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Project Summary

Measurements of Exhaled Breath Using a New Portable Sampling Method

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This report documents the development and demonstration of a new breath sampling method for volatile organic compounds (VOCs). The project, part of EPA's Total Exposure Assessment Methodology (TEAM) Program, was aimed at improving the existing field method for sampling exhaled breath. The new method was tested on four subjects exposed to elevated chemical levels in six microenvironments (hardware stores, swimming pools, garages, etc.). Repeated breath measurements before and after exposure provided data on the uptake and excretion of 20 VOCs.

This Project Summary was developed by EPA's Atmospheric Research and Exposure Assessment Laboratory, Research Triangle Park, NC, to announce key findings of the research project that is fully documented in a separate report of the same title (see Project Report ordering information at back).

Introduction

EPA's TEAM Study (1) of human exposure to VOCs has always included measurements of exhaled breath to determine time-integrated dose and to confirm that exposure measurements have included all important routes of exposure. The original method used in all TEAM Studies between 1979 and 1987 employed a van-mounted spirometer (2). The principle of the method was to collect about 40 L of expired air in a bag and then pull the air across two Tenax cartridges for later analysis by gas chromatography-mass spectrometry (GC-MS). The subject breathed clean air supplied by a cylinder in the van. Normal breathing was employed, and all the exhaled air was collected; thus the exhaled air was a mixture of alveolar air and air from the upper airways, or "deadspace" area.

The above method was employed to collect breath samples from about 800 people in eight cities during the 1979-1987 period. The method had several important advantages, including (1) transportability–the van drove to people's homes to reduce the burden on them of supplying a sample; and (2) simplicity of breathing technique–untrained persons from 5 to 85 had little difficulty giving samples.

However, three important disadvantages of the method were also identified:

(1) Although the time to provide 40 L of breath was only about 5-6 minutes, the total cycle time (time to complete one breath sample and be ready to collect another) was about 20 minutes. In situations where repeated breath measurements are desirable, this represents an irreducible limit on frequency of collection.

(2) The breathing technique resulted in a mixture of alveolar air with the clean inhaled air that failed to penetrate the alveolar region ("deadspace air"). Thus the actual alveolar concentration would be higher than the measured concentration by an unknown factor, depending on the relative proportion of deadspace air for each subject.

(3) The amount of bulky equipment required (cylinder of clean air, 40-L bags, pumps) reduced the ability to collect samples at any time and place desired.

Therefore EPA decided to develop a new method for sampling exhaled breath. The performance goals of the new method were as follows:

(1) Reduce the sampling time to 1-2 minutes and the cycle time to 5 minutes.

(2) Collect alveolar air predominantly.
(3) Be portable with no power requirements.

Following development and laboratory testing of the method, it was employed in field studies of exposure to common microenvironments with suspected high concentrations of certain toxic or carcinogenic VOCs. Following exposure, volunteers supplied repeated breath samples over a period of 2-4 hours. The goals of the study were to measure concentrations of a number of VOCs in common microenvironments, and determine the uptake of these VOCs in the body and their subsequent excretion.

Results

Development of the Method

The new method includes the following fundamental components:

(1) A charcoal cartridge to clean ambient air as a source of inhaled air. This eliminates the need to provide a separate source of clean air.

(2) A critical-orifice canister to collect a known volume of expired air in 1-2 minutes. This eliminates the need for a pump and the associated power requirements.

(3) A long narrow tube to isolate alveolar air from deadspace air for the majority of the breath cycle time.

The complete device is mounted in an aluminum suitcase and weighs 10.5 kg, including two 1.8-L evacuated canisters (Figure 1). It can be carried by one person, set up in less than five minutes, and collect alveolar breath samples in less than two minutes. All components are attached to an aluminum plate mounted on pivoting slides. These slides allow the entire mounting plate to slide out horizontally and elevate vertically to six different mounting heights to accommodate children and adults of all heights.

