Applied Industrial Hygiene

ISSN: 0882-8032 (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/uaph20

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To cite this article: Michael S. Morgan , Mark H. Litzinger & Stuart T. Cordts (1988) Design and Laboratory Evaluation of a Breath Sampling Respirator for Organic Solvent Biological Monitoring, Applied Industrial Hygiene, 3:2, 41-46, DOI: 10.1080/08828032.1988.10388507

To link to this article: https://doi.org/10.1080/08828032.1988.10388507

Design and Laboratory Evaluation of a Breath Sampling Respirator for Organic Solvent Biological Monitoring

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A modified half-face air purifying respirator was developed as a technique for large-scale monitoring that will be acceptable to workers, simple to apply, and relatively sensitive. Exhaled air was directed through the respirator exhaust port and then through a two-part cartridge. The first part contained four layers of activated charcoal cloth which adsorbed organic solvent vapors; the cloth was subsequently desorbed for standard gas chromatographic analysis. The second part contained 70 g of 8–12 mesh molecular sieve whose weight gain was proportional to the volume of air exhaled. The proportionality was determined by independent measurement of volume in subjects while at rest and while exercising. Controlled atmospheres containing toluene at relative humidities near saturation were passed through the cartridge at steady flows equal to resting human ventilatory rates. Toluene recovery was 70 percent for simulated breath concentrations of 0.75 mg/m³ to 60 mg/m³. Nine adult males volunteered to breathe toluene in air at 40 ppm for four hours (TLV = 100 ppm TWA). About 18 hours later, their breath was sampled to simulate a worksite measurement at the start of the next shift. Samples of at least 140 liters were taken from each subject, and the mean exhaled concentration was 344 µg/m³ (0.23% of exposure TWA), in good agreement with literature reports using more complicated methods not appropriate for field application. The device can be used to collect samples of up to 300 liters in 30 minutes, and its sensitivity and selectivity are then limited only by the desorption and analysis of the charcoal adsorbent. The lower limit of quantitation for toluene, with conventional GC analysis, was about 65 µg/m³ (18 ppb). The technique can be applied to most solvents capable of adsorption on charcoal and will permit sampling large numbers of workers with minimal job disruption. **Morgan, M.S.; Litzinger, M.H.; Cordts, S.T.: Design and Laboratory Evaluation of a Breath Sampling Respirator for Organic Solvent Biological Monitoring. Appl. Ind. Hyg. 3:41–46; 1988.**

Introduction

Among methods available for biological monitoring, exhaled breath analysis offers potential advantages as it is less intrusive than drawing blood and gives a better reflection of blood composition than does urinalysis. However, breath analysis has not become widespread in the workplace because of practical problems in sampling large numbers of workers and in interpreting the results. Because concentrations of contaminants in exhaled air are low and the air is moist, previous research has relied either on elaborate and expensive equipment or on sampling methods subject to moisture-related loss of contaminant. Further, evaluating the results of breath sampling requires consideration of the complex excretion kinetics of most volatile compounds and of the effects of respiratory dead space on the composition of exhaled breath. The last point has led to efforts to sample alveolar air, requiring much cooperation from the worker. This study addresses some of these problems. A portable, simplified breath sampling system has been developed which is suitable for mass screening, is capable of collecting a relatively large sample, and gives good performance in sampling moist air.

The primary value in breath sampling lies in the fact that alveolar gas is very nearly in equilibrium with arterial blood.[1] Mixed expired air, however, is not equal in composition to alveolar air because of the addition of air from the respiratory dead space. Nevertheless, for samples taken over periods of ten minutes or more, such that all the expired air is collected and its volume measured, there is usually a predictable relationship between alveolar and mixed expired air, so that the latter can still be used to make estimates of the blood levels of trace compounds.[1–3] A more serious problem in sampling either alveolar or mixed expired air is the effect of the passage of time after exposure has ended. Models and experimental measurements of excretion kinetics of volatile compounds have shown that within two to four hours after the end of exposure, the breath levels decrease rapidly and are strongly correlated with the concentration in the inhaled air at the end of exposure.[4–6] At longer times post-exposure, the breath levels are less time dependent and are more closely proportional to the time-weighted average expo-

Supported by Grant No. 5 R01 OH01490-02 from the National Institute for Occupational Safety and Health.

sure, or body burden, of the compound.[5] The goal of this work was to design and demonstrate a field-portable technique for sampling mixed expired air at times long after exposure, when the breath level is indicative of body burden. The use of mixed expired air represents a concession to the need for simplicity in sampling, but the method should still give a result useful in biological monitoring. The sampling method was demonstrated in human volunteers long after a relatively low inhalation exposure (20% of the time-weighted average threshold limit value, TLV) as a severe test of performance.

