Journal of Environmental Monitoring

Cite this: *J. Environ. Monit.*, 2012, **14**, 977

www.rsc.org/jem

**PAPER**

# Validation of evacuated canisters for sampling volatile organic compounds in healthcare settings

**Ryan F. LeBouf,* Aleksandr B. Stefaniak and M. Abbas Virji**

***Received 9th November 2011, Accepted 25th January 2012***
**DOI: 10.1039/c2em10896h**



Healthcare settings present a challenging environment for assessing low-level concentrations of specific volatile organic compounds (VOCs) in the presence of high background concentrations of alcohol from the use of hand sanitizers and surface disinfectants. The purposes of this laboratory-based project were to develop and validate a sampling and analysis methodology for quantifying low-level VOC concentrations as well as high-level alcohol concentrations found together in healthcare settings. Sampling was conducted using evacuated canisters lined with fused silica. Gas chromatography/mass spectrometry analysis was performed using preconcentration (for ppb levels) and loop injection (for ppm levels). For a select list of 14 VOCs, bias, precision, and accuracy of both the preconcentration and loop injection methods were evaluated, as was analyte stability in evacuated canisters over 30 days. Using the preconcentration (ppb-level) method, all validation criteria were met for 13 of the 14 target analytes—ethanol, acetone, methylene chloride, hexane, chloroform, benzene, methyl methacrylate, toluene, ethylbenzene, *m*,*p*-xylene, *o*-xylene, alpha-pinene, and limonene. Using the loop injection (ppm-level) method, all validation criteria were met for each analyte. At ppm levels, alpha-pinene and limonene remained stable over 21 days, while the rest of the analytes were stable for 30 days. All analytes remained stable over 30 days at ppb levels. This sampling and analysis approach is a viable (*i.e.*, accurate and stable) methodology that will enable development of VOC profiles for mixed exposures experienced by healthcare workers.

## Introduction

Recent epidemiologic studies in a range of healthcare occupations have reported increased risk of work-related asthma (WRA) associated with exposure to groups of agents such as latex, indoor air pollution, volatile organic compounds (VOCs), bioaerosols, ammonia- or chlorine-containing products, chemicals used for cleaning instruments or indoor surfaces, and aerosolized medicines.[1–6] However, much remains to be understood about specific agents and exposure levels responsible for WRA among healthcare workers. Many studies are affected to some degree by exposure misclassification due to a lack of quantitative exposure characterization. These studies have used general or asthma-specific job-exposure matrices, performance of tasks or activities, or self-reported exposures and their duration and frequency as proxies for exposure. A review by Becklake and colleagues noted the need for quantitative exposure data in studies of occupational asthma to minimize exposure misclassification and to obtain quantitative exposure-response relationships, thus supporting the development of exposure limits to minimize asthma outcomes.[7]

The current study is part of a larger epidemiologic investigation aimed at assessing exposures to agents, including cleaning and disinfecting products, that may cause or exacerbate asthma

*National Institute for Occupational Safety and Health, 1095 Willowdale Road, Morgantown, WV, USA 26505. E-mail: rlebouf@cdc.gov; Fax: +304.285.5820; Tel: +304.285.6287*

### Environmental impact

The validation of evacuated canisters for sampling volatile organic compounds (VOCs) in a mixed concentration environment is essential prior to use in exposure assessments. The current study validated a canister method for 14 VOCs at ppb and ppm concentration levels using a statistical approach from the National Institute for Occupational Safety and Health. The use of evacuated canisters may be more beneficial than traditional sorbent-based active sampling: multiple analyses may be performed on the same sample; a wide range of VOC classes may be accurately sampled and quantified; no sampling pumps are required; and samples do not require refrigerated storage.

among healthcare workers. In 2009, the authors conducted a preliminary sampling campaign at a Veterans Affairs (VA) hospital to assess chemical exposures using thermal desorption tubes for personal sampling and 6 liter (L) evacuated canisters for area sampling. Passive sampling (*e.g.*, through the use of a flow controller) into evacuated stainless steel canisters lined with fused silica allows a whole-air, time-integrated sample to be collected, provides a large volume sample for multiple analyses, and does not require a sampling pump.[9] The results of the preliminary sampling (data not published) showed that low (ppb-level) concentrations of ketones, aromatics, terpenes, and halogenated hydrocarbons were present among high (ppm-level) concentrations of alcohols. This combination of chemicals and concentrations presents a very challenging mixed exposure environment for sampling and analysis. In our preliminary sampling, thermal desorption tube sorbent was overwhelmed by the high-level concentrations of alcohols, making such tubes unsuitable for quantifying the low-level exposures in this environment. Evacuated-canister, whole-air samples also present an analytical challenge because, when alcohols are present in the air at three orders of magnitude greater signal than the other chemical constituents, the 45 *m/z* (mass-to-charge ratio) in the mass spectrometer fragmentation pattern from the alcohols can dominate and obscure signals from low-level analytes. However, evacuated canister sampling offers a uniquely suitable approach for handling this wide range of exposures because a single sample can be split for multiple analyses at both ppb- and ppm-level concentrations.