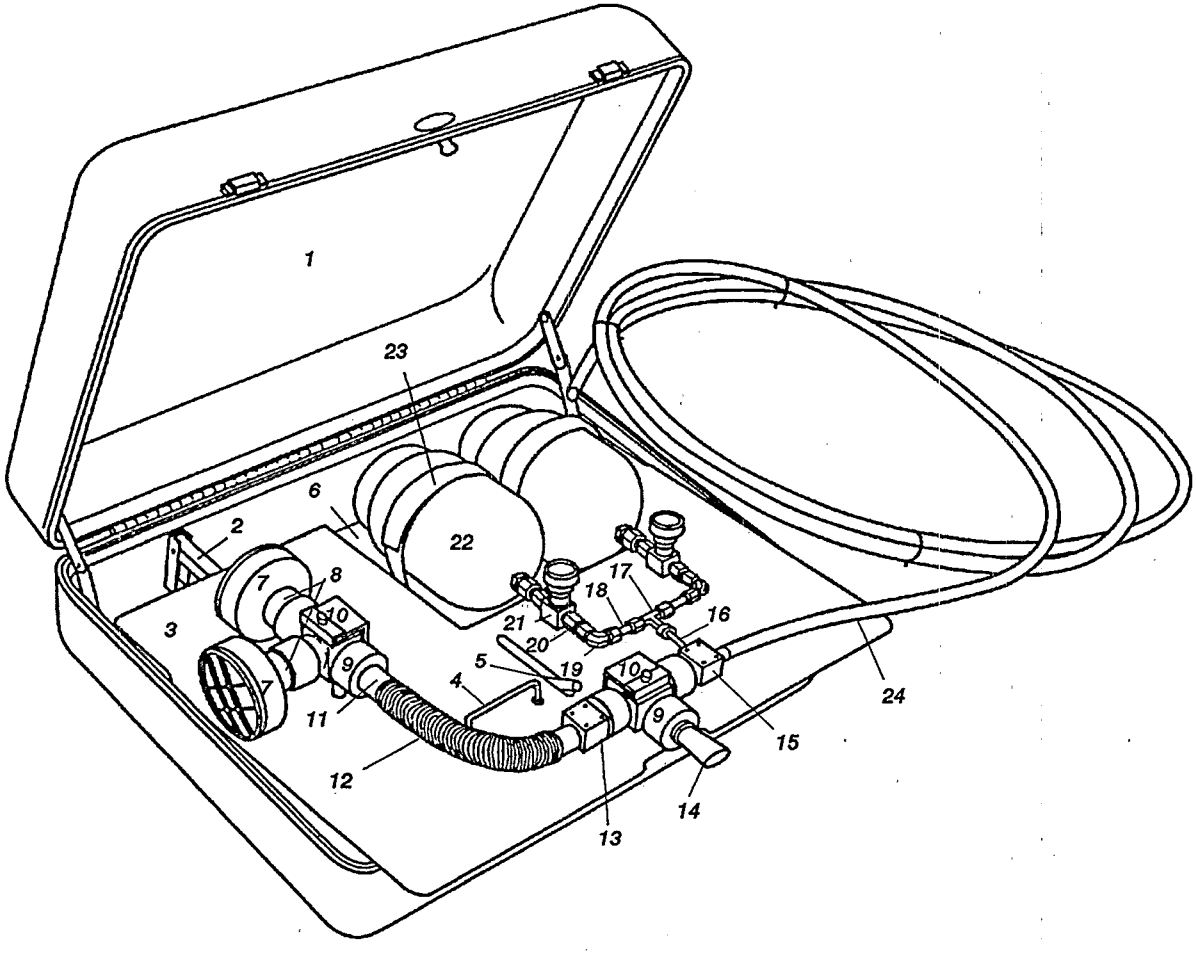

Figure 1. *Portable spirometer for the collection of VOCs in alveolar breath.*

The procedure for collecting a breath sample is as follows: following adjustment of the system to the correct height, the participant dons pinch-type nose clamps to prevent nose-breathing, and places his/her mouth tightly over a previously sterilized mouthpiece unit and breathes as normally as possible. (Due to resistance from the valves and the breath containment tube, breathing is probably slower and deeper than normal–this should enhance the proportion of alveolar air collected.) As the participant inhales, air is pulled through two charcoal-filled respirator cartridges mounted in parallel. Four full breaths are taken before sample collection begins in order to clear the spirometer and the participant airways of ambient air trace chemicals. The inhaled air passes through the unidirectional inhale valve and into the lungs; exhaled air passes through the unidirectional exhale valve and the sampling port into the breath containment tube. Following completion of the fourth breath, the canister valve is opened and pressure-driven flow commences through the fixed needle orifice. The orifice is designed to collect 1.4 L of air in about 1.5 minutes, at which time the canister valve is closed.

The breath containment tube was designed to collect over 95% alveolar air. As the participant exhales, the deadspace air passes rapidly by the sampling port, into the tube and out the other end. At the completion of an exhalation, all the air remaining in the breath containment tube is alveolar. This alveolar air is then sampled by the canister during the remainder of the breath cycle (resting time plus the inhalation portion of the next breath). Although the deadspace air is briefly sampled by the canister during the fraction of a second that it passes by the sampling port, the actual volume sampled is only about 1-2% of the volume of alveolar air sampled during the remainder of the breathing cycle.

The respirator cartridges (Survivaire®) were tested to determine background levels and breakthrough volumes of 11 VOCs selected to provide a variety of different classes and volatilities. Background levels of all chemicals with the exception of tetrachloroethylene and methylene chloride were below the quantifiable limit. Since these chemicals were at high levels in laboratory air, and since later spirometer blanks indicated that the filter cartridges themselves were not contaminated, the true source appears to have been residual laboratory air in the system. Estimated quantifiable limits in a 150-ml sample were less than one $\mu g/m^3$ for 10 VOCs, and ranged from 1.6-4.4 $\mu g/m^3$ for seven additional compounds. The breakthrough volume for dichloromethane was determined to be 320 L per cartridge. The cartridges were also tested to determine the effects of storage time and intermittent reuse of the type expected for field sampling conditions. Intermittent use over a period of five days resulted in identical breakthrough volume of 320 L. Since two cartridges are used in parallel, they would not need to be replaced until 640 L of air had passed through them. Assuming 20 L inhaled during two minutes, this corresponds to about 30 breath samples.

The system was also tested to determine whether VOCs are adsorbed on any interior surfaces. Only two of 26 chemicals showed evidence of adsorption: *n*-dodecane and 4-phenylcyclohexene. "Carryover" experiments (collection of a low-concentration mixture following a high-concentration one) identified the same two chemicals as showing evidence of adsorption followed by release during later use of the system. Therefore it is expected that compounds more volatile than *n*-dodecane can be collected successfully by the system in normal use. To collect the less volatile compounds successfully, a small amount of "conditioning" of the system (about two minutes of breathing through the device by the participant before collection of the sample) may improve recoveries.

Breath Measurements Using the New Method

Previous TEAM Studies have indicated that consumer products and personal activities, particularly in enclosed spaces (microenvironments) provide the major sources of exposure to many VOCs (3). Only limited data are available on the thousands of consumer products and hundreds of different microenvironments where exposure can occur. Even fewer data are available showing the uptake and excretion of VOCs during and after exposure in these microenvironments. Therefore a study was planned to screen a number of possible high-exposure microenvironments, consumer products and personal activities. A small number of these would then be selected for study of exposure, uptake, and excretion of a number of target compounds for several volunteer subjects.

A total of 24 target chemicals were selected for study (Table 1). The chemicals were selected on the basis of their toxic, mutagenic, or carcinogenic properties; high

Table 1. *Target Chemicals for Screening and Breath Exposure Study Samples*

Compound	*Canister*	*Tenax*
Vinyl chloride	√	
Isopentane	√	
Vinylidene chloride	√	
n-*Pentane*	√	
Dichloromethane	√	
2-Methylpentane	√	
Chloroform	√	
1,1,1-Trichloroethane	√	
Carbon tetrachloride	√	
Benzene	√	
Trichloroethylene	√	
n-Octane	√	√
Toluene	√	
n-Nonane	√	
Tetrachloroethylene	√	
Ethylbenzene	√	
p-Xylene (or m-)	√	√
Styrene	√	
o-Xylene	√	√
α-Pinene		√
n-Decane	√	√
Limonene		√
p-Dichlorobenzene		√
n-Dodecane		√

