

5. DISCUSSION

5.1. Analysis of Exhaled Breath versus Ambient VOCs in Relation to Asthma Symptoms

The correspondence was poor between diary reports of asthma symptoms and the subject's verbal classification of breath canisters as being given on days with an asthma event versus baseline days. Preliminary analyses of potential health effects of breath VOCs and other data suggested that the diary data was more valid than the canister classification. Therefore, the epidemiologic analysis focused on diary reports of symptom severity.

The comparison of exhaled breath VOCs with ambient VOCs measured on the same person-days showed some interesting inconsistencies. Ambient benzene was significantly and strongly associated with bothersome or more severe symptoms (symptom scores > 1) (OR 5.93, $p < 0.01$) whereas the effect of breath benzene for the same subset of person-days was much smaller (OR 2.03, $p < 0.14$) (Table 4.14). Similarly, strengths of association with symptom scores > 1 for toluene, tetrachloroethylene, *m,p*-xylene and *o*-xylene were larger for ambient than breath samples. However, both ambient and breath benzene were significantly associated with more severe symptoms interfering with daily activities (symptom scores > 2) and similar in magnitude (2.75, $p < 0.001$, vs. OR 2.56, $p < 0.01$, respectively). Unlike benzene, strengths of association for xylene compounds with symptom scores > 2 were greater in magnitude for ambient than for breath measurements. Three of 4 models for ambient xylene compounds were significant. Breath *m,p*-xylene showed a borderline significant relationship to symptom scores > 2 ($p < 0.08$). Note that the sample size of ambient exposure used in comparison with breath samples is actually a subset of breath sample days (i.e., ambient data is restricted to the same person-days subjects gave breath samples). This is in contrast to the larger sample size in the analysis involving ambient exposures across all days of the panel study (discussed below). Breath toluene was significantly associated with symptom scores > 2 (OR 2.34) in the model without respiratory infections as a covariate, but the model adding the covariate failed to converge because of small cell size (Table 4.13).

If the VOC compounds analyzed are causally related to acute asthma, then the expectation is that a biomarker of exposure like exhaled breath concentrations of VOCs would be more strongly associated with symptoms than ambient measurements. We offer three hypotheses to explain our finding of greater associations with ambient measurements, as follows:

- 1) ambient measurements could serve as better surrogates for true causal air pollutants in ambient air than breath VOCs;
- 2) breath concentrations may less accurately reflect pulmonary doses during the time frame relevant to acute responses; and
- 3) weak causal strengths of VOCs were not detected by the small sample sizes of breath VOCs, and systematic or random biases led to associations with ambient VOCs for the subset of person-days when breath samples were given.

Hypothesis 1: Ambient measurements of VOCs may track other ambient air toxics, ultrafine particles or other unmeasured pollutant gases that may be more causally related to acute asthma outcomes than the measured VOCs. Breath VOCs, on the other hand, are likely to be influenced by other non-ambient sources in locations such as indoor home or other microenvironments. There were weak correlations between breath VOCs and outdoor VOCs used in the epidemiologic analysis (Table 4.11) (e.g., benzene, $r = 0.30$, $p < 0.01$) and between personal VOC and outdoor VOCs in the exposure assessment study. This suggests that personal exposures are not notably linked to outdoor levels, which is consistent with the overall results of the EPA TEAM Study (Wallace et al., 1991). On the other hand, the ambient

measurement may be a better surrogate because either the breath sampling method or subject compliance with breath measurements led to inaccuracies.

Criteria air pollutant gases could be among the causal agents in ambient air explaining the difference in association between breath and ambient VOCs. However, ambient criteria pollutant gases did not confound relationships between breath benzene and symptom scores > 2 (Table 4.16). Problems of multicollinearity prevented a clear interpretation of inter-pollutant confounding for models predicting symptom scores > 1 (Table 4.16). Similarly, 2-pollutant models for ambient VOCs and criteria pollutant gases measured across the entire panel study period did not clarify whether associations were due to one or the other pollutant (Table 4.28). This was due to high inter-pollutant correlations and interactions between VOCs and criteria pollutant gases in relation to symptoms. Unfortunately, there was insufficient particulate air pollution data to test whether particle mass confounds ambient or breath VOC associations.

Hypothesis 2: The alternative explanation for stronger associations with ambient than breath VOCs is that even if VOCs are causal, breath concentrations may not accurately reflect pulmonary doses during the time frame relevant to acute responses. This is because the half-life of VOC following deposition to pulmonary sites is on the order of minutes in blood to a few hours in various other compartments. An exception is in adipose tissue where half-lives may extend for up to 3 days. Inaccuracy in breath sampling maneuvers is another source of misclassification of breath VOC concentrations, but our evidence suggests that subjects performed the procedure adequately. The U.S. EPA TEAM Studies of 800 people showed correlations between breath and previous personal air measurements were significant ($p < 0.0001$) but small (correlation coefficients 0.3 to 0.4) (Wallace, 1996). The small correlation coefficients are likely due in large part to inaccuracies in personal exposure and VOC breath measurements, as well as variability in pulmonary dose and metabolism.

The kinetics of VOC exhaled air concentration as it relates to exposure and to metabolism is complex. We expect our breath sample VOC concentrations reflect some component concentrations in the first compartment (blood) for the half hour prior to the breath sample, and in the second compartment (vessel-rich tissues) from the prior hour and up to 4 hours in the past for some compounds (Gordon et al., 1992; Pellizari et al., 1992; Wallace et al., 1993; Wallace et al., 1996). Also, we likely detected high VOC exposures occurring during the last several hours up to 12 hours in the past, which leads to elevated concentrations in the third compartment (other vessel-poor tissues), and high exposures occurring up to 3 days in the past, which leads to elevated concentrations in the fourth compartment (fatty tissue) (Wallace et al., 1996). Therefore, measured breath concentrations can reflect long-term equilibrium concentrations over several hours to days. Thus, the relationship between asthma episodes and breath VOC samples may be limited in accuracy because the interplay between the half-life of the VOC and the causal temporality of the exposures. Similarly, the accuracy of the estimated relationship between asthma episodes and ambient air VOCs may be a function of the length of period over which the time-weighted average is obtained prior to the episode. The VOC concentrations in ambient air (as collected here) represent a time-weighted average value over the 24-hr sampling time period. In addition, we may have also missed bronchoconstrictive responses to short-term peak exposures, which could occur at times distant to the breath sample, and which may also not be reflected by the 24-hr average ambient measurements. This is important because the time frame of the asthmatic response can be short. For instance, initial IgE-mediated response induced by an allergen is characterized by both an immediate and late phase bronchospastic reactions (4-6 hours later) (O'Byrne et al., 1987). A more chronic phase of the response is evidenced by additional inflammatory cell changes 24 hours after inhalation challenge with allergen in asthmatics (Bentley et al., 1993). Irritant or neuroinflammatory responses to pollutants leading to changes in bronchomotor tone are expected to be fairly acute. This is evidenced by increases in airway responsiveness to methacholine at 1 hour and allergen responsiveness at 3 hours after O₃ challenge in subjects with mild asthma (Jörres et al., 1996).

Although we do not know what the optimal ambient air sampling time should, these results suggest it is likely to be longer than the half-life of the VOC. The optimal sampling time frame for understanding whether VOCs are involved in asthma exacerbations would need to be determined using real-time measurements.

Hypothesis 3: The limited number of breath VOC samples may have reduced the statistical power to detect adverse health effects. For instance, the number of breath analyses was limited to 96 person-days in 19 subjects in the final models (Table 4.14). The significant findings for ambient exposures on canister days (despite the small sample size) could have occurred as a result of some bias in the subject-selected sampling schedule for breath canisters. It is notable that ambient toluene was significantly associated with asthma symptom scores > 1 and > 2 in the model used in comparison with the model showing no significant associations with breath toluene (Table 4.14, 80 person-days). On the other hand, in the analysis of all person-days of observation ambient toluene was not associated with symptom scores > 2 (Table 4.27, 938 person-days), although toluene showed a borderline significant relationship to symptom scores > 1 . Some limited consistency was found between models for ambient VOCs on canister days versus all panel days for benzene, tetrachloroethylene, *m,p*-xylene and *o*-xylene. Again, however, strengths of association were stronger for canister days. We speculate that the added days across the entire panel study brought in more variability in the etiology of responses for the non-canister days.

5.2. Analysis of Ambient Exposures in Relation to Asthma Symptoms

Numerous positive associations were found between asthma symptoms and ambient exposures to VOCs across the 3-month daily panel. These associations were unlikely to have occurred by chance from multiple testing bias, which can lead to Type I errors with a probability of α (5%). There were 9 out of 22 tests for symptom scores > 1 (41%) that were significant or nearly so and 6/22 for symptom scores > 2 (27%). The two symptom cut-off points led to different results between same day concentrations of carbonyl and non-carbonyl compounds (Table 4.26). Asthma symptom scores > 2 were not associated with lag 0 acetaldehyde, but were positively associated with acetone and formaldehyde. The association with formaldehyde was strong (OR 7.30, $p < 0.05$). Many models for the relationship between asthma symptom scores > 1 and the non-carbonyl VOCs were positive and significant or near significant, including benzene, ethylbenzene, tetrachloroethylene, toluene, and *m,p*-xylene and *o*-xylene. However, none of the lag 0 non-carbonyl VOCs were associated with asthma symptom scores > 2 . As discussed above, only 7 subjects reported asthma symptoms that interfered with daily activities (scores > 2) as compared with 16 reporting symptom scores > 1 . Also, associations for symptom scores > 2 , particularly those for the carbonyl compounds and NO₂, were strongly influenced by one subject who was the most symptomatic, who was not on anti-inflammatory medications, and who had the worst predicted FEV₁ measurements ($< 64\%$). Thus, differing results for the two cut-points could have resulted from different sets of subjects with positive symptom responses. We speculate that some asthmatics such as this one subject with persistent symptoms and moderately severe lung function may be particularly susceptible to air pollutant-induced exacerbations that interfere with daily activities. Our results examining interaction with asthma severity (discussed below) only weakly support this view, suggesting that unmeasured host susceptibility factors and/or differences in personal exposure could have been important effect modifiers.

For lagged exposures, there were significant associations of asthma symptom scores > 1 with carbonyl compounds at lag 1 day, including acetaldehyde and formaldehyde. Several of the 2-day moving averages for VOCs (mean of lag 0 + 1) were significant or borderline significant with ORs for symptom scores > 1 between 1.5 and 2.0, including benzene, ethylbenzene, 1,3-butadiene, *m,p*-xylene and *o*-xylene. Few of the lagged non-carbonyl VOC or criteria air pollutant gases were significantly associated with symptom

scores > 2. However, there were significant associations of asthma symptom scores > 2 and lagged carbonyl compounds. Associations were also found for 2-day moving averages of acetone and formaldehyde. Some of these associations for symptom scores > 2, particularly the 2-day moving average, were due largely to the most symptomatic subject discussed above.

Positive associations were also found between asthma symptoms and ambient exposures to criteria air pollutant gases (Table 4.27). Ozone was significantly associated with asthma symptom scores > 2, but not scores > 1. Both symptom variables were associated with NO₂ and SO₂. Asthma symptoms were not associated with CO. Two-day moving averages of NO₂ and SO₂ were associated with symptom scores > 1 and scores > 2. Again, the associations for symptom scores > 2 were strongly influenced by the most symptomatic subject. Larger odds ratios were observed between NO₂ and symptoms on days that VOC breath samples were collected (Table 4.15). This may have been a function of the subset of days selected because odds ratios drop considerably with the use of the full number of sampling days (Table 4.27).

In general, our findings for criteria air pollutant gases are consistent with other studies of asthmatics (reviewed by Bascom et al., 1996).

5.2.1. Summary of Symptom Models for lag 0 through lag 4 Ambient Exposures to VOCs and Criteria Pollutant Gases:

- *Non-carbonyl VOCs:* Symptom scores > 1 were associated with most lag 0 petroleum-related VOCs (benzene, ethylbenzene, toluene, and *m,p*-xylene and *o*-xylene) and one process-related VOC (tetrachloroethylene). Although symptom scores > 1 were not significantly associated with lag 1 petroleum-related VOCs (Table 4.27), they were associated with 2-day moving averages of benzene, ethylbenzene, 1,3-butadiene, *m,p*-xylene and *o*-xylene. Symptom scores > 2 were only associated with one process-related VOC, styrene, at lags 3 and 4, and with the 2-day (lags 0-1) and 4-day (lags 0-4) moving averages of styrene.
- *Carbonyls:* Carbonyl compounds showed a variety of modest to strong associations depending on the symptom cut-point and lag. Symptom scores > 1 were most clearly associated with lag 1 carbonyls (acetaldehyde and formaldehyde). Symptom scores > 2 were associated with carbonyls (acetone, acetaldehyde and formaldehyde) at various lags (0, 1, 2 and 4) and with multi-day moving averages of carbonyls. Effects on symptom scores > 2 were strongly influenced by the most symptomatic subject.
- *Criteria pollutant gases:* Lag 0 criteria pollutant gases NO₂, SO₂ and O₃, but not CO, were associated with symptom scores > 1 and > 2. Lag 1 NO₂ and SO₂ showed some borderline relationships, which contributed to significant associations with symptom scores > 1 and > 2 for 2-day moving averages of these two gases. The association between O₃ and symptom scores > 2 were strongly influenced by the most symptomatic subject.

5.2.2. Two-pollutant Models and Interactions:

Results of 2-pollutant regression models including an individual VOC with a criteria air pollutant gas did not clarify whether associations were due to one or the other pollutant (Table 4.28). When regressing two air pollutants, moderate to high levels of correlation between pollutant variables generally prevented an interpretation of independent effects. This was likely due to problems of multicollinearity in regression models as indicated by variance inflation and reductions in regression parameters for both co-regressed pollutants. Furthermore, significant interactions between carbonyl compounds and criteria air pollutant gases were found preventing a clear interpretation of 2-pollutant models without product terms. The interaction could have resulted from days when high concentrations of measured and unmeasured

pollutants drove associations, and such days were best represented by high concentrations of both regressed pollutants. This statistical interaction does not necessarily imply biological interaction. It may represent an atmospheric condition wherein a third unmeasured factor is causal. Also, it may be inappropriate to use multi-pollutant modeling to test independent air pollutant effects by treating one or the other pollutant as a confounder if the pollutants are surrogates for some underlying causal mixture.

In summary, the presentation of two-pollutant models and interactions was exploratory in scope. The results suggest that other approaches are necessary to identify independent pollutant effects. Experimental designs are an option, but many of the air toxics have known non-respiratory adverse effects possibly prohibiting their use in human models. Studies utilizing personal exposures hold some promise in separating independent pollutant effects as evidenced in the studies by Sarnat et al. (2000; 2001). They found that in contrast to high inter-pollutant correlations between ambient pollutant measurements, personal PM_{2.5} exposures were not significantly correlated with personal exposures to O₃ or NO₂.

5.2.3. Particulate Air Pollutants:

Despite the small number of days monitored by the SCAQMD (24 days, 408 person-days), gravimetric mass variables were positively associated with asthma symptoms (Table 4.29). These findings are consistent with other studies of asthmatics (reviewed by EPA, 1996). Strengths of association were OC > EC > PM₁₀. In two-pollutant models, PM₁₀ did not confound the associations with EC or OC, but the OR for PM₁₀ was reduced to around 1.0 when regressed with either EC or OC. Confidence limits were widened for EC and OC in the 2-pollutant models. These findings suggest that particle effects were more accurately detected with EC and OC measurements than with PM₁₀. Organic compounds such as polycyclic aromatic hydrocarbons (PAH) or other combustion products may have driven particle associations. Organic constituents of PM are capable of generating reactive oxygen species (ROS) that then induce subsequent oxidant injury and inflammatory responses (reviewed by Nel et al., 2001). The actual mass of organic compounds in PM₁₀ is mostly in the submicrometer fraction, and are, therefore, capable of reaching target sites in the small airways and alveoli. Ultrafine (< 0.1 µm) and accumulation mode (0.1-1.0 µm) particles in nearby Downey, CA, are largely made up of elemental and organic carbon (Kim et al., 2002). There is sufficient reason to believe that ultrafine particles are capable of inducing the greatest amount of inflammation per unit PM mass due to high particle number, high deposition efficiency, and surface chemistry, which includes a high surface area that can carry adsorbed or condensed toxic air pollutants (organic compounds, oxidant gases, and transition metals) (Oberdörster, 2001). Diesel exhaust particles (DEP) likely contributed considerable mass and particle numbers to the ultrafine and accumulation mode fractions in the Huntington Park region.

There is experimental evidence that suggest airborne PAH exposures linked to DEP have pro-inflammatory effects on airways, thus playing an important role in allergic respiratory illnesses (Nel et al., 1998; 2001). DEP have been shown to induce a broad polyclonal expression of cytokines in respiratory epithelium possibly due to PAH (Nel et al., 1998; 2001). Numerous epidemiological studies have shown associations between allergic responses or asthma with exposures to ambient air pollutant mixtures with PAH components, including black smoke, and high home or school traffic density (particularly truck traffic) (Delfino, 2002a). Other particle-phase and gaseous co-pollutants are likely causal in these associations as well.

TEOM PM₁₀ was also significantly associated with asthma symptoms despite the small number of monitored days (10 days, 54 person-days). Large odds ratios were observed for TEOM PM₁₀, but this may have been a function of the subset of days monitored (Table 4.29). Strengths of association for the various TEOM PM₁₀ averaging times showed the relative magnitudes to be: 1-hr \cong 8-hr > 24-hr PM₁₀. These findings are consistent with previous asthma panels studies conducted in San Diego County

(Delfino et al, 1998; Delfino et al, 2002b). Two hypotheses are offered to explain the greater magnitude of association for peak than for 24-hr average PM₁₀, as follows:

- 1) Changes in particle exposure concentrations over the course of the day will alter the dose of particles in the lung in a time-dependent manner. Therefore, it is expected that biological responses may intensify with high peak excursions that overwhelm certain lung defense mechanisms, as compared with integrated exposure metrics that may be inappropriate unless concentrations are stable. Particles may be effectively neutralized or cleared from the lungs in the absence of short-term high excursions.
- 2) Ambient peak PM₁₀ exposure shows stronger effects than ambient 24-hour average exposure because it is a better surrogate for personal outdoor exposures during the daytime, exposures that can often occur at times of high physical activity in children leading to greater particle doses.

5.2.4. Susceptible Subpopulations:

Models for symptom scores > 1 with product terms testing for interaction between ambient air pollutants and classification of asthma severity level showed no significant interactions (p -values ≥ 0.2). For most models, regression parameters were either moderately greater or close in magnitude for more severely asthmatic subjects as compared with less severely asthmatic subjects. Parameters were generally positive for both groups.

Models for symptom scores > 1 with product terms testing for interaction between the ambient air pollutants and regular use of anti-inflammatory medications were not significant in most models ($p \geq 0.10$). However, product term models for 8-hr CO, acetaldehyde and formaldehyde revealed higher response magnitudes among those not on anti-inflammatory medications ($p < 0.07$). For the remaining models, although there were no significant differences between medication groups, those on anti-inflammatory medications generally showed regression parameters that were either moderately greater or close in magnitude to those not on anti-inflammatory medications. However, symptom severity was significantly greater among subjects on anti-inflammatory medications, showing that prescriptions for maintenance medications were used by more severe asthmatics. The problem illustrated here is that between-subject severity of asthma during follow-up can confound the expected protective effects of anti-inflammatory medications against the putative pro-inflammatory effects of air pollutants such as O₃. Two panel studies showed stronger associations between asthma outcomes and air pollutants among medicated than non-medicated subjects, but they did not separate subjects on versus not on anti-inflammatory medications (Peters, 1997; Roemer, et al., 1999). Mortimer, et al. (2000) compared effects on asthma outcomes by outdoor O₃ levels across medication groups based on baseline data for prescribed medication rather than actual medications used during the repeated measures follow-up. The magnitude of association between incidence of symptoms and increase of 15 ppb in O₃ was largest among those prescribed cromolyn but not steroids. The results could have been influenced by differences in asthma severity reflected by baseline differences in prescribed medications. Ostro, et al. (2000) found little difference in PM₁₀ effects among those reporting and not reporting regular use of anti-inflammatory medications at baseline, whereas associations with *Alternaria* were somewhat stronger in medicated subjects. We found in our asthma panel study in Alpine, CA that symptom associations with PM₁₀, NO₂ and O₃ were notably stronger in 12 asthmatics not taking anti-inflammatory medications as compared with 10 subjects that did (Delfino et al., 2002a). In another of our previous panel studies in Alpine, CA, we controlled for severity by stratification and found stronger associations between asthma symptoms and both PM₁₀ and O₃ among 7 mild asthmatic subjects not on anti-inflammatory medications as compared with 7 other mild asthmatic subjects on anti-inflammatory medications (Delfino et al., 1998). This stratification was not possible in the present study because subjects on anti-inflammatory medications were more symptomatic. Furthermore, our findings may have been influenced by the smaller number of subjects on (N=6) than not on anti-inflammatory medications (N=14).

5.3. Analysis of Peak Expiratory Flow Rates

5.3.1. *Breath versus Ambient VOCs:*

There was some consistency between the analysis of asthma symptoms and the analysis of PEF in relation to breath versus ambient VOCs measured on breath sample days. A significant decrease in evening PEF of -21 L/min was found for a mean increase in ambient benzene. Borderline significant deficits in evening PEF were found in relation to ambient methylene chloride ($p < 0.08$) and ambient toluene ($p < 0.09$). A significant decrease in evening PEF of -29 L/min was found for a mean increase in breath tetrachloroethylene. Recall that tetrachloroethylene was not significantly associated with asthma symptoms, although the OR was suggestive of an effect for symptom scores > 2 (OR 1.62, $p < 0.15$). There was no association of PEF with ambient tetrachloroethylene. The statistical significance of the association of PEF deficits with breath tetrachloroethylene (1 out of 16 models tested) could have occurred by chance. The same assessment can be made for association of PEF deficits with ambient benzene. However, it is of note that PEF deficits were found for 12 out of 16 models for breath VOCs and 14 out of 16 models for ambient VOCs, although some deficits were very small with wide confidence intervals (Table 4.17). Two-pollutant models gave no evidence that ambient criteria pollutant gases confounded the significant PEF effects.

5.3.2. *Personal VOC Exposure:*

The analysis of personal VOC exposures in relation to PEF in the 4 subjects wearing samplers showed that personal VOC exposures were more strongly associated with PEF deficits than ambient VOC exposures. Six models were significant or nearly so for evening PEF in relation to personal exposures to *p*-dichlorobenzene, styrene, *m,p*-xylene and *o*-xylene. Overall results for personal VOCs show that regression parameters were negative for 18 out of 21 models (86%), with 12 being -10 L/min or less (57%) for a mean increase in VOC. In comparison, overall results for ambient VOCs showed that regression parameters were negative for 14 total of out of 21 models (67%), with only 4 being -10 L/min or less (19%) for a mean increase in VOC.

5.3.3. *Ambient VOC and Criteria Pollutants:*

There was no consistency between the analysis of asthma symptoms and the analysis of PEF in relation to ambient VOCs or criteria pollutant gases for exposures across the entire 3-month panel study. Neither morning nor evening PEF were associated with these pollutants. There were some inverse associations between PEF and the particulate air pollutant variables. One-hr maximum TEOM PM₁₀ was associated with significant and large PEF deficits in the morning (-64.5 L/min at a mean of $92 \mu\text{g}/\text{m}^3$). However, there were no consistent deficits in evening PEF in relation to TEOM PM₁₀. Gravimetric PM₁₀, EC and OC showed inverse relationships with evening PEF but none were significant and there was no suggestion of an effect on morning PEF.

5.3.4. *Conclusions Regarding PEF Models:*

The paucity of statistically significant adverse associations of air pollutants with PEF could be the result of biases in performing or reporting PEF by children. We presented evidence consistent across a number of parameters that two subjects repeatedly falsified PEF data. Although this data were excluded in analyses, we could not verify that other PEF data were valid. Falsification of PEF data is a strong possibility with non-electronic methods. Evidence from two studies showed that around a third of non-electronic PEF data was falsified (Verschelden et al., 1996; Redline et al., 1996). Also, PEF is intended as a surrogate measure of FEV₁, but studies have shown that PEF does not accurately reflect FEV₁ (Meltzer et al., 1989) or reflect bronchial hyperresponsiveness as measured by FEV₁ (Malmberg et al., 2001). PEF has a high probability of false negative detection of abnormal FEV₁, forced expiratory flow rate at 50% of FVC (FEF₅₀) or at 25-75% of FVC (FEF₂₅₋₇₅) (Ferguson, 1988; Sly et al., 1994; Goldberg et al., 2001) particularly as air trapping increases (residual volume/total lung capacity) (Eid et al., 2000). The inability

to confirm that lung function maneuvers were performed correctly or even performed at all, along with a lack of FEV₁ data, likely explains part of the inconsistency between results of the analysis of symptoms and lung function. In addition, the symptom scoring system we use allows the asthmatic subject to gauge his or her daily quality of life resulting from asthma, whereas FEV₁ and PEF represent a snap-shot of one physiological parameter, which may not be representative of the daily severity of asthma. This is particularly likely if the patient has been using as-needed β -agonist inhalers. In a large study of over 1500 patients in clinical trials, the canonical correlation coefficients between airway obstruction (FEV₁ and PEF) and patient-reported endpoints (asthma symptoms and as-needed β -agonist use) was low (0.20-0.27) (Shingo et al., 2001). Finally, PEF represents large airways function, whereas asthma is thought to be a mixture of large and small airways obstruction. Some asthma symptoms may be driven more by small airways obstruction. Chan-Yeung and colleagues (1996) found in 41 asthmatics that a significant increase in asthma symptoms occurred before a significant reduction in PEF in both children and adults with acute exacerbations leading to physician contact.

6. SUMMARY AND CONCLUSIONS

6.1. Background, Aims and Significance

Acute adverse respiratory effects have been established for principal criteria air pollutants (for which the US EPA has established so-called National Ambient Air Quality Standards (NAAQS), namely, ozone, nitrogen dioxide, sulfur dioxide and carbon monoxide, PM₁₀, and PM_{2.5}). However, there is little epidemiologic information on the public health impact from air pollutants such as volatile organic compounds (VOCs) from outdoor toxic emission sources, which include automobiles and trucks. Therefore, there is a need to evaluate health effects of toxic air pollutants in communities near such emission sources. This project aimed to evaluate acute respiratory health effects of air toxics in a potentially susceptible population of asthmatic school children living close to an air toxics monitoring site of the South Coast Air Quality Management District (Section 4.). An additional aim of the study was to characterize exposures to air toxics using subject reports of their time-activity patterns and a variety of approaches to measuring exposure to VOCs including chemical analysis of exhaled breath samples, and air samplers located on the person (personal exposure), indoors at the home, and at outdoor stationary regional sites (Section 3.). Results of this study will be useful in determining the type and scope of studies needed to evaluate exposures and acute health effects in California communities affected by multiple emission sources. This will guide the assessment of resources needed to fund various research designs, experimental and epidemiologic, to address environmental justice-related issues.

6.2. Methods

We recruited 26 Hispanic school children with asthma, ages 10-16, who lived in the Huntington Park area of East Los Angeles County, an area flanked by major freeways and trucking routes. Two dropped out and 4 had invalid diary or PEF data, leaving 20 subjects with 1,035 asthma symptom-days of observation over the period with outdoor air pollution data (Nov. 4, 1999 through Jan. 23, 2000). Selected VOCs were measured in self-administered exhaled breath samples during a 3-month daily diary study. Subjects were instructed to give breath samples during asthma flares and following baseline periods free of symptoms. Ambient air pollutants were measured daily over the same period at centrally located stationary outdoor monitors. These pollutants included VOCs, criteria pollutant gases, and a subset of days with PM₁₀, organic and elemental carbon. Four volunteers were recruited from 24 participants in the panel for daily personal VOC exposure measurements and indoor home VOC exposure sampling over a 5-week period.

They recorded in diaries their activities relevant to exposures. All subjects recorded health outcomes in paper diaries, and peak expiratory flow of the lungs using a non-electronic device twice daily. This allowed an analysis of health effects across all days in 20 subjects. Health effects were tested in longitudinal regression models controlling for temporal factors, weather and respiratory infections. Time series models predicting personal VOC exposure were estimated from the different exposure measurements and time-activity diary data for the 4 subjects.

6.3. Exposure Assessment

6.3.1. VOCs in the exhaled breath of 24 subjects:

Twelve VOCs, including 1,1-dichloroethane, benzene, carbon tetrachloride, chloroform, styrene, tetrachloroethylene, toluene, *m,p*-xylene, *o*-dichlorobenzene, *o*-xylene, and *p*-dichlorobenzene were found in the breath samples. Except for 1,1-dichloroethane, carbon tetrachloride, chloroform, and *o*-dichlorobenzene, 8 of the 12 compounds were found in more than 75% of the breath samples.

The ratios of VOC concentrations in the breath samples over indoor concentration were smaller than 1 for all of the chemicals, except *p*-dichlorobenzene, suggesting that these VOCs were likely produced environmentally rather than endogenously, and that air was perhaps the dominant pathway for exposure. The chemical *p*-dichlorobenzene, a solvent that can be found in soap and other products, likely had exposure pathways (such as dermal or ingestion) other than air.