The focus of the current study was to establish and validate an evacuated canister-based (passive) sampling approach followed by preconcentration of samples (for ppb-level VOCs) and loop injection (for ppm-level VOCs) into a gas chromatograph/mass spectrometer (GC-MS). The specific objectives were to: (1) develop a sampling and analysis protocol for the characterization of a mixed concentration exposure consisting of low-level VOC concentrations in the presence of a high-level VOC background (*i.e.*, alcohols); and (2) statistically validate the sampling and analysis methods used in the protocol per NIOSH method development guidelines.[8]

## Methods

### Target analytes

A target list of 14 specific analytes of interest was selected because they are agents that contribute to asthma,[12] surrogates of exposures that contribute to asthma, or prevalent workplace exposures observed in the preliminary sampling (see Introduction). These analytes were ethanol, hexane, benzene, toluene, and alpha-pinene (Sigma-Aldrich, St. Louis, MO), acetone and methylene chloride (Fisher Scientific, Pittsburgh, PA), 2-propanol (Spectrum Chemical, Gardena, CA), chloroform, methyl methacrylate, ethylbenzene, m,p-xylene, o-xylene, and limonene (Acros Organics, Pittsburgh, PA).

### Canister samplers

Evacuated 6 L Silonite®-coated canisters (Entech Instruments, Inc.) and 400 mL Silonite®-coated Minicans™ (Entech Instruments, Inc.) were used to prepare gas-phase calibration standards. EPA Method TO-15 provided guidance for sampling and analysis of air contaminants collected in canisters.[11]

### Sample preconcentration

The canister samples require preconcentration prior to analysis in order to detect low ppb-level VOC concentrations. Air samples were concentrated prior to analysis using an Entech 7032A Autosampler (Minicans) or an Entech 7016CA (6 L canister) Autosampler with a 100 °C transfer line attached to an Entech 7100 Preconcentrator. The preconcentrator was attached to a 6890N/5973N GC-MS system (Agilent Technologies, Inc., Santa Clara, CA) with a RTX-1 capillary column 60m long × 0.32mm ID × 1μm film thickness (Restek Corporation, Bellefonte, PA). Preconcentration conditions were the following: a modified cold trap dehydration; module 1 (empty) at −20 °C, desorbed at 10 °C, and baked at 150 °C for 7 min; module 2 (glass beads) focused at −80 °C, desorbed at 180 °C, and baked at 190 °C; and module 3 (focuser) focused at −150 °C. The loop injection (for ppm levels) followed the same parameters with a 1 mL loop flushed onto the traps.

### Instrument setup

Gas chromatograph analysis conditions were set as follows: the oven temperature program was set to 35 °C for 2 min, followed by 8 °C $min^{-1}$ ramp to 170 °C and then 20 °C $min^{-1}$ ramp to a final temperature of 220 °C, which was held for 3 min; injector temperature was set to 250 °C with a 20 : 1 split (split flow 20.2 mL $min^{-1}$); detector temperature was set to 280 °C; and column flow rate was set to 1 mL $min^{-1}$. Mass spectrometer analysis conditions were set as follows: scan mode to 35–350 amu to capture alcohols; threshold at 150; scan speed at 2.84 scans/s; solvent delay to 4.5 min; source temperature at 230 °C; and quadrapole temperature at 150 °C.

### Quality assurance and quality control

Quality assurance/quality control (QA/QC) protocols were established to ensure analytical system stability and data integrity. Bromofluorobenzene was used to monitor instrument response over time. MS tuning and calibration curves were analyzed periodically to ensure sample analysis stability. A one-point calibration check standard (10 ppb), bromofluorobenzene, and instrument blank (UHP nitrogen gas) were analyzed with each set of samples within a 24-hour period per EPA Method TO-15.[11]

### Data analysis

MSD Chemstation D.02.00.275 (Agilent Technologies, Inc.) was used for data acquisition. Chromatograms were integrated and the resulting data was transferred to Microsoft Excel® spreadsheets for subsequent blank correction and data handling prior to statistical analysis. Canister concentrations were calculated based on the response of the closest internal standard.

 

### Calibration

Liquid target analytes were used to produce gas standards in a 2 L glass bulb. A known gas volume from the bulb was introduced to a single 6 L canister followed by pressurization using humidified UHP nitrogen using an Entech 4600A Dynamic Diluter. For ppb-level calibration, the gas standard was introduced to the preconcentrator to yield varying concentrations using injection volumes from 25 to 500 mL. For ppm-level calibration, the protocol was the same except individual standards were produced in multiple Minicans; they were pressurized to 1.5 times atmospheric pressure to provide enough excess pressure to flush a 1 mL loop.

Internal standards (46 mL of 100 ppb bromochloromethane, 1,4-difluorobenzene, and chlorobenzene-d5; Restek Corporation) were added to the first stage of the preconcentrator during analysis to account for variability in sample preconcentration and analysis. For each analyte, response factors were calculated as the ratio of the response of the analyte to that of the internal standard, both at known concentrations. Average response factors of analyte to internal standard were used for quantifying concentrations of analytes.