Table 2. *Microenvironment Screening Sample Locations for Canister Air Sampling*

Microenvironment	Sample Collection Duration	Full Scan or MID [a] GC/MS Analysis
Photocopier room	<1 min	FS
High volume photocopy/print center	<1 min	FS
Room painting (oil based paints)	<1 min	FS
Metal shop	<1 min	FS
Woodshop	<1 min	FS
Wood staining area	<1 min	FS
Home No. 1 with moth crystals	<1 min	FS
Home No. 2 with moth crystals	<1 min	FS
Office with one heavy smoker	<1 min	FS
Indoor swimming pool	<1 min	FS
Furniture stripping shop	<1 min	FS
Hardware store No. 1	<1 min	FS
Hardware store No. 2	<1 min	FS
Interior decorating store No. 1	<1 min	FS
Interior decorating store No. 2	<1 min	FS
Beauty school No. 1	<1 min	FS
Beauty school No. 2	<1 min	FS
Laundromat	<1 min	FS
Bar/nightclub with smoking	<1 min	MID
Driving and smoking during rush hour	1 h	MID
Outdoors at a truckstop	<1 min	MID
Auto and mower refueling	20 min	MID
Inside a new pickup truck cab	<1 min	MID
Home garage, morning	<1 min	MID
Home garage, evening after driving in car	<1 min	MID
Commercial repair garage	<1 min	MID
Body and repair shop	<1 min	MID
Paint and body shop	<1 min	MID
Home with diapers soaking in bleach	12 h	MID
Mass spectrometer laboratory facility	<1 min	MID
Laboratory recently re-roofed	<1 min	MID
Packaging facility with much styrofoam	<1 min	MID

[a] *FS = full scan, MID = multiple ion detection.*

Table 3. *Consumer Product Emission Samples Collected on Tenax Using a Dynamic Headspace Purge*

Product Name	Test Temperature	Headspace Volume Analyzed
Pine-Sol® (19% pine oil)	40°C	0.23 L
Airwick® Solid Room Deodorizer (lemon scent)	30°C	0.45 L
Wood Plus® Polish (lemon scent)	30°C	0.48 L
Johnny Fresh® Bathroom Bowl Cleaner (pine scent)	26°C	0.30 L
Old English® Furniture Polish	26°C	0.23 L
Renuzit Roomate® Liquid Air Freshner	26°C	0.22 L

production volumes; or their prevalence in homes and buildings.

Phase I: Screening Microenvironments

A total of 32 microenvironments (Table 2) and six consumer products (Table 3) were selected for screening. Air samples were collected in evacuated canisters in each location and were analyzed by GC-MS. Tenax cartridges were employed in three of the microenvironments and also for headspace analysis of the consumer products, since sources of elevated α-pinene, limonene, and para-dichlorobenzene were being sought, and these target chemicals are not sufficiently volatile to be recovered efficiently from the canisters.

Concentrations of the target VOCs in each microenvironment as measured by the canisters are shown in Table 4. Many of the microenvironments had elevated levels of individual VOCs, often exceeding 100 $\mu g/m^3$. Of the 24 target VOCs, only three (vinyl chloride, vinylidene chloride, and carbon tetrachloride) were not found above 10 $\mu g/m^3$ in any of the 32 microenvironments.

Nine microenvironments were investigated for nontarget chemicals (Table 5). Tenax results for the consumer products and the three microenvironments are provided in Tables 6 and 7.

Table 4. *Air Concentrations ($\mu g/m^3$) in Microenvironment Screening Canister Samples*

Compound	Photocopier Room	Photocopy & Print Center	Oil-Based Painting	Metal Shop	Wood Shop	Wood Staining	Home No. 1 with Moth Crystals
Vinyl chloride	ND [a]	ND	ND	ND	ND	ND	ND
Isopentane	ND	ND	ND	ND	ND	ND	56
n-Pentane	ND	180	150	62	ND	1100	28
Vinylidene chloride	ND	ND	ND	4	ND	ND	ND
2-Methylpentane	2	2	ND	12	ND	58	1
Dichloromethane	20	10	25	23	5	2	3
Chloroform	7	50	77	36	ND	ND	14
1,1,1-Trichloroethane	2	5	3	21000	140	18	ND
Carbon tetrachloride	ND	ND	ND	ND	ND	ND	ND
Benzene	3	6	ND	ND	ND	10	8
Trichloroethylene	35	ND	5	8	15	5	ND
Toluene	8	9	20	130	120	2700	26
n-Octane	ND	ND	16	27	53	350	ND
Tetrachloroethylene	ND	ND	ND	1200	100	2	ND
Ethylbenzene	ND	1	24	4	90	11	7
m,p-Xylene	ND	5	88	11	200	30	13
n-Nonane	ND	2	230	26	8200	340	ND
o-Xylene	ND	4	39	4	75	11	9
Styrene	ND	ND	ND	ND	ND	2	ND
n-Decane	ND	ND	1200	63	1500	810	ND
p-Dichlorobenzene	ND	ND	ND	ND	ND	ND	22
n-Dodecane	ND	ND	46	NC [b]	NC	NC	NC

Compound	Home No. 2 with Moth Crystals	Office with One Smoker	Indoor Swimming Pool	Furniture Stripping Shop	Hardware Store No. 1	Hardware Store No. 2
Vinyl chloride	ND	ND	ND	ND	ND	ND
Isopentane	3	ND	24	10	29	630
n-Pentane	3	66	15	6	16	180
Vinylidene chloride	ND	ND	ND	3	2	ND
2-Methylpentane	3	ND	7	26	41	120
Dichloromethane	77	39	ND	7100	900	100
Chloroform	ND	36	240	2	ND	1
1,1,1-Trichloroethane	34	7	2	280	210	46
Carbon tetrachloride	ND	ND	ND	ND	ND	ND
Benzene	2	9	6	4	9	34
Trichloroethylene	ND	ND	ND	120	ND	6
Toluene	61	21	7	2500	650	250
n-Octane	1	ND	1	29	80	50
Tetrachloroethylene	ND	ND	ND	23	27	6
Ethylbenzene	47	1	3	120	590	17
m,p-Xylene	180	7	10	430	1700	64
n-Nonane	5	ND	2	61	290	200
o-Xylene	11	ND	4	160	110	23
Styrene	ND	ND	ND	68	38	7
n-Decane	9	ND	4	180	570	390
p-Dichlorobenzene	>540	ND	18	ND	39	ND
n-Dodecane	3	NC	ND	35	57	25

Table 4 (Continued)