Day-to-day variations in breath VOC concentrations within a subject appeared to be larger than the between-subject variations. Given the sporadic nature of breath sample collection (see Epidemiologic Analysis) this suggests that daily collection is needed to further understand the temporal exposure patterns of individuals.

6.3.2. Relationships between personal exposures, indoor exposures, outdoor exposures, personal activity patterns, and other exposure sources:

- 1) Time-series analysis suggest that personal exposures were correlated with indoor exposures for all the target VOCs;
- 2) Time-series models were subject specific, i.e., same subject, rather than same chemical, tends to have one general model format. This suggests that personal or household characteristics have greater influence on the correlation between personal, indoor, outdoor exposures than the chemical properties of these compounds.
- 3) Personal exposures did not correlate with outdoor measurements for most of the target compounds except for tetrachloroethylene and *m,p*-xylene.
- 4) Among the VOC exposure sources reported in time-activity diaries, only being at a gas station or garage significantly correlated the personal VOC measurements.

6.3.3. Analyses of Breath VOC measurements:

- 1) The ratios of breath VOC/indoor VOC were less than 1.0 for most of the chemicals, which agrees with previous studies done cross-sectionally. Because the participants spent most of their time indoors, these results suggest that the VOCs were produced exogenously rather than endogenously.
- 2) For most of the target compounds, breath measurements did not correlate with outdoor measurements. However, outdoor benzene, styrene and *m,p*-xylene of previous two days appeared to be correlated with current day breath measurements. This suggests an outdoor source for these chemicals. Slow release of VOCs from fatty tissue could explain part of the lagged relationship.

- 3) Within-individual variances appeared to be larger than between-individual variances, a phenomenon observed for many occupational exposures. This suggests that to quantify an individual's breath exposure, multiple measurements should be taken.

6.3.4. Correlation between the VOCs:

The target VOCs were correlated with one another within personal and within indoor measurement datasets. However, only benzene, xylene and toluene were correlated among breath VOCs. This difference in correlation for breath versus personal or indoor VOC could be explained by different datasets used for analysis. While personal and indoor measurements were from the subset of 4 subjects, the breath VOC measurements were from all 24 subjects.

6.3.5. Conclusion: This pilot exposure assessment study has provided valuable insight regarding the measurement methods needed to assess personal exposures and doses in a potentially sensitive group of children. Evidence was found with both breath and personal VOC measurements suggesting an outdoor source for these chemicals. The variability in breath VOC concentrations within individuals suggests that to quantify an individual's exposure with exhaled breath VOC samples, multiple daily measurements should be taken. Furthermore, the characteristics of models predicting personal VOC exposure suggests personal or household characteristics are key and need to be evaluated with greater accuracy. The applicability of these findings to the general population will need to be established with larger studies.

6.4. Health Effects

6.4.1. Summary of findings:

In the epidemiologic study, we found the following:

- 1) The correspondence was poor between diary reports of asthma symptoms and the subject's verbal classification of breath canisters as being given on days with an asthma event versus baseline days. Preliminary analyses of health effects of breath VOCs and other data suggested that the diary data was more valid than the canister classification. Therefore, the epidemiologic analysis of exhaled breath VOCs focused on diary reports of symptom severity.
- 2) Associations were found between bothersome or more severe asthma symptoms recorded in diaries and breath concentrations of benzene (93 person-days), particularly for episodes when asthma symptoms interfered with the daily activities of subjects. This last result was based on a small number of such asthma flares.
- 3) Other breath VOCs were not significantly associated with asthma symptoms.
- 4) An analysis of ambient VOCs measured on the same person-days as breath VOCs showed notably stronger and significant associations with symptoms, including benzene, toluene, *m,p*-xylene and *o*-xylene.
- 5) In the analysis of daily outdoor VOCs across the full time period (3 months, up to 938 person-days) we found numerous positive associations of asthma symptoms with VOCs. Significant associations of ambient VOCs with asthma symptoms were found for benzene, 1,3-butadiene, ethylbenzene, styrene, tetrachloroethylene, toluene, *m,p*-xylene, *o*-xylene, acetone, acetaldehyde and formaldehyde. Most effects were at lag 0.
- 6) Associations between episodes when asthma symptoms interfered with the daily activities of subjects and carbonyl compounds at various lags (acetone, acetaldehyde and formaldehyde) were strongly influenced by the most symptomatic subject with the worst lung function. Lag 1 acetaldehyde and formaldehyde were associated with bothersome or more severe asthma symptoms.
- 7) Associations were found between bothersome or more severe asthma symptoms and ambient concentrations of NO₂ and SO₂, and between asthma symptoms that interfered with daily activities

and ambient concentrations of NO₂, SO₂ and O₃. Effects on more severe symptoms strongly influenced by the most symptomatic subject with the worst lung function.

- 8) A subset of days with particulate air pollution data (408 person-days) showed associations between asthma symptoms and organic carbon, elemental carbon and PM₁₀. The strongest and most robust particle association was with organic carbon followed by elemental carbon, then PM₁₀. In two-pollutant models, PM₁₀ did not confound associations with organic and elemental carbon, but organic and elemental carbon confounded associations with PM₁₀.
- 9) TEOM PM₁₀ was significantly associated with asthma symptoms despite the small sample size (54 person-days). Strengths of association showed the relative magnitudes to be: 1-hr maximum \cong 8-hr maximum > 24-hr average PM₁₀.
- 10) Although deficits in peak expiratory flow of the lungs were found in relation to increases in some air pollutants, most findings were not statistically significant. However, we presented evidence that falsification of PEF data was a strong possibility with the non-electronic meters used.

6.4.2. Susceptibility and Causal Components:

Aside from the influence of one moderately severe asthmatic on regression models for carbonyl compounds, we found limited evidence that the more severe asthmatics were at greater risk from pollutant exposures. For most models with product terms testing for interaction between ambient air pollutants and classification of asthma severity level, regression parameters were either moderately greater or close in magnitude for more severely asthmatic subjects as compared with less severely asthmatic subjects (p -values ≥ 0.2). Furthermore, the low frequency of asthma flares diminished our ability to assess effects of breath VOCs, and to assess pollutant effects on symptoms interfering with daily activities. Testing for differences by use of anti-inflammatory medication showed some pollutants had greater effects on those without such medication use while other pollutants showed greater effects on those with such medication use. This difference could have been due in part to the fact that symptom severity was significantly greater among subjects on anti-inflammatory medications.

At this time, it is unclear what are the characteristics of susceptible sub-populations and which pollutants play key roles in the associations. This is analogous to the current situation for community exposures to PM₁₀ or PM_{2.5} for which adverse health effects have been repeatedly found in epidemiologic studies, but the causal components and susceptible subgroups have yet to be clearly defined (NRC, 1998). Similarly, the VOC exposures in the present analyses are best considered to be surrogates of a varying mix of ambient exposures. This is because we were not able to measure all potentially relevant exposures, and because we do not know which, if any, of the VOC compounds are causally related to the health outcomes. There is only limited evidence on the possible mechanisms by which VOCs might exacerbate asthma, such as irritant triggering of neurogenic inflammation (American Thoracic Society, 1999; Meggs, 1993). There is little supportive evidence that non-reactive VOCs (e.g., benzene), particularly at low concentrations, act as airway irritants, while there is more support in the literature for an irritant mechanism for reactive VOCs such as formaldehyde (Wolkoff and Nielsen, 2001).

Some of the VOCs, NO₂, organic and elemental carbon may be markers for a causal mixture of traffic-related pollutants in an area with high traffic density. Our findings, coupled with experimental and epidemiologic evidence in the literature (Delfino, 2002a; Nel et al., 1998; 2001) suggest that the adverse health effects in asthmatic children were due to the pro-inflammatory and irritant nature of traffic-related pollutants. Some limited evidence was found for adverse effects of process-related VOCs (styrene and tetrachloroethylene). Results suggest more work is needed on potentially causal air toxics in the pollutant mix from traffic and industrial sources. This research must include more than the principle criteria air pollutants in the EPA NAAQS.

6.4.3. Consistency with Other Epidemiological Studies:

Cross-sectional and case-control studies of children have shown associations of allergic responses, asthma symptoms, and prevalence of asthma or allergic sensitization with proximity to high home or school traffic density (particularly truck traffic) (Delfino, 2002a). Our findings of acute exposure-response relationships in an area with high traffic density are consistent with these studies, but have the advantage of a more temporally valid exposure-response relationship, i.e., the exposure precedes or is concurrent with the measured response. Other literature on community asthma and indoor VOCs such as formaldehyde (Delfino, 2002a), and studies of occupational asthma and air toxics (Bernstein et al., 1999), suggest that asthma is an illness relevant to the hazardous effects of air toxics in addition to cancer, neurological illnesses and congenital defects. There have been no other studies conducted in California on the acute health effects of community exposures to VOCs or other air toxics in asthmatic children. The only other epidemiologic study in the U.S. that evaluated ambient VOC effects on respiratory health in children showed positive associations of VOCs with lower respiratory symptoms and with prevalence of asthma diagnoses in the industrial area of Kanawha Valley, WV (Ware et al. (1993).

To our knowledge, only three epidemiologic time series investigations of aggregate hospital data have evaluated effects of specific air toxics, and all of these support our general finding that criteria air pollutants did not clearly show stronger or more robust associations than VOCs. Thompson et al (2001) found associations between emergency room visits for asthma by children and ambient benzene in Belfast, Northern Ireland. Smaller significant associations were found for criteria air pollutants (PM₁₀, NO₂, SO₂ and CO). Hagen et al., (2000) studied hospital admissions for aggregate respiratory diseases in Drammen, Norway and also found stronger associations for benzene than for criteria air pollutants, but also found significant associations for toluene and formaldehyde at magnitudes similar to the criteria air pollutants. Both studies found associations with the VOCs were more robust in 2-pollutant models than PM₁₀. Another time series investigation in London evaluated an extensive database of hydrocarbon data and found that most of the hydrocarbons, including benzene, toluene, 1,3-butadiene, ethylbenzene, *m,p*-xylene, and *o*-xylene were associated with emergency room visits for symptoms of acute wheeze in children 16 years old (Buchdahl et al., 2000). Associations with criteria pollutants (PM₁₀, NO₂, SO₂) were of similar magnitude but confidence intervals were wider, and ozone showed a U shaped relationship across seasons. In conclusion, these studies suggest that the lung may be responding to a large number of compounds, and that attributing effects to any one agent ignores the importance of the mixture.

6.4.4. Conclusions:

The present study is the first epidemiologic study to evaluate the longitudinal relationship of acute asthma to exhaled breath measurements of VOC. The main contribution of the present study is that it provides preliminary evidence of acute adverse associations of VOC with asthma in children. This study lays the foundation for more definitive studies in larger population groups. Overall, the literature on the relationship of asthma exacerbations to air pollutants provides sufficient evidence to justify further advancements in etiologic research of sensitive asthmatic subpopulations to improve understanding of causal components. Asthma may represent a key sentinel for the effects of toxic compounds on diseases of the pulmonary system.

In conclusion, our findings, coupled with experimental and other epidemiologic evidence in the literature, suggest that the pro-inflammatory and irritant nature of traffic-related pollutants can lead to adverse health effects in asthmatic children. Some VOCs measured in the present study, criteria air pollutants, organic and elemental carbon may be markers for a causal mixture of combustion-related pollutants in an area with high traffic density.

7. RECOMMENDATIONS

We believe that the findings for asthma symptoms show that adverse respiratory effects of air toxics can be found in small groups of symptomatic children with asthma. The low frequency of asthma flares limited our ability to assess effects of breath VOCs, and to assess effects of ambient air pollutants on clinically relevant symptoms interfering with daily activities. This was a consequence of having an insufficient number of asthmatics with persistent asthma. If the associations with VOC we found represent a true underlying causal relationship, then future studies will require more patients with at least mild persistent asthma in order to clearly detect associations that impact the quality of life of asthmatic children. The design will require sufficient funding to provide a larger recruitment effort and in-clinic evaluations of volunteers, including full spirometry and allergy testing.

The problem of potentially invalid or falsified PEF is a major consideration in interpreting the analyses of PEF. As discussed, the null results could be attributable to this. Because the PEF data were not collected using electronic lung function meters, we could not confirm whether maneuvers were actually performed. There is prior evidence that this may be a major problem in studies using handheld PEF meters (Verschelden, 1996; Redline, 1996). As with the PEF data, the asthma symptom and other health outcome data, as well as time-activity data, were not collected by electronic means, so we could not verify that answers to diary questions were given at the appropriate times during each and every day. If answers were recorded later in time, the data are subject to recall bias and temporal inaccuracies. We recommend that despite increased costs, future studies should employ both electronic PEF/FEV₁ meters and electronic diaries similar to our other recent asthma panel studies (Delfino et al., 2001a; 2001c). This will ensure reproducibility and compliance for lung function maneuvers and will confirm diary compliance at the expected time of data entry by subjects. Nevertheless, we feel that much of the data collected in the present manner was informative in the epidemiological analysis as it has been in other similar studies, particularly after sensitivity analyses are done to exclude suspect data. Our results for asthma symptoms support this view.

We used outcome data collection methods that are typically used by researchers worldwide for asthma panel studies. Findings such as ours that led to the need for exclusion of subject diary and PEF data should be emphasized in light of strong recommendations of an NRC Committee for improvements in particulate air pollution exposure assessment data for epidemiologic research (NRC, 1998; 1999). It is unclear how needed improvements in exposure data without similar improvements in outcome assessments will be sufficient to fully characterize populations at risk from the adverse effects of air pollutants. As discussed previously, despite increased costs of research, we strongly recommend that future investigations move toward electronic methods of ambulatory data acquisition from subjects. Assuring valid and relevant health outcome data will require advancements in methods in parallel with exposure assessment work. This may be particularly challenging in highly exposed populations living in urban areas characterized by lower socioeconomic status. Residents of the Huntington Park region are a key example of such a population.

Our weaker results for the adverse effects of breath versus ambient VOC exposures suggest the need for an improved study approach, including, a more extensive evaluation of:

- 1) other correlated air toxics exposures in ambient air such as polycyclic aromatic hydrocarbons (PAH) from diesel exhaust that have been proposed to be relevant to allergic respiratory diseases (Nel 2001; Pandya 2002);
- 2) personal exposures, including air toxics exposures of outdoor origin versus microenvironmental exposures, with assessments of exposure sources; and
- 3) advancement in the approach to VOC breath sample collection, including daily longitudinal samples, and/or the use of other biomarkers of air toxics exposures.

The need for items 2 and 3 are supported by the exposure assessment results. We found marked day-to-day variability in breath sample measurements in each participant. It is important to learn the reasons for the variability for future studies that aim to use breath VOCs as biomarkers. We also found relationships between personal and lagged outdoor benzene and xylene, and between breath and lagged outdoor benzene, styrene and xylene. This suggests fairly strong outdoor source for these chemicals (which are gasoline combustion products) and a time interval for outdoor exposures to penetrate indoors during the cool season of November to January in California. However, given the small number of subjects, it was unclear if the observation was externally valid. The overall findings of the exposure assessment study support a need to conduct a longitudinal study where indoor, outdoor, personal, and breath samples are collected daily. This will enable researchers to better describe within-subject variability and temporal relationships between microenvironmental exposures and breath VOC concentrations.

The results of this study are useful in determining the type and scope of studies needed to evaluate health impacts in California communities affected by multiple emission sources. This will guide the assessment of resources needed to fund various research designs, experimental and epidemiologic, to address environmental justice-related issues. In addition, this pilot study has provided valuable insight regarding personal exposures in a potentially sensitive group of children. Our finding of positive association between acute adverse symptom outcomes in asthmatic children and ambient air toxics supports the need to evaluate both acute and chronic health effects using additional research designs in populations at risk. We strongly recommend the advancement of epidemiologic methods to investigate this important area of public health.

FIGURES

Figure 1. Huntington Park Region Study Map. The radius of study participant homes is 2.57 miles, excluding one outlying home labeled number 1 in box. Two outdoor stationary monitors are mapped, Nimitz and Heliotrope Schools. Homes are not mapped.

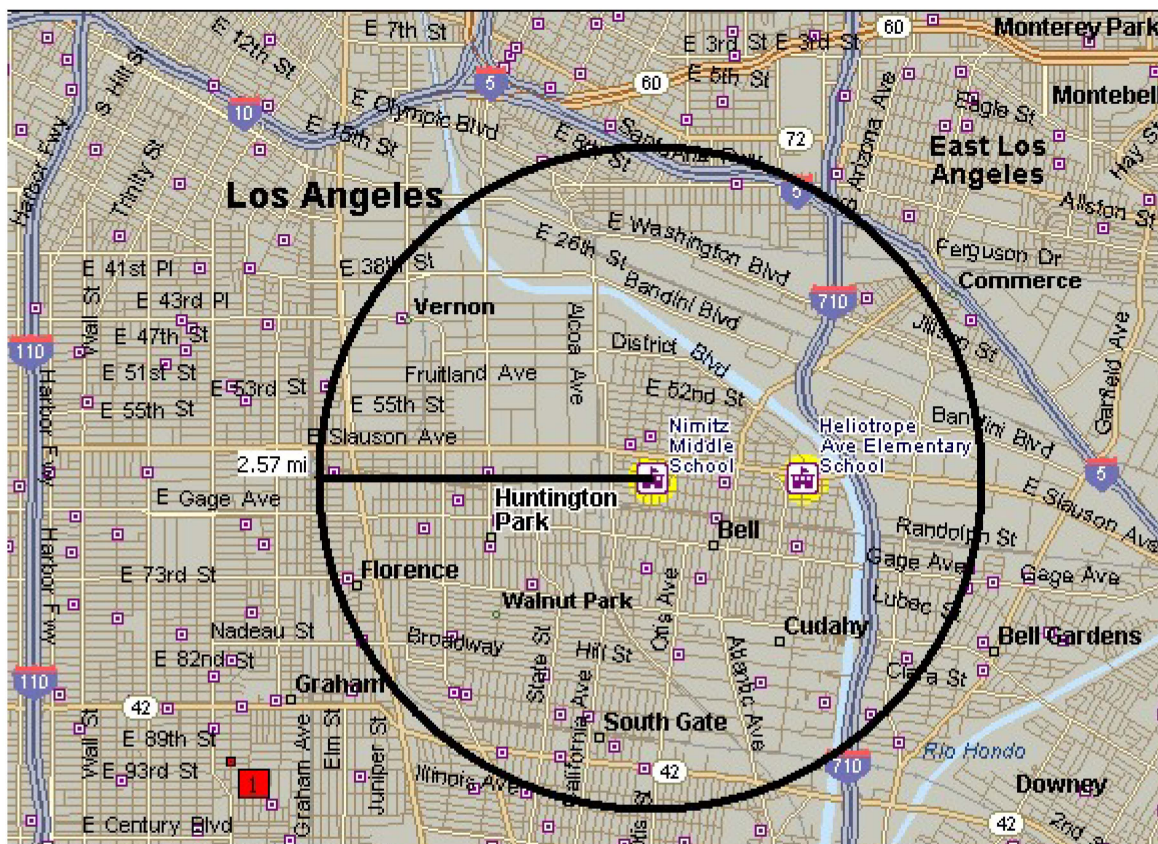


Figure 2a. Time plot for 1,1-Dichloroethane

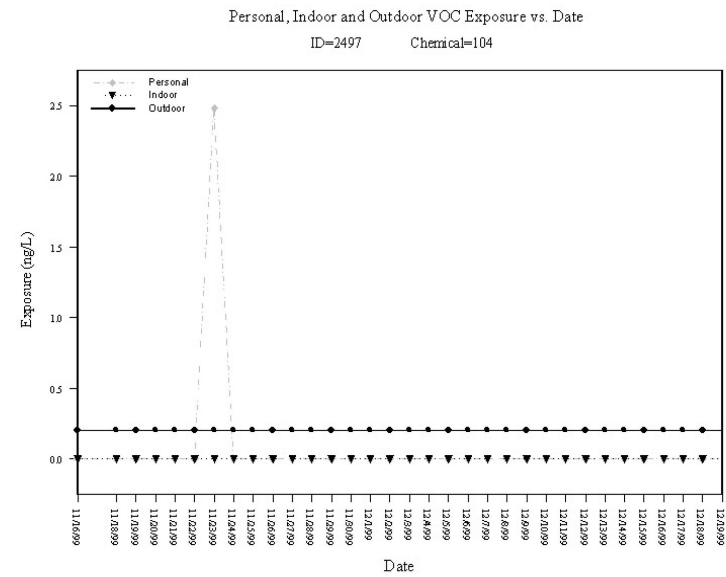
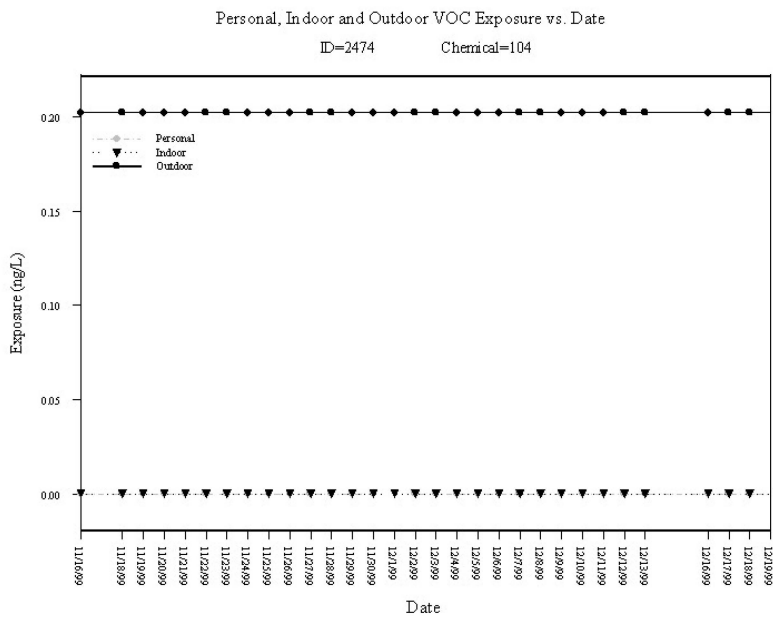
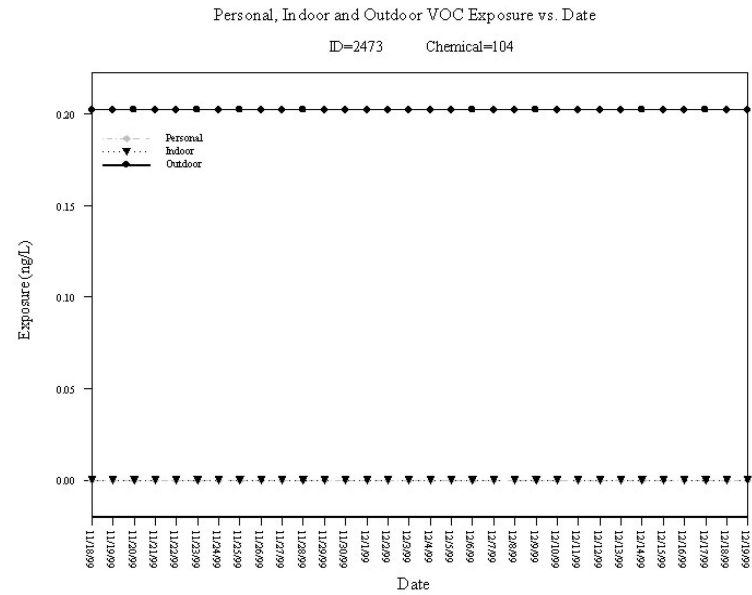
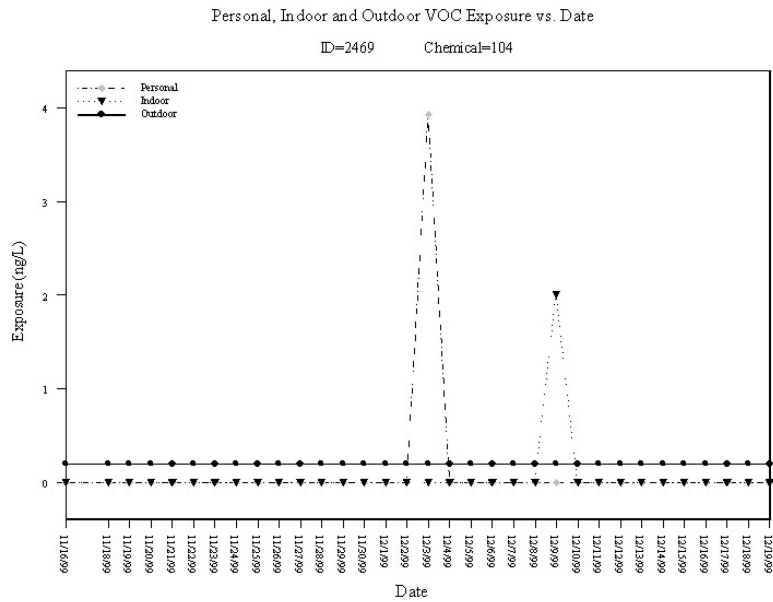


