Evaluation and Identification of Volatile Organic Compounds in Childhood Education Facilities

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Abstract

Little information exists about volatile organic compound (VOC) exposures in early childhood education (ECE) environments. As part of an earlier California Air Resources Board (CARB) contract (Agreement Number 08-305), we measured VOCs in single-day air samples collected in 2010-2011 from 40 early childhood education (ECE) facilities in California. VOCs were detected more frequently and at much higher concentrations indoors compared with outdoors and were inversely associated with ventilation rates. We also observed numerous unknown peaks in the gas chromatography-mass spectrometry (GC/MS) chromatographs for indoor samples. We verified identification of 119 of these non-targeted compounds using automated mass spectral de-convolution and identification software (AMDIS) and mass spectral libraries and ran 14 pure standards for selected chemicals to independently verify the identification. Retention times for the identified chemicals and the pure standards matched almost perfectly (R^2=0.998). Probability-based matching also demonstrated strong agreement between the mass spectra, indicating that the 14 compounds were correctly identified, confirming the general validity of the method used to identify unknown VOCs. Estimated exposures to naphthalene, identified using the mass spectral libraries, exceeded age-adjusted "safe harbor levels" based on California's Proposition 65 guidelines (10^{-5} lifetime cancer risk) in 97% of the facilities, as did several compounds described in the parent report (benzene, chloroform, ethylbenzene, formaldehyde, and acetaldehyde). While exposures to 17 of the VOC compounds we measured were below non-cancer health benchmarks, more than 70% of the compounds lacked any health-based exposure standards that could be used to assess potential risks. Through extensive review of databases aggregating toxicological information and the application of quantitative structure–activity relationship (QSAR) modeling methods, we identified 12 chemicals that warrant additional exposure and health evaluation due to their potential for carcinogenic, neurologic, or other health effects (acetic acid, butyl ester; camphor; octamethylcyclotetrasiloxane (D4); D5; n-heptane; heptanal; d-limonene; n-pentane; 3-phenyl-2-propenal; α-pinene; α-terpineol; and 1,2,4-trimethylbenzene). These chemicals include commonly used terpenes and fragrance-related compounds, which have been associated with respiratory or other health problems. The use of AMDIS processing, identification with mass spectral libraries, and follow-up confirmation with pure standards is an effective tool to identify unknown VOCs in indoor environments. Future indoor air quality studies should consider these methods to identify unknown chemicals beyond the *a priori* list of target analytes, allowing a broader assessment of exposures and potential health risks. The library of chemicals identified in this study also provide guidance on the choice of target analytes for future studies in child care. Given the seriousness of the health risks associated with the VOC levels we observed, our findings demonstrate that potentially harmful VOC exposures are occurring in ECE environments and indicate that more research is needed to fully assess the potential health risks to young children and adult staff and identify major sources of VOCs present in ECE facilities. If warranted, restrictions on the use of some compounds should be considered as well as outreach to child care providers on strategies to improve indoor air quality, such as ensuring proper ventilation, to mitigate these exposures. Published and submitted manuscripts are appended to this report.

Executive Summary

Background

Many infants and young children spend as much as ten hours per day, five days per week, in child care and preschool centers. California, where approximately 1.1 million children five years or younger attend child care or preschool, has the largest number of licensed child care centers in the United States at 49,000, 80% of which are family-based centers located in homes. By the time they enter kindergarten, over 50% of all California children have attended some type of licensed child care facility. Additionally, 146,000 staff work in California's licensed child care facilities. Similar to other indoor environments, early childhood education (ECE) facilities contain volatile organic compounds (VOCs) and other contaminants hazardous to children's health. Children have higher exposures to air contaminants because they breathe more air per unit of body weight compared with adults. They are also less developed immunologically, physiologically, and neurologically and therefore may be more susceptible to the adverse effects of chemicals and toxins.

Under a prior contract, we measured aldehydes and targeted VOCs in 40 ECE facilities (Agreement Number 08-305). We also observed numerous unknown peaks in the gas chromatography-mass spectrometry (GC/MS) chromatographs; 119 of these non-targeted compounds were identified using mass spectral libraries, however most of the compounds lacked health-based exposure benchmarks to evaluate potential risks. Under the current contract, our objectives were to confirm the identity of the non-targeted VOCs, including the use of pure standards to verify the identity of a subset of the non-targeted compounds, and to evaluate potential exposure determinants and health risks. Because many compounds lack health-based exposure benchmarks, we also conducted extensive toxicological reviews and applied quantitative structure–activity relationship (QSAR) models to identify potential health concerns and prioritize compounds for additional exposure and health evaluation.

This study is the first to examine targeted and non-targeted VOC air contaminants in ECE facilities in California and the nation, and apply novel methods to evaluate potential health risks from these exposures. This information will help the California Air Resources Board (CARB) and other agencies better protect children's health by identifying key exposures that can be reduced through regulations or other approaches.