Compound	Interior Decorating Store No. 1	Interior Decorating Store No. 2	Beauty School No. 1	Beauty School No. 2	Laundromat	Bar/Club with Smokers	Rush Hour Driving with Smoking
Vinyl chloride	ND	ND	ND	ND	ND	ND	ND
Isopentane	35	9	21	43	11	74	61
n-Pentane	19	5	10	11	11	27	30
Vinylidene chloride	ND	ND	ND	ND	ND	ND	ND
2-Methylpentane	12	5	3	3	3	22	24
Dichloromethane	240	74	17	ND	6	6	5
Chloroform	ND	ND	20	6	36	6	2
1,1,1-Trichloroethane	22	12	72	8	2	3	5
Carbon tetrachloride	ND	ND	ND	ND	ND	ND	NC
Benzene	9	3	15	8	4	20	52
Trichloroethylene	ND	ND	12	7	ND	ND	ND
Toluene	310	37	240	320	6	54	120
n-Octane	21	53	2	ND	ND	2	3
Tetrachloroethylene	9	ND	ND	4	17	1	6
Ethylbenzene	28	7	5	2	1	10	23
m,p-Xylene	93	26	16	8	3	31	72
n-Nonane	380	190	6	3	ND	6	3
o-Xylene	22	11	5	2	1	13	23
Styrene	6	ND	7	ND	ND	6	17
n-Decane	700	590	14	2	ND	7	3
p-Dichlorobenzene	ND	90	3	3	2	NC	NC
n-Dodecane	NC	ND	6	2	ND	NC	NC

Compound	Truckstop Outdoors	Auto & Mower Refueling	Inside New Truck Cab	Home Garage A.M.	Home Garage P.M.	Commercial Repair Garage	Body & Repair Shop
Vinyl chloride	NC	1	ND	ND	ND	ND	ND
Isopentane	80	>1500	11	250	>370	79	88
n-Pentane	32	>3600	8	120	222	28	28
Vinylidene chloride	ND	1	1	ND	ND	ND	1
2-Methylpentane	18	>1900	15	62	110	19	23
Dichloromethane	ND	NC	7	2	1	4	4
Chloroform	ND	NC	2	1	1	ND	ND
1,1,1-Trichloroethane	1	2	160	3	2	1	68
Carbon tetrachloride	ND	NC	3	ND	3	ND	1
Benzene	8	>380	3	30	53	10	10
Trichloroethylene	ND	ND	1	ND	ND	ND	ND
Toluene	21	920	240	120	160	36	520
n-Octane	2	22	3	4	7	2	7
Tetrachloroethylene	ND	ND	2	ND	ND	ND	16
Ethylbenzene	5	110	27	26	32	7	56
m,p-Xylene	16	340	140	93	110	22	>210
n-Nonane	2	20	8	4	7	3	56
o-Xylene	6	120	68	32	40	10	71
Styrene	ND	13	33	6	10	ND	46
n-Decane	2	10	45	5	8	8	56
p-Dichlorobenzene	NC	NC	NC	NC	NC	NC	NC
n-Dodecane	NC	NC	NC	NC	NC	NC	NC

Table 4. (Continued)

Compound	Paint & Body Shop	Home Diapers in Bleach	Mass Spec. Laboratory Facility	Laboratory with New Roof	Packaging Facility with Styrofoam
Vinyl chloride	ND	ND	NC	ND	ND
Isopentane	260	20	4	4	ND
n-Pentane	110	16	56	4	ND
Vinylidene chloride	ND	ND	ND	2	ND
2-Methylpentane	61	ND	9	2	ND
Dichloromethane	7	41	450	>1400	97
Chloroform	1	94	49	3	100
1,1,1-Trichloroethane	3	ND	13	53	ND
Carbon tetrachloride	ND	ND	1	ND	ND
Benzene	68	4	3	2	ND
Trichloroethylene	ND	ND	5	1	ND
Toluene	2100	11	180	3	14
n-Octane	35	ND	5	ND	ND
Tetrachloroethylene	ND	ND	1	ND	ND
Ethylbenzene	67	1	1	1	ND
m,p-Xylene	220	7	4	2	14
n-Nonane	36	2	1	2	ND
o-Xylene	80	2	1	1	ND
Styrene	19	2	1	ND	1
n-Decane	5	3	1	37	ND
p-Dichlorobenzene	NC	NC	NC	NC	NC
n-Dodecane	NC	NC	NC	NC	NC

[a] *ND = not detected.*
[b] *NC = not calculated.*

Phase II: Microenvironmental Exposures and Breath Sampling

Based on the results from the screening phase, six microenvironments (the furniture stripping shop, the wood/metal shop, the indoor swimming pool, hardware store #1, a home garage with fuel handling and wood staining, and a home with moth crystals and wood polish selected from the consumer product evaluation) were selected for the exposure study. Four volunteers (Table 8) were asked to spend 2-4 hours in one or more of the selected microenvironments, followed by 4 hours in a nearby location where repeated breath samples could be collected to follow the decline of the compounds in the body.

A total of 10 separate exposure experiments were carried out. In each case, personal air samples were collected for the volunteers during the 12-hour period prior to exposure to identify any unplanned exposure. Air samples were also collected during the exposure period, and in the location where the breath samples were collected. Breath samples were collected just before the exposure period and for the four-hour post-exposure period using the new alveolar breath system and the older "whole-breath" system. About 12 alveolar and 8-9 whole breath samples were collected during the 4-hour post-exposure period, with a higher frequency of collection (every 10 minutes for the alveolar samples, every 20 minutes for the whole breath samples) during the early part of the period (when the steepest decline in breath concentration was expected).

Results were analyzed to determine whether participants had had unplanned exposures or unexplained elevated breath concentrations prior to the exposure period. For cases where both previous exposures and breath concentrations were negligible, the data from the post-exposure breath concentrations were analyzed to determine the best-fit decay curve.

A simple pharmacokinetic model has previously been developed to describe the breath data collected in the TEAM Study (4). The main feature of the model is that it is based on a multicompartment mass-balance set of differential equations. The first compartment is identified with the blood, and additional compartments with successively "deeper" body systems, such as vessel-rich tissues, muscle, and fat. The number of compartments may be selected according to the situation, and range typically from 1 to 3. One important feature of the model is the existence of an intrinsic "residence time" associated with each compartment. Knowledge of these residence times is essential if breath measurements are to be used to estimate previous exposures. For the case of a negligible air concentration, the alveolar concentration at any time t following exposure is given by:

$$C_{ALV} = \Sigma A_i e^{r_i t}$$

where i indexes the compartment, the A_i are determined by the initial concentrations in each compartment, and the r_i are functions of the intrinsic residence times associated with each compartment.