Figure 2b. Time plot for o-Dichlorobenzene

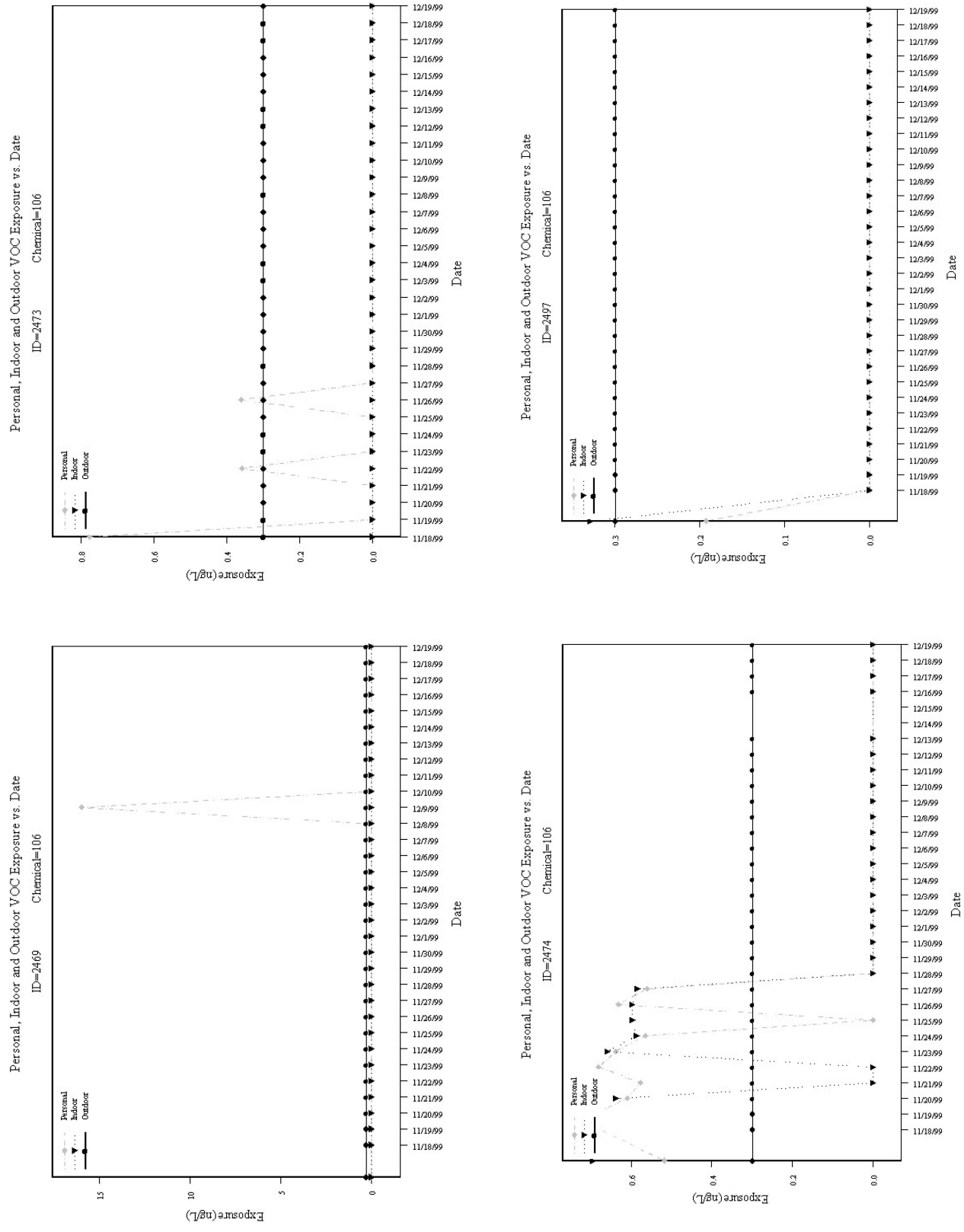


Figure 2c. Time plot for p-Dichlorobenzene

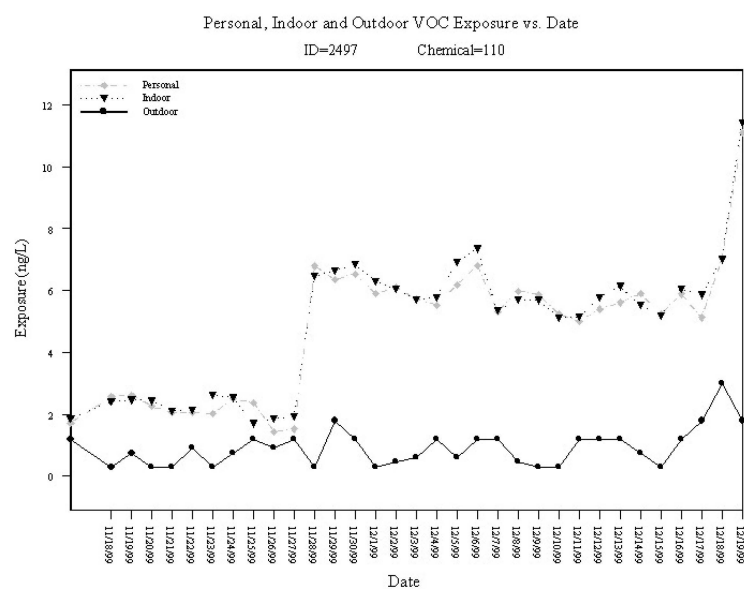
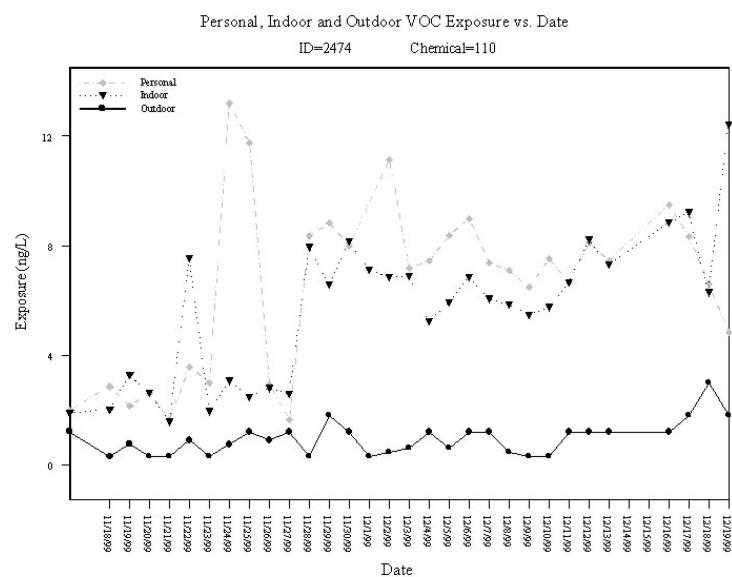
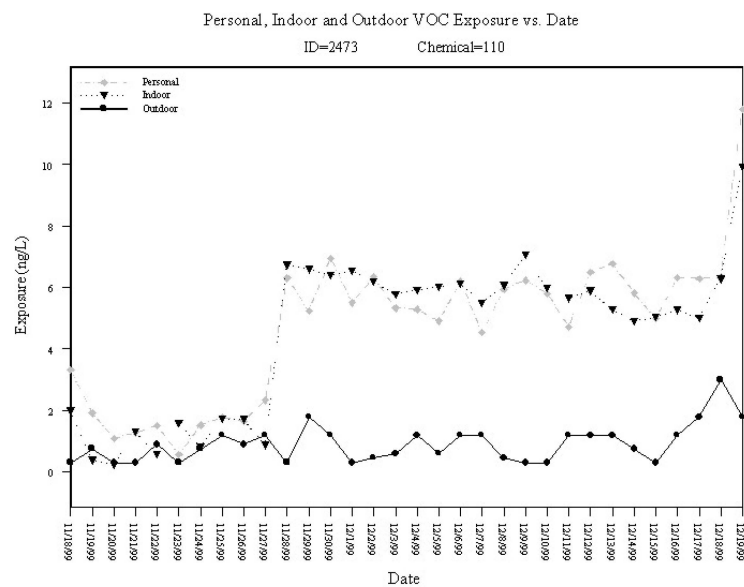
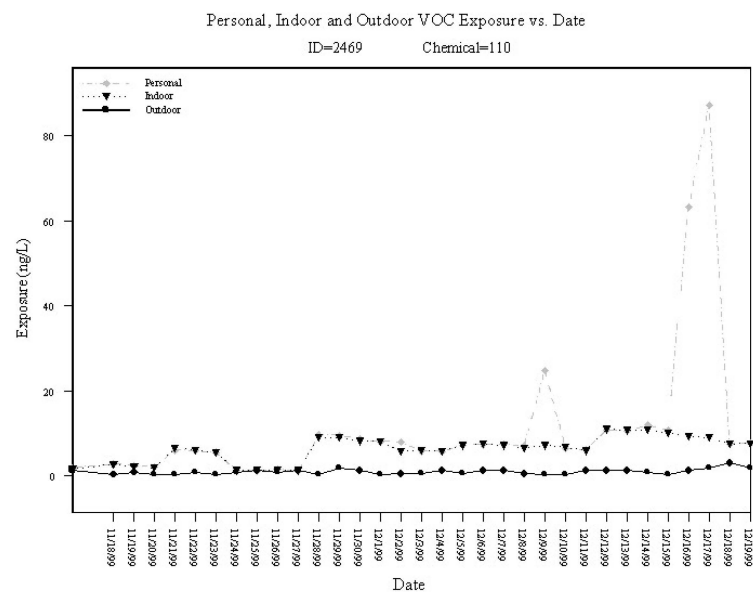


Figure 2d. Time plot for Benzene

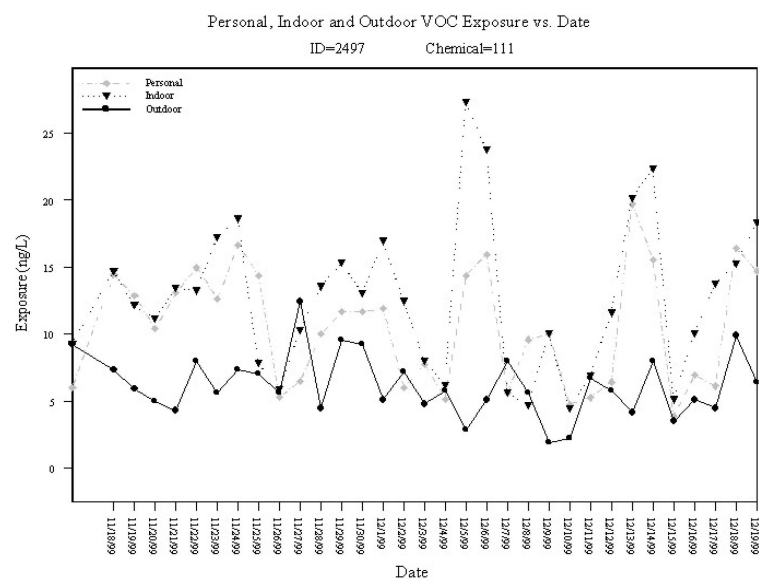
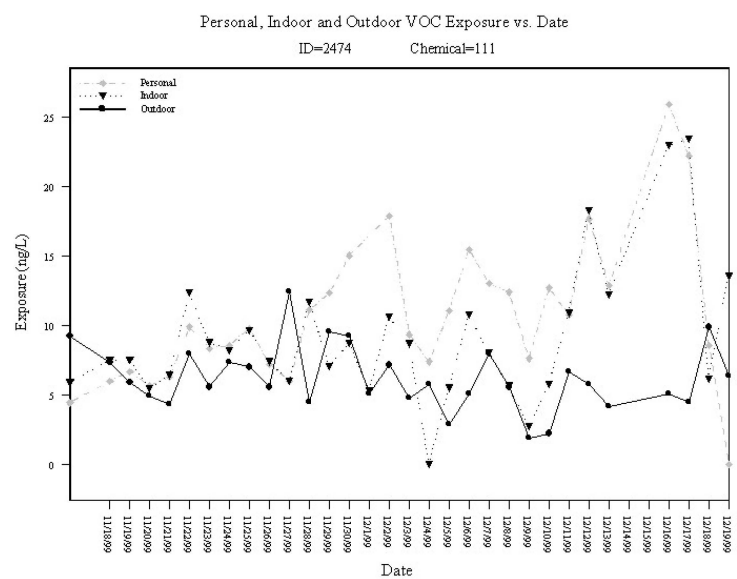
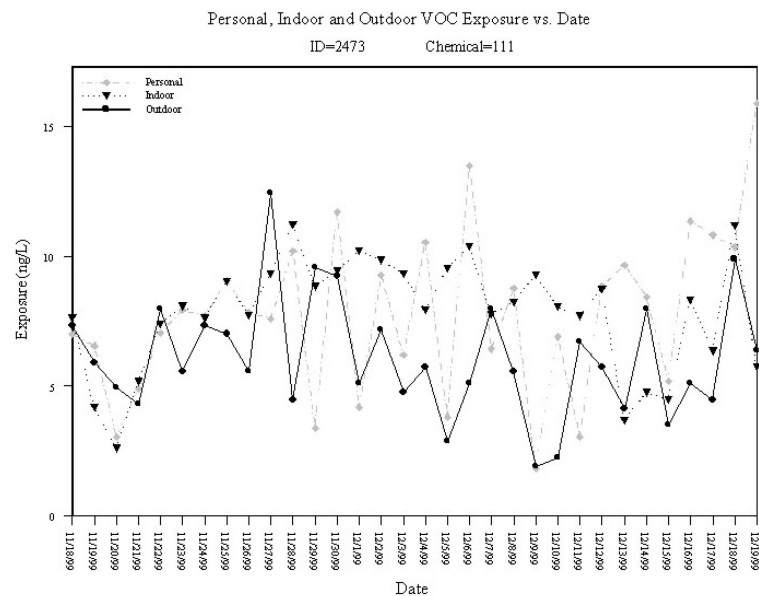
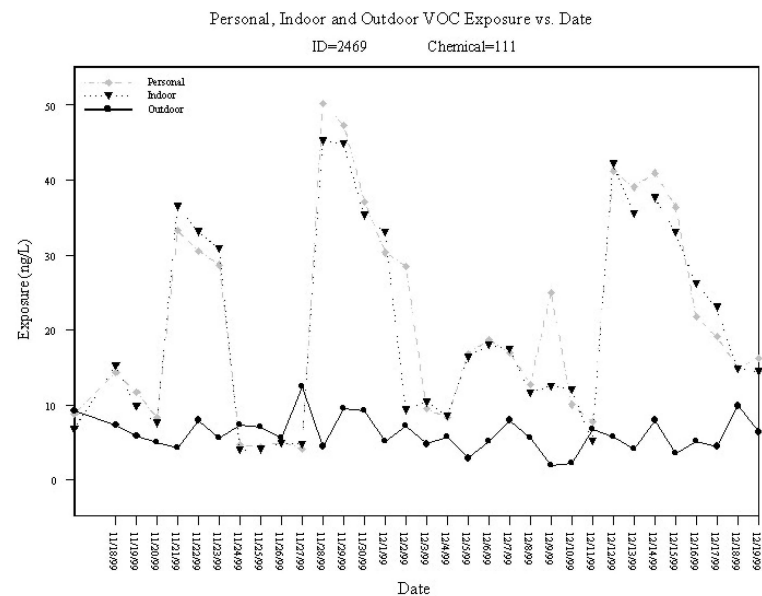


Figure 2e. Time plot for Chloroform

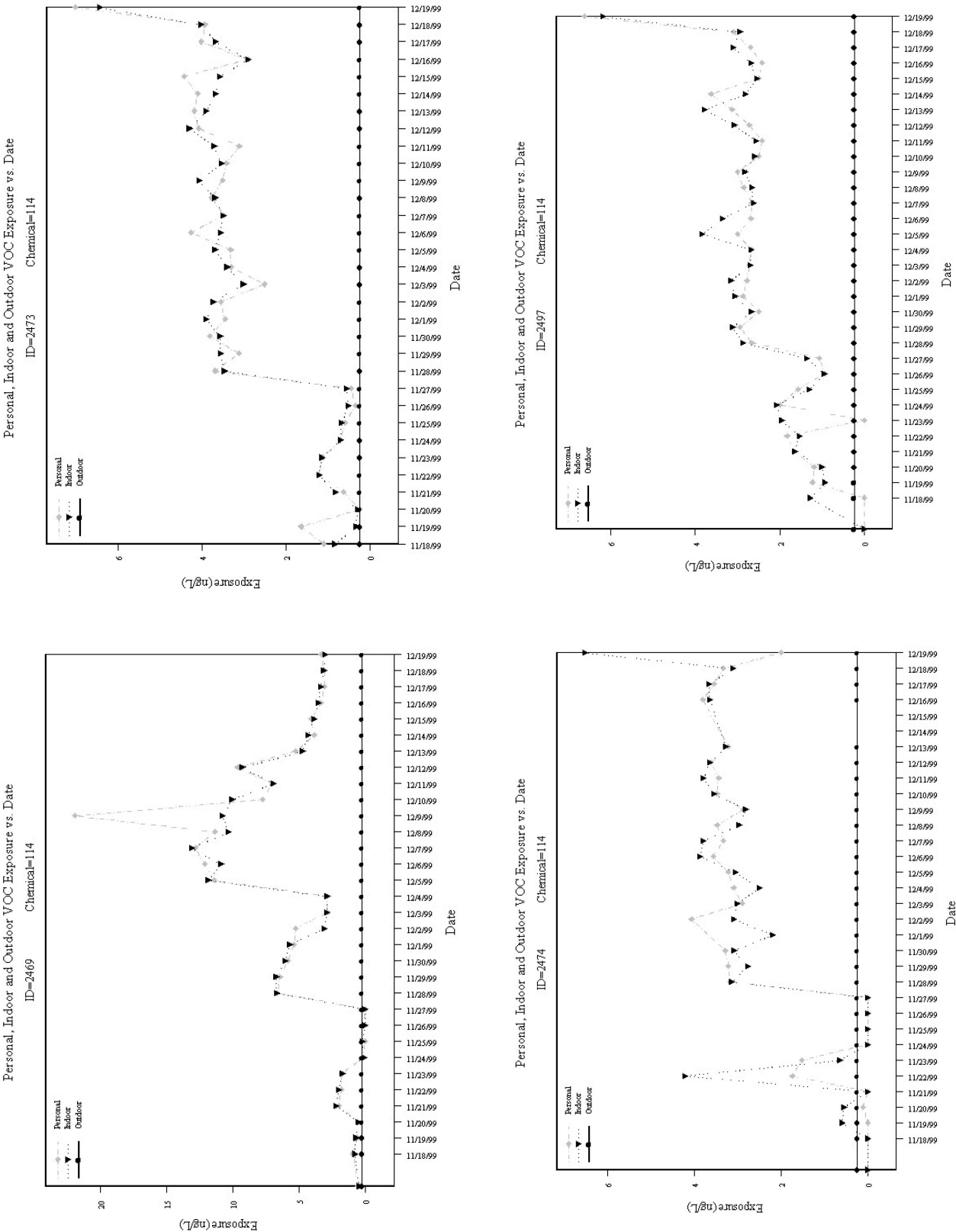


Figure 2f. Time plot for Styrene

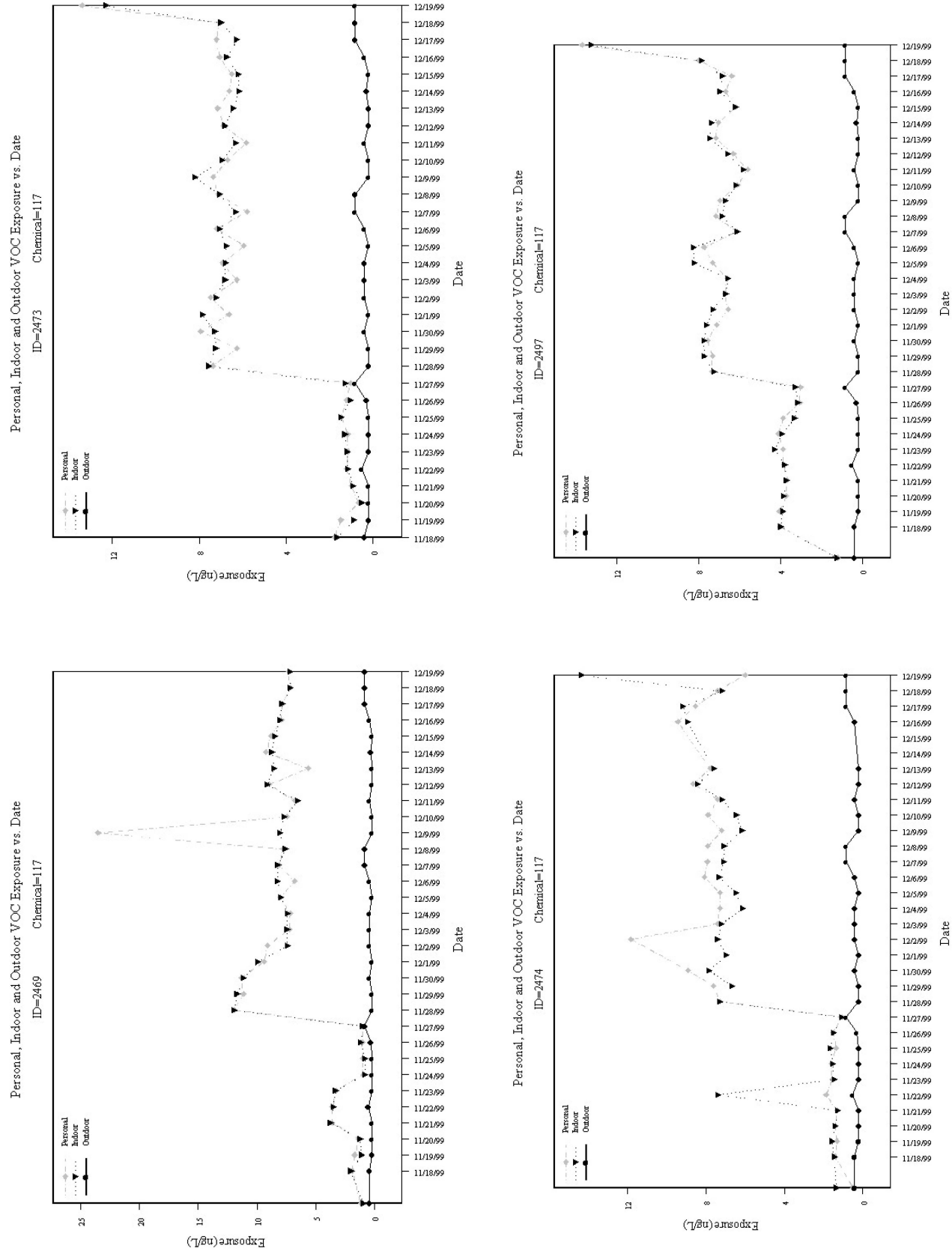


Figure 2g. Time plot for Tetrachloroethylene

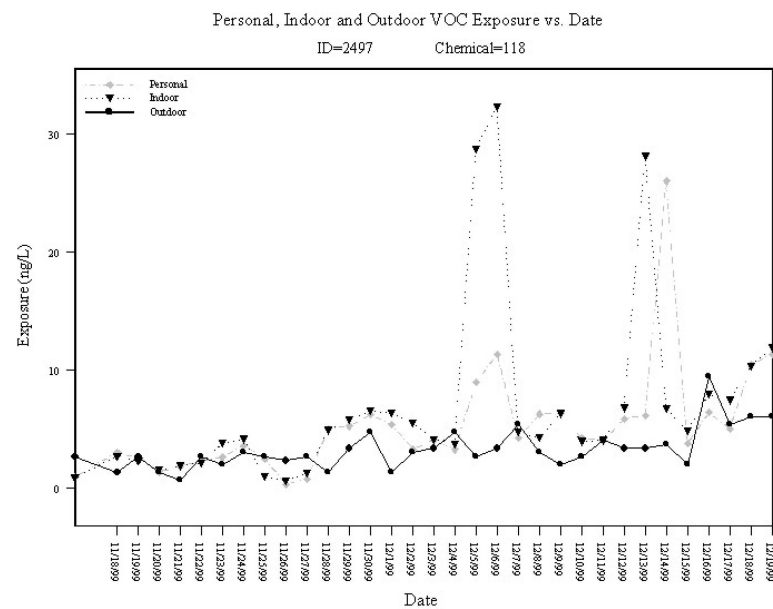
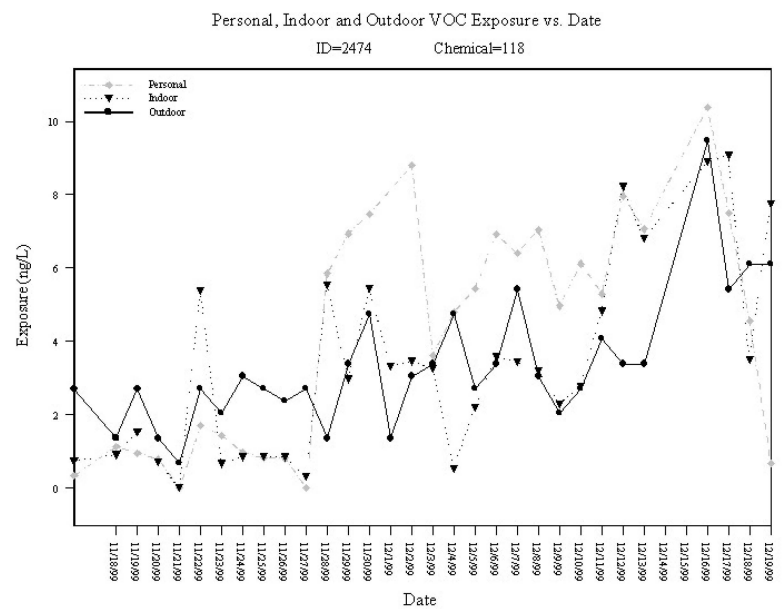
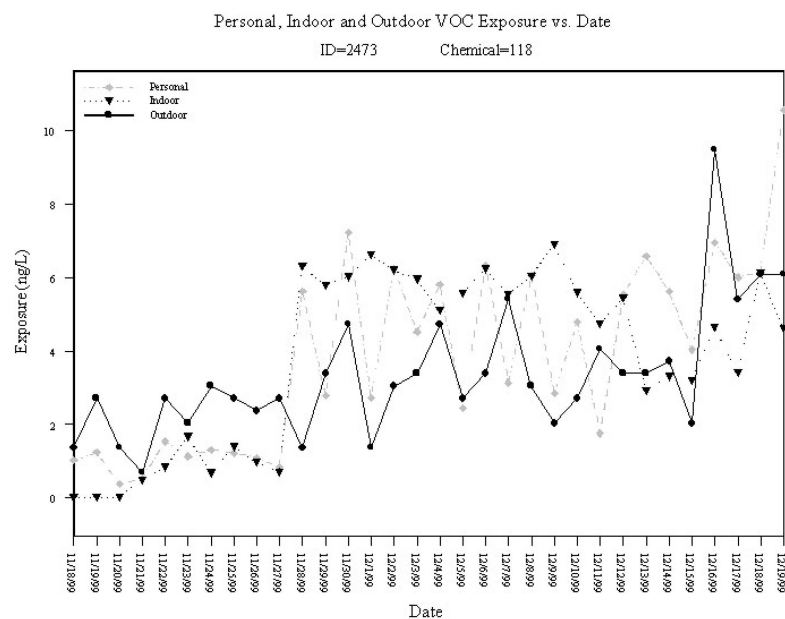
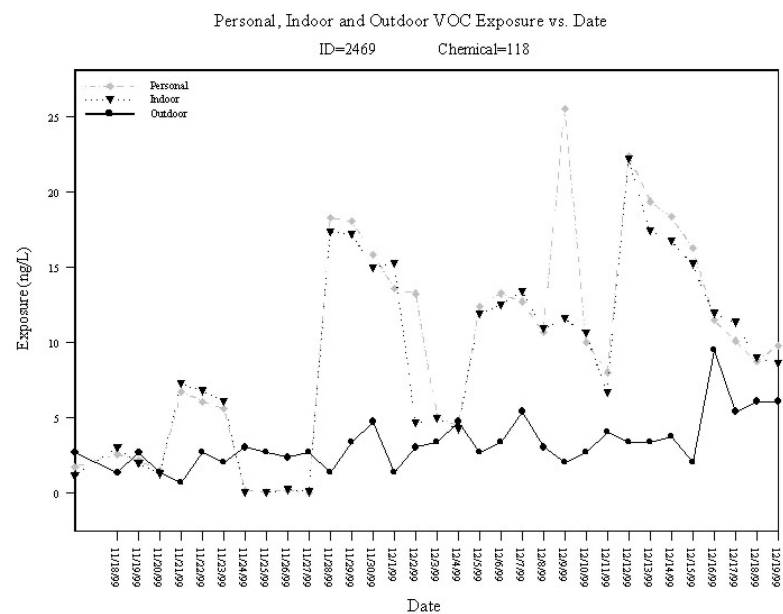