Methods

We measured acetaldehyde, formaldehyde and 38 VOCs in single-day air samples collected in 2010-2011 from ECE facilities serving California children and evaluated potential health risks. We also examined unknown peaks in the GC/MS chromatographs for indoor samples and identified 119 of these compounds using mass spectral libraries. We also ran 14 pure standards for selected chemicals on the GC/MS column to independently verify the prior identification. Retention times for the previously identified chemicals and the pure standards matched almost perfectly (R^2=0.998), and probability-base matching also indicated strong agreement between the mass spectra, indicating that the 14 were correctly identified and confirming the validity of our prior mass spectral library matches. Semiquantitative levels for the non-targeted VOCs were estimated using a toluene model.

We then used both quantified VOC and "non-targeted" VOC measurement data to characterize contaminant levels in ECE environments and evaluate potential determinants of indoor contaminants. For commonly detected aldehydes and targeted VOCs, we used bivariate

analyses or statistical models to evaluate potential predictors and sources of individual compounds. Predictors and sources considered included ECE facility type (home based versus center based), building type, type of furniture present, carpeting, floor type, cleaning materials, nearby traffic, air exchange rates, relative humidity, temperature, etc.

Where appropriate, concentrations were compared to California Office of Environmental Health Hazard Assessment (OEHHA) chronic or acute reference exposure levels (RELs) and U.S. Environmental Protection Agency (EPA) reference concentrations (RfDs). For compounds identified as carcinogens by the State of California, we compared daily intake to OEHHA No Significant Risk Levels (NSRLs), defined as intake rates with cancer risks of 1 in 100,000 (10^{-5}). For VOCs without health benchmarks, we reviewed extensive toxicological information and applied quantitative structure-activity relationship (QSAR) models to assess potential health concerns. Toxicological information was compiled from authoritative lists, including ScoreCard and the Pharos Project, reports from government agencies, non-governmental organizations (NGOs), and other expert bodies. We used the VEGA QSAR model (Virtual models for Evaluating chemicals within a Global Architecture (VEGA) developed by the non-profit Istituto di Ricerche Farmacologiche "Mario Negri" in Milan, Italy) and includes algorithms developed by the European Union and U.S. EPA. We classified the compounds into potential hazard groups based on findings from VEGA, ScoreCard, and Pharos, including: potential carcinogen or mutagen (Group 1), developmental toxicants (Group 2), reproductive toxicants (Group 3), endocrine disrupting chemicals (Group 4), neurotoxicants (Group 5), immunotoxicants/sensitizers (Group 6), specific organ or acute toxicants (Group 7), irritants (Group 8), persistent or bioaccumulative chemicals (Group 9), and no information (Group 10). To quantify the breadth of hazard data, we allotted a binary score to each group according to the presence or absence (score=1 or 0) of positive toxicity data. We summed the scores for each chemical, creating a cumulative "hazard score." We selected a hazard score of >3 to prioritize compounds for further review.

Results

Aldehyde levels in Air: Acetaldehyde and formaldehyde were detected in 100% of ECE facilities measured (n=40). Aldehyde levels were significantly higher indoors compared to outdoors ($p<0.05$), indicating that indoor sources are primary contributors to indoor formaldehyde and acetaldehyde concentrations. Final multivariate regression model results for formaldehyde and acetaldehyde concentrations showed significant inverse associations between aldehyde levels and air exchange rate (AER) and significant positive associations with average indoor temperature ($p<0.05$).

Targeted VOC Levels in Air: For the 15 targeted VOCs with indoor mixed and mobile sources (MMS), the median indoor concentration ranged from 0.1 µg/m³ for 1,2,3-trimethylbenzene to 3.1 µg/m³ for toluene. Seven compounds were detected in 100% of indoor samples – including toluene, ethylbenzene, and xylenes. Benzene was detected in 70.6% of samples. Many of the MMS VOCs were moderately to strongly correlated with each other (rho>0.35-0.99, $p<0.05$), indicating common sources. The MMS VOCs were detected more frequently indoors than outdoors, and 93% had significantly higher levels indoors than outdoors, with the mean indoor to outdoor (I/O) ratios ranging from 1.1 for benzene to 59.4 for n-tetradecane, underscoring that several of these compounds also have indoor sources. Several indoor MMS VOC air concentrations (including benzene; n-heptane; n-hexadecane; n-tetradecane; toluene; and 1,2,4-trimethylbenzene) were inversely and significantly associated with AER (Spearman rho=

-0.38 to -0.67, $p<0.05$). Three MMS VOCs, benzene, n-heptane, and n-hexadecane, were positively correlated with proximity to traffic (Spearman rho= 0.38-0.44, $p<0.05$).