If the residence times differ sharply between compartments, the model simplifies to

$$C_{ALV} = \Sigma A_i e^{-t/\tau_i}$$

where τ_i is the residence time of the *i*th compartment.

Previous chamber studies of washout times following exposure have indicated that the residence times associated with the second and third compartments are on the order of 1-3 hours and 6-8 hours, respectively, for a number of target VOCs. However, no direct measurements of the residence

Table 5. *List of Nontarget Compounds Present in Selected Screening Canister Samples*

Furniture Stripper	Interior Decorating Store #1	Interior Decorating Store #2
trichlorofluoromethane	2-methyl-1,3-butadiene (tent.)	2-methylheptane
trimethylsilanol	3-methylhexane (tent.)	3-methylheptane
2-methylhexane	trimethylcyclohexane iso.	dimethylcyclohexane iso.
3-methylhexane	ethylcyclohexane	dimethylcyclohexane
acetic acid, 2-methylpropyl ester (tent.) [a]	trimethylcyclohexane	ethylcyclohexane (tent.)
ethylcyclohexane (tent.)	2-methyloctane	trimethylcyclohexane iso.
trimethylcyclohexane iso. [b]	3-methyloctane	2-methyloctane
3-methyloctane	methylethylcyclohexane	3-methyloctane
butanoic acid, 2-methylpropyl ester (tent.)	propylcyclohexane	ethylmethylcyclohexane
decane, branched chain (tent.)	4-cyclohexadecane (tent.)	alkylcyclohexane (tent.)
4-methylnonane		alkane, branched
1,2,4-trimethylbenzene (tent.)		n-undecane
1-ethyl-2-methylbenzene (tent.)		alkylcyclohexane
trimethylbenzene iso.		

Hardware Store #1	Hardware Store #2	Beauty School #1
1,2-pentadiene (tent.)	trichlorofluoromethane	trichlorofluoromethane
methylcyclopentane	pentene iso.	pentadiene
2-methylhexane	alkane (tent.)	2-ethylcyclobutanol (tent.)
3-methylhexane	alkane (tent.)	cyclic alkene or diene (tent.)
methylethylhexane (tent.)	hexane	n-undecane
ketone (tent.)	methylcyclohexane (tent.)	
2-methylheptane	dimethylpentane (tent.)	
3-methylheptane (tent.)	methylhexane	
acetic acid, 2-methylpropyl ester	branched alkane	
aldehyde or ketone (tent.)	branched alkane	
1,3,5-trimethylcyclohexane	alkyl cyclopentane (tent.)	
2-methyloctane (tent.)	branched alkane	
3-methyloctane	alkyl cyclohexane	
trans-1-ethyl-4-methylcyclohexane (tent.)	trimethylcyclohexane	
methylnonane iso. (tent.)	methyloctane iso.	
(1-methylethyl)-benzene	methyloctane iso.	
methylnonane iso. (tent.)	branched alkene iso.	
trimethylbenzene iso. (tent.)	alkyl cyclohexane	
1,3-cyclopentadiene,5-(1-methyl-propylidene) (tent.)	alkane, branched	
ketone (tent.)	alkane, branched	
	alkane, branched	

Beauty School #2	Swimming Pool	Laundromat
With Perma Pure Dryer:		
trichlorofluoromethane	dimethyl disulfide (tent.)	ester (tent.)
pentadiene (tent.)		
decane, branched (tent.)		
decane, branched (tent.)		
undecane, branched (tent.)		
alkane, branched		
alkane, branched		
Without Perma-Pure Dryer:		
acetic acid, anhydride (tent.)		
acetic acid, butyl ester		

[a] tent. = Tentative GC/MS identification.
[b] iso. = Isomer.

Table 6. *Qualitative Results of the GC/MS Analysis of Product Headspace Samples for α-Pinene and Limonene*

Product Name	α-Pinene	Limonene	Potential Interfering Compounds
Pine-Sol® (19% pine oil)	Present	Present	Many
Airwick® Solid Room Deodorizer (lemon scent)	Present	Present	Many
Wood Plus® Polish (lemon scent)	Present	Present	Few
Johnny Fresh® Bathroom Bowl Cleaner (pine scent)	Absent	Absent	-[a]
Old English® Furniture Polish	Absent	Absent	-
Renuzit Roomate® Liquid Air Freshner	Present	Present	Many

[a] *Not applicable since target compounds were absent.*

Table 7. *Air Concentrations (μg/m³) in Microenvironmental Screening Tenax Samples*

Compound	Furniture Stripping Shop	Hardware Store No. 1	Wood Shop
n-Octane	26	29	110
m,p-Xylene	280	620	180
Styrene	35	15	3
o-Xylene	110	230	80
n-Nonane	71	110	730
α-Pinene	11	24	34
p-Dichlorobenzene	2	3	ND[a]
n-Decane	120	100	770
Limonene	2	5	12
n-Dodecane	25	1	68

[a] *ND = not detected.*

Table 8. *Participant Characteristics and Approximate Alveolar Spirometer Breathing Rates*

Participant Number	Sex	Age	Height	Weight	Alveolar Spirometer Breathing Rate (breaths/min)
1	Male	35	178 cm	82 kg	4.8
2	Male	31	168 cm	57 kg	5.2
3	Male	32	185 cm	79 kg	5.6
4	Female	25	180 cm	61 kg	8.0

time associated with the first compartment have been possible, due to the slow cycle time (20 minutes) of the breath sampling system then available. However, indirect observations from these chamber studies, and theoretical considerations using the model above with observed chemical and biological data, have suggested that the residence time associated with the first compartment (the blood) is very short (on the order of a few minutes for very volatile compounds, and 25-30 minutes for relatively nonvolatile compounds such as tetrachloroethylene.

In view of the 4-hour sampling period for the post-exposure breath measurements, it is expected that only the first two (or possibly three) compartments would be observable in the decay curves. Therefore a simple biexponential curve was fit to both the alveolar and whole breath data. As a check, other types of curves were also fit to the data, including single exponential, inverse, logarithmic, and power functions. In all cases, the biexponential curve provided the best fit, with typical R^2 values of 99.9% (Figure 2).