### Limits of detection and quantification

For the preconcentration method used to quantify ppb levels of the target analytes, limits of detection and quantification (LOD and LOQ) for each analyte were determined with five low-level calibration spikes ranging from 0.03 to 1.1 ppb (depending on the analyte) prepared in 6 L canisters and analyzed with a nominal injection volume of 500 mL. For the loop method used to quantify ppm levels, LODs and LOQs were determined with five calibration spikes ranging from 0.1 to 2 ppm (depending on the analyte). The LOD was calculated as 3 times the standard error of the regression divided by the slope of the regression, while the LOQ was calculated as 3.33 times the LOD.[8]

### Method validation

The measurement data studied here are assumed to follow the normal distribution. Method bias, precision, and accuracy were assessed in the range of 1 to 10 ppb and 0.8 to 2 ppm following NIOSH guidelines.[8] For comparison, accuracy was also assessed using the symmetric range accuracy method.[13] Storage stability in the canisters was assessed because air concentration of a chemical in the canister may change over time due to adsorption onto internal canister walls or transformation effects within the canister.[10,11]

Bias was assessed as the ratio of the measured to the theoretical concentration

$$B_{Avg} = \sum_{i=1}^{k}\sum_{j=1}^{l}\frac{\left(\frac{C_{ij}}{\theta_{ij}} - 1\right)}{k} \quad (1)$$

where $B_{Avg}$ = average bias, k = number of concentration levels, $C_{ij}$ = $j^{th}$ of l measurements at concentration level i, $\theta_{ij}$ = $j^{th}$ theoretical or target concentration at level i (note: since individual standards were prepared at each level, the theoretical concentration may vary slightly due to final pressurization). The upper and lower 95% confidence limit ($B_{Avg} \pm 95\%CL$ in Tables 3 and 5) of the average bias was calculated (*i.e.*, ±1.96*standard error). To be acceptable either both bias limits must have an absolute value less than 0.10, or an absolute value of 0.10 must fall between the limits.

Precision was measured as the relative standard deviation and pooled across concentrations

$$S_{rx} = \sum_{i=1}^{k}\frac{f_i\ (S_{rxi})^2}{f} \quad (2)$$

where $S_{rx}$ = pooled precision as relative standard deviation, $f_i$ = degrees of freedom, equal to the number of observations minus one at the $i^{th}$ concentration, k = number of concentrations, $S_{rxi}$ = relative standard deviation of the observations at the $i^{th}$ concentration, f = sum of $f_i$ for k concentrations, and i = index for the k concentrations.

Assumption of homogeneity of precision across all concentrations for each analyte was assessed using Bartlett's test

$$\chi^2 = \frac{f\ln(S_{rx})^2 - \sum_{i=1}^{k} f_i\ln(S_{rxi})^2}{1 + \frac{1}{3\ (k-1)} + \left[\left(\sum_{i=1}^{k}\frac{1}{f_i}\right) - \frac{1}{f}\right]} \quad (3)$$

where $S_{rx}$ = pooled precision as relative standard deviation, $f_i$ = degrees of freedom, equal to the number of observations minus one at the $i^{th}$ concentration, k = number of concentrations, $S_{rxi}$ = relative standard deviation of the observations at the $i^{th}$ concentration, f = sum of $f_i$ for k concentrations, and i = index for the k concentrations. Results of Bartlett's test for homogeneity of precision across concentrations were used to determine how accuracy was calculated (see below).

For a method to meet the NIOSH "25% accuracy" criterion, the 95% confidence statistic for accuracy ($A_{0.95}$ in Tables 3 and 5) estimated with the hyperbolic approximation formula shown in eqn (4) must be below 0.25. The 95% confidence statistic for accuracy was most often estimated with the hyperbolic approximation formula for nine measurements at three concentrations shown in eqn (4):

$$A_{0.95} = 1.8\ (B_{Avg} + 1)\ \sqrt{(1.37\ S_{rx})^2} + \sqrt{(0.16\ (B_{Avg} + 1))^2 * (1.37\ S_{rx})^2 + B_{Avg}{}^2} \quad (4)$$

where $A_{0.95}$ = the upper limit or 95% confidence statistic for accuracy, $B_{Avg}$ = the average bias across the three concentrations, and $S_{rx}$ = pooled precision as relative standard deviation. However, where Bartlett's test failed to show homogeneity of precision across concentrations, the 95% confidence statistic for accuracy was estimated by substituting the highest precision value from an individual concentration ($S_{rxi}$) for the pooled estimate of precision ($S_{rx}$) in eqn (4). In addition, the highest $B_{Avg}$ from an individual concentration, which may or may not be at the same concentration level as the highest precision chosen, was used as well as adjustment of the confidence statistics for a single concentration level (*i.e.* a decrease in degrees of freedom); this results in a conservative estimate of accuracy. Regardless of the results of Bartlett's test, accuracy was also calculated using the symmetric range method for comparison, and assessed against the same "25% accuracy" criterion.[13] For each concentration

condition used to determine accuracy, percent recoveries were also calculated.