Materials and Methods

Sampler Design and Performance

The sampler is based on a half-face, dual-cartridge respirator whose inhalation ports are fitted with standard air purifying elements.[7] On the exhalation port is mounted a special cartridge for sampling exhaled air. The operating principle of this cartridge is based on 1) quantitative adsorption of organic vapors and subsequent analysis by standard methods and 2) determination of the air volume sampled by taking advantage of the nearly invariant concentration of water vapor in expired air among individuals over a wide range of activity levels.[8,9]

The sampling cartridge is shown in cutaway view in Figure 1. The upper section contains four layers of activated charcoal cloth mounted in pairs separated by Teflon gaskets. This adsorbent is a woven material having properties similar to granular charcoal, except that its collection performance, based on studies with volatile anesthetics, is reported to be much better at high water vapor content.[10] The lower section contains 70 g of 8–12 mesh molecular sieve of 3 Å pore size which collects the water vapor. The organic vapors collected on the charcoal cloth were recovered by desorption in 10 ml carbon disulfide for one hour. The eluent was analyzed by gas chromatograph using a flame ionization detector following recommended procedures.[11] Generally, the cloth layer pairs were analyzed separately to permit detection of breakthrough past the first pair of layers. The collected water vapor was determined gravimetrically. The sampling cartridge dimensions are also shown in Figure 1. It was fabricated from polyvinyl chloride pipe with stainless steel screens to retain the adsorbents. The loaded cartridge weighed about 180 g and thus, added about 60 percent to the weight of the respirator. Resistance to airflow through the cartridge was not more than 2 cm H_2O/L/s at flow rates up to 1 L/s.

The sampling cartridge was tested for recovery efficiency with controlled atmospheres designed to simulate human breath containing low levels of organic vapor. Toluene was selected for this study because it is used in large quantities in industry and because studies of its toxicokinetics have been reported by several authors.[2,12–15] The atmospheres were generated in a 90-liter glass mixing chamber equipped with a cooled-mirror dew point hygrometer and a photoionization detector. Compressed breathing quality air was passed through a high efficiency filter and a bed of granular charcoal before entering the chamber at 40 lpm. Water was atomized into the chamber, and liquid toluene was metered via motor-driven syringe through a heated metal tube. Both relative humidity (RH) and solvent concentration were monitored continuously. The generator was capable of producing stable atmospheres at between 5 percent and 95 percent RH and containing between 0.1 ppm and 400 ppm of toluene. Recovery data were obtained over a range of RH and air temperatures, whose selection was based on preliminary measurements of the air stream leaving respirators while being worn. Cartridges were challenged at toluene levels between 0.75 mg/m³ (0.20 ppm) and 150 mg/m³ (40 ppm), based on the results of toxicokinetic studies.

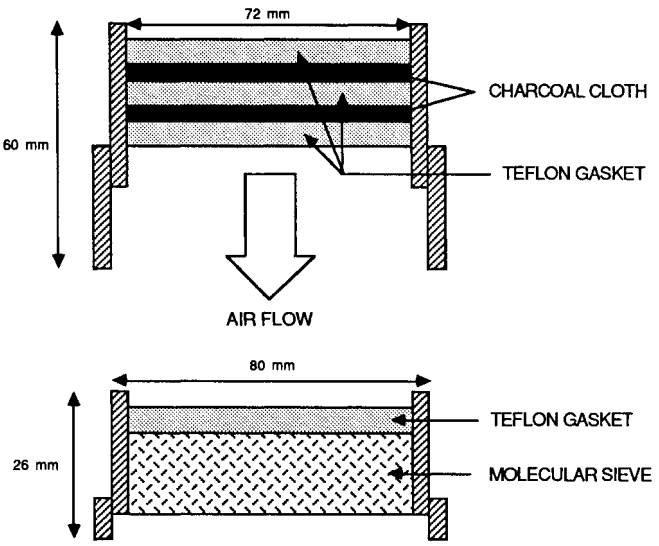

FIGURE 1. Cutaway view of the breath sampling cartridge showing the upper section for organic solvent vapor collection and the lower section for moisture collection; the two sections nest tightly together when in use. The upper section is threaded to fit a standard respirator cartridge holder which is mounted in the exhaust port of the mask.