The half-lives calculated from the one- and two-compartment models are displayed for alveolar breath (Table 9) and whole breath (Table 10). (The half-life is the product of the residence time and the natural logarithm of 2.) The half-lives calculated for the first compartment in the two-compartment model are 2-20 minutes, in excellent agreement with the values predicted earlier. The half-lives for the second compartment are typically 1-3 hours, again in good agreement with previously measured values.

No consistent correlation of measured half-lives with exposure level was noted.

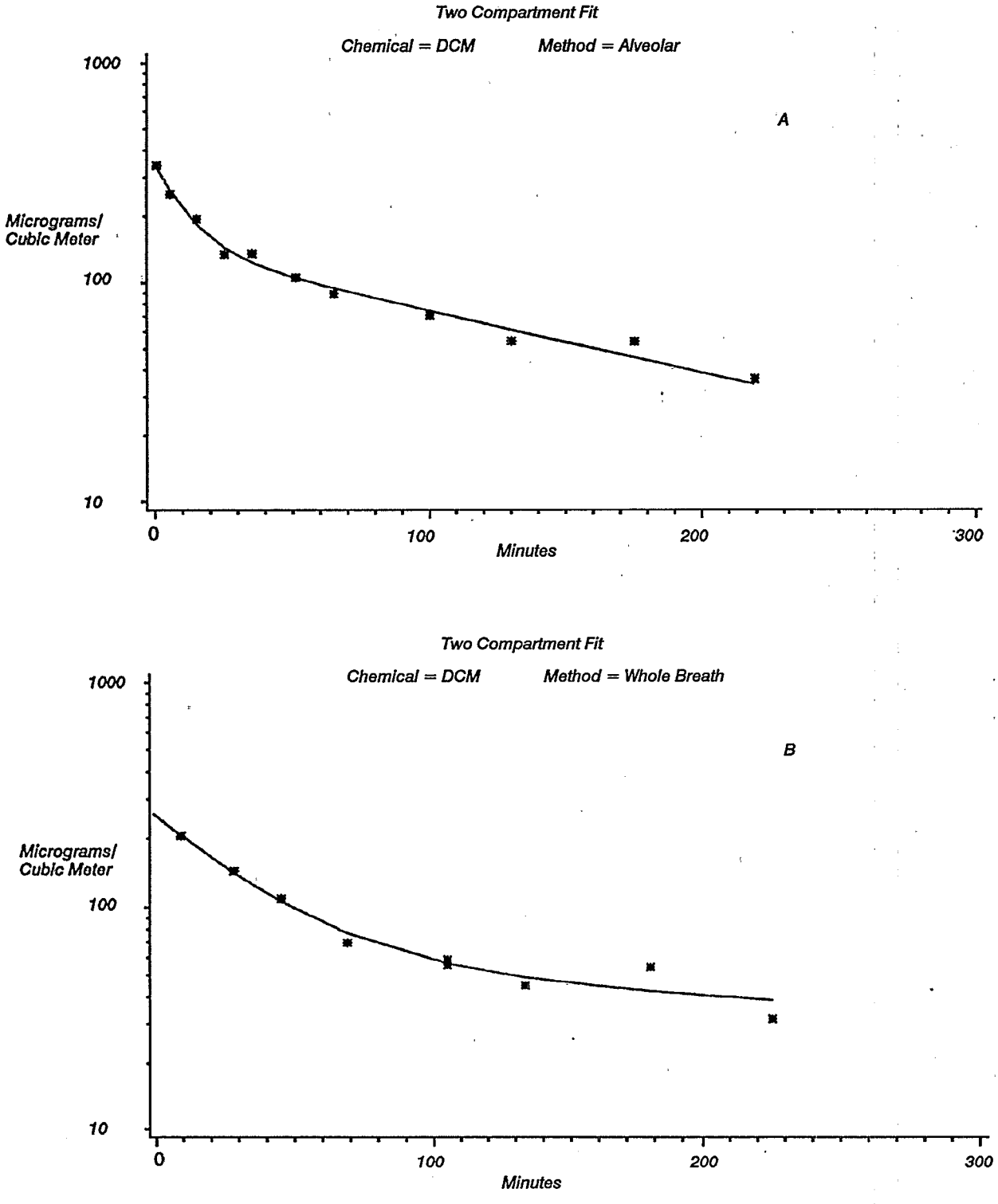

Figure 2. *Ln-linear display of decay data measured for dichloromethane in alveolar (A) and whole (B) breath. The solid curve indicates a curve defined by data showing an ideal fit to a two compartment model.*

Table 9. *Calculated Half-Lives for Halogenated Hydrocarbons in Alveolar Breath*

Compound	Exposure Conc. ($\mu g/m^3$)	Participant	One Compartment Model	Two Compartment Model	
			One Compart. $t_{1/2}$ (h)	First $t_{1/2}$ (h)	Second $t_{1/2}$ (h)
Halogenated Hydrocarbons					
Vinylidene chloride	56	1	2.97	0.12	11.60
Dichloromethane	5000	1	0.60	0.13	1.80
Dichloromethane	470	2	0.40	0.10	1.07
Dichloromethane	460	1	1.07	0.78	IC [a]
Dichloromethane	320	3	1.65	0.08	1.14
Dichloromethane	220	4	1.86	0.17	2.07
Chloroform	600	2	0.72	0.08	1.58
1,1,1-Trichloroethane	16000	1	0.88	0.10	1.90
1,1,1-Trichloroethane	340	2	1.33	0.13	2.60
1,1,1-Trichloroethane	200	2	4.30	0.00	3.81
1,1,1-Trichloroethane	200	1	0.99	0.17	3.18
1,1,1-Trichloroethane	200	4	3.39	0.17	6.08
1,1,1-Trichloroethane	140	1	1.00	0.08	1.80
Trichloroethylene	77	1	0.65	0.20	IC
Tetrachloroethylene	280	2	2.42	0.18	3.70
Tetrachloroethylene	190	3	0.85	0.11	1.67
Tetrachloroethylene	150	4	2.06	CF [b]	CF

[a] *IC = insufficient concentration change; model reflects insufficient change in concentration to calculate a half-life over this time interval.*
[b] *CF = convergence failure; residuals failed to converge in 50 steps during iterative computation.*