Sample storage stability at room temperature was assessed at 5 ppb and 0.6 ppm over a period of 30 days. For the 5 ppb concentration, a total of twelve 6 L canisters were stored and analyzed repeatedly on days zero, 7, 14, 21, and 30. For the 0.6 ppm concentration, 30 canisters were generated and analyzed only once according to the following schedule: 12 canisters on day zero, six canisters on day 7, and three canisters each on days 14, 21, and 30. The stability metric is bias comparing average concentration on day 30 to average concentration on day zero; the absolute value of the stability metric must be less than 0.10 to be acceptable per NIOSH guidance.[8] If the analyte is not stable for 30 days, the method is still acceptable as long as a shorter stability time is confirmed.

## Results

### Quality assurance and quality control

Stability of the GC-MS system during the canister validation study was evidenced by consistent bromofluorobenzene recoveries between runs and by 10 ppb check standard concentrations within ±10% of their theoretical value for 10 of the 14 target analytes. The other four analytes—ethanol, acetone, 2-propanol, and methylene chloride—each had measurement variability up to ±20%. Instrument blanks had an average background of 0.09, 0.22, 0.24, and 0.11 ppb for ethanol, acetone, 2-propanol, and methylene chloride, respectively. All sample and standard values for these four analytes were blank-corrected to account for background signal. Instrument blanks for the remaining 10 target analytes had no signal.

### Calibration

Average response factors and percent relative standard deviations for each of the 14 target analytes are shown in Table 1. The percent relative standard deviations of the response factors for ppm-level concentrations using the loop method were generally larger than those for ppb-level concentrations using the preconcentration method, primarily due to the different methods used to prepare standards (single aliquots from individually prepared canisters for the ppm-level measurements *vs.* multiple aliquots from a single standard for the ppb-level measurements).

**Table 1** Average response factors for target analytes

| | ppb-level ($n = 12$)[b] | | ppm-level ($n = 12$)[b] | |
|---|---|---|---|---|
| Analyte | Average | %RSD[a] | Average | %RSD[a] |
| ethanol | 0.29 | 2.3 | 0.25 | 8.3 |
| acetone | 0.39 | 4.3 | 0.43 | 8.7 |
| 2-propanol | 1.48 | 3.0 | 1.43 | 2.9 |
| methylene chloride | 1.05 | 9.2 | 1.03 | 13.9 |
| hexane | 1.27 | 2.4 | 1.21 | 3.5 |
| chloroform | 1.82 | 5.8 | 2.24 | 3.7 |
| benzene | 2.47 | 2.6 | 3.11 | 4.0 |
| methyl methacrylate | 0.22 | 2.6 | 0.25 | 8.6 |
| toluene | 0.74 | 2.6 | 0.97 | 7.3 |
| ethylbenzene | 1.20 | 4.8 | 1.09 | 8.1 |
| *m*,*p*-xylene | 0.94 | 4.3 | 1.10 | 8.1 |
| *o*-xylene | 0.98 | 4.7 | 1.17 | 9.1 |
| alpha-pinene | 0.83 | 6.7 | 1.01 | 10.7 |
| limonene | 0.45 | 5.1 | 0.47 | 20.1 |

[a] %RSD = percent relative standard deviation. [b] 6 standards, each analyzed in duplicate.

### Limits of detection and quantitation

LODs and LOQs for target analytes are listed in Table 2. LODs for ppb-level concentrations range from 0.07 ppb for 2-propanol to 0.33 ppb for acetone. LODs for ppm-level concentrations range from 0.08 ppm for o-xylene to 0.32 ppm for methylene chloride.

### Method validation

**ppb-level method.** Method bias ($B_{Avg}$), precision ($S_{rx}$), accuracy ($A_{0.95}$, estimated from the hyperbolic approximation formula), and stability results for ppb-level concentrations for each target analyte are shown in Table 3. At ppb-level concentrations, bias was acceptable for all analytes. Chloroform failed Bartlett's test of precision homogeneity; accuracy values displayed for these chemicals were conservatively estimated based on concentration-specific precision and bias values. 2-propanol failed the 25% accuracy criterion (*i.e.*, $A_{0.95} \geq 0.25$). All 14 analytes were stable (*i.e.*, less than 10% change) while stored in 6 L canisters over a period of 30 days.

Percent recoveries and relative standard deviations for ppb-level concentrations are displayed for each target analyte in Table 4. Recoveries at 10 ppb ranged from 89% for ethanol and 2-propanol to 98% for toluene. A wider range of recoveries, from 74% for methyl methacrylate to 104% for methylene chloride, were seen at 1 ppb. At 4 ppb, measured concentrations for all but two of the analytes showed a positive bias, presumably due to a systematic error in sample preparation. Relative standard deviations were generally lower at 10 ppb than at 1 ppb.