Figure 2h. Time plot for Toluene

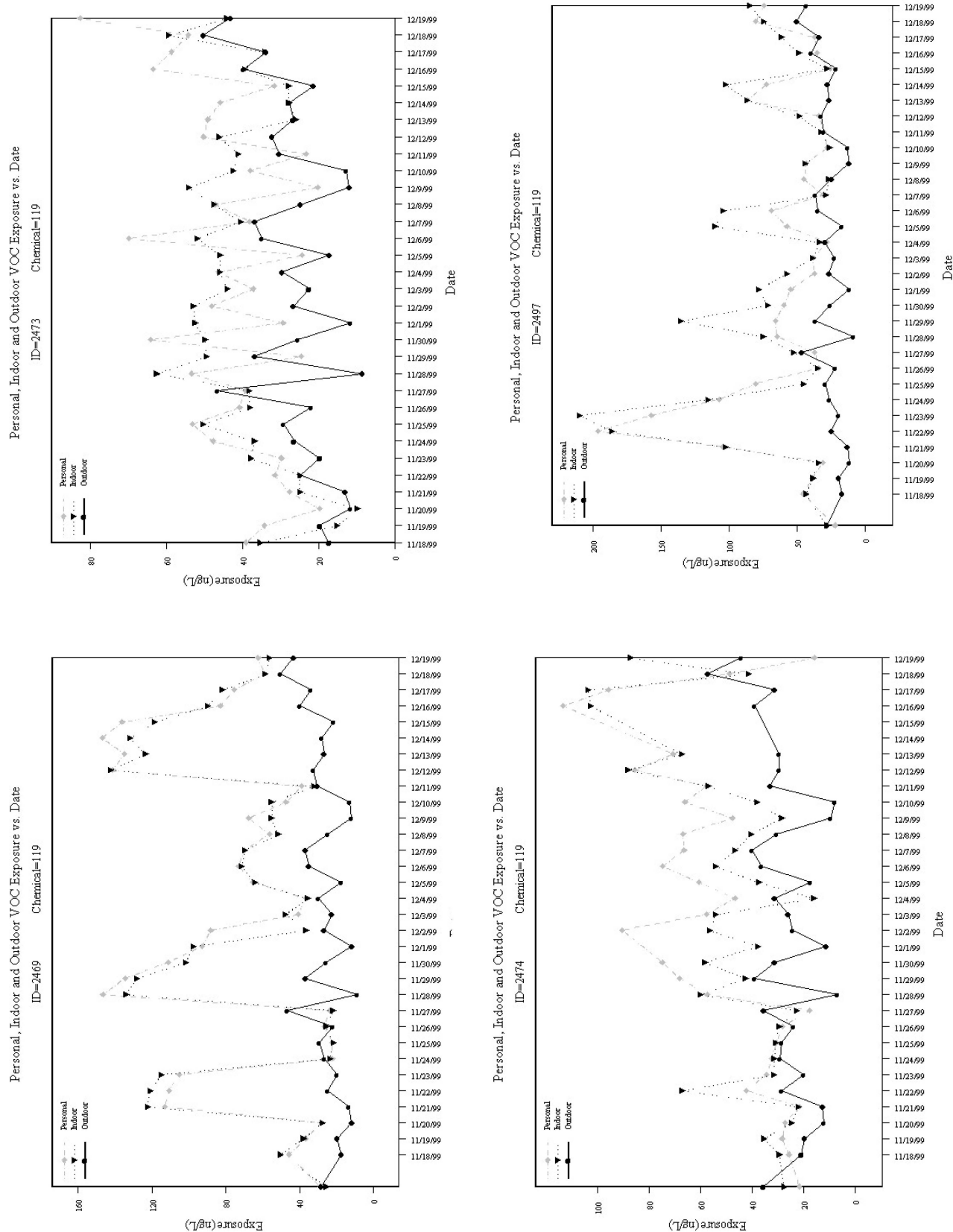


Figure 2i. Time plot for m,p-Xylene

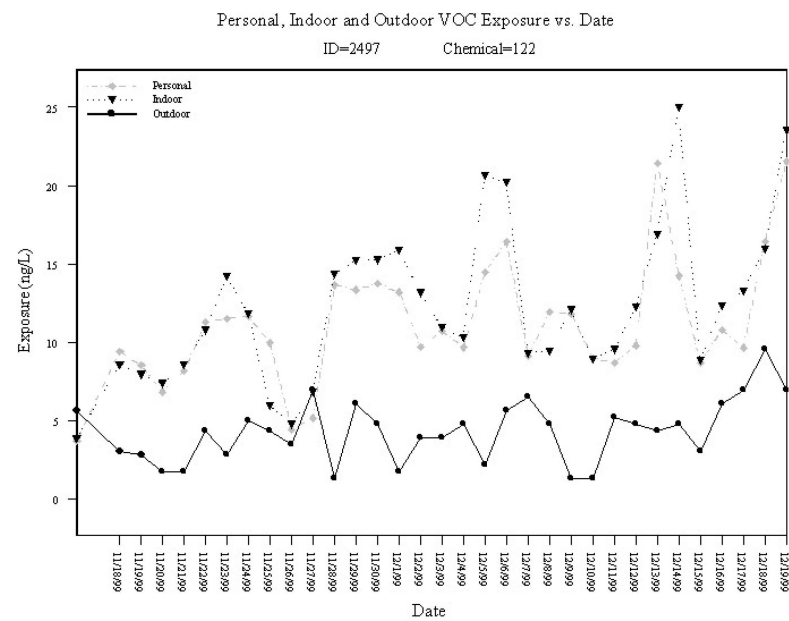
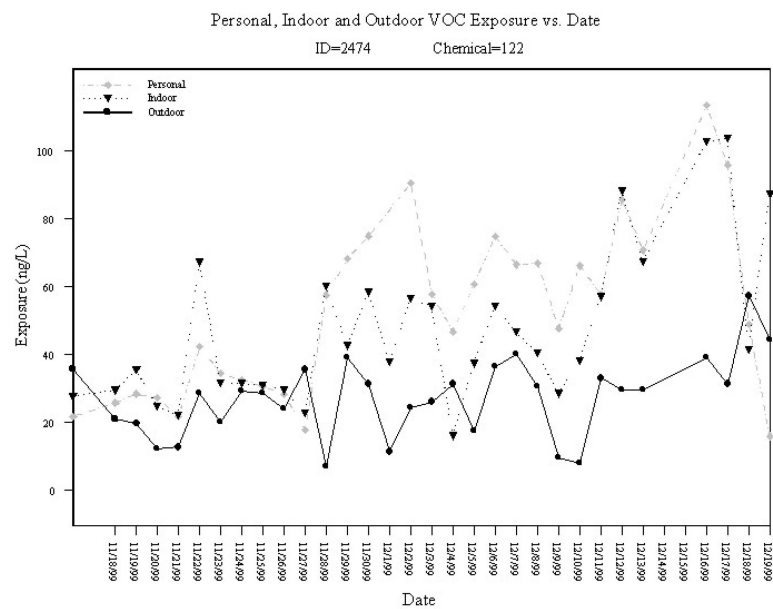
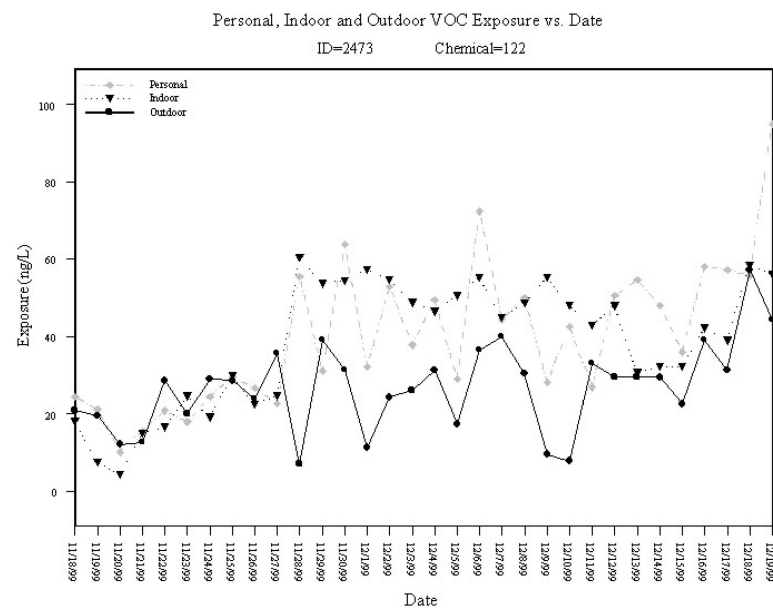
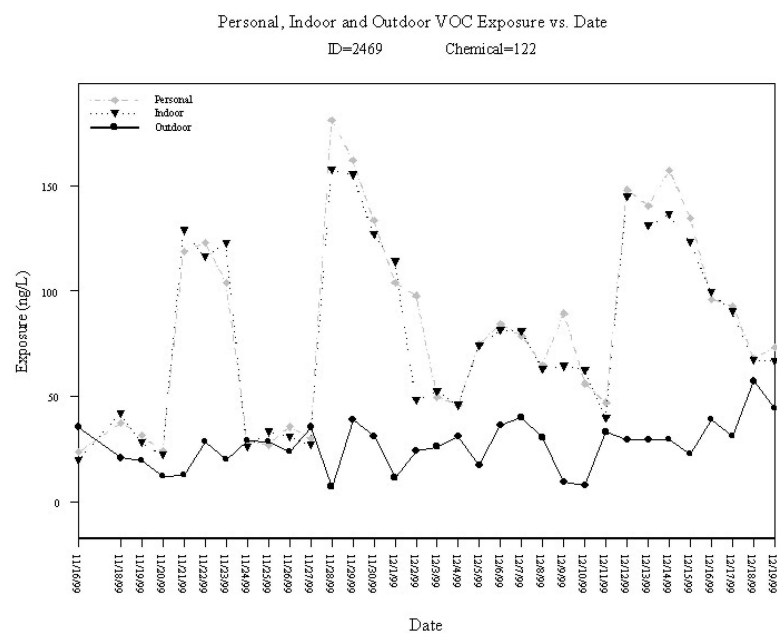


Figure 2j. Time plot for o-Xylene

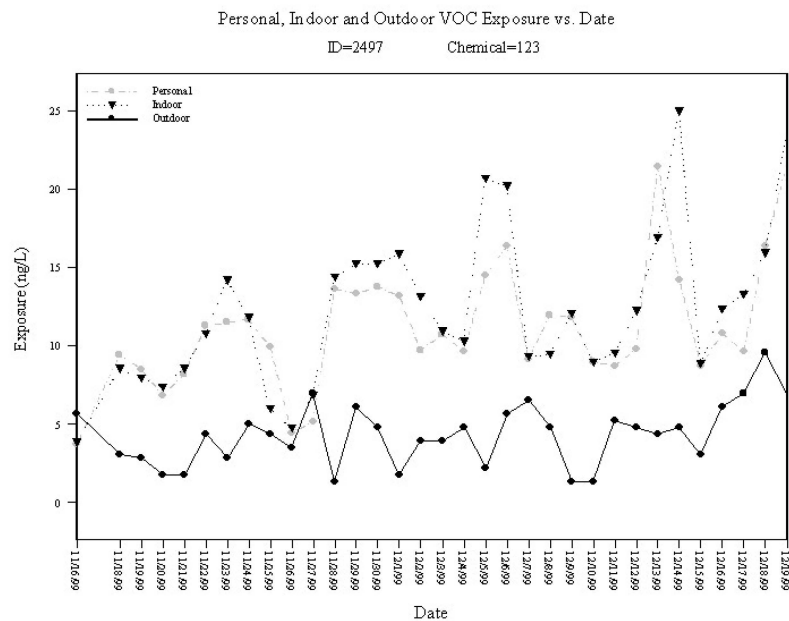
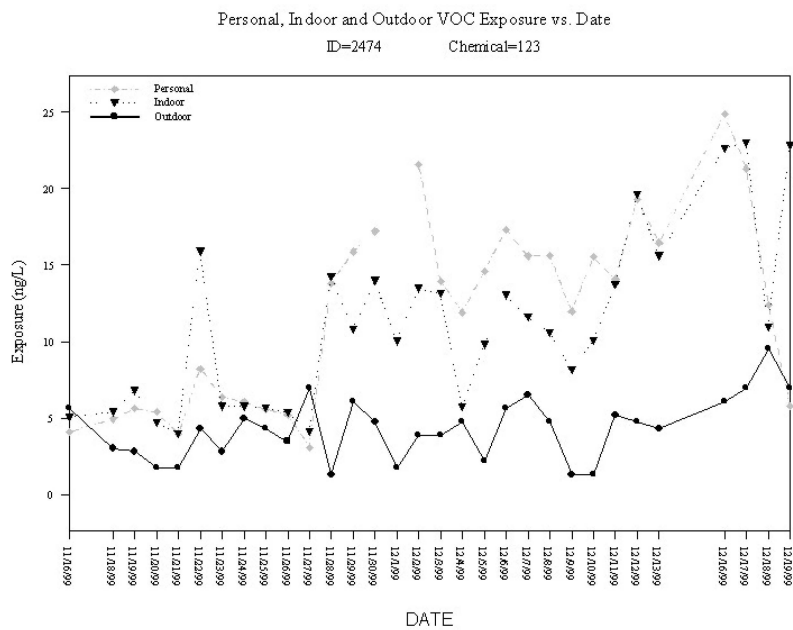
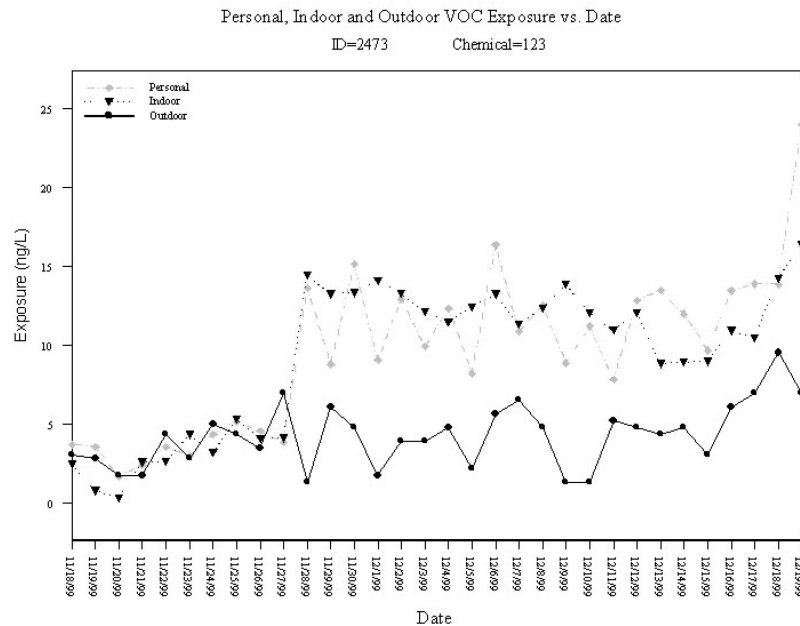
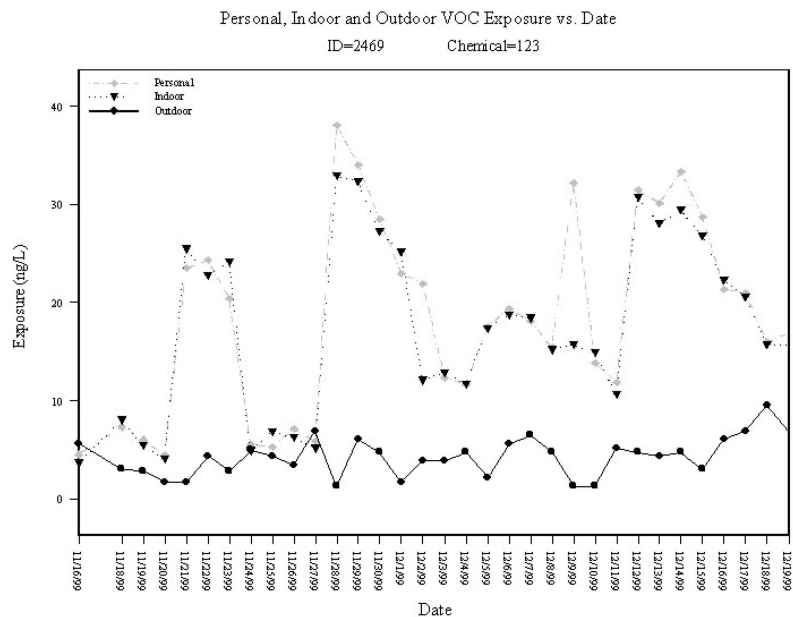


Figure 3a. Distribution of the differences >10 L/min between the largest and second largest evening PEF within a test session.

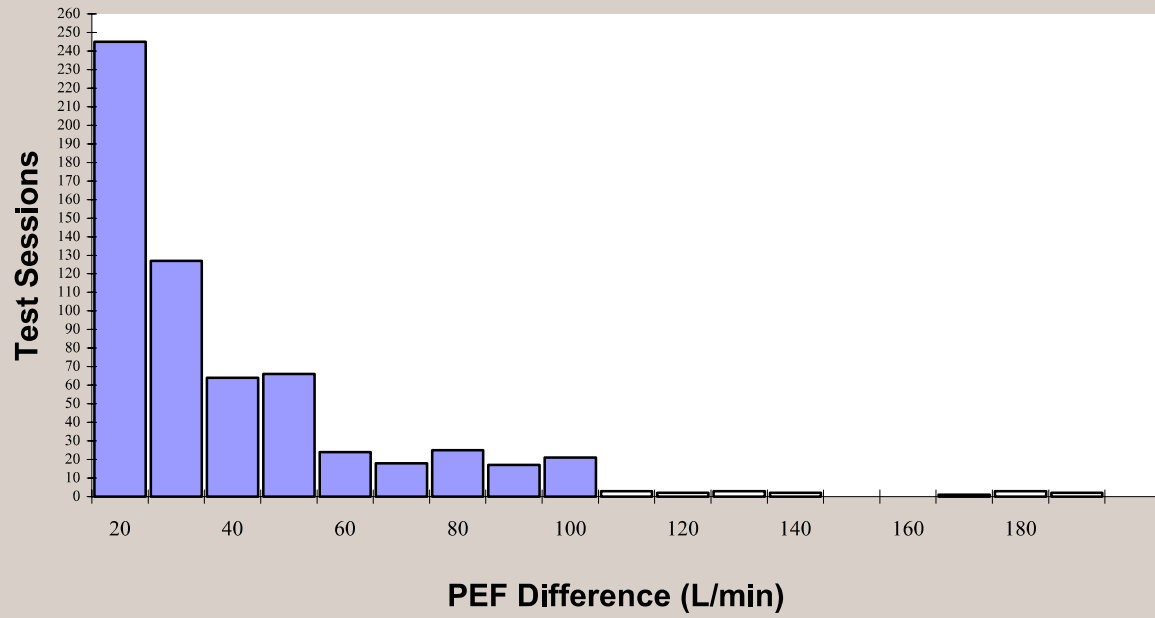


Figure 3b. Distribution of differences >10 L/min between the largest and second largest morning PEF within a test session.

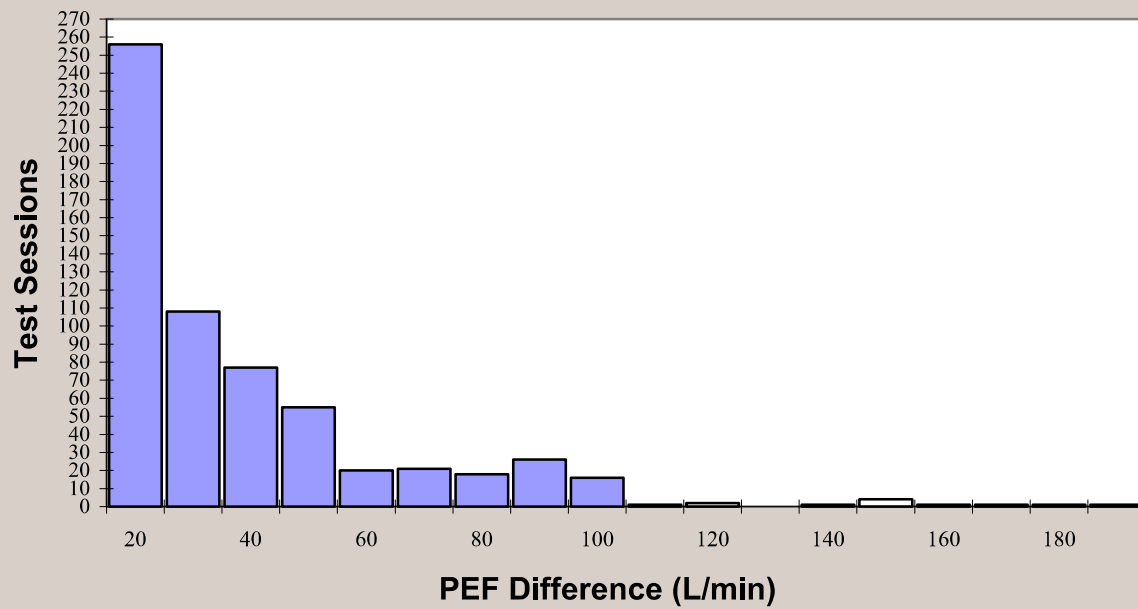


Figure 4. Time plot of daily 8-hr maximum NO₂ (ppb) compared with 24-hr mean benzene (ppb), Nov 4, 1999 through Jan 23, 2000, Huntington Park, Los Angeles County, California.

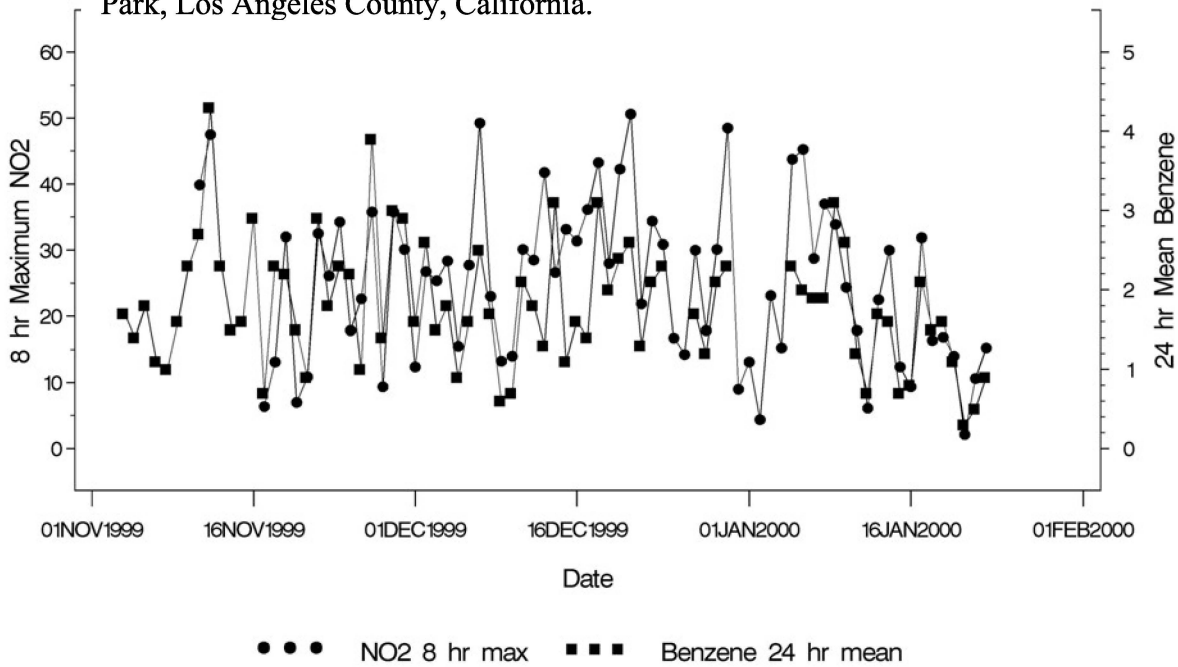


Figure 5. Time plot of daily 8-hr maximum NO₂ (ppb) compared with 24-hr mean m,p-xylene (ppb), Nov 4, 1999 through Jan 23, 2000, Huntington Park, Los Angeles County, California.

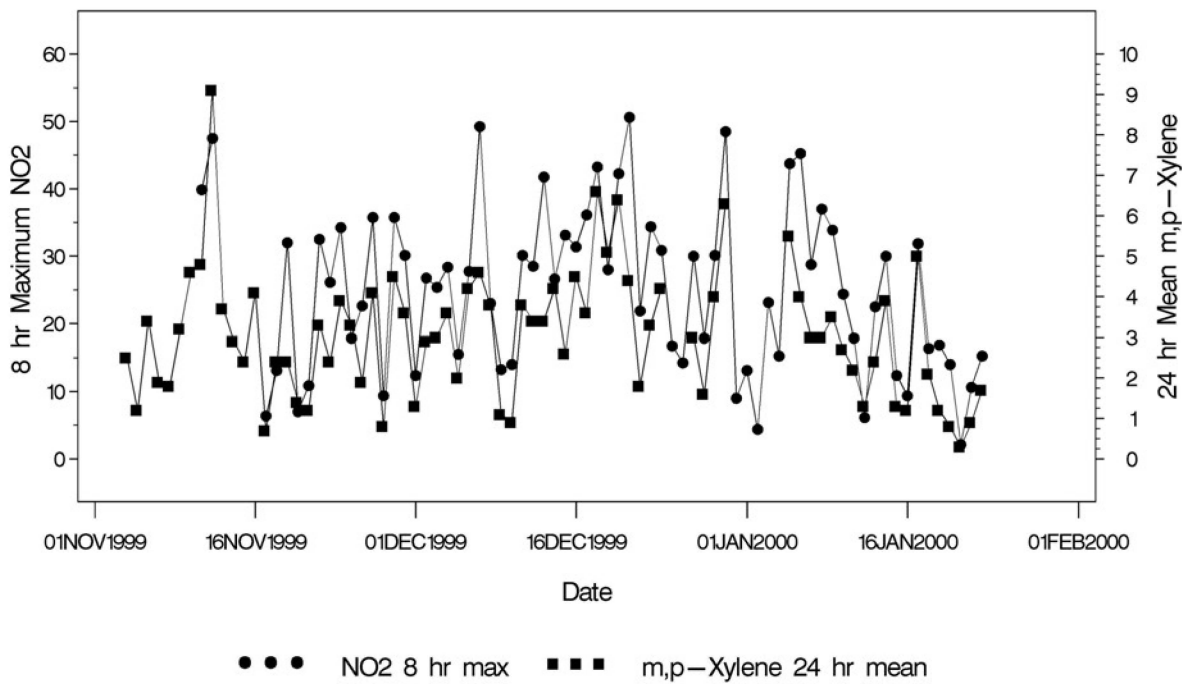


Figure 6. Time plot of daily 8-hr maximum NO₂ (ppb) compared with 24-hr mean acetone (ppb), Nov 6, 1999 through Jan 23, 2000, Huntington Park, Los Angeles County, California.

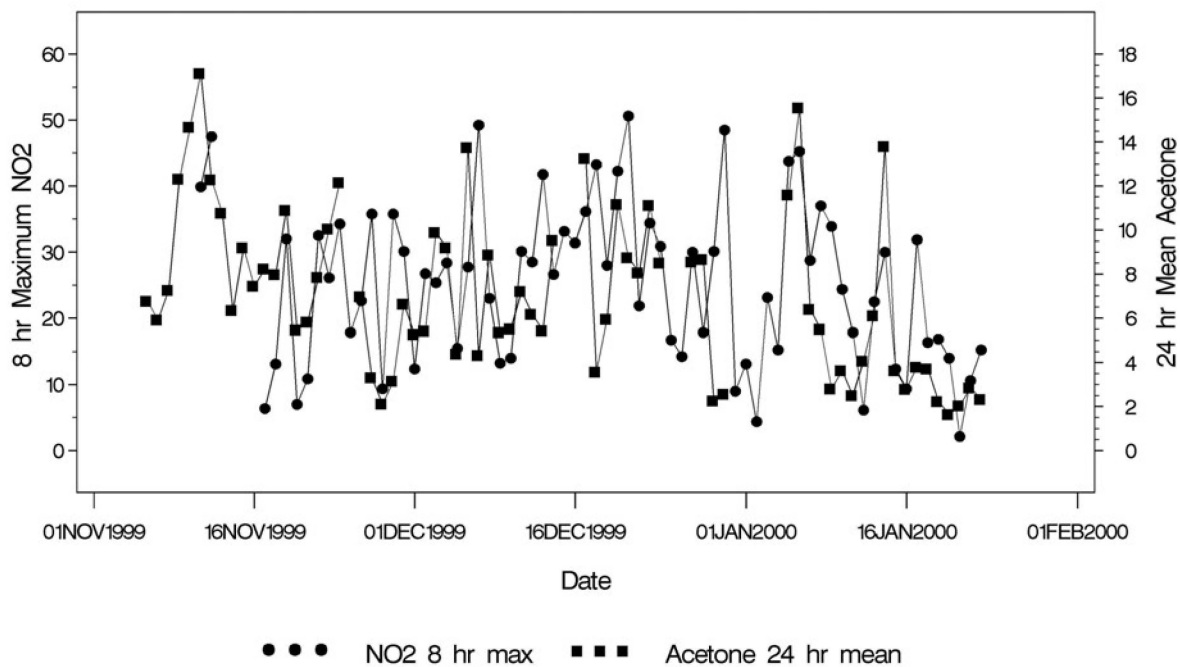


Figure 7. Time plot of daily 8-hr maximum NO₂ (ppb) compared with 24-hr mean formaldehyde (ppb), Nov 6, 1999 through Jan 23, 2000, Huntington Park, Los Angeles County, California.

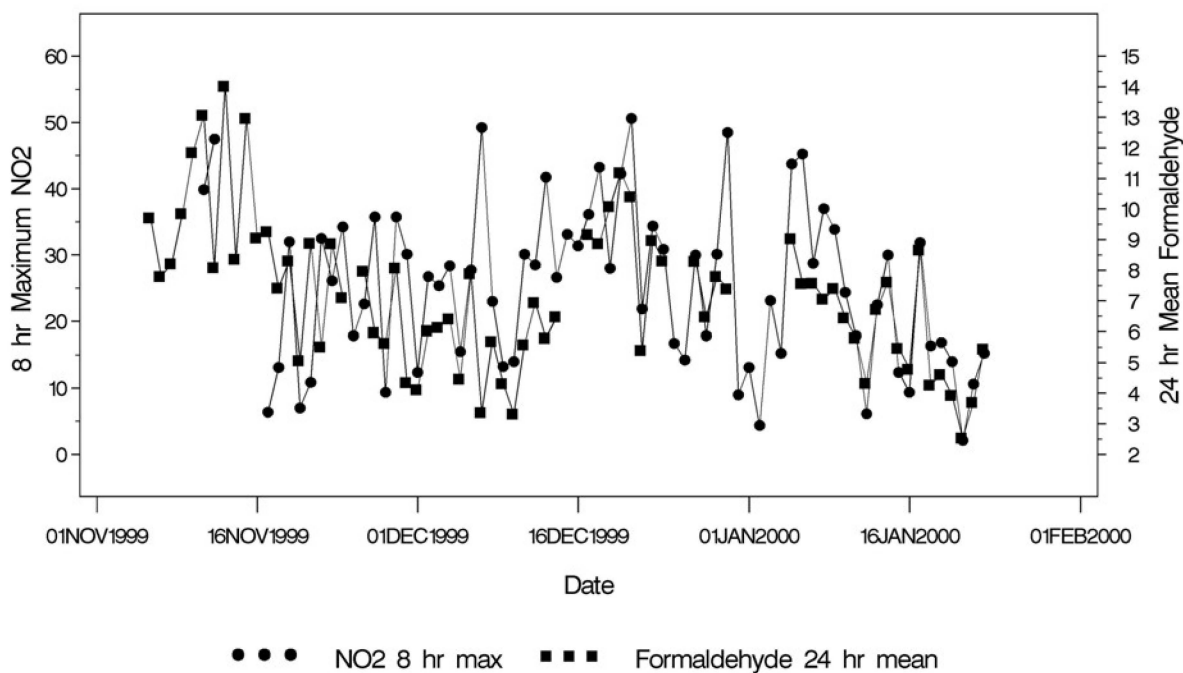


Figure 8. Time plot of daily 8-hr maximum NO₂ (ppb) compared with 8-hr maximum O₃ (ppb), Nov 11, 1999 through Jan 23, 2000, Huntington Park, Los Angeles County, California.