For the 23 targeted VOCs with household sources (HS), the median indoor concentrations ranged from 0.1 for tetrachloroethylene to 51.4 µg/m³ for decamethylcyclopentasiloxane [D5]. The fragrance VOCs were frequently detected indoors with nine (of twelve) compounds detected in >90% of ECE facilities. D-limonene was detected in all facilities and had a median (range) of 33.1 µg/m^3 (0.8-81.5 µg/m^3). The siloxane D5 had the highest median concentration (51.4 µg/m³, range: 2.6-88.2 µg/m^3). Octamethylcyclotetrasiloxane (D4) also had a high detection frequency (90.9%) with a median concentration (range) of 0.9 µg/m^3 (0.1-78.5 µg/m^3). Many of the indoor HS VOC concentrations were also moderately correlated (rho>0.36), albeit less strongly than the MMS VOCs. HS VOCs were detected more frequently indoors than outdoors (n=20). The mean I/O ratios for HS VOCs ranged from 1.2 (carbon tetrachloride and methylene chloride) to 1,603.9 (d-limonene) and were higher than the MMS ratios, indicating that indoor sources were dominant for these compounds. Butanal, hexanal, α-pinene, 2-ethyl-1-hexanol, and D4 were significantly and inversely associated with AER (Spearman rho= -0.42 to -0.62, $p<0.05$), indicating indoor sources of these chemicals. Indoor concentrations of analytes found in fragrances (hexanal, decanal and D5) were significantly and positively correlated with reported air freshener use ($p<0.05$).

Non-targeted VOC Levels in Air: Levels of 119 non-targeted VOC analytes are reported by chemical class. For 31 alkane compounds, median concentrations ranged from <MDL (method detection limit) to 0.29 µg/m^3 for methylcyclohexane. For 31 oxygenated hydrocarbon compounds, median concentrations ranged from <MDL to 7.36 µg/m^3 for propylene glycol. For 34 aromatic compounds, median concentrations ranged from <MDL to 1.13 µg/m^3 for phenol. Naphthalene, a possible carcinogen, was detected in 96.9% of samples with a median concentration of 0.34 µg/m^3. Siloxane median concentrations ranged from <MDL to 1.89 µg/m^3 for dodecamethylcyclohexasiloxane (D6). For the 15 terpenes, median concentrations ranged from <MDL to 1.66 µg/m^3 for 2,6-dimethyl-7-octen-2-ol.

Non-cancer Risk Evaluation: The 50th and 95th percentile formaldehyde air concentrations (17.8 and 37.3 µg/m^3, respectively) exceeded the 8-hour Reference Exposure Level (REL) and chronic REL (both 9 µg/m^3), with ratios of 2.0 and 4.1, respectively. Formaldehyde levels exceeded the 8-hour REL and chronic REL in 87.5% of facilities. Acetaldehyde concentrations were lower than OEHHA RELs, but exceeded the U.S. EPA Reference Concentration (RfC) in 30% of facilities. Of the 10 targeted VOCs and six non-targeted VOCs with RELs or RfCs, none of the risk ratios exceeded one and were often much lower.

Cancer Risk Evaluation: If reflective of long-term averages, estimated acetaldehyde or formaldehyde intake rates exceeded age-adjusted NSRL benchmarks based on California's Proposition 65 guidelines (10^{-5} lifetime cancer risk) in all ECE facilities. In addition, estimated intake rates exceeded age-adjusted NSRL benchmarks for benzene, chloroform, ethylbenzene, and naphthalene in 71%, 38%, 56% and 97% of facilities, with all facilities having exposures to at least one VOC exceeding the respective NSRL.

Hazard Assessment and Prioritization for Future Study: Of the targeted VOCs without non-occupational health-based exposure benchmarks, two were excluded from detailed review due to lower detection frequency (<60%). Twenty-four of the remaining 25 compounds had positive toxicological information cited by our toxicological review or QSAR predictions. The 24 VOCs were distributed into respective hazard groups (Groups 1-9) as follows: 8% (n=2) for carcinogenicity or mutagenicity, 29% (n= 7) for developmental toxicity, 4% (n=1) for

reproductive toxicity, 4% (n=1) for endocrine activity, 25% (n=6) for neurotoxicity, 58% (n=14) for immunotoxicity or sensitization, 71% (n=17) for specific organ or acute toxicity, 63% (n=15) for irritation, and 25% (n=6) for persistence or bioaccumulation. Each hazard group is not mutually exclusive. We identified 7 compounds with hazard scores >3 for additional evaluation: d-limonene; α-pinene; α-terpineol, 1,2,4-trimethylbenzene; D4; n-heptane; and heptanal. The persistent and bioaccumulative nature of cyclosiloxanes (D4 and D5) raises health concerns, especially given adverse reproductive effects reported in animals. These compounds are also listed as priority chemicals for biomonitoring by the California Biomonitoring Program. Thus, we recommend additional evaluation of D5 because of health concerns raised by OEHHA, and the high detection frequency and levels measured.