**ppm-level method.** Method bias, precision, accuracy, and stability results for ppm-level concentrations are displayed in Table 5. Bias was acceptable for all analytes. Only methylene

**Table 2** Limits of detection (LODs) and limits of quantitation (LOQs) for target analytes

| | ppb-level | | ppm-level | |
|---|---|---|---|---|
| Analyte | LOD | LOQ | LOD | LOQ |
| ethanol | 0.29 | 0.97 | 0.18 | 0.60 |
| acetone | 0.33 | 1.11 | 0.23 | 0.76 |
| 2-propanol | 0.07 | 0.23 | 0.19 | 0.63 |
| methylene chloride | 0.30 | 1.01 | 0.32 | 1.07 |
| hexane | 0.21 | 0.70 | 0.18 | 0.61 |
| chloroform | 0.19 | 0.64 | 0.27 | 0.89 |
| benzene | 0.19 | 0.64 | 0.17 | 0.55 |
| methyl methacrylate | 0.24 | 0.79 | 0.20 | 0.66 |
| toluene | 0.18 | 0.58 | 0.23 | 0.77 |
| ethylbenzene | 0.19 | 0.65 | 0.25 | 0.83 |
| *m*,*p*-xylene | 0.20 | 0.68 | 0.26 | 0.85 |
| *o*-xylene | 0.22 | 0.73 | 0.08 | 0.27 |
| alpha-pinene | 0.22 | 0.73 | 0.25 | 0.83 |
| limonene | 0.30 | 1.01 | 0.31 | 1.02 |

**Table 3** Bias, precision, accuracy, and stability results for target analytes at ppb-level concentrations[a]

| Analyte | $B_{Avg} \pm 95\%CL$ | $S_{rx}$ | $\chi^2$ | $A_{est}$ | $A_{0.05}$ | $A_{0.95}$ | Stability |
|---|---|---|---|---|---|---|---|
| ethanol | −0.093 ± 0.026 | 0.058 | 1.35 | 0.176 | 0.144 | 0.222 | −0.005 |
| acetone | −0.032 ± 0.032 | 0.064 | 5.69 | 0.137 | 0.101 | 0.186 | 0.031 |
| 2-propanol | −0.123 ± 0.036 | 0.098 | 0.36 | 0.231 | 0.189 | **0.289** | 0.078 |
| methylene chloride | 0.029 ± 0.029 | 0.017 | 1.82 | 0.056 | 0.045 | 0.071 | −0.041 |
| hexane | −0.001 ± 0.042 | 0.020 | 5.10 | 0.040 | 0.029 | 0.055 | 0.031 |
| chloroform | −0.003 ± 0.025 | 0.020 | **8.35** | 0.119 | 0.095 | 0.165 | 0.003 |
| benzene | −0.030 ± 0.037 | 0.022 | 5.83 | 0.065 | 0.051 | 0.083 | 0.016 |
| methyl methacrylate | −0.102 ± 0.051 | 0.066 | 4.89 | 0.197 | 0.161 | 0.249 | −0.060 |
| toluene | −0.040 ± 0.051 | 0.020 | 4.15 | 0.070 | 0.058 | 0.086 | −0.014 |
| ethylbenzene | −0.044 ± 0.047 | 0.020 | 0.72 | 0.074 | 0.062 | 0.091 | 0.033 |
| *m*,*p*-xylene | −0.067 ± 0.046 | 0.025 | 1.64 | 0.105 | 0.090 | 0.126 | 0.031 |
| *o*-xylene | −0.060 ± 0.050 | 0.027 | 0.44 | 0.101 | 0.085 | 0.123 | 0.040 |
| alpha-pinene | −0.047 ± 0.041 | 0.028 | 0.58 | 0.091 | 0.074 | 0.114 | −0.096 |
| limonene | −0.046 ± 0.048 | 0.069 | 6.06 | 0.156 | 0.118 | 0.211 | 0.066 |

[a] Notes: To be acceptable either both bias limits must have an absolute value less than 0.10, or an absolute value of 0.10 must fall between the limits. $S_{rx}$ is an estimate of pooled precision. $\chi^2$ for 2 degrees of freedom (*i.e.*, 3 concentration levels) must be <7.38 to pass Bartlett's test at 2.5% significance level. $A_{est}$ is the point estimation of accuracy using the hyperbolic approximation formula. $A_{0.05}$ and $A_{0.95}$ are the 5% and 95% confidence limits for the estimate of accuracy. $A_{0.95}$ must be less than 0.25 to pass accuracy criterion. Stability metric is bias comparing average concentration on day 30 to average concentration on day zero; the absolute value of the stability metric must be less than 0.10.



chloride and methyl methacrylate failed Bartlett's test of precision homogeneity. All 14 analytes passed the 25% accuracy criterion. With the exception of alpha-pinene and limonene, all analytes were stable while stored in 6 L canisters over a period of 30 days. Alpha-pinene and limonene were stable for 21 days with biases of 0.06 and −0.03, respectively. The dramatic drop on day 30 of the storage stability was due to a single canister. When removed, alpha-pinene and limonene showed acceptable bias for day 30, 0.07 and −0.05, respectively.

Percent recoveries and relative standard deviations for ppm-level concentrations are displayed in Table 6. For the most part, recoveries and relative standard deviations were consistent across concentration levels. Recoveries at 0.8 ppm ranged from 105% for toluene to 118% for limonene. Recoveries at 2 ppm ranged from 94% for methylene chloride to 106% for limonene.