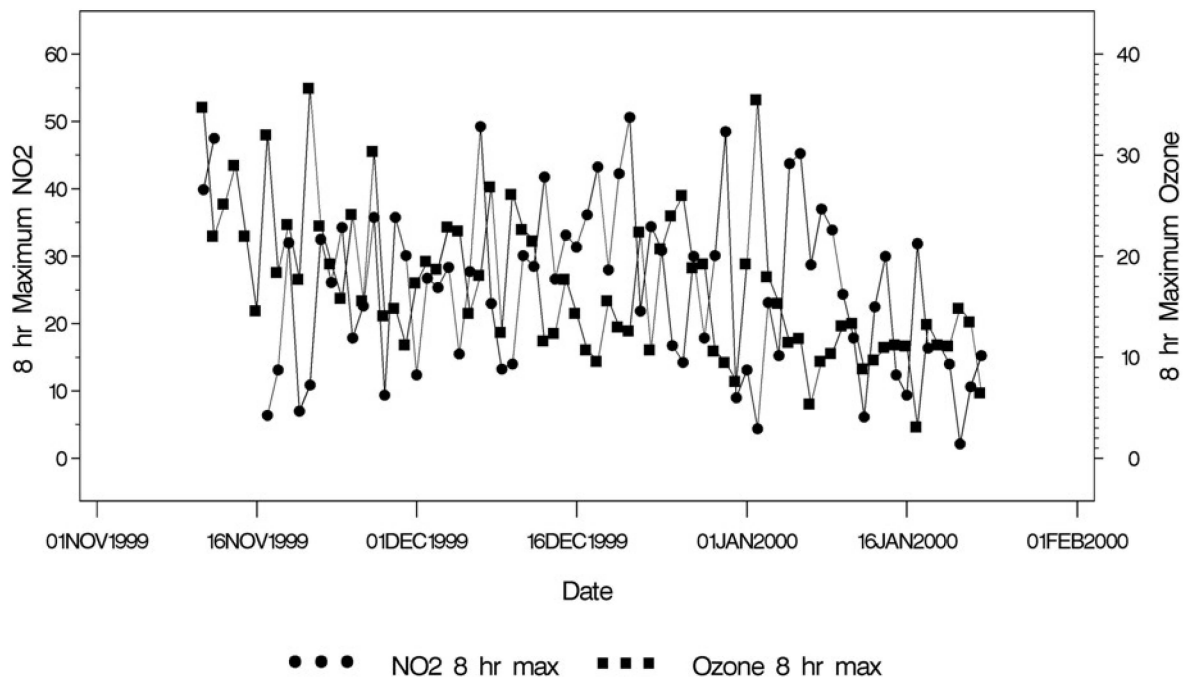


Figure 9. Time plot of daily 8-hr maximum NO₂ (ppb) compared with 8-hr maximum SO₂ (ppb), Nov 11, 1999 through Jan 23, 2000, Huntington Park, Los Angeles County, California.

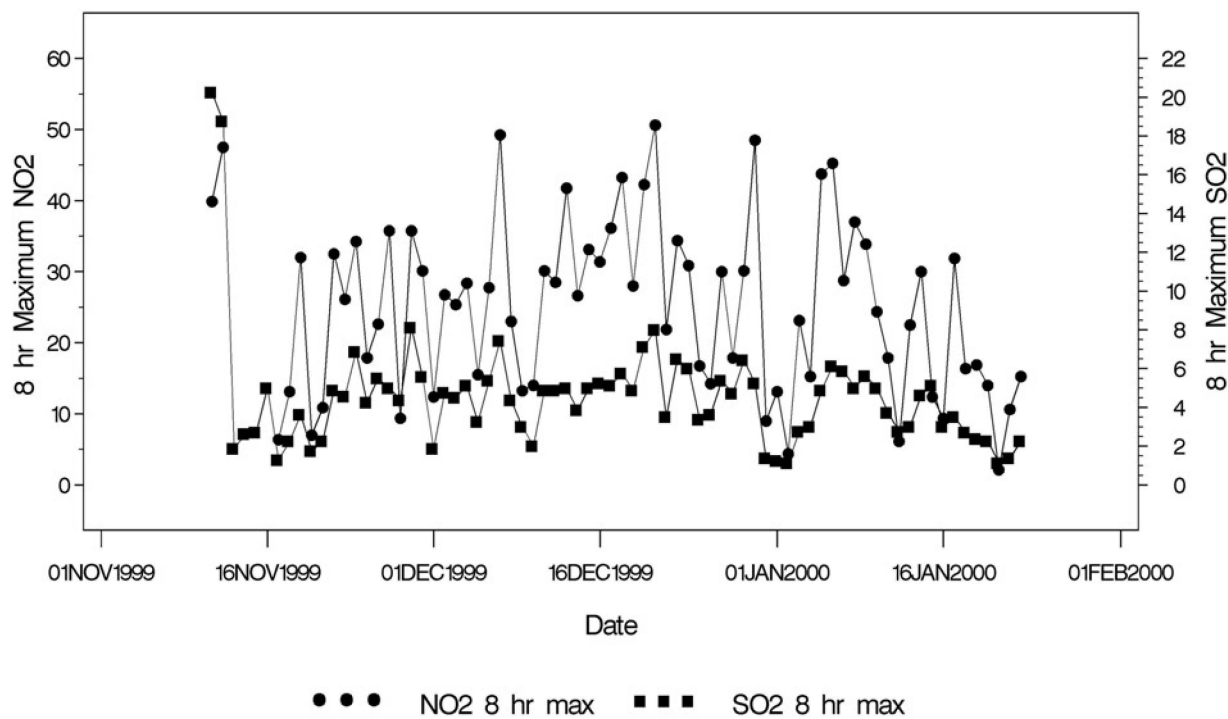


Figure 10. Time plot of daily 24-hr mean organic carbon ($\mu\text{g}/\text{m}^3$) compared with 24-hr mean m,p-xylene (ppb), Nov 4, 1999 through Nov 26, 2000, Huntington Park, Los Angeles County, California.

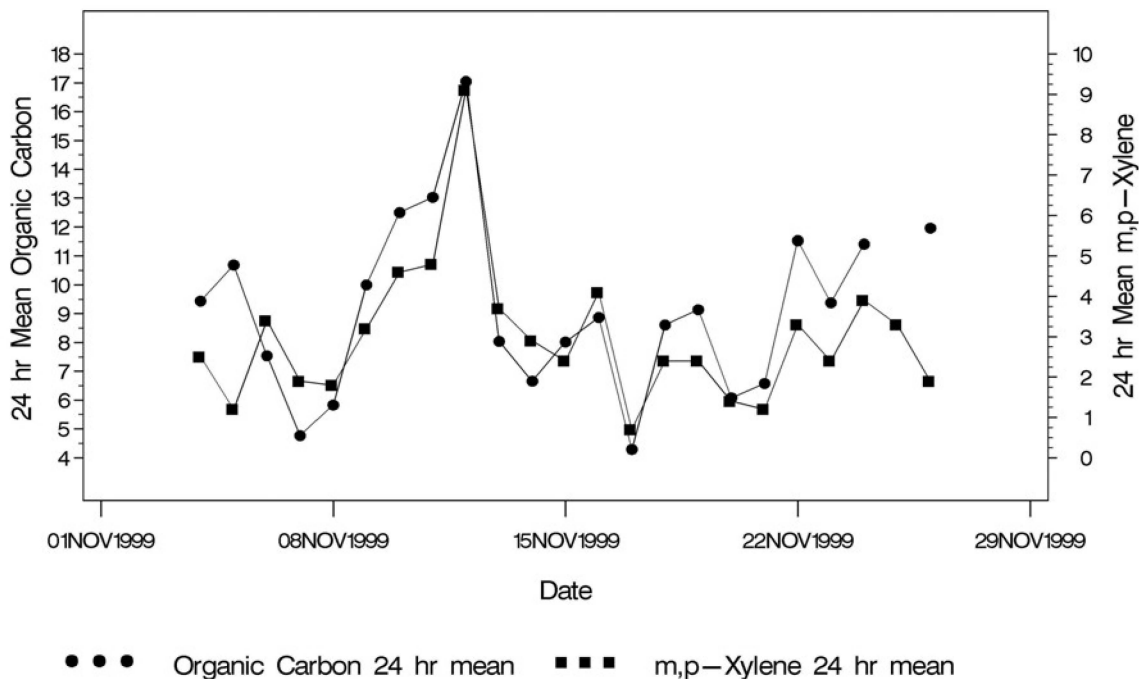


Figure 11. Time plot of daily 24-hr mean elemental carbon ($\mu\text{g}/\text{m}^3$) compared with 24-hr mean m,p-xylene (ppb), Nov 4, 1999 through Nov 26, 2000, Huntington Park, Los Angeles County, California.

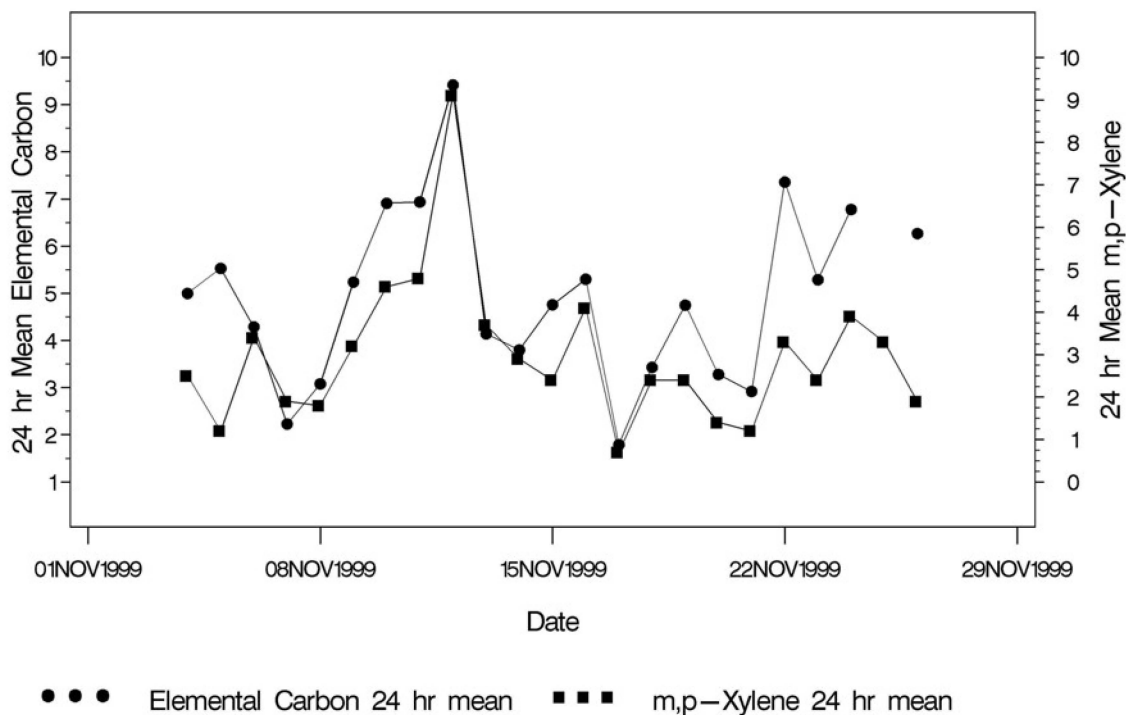


Figure 12. Time plot of daily 24-hr mean organic carbon ($\mu\text{g}/\text{m}^3$) compared with 24-hr mean gravimetric PM10 ($\mu\text{g}/\text{m}^3$), Nov 4, 1999 through Nov 26, 2000, Huntington Park, Los Angeles County, California.

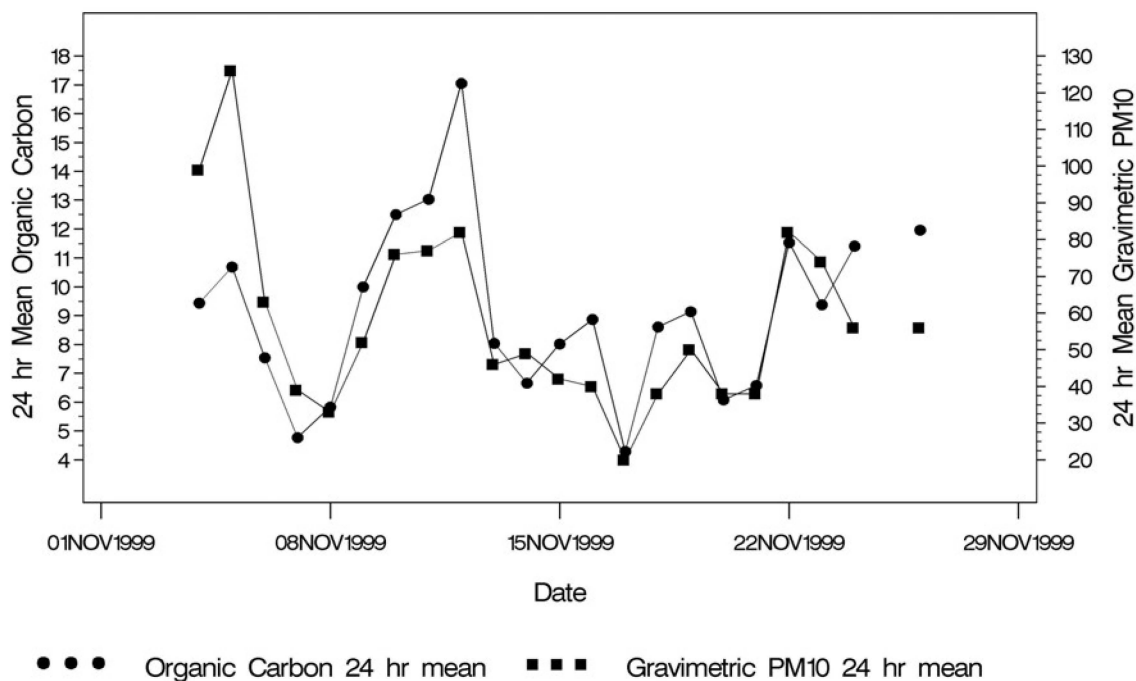
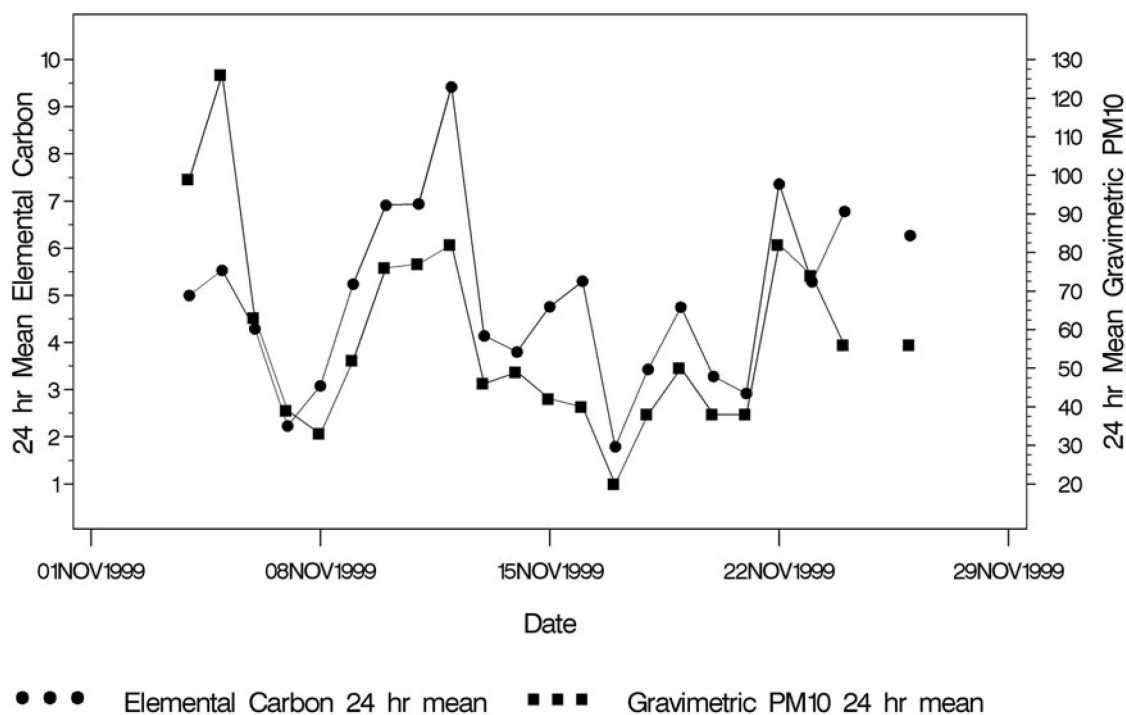


Figure 13. Time plot of daily 24-hr mean elemental carbon ($\mu\text{g}/\text{m}^3$) compared with 24-hr mean gravimetric PM10 ($\mu\text{g}/\text{m}^3$), Nov 4, 1999 through Nov 26, 2000, Huntington Park, Los Angeles County, California.



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GLOSARRY OF TERMS, ABBREVIATIONS, AND SYMBOLS

AIC: Akaike's information criterion
CI: confidence interval
DEP: diesel exhaust particles
EC : elemental carbon
ETS: environmental tobacco smoke
FEF₅₀: forced expiratory flow rate at 50% of FVC
FEF₂₅₋₇₅: forced expiratory flow rate at 25-75% of FVC
FEV₁: forced expiratory volume in 1 sec
FVC : forced vital capacity
IgE: immunoglobulin E
NEP: neutral endopeptidase
OR: Odds ratio
OC: organic carbon
PAH: polycyclic aromatic hydrocarbon
PEF: peak expiratory flow
PM: particulate matter
PM₁₀: particulate matter < 10 µm in aerodynamic diameter
PM_{2.5}: particulate matter < 2.5 µm in aerodynamic diameter
RNRC: Rancho National Rehabilitation Center
RAST: radioimmunoassay test
RTI: Research Triangle Institute
SES: socioeconomic status
SPT: skin prick test
TDI: toluene diisocyanate
TEOM: tapered-element oscillating microbalance
UCI: University of California, Irvine
U.S. NAAQS: National Ambient Air Quality Standards
VOC: volatile organic compounds

APPENDICES

APPENDIX A.

Recruitment Flyer (English)

Recruitment Flyer (Spanish)

Screening Eligibility Questionnaire

Volunteers Needed

We are looking for subjects to participate in a research project lasting 6-9 weeks, to help us in studying how the air pollution and toxins present in Huntington Park and the surrounding communities effects the children and adolescents living there.

- **You must be between the ages of 10 and 15 years old**
 - **Have asthma that bothers you atleast once a week**
 - **Plan to be in and around your home in Huntington Park for the entire summer**

Subjects will be asked to keep track of their daily symptoms and activities and to perform simple breath sampling maneuvers

Compensation will be paid to participants.

If you are interested and would like further information, please contact Marisela Avila @ (562) 401-7563

Voluntarios Necesitados

Buscamos a participantes para tomar parte de un Estudio Del Medio Ambiente que durara de 6 a 9 semanas, y ayudarnos a estudiar cómo la contaminación del aire y los toxicos presentes en Huntington Park y las comunidades circundantes afecta a los niños/as y a adolescentes que viven allí.

- Usted debe estar entre las edades de 10 y 15 años
- Tener asma que le molesta usted aunque sea una vez a la semana
- Planear estar en y alrededor de su hogar en Huntington Park por el verano entero

A los participantes se pedirán apuntar sus síntomas y las actividades diarios y coleccionar ejemplos sencillos de su aliento

Una compensación será pagada a los participantes. Si usted es interesado y apreciaría información adicional, por favor llame a (562) 401-7563 contacto: Marisela Avila

VOC/CHILDREN'S HEALTH STUDY

Last Name _____ First Name _____

Address _____

Nearest Major Cross Street _____

Day Phone # () _____ Best time to be reached _____

DOB _____ Age _____ Grade __ Name of school _____

ADULT CONTACT:

ADDRESS IF DIFFERENT:

PHONE NUMBER IF DIFFERENT: () _____

ASTHMA HISTORY:

Date of Onset? _____ Seasonal or Year-Round _____

MEDICATIONS: _____

Name, Doses

Do you have Dr. diagnosed asthma? Y / N

Number of attacks in 1 week? _____

Are you able to control it with your usual medications? Y / N

How many visits to the emergency room in a year? _____

Do you smoke? Y / N

Any smokers living in your home? Y / N

Do you plan to remain in your city for the entire summer? Y / N

Does your home have an air conditioner, swamp cooler? Y / N

If so, where is it located? _____

Screened by: _____ Date: _____

APPENDIX B.

Health Questionnaire

Health Questionnaire
Environmental Health Service
Los Amigos Research and Education Institute, Inc.
Rancho Los Amigos Medical Center
Medical Science Building, Room # 51
7601 East Imperial Highway
Downey, California 90242
Telephone (562) 401-7561 Facsimile (562) 803-6883

Thank you for volunteering to be screened for possible participation in a research study.

The purpose of this questionnaire is to determine your medical and health background for the study we are planning (or may plan in the future).

All information given in the questionnaire is strictly **CONFIDENTIAL** and will be used for medical research only.

This questionnaire should be **COMPLETELY FILLED OUT** to the best of your ability by your next scheduled visit _____.

SUBJECT NO. _____

REV. 3/99

**LOS AMIGOS RESEARCH AND EDUCATION INSTITUTE, INC.
OF RANCHO LOS AMIGOS MEDICAL CENTER
ENVIRONMENTAL HEALTH SERVICE
7601 E IMPERIAL HWY MSB 51
DOWNEY CALIFORNIA 90242**

**TELEPHONE NUMBER
(562) 401-7561**

FILL IN NAME, SEX, BIRTH DATE, BIRTHPLACE, DATE OF TREATMENT

NAME _____ DATE _____
SEX _____
BIRTH DATE _____
BIRTHPLACE _____
APPROXIMATE DATE(S) OF TREATMENT: _____

Dear Doctor:

The above named is being considered for an environmental health research study. We understand that he/she was previously examined by you. At your earliest convenience, we would appreciate receiving a copy of his medical record.

Very truly yours,

DEPARTMENT OF ENVIRONMENTAL HEALTH
RANCHO LOS AMIGOS MEDICAL CENTER

By _____
Clinical Research Coordinator

FILL IN NAME OF DOCTOR AND SIGN BELOW:

Who is your primary care physician? NAME: _____
ADDRESS _____

CONSENT TO RELEASE MEDICAL INFORMATION

I hereby authorize _____ to release the desired information about myself to the Los Amigos Research and Education Institute, Inc, Department to Environmental Health, Rancho Los Amigos Medical Center, Room 51, Medical Science Building, 7601 E. Imperial Hwy., Downey, California 90242.

WITNESS (Signature)

Date

VOLUNTEER SUBJECT (Signature)

Date

IMPORTANT---PLEASE BRING COMPLETED QUESTIONNAIRE WITH YOU AT TIME OF APPOINTMENT.

ENVIRONMENTAL HEALTH SERVICE
LOS AMIGOS RESEARCH AND EDUCATION INSTITUTE, INC.
OF RANCHO LOS AMIGOS MEDICAL CENTER

Date:

	/ /	
Name	date of birth	age (yrs.)

Address	height (ins.)	weight (lbs)
---------	---------------	--------------

 City

 Zip code

Daytime phone #: () -
 Evening phone #: () -
 Message/pager #: () -

Social security no.

Name of school (if applicable)	Grade (0 – 12)
--------------------------------	----------------

Daytime # () -
Evening # () -

Relative or friend who we can contact in case of emergency

What is your gender: 1:male 2:female

Race: 1: White 4:Hispanic
 2: Black 5:American Indian
 3: Oriental 6:Other (Specify)

Parent and/or guardian if applicable:

[illegible]

1. Have you ever had any serious illness(es) or surgery other than simple tonsil, adenoid removal? Explain.

2. Have you ever been hospitalized or gone to an emergency room for any reason?

0:no 1:yes

If yes, please list all hospitalizations in the last 5 years below:

Reason:	age or date:	length of stay:
<hr/>	<hr/>	
<hr/>	<hr/>	
<hr/>	<hr/>	
<hr/>	<hr/>	

Please list the number of hospitalizations for asthma or other respiratory problems:

3. Are you allergic to any medicines?

0: no 1: yes **if yes**, describe:

Medical History

Do you or any members of your family have a history of any of the following?

	Self		Family	
	Yes or no	Date (Mo./Yr.)	Yes or No	Relationship to you
Heart disease				
Hypertension				
Diabetes				
Emphysema				
Chronic bronchitis				
Bronchial asthma				
Hay fever/unknown allergies				
Tuberculosis				
Coronary artery disease				
Thyroid disorder				
Anemia				
Epilepsy				
Hepatitis				
HIV infection / AIDS				

For females:

1. Do you think that you might be/ or that you will try to become pregnant during the next __ months?

0:no 1:yes

2. Are you at the present time nursing?

0:no 1:yes

(I am not now, nor do I plan to become pregnant during the course of the study. If I do become pregnant I will inform the study coordinator or doctor as soon as I find out.)

Signature of subject:_____ date:___/___/___

Respiratory Health Questionnaire

Cough

1. Do you usually cough first thing in the morning in bad weather?

0: no 1: yes

2. Do you usually cough at other times during the day or night in bad weather?

0: no 1: yes

if yes, do you know what causes your cough?

3. Do you cough on most days for as much as three months of the year?

0: no 1: yes

if yes, how many years (or months) have you had this cough? _____Yrs. _____Mos.

Sputum

4. Do you usually bring up phlegm, sputum, mucus from your chest in the morning?

0: no 1: yes

5. Do you usually bring up phlegm, sputum, mucus from you chest at other times during the day or night?

0: no 1: yes

if yes to questions 4 or 5:

- a) what color is your sputum?

b) do you know what causes you to bring up mucus?

6. Do you bring up phlegm, sputum, or mucus from your chest on most days for as much as 3 months of the year?

0: no 1: yes

if yes, how many years (or months) have you raised phlegm, sputum, or mucus from your chest?

_____Yrs. _____Mos.

Wheezing

7. Does your breathing ever sound wheezy or whistling?

0: no 1: yes

8. Has your breathing ever sounded wheezy or whistling?

0: no 1: yes

if yes, what causes you to wheeze

9. Have you ever had attacks of shortness of breath with wheezing?

0: no 1: yes

10. Do you wheeze or have you ever wheezed on most days for as much as 3 months of the year?

0: no 1: yes

Breathlessness

11. Do you ever get short of breath?

0: no 1: yes

12. Have you had shortness of breath for as much as 3 months of the year?

0: no 1: yes

if yes to question 11:

- a) How many years (or months) have you had shortness of breath? _____yrs. _____mos.
- b) what causes you to become short of breath?

13. Are you troubled by shortness of breath when hurrying on level ground or walking up a slight hill?

0: no 1: yes

14. Do you get short of breath walking with other people of your own age on level ground?

0: no 1: yes

Chest illness

15. During the past 3 years, how much trouble have you had with illnesses such as chest colds, bronchitis, pneumonia? (Do not include head colds).

1: none 2: 1-2 3: 3-4 4: 5+

16. During the past 3 years, how often were you unable to do your usual activities because of illnesses such as chest colds, bronchitis, or pneumonia?

1: none 2: 1-2 3: 3-4 4: 5+

17. Do you think you have ever had any of these chest disorders: asthma, any kind of bronchial trouble, or emphysema?

0: no 1: yes 2: don't know

18. Have you ever had a mini film or chest x-ray questioned?

0: no 1: yes if yes, when
What was the outcome?

19. Did you have bronchial asthma as a child?

0: no 1: yes

If yes, at what age were you first diagnosed?

/_____
yrs. mos.

Smog sensitivity

20. Are you ever bothered by sneezing, nasal congestion, or sore throat more on smoggy days than on clear days?

0: no 1: yes

21. Are you ever bothered by coughing, wheezing, chest pain, or shortness of breath when walking or doing other light exercise outdoors?

0: no 1: yes

if yes to question 21,
a) are you bothered more by this problem on smoggy days than on clear days?

0: no 1: yes

22. Are you ever bothered by coughing, wheezing, chest pain, or shortness of breath while resting?

0: no 1: yes

If yes to question 22,
a) are you bothered more by this problem on smoggy days than on clear days?

0: no 1: yes

23. Do you feel you are more sensitive to smog than most people your own age?

0: no 1: yes

24. On smoggy days or when heavy smog is predicted, do you try to stay indoors or avoid exercise?

0: no 1: yes

Changes In Breathing

Is your breathing or asthma worsened or caused by the following? (Include items that cause wheezing, shortness of breath, chest tightness and/or coughing)

- | | | | |
|----------------------------|------------|----------------------------|------------|
| 1. Heat | 1:yes 0:no | 13. Cut grass | 1:yes 0:no |
| 2. Cold | 1:yes 0:no | 14. Flowers | 1:yes 0:no |
| 3. Rain or dampness | 1:yes 0:no | 15. Varnish | 1:yes 0:no |
| 4. Sudden temp.changes | 1:yes 0:no | 16. Household cleaners | 1:yes 0:no |
| 5. Dust | 1:yes 0:no | 17. Respiratory Infections | 1:yes 0:no |
| 6. Tobacco smoke | 1:yes 0:no | 18. Ammonia or bleach | 1:yes 0:no |
| 7. Cooking or frying odors | 1:yes 0:no | 19. Solvents | 1:yes 0:no |
| 8. Fumes | 1:yes 0:no | 20. Fuel oil (gasoline) | 1:yes 0:no |
| 9. Colognes or Perfumes | 1:yes 0:no | 21. Cosmetics | 1:yes 0:no |
| 10. Hair & other sprays | 1:yes 0:no | 22. Sawdust | 1:yes 0:no |
| 11. Soap powder | 1:yes 0:no | 23. High air pollution | 1:yes 0:no |
| 12. Antiperspirants | 1:yes 0:no | 24. Animals (cats,dogs) | 1:yes 0:no |

Total number positive

Is there any one substance that **always** makes you wheeze when you come into contact with it?