Applying the same methods to the 119 non-targeted VOCs with no non-occupational health-based exposure benchmarks, we identified 4 additional compounds with hazard scores >3 for further evaluation: butyl ester acetic acid; camphor; n-pentane; 2-propenal, 3-phenyl-.
In summary, we identified 12 chemicals that warrant additional exposure and health evaluation due to their potential for carcinogenic, neurologic, or other health effects. Four of these– d-limonene, α-pinene, α-terpineol, and camphor– are terpenes. The remaining 8 compounds identified were: acetic acid, butyl ester; D4; D5; n-heptane; heptanal; n-pentane; 3-phenyl-2-propenal; and 1,2,4-trimethylbenzene. These chemicals include commonly used terpenes and fragrance-related compounds, which have been associated with respiratory symptoms, a common health problem in child care.

Conclusions and Recommendations

a. The use of automated mass spectral de-convolution and identification software (AMDIS) combined with matching to mass spectral libraries and follow-up confirmation with pure standards is an effective tool to identify unknown VOCs in indoor environments. Future indoor air quality studies should consider these methods to identify significant unknown chemicals beyond the *a priori* list of target analytes, allowing a broader assessment of exposures and potential health risks. The library of chemicals identified in this study provide guidance on the choice of target analytes for future studies of indoor air quality in child care.

b. More research is needed to determine the relative contribution of composite wood products versus other sources (i.e., other building materials and furnishings, cleaning materials, personal care products, etc.) to indoor formaldehyde contamination in new and older buildings serving child care.

c. Additional studies determining sources and health impacts of VOC compounds where levels exceeded exposure benchmarks based on carcinogenicity should be a high priority, including benzene, chloroform, ethylbenzene, and naphthalene.

d. Based on extensive toxicological review and the application of QSAR models, the following 12 chemicals should be prioritized for additional exposure and health evaluation due to their potential for carcinogenic, neurologic, respiratory, or other health effects: acetic acid, butyl ester; camphor; D4; D5; n-heptane; heptanal; d-limonene; n-pentane; 3-phenyl-2-propenal; α-pinene; α-terpineol; 1,2,4-trimethylbenzene). These include chemicals commonly used terpenes and fragrance-related compounds, which have been associated with respiratory symptoms, common problems among children in child care.

e. The lack of toxicological information for many of the chemicals we measured is a basic limitation, and even QSAR programs are constrained by the availability of adequate

toxicological data for reference chemicals to make accurate hazard predictions. Additional toxicological evaluations are needed for many of the chemicals we identified to fully inform health risk assessments of these exposures.

f. While the chemicals we identified are not uniquely found in child care, the seriousness of the health risks associated with the VOC levels observed in ECE environments demonstrate that potentially harmful exposures are occurring and indicate that more research is needed to fully assess potential health risks and identify sources of indoor air contamination. If warranted, restrictions on the use of some compounds should be considered as well as outreach to child care providers on strategies to improve indoor air quality, such as ensuring proper ventilation, to mitigate these exposures.

Body of Report

1 Introduction

Young children spend up to 90% of their time indoors, mostly at home.[1-3] However, many infants and young children spend as much as 10 hours per day, 5 days per week, in child care and preschool centers.[4,5] Nationally, 13 million children, or 65% of all U.S. children, spend some portion of the day in child care or preschool.[5] California, where approximately 1.1 million children five years or younger attend child care or preschool,[6] has the largest number of licensed child care centers in the United States[7] at 49,000. By the time they enter kindergarten, over 50% of all California children have attended some type of licensed child care facility.[8] Additionally, 146,000 staff work in California's licensed child care facilities.[8]

Collectively, Early Childhood Education (ECE) facilities are varied and include home-based child care providers, centers operated like private schools, and programs run by government agencies (e.g., preschool in school districts or Head Start) or religious institutions. These facilities are located in a variety of building types, including homes, schools, private commercial buildings, and portable classrooms. During the last two decades, U.S. Environmental Protection Agency (EPA), state, and local environmental agencies and school districts have developed programs addressing environmental exposures in elementary and high schools, but only recently have research and education programs begun focusing on ECE environments. These new programs are important because very young children have higher exposures to contaminants because they breathe more air, eat more food, and drink more water per unit of body weight compared with adults. They are also less developed immunologically, physiologically, and neurologically and therefore may be more susceptible to the adverse effects of chemicals and toxins.