## Discussion

Evacuated canisters have traditionally been used to sample ambient air toxics using the TO-15 method developed by the Environmental Protection Agency.[11,14,15] Besides the initial method validation by the EPA, there is a paucity of data on validation of canisters for other exposure scenarios, in particular for work environments with mixed exposures to multiple chemicals at widely differing concentrations. To our knowledge, the current study and a study by Coffey *et al.*[8] are the only published method validation studies for evacuated-canister air sampling that have used the NIOSH guidelines.[17] The current study is the first to provide method validation data for VOC air contaminants at ppm- and ppb-level concentrations.

This study established LODs that are sufficiently sensitive to measure ppb-level as well as ppm-level concentrations of target analytes from the same canister sample, thereby enabling quantitative assessments of mixed level exposure environments

**Table 4** Percent recoveries (Rec) and percent relative standard deviations (RSD) for target analytes at ppb-level concentrations

| | 1 ppb ($n = 8$) | | 4 ppb ($n = 8$) | | 10 ppb ($n = 9$) | |
|---|---|---|---|---|---|---|
| Analyte | Rec (%) | RSD (%) | Rec (%) | RSD (%) | Rec (%) | RSD (%) |
| ethanol | 88 | 4.8 | 96 | 5.8 | 89 | 7.2 |
| acetone | 98 | 9.9 | 102 | 6.2 | 90 | 3.9 |
| 2-propanol | 79 | 7.6 | 94 | 9.2 | 89 | 7.5 |
| methylene chloride | 104 | 2.0 | 111 | 2.2 | 94 | 1.4 |
| hexane | 91 | 2.8 | 115 | 2.5 | 94 | 1.0 |
| chloroform | 97 | 2.4 | 108 | 2.7 | 94 | 1.0 |
| benzene | 87 | 2.9 | 109 | 2.5 | 95 | 1.1 |
| methyl methacrylate | 74 | 6.7 | 101 | 7.3 | 95 | 4.1 |
| toluene | 80 | 2.7 | 111 | 2.4 | 98 | 1.3 |
| ethylbenzene | 81 | 1.8 | 110 | 1.9 | 96 | 1.8 |
| *m*,*p*-xylene | 78 | 2.2 | 107 | 2.3 | 95 | 2.2 |
| *o*-xylene | 78 | 2.3 | 108 | 2.7 | 96 | 2.5 |
| alpha-pinene | 83 | 2.6 | 108 | 3.5 | 95 | 3.0 |
| limonene | 83 | 4.1 | 107 | 10.6 | 96 | 6.0 |

**Table 5** Bias, precision, accuracy, and stability results for target analytes at ppm-level concentrations[a]

| Analyte | $B_{Avg} \pm 95\%CL$ | $S_{rx}$ | $\chi^2$ | $A_{est}$ | $A_{0.05}$ | $A_{0.95}$ | Stability |
|---|---|---|---|---|---|---|---|
| ethanol | 0.094 ± 0.032 | 0.028 | 2.45 | 0.143 | 0.124 | 0.170 | −0.092 |
| acetone | 0.087 ± 0.031 | 0.019 | 1.11 | 0.120 | 0.107 | 0.138 | −0.016 |
| 2-propanol | 0.089 ± 0.027 | 0.027 | 1.01 | 0.135 | 0.117 | 0.161 | −0.029 |
| methylene chloride | 0.030 ± 0.042 | 0.041 | **10.4** | 0.137 | 0.108 | 0.178 | −0.047 |
| hexane | 0.061 ± 0.025 | 0.012 | 2.50 | 0.082 | 0.074 | 0.094 | 0.001 |
| chloroform | 0.057 ± 0.027 | 0.012 | 1.65 | 0.077 | 0.069 | 0.089 | −0.019 |
| benzene | 0.063 ± 0.020 | 0.011 | 2.82 | 0.082 | 0.074 | 0.093 | 0.073 |
| methyl methacrylate | 0.057 ± 0.019 | 0.016 | **7.93** | 0.113 | 0.090 | 0.156 | 0.014 |
| toluene | 0.055 ± 0.018 | 0.015 | 6.12 | 0.080 | 0.070 | 0.093 | 0.064 |
| ethylbenzene | 0.047 ± 0.019 | 0.017 | 0.56 | 0.076 | 0.065 | 0.092 | 0.008 |
| *m*,*p*-xylene | 0.039 ± 0.021 | 0.019 | 1.56 | 0.071 | 0.058 | 0.088 | −0.021 |
| *o*-xylene | 0.054 ± 0.020 | 0.019 | 0.62 | 0.086 | 0.073 | 0.103 | −0.003 |
| alpha-pinene | 0.067 ± 0.016 | 0.022 | 1.06 | 0.105 | 0.090 | 0.125 | **−0.174** |
| limonene | 0.131 ± 0.032 | 0.039 | 0.44 | 0.202 | 0.174 | 0.240 | **−0.279** |