To determine the relationship between water vapor collected and the volume of expired air sampled, a group of six volunteers wore the respirator while at rest or while walking on a treadmill at various work rates. Expired air was passed through the sampling cartridge in series with a calibrated pneumotachometer. The flow signal from the pneumotachometer was integrated electronically to give an accurate measurement of air volume. The weight gain of the molecular sieve in the cartridge was then compared to the independent measurement of volume. The sampling periods were between 14 and 20 minutes.

Performance in Controlled Human Exposures

As a demonstration of the device under realistic conditions of use, nine male volunteers were exposed to 150 mg/m³ (40 ppm) toluene at 50 percent RH for four hours using the generator described above. After giving informed consent, each subject was sampled for the baseline level of toluene in expired breath. Then toluene-laden air from the generator was passed through a mask covering the subject's nose and mouth at 35 lpm. Between 17 and 20 hours later, corresponding to the start of the next work shift, a breath sample was taken and analyzed. The sampling procedure consisted of first wearing the respirator without the special sampling cartridge for seven to ten minutes to allow air temperature and RH inside the mask to stabilize. Then the sampling cartridge was attached, and the subject continued to breathe at rest for 15 to 20 minutes. The cartridge was then disassembled, and the adsorbents were analyzed within one hour. Routine sampling of laboratory ambient air indicated that toluene levels were always less than 10 μg/m³.

The observed breath concentrations were corrected for the dilution effect of the respirator cavity dead space. In a separate experiment, the correction factor for each subject was estimated by measuring the concentration of carbon dioxide in mixed expired air collected 1) at the respirator outlet port and 2) at the mouth. It was assumed that the dilution of expired carbon dioxide by the respirator dead space approximates closely the dilution of expired trace organics.

TABLE I. Recovery of Toluene from Charcoal Cloth

Toluene Concentration (mg/m³)	Temp (°C)	RH (%)	No. of Layers	% Recovery[A]
0.75	22	80	4	69.1 ± 6.2 (n = 7)
1.30	30	90	4	63.6 ± 7.5 (n = 6)
2.00	30	90	4	70.5 ± 7.5 (n = 6)
7.4	22	80	4	68.8 ± 5.2 (n = 5)
60.0	22	80	6	67.0, 70.0 (n = 2)
150.0	22	80	6	38.0, 25.0[B] (n = 2)

[A]Mean ± standard deviation (no. of replicate runs).
[B]Breakthrough detected on second pair of layers in each replicate run.

Results

Recovery of toluene from the charcoal cloth at a range of simulated breath concentrations is shown in Table I. At concentrations up to 60 mg/m³ (16 ppm), the recovery was between 60 and 70 percent. The recovery dropped at higher concentrations, presumably due in part to breakthrough. At 60 mg/m³ or less, the recovery precision was good, indicating that sample results can be corrected for recovery efficiency with reasonable confidence.

The results for the comparison of exhaled air volume and water vapor collected are given in Figure 2. There was a good correlation between the two, despite the fact that among the subjects there was considerable variation in tidal volume, breathing pattern, and rate of ventilation (ventilatory rates were between 4.0 and 28.3 lpm). The data suggest that there is a simple, reliable relationship between weight gain of the dessicant and exhaled volume which can be applied as the calibration for the sampler when used under the conditions described. From linear regression, this calibration is

$$\text{Moisture gain (g)} = 0.0268 \times \text{Expired volume (L)} + 0.73\ \text{g}.$$

The correlation coefficient (r) was 0.9789.

When the subjects' breath was sampled 17 to 20 hours after exposure, toluene was readily quantitated in each, while no toluene was detected in background breath samples and blanks. In the post-exposure samples, the amount of toluene found on the second pair of layers was less than 5 percent of the total recovered. Table II summarizes the results for all subjects and indicates the range of sample volumes and resulting toluene concentrations, corrected for recovery efficiency and for respirator dead space. With one exception, the toluene levels were very consistent, giving an overall mean exhaled concentration that was 0.23 percent of the exposure concentration inhaled the previous day.