Obtaining data on environmental exposures in these facilities is a necessary first step to assess potential exposures and health risks to children and adult staff. However, many of the measureable chemicals, especially in air, lack health-based standards to characterize risk. In this report, we describe additional research aiming to characterize young children's exposures to volatile organic compounds (VOCs) previously measured in California ECE facilities,[9] and perform Quantitative Structural Activity Relationship (QSAR) modeling to identify additional compounds with potential health risks requiring further assessment.

1.1 Health Effects from Exposures to VOCs

A growing body of evidence suggests that indoor exposures are determinants of asthma prevalence and morbidity in children.[1] Known environmental triggers of asthma include VOCs, combustion by-products, and some common home-use pesticides and cleaners and sanitizers.[10-26] Exposure to VOCs in indoor air, from sources such as newly painted surfaces; cleaning, sanitizing and disinfecting products; and room fresheners, has been associated with increased risk of asthma in children[27,28] and respiratory symptoms including decreased lung function, inflammation, and airway obstruction.[20,26,29,30] Exposures to benzene, toluene, ethyl benzene, and xylene (BTEX), a subset of VOCs commonly found in vehicular exhaust, can also cause neurological and developmental adverse health effects.[31] Glycol ethers (i.e., 2-butoxyethanol) are frequently used as solvents in household products such as paints and have been associated with increased risk of asthma, rhinitis, and eczema.[32,33] Terpenes (i.e., d-limonene), frequently used in cleaning products, may react with ozone to produce hazardous

secondary pollutants such as formaldehyde and hydroxyl radicals.[34] Aldehydes (formaldehyde and acetaldehyde) are VOCs present in pressed wood and laminated products like shelving, paneling, and furniture and are of particular concern in new buildings and homes.

Formaldehyde is listed as a Class B1 compound (probable human carcinogen) by U.S. EPA[35] and a Group 1 compound (carcinogenic to humans) by the International Agency for Research on Cancer (IARC).[36] Acetaldehyde is listed by U.S. EPA as a Class B2 (probable human carcinogen) compound[37] and by IARC as a Group 2B (possibly carcinogenic to humans) compound.[38] Numerous rodent studies have reported adenocarcinomas and squamous cell carcinomas subsequent to aldehyde exposure[39-42] while occupational cohort studies have reported associations between formaldehyde exposure and lung, nasal, and nasopharyngeal cancer mortality.[43-45] Additionally, exposure to aldehydes has been associated with adverse respiratory outcomes, including increased risk of childhood asthma[46] and nocturnal breathlessness.[20,47] CARB's "new home" study found that concentrations of both formaldehyde and acetaldehyde exceeded accepted cancer and chronic non-cancer health benchmark levels in nearly all homes studied and exceeded benchmarks for acute health effects in most homes.[48,49] In the CARB's study of portable classrooms, indoor concentrations of formaldehyde were elevated above the California Office of Environmental Health Hazard Assessment (OEHHA) 8-hour Reference Exposure Level (REL) for acute eye, nose, and lung irritation in 4% of the classrooms. Levels in all classrooms exceeded the OEHHA chronic REL for irritant effects.[50]

A large body of research has raised concerns about the health effects of aldehyde exposure in children.[20,46] Exposure to these compounds has been associated with increased risk of pediatric asthma [51] and respiratory symptoms including decreased lung function, inflammation, and airway obstruction.[20,52] Numerous rodent studies have reported adenocarcinomas and squamous cell carcinomas subsequent to aldehyde exposure [40,42]; while occupational cohort studies have reported associations between formaldehyde exposure and nasopharyngeal cancer and myeloid leukemia mortality.[53,54] The International Agency for Research on Cancer (IARC) and National Toxicology Program (NTP) recognize formaldehyde as a known human carcinogen.[55,56] The U.S. Environmental Protection Agency (EPA) lists both formaldehyde and acetaldehyde as probable human carcinogens.[57,58]

Recent studies have shown poor indoor air quality in schools and residences, documenting elevated levels of formaldehyde and acetaldehyde above established cancer and non-cancer health benchmark levels.[59-61] Reflecting concerns about the health effects of formaldehyde exposure, the California Air Resources Board (CARB) finalized new rules in 2008 to reduce formaldehyde emissions from composite wood products.[62] The U.S. EPA proposed similar standards in May 2013, and is currently reviewing comments last received in October 2013.[63] Thus, national regulation of formaldehyde emissions is still pending.

Recent studies also indicate that ECE environments contain environmental contaminants hazardous to children's health,[1,5,64] including VOCs. Compared to adults, children are more vulnerable to the adverse effects of environmental contaminants because they are less developed immunologically, physiologically, and neurologically than adults.[65-67] They also breathe more per kg of body weight and are thus more highly exposed when air contaminants are present.