[a] Notes: To be acceptable either both bias limits must have an absolute value less than 0.10, or an absolute value of 0.10 must fall between the limits. $S_{rx}$ is an estimate of pooled precision. $\chi^2$ for 2 degrees of freedom (*i.e.*, 3 concentration levels) must be <7.38 to pass Bartlett's test at 2.5% significance level. $A_{est}$ is the point estimation of accuracy using the hyperbolic approximation formula. $A_{0.05}$ and $A_{0.95}$ are the 5% and 95% confidence limits for the estimate of accuracy. $A_{0.95}$ must be less than 0.25 to pass accuracy criterion. Stability metric is bias comparing average concentration on day 30 to average concentration on day zero; the absolute value of the stability metric must be less than 0.10.



characterized by widely differing concentrations of VOCs. These LODs could be improved by setting the MS to selected ion monitoring (SIM) mode, but unknown chemicals from field samples would be lost by doing so. Using scan mode allows unknown chemicals to be qualitatively identified and concentrations estimated based on the closest internal standard and an assumed response factor. Scan and SIM mode have been previously shown to provide roughly equivalent detection limits for aromatics, alkanes, and terpenes when using a thermal desorption/GC-MS system.[16]

With respect to method validation for the preconcentration method used to measure ppb-level concentrations, all bias, accuracy, and stability criteria were within acceptable limits for 13 of the 14 target analytes—ethanol, acetone, methylene chloride, hexane, chloroform, benzene, methyl methacrylate, toluene, ethylbenzene, m,p-xylene, o-xylene, alpha-pinene, and limonene.

For the ppb-level method, bias was acceptable for all analytes. The average bias for 2-propanol was greater than 0.10; further evaluation to confirm or refute this excessive bias result is warranted, particularly because bias values in the current study may have been influenced by error introduced during the preparation of standards (*e.g.*, liquid injection into glass bulb or concentration dilution). 2-propanol failed the accuracy criterion at ppb-level concentrations, perhaps because the water management step in the preconcentration may have affected the concentrations of this analyte due to its polar nature. Ethanol, however, passed the accuracy criterion despite its similar polarity.

Because chloroform failed Bartlett's test of homogeneity (*i.e.*, precision varied across concentrations), the accuracy value for this analyte displayed in Table 3 was not calculated based on a value for precision that was pooled across all concentrations investigated. Rather, they were calculated based on the worst-case concentration-specific precision and bias and a modified eqn (4) that accounts for the reduced degrees of freedom. Further investigation of the precision for chloroform using the ppb-level method is warranted. In the meantime, the method can be used to quantify this analyte, but the analyst must be cognizant of the concentration-dependence of measurement variability.

**Table 6** Percent recoveries (Rec) and percent relative standard deviations (RSD) for target analytes at ppm-level concentrations

| | 0.8 ppm ($n = 9$) | | 1 ppm ($n = 9$) | | 2 ppm ($n = 8$) | |
|---|---|---|---|---|---|---|
| Analyte | Rec (%) | RSD (%) | Rec (%) | RSD (%) | Rec (%) | RSD (%) |
| ethanol | 112 | 2.8 | 115 | 3.3 | 102 | 1.9 |
| acetone | 115 | 1.9 | 111 | 2.0 | 100 | 1.5 |
| 2-propanol | 113 | 2.4 | 113 | 3.1 | 101 | 2.5 |
| methylene chloride | 117 | 1.3 | 98 | 5.0 | 94 | 4.9 |
| hexane | 112 | 1.0 | 107 | 1.0 | 99 | 1.7 |
| chloroform | 113 | 1.4 | 104 | 1.0 | 100 | 1.2 |
| benzene | 108 | 1.3 | 108 | 1.0 | 102 | 0.9 |
| methyl methacrylate | 106 | 2.3 | 107 | 1.2 | 104 | 0.8 |
| toluene | 105 | 1.9 | 106 | 1.0 | 105 | 1.2 |
| ethylbenzene | 108 | 1.7 | 103 | 1.7 | 103 | 1.5 |
| *m*,*p*-xylene | 108 | 2.1 | 101 | 1.5 | 103 | 1.9 |
| *o*-xylene | 108 | 1.9 | 104 | 1.7 | 104 | 1.8 |
| alpha-pinene | 110 | 2.2 | 105 | 2.3 | 105 | 1.7 |
| limonene | 118 | 3.5 | 115 | 4.4 | 106 | 3.7 |

Coffey *et al.* performed a similar method validation study for fused-silica lined, evacuated-canister air sampling analyzed using a microscale purge and trap preconcentrator configuration.[17] They found that acetone passed the accuracy criterion but failed the stability criterion, while the current study found that acetone passed both the accuracy and stability criteria. Also, LODs established by Coffey *et al.*[17] were not so low as those established in the current study, presumably due to a difference in trap configurations. In contrast to the Coffey *et al.* study, the preconcentrator configuration for the current study did not employ a sorbent in trap 2. This appears to have increased sensitivity for acetone, chloroform, hexane, and methylene chloride, which may explain the discrepancy in acetone results and LODs.