Allergies

Check the appropriate boxes for allergies of yourself and/or your family:

<u>Allergy type (self)</u>	<u>Allergy type (family)</u>	<u>Who</u>
<input type="checkbox"/> Unknown	<input type="checkbox"/> Unknown	_____
<input type="checkbox"/> None	<input type="checkbox"/> None	_____
<input type="checkbox"/> Non-specific	<input type="checkbox"/> Non-specific	_____
<input type="checkbox"/> Food	<input type="checkbox"/> Food	_____
<input type="checkbox"/> Pollen	<input type="checkbox"/> Pollen	_____
<input type="checkbox"/> Dust	<input type="checkbox"/> Dust	_____
<input type="checkbox"/> Hay fever (rhinitis)	<input type="checkbox"/> Hay fever (rhinitis)	_____
<input type="checkbox"/> Drugs	<input type="checkbox"/> Drugs	_____
<input type="checkbox"/> Uticaria (skin "blotchiness")	<input type="checkbox"/> Uticaria	_____
<input type="checkbox"/> Eczema (skin "flaking")	<input type="checkbox"/> Eczema	_____
<input type="checkbox"/> Asthma	<input type="checkbox"/> Asthma	_____
<input type="checkbox"/> Animals	<input type="checkbox"/> Animals	_____
<input type="checkbox"/> Other, specify: _____	<input type="checkbox"/> Other, specify: _____	_____

1. Do you have a sensitivity to aspirin?

0: no 1: yes

2. (*) Have you ever had allergy skin tests performed?

0:no 1:yes

If yes, please give name of doctor (hospital) and date:

Name

address

date

***Circle** any of the above allergies which were identified by the skin test.

Medication use

1. Are you now taking, or have you taken any medication in the past month?

0: no 1: yes

If yes, fill in type, dosage, and frequency of all medicine you take (please include, aspirin, antibiotics, vitamins, etc.)

A. Medication: _____

Dosage: _____

Frequency: _____

Still taking? 0: no 1: yes **if no**, last date taken: _____

B. Medication: _____

Dosage: _____

Frequency: _____

Still taking? 0: no 1: yes **if no**, last date taken: _____

C. Medication: _____

Dosage: _____

Frequency: _____

Still taking? 0: no 1: yes **if no**, last date taken: _____

D. Medication: _____

Dosage: _____

Frequency: _____

Still taking? 0: no 1: yes **if no**, last date taken: _____

E. Medication: _____

Dosage: _____

Frequency: _____

Still taking? 0: no 1: yes **if no**, last date taken: _____

2. Are you taking any of the following medicines on a regular basis (daily or weekly) or frequently?

Aspirin	1: yes	0: no
motrin, advil, nuprin, aleve, etc.	1: yes	0: no
multi vitamins, vit. C, vit. E, etc.	1: yes	0: no
antibiotics	1: yes	0: no
over the counter inhalers (primatene mist, etc)	1: yes	0: no
over the counter allergy pills/ cold pills	1: yes	0: no

Miscellaneous

1. What regular work exercise do you do outside? What type (light, medium, heavy work)? How many hours per week?

<u>Work exercise</u>	<u>type</u>	<u>hours/week</u>
----------------------	-------------	-------------------

_____	_____	_____
_____	_____	_____
_____	_____	_____

2. What regular recreational exercise do you do outside? How many hours per week?

<u>Recreational exercise</u>	<u>hours/week</u>
------------------------------	-------------------

Smoking information

1. Have you ever smoked cigarettes?

0: NO 1: YES

if no -> skip to question 2

if yes:

1a. Do you now smoke cigarettes?

0: no 1: yes

1b. How old were you when you first started regular cigarette smoking?

1c. If you have stopped smoking cigarettes completely, how old were you when you stopped?

1d. How many cigarettes do you smoke per day now?

1e. Of entire time you smoked, on average how many cigarettes did you smoke per day?

1f. Do you or did you inhale the cigarette smoke?

1: not at all 3: moderately
2: slightly 4: deeply

2. Have you ever smoked a pipe regularly?

0: no 1: yes

if no -> skip to question 3

if yes:

2a. How old were you when you first started regular pipesmoking? _____

2b. If you have stopped smoking pipe completely, how old were you when you stopped _____

2c. How much tobacco do you smoke now? (A standard pouch of tobacco = 1-1/2oz)

2d. Do you or did you inhale the pipe smoke?

1: not at all 3: moderately
2: slightly 4: deeply

3. Have you ever smoked a cigar regularly?

0: no 1: yes

if no -> skip to question 4

if yes:

3a. How old were you when you first started smoking cigars?

3b. If you have stopped smoking cigars completely, how old were you when you stopped?

3c. How many cigars do you smoke per day?

3d. Do you or did you inhale the cigar smoke?

1: not at all 3: moderately
2: slightly 4: deeply

4. Does anyone living in your home smoke in your home?

0: no 1: yes

If no -> skip to question 5

if yes:

4a. How many people smoke?

4b. How much do they smoke in a typical week?

cigarettes _

cigars _

pipes _

Other:

5. Do you ever smell tobacco smoke at work or at school?

0: no 1: yes

if yes:

5a. Estimate the amount:

1: a lot 2: some 3: little

5b. Does the tobacco smoke at work or at school physically affect you in any way?

1: usually 3: rarely
2: sometimes 4: never

Home Environment

A. Location data

Please give city, state, and length of time in residence:

Present address:

Years: ____ months: __

Prior address: _____

Years: ____ months: ____

How close are you to a busy street?

____ I live on one ____ blocks away

Name of the nearest busy street _____

B. Housing characteristics

- b1. How many rooms do you have in your living quarters? (Do not count bathrooms, porches, balconies, foyers, halls, or half-rooms).
- Please circle: 1 2 3 4 5 6 7 8 9+
- b2. Are your living quarters?
____ owned ____ rented
____ other : _____
- b3. Which best describes this building?
- a. Mobile home or trailer.
 - b. 1 family house detached from otherhouses.
 - c. 1 family house attached to 1 or more houses.
 - d. Building for 2 families.
 - e. Building for 3 or 4 families.
 - f. Building for 5 to 9 families.
 - g. Building for 10 to 19 families.
 - h. Building for 20 or more families.
 - i. Boat, tent, van, etc.
 - j. Other, please specify
- b4. How many stories (floors) are in this building?
(Count an attic or basement as a story if it has any finished rooms for living purposes).
- a: 1 to 3 b: 4 to 6 c: 7 to 12
d: 13 or more
- b5. About when was the building originally built?
(Circle when the building was first constructed, not when it was remodeled or added on to).
- a: 1986 to present e: 1950 to 1959
b: 1980 to 1985 f: 1940 to 1949
c: 1970 to 1979 g: before 1939
d: 1960 to 1969 h: Don=t know
- b7. How many bedrooms do you have?
(Count rooms used mainly for sleeping even if used also for other purposes).
- a: No bedrooms d: 3 bedrooms
b: 1 bedrooms e: 4 bedrooms
c: 2 bedrooms f: 5 or more
- b8. Where are cars / vehicles usually parked near your living quarters? (Circle all that apply)
- a: In an underground garage
b: In an attached garage
c: In an attached carport
d: On the street next to living quarters
e: Other specify _____
- b9. How many motor vehicles are kept at your home for use by members of your household?
- a: None b: One
c: Two d: Three or more
- b10. How would you describe the traffic on your street?
- a: very quiet residential street
b: average residential street (mostly residents)
c: busy residential street
d: very busy residential street
e: average 2 lane highway traffic
f: busy, with more than 2 lanes of traffic
- b11. Is any building or road construction underway nearby?
- a: No b: Yes

C. Occupant characteristics

1. Number in household

a. How many children under age 18 are there living in the household? _____ children

b. How many adults, ages 18 and older, are there living in the household?

_____ ages 18-61 years

_____ age 62 years or greater

2. Are there pets in the home?

0: No 1: Yes, **if yes** list type and how many?

dog(s): _____ cat(s): _____

hamster(s): _____ bird(s): _____

3. How many minutes does it usually take for you to get from home to school, one way (including walking time)?

a) Door to door minutes per trip _____

b) Minutes spent in car _____

D. Cooking and other appliance Usage

1. Cooking

a. Do you have a gas range or oven?

0: No 1: Yes

If no> skip to 2 **if yes**>continue below

b. During the winter, do you ever use the range or oven to help heat the living quarters?

1. Yes, three or more days per week
2. Yes, one or two days per week
3. Yes, only in the morning to take the chill off (less than one hour)
4. No

2. Water heater

a. Where is your water heater located? (circle all that apply)

1. In a room within the living quarters, such as the kitchen.
2. In a closet or storage room in part of the main living quarters.
3. In a utility or closet room separate from the main living quarters.
4. In the garage.
5. In the basement.
6. Outside.

3. Clothes Dryer (cont.)

a. Is there a clothes dryer in your living quarters?

0: No 1: Yes

If no>skip to D4 **if yes**>continue below

b. Is your clothes dryer gas or Electric?

1. Gas
2. Electric
3. Do not know

c. Where is the clothes dryer located?

1. In a room within the living quarters, such as the kitchen
2. In a closet or storage room in part of the main living quarters.
3. In a utility or closet room separate from the main living quarters.
4. In the garage.
5. In the basement
6. Outside
7. Other, specify _____

d. Is the dryer vented?

1. Yes, always outside
2. Yes, with an inside/outside switch
3. Not vented to outside.
4. Do not know

4. Air conditioning

- a) Is there an air conditioner in your living quarters?

0: No 1: Yes

If no>skip to d5, **if yes**>continue below

- b) Is air conditioning:

1. Single unit 3. Central
2. Multiple unit 4. Other

- c) Is the unit:

1. Swamp cooler/evaporative
2. Refrigeration/closed

5. Heating system

- a) What is the main type of fuel used to heat your living quarters? (Circle the one most often used)

1. Gas 6. Wood
2. Electric 7. Solar
3. Fuel oil 8. None>skip to
4. Kerosene 9. Other
5. Coal

- b) What is the main type of furnace or heating system used to heat your living quarters? (Circle one)

1. Forced air (central system with ducts that blow air into most rooms)
2. Wall furnace
3. Steam
4. Hot water
5. Floor furnace
6. Gravity furnace
7. Portable heater
8. Other
9. None

6. Air Purification device

- a) Do you use an air purifier ?

0: No 1: Yes

If no skip to 7, **if yes**:

- b) Do you use it regularly, several days a week for several months at a time?

0: No 1: Yes

If no, skip to 7, **if yes**:

1. Cool season only (between Nov & Feb)
2. Warm season only (between March & Oct)
3. All year long.

- c) What type?

brand and model

- d) How many?

- e) Location(s)?

7. Wood stove and/or fireplace

- a) During the cold weather, do you use a wood burning stove to help heat your living quarters?

0: No 1: Yes

If no>skip to E , **if yes**>how many? _____

- b) How often do you use a wood burning stove during the cold weather?

1. Three or more days per week
2. One or two days per week
3. Only in the morning to take the chill off (less than one hour)

- c) How often do you use your fireplaces during the cold Weather?

1. Three or more days per week
2. One or two days per week
3. Only in the morning to take the chill off.

8. Organic pollutants

- a) Have you worked with or used pesticide or herbicides outdoors for more than 1 hour at a time in the past 6 months?

0: No 1: Yes

b) Did you or any member of the household, or a commercial applicator use pesticides in the living quarters in the past 6 months?

0: No 1: Yes

If no>skip to f3, **if yes**>answer below specify brand names if known :

c) Specifically, where are you using them?

- | | |
|----------------|-------------------|
| 1. living room | 4. master bedroom |
| 2. dining room | 5. other bedrooms |
| 3. kitchen | 6. other rooms |

d) In the past 6 months, were the drapes, carpeting or furniture in your home steam or dry cleaned?

0: No 1: Yes

e) Are you now using mothballs or moth-crystals in your living quarters?

0: No 1: Yes

If no>skip to 8f, **if yes**>specifically, where are you using them?

- | | |
|----------------|-------------------|
| 1. Living room | 4. Master bedroom |
| 2. Dining room | 5. Other bedrooms |
| 3. Kitchen | 6. Other rooms |

f) Is ornamental or fragrant burning (incense, candles, potpourri, etc.) performed at home?

0: No 1: Yes

If no>skip to 8g, **if yes** please identify:

- | | |
|------------|--------------|
| 1. Incense | 3. Potpourri |
| 2. Candles | 4. Other |

g) Do you have or do any hobbies or crafts that expose you to chemicals, dust or other irritants? (Please explain)

0: No 1: Yes

If no>skip to f8, **if yes**> explain below:

g) Are there any noticeable obvious industrial/commercial pollutants odors (dairy, factory, paint, etc.)

0: No 1: Yes

If no>skip to 8h, **if yes**>please describe:

h) Has new or different furniture been purchased and/or delivered in the past year or so?

0: No 1: Yes

i) Have new carpets been installed in the past year or so?

0: No 1: Yes

j) Is mildew in apparent problem in your home?

0: No 1: Yes

k) Are there potted plants in the home?

0: No 1: Yes

l) Has there been any flooding damage to the inside of your home?

0: No 1: Yes

Asthma
Triggers:

Which of the following <u>do you feel</u> triggers your asthma?			
Trigger	No	Yes	Don't know
Animals			
Pollen			
Mold			
Dust			
Exercise			
Respiratory Infection			
Tobacco Smoke			
Change in the Weather			
If yes, describe the changes:			
Air Pollution			
If yes, explain how you know:			
Food			
If yes, specify which foods:			
Aspirin			
Others:			
If yes, specify			
Any others, specify:			

History and Treatment:

- 1) How long have you had asthma? _____ years and _____ months.
- 2) At what age did you have your first attack? _____ years old.
- 3) Does your asthma require treatment with medication? 0: No 1: Yes, if no skip to , **if yes** continue below.
- 4) How often in the pas 12 months? (Circle the appropriate number)
 - 1: less than once per week 2: at least once per week 3: several times per week 4: always take medication routinely, including daily and as needed us of inhalers.

Asthma (cont.)

5) Are you ever prescribed oral steroids for worsening of your asthma? (ie Medrol, Prednisone, Decadron, Pediapred, Prednisolone, Prelone) 0: No 1: Yes

6) How many times during the last 12 months was your asthma bad enough to require the following?

- a. Admission to a hospital _____ times
- b. Visit to an emergency or urgent care facility _____ times
- c. Non-routine visit to Dr.'s office or clinic _____ times
- d. School absence _____ times

7) Which if any of the following are the main symptoms you experience: (Mark the appropriate box)

Symptom	No	Yes	Don't know
Wheeze			
Chest Tightness			
Shortness of Breath			
Cough			
Sputum or phlegm			
Other, specify:			

Circle the number corresponding to the appropriate response for the questions below:

8) When does your asthma usually occur?

- a. Certain seasons ? 0: No 1: Yes 9: Don't know
- b. All seasons ? 0: No 1: Yes 9: Don't know

9) Is your asthma worse during the

- a. Spring 0: No 1: Yes 9: Don't know
- b. Summer 0: No 1: Yes 9: Don't know
- c. Fall 0: No 1: Yes 9: Don't know
- d. Winter 0: No 1: Yes 9: Don't know

10) When your asthma is a problem, on average, how often do your attacks occur?

- 1: Once per month.
- 2: 2 – 3 times per month
- 3: 1 to several days or nights per week
- 4: Almost every day and/or night

11) Does your asthma tend to occur most often during the daytime?

- 0: No 1: Yes, some of the time 2: Yes, most of the time 9: Don't know

Asthma (cont.)

12) Does your asthma tend to occur most often during the nighttime?

0: No 1: Yes, some of the time 2: Yes, most of the time 9: Don't know

13) Do you ever get hay fever (nasal allergy, allergic rhinitis, sneezing with a runny, stuffy nose, itchy watery eyes or itchy throat)?

0: No 1: Yes 9: Don't know, **if yes** continue below, if not yes skip #'s 14 – 16.

14) Is your hay fever present during?

- | | | | |
|--------------|-------|--------|---------------|
| a. Spring | 0: No | 1: Yes | 9: Don't know |
| b. Summer | 0: No | 1: Yes | 9: Don't know |
| c. Fall | 0: No | 1: Yes | 9: Don't know |
| d. Winter | 0: No | 1: Yes | 9: Don't know |
| e. Daytime | 0: No | 1: Yes | 9: Don't know |
| f. Nighttime | 0: No | 1: Yes | 9: Don't know |

15) How long have you had hay fever?

_____ years 9: Don't know

16) How often do symptoms of asthma occur at the same time as hay fever does?

1: almost never 2: occasionally 3: often 4: almost always

Additional Optional Questions for Parents/Guardians

The answers to these questions will not be used in the analysis of the data obtained but to document the environmental justice of this project. You will in no way be penalized if you chose to not answer any or all of the questions. Your responses will be kept strictly confidential.

Fill in the blanks using the corresponding list or circle the appropriate number.

Education level of Mother or female guardian: _____ Education level of Father or male guardian: _____

- _____
- 1 = Elementary K – 8
 - 2 = High School
 - 3 = Trade, technical or business school
 - 4 = Community College (2 years)
 - 5 = Undergraduate College (4 years)
 - 6 = Professional or Graduate School
 - 7 = Unknown

Occupation of Mother or female guardian: _____ Occupation of Father or male guardian: _____

- 1 = unemployed
- 2 = housewife / househusband
- 3 = blue collar worker
- 4 = white collar worker
- 5 = professional
- 6 = unknown

Which of the following ranges represents your total family gross income before taxes and deductions.

- 1 = less than \$15,000
- 2 = \$15,000 to \$29,999
- 3 = \$30,000 to \$49,999
- 4 = \$50,000 to \$75,000
- 5 = over \$75,000
- 6 = don't know

APPENDIX C.

Environmental Inventory

VOC and Asthma Study - Environmental Inventory

Name of the Participant _____

Participant Identification Number _____

Completed by _____ (if other than participant)

Relationship to participant _____

Home Phone _____ Date: ____/____/____

Address: _____

Demographics

1. What is your (your child's) date of birth? _____/_____/_____
2. Gender: Male Female
3. How tall are you (is your child) without shoes ? _____ft _____inches
4. How much do you(does your child) weigh ? _____ pounds
5. Which school do you (your child) attend? _____
Address: _____
6. What grade are you (is your child) in? _____

Personal Exposure Activities

7. On average, home many hours per day do you (does your child) sleep ? _____
8. On average, how many hours per day do you (does your child) spend at home?
 - a. On weekdays _____
 - b. On weekends _____
9. On average, how many hours per day do you (does your child) spend outdoors?
 - a. On weekdays _____
 - b. On weekends _____
10. How long have you lived at the current address? _____
11. When was your dwelling originally built? Indicate when the dwelling was constructed, not when it was remodeled, added to, or converted. (Circle the number beside the best answer below.)
 - 1 1990 or later
 - 2 1980 to 1989
 - 3 1970 to 1979
 - 4 1960 to 1969
 - 5 1950 to 1959
 - 6 1940 to 1949
 - 7 1939 or earlier
 - 8 Not sure

12. In the past six months, have any of the following activities occurred in your home? (Circle the number beside the activities which apply. More than one is acceptable.)

1. Interior painting (Specify which room(s)) _____
2. Exterior painting
3. Refinishing floors (Specify which room(s)) _____
4. Installed new carpet (Specify which room(s)) _____
5. Added new furniture (Specify which furniture) _____
6. Major renovations to the house (Specify which room(s)) _____
7. None of the above

13. How is your home heated? Indicate the one source of heat used most frequently.

- 1 Steam or hot water system
- 2 Central warm-air furnace with ducts to each room
- 3 Electric heat pump
- 4 Other built-in electric units (permanently installed in wall, ceiling, or baseboard)
- 5 Floor, wall, or pipeless furnace
- 6 Room heaters with flue or vent, burning gas, oil, or kerosene
- 7 Room heaters without flue or vent, burning gas, oil, or kerosene
- 8 Fireplaces, stoves, or portable room heaters of any kind, including kerosene or electric heaters.
- 9 No heating equipment

14. Which fuel or energy source is used most frequently for heating your home?

- 1 gas: from underground pipes serving the neighborhood
- 2 gas: bottled, tank, or LP
- 3 electricity
- 4 fuel oil, kerosene, or other petroleum product
- 5 coal or coke
- 6 wood
- 7 solar energy
- 8 other fuel (specify) _____
- 9 no fuel used

15. On average, how many hours did you use heating last week? _____

16. Which fuel or energy source is used most frequently for cooking?

- 1 gas from underground pipes serving the neighborhood
- 2 gas from bottles, tanks
- 3 electricity
- 4 fuel oil, kerosene, or other petroleum product
- 5 coal or coke
- 6 wood
- 7 other fuel (specify) _____
- 8 no fuel used

17. On average, how many hours were spent cooking last week? _____

18. Do you use air conditioning to cool your home?

- 1 yes, central air conditioning system
- 2 yes, one window unit
- 3 yes, two or more window units
- 4 yes, evaporative (swamp) cooler
- 6 yes, other (specify) _____
- 7 no

19. On average, how many hours did you use air conditioning last week? _____

20. On average, how many hours did you have doors leading to the outside and windows open last week?

Doors _____
Windows _____

21. Does your home qualify for an energy conservation discount from your utility company?

- 1 yes
- 2 no
- 3 uncertain

22. Is an enclosed garage attached to or within the structure in which you live?

- 1 yes, used for motor vehicles and other gasoline engine devices, such as chain saws, lawn mower, and jet skis.
- 2 yes, not used for motor vehicles
- 3 no

23. If yes to question 22, does the attached garage share a common door with your living quarters?

- 1 yes
- 2 no

24. Is gasoline stored in any room, basement, or attached garage in your home?

- 1 yes
- 2 no
- 3 uncertain

25. How many people smoke on a daily regular basis within your living quarters?

- 1 One
- 2 Two
- 3 Three or more
- 4 None

26. During the past week, how many hours did you spend:

- 1. Inside your home with someone who was smoking tobacco? _____
- 2. Elsewhere with someone who was smoking tobacco? _____

27 a What methods of transportation do you usually use to go to school?

- 1 Car, truck, van or taxi cab
- 2 Bus
- 3 Subway
- 4 Bicycle
- 5 Walk
- 6 Other

27 b How many minutes do you usually spend going to school (one way)? _____

27 c How many minutes during an average week do you usually spend in a motor vehicle? _____

28 During the last week, did you or others in your household use any cosmetics (example: lipstick, nail polish)?

- 1 yes, list: _____

2 no

29 During the last week, did you or others in your household use any household products such as waxes, polishes, glues, or crafts?

- 1 yes, list: _____

- 2 no

30 During the last week, did you use in your home any paints, wall paper products, or cleaning products (including disinfectants, bleach, washing detergents)?

- 1 yes, list: _____ How often per week? _____
_____ How often per week? _____
_____ How often per week? _____
- 2 no

31 During the last week, did you or others in your household use any pesticides in your home?

1 yes, list product name: _____

2 no

32 Did anyone bring home clothes from the dry cleaner during the past week?

1 yes

2 no

3 uncertain

33 a. How often do you (does your child) swim?

1 One to three times per month

2 One or two times per week

3 3-6 days per week

4 Daily

5 Never

33 b. If yes, how long do you (does your child) typically spend in the swimming pool? _____

34. How often do you (does your child) use crafts such as paint and glue for hobbies or school projects?

1 One to three times per month

2 One or two times per week

3 3-6 days times week

4 Daily

5 Never

35. Are mothballs used in your home?

1. Yes

2. No

3. Don't know

36. During the past month, have room deodorizers been used in your home?

1. Yes

2. No

3. Don't know

37. Did you have any trouble understanding or answering any of the questions on this questionnaire?

1 yes Specify the question number(s) which caused you the problem: _____

2 no

APPENDIX D.

Huntington Park Asthma Research Study Guide for Kids

Sample Collection Procedures for Alveolar Air Sampler

HUNTINGTON PARK ASTHMA RESEARCH STUDY

GUIDE FOR KIDS

INTRODUCTION

The diaries that you have been given are for you to write down how your asthma is, how well you breath, what medications you use, and other factors which may affect your asthma. We will compare these things to what we are studying in your community. It is very important for you to write down the information carefully. You need to make sure that all of the information is correct. In a way you are the most important scientist on our team because the information that you give to us could not only help you, but other asthmatics as well.

This guide is divided into 3 parts.

- 1) What will happen;
- 2) How to use the Asthma Study Diary and Time-Place Activity Diary;
- 3) How to use the peak flow meter; (Breath Machine).

WHAT WILL HAPPEN

You need to start writing down information into your diary on Monday, October 25, 1999. Continue writing down information in the diary every day through the end of the study on Monday, December 20, 1999. This is a total of 8 weeks.

Every week, at a time that you and one of your parents are home, a member of our project staff will come by, collect, and go over the diary with you, to make sure that you are filling it out correctly. This is when you should ask any questions that you have about how to use the diaries.

HOW TO USE THE DAILY ASTHMA STUDY DIARY

You will be given one diary each week. It will be one page, with the days of the week, and the date printed at the top of the page. **It is important for you to fill in the boxes in the column that has today's date printed at the top.** (see example diary) Begin each week by entering your name or initials at the top of the page. A sample diary which has been filled out as an example has been given to you.

Do not wait at all to write down your information into the diary. You must write down the information every day so you will not forget. You must also remember to write down your peak flow rates as soon as you take them in the morning and in the evening, **no matter what else you do.**

DOING PEAK FLOWS AND ENTERING NUMBERS IN THE DIARY:

The first time that you write in the diary will be **BEFORE** you take your **MORNING** asthma medications. You will record **3 PEAK FLOW (BREATH MACHINE)** measurements, and answer a question on the **NUMBER OF TIMES** you **WOKE UP** in the night because of your asthma. It is important to use the peak flow meter before taking your asthma medication. This is because your medication might quickly clear up your asthma. A good time to do this is before **9:00 A.M.**. Remember to always enter the time into the diary no matter when you take the measurement, as long as it is in the morning. If you need your inhaler earlier because of asthma symptoms, do the peak flows before you take the puffs.

The second time you write in the diary will be **BEFORE** you take your **EVENING** asthma **MEDICINE**. A good time to do this is after **8:00 P.M.**. As before, you must enter the **TIME** that you do this, no matter what time it is, as long as it is late in the day. If you need your inhaler earlier because of asthma symptoms, do the peak flows before you take the puffs. Filling out this part of the diary involves recording **3 PEAK FLOW** readings, and answering the following questions.

OTHER DIARY QUESTIONS:

1) What was the **HIGHEST** level of **ASTHMA SYMPTOM SEVERITY** for that day from the time you filled out your diary last night up to the time you are now filling out the diary? In other words, how bad was your asthma when it was its worst? For example, if you finished filling out your diary for yesterday at 9:00 P.M. last night and you are now filling out the diary at 8:00 P.M., then you would try to remember how bad your asthma was when your asthma was at its worst between 9:00 P.M. last night and now. For the first day of the study just report about symptoms since 8:00 P.M. the night before. **It is important for you to remember not to skip a day.** You will write down a number from **0** to **5**, when telling us how bad your asthma symptoms were. These symptoms are given on the back of the diary page, under the title **ASTHMA SYMPTOMS SEVERITY SCALE**,

They include: wheeze, cough, shortness of breath and chest tightness.

Put down **0** if you had **none** of the **ASTHMA SYMPTOMS** listed on the back of the diary page.

You will write down a **1** if one or more of the listed **asthma symptoms were present**, but did not cause you any discomfort.

A mark of **2** indicates that one or more of the listed **symptoms were present**, you **probably did not feel good**, and you may have needed to take some puffs from your as-needed inhaler. However, at level **2**, you were **still able to do the activities** (go to school, play) that you normally do and you slept OK without being awakened by your asthma.

If your asthma symptoms **interfered a little with your daily activities or sleep**, you would mark down a **3**. A good example of **3** would be that you were able to go to school, but had to sit down during most of your P.E. class because Of asthma symptoms which were already **present before P.E.**.. If PE or any exercise usually makes your asthma bad, then you would write down a **2**, only if you were bothered by your asthma more than usual after exercise, and the asthma lasted longer than usual.

A mark of **4** would indicate that your **asthma symptoms interfered with most of your daily activities** (school sport etc.). Reasons for marking down a **4** would include being driven home from school early, or not going to school at all.

If at any time during the day you have to go and **see a doctor because your asthma is getting worse** you would mark down a **5**. Do not put down a **5** for a day that you have a regular visit to the doctor. If you are not sure which number to mark down, make your best guess. You or your parent can talk about it with the staff member when he/she comes to visit.

2) When did your symptoms first reach the **HIGHEST SEVERITY LEVEL** listed above. If the number you put down for **HIGHEST ASTHMA SEVERITY LEVEL** was 0, you can skip this question. If you put down a number from 1 to 5, then check the box for the time of day when the **HIGHEST SEVERITY LEVEL** was reached. For example, if your symptoms were at their worst level just after getting to school, you would mark the box next to **THIS MORNING**, even if you got better later on in the morning, but got just as sick later in the day. If your symptoms were first at their worst last night before getting up this morning, you would mark **BEDTIME UNTIL SUNRISE**, and so on.