1.2 Relevant Research

School environments are known to contribute to children's exposures to several contaminants, including mold, lead, pesticides, and VOCs.[5,50,68] These exposures can

exacerbate asthma and other respiratory illnesses or impair neurological development of children. Beyond preventing children's exposure to lead, however, few states have programs or licensing regulations that address children's exposures to environmental contaminants such as VOCs in ECE facilities, and very limited information is available on environmental contaminants present in ECE environments.

California has examined indoor environmental exposures to contaminants in school settings for school-aged children. For example, the 2003 California Portable Classroom Study sponsored by CARB investigated conditions inside traditional and portable classrooms in California public schools.[5,50,68] Aldehydes and other carbonyls and VOCs were measured over a school day in classrooms. Of 15 aldehydes and other carbonyls measured in air, formaldehyde and acetaldehyde were detected most often (detection frequency >75%). Mean air concentrations of formaldehyde in both portable classrooms (15 ppb) and traditional (12 ppb) classrooms were higher than outdoor measurements (3.5 ppb). Mean VOC concentrations were similar between portable classrooms and traditional classrooms and were also higher than outdoor levels.

In a 2009 report, The Environmental Working Group[69] described 21 cleaners used in 13 large K-12 California school districts that, when used as directed, released 457 chemicals, many with little or no hazard information. Cleaners, sanitizers, and disinfectants are heavily used in ECE facilities to comply with regulations aiming to reduce the spread of infectious disease.

Volatile organic compounds (VOCs) are also emitted from building materials and furnishings and are often found at higher concentrations indoors than outdoors.[70] Formaldehyde is emitted from a variety of materials and consumer products.[71] Composite wood products containing urea-formaldehyde (UF) resin have been identified as a significant contributor to indoor formaldehyde.[72] Other sources include wallpaper; paints; permanent press fabrics; acid-catalyzed UF coatings on shelving, paneling, and furniture; cosmetic products; and combustion sources.[73] Indoor sources of acetaldehyde include phenol-formaldehyde wood products, rigid polyurethane foams, adhesives, coatings, lubricants, and inks. [74,75] Formaldehyde and acetaldehyde are also formed from chemical reactions between ozone and VOCs emitted from household items such as carpets, art supplies, disinfectants, and air fresheners.[76,77] Indoor aldehyde sources are common in child care environments and may present health risks to children. While a few international studies have examined aldehyde air levels in child care facilities[78-82], scarce information is available about U.S. facilities.

2 Materials and Methods

Additional information on recruitment, administration of questionnaires and inspections, and evaluation of building parameters are described in the parent report (Agreement Number 08-305).[9]

2.1 Recruitment

Forty ECE facilities located in two northern California counties [Monterey (n=20) and Alameda (n=20)] participated in this study.[9] Monterey County, CA is largely rural and agricultural, while Alameda County, CA, is predominantly urban or suburban. To recruit a diverse sample, we geographically stratified center and large home-based licensed (>8 children) ECE facilities by zip code using publicly available databases.[83] Participating ECE facilities were recruited by mail or direct phone solicitation. We ultimately completed assessments at 28 child care centers and 12 home-based facilities between May 2010 and May 2011. All procedures

were reviewed by the UC Berkeley Committee for the Protection of Human Subjects and written informed consent was obtained by each director or a senior administrator.

2.2 Questionnaire and Facility Inspection

Upon enrollment into the study, a questionnaire was administered to a site supervisor and a detailed inspection was conducted.[9] Questionnaire and inspection forms were developed to assess environmental quality in the facility. Information obtained included building type (home, school, or office and if portable or manufactured), building age, ECE type (home versus center), building materials, renovations (within the last five years), new flooring (within the last year), air freshener use, and the presence of composite wood products.

2.3 Building and Environmental Parameters

We used TSI, Inc. 8554 QTraks to measure real-time indoor carbon dioxide (CO_2), relative humidity (RH), and temperature over the entire school day. TSI calibrated the instruments in the spring of 2010. Air exchange rates (AERs) were estimated using both continuous indoor CO_2 measurements and the release of medical grade CO_2 as a tracer gas.[84,85] To track changes in CO_2 emissions from room occupants, we recorded minute-by-minute occupancy of three different age groups and assumed children <5 years old and adults to have a CO_2 emission rate of 10.44 L/h and 18.72 L/h, respectively.[86] Adult ERs were used for child occupants between ages of 5-18 years. We compared average AERs to the California Residential Code for ventilation.[87]

To investigate the relationship between indoor and outdoor air pollution in ECE facilities, we obtained traffic length-adjusted traffic volumes (∑LATV) within a one kilometer (km) radius buffer from the California Environmental Health Tracking Program (CEHTP) traffic linkage service,[88] which is based on data recorded in the CalTrans Highway Performance Monitoring System (HPMS) 2004. Length-adjusted traffic volumes (LATV) are the length of a road segment (km) multiplied by the average daily traffic volume (vehicles per hour).