For the loop method used to measure ppm-level concentrations, all accuracy and bias criterion were within acceptable limits for each analyte. Bartlett's test demonstrated that measurement precision was non-homogeneous over concentrations for both methylene chloride and methyl methacrylate, so the analyst must be cognizant of the concentration-dependence of measurement variability when this method is used to quantify these two analytes. All analytes were stable for 30 days, except alpha-pinene and limonene, which remained stable for 21 days. The shorter acceptable storage time for alpha-pinene and limonene may be due to a single erroneous storage sample or to losses from chemical reactions with other components of canister contents, particularly oxidizing species such as ozone or hydroxyl and nitrate radicals naturally found in indoor air.[18,19]

## Conclusions

Protocols for monitoring VOCs in healthcare settings are needed by industrial hygienists for air sampling to assess exposures and by epidemiologists to evaluate potential risks of exposure among healthcare workers. This study evaluated sampling and analysis parameters that can be used for assessing a mixed concentration level scenario, where some low-level VOCs of interest are present in a high-level VOC background.

Results of this validation study demonstrate that evacuated canister sampling coupled with preconcentration and GC-MS analysis is a viable (accurate and stable) air sampling methodology for measuring very low air concentrations of some VOCs as well as much higher VOC concentrations (*e.g.*, alcohols) found together in the same setting. This sampling and analysis approach will enable development of VOC exposure profiles for healthcare workers, and may also be applicable to other settings involving exposure to indoor air contaminants.

## Acknowledgements

The authors would like to thank J.E. Slaven and S.A. Shulman for their assistance with statistical analyses, as well as J.R. Wells, C.C. Coffey, and R.M. Castellan for their comments and suggestions. The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the National Institute for Occupational Safety and Health. Mention of any commercial product or trade name does not constitute endorsement by the Centers for Disease Control and Prevention/National Institute for Occupational Safety and Health.

## References

1 J.-P. Zock, N. Cavalle, H. Kromhout, S. Kennedy, J. Sunyer, A. Jaen, N. Muniozguren, F. Payo, E. Almar, J. Sanchez, J. Anto and M. Kogevinas, *J. Exposure Anal. Environ. Epidemiol.*, 2004, **14**, 397–403.
2 J.-P. Zock, D. Vizcaya and N. Le Moual, *Curr. Opin. Allergy Clin. Immunol.*, 2010, **10**, 114–120.
3 A. A. Arif and G. L. Delclos, *Occup. Environ. Med.*, 2012, **69**, 35–40.
4 G. Liss, L. Buyantseva, C. Luce, M. Ribeiro, M. Manno and S. Tarlo, *Am. J. Ind. Med.*, 2011, **54**, 278–284.
5 M. Mirabelli, J.-P. Zock, E. Plana, J. Anto, G. Benke, P. Blanc, A. Dahlman-Hoglund, D. Jarvis, H. Kromhout, L. Lillienberg, D. Norback, M. Olivieri, K. Radon, J. Sunyer, K. Toren, M. van Sprundel, S. Villani and M. Kogevinas, *Occup. Environ. Med.*, 2007, **64**, 474–479.
6 A. A. Arif, G. L. Delclos and C. Serra, *Occup. Environ. Med.*, 2009, **66**, 274–278.
7 M. Becklake, J. L. Malo and M. Chan Yeung, *Asthma in the Workplace*, Taylor and Francis Group, New York, NY, 2006.
8 E. R. Kennedy, T. J. Fischbach, R. Song, P. M. Eller and S. A. Shulman, *Guidelines for Air Sampling and Analytical Method Development and Evaluation, 95–117*, National Institute of Occupational Safety and Health, Cincinatti, 1995.
9 N. Ochiai, S. Daishima and D. Cardin, *J. Environ. Monit.*, 2003, **5**, 997–1003.
10 C. C. Hsieh, S. H. Horng and P. N. Liao, *Aerosol Air Qual. Res.*, 2003, **3**, 17–28.
11 EPA, *Compendium Method TO-15: Determination of Volatile Organic Compounds (VOCs) in Air Collected in Specially-Prepared Canisters and Analyzed by Gas Chromatography/Mass Spectrometry (GC/MS)*, Second edn, Cincinnati, OH, 1999.
12 CHE, The Collaborative on Health and the Environment, 2011, http://www.healthandenvironment.org/tddb/, accessed 14 September 2011.
13 D. L. Bartley, *Ann. Occup. Hyg.*, 2001, **45**, 357–364.
14 G. F. Evans, T. A. Lumpkin, D. L. Smith and M. C. Somerville, *J. Air Waste Manage. Assoc.*, 1992, **42**, 1319–1323.
15 T. F. Dann and D. K. Wang, *J. Air Waste Manage. Assoc.*, 1995, **45**, 695–702.
16 C. Jia, S. Batterman and S. Chernyak, *J. Environ. Monit.*, 2006, **8**, 1029–1042.
17 C. C. Coffey, R. F. LeBouf, C. A. Calvert and J. E. Slaven, *J. Air Waste Manage. Assoc.*, 2011, **61**, 826–833.
18 R. Atkinson and J. Arey, *Atmos. Environ.*, 2003, **37**, S197–S219.
19 C. Forester and J. Wells, *Environ. Sci. Technol.*, 2009, **43**, 3561–3568.