The dead space correction factor, $C_{mouth}/C_{respirator}$, ranged from 1.10 to 1.46 with a mean of 1.31 and a standard deviation of 0.11. That is, the carbon dioxide in mixed expired air collected at the mouth was on average 31 percent higher than the level in air collected at the respirator outlet. The effective dead space of a face mask clearly will depend on geometric factors (mask and face shapes), but it also is reported to increase in an individual when the tidal volume is increased above about 1 liter.[21] To avoid the tidal volume effect, sampling is best done with the subject sitting at rest.

Discussion

In designing the breath sampling cartridge, the primary goal was to measure toluene in breath at the start of the next shift. This was based on the predictions from toxicokinetic models and limited experimental data, showing that one must wait at least two to four hours after the end of exposure before the breath level of solvent reflects the integrated dose over the previous shift (or shifts), rather than the most recent concentration inhaled. Since it appears impractical to ask workers to remain at work until two to four hours after the shift ends, the first chance to obtain the desired sample is 16 to 20 hours after the shift ends. Then the breath levels of solvent are expected to be less than 1 percent of the previous time-weighted average exposure concentration.[4] The sampling and analytical procedure must, therefore, have a quantitation limit that is much lower than that required of methods for sampling workroom air for contaminants at concentrations near the permissible exposure limits (PEL) or the TLV.

The performance of the sampling cartridge was satisfactory, considering the conditions employed: very moist expired air containing toluene at concentrations between 0.75 mg/m³ and 60 mg/m³, as compared to the PEL of 750 mg/m³ and the TLV of 375 mg/m³ which are usually measured at RH levels less than 75 percent. Granular forms of activated charcoal have been reported to show serious degradation in capacity and breakthrough time at RH levels above 80 percent.[16] In addition, recovery of solvents from granular charcoal is known to be adversely affected by low sampling flow rates.[17] Recovery is also lower for vapor loading as compared to liquid loading.[18,19] There are no published data on recovery of solvents from charcoal cloth, but recovery efficiency may be subject to the same effects seen in granular charcoal. Although the influences of humidity, flow rate, and other factors remain to be fully investigated in the adsorbent used in this study, the consistency of the recovery results justified their use in correcting the measurements of toluene vapor in these experiments.

The relationship between moisture collected and the volume of breath exhaled was approximately 27 mg/L. This is in good agreement with the work of others who have reported values between 25 and 31 mg/L using more sophisticated methods.[9,20] Those authors also reported that the moisture content of exhaled breath is moderately dependent on ambient temperature and RH. This effect is very small for temperature or RH above room conditions, but it becomes important below 10°C or below 20 percent RH. Under such conditions, the volume measuring por-

TABLE II. Results for 4-hour Exposure to 150 mg/m³ Toluene

Subject	Hours After Exposure	Sample Volume (L)	Breath Toluene* (mg/m³)
1	18	174	0.246
2	20	311	0.356
3	18	231	0.389
4	17	184	0.309
5	18	214	0.453
6	19	200	0.246
7	19	237	0.211
8	19	137	0.606
9	18	200	0.282
		mean	0.344
		std. dev.	0.125

*Corrected for recovery efficiency and for mask dead space.

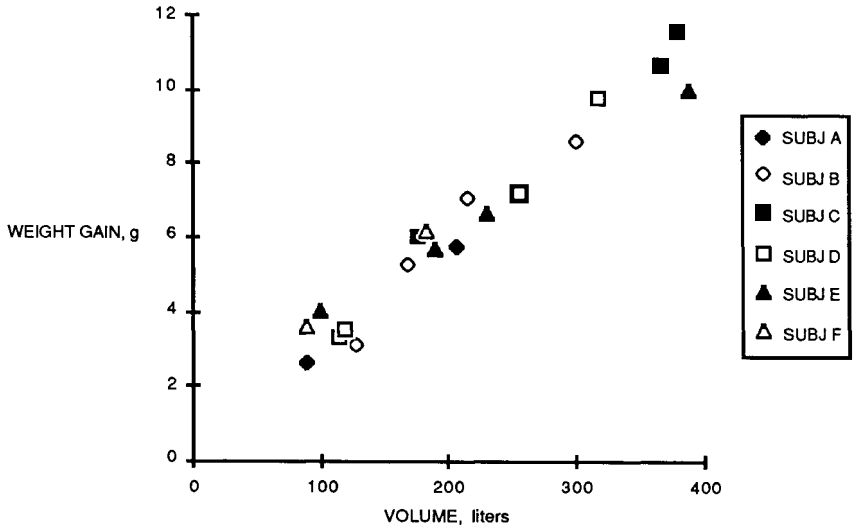

FIGURE 2. Relationship between molecular sieve weight gain and exhaled volume measured by an independent method (see text) in volunteer subjects, measured at 20°C and 40% RH ambient conditions.