Calculated Half-Lives for Aromatic Hydrocarbons in Alveolar Breath

Compound	Exposure Conc. ($\mu g/m^3$)	Participant	One Compartment Model	Two Compartment Model	
			One Compart. $t_{1/2}$ (h)	First $t_{1/2}$ (h)	Second $t_{1/2}$ (h)
Aromatic Hydrocarbons					
Benzene	430 [a]	1	1.68	0.14	3.38
Toluene	5700	1	0.82	0.10	1.82
Toluene	1200 [a]	1	1.84	0.05	2.64
Toluene	640	2	1.53	0.07	1.88
Toluene	640	1	1.06	0.08	1.68
Toluene	510	1	1.15	CF [b]	CF
Toluene	460	3	1.13	0.05	4.05
Toluene	320	2	0.52	0.27	3.23
Toluene	280	4	1.64	CF	CF
Ethylbenzene	2600 [a]	1	2.46	0.03	2.90
Ethylbenzene	360	2	0.22	0.08	2.12
Ethylbenzene	150	2	1.70	0.04	2.49
Ethylbenzene	150	1	1.02	0.08	1.43
m,p-Xylene	1700 [a]	1	1.60	CF	CF
m,p-Xylene	1600	2	0.92	0.03	1.10
m,p-Xylene	560	2	0.64	0.13	2.42
m,p-Xylene	560	1	0.45	0.11	2.15
m,p-Xylene	230	3	0.08	0.03	2.16
m,p-Xylene	160	4	0.58	0.08	2.12
o-Xylene	700 [a]	1	0.67	0.11	2.94
o-Xylene	440	2	0.25	0.08	1.17
o-Xylene	190	2	1.61	0.04	9.95

[a] *Exposure concentrations from the garage experiments are approximate.*
[b] *CF = convergence failure; residuals failed to converge in 50 steps during iterative computation.*

Table 9 (continued) Calculated Half-Lives for Aliphatic Hydrocarbons in Alveolar Breath

Compound	Exposure Conc. ($\mu g/m^3$)	Participant	One Compartment Model: One Compart. $t_{1/2}$ (h)	Two Compartment Model: First $t_{1/2}$ (h)	Two Compartment Model: Second $t_{1/2}$ (h)
Aliphatic Hydrocarbons, Straight-Chain					
n-Pentane	3400 [a]	1	0.70	0.08	2.34
n-Pentane	340	1	1.15	0.07	2.07
n-Octane	320 [a]	1	0.67	0.19	2.84
n-Octane	39	2	0.87	0.17	IC [b]
n-Nonane	12000 [a]	1	1.37	0.02	1.73
n-Nonane	210	2	1.13	0.06	2.01
n-Nonane	210	1	0.68	0.15	2.06
n-Nonane	180	2	0.08	0.02	0.48
n-Nonane	130	3	0.21	0.04	1.53
n-Nonane	110	4	0.61	CF [c]	CF
n-Decane	14000 [a]	1	1.54	0.37	16.40
n-Decane	360	2	0.22	0.08	1.39
n-Decane	360	1	0.17	0.04	1.06
n-Decane	260	2	0.08	0.07	IC
n-Decane	210	3	0.27	0.19	2.82
n-Decane	170	4	0.11	0.05	IC
n-Undecane	5600 [a]	1	0.28	0.07	1.36
Aliphatic Hydrocarbons, Branched-Chain					
Isopentane	10000 [a]	1	0.65	0.08	2.33
2-Methylpentane	2000 [a]	1	0.86	0.21	3.18
2-Methylhexane	340 [a]	1	0.26	0.13	3.16
3-Methylhexane	410 [a]	1	0.39	0.13	2.54
3-Methylhexane	39	1	0.42	CF	CF
2-Methyloctane	5400 [a]	1	0.60	0.28	2.48
Ethylcyclohexane	900 [a]	1	0.89	0.19	2.53

[a] *Exposure concentrations from the garage experiments are approximate.*
[b] *IC = insufficient concentration change; model reflects insufficient change in concentration to calculate a half-life over this time interval.*
[c] *CF = convergence failure; residuals failed to converge in 50 steps during iterative computation.*

Also, no clear differences in measured half-lives among the participants could be discerned. However, the data are quite limited for this purpose.

Alveolar Values Compared to Whole Breath

Since deadspace air volume is usually considered to be about a third of the volume of a normal breath, a simplistic assumption would suggest that the alveolar concentrations measured in this study would be about 50% higher than the whole breath concentrations. However, a comparison of alveolar to whole breath concentrations displayed the anticipated behavior for only two or three of 16 VOCs (Table 11). The reasons for this are presently not clear; however, it is important to determine the relation between alveolar and whole breath samples in order to interpret more meaningful the whole breath measurements made in previous TEAM Studies. The relative impact of factors such as changed breathing patterns resulting from the increased effort of forced expiration or the effect of time lapse between inhalation of clean air and expiration need further investigation using controlled experimental conditions and a rigorous quality assurance program.

Summary and Conclusions

A new portable alveolar breath sampling method suitable for environmental (ppb) concentrations of many VOCs has been developed and tested in the laboratory and in field experiments. The system can be carried and set up by a single technician, requires no power, and collects 98-99% alveolar breath samples in 1-2 minutes from untrained participants of any age above 5. Organic compounds more volatile than *n*-dodecane are recoverable with 95+% efficiency. Less volatile compounds can also be measured using a slightly longer (2 minutes) conditioning period. The ability to collect many samples in rapid succession following exposure should greatly improve our understanding of the uptake and decay characteristics for a large number of VOCs.

Thirty-two common microenvironments (homes, cars, garages, shops) were screened for elevated concentrations of 24 VOCs. Many of these microenvironments were found to have elevated concentrations of multiple VOCs. Six microenvironments were selected for exposure studies involving four volunteers. Breath concentrations of 21 VOCs were sufficiently elevated to allow calculating residence times in the blood and a second compartment of the body. These measurements are among the first that have allowed direct observation of decay times for blood concentrations resulting from exposure to common environmental sources. The measured decay times agree well with theoretical predictions of a pharmacokinetic model developed in conjunction with earlier TEAM Study results.