3) What was your **HEADACHE SEVERITY TODAY?** In other words, how bad was your worst headache from the time you woke up this morning until the second time you filled out the diary today, at 8:00 P.M.?

You will write down a number from **0** to **4**, when telling us how bad your headache was today. The levels of severity are given on the backside of the diary page, under the title **HEADACHE SEVERITY**.

Put down **0** if you **did not have a headache** today.

You will write down a **1** if you had a **very light headache** that went away on its own, without any medication.

Mark a **2** if your headache was **somewhat painful**, but **went away after you took some medication** like Tylenol or Aspirin. Only mark a **2** if your headache went away after you took pain medication once.

Put down a **3** if your headache was **very painful**, and you **needed to take pain medication more than once** to make it go away.

If your headache was so bad that it **still hurt even after taking pain medication a number of times**, you would mark a **4**. You would also want to put down a **4** if you had to take a migraine medication that your doctor prescribed to make your headache go away.

4) Did you have any **ALLERGY SYMPTOMS** today? This is a simple **YES** or **NO** answer. The types of allergy symptoms that we are asking about are listed at the bottom of the diary page. It is important that you make sure that the symptoms are **NOT DUE TO A COLD OR THE FLU**, and you must also make sure that there are **MORE THAN ONE OF THE SYMPTOMS PRESENT**. If you just sneezed a few times, with no other symptoms, then the answer would be no.

5) Did you have a **RESPIRATORY INFECTION** today? This is a simple **YES** or **NO** answer. The types of respiratory infections that we are asking about are located on the backside of the diary page under allergy symptoms. They include a cold, sore throat, up to pneumonia. Put a yes for every day that you have the respiratory infection. Put **No** if you do not have a respiratory infection or if you have a different illness such as the stomach flu.

6) **JUST BEFORE OR WHILE YOU WERE AT HOME INDOORS, WAS THE GAS STOVE OR OVEN IN USE FOR MORE THAN 1 HOUR?** Even though this is a simple **YES** or **NO** answer, it should be answered by your parent, or the person who controls these appliances. If you do not have a gas stove or oven, then always skip this question.

7) How many **PUFFS** did you take from your **AS-NEEDED INHALER** since last night? This **DOES NOT INCLUDE** inhaler puffs that your doctor has you take every day on a **REGULAR** basis. If you use more than one inhaler each day **TAKEN ONLY AS-NEEDED**, you will simply write down the **NAME** of the **INHALER**, and number of puffs from each inhaler.

Remember, **EACH PUFF COUNTS AS 1**, so that if you take **2** puffs at one time in the afternoon for asthma symptoms, and **2** puffs at one time at night you would record a number **4** in your diary.

The as-needed inhalers **DO NOT INCLUDE INHALERS YOU USE BEFORE EXERCISE**, those go below as prescription medications.

8) How many **DOSES OR TIMES** did you take **REGULAR PRESCRIPTION MEDICATIONS TODAY?**

On the left lower side of the diary, there are five spaces for you to use. You need to write in the **NAME** of each **MEDICATION** that you use. It is also important to write down **HOW STRONG** it is. This is usually written in milligrams (mg). We will help you with this. Remember to write down only medicines that are for your asthma.

It is also important to write down the number of doses that **you actually took for that day**, and not the number that you are prescribed. **Each dose** would be either **one pill** for medicine that you take by mouth, or **one puff** for inhalers. **For example**, you **TOOK** 2 puffs from your inhaler 3 times a day, every day, you would mark down a "6". **Do not mark down** the extra puffs you take as-needed during the day when your asthma flares up.

If your doctor gives you a **NEW** medicine or takes you off one that you are currently on, you need to write it down, and begin writing down the regular prescribed doses that you are to take, or stop marking those that you are now not taking. **If your doctor** gives you a medicine and tells you to take it and you do not, still write down the name of the medicine, and **put a 0 for every day that you do not take it**, even if it is for the whole study.

HOW TO USE THE DAILY TIME-PLACE-ACTIVITY DIARY

The Time-Place-Activity Diary is different from the Asthma Patient Diary. You have one of these diaries for each day. You will use a pencil or pen to bubble in different sections of the chart that show us what you were doing at different times of the day. This would be things like slow walking, or doing dishes, resting, or riding your bike. The guide which tells you what each of those pictures represent can be found on the backside of the Time-Place-Activity Diary.

The best way to do this is to keep the log with you at all times while you are awake. This is because you will need to mark down things at different times during the day. You also should CHECK YOUR WATCH EVERY TIME you go OUTSIDE, and again when you go INSIDE, or go IN A CAR OR BUS. You will be asked to **RECORD YOUR ACTIVITIES IN HALF HOUR BLOCKS**, which are on the chart. In most cases you will have to round out your answers. This is very simple. For example, if you rode your bike outside at 8:24 p.m., you would bubble in 8:30, and not 8:00. You would do this because 8:24 is closer to 8:30 than it is to 8:00.

If you completely leave Huntington Park, Please write down where you went while you were gone. **REMEMBER** if you do leave, you need to fill out your diary.

HOW TO USE THE PEAK FLOW METER.

What it does: The peak expiratory flow rate meter (**peak flow meter**) measures the greatest flow of air that comes out of your lungs when you blow through the meter. In order to get the best readings your lungs must be **FULL** of air, and you must blow out as **HARD** as you can. The information that this meter provides lets the doctors know how much your airway is obstructed, which helps in determining how bad your asthma is.

How to use it:

The test must be done **before** YOU take asthma **medications**, the reason is that the medications could immediately influence the function of the lungs more than anything else.

The success of the test depends on your **EFFORT** and the **AMOUNT OF AIR** you get out.

1. **Stand up.**
2. Take **as deep a breath as you can** rapidly inhaling and **completely** filling your lungs.
3. **Immediately** insert the meter in the your mouth and close your lips around the mouthpiece to create an **airtight seal**.
4. As soon as your lips are sealed around the mouthpiece, **blow out as hard and as fast as you possibly can** (it is very important that you make the greatest effort possible here).
5. **Repeat** the above procedure 3 more times, waiting at least 1 minute between procedures.

When to use the peak flow meter (breath machine):

You need to take these measurements two times a day:

Once in the morning **BEFORE** you take your medicine, but after you have had time to wake up.

Once at night **BEFORE** you take your medicine. It is best if this is done around or after 8:00 P.M.. If you have to use your inhaler earlier in the evening because of asthma, then do the peak flows first. You can fill out the other parts of the diary later at 8:00 P.M..

Conclusion

This may seem like a lot of work, but stick with it and do not give up! It will be easier to be in this study than you think, and filling out the diary will become much easier after the first week.

If you have any questions about how to use the diary, and you cannot wait until the weekly visit or phone call, please feel free to call the office at any time. **YOU SHOULD ASK YOUR DOCTOR ABOUT ANY MEDICAL QUESTIONS YOU HAVE ABOUT YOUR ASTHMA.**

It is important for scientific reasons that you do not change your usual daily activities. In other words **ACT NORMAL, and do everything that you would normally do in a regular day**. This includes school, sports, being with friends, and taking your medicine when you usually do. Remember the success of the study depends on you being honest, and taking the time to fill out the diary completely. The results may benefit you and other asthmatics as well.

NAME _____

ID # _____

DATE _____

CANISTER # _____

SAMPLE COLLECTION PROCEDURES FOR ALVEOLAR AIR SAMPLER

1. Place noseclip on nose making sure to completely close the nostrils.
2. Exhale.
3. ***PLACE LIPS TIGHTLY AROUND MOUTH PIECE*** so that all of the air you breath comes through the sampler and not from around the mouth piece.
4. **INHALE AND EXHALE 4 TIMES**, keeping mouth around mouth piece.
5. **IMMEDIATELY AFTER THE FINAL EXHALE**, open the green canister valve at least 2 turns.
6. **START THE STOPWATCH.**
7. Continue to breathe as normally as possible. **BREATHS SHOULD BE DEEP ENOUGH THAT YOUR LUNGS FILL WITH AIR.**
8. **AFTER 80 SECONDS** of breathing and with your mouth still on the mouth piece, close the canister valve. **MAKE SURE THAT THE VALVE IS FIRMLY CLOSED.**
9. ***If you CANNOT breathe for 80 seconds, NOTE TIME THAT YOU STOPPED TIMER.***

TIMER STOPPED AT: _____ SECONDS

COMMENTS: _____

APPENDIX E.

Children's Asthma Study Diary (English)

Children's Asthma Study Diary (Spanish)

CHILDREN'S ASTHMA STUDY DIARY

Day of Week – MONTH/DAY	MON	TUES	WED	THUR	FRI	SAT	SUN
COMPLETE BEFORE MORNING MEDICATIONS TIME	<u> </u> : <u> </u> AM	<u> </u> : <u> </u> AM	<u> </u> : <u> </u> AM	<u> </u> : <u> </u> AM	<u> </u> : <u> </u> AM	<u> </u> : <u> </u> AM	<u> </u> : <u> </u> AM
PEAK FLOWS (DO THIS BEFORE USING INHALER)	1. 2. 3.						
NUMBER OF TIMES AWAKENED BY ASTHMA LAST NIGHT							
COMPLETE BEFORE EVENING MEDICATIONS TIME	<u> </u> : <u> </u> PM	<u> </u> : <u> </u> PM	<u> </u> : <u> </u> PM	<u> </u> : <u> </u> PM	<u> </u> : <u> </u> PM	<u> </u> : <u> </u> PM	<u> </u> : <u> </u> PM
PEAK FLOWS (DO THIS BEFORE USING INHALER)	1. 2. 3.						
HIGHEST ASTHMA SYMPTOM SEVERITY (see scale below)							
WHEN DID SYMPTOMS REACH THIS HIGHEST SEVERITY LEVEL? (If above Symptom Severity = 0, leave blank: For Symptom Severity = 1-5, check 1 of the following)							
BEDTIME UNTIL SUNRISE							
THIS MORNING							
THIS AFTERNOON							
THIS EVENING							
ALLERGY SYMPTOMS?	<u> </u> yes <u> </u> no	<u> </u> yes <u> </u> no	<u> </u> yes <u> </u> no	<u> </u> yes <u> </u> no	<u> </u> yes <u> </u> no	<u> </u> yes <u> </u> no	<u> </u> yes <u> </u> no
RESPIRATORY INFECTIONS?	<u> </u> yes <u> </u> no	<u> </u> yes <u> </u> no	<u> </u> yes <u> </u> no	<u> </u> yes <u> </u> no	<u> </u> yes <u> </u> no	<u> </u> yes <u> </u> no	<u> </u> yes <u> </u> no
GAS STOVE/OVEN USE Just Before or While the participant was Home Indoors were the Appliances in Use More Than 1 Hour? (if no gas stove/oven then skip)	<u> </u> yes <u> </u> no	<u> </u> yes <u> </u> no	<u> </u> yes <u> </u> no	<u> </u> yes <u> </u> no	<u> </u> yes <u> </u> no	<u> </u> yes <u> </u> no	<u> </u> yes <u> </u> no
NUMBER OF AS-NEEDED INHALER PUFFS: IF YOU DID NOT USE A MEDICATION LISTED BELOW, PLEASE PUT A "0" IN THE APPROPRIATE BOX.							
NUMBER OF PUFFS:	As Needed Inhaler 1						
	As Needed Inhaler 2						
	As Needed Inhaler 3						
NUMBER OF DOSES OF DAILY PRESCRIPTION MEDICATIONS TAKEN:							

ASTHMA SYMPTOMS include the following: Wheeze, Cough, Shortness of Breath, and Chest Tightness	
OVERALL ASTHMA SYMPTOM SEVERITY SCALE (choose the single highest level reached)	
0	No asthma symptoms today.
1	Asthma symptom(s) present, but did not cause any discomfort.
2	Asthma symptom(s) caused discomfort, but no interference with daily activities or sleep.
3	Asthma symptom(s) interfered somewhat with daily activities or sleep.
4	Asthma symptom(s) interfered with most activities, and may have required any of the following examples: staying home in bed; being driven home early from school; calling a doctor or nurse for advice.
5	Asthma symptoms required any of the following: seeing a doctor or going to a hospital or emergency clinic.
DEFINITIONS	
ALLERGY SYMPTOMS: Did you have symptoms of Hayfever today, which were not due to a cold or flu. Those symptoms should include more than 1 of the following: sneezing, runny nose (including Post-Nasal Drip), sinus or nasal congestion, itchy and watery eyes, itchy throat?	
RESPIRATORY INFECTIONS: Were any of the following conditions present today: a cold, sore throat, fever, doctor-diagnosed flu, doctor diagnosed respiratory infection (pneumonia, bronchitis, croup, pharyngitis, laryngitis, middle ear infection, upper respiratory tract infection, or a sinus infection)	
HEADACHE SEVERITY	
0	NONE
1	MILD: no pain medications needed -- went away on its own
2	MODERATE: bothersome pain, needed to use pain medications one time
3	SEVERE: needed to use pain medications more than once, very painful
4	VERY SEVERE: repeated doses of pain medications didn't take away pain, or needed to use prescription migraine medication
Pain medications (analgesics) include: over-the-counter pain medications such as Tylenol, ibuprofen, aspirin, Aleve, etc.	

COMMENTS: (please refer to specific dates) _____

PEAK FLOW MEASUREMENT INSTRUCTIONS

- PEF Represents Peak Flow
 - Since PEF is both effort- and volume- dependent, maximum subject cooperation is essential
 - Make sure you are sitting up straight and the flow meter is set at zero
1. First, you will rapidly inhale completely filling your lungs.
 2. Immediately insert the mouthpiece and close your lips around it.
 3. Blow as hard, fast and sharp as you can as soon as your lips are sealed around the mouthpiece.
 4. You do not need to blow until you are empty as in Spirometry.
 5. Just a short, hard burst lasting only 1 or 2 seconds.
 6. Record the value, zero the meter and repeat the process 2 more times.
- Make note of any irregularities or problems that occurred.
 - Record all three values obtained on the sheet provided.
 - Record the actual time of the tests.

EL DIARIO DEL ESTUDIO DE ASMA DE NINOS

NOMBRE _____ ID _____

DIA DE LA SEMANA – MES/DIA	LUN	MAR	MIE	JUE	VIE	SAB	DOM
COMPLETE ANTES DEL HORA: MEDICAMENTO DE LA MAÑANA	—:— AM	—:— AM	—:— AM	—:— AM	—:— AM	—:— AM	—:— AM
INSTRUMENTO DE MEDIR (HAGA ESTO ANTES DE USAR SU MEDICAMENTO)	1. 2. 3.						
EL NUMERO DE VECES DESPERTADO POR EL ASMA EN LA NOCHE							
COMPLETE ANTES DEL HORA: MEDICAMENTO DE LA TARDE	—:— PM	—:— PM	—:— PM	—:— PM	—:— PM	—:— PM	—:— PM
INSTRUMENTO DE MEDIR (HAGA ESTO ANTES DE USAR SU MEDICAMENTO)	1. 2. 3.						
LA SEVERIDAD MAS ALTA DEL SINTOMA DEL ASMA (vea la escala atras)							
CUANDO ALCANZARON LAS SINTOMAS A ESTE NIVEL MÁS ALTO DE SEVERIDAD?(Si encima de la severidad del) Síntoma= 0, Deje en blanco: Para la Severidad del Síntoma= 1-5, apunte 1 del siguiente)							

RTI/ ACS-AP-209-112
Revision 0

LA HORA DE ACOSTARSE HASTA LA SALIDA DEL SOL								
ESTA MAÑANA?								
ESTA TARDE?								
ANOCHECER?								
SINTOMAS DE ALERGIA?		___ si ___ no	___ si ___ no	___ si ___ no	___ si ___ no	___ si ___ no	___ si ___ no	___ si ___ no
INFECCIONES RESPIRATORIAS?		___ si ___ no	___ si ___ no	___ si ___ no	___ si ___ no	___ si ___ no	___ si ___ no	___ si ___ no
ESTUFA DEL GAS/EL USO DE HORNO Antes o Mientras el participante estuvo dentro del hogar, fueron usados algunos de estos Aparatos por mas de 1 Hora? (si ninguna estufa de gas/horno entonces se salta)		___ si ___ no	___ si ___ no	___ si ___ no	___ si ___ no	___ si ___ no	___ si ___ no	___ si ___ no
EL NUMERO DE INHALADAS NECESARIAS: SI USTED NO USO UN MEDICAMENTO LISTO ABAJO, ESCRIBA POR FAVOR UN "0" EN LA CAJA APROPIADA.								
EL NUMERO DE SOPLOS:	Como Necesitado Inhaler 1							
	Como Necesitado Inhaler 2							
	Como Necesitado Inhaler 3							
EL NUMERO DE DOSIS DE LA PRESCRIPCION DIARIA DE								

ESCALA DE LA SEVERIDAD DEL SINTOMA DEL ASMA (escoja solo el nivel más alto alcanzado)

0	Ningún síntomas de asma hoy.
1	El síntoma (s) del asma presente, pero no causó ninguna molestia.
2	El síntoma (s) del asma causó molestia, pero ningun interferencia con actividades ni con el sueño.
3	El síntoma (s) del asma intervino algo con actividades y sueño.
4	El síntoma (s) del asma intervenido con la mayoría de las actividades, y puede haber requerido cualquiera de los ejemplos siguientes: permaneciendo en la cama; ser manejado al hogar temprano de la escuela; llamar un doctor o enfermero para un consejo.
5	Los síntomas del asma requirieron ver a los siguientes: a un doctor o ir a un dispensario del hospital o de emergencia.

LAS DEFINICIONES

LOS SINTOMAS DE ALERGIA: Tuvo un sintoma de Fiebre Del Heno hoy, no causados por un gripe o resfriado. Deben incluir esos síntomas más de 1 de los siguientes:, destornudad, la nariz suelta (incluyendo gota de nasal), sinusitis o congestión nasal, comezon y ojos llorosos, comezon en la garganta?

LAS INFECCIONES RESPIRATORIAS: Fueron cualquiera de las condiciones siguientes presente hoy: un resfriado, garganta adolorida, la fiebre, gripe diagnosticada de doctor, infección respiratoria diagnosticada por doctor (la pulmonía, bronquitis, tos ferina, bronquiolitis, una infección en el oido, una infección respiratoria superior de trecho, o una infección de sinusitis)

COMENTARIOS: (se refiere porfavor a fechas específicas)_____

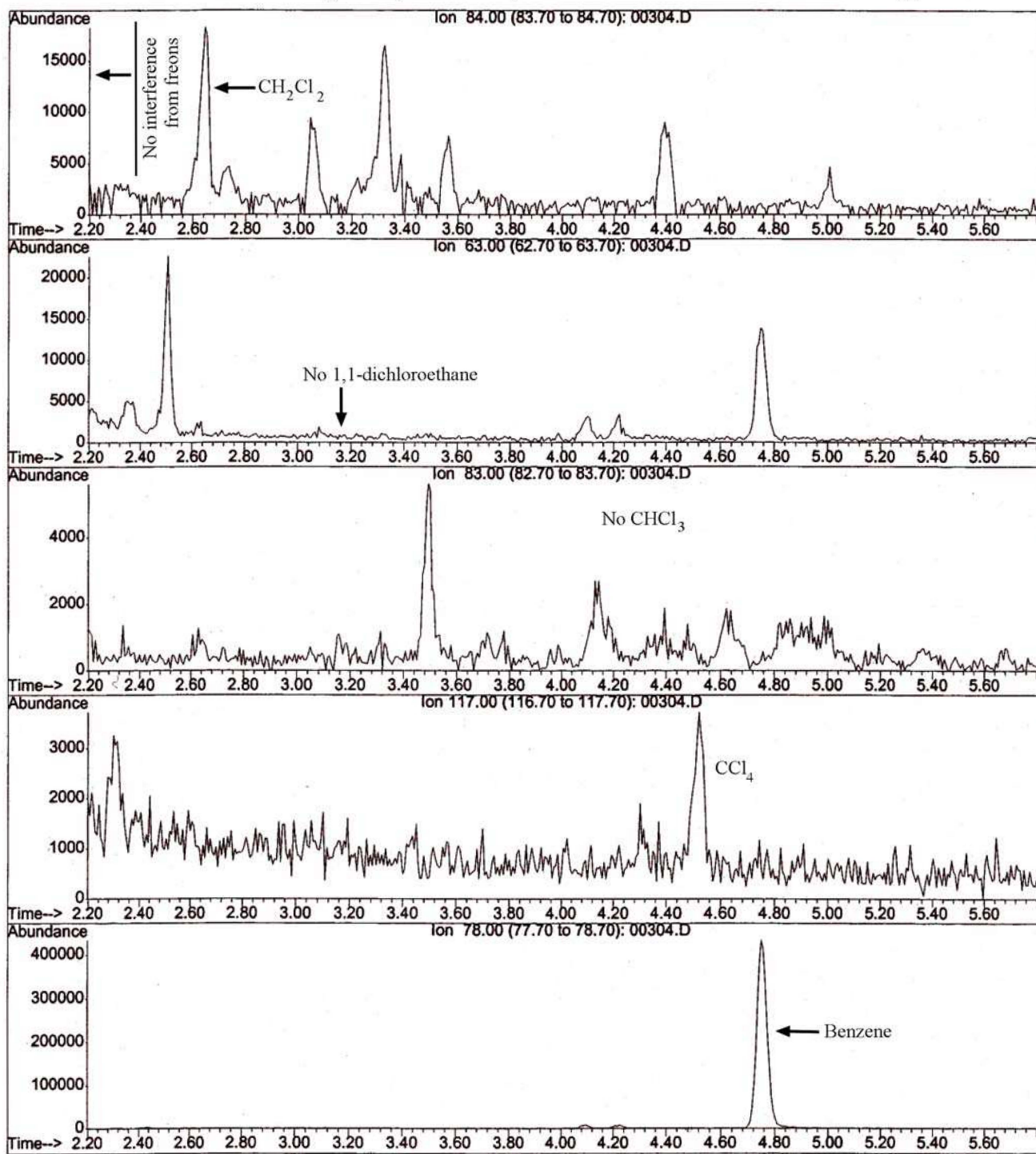
INSTRUCCIONES PARA MEDIR EL PICO FLUYE

- PEF Representa el Pico Fluye
 - La maxima cooperacion es esencial
 - Asegurase que este sentado derecho y que el medidor del flujo este a zero (0)
1. Primero, usted inhalará rápidamente y completamente llene sus pulmones.
 2. Inmediatamente insierte la piesa en la boca y cierre los labios alrededor.
 3. Sople lo mas duro, rápido y fuerte que usted pueda en cuanto cierre sus labios.
 4. Usted no necesita soplar profundamente.
 5. Nomas sople corto y duro por sólo 1 o 2 segundos.
 6. Registre el valor, ponga el contador a zero y repita el proceso 2 veces mas.
- Haga nota de cualquier irregularidad o los problemas que ocurrieron.
 - Registre los tres valores obtenidos en la hoja proporcionada.
 - Registre el tiempo verdadero de las pruebas.

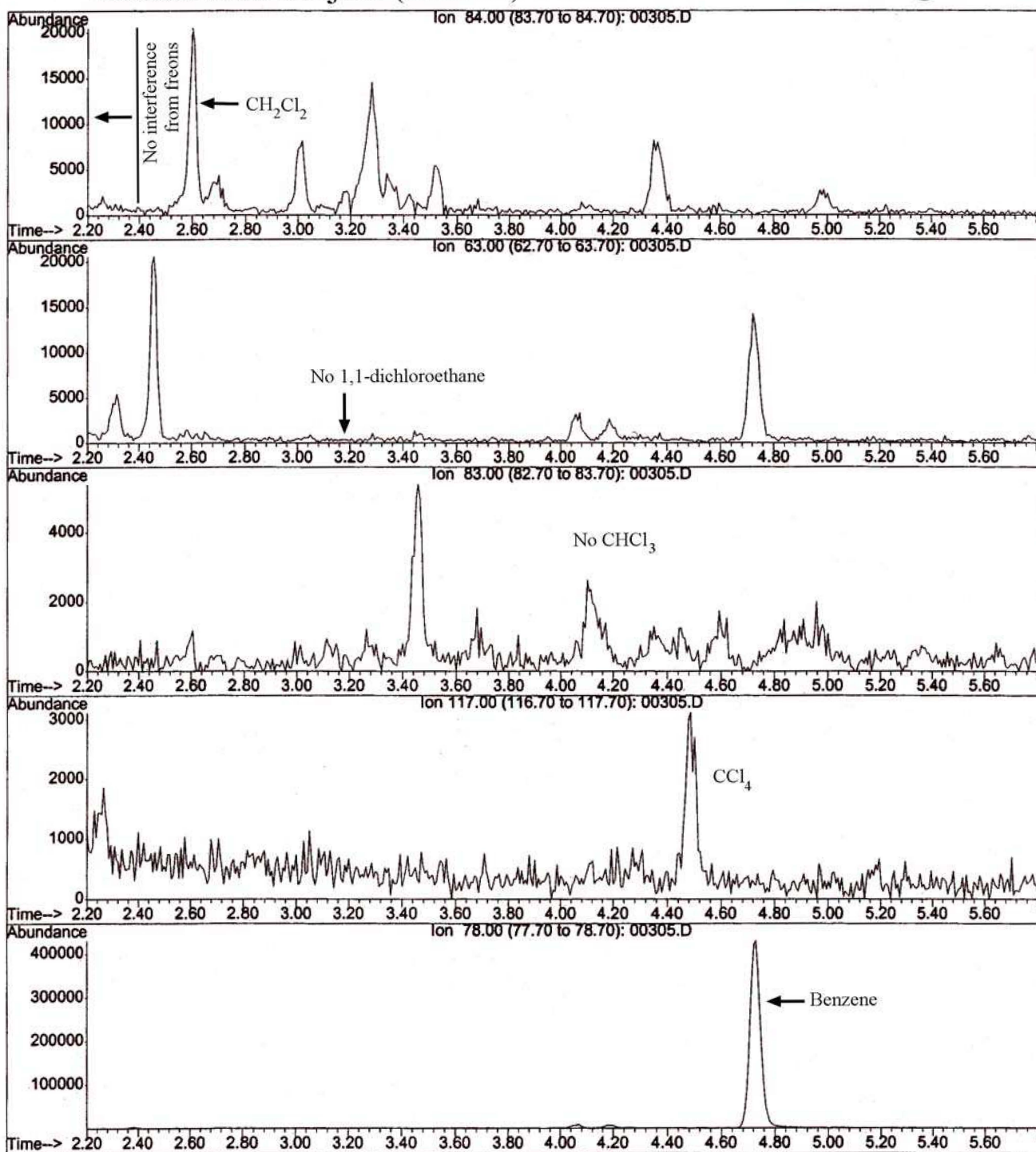
APPENDIX F.