tion of the breath sampler described here would have to be recalibrated.

When the sampler is used as reported in this work, the lower limit of quantitation for toluene in breath is 65 μg/m³ (0.018 ppm at room temperature). This is based on a sample volume of 240 liters, a dead space correction factor of 1.31, desorption of the cloth in 10 ml of carbon disulfide with a recovery efficiency of 70 percent, injection of 1.0 μL eluate, and a rather modest gas chromatograph quantitation limit of 0.87 ng. With the exception of dead space, each of these factors is subject to improvement so that a much better detection limit could be achieved readily. However, a breath level of 65 μg/m³ would correspond to a previous day's exposure to toluene at an eight-hour time-weighted average of about 15 mg/m³, or 4 percent of the present TLV. Thus even with moderate analytical sensitivity, relatively low exposures may be monitored with this technique.

The findings from the controlled human exposure may be compared to other published reports of breath sampling for toluene in which plastic bags, glass tubes, or more elaborate methods (not suitable for workplace screening) were used. Figure 3 shows the data from this study, corrected for dilution by the respiratory dead space (assuming a physiological dead space of 30 percent of tidal volume) and mask dead space. The figure also shows results from other studies.[2,12–15] All concentrations have been normalized to the inhaled dose calculated as the product of exposure concentration and duration. Note that only one previous study included data at 18 hours post-exposure, and that value is close to the result from this work. At earlier sampling times, the data from other studies show considerable variation. That variation might be attributed to differences in sampling technique or to variable excretion kinetics at short post-exposure times. When the breath results from all studies were normalized by the inhaled concentration (Figure 4), no improvement in agreement was noted at short times; the results of previous work and of this study at 18 hours again are in good accord. A very recent report of toluene monitoring in breath 17 hours after exposure was not included in the comparisons shown. In that study, the reported infirmary ambient toluene concentration was higher than the values found for breath samples taken in that room.[13]

The sampling method used in this work offers several advantages over other techniques. Conversely, there are some relative disadvantages which must be considered when a breath sampling program is being developed. The sampling respirator would not

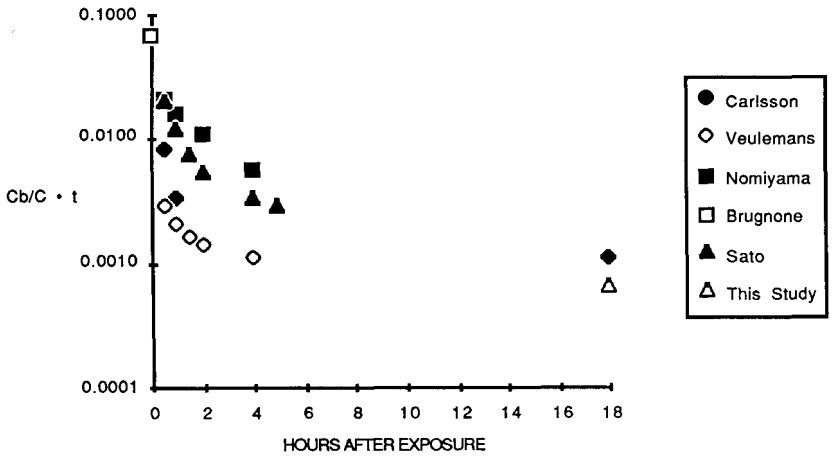

FIGURE 3. Breath toluene after exposure (Cb), normalized to dose expressed as exposure concentration (C) multiplied by exposure duration (t) in hours. Note that the ordinate is a logarithmic scale. Results are shown for this study and for five others, identified by first author of report.