Table 10. *Calculated Half-Lives for Aromatic and Halogenated Hydrocarbons in Whole Breath*

Compound	Exposure Conc. ($\mu g/m^3$)	Participant	One Compartment Model: One Compart. $t_{1/2}$ (h)	Two Compartment Model: First $t_{1/2}$ (h)	Two Compartment Model: Second $t_{1/2}$ (h)
Aromatic Hydrocarbons					
Benzene	430 [a]	1	1.30	0.46	4.12
Toluene	5700 [a]	1	1.03	0.32	2.28
Toluene	1200	1	1.24	0.31	1.86
Toluene	320	2	1.03	CF [b]	CF
Ethylbenzene	2600 [a]	1	1.25	0.48	2.45
Ethylbenzene	360	2	0.95	0.25	2.17
m,p-*Xylene*	1700 [a]	1	1.06	0.52	4.98
m,p-*Xylene*	1600	2	1.05	0.18	1.60
m,p-*Xylene*	240	1	0.55	0.25	2.52
o-*Xylene*	700 [a]	1	1.21	0.53	6.02
o-*Xylene*	440	2	0.93	0.08	1.48
Halogenated Hydrocarbons					
Dichloromethane	5000	1	0.95	0.40	7.98
Dichloromethane	470	2	0.55	0.33	5.40
1,1,1-Trichloroethane	340	2	1.33	1.38	IC [c]
1,1,1-Trichloroethane	140	1	1.10	0.52	IC
Tetrachloroethylene	280	2	2.13	1.68	IC
p-*Dichlorobenzene*	9400	2	1.57	0.53	21.00

[a] *Exposure concentrations from the garage experiment are approximate.*
[b] *CF = convergence failure; residuals failed to converge in 50 steps during iterative computation.*
[c] *IC = insufficient concentration change; model reflects insufficient change in concentration to calculate a half-life over this time interval.*

Calculated Half-Lives for Aliphatic and Cyclic Hydrocarbons in Whole Breath

Compound	Exposure Conc. ($\mu g/m^3$)	Participant	One Compartment Model: One Compart. $t_{1/2}$ (h)	Two Compartment Model: First $t_{1/2}$ (h)	Two Compartment Model: Second $t_{1/2}$ (h)
Aliphatic Hydrocarbons, Straight-Chain					
n-*Pentane*	3400 [a]	1	0.88	0.26	2.32
n-*Octane*	320 [a]	1	0.95	0.00	0.61
n-*Nonane*	12000 [a]	1	0.74	0.42	5.55
n-*Decane*	14000 [a]	1	0.88	0.00	0.88
n-*Undecane*	5600 [a]	1	0.86	0.19	1.61
Aliphatic Hydrocarbons, Branched-Chain					
Isopentane	10000 [a]	1	0.89	0.24	2.85
2-Methylpentane	2000 [a]	1	1.02	0.26	2.25
2-Methylhexane	340 [a]	1	0.87	0.29	3.47
3-Methylhexane	400 [a]	1	0.88	0.31	3.57
2-Methyloctane	5400 [a]	1	0.96	0.57	5.20
Cyclic Hydrocarbons					
Ethylcyclohexane	900 [a]	1	0.99	0.40	6.64
α-Pinene	97	2	0.79	0.13	1.60
Limonene [b]	160	2	0.16	0.33	58.70

[a] *Exposure concentrations from the garage experiments are approximate.*
[b] *Participant was exposed to limonene at the end of the period over which breath samples were provided.*

Table 11. *Percent Difference Between Alveolar and Whole Breath Organic Compound Concentrations at 12, 60, and 185 Minutes Post-Exposure* [a]

Compound	12 Min Concentrations		60 Min Concentrations		185 Min Concentrations		(Alveolar-Whole)/ Alveolar		
	Whole	Alveolar	Whole	Alveolar	Whole	Alveolar	T=12	T=60	T=185
Isopentane	180	140	71	64	38	42	-28.6	-10.9	9.5
n-Pentane	99	87	42	43	19	26	-13.8	2.3	26.9
2-Methylpentane	50	66	25	29	12	15	24.2	13.8	20.0
2-Methylhexane	44	38	11	13	8.8	7.5	-15.8	15.4	-17.3
3-Methylhexane	27	25	11	9.2	6.3	5.7	-8.0	-19.6	-10.5
Benzene	24	17	13	10	6.2	6.5	-41.2	-30.0	4.6
Toluene	40	35	22	23	8.8	15	-14.3	4.3	41.3
n-Octane	8.6	5.4	4.3	2.4	1.5	1.5	-59.3	-79.2	0.0
Ethylcyclohexane	20	24	9	11	4.9	5.5	16.7	18.2	10.9
3-Methyloctane	120	131	62	52	25	16	8.4	-19.2	-56.3
Ethylbenzene	38	36	21	26	8.5	17	-5.6	19.2	50.0
p-Xylene	23	27	11	18	4.7	7.3	14.8	38.9	35.6
n-Nonane	230	154	90	90	37	50	-49.4	0.0	26.0
o-Xylene	8.5	8.6	4.6	4.1	1.9	2.6	1.2	-12.2	26.9
n-Decane	160	143	71	83	28	55	-11.9	14.5	49.1
n-Undecane	36	61	15	23	6	11	41.0	34.8	45.5

[a] *Concentration ($\mu g/m^3$) for whole breath at 12 and 185 minutes and alveolar breath at 60 minutes were as measured. The corresponding data point in whole or alveolar breath was calculated using the equation of best fit from StatPlan as in Table 6-10 or 6-12.*

Both alveolar and whole breath samples were collected into 6 L canisters and analyzed in the same manner.

Recommendations

The breath sampling method could be further miniaturized. Additional VOCs commonly found in breath (e.g., ethane and acetylene) should be tested for applicability to this method. Extension of the method to polar compounds would also be desirable. Investigating more fully the factors affecting the fraction of whole breath represented by alveolar air will enable the whole breath measures collected in previous TEAM Studies to be better interpreted. Additional study of VOC concentrations in other common microenvironments will help fill in our knowledge of how and where people are exposed to VOCs. Additional exposure and breath decay experiments for the same and additional VOCs will provide information needed to estimate exposures from breath measurements and vice versa. The effect of physiological characteristics (body build, exercise, breathing rate, etc.) on residence time in the blood and other compartments should be studied. The pharmacokinetic model should be tested on a set of different participants exposed to the same chemicals to determine the usefulness of the model.

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The complete report, entitled "Measurements of Exhaled Breath Using a New Portable Sampling Method," (Order No. PB 90-250 135/AS; Cost: $39.00, subject to change) will be available only from:

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