2.3.1 Air Exchange Rate Computations

Given the highly fluctuating indoor environment, we used mass balance and tracer gas methods to calculate air exchange rates (AERs). We selected carbon dioxide (CO_2) as the tracer gas due to its low toxicity and acceptability to ECE directors. See Appendix *Air Exchange Rate Computations*.[9,89,90]

2.4 Air Sampling

Indoor air samples were collected in the main child care room during a single day at each facility.[9] Samplers were deployed at the height of a child's breathing zone (~1 meter) and were protected by a "kiddie-corral" made of untreated wood. The air sampling system used a rotary vane pump to provide vacuum for multiple sampling lines used during monitoring. The pump was placed in a stainless steel box lined with sound-insulating foil-faced fiberglass; the exhaust system included a muffler to reduce noise and a HEPA and carbon filter to eliminate possible emissions by the pump. Airflow was regulated by inline taper flowmeters. Calibration curves were determined for each flowmeter using a Gilibrator® air flow calibrator. Calibration curves were checked after sampling was completed and were consistent with prior results. Outdoor air

samples were collected from a random subset of ECE facilities (n=20) using SKC AirChek 2000 pumps. Flow rates for both the inline flowmeters and AirChek pumps were calibrated using a Gilibrator® air flow calibrator.

2.5 Aldehydes

2.5.1 Aldehyde Air Sampling

Aldehyde samplers, consisting of silica gel cartridges coated with 2,4-dinitrophenyl-hydrazine (Sep-Pak XPoSure; Waters corporation) with ozone scrubbers (P/N WAT054420; Waters) upstream. Air was pulled at approximately 0.25 liters per minute (LPM). Aldehyde Laboratory Measurements.

Aldehyde samplers were analyzed following U.S. EPA Method TO-11A.[91] Cartridges were extracted by eluting with 2 ml of high-purity acetonitrile and analyzed by high-performance liquid chromatography (1200 Series; Agilent Technologies) using a C_{18} reverse phase column with 65:35 H_2O:acetonitrile mobile phase at 0.35 ml/minute and UV detection at 360 nm. Multipoint calibrations were prepared for the target aldehydes using commercially available hydrazone derivatives of formaldehyde and acetaldehyde. The method detection limit (MDL) for formaldehyde and acetaldehyde were 10 and 1.0 ng, respectively. Using the average total collected air volume (0.12 m^3), formaldehyde and acetaldehyde MDLs as a concentration were 0.08 and 0.008 µg/m³, respectively.

2.5.2 Aldehyde Data Analysis

For the facilities with duplicate aldehyde measurements (n=12), the average of the two measurements were used for data analysis. We first computed descriptive statistics for formaldehyde and acetaldehyde air concentrations and emission rates. We then examined predictors of indoor air formaldehyde and acetaldehyde air concentrations. Based on visual inspection of quantile-quantile plots of the concentration data and the Shapiro–Wilk test ($p>0.05$), we determined that untransformed formaldehyde concentrations and log-transformed acetaldehyde concentrations approximated normal distributions. For statistical analyses, we used untransformed formaldehyde and log-transformed acetaldehyde data. The t-test was used to assess bivariate associations between indoor aldehyde air concentrations with potential determinants including: presence of composite wood products (yes/no); air freshener use (yes/no); presence of carpets (yes/no); occurrence of renovations within the last five years (yes/no); installation of new floor coverings within the last year (yes/no); building type (portable or manufactured/non-portable or non-manufactured); and license type (center- vs. home-based). Pearson correlations were used to assess associations between aldehyde levels with building age (in years), air exchange rate (AER) (hr^{-1}), relative humidity (RH) (%), and temperature (°C). We then used multivariable linear regression models to examine associations between indoor aldehyde levels and all the potential determinants identified a priori (listed above). All variables were included in the model except variables with p-values>0.1, which were eliminated in a step-wise fashion.

Because formaldehyde and acetaldehyde emission rates were not normally distributed, we used the non-parametric Mann-Whitney rank sum test to evaluate bivariate associations between emission rates and the presence of composite wood products, air freshener use, presence of carpets, occurrence of renovations, installation of new floorings, building type, and

license type. The Spearman rank correlation test was used to assess associations of formaldehyde and acetaldehyde emission rates with building age, RH, and temperature.

Differences in aldehyde levels stratified by geographic location (Monterey County vs. Alameda County) were analyzed using t-tests.