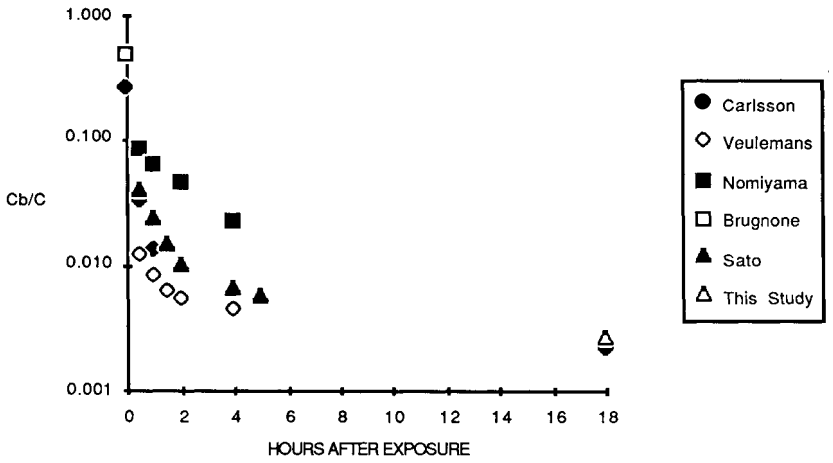

FIGURE 4. Breath toluene after exposure (Cb), normalized to exposure concentration (C). Note that the ordinate is a logarithmic scale. Results are for the same studies shown in Figure 3.

be intimidating to the majority of workers exposed to solvents, as many are undoubtedly familiar with air purifying respirators already. The sampling and analytical techniques are relatively simple and inexpensive, and thus many workers can be monitored simultaneously. The ability to sample a large volume of expired air gives the method very good sensitivity. Finally, leakage of expired air around the face seal produces no error as this lost air does not reach the adsorbent or dessicant in the cartridge. Therefore, the device measures only the volume of air from which organic vapor is also collected.

There are some features which could limit the value of this approach under certain circumstances. The sampler as described is rather heavy, and sampling for longer than 15 to 20 minutes may prove uncomfortable. Use of lighter weight materials in constructing the cartridge should reduce this problem. The need to correct for the effect of mask dead space is a disadvantage relative to use of bags or other methods permitting sampling directly at the mouth. The range of correction factors in adult males at rest was relatively narrow, however, so that using a group mean correction for dead space would have produced a maximum error of less than 15 percent in our group of subjects. The technique also does not permit the estimation of true alveolar concentration, but there is some doubt that any of the published methods could accomplish this in the field. When the features of this device are weighted, it may be an attractive means of monitoring the body burdens of volatile organic compounds in a wide variety of industries and processes.

Recommendations

In workplaces where exposure to volatile solvents occurs via inhalation or skin contact or both, and where monitoring the body burden over periods longer than one shift is desired, it is recommended that a technique such as that described here be used. The Biological Exposure Indices (BEIs), now listed in the TLV booklet, suggest that styrene (established) and benzene (proposed) may be monitored using mixed expired air sampled before the shift. Other substances, such as toluene, for which BEIs on mixed expired air have not been established, may still be suitable for longitudinal monitoring in an exposed worker population. A program based on regular mixed expired air sampling, in conjunction with air monitoring, would permit the identification of individuals showing excessive solvent absorption.[22] This could result from dermal exposure, from nonoccupational exposure, or from individual variation in uptake and disposition. Once identified, these individuals should be the subjects of further investigation.

The respirator-based technique for sampling mixed expired breath appears to be a useful method for pre-shift monitoring. Its use in practice will require measuring the efficiency of recovery from the sampling cartridge for solvents of interest. Data are available now for toluene and soon will be complete for the xylene isomers, methy ethyl ketone, and methyl isobutyl ketone. The procedure for determining recovery efficiency has been outlined above. It requires the generation of a controlled atmosphere in a fashion identical to that used to certify solvent recovery from charcoal tubes, with the controlled addition of moisture at 90 percent RH.

Once the recovery efficiency has been determined, pre-shift breath sampling may be conducted. It is recommended that workers' breath be sampled in an uncontaminated room so that background exposure does not interfere. Results should be corrected for mask dead space (the factor of 1.31 is suggested for half-face masks) to give the corresponding exhaled concentrations at the mouth.

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Received 12/1/86; review/decision 3/9/87; revision 7/7/87; accepted 7/15/87