Chromatograms for CFC Analysis

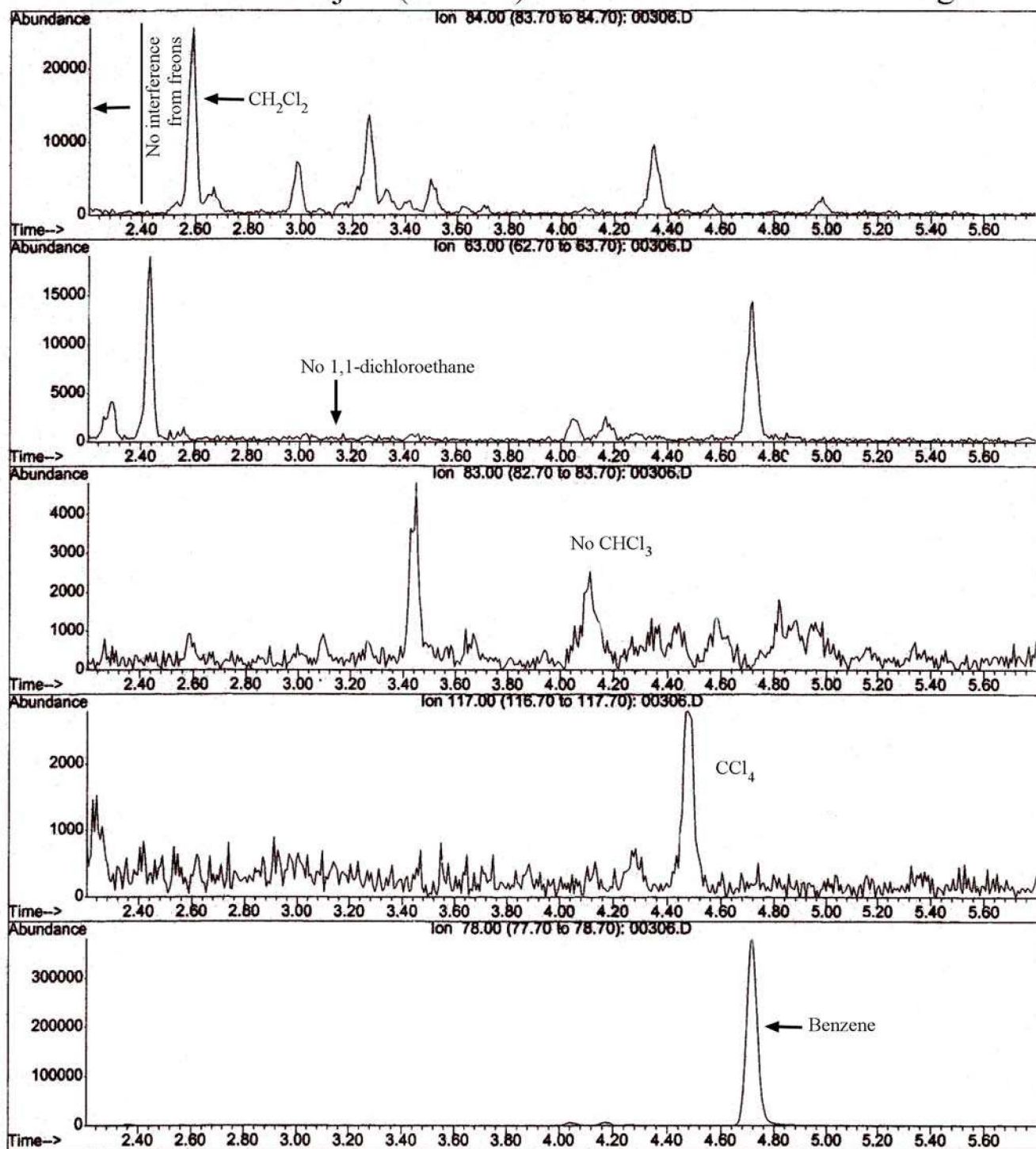
Breath from subject (smoker) 1 minute after inhaler usage



Breath from subject (smoker) 5 minutes after inhaler usage



Breath from subject (smoker) 15 minutes after inhaler usage



Breath from subject (smoker) 15 minutes after inhaler usage


Internal Standards		R.T.	QIon	Response	Conc	Units	Dev(Min)
1) 1-bromo-4-fluorobenzene	17	13.15	174	96386	471.00	pg	0.00
Target Compounds							Qvalue
2) 1-bromo-4-fluorobenzene	95	13.16	95	65142	455.63	pg	94
3) Methylene chloride	84	2.59	84	50050	518.25	pg	92
4) Methylene chloride	86	2.58	86	34686	522.33	pg	90
5) 1,1-Dichloroethane	63	0.00	63	0	N.D.	d	
6) 1,1-Dichloroethane	65	0.00	65	0	N.D.	d	
7) Chloroform	83	4.11	83	7680m	5.20	pg	
8) Chloroform	85	4.13	85	9896m	38.99	pg	
9) Carbon tetrachloroethylene		4.48	117	9343	21.69	pg	98
10) Carbon tetrachloroethylene		4.48	121	3488m	21.81	pg	
11) Benzene	78	4.72	78	1107933	Below	Cal	97
12) Benzene	77	4.72	77	272400	Below	Cal	89
13) Toluene	91	7.67	91	1510929	Below	Cal	98
14) Toluene	92	7.67	92	904686	Below	Cal	97
15) Tetrachloroethylene	166	8.69	166	6253m	Below	Cal	
16) Tetrachloroethylene	129	8.69	129	3695m	0.29	pg	
17) m, p-Xylene	91	11.04	91	125707	1102.97	pg	99
18) m, p-Xylene	106	11.05	106	69396	1124.20	pg	99
19) o-Xylene	91	11.91	91	27538	130.87	pg	98
20) o-Xylene	106	11.92	106	15481	138.46	pg	97
21) Styrene	104	11.97	104	29909	308.21	pg	# 70
22) Styrene	78	11.96	78	9398m	200.77	pg	
23) p-Dichlorobenzene	146	16.11	146	5771m	Below	Cal	
24) p-Dichlorobenzene	148	16.10	148	4616m	0.88	pg	

APPENDIX G.

















Time-Activity Diary

Time-Activity Diary Guide

- 1). The diary card should be filled out every 30 minutes with any pen or pencil.
- 2). There are four categories in the diary: location, activity level, exposure source and use of inhaler. Mark one answer in the location columns and one answer in the activity level columns. Mark the exposure source columns and the use of inhaler column when applicable.



Symbol Legend

 Indoor in HP  Outdoor in HP  Indoor outside HP  Outdoor outside HP  Rest	 Light to moderate activity  Strenuous activity  In car  Garage/Gas station  Near smoker	 Laundromat  Swimming  Painting  Hair salon  Detergent use  Use of inhaler
---	---	--

RTI/ACS-AP-209-112
Revision 0

















ID#		Date														
AM	Location				Activity			Exposure Source							Inh.	
6:30 AM																
7:00 AM																
7:30 AM																
8:00 AM																
8:30 AM																
9:00 AM																
9:30 AM																
10:00 AM																
10:30 AM																
11:00 AM																
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12:00 AM																
12:30 PM																
1:00 PM																
1:30 PM																
2:00 PM																
2:30 PM																
3:00 PM																

ID#		Date														
PM	Location				Activity			Exposure Source							Inh.	
3:30 PM																
4:00 PM																
4:30 PM																
5:00 PM																
5:30 PM																
6:00 PM																
6:30 PM																
7:00 PM																
7:30 PM																
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8:30 PM																
9:00 PM																
9:30 PM																
10:00 PM																
10:30 PM																
11:00 PM																
11:30 PM																
12:00 - 6:30 AM																

Weekend Example

ID# _____		Date _____													
AM	Location					Activity			Exposure Source						Inh.
6:30 AM															
7:00 AM															
7:30 AM															
8:00 AM															
8:30 AM															
9:00 AM															
9:30 AM															
10:00 AM															
10:30 AM															
11:00 AM															
11:30 AM															
12:00 AM															
12:30 PM															
1:00 PM															
1:30 PM															
2:00 PM															
2:30 PM															
3:00 PM															

Weekday Example

ID# _____		Date _____																	
AM	Location					Activity			Exposure Source										Inh
																			
6:30 AM	●					●													
7:00 AM		●			●	●													
7:30 AM	●					●													
8:00 AM	●					●													
8:30 AM	●					●													
9:00 AM	●					●													
9:30 AM	●					●													
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1:00 PM	●					●													
1:30 PM	●					●													
2:00 PM		●				●													
2:30 PM	●					●													
3:00 PM		●			●	●													

APPENDIX H.

Procedures for Analysis of VOCs in the Badge

Procedures for Analysis of VOCs in the Badge

ANALYSIS OF VOLATILE ORGANIC COMPOUNDS FROM CHARCOAL BADGES BY
GAS CHROMATOGRAPHY/MASS SPECTROMETRY

TABLE OF CONTENTS

<u>Section</u>	<u>Page</u>
1.0	Scope and Application 3
2.0	Summary of the Method 3
3.0	Interferences 3
4.0	Safety 4
5.0	Equipment 4
6.0	Reagents and Standards..... 6
7.0	Sample Storage..... 7
8.0	Quality Control 7
9.0	Sample Extraction..... 9
10.0	Calibration and Standardization 9
11.0	Procedure 12
12.0	Method Performance..... 13
13.0	Data Management..... 13

LIST OF FIGURES

<u>Number</u>	<u>Page</u>
1	Example Sample Information and Custody Record 22
2	Example Sample Batch Submission Form 23

LIST OF TABLES

<u>Number</u>	<u>Page</u>
1	Target VOC Analytes 16
2	Nominal Calibration Solutions 17
3	Percent Recoveries of VOCs from Charcoal Badge..... 18
4	Operating Parameters for the Capillary GC/MS System 19
5	Analyte SIM Ions 20

1.0 SCOPE AND APPLICATION

1.1 This is a general purpose method that provides for the determination of volatile organic hydrocarbons (VOCs) in air samples by gas chromatography/mass spectrometry (GC/MS).

1.2 Analytes appropriate to this analysis are shown in Table 1.

2.0 SUMMARY OF THE METHOD

This method is for the analysis of VOCs in air by GC/MS in the selected ion monitoring mode (SIM). Charcoal badge samplers are extracted with a suitable solvent (acetone/carbon disulfide; 2:1 v/v) containing internal standards and then the sample extract is injected into a GC/MS having a fused silica capillary column. The compounds are identified by retention time and at least two representative mass fragment ions as compared to standards. One ion, a primary ion, is used for the quantitation of a given compound. The secondary ion is utilized as a confirmation ion for a given compound. Quantitation is carried out by the method of internal standards by utilizing the areas of the primary ion and internal standard to determine relative response factors for each specific analyte of interest.

Method Reference

Pellizzari, E., L. C. Michael, and S. Cooper. "Performance and Validation of VOC Collection and Analysis Using OVM 3500 Charcoal Badges", manuscript in preparation.

3.0 INTERFERENCES

3.1 During analysis, major contaminant sources are reagents and sample collection materials. Analysis of field and method blanks provide information about the presence of contaminants.

3.2 Carry over contamination may occur when a sample containing low concentrations of compounds is analyzed immediately after a sample containing relatively high concentrations of compounds. Syringes and splitless injection port liners must be cleaned carefully or replaced as needed.

3.3 Method interferences may be caused by contaminants in solvents, reagents, glassware and other sample processing apparatus that lead to discrete artifacts or elevated baselines in gas chromatograms. All reagents and apparatus must be routinely demonstrated to be free from interferences under the conditions of the analysis by method blanks as described in Section 8.2.

4.0 SAFETY

4.1 The toxicity and carcinogenicity of chemicals used in this method have not been precisely defined; each chemical should be treated as a potential health hazard, and exposure to these chemicals should be minimized. Each laboratory is responsible for maintaining awareness of OSHA regulations regarding safe handling of chemicals used in this method. Additional references of laboratory safety are available for the information of the analyst.

4.2. Some method analytes have been tentatively classified as known or suspected human or mammalian carcinogens. Pure standard materials and stock standard solutions of these compounds should be handled with suitable protection to skin, eyes, etc.

5.0 EQUIPMENT

5.1 Laboratory Equipment

5.1.1 All glassware must be meticulously cleaned. This may be accomplished by washing with detergent and water, rinsing with water, distilled water, or solvents, air-drying, and heating (where appropriate) in an oven.

5.1.2 Volumetric flasks, various sizes.

5.1.3 Micro syringes, various sizes.

5.1.4 Vials. Various sizes of amber vials with Teflon-lined screw or crimpseal caps.

5.1.5 Analytical balance. Capable of weighing 0.0001 g accurately.

5.2 Gas Chromatograph/Mass Spectrometer/Data System (GC/MS/DS)

5.2.1 The GC must be capable of temperature programming and be equipped for splitless/split injection. The injection tube liner should be quartz and about 3 mm in diameter. The injection system must not allow the analytes to contact hot stainless steel or other metal surfaces that promote decomposition.

5.2.2 The GC may be equipped with an autosampler capable of handling the sample vials and injecting the samples in a specific run sequence. Both the sample injection size and the number of syringe rinses should be controllable by the operator.

5.2.3 The GC/MS interface should allow the capillary column or transfer line exit to be placed within a few mm of the ion source. Other interfaces, for example the open split interface, are acceptable as long as the system has adequate sensitivity.

5.2.4 The mass spectrometer must be capable of electron ionization at a nominal electron energy of 70 eV. The spectrometer must be capable of scanning from 45 to 450 amu or selected ion monitoring with a complete scan cycle time (including scan overhead) of 1.5 sec or less. (Scan cycle time = Total MS data acquisition time in sec divided by number of scans in the chromatogram.) The spectrometer must produce a mass spectrum that

meets all criteria for the tune of perfluorotributylamine (FC-43) as described in RTI/ ACS-SOP-184-002.

- 5.2.5 A data system is required to acquire, store, reduce, and output mass spectral data. The software must allow integration of the ion abundance of any specific ion between specified time or scan number limits, calculation of response factors as defined in Section 10.1.5 (or construction of a first or second order regression calibration curve), calculation of response factor statistics (mean and standard deviation), and calculation of concentrations of analytes using either the calibration curve or the equation in Section 13. Optionally, data may be transferred from the instrument to another computer to carry out calculations after identifications and integrations are complete.

6.0 REAGENTS AND STANDARDS

6.1 Helium Carrier Gas

6.2 Solvents

Methylene chloride, carbon disulfide, toluene and acetone (pesticide grade or equivalent).

6.3 Stock Standard Solutions

Individual solutions of analytes, surrogates, and internal standards are prepared from certified solutions or from pure (neat) materials. The solutions are prepared in a suitable solvent (i.e., acetone/carbon disulfide; 2:1 v/v). The stock solutions are stored in vials with Teflon lined caps at -10EC or sealed in clean glass ampules for storage.

6.4 Primary Dilution Standard

The stock standards are used to prepare a primary dilution standard solution that contains multiple analytes. Aliquots of each of the stock standard solutions are combined to produce the primary dilution standard in which the concentration of the analytes is at least equal to the concentration of the highest calibration solution. Store the primary dilution standard solution in a vial sealed with a Teflon lined cap at 4EC or less.

6.5 Internal Standard Solution

The stock internal standard solutions are used to prepare a primary dilution standard containing the internal standards. The solution is prepared at a level which facilitates the delivery of an appropriate amount of internal standards to the final sample extracts with a small (i.e., 5-50 μ L) volume. The solution is also used in the preparation of the calibration solutions.

6.6 Calibration Solutions

A series of calibration solutions are prepared to span the expected range of analyte concentrations found in the sample extracts. Typically five concentration levels are prepared and analyzed in duplicate. The calibration should cover the nominal range from 0.075 to 250 Φ g/mL of each target analyte. The specific analytes contained in the calibration solutions may be prepared at different concentration levels which reflect the ratios found in typical environmental extracts. Each calibration solution contains equal amounts of the selected internal standards. Table 2 lists the suggested calibration levels, target analytes, and internal standards for the calibration curve standards. Octafluorotoluene (PFT) will be used as the internal standard for quantitation. The solutions are stored in vials with Teflon caps at 4EC. Aliquots of the solutions are transferred to amber autosampler vials and sealed with Teflon lined septa for analysis by GC/MS.

7.0 SAMPLE STORAGE

All sample extracts are stored in a freezer at -10EC.

8.0 QUALITY CONTROL

8.1 Field Blanks

Processing of field blanks will be performed by extracting unexposed charcoal badges. The results of these analyses will help define contamination resulting from field sampling and transport activities and lot to lot variations. Field blanks are unspiked cartridges taken to the field and treated exactly as field samples.

8.2 Method Blanks

Laboratory processing of method blanks will be performed along with each batch of samples extracted as a means of assessing the contamination resulting from the sample extraction and cleanup procedures. Method blanks are simply extraction solvent processed and analyzed with field samples.

8.3 Field Controls

Field controls, containing known quantities of target analytes, will be processed for each sample type. The results of these analyses will be a means of assessing the overall recovery of the target analytes from the charcoal badge. The recovery of the target analytes will be monitored. Field controls are spiked then taken to the field, returned, and stored along with field samples.

The chosen levels of each analyte loaded onto charcoal badges will yield a nominal level of 500 pg/ Φ L in the final extract.

8.4 Laboratory Controls

Laboratory controls will be processed and analyzed prior to processing field controls. Laboratory controls are used to demonstrate acceptable method performance prior to extracting field samples. Laboratory controls will contain all target analytes, and undergo all extraction and procedures which the samples are subjected to. The recovery of the target analytes will be monitored.

The chosen levels of each analyte loaded onto charcoal badges will be identical to field controls.

8.5 Method Controls

Method controls will be processed and analyzed with each extraction batch to evaluate recovery of target VOCs during sample manipulation and analyses. Method controls are extracting solvent spiked with all target VOCs then processed and analyzed with field samples.

The chosen levels of each analyte in the extraction solvent will be at a nominal level of 500 pg/ Φ L.

9.0 SAMPLE EXTRACTION

Samples received from the field or retrieved from storage are first inspected for (a) the closure cap being firmly snapped to the monitor body and (b) the closure cap plugs being firmly sealed in the cap parts. [NOTE: If these conditions are violated, the sample may be compromised.]

The center port of the cap is opened and 1.5 mL of acetone/carbon disulfide [2:1 v/v] desorption solvent which contains the three internal standards (Table 2, 5 ng/ Φ L each) is injected. The rim part may be open to allow venting. Both ports are resealed. With occasional gentle agitation the monitor is let stand for 1/2 hour.

Both ports are carefully opened. The decanting spout is inserted into the rim port and the liquid is carefully transferred into a sampler vial used with the automatic sampler of the GC/MS system. The vial is immediately sealed, and is ready for analysis.

Recoveries of analytes from charcoal badges exposed to atmospheres containing known levels and processed by this procedure followed by GC/MS analysis has been shown to be 70-110% (Table 3). Precision of duplicate 144 hr samples from six participants ranged from 0-28% RSD across all analytes and samples (avg. RSD \square 10%).

10.0 CALIBRATION AND STANDARDIZATION

Demonstration and documentation of acceptable initial calibration are required before any samples are analyzed and are required intermittently throughout sample analysis as dictated by results of continuing calibration checks. After initial calibration is successful, a continuing calibration check is required at the beginning of each 8 hour period during which analyses are performed. Additional periodic calibration checks are good laboratory practice.

10.1 Initial Calibration

- 10.1.1 Calibrate the mass and abundance scales of the MS with calibration compounds and procedures prescribed by the manufacturer with any modifications necessary to meet the requirements in Section 10.1.2.
- 10.1.2 Configure the GC/MS system as described in Table 4.
- 10.1.3 Inject a 1 μ L aliquot of a medium concentration calibration solution (5 Φ g/mL nominal concentration) and acquire and store data from the selected ions with a total cycle time (including scan overhead time) of 1.5 sec or less. Cycle time should be adjusted to measure at least five or more spectra during the elution of each GC peak.

- 10.1.4 If medium standard demonstrates acceptable chromatographic performance, as described in Section 13.1.4, inject a 1 μ L aliquot of each of the other calibration solutions using the same GC/MS conditions.
- 10.1.5 Calculate a response factor (RF) for each analyte for calibration solution using the octafluorotoluene (PFT) internal standard. Table 5 contains quantitation ions for all selected compounds and internal standard. RF is a unitless number, but units used to express quantities of analyte and internal standard must be equivalent. RF is calculated

$$\text{func RF} = \frac{(A_x)(Q_{is})}{(A_{is})(Q_x)}$$

as:

where:

A_x = integrated abundance of the quantitation ion of the analyte.

A_{is} = integrated abundance of the quantitation ion internal standard.

Q_x = quantity of analyte injected in concentration units.

Q_{is} = quantity of internal standard injected in concentration units.

For each analyte and surrogate, calculate the mean (M) RF from the analysis of the multipoint calibration solutions. Calculate the standard deviation (SD) and the percent relative standard deviation (%RSD) for each mean: %RSD = 100 (SD/M). If the RSD of any analyte mean RF exceeds 25%, either analyze additional aliquots of appropriate calibration solutions to obtain an acceptable RSD of RFs over the entire concentration range, or take action to improve GC/MS performance.

- 10.1.6 As an alternative to calculating mean response factors and applying the RSD test, use the GC/MS data system software or other available software to generate a linear or second order regression calibration curve. Acceptable calibration curves must have correlation coefficients (r) values ≥ 0.99 .

10.2 Continuing Calibration Check

Verify the MS tune and initial calibration at the beginning of each 8 hr work shift during which analyses are performed using the following procedure.

- 10.2.1 Inject a 1 μ L aliquot of a medium concentration calibration solution (5 Φ g/mL) and analyze with the same conditions used during the initial calibration.
- 10.2.2 Demonstrate acceptable chromatographic performance.
- 10.2.3 Determine that the absolute areas of the quantitation ions of the internal standards and surrogate(s) have not decreased by more than 25% from the areas measured in the most recent continuing calibration check, or by more than 50% from the areas measured during initial calibration. If these areas have decreased by more than these amounts, adjustments must be made to restore system sensitivity. These adjustments may require cleaning of the MS ion source, or other maintenance as indicated in Section 10.3.5 and recalibration.
- 10.2.4 Calculate the RF for each analyte from the data measured in the continuing calibration check. The RF for each analyte is in control if its primary ion RF is within $\pm 25\%$ of the mean value of the same level standard measured in the initial calibration. Record the performance of the RF for each analyte and surrogate on a control chart. Acceptable performance for the analytical system is met if:
- All primary target analytes, (see Table 1), are in-control.
 - No more than two (2) secondary target analytes are out-of-control.
- If these conditions are not achieved, remedial action must be taken, which may include recalibration.

10.2.5 Remedial Actions

Possible remedial actions include major maintenance such as cleaning an ion source, cleaning quadrupole rods, etc. require recalibration.

10.2.5.1 Check and adjust GC and/or MS operating conditions; check MS resolution, and calibrate the mass scale.

10.2.5.2 Clean or replace the splitless injection liner, silanize a new injection liner.

10.2.5.3 Flush the GC column with solvent according to the manufacturer's instructions.

10.2.5.4 Break off a short portion (about 1 meter) of the column from the end near the injector; or replace GC column. This action may cause a change in retention times, requiring recalibration of retention windows.

10.2.5.5 Prepare fresh calibration solutions, and repeat the initial calibration step.

10.2.5.6 Clean the MS ion source and rods (if a quadrupole).

10.2.5.7 Replace any components that allow analytes to come into contact with hot metal surfaces.

10.2.5.8 Replace the MS electron multiplier, or any other faulty components.

11.0 PROCEDURE

11.1 Analyze a 1-2 μL aliquot of each sample with the GC/MS system under the same conditions used for the initial and continuing calibrations (Section 10.2.2). The samples are analyzed in sets which consist of calibration check standards, method controls and blanks, a NIST reference check, and eight (8) sample extracts. The order of analysis is:

Continuing calibration check standard

Method control

Method blank

NIST reference standard

Sample extracts

Continuing calibration check standard

11.2 At the conclusion of data acquisition, use the same software that was used in the calibration procedure to tentatively identify peaks in retention time windows of interest.

11.3 Identification of analytes - identify a sample component by its retention time and extracted ion profiles. The GC retention time of the sample components should be within 10 sec of the time observed for that same compound when a continuing calibration solution was analyzed. Manually check the peak integration to verify that the extracted ion profile was properly integrated and the most accurate peak area was obtained.

12.0 METHOD PERFORMANCE

Method detection limits (MDLs) are based upon the lowest calibration concentration used for the sample analysis.

13.0 DATA MANAGEMENT

13.1 Calculations

Complete chromatographic resolution is not necessary for accurate and precise measurements of analyte concentrations if *unique* ions with adequate intensities are available for quantitation.

func $C_x \sim \frac{(A_x)(Q_{is})}{(A_{is})(RF)}$

13.1.1 Calculate analyte and surrogate concentrations using the following equations:

where:

C_x = concentration of analyte or surrogate in ng/sample in the sample extract.

A_x = integrated abundance of the quantitation ion of the analyte in the sample.

A_{is} = integrated abundance of the quantitation ion of the internal standard in the sample.

Q_{is} = total quantity (in nanograms) of internal standard added to the sample.

RF = mean response factor of analyte from the initial calibration.

13.1.2 Alternatively, use the GC/MS system software or other available proven software to compute the concentrations of the analytes and surrogates from first or second order regression curves.

13.1.3 Calculations should utilize all available digits of precision, but final reported concentrations should be rounded to an appropriate number of significant figures (one digit of uncertainty).

13.1.4 Chromatographic performance will be evaluated at the beginning of analysis. The retention characteristics of target analytes, resolution of target analytes, and chromatographic peak shapes of target analytes will be used to evaluate

chromatographic performance. In addition, the instrument operator will visually monitor analyte resolution for standards daily. Resolution (R) will be measured using a pair of closely eluting analytes (methyl chloroform and benzene) by

$$R = \frac{2 \times (\Delta RT)}{(W_1 + W_2)}$$

where:

ΔRT is the difference in retention (benzo[a]pyrene and benzo[e]pyrene), W_1 , and W_2 are peak widths measured at 10% above the baseline for each compound.

Resolution must be ≥ 1.0 .

13.2 Data Management

13.2.1 Sample Management

A series of unique sample codes will be used for sample identification. These sample codes will be placed on all samples and associated documents.

A sample protocol record will be used to document sample preparation. Custody records for the sample are completed in the same record (Figure 1). Detailed information regarding sample extraction will be recorded in RTI Laboratory Notebooks. Samples batched for extraction and submitted to the GC/MS lab for analysis will be tracked using a batch sample submission form (Figure 2). This form will assist in tracking samples and will include important processing information such as amounts of internal standards added.

13.2.2 Sample Custody

Sample custody procedures will be used to track samples and sub-samples generated during this work assignment. Custody documents will be utilized for all sample preparation and analysis activities. The analyst is responsible for sample custody. Sample chain-of-custody and batch records are kept in the laboratory until the data has been electronically transferred to the database manager. Upon complete review of the data once it is merged into the database, the chain-of-custody and batch records will be returned to the field supervisor.

13.2.3 Electronic Datafile Management

Electronic datafiles containing the sample results as ng/sample will be created for each individual sample. These files will be incorporated into a project database where calculations to determine the actual concentration in air will be performed (RTI/ACS-AP-209-400). The laboratory manager is responsible for reviewing the data prior to its transfer as electronic data files to the database manager. This review will be for

completeness of the dataset to insure that all samples, blanks and QC samples have been included in the electronic datafile.

TABLE 1. TARGET VOC ANALYTES

Primary Analytes	Secondary Analytes
Benzene	Methylchloroform
Chloroform	Methylene Chloride
Perchloroethylene	Styrene
Trichloroethylene	Toluene
	<u>o</u> -Xylene
	<u>m,p</u> -Xylenes
	<u>p</u> -Dichlorobenzene

TABLE 2. NOMINAL CALIBRATION SOLUTIONS

Compound	Concentration of Analytes in (Φg/mL) Levels				
	0.1X	0.3X	5X	50X	250X
Benzene	0.075	0.30	5.0	50	250
Chloroform	0.075	0.30	5.0	50	250
Perchloroethylene	0.075	0.30	5.0	50	250
Trichloroethylene	0.075	0.30	5.0	50	250
Methylchloroform	0.075	0.30	5.0	50	250
Methylene Chloride	0.075	0.30	5.0	50	250
Styrene	0.075	0.30	5.0	50	250
Toluene	0.075	0.30	5.0	50	250
<u>o</u> -Xylene	0.075	0.30	5.0	50	250
<u>m,p</u> -Xylene	0.075	0.30	5.0	50	250
<u>p</u> -dichlorobenzene	0.075	0.30	5.0	50	250
Internal Standards					
Octafluorotoluene (PFT)	5.0	5.0	5.0	5.0	5.0
Hexafluorobenzene (PFB)	5.0	5.0	5.0	5.0	5.0
Bromopentafluorobenzene (BFB)	5.0	5.0	5.0	5.0	5.0

TABLE 3. PERCENT RECOVERIES OF VOCs FROM CHARCOAL BADGE

Chemical	Low ^a	Medium	High
Chloroform	81±4.2	80±2.8	86±1.4
1,1,1-Trichloroethane	80±2.1	80±2.1	86±2.8
Benzene	78±4.9	71±2.8	78±3.5
Trichloroethylene	74±2.8	72±2.1	79±5.7
Toluene	95±5.7	81±4.2	88±4.9
p-Xylene	84±3.5	82±2.1	92±4.9

^a Low = 0.9 - 3 Φg total spiked onto badge from atmosphere.
Medium = 6.4 - 20 Φg total spiked onto badge from atmosphere.
High = 12.8 - 41 Φg total spiked onto badge from atmosphere.

TABLE 4. OPERATING PARAMETERS FOR THE CAPILLARY GC/MS SYSTEM

Parameter	Setting
GAS CHROMATOGRAPH	
Instrument	Hewlett-Packard 5890
Column	60m x 0.32 mm DB-5 fused silica capillary column
Temperature Program	0EC (3 min) to 150EC @ 4EC/min
Carrier Gas Flow Rate	1.0 mL/min
Capillary Injector	1 min splitless
Injector Temperature	200EC
MASS SPECTROMETER	
Instrument	Hewlett Packard, Model 5988A
Ionization Mode	Electron Ionization Selected Ion Monitoring
Emission Current	0.3 mA
Source Temperature	200EC
Electron Multiplier	2000 volts ^a

^a Typical value

TABLE 5. ANALYTE SIM IONS

Compound	Primary	Secondary
Benzene	78	74
Chloroform	83	85
Perchloroethylene	166	94
Trichloroethylene	130	95
Methylchloroform	61	97
Methylene chloride	84	86
Styrene	104	78
Toluene	91	92
<u>m</u> /p-Xylene	91	106
<u>o</u> -Xylene	91	106
p-Dichlorobenzene	146	148

RESEARCH TRIANGLE INSTITUTE SAMPLE PROTOCOL AND CUSTODY RECORD PROJECT NO.-XXXXXXXX				
SAMPLE CODE:				
INITIALS	I.D. NO.	DATE	TIME	OPERATION PERFORMED

Research Triangle Institute
Post Office Box 12194
Research Triangle Park, NC 27709

Figure 1. Example sample information and custody record

ACS MASS SPECTROMETRY SAMPLE SUBMISSION FORM				
PROJECT		SAMPLE SET OF		
PLEASE LIST SAMPLE CODES OF SAMPLES SUBMITTED ON / / . Page 1 of				
SURROGATES	CONCENTRATION LEVELS	INTERNAL STDs	CONCENTRATION LEVELS	COMMENTS
TARGET ANALYTES				

Figure 2. Example sample batch submission form.