2.6 VOCs

2.6.1 Targeted VOC Air Sampling

Air was pulled at approximately 0.015 liters per minute (LPM). Initial VOC samplers used glass sorbent tubes containing Tenax-TA® backed with Carbosieve™. However, alcohols released by hand sanitizers produced large interferent peaks in chromatograms, rendering samples from six facilities unusable. To resolve these problems, final protocols used separate Tenax-TA® and CarboTrap™ sorbent glass tubes (P/N 012347-005-00; Gerstel or equivalent) to sample VOCs. In one facility without alcohol interference, VOC levels were collected on a Tenax-TA with a Carbosieve sorbent glass tube. In summary, we report valid indoor VOC measurements for a total of 34 ECE facilities, including 20 with outdoor measurements.

2.6.2 Targeted VOC Laboratory Measurements

The samples were analyzed at Lawrence Berkeley National Laboratory (LBNL) following U.S. EPA Methods TO-17.[92] Multipoint calibrations were prepared from standards to quantify 38 target analytes. All standards and analytes were referenced to an internal standard (~120 ng) of 1-bromo-4-fluorobenzene. All compounds over the method detection limit (MDL) (< 1 to several ng) were evaluated using the NIST spectral library followed by comparison to reference standards. On a mass/volume basis, the MDLs ranged from 0.03–1.80 μg/m³.[90] VOC levels below the MDL were imputed to MDL/√2.[93] Decamethylcyclopentasiloxane (D5), d-limonene, and octamethylcyclotetrasiloxane (D4) masses exceeded the highest calibration standard in 15 (44%), 11 (32%), and 2 (6%) of the ECE facilities, respectively. The analytical methods did not allow for reanalysis of these samples because the entire sample was consumed during the analyses. For these samples, the calibration high mass was used to calculate air concentration (using the sample-specific volume, which averaged ~7 liters).

For three duplicate VOC samples, the mean relative percent difference (RPD) was 15.2±4.8%, showing good precision overall. Seventeen travel blanks were analyzed for possible contamination. Of the 38 analytes measured, only two had median blank masses above the method detection limit: hexamethylcyclotrisiloxane (4.1 ng) and benzaldehyde (1.5 ng). Three Tenax travel spikes were used to quantify recovery. For all 38 analytes, average recovery for the travel spikes was 96.0% (SD=8.0). See Appendix Table 24 for additional QA/QC results. Note, when duplicate samples were collected, the average was used for final analyses.

2.6.3 Identification and Quantification of Non-targeted VOCs

For 32 facilities, we identified unknown peaks on the chromatograms from indoor air samples by conducting a mass spectral library search with the National Institute of Science and Technology (NIST) NIST08 database.[94] This approach utilizes automated deconvolution information software (AMDIS), which improves resolution of complex chromatograms with large numbers of unresolved or partially resolved peaks. For especially complex chromatograms, we used a dominant and/or unique fragment ion chromatogram in the mass spectra, referred to

here as the extracted ion chromatogram (EIC). The chemical name and retention time for each peak was recorded if the match quality was >80% as determined by the Chemstation software. This approach resulted in the identification of 151 chemicals, including overlap with the previously reported *a priori* target analytes (where standard calibration curves were used).[90] See Appendix Table 27 for more information.

We applied a modified toluene equivalent mass calibration to compute semi-quantitative estimates of the mass of each VOC identified with the spectral libraries. See Appendix Table 25. Toluene equivalent mass has long been used in reporting total volatile organic compounds (TVOC) for unidentified chemicals, and is optimal for total ion chromatographs (TIC) with well-resolved peaks.[95] We report values for each VOC if the peaks were >5 ng toluene equivalent in the chromatographs. In total, 119 additional VOC analytes were identified and quantified. To assess the quality of the estimated values, we compared levels of the 38 VOCs quantified *a priori* with the standard calibration curve versus estimated values from the toluene equivalent mode. The R^2 of the regression was 0.75, indicating reasonable estimation, with a tendency to underestimate true values with the toluene model.[90] See Appendix Figure 3. Overall, these results indicate that we correctly identified the non-targeted VOCs and the estimated values are a good indicator of the likely concentrations. See Appendix Table 26.

2.6.4 Comparison to Pure Standards and Probability-based Matching (PBM)

As additional verification, we ran pure standards for 14 selected non-targeted chemicals diluted to levels comparable to our estimated concentrations and compared the retention times. The retention times matched almost perfectly (R^2=0.998), confirming the accuracy of our prior identification based on the spectral libraries (Figure 1).

Probability-based matching (PBM)[96] was also performed and provided further confirmation of VOC identification. All PBM mass spectra were selected from ECE 32 sample results, except for acetophenone and phenol, which were selected from ECE 19 due to higher detectable masses. Of the VOCs detected, seven had a PBM score above 90% and all were above 70% (Range 72-96%), affirming a high quality of accuracy in VOC identification (Table 1).[96] The PBM test could not detect cyclohexanone and 1-butoxy-2-propanol in the selected samples due to their low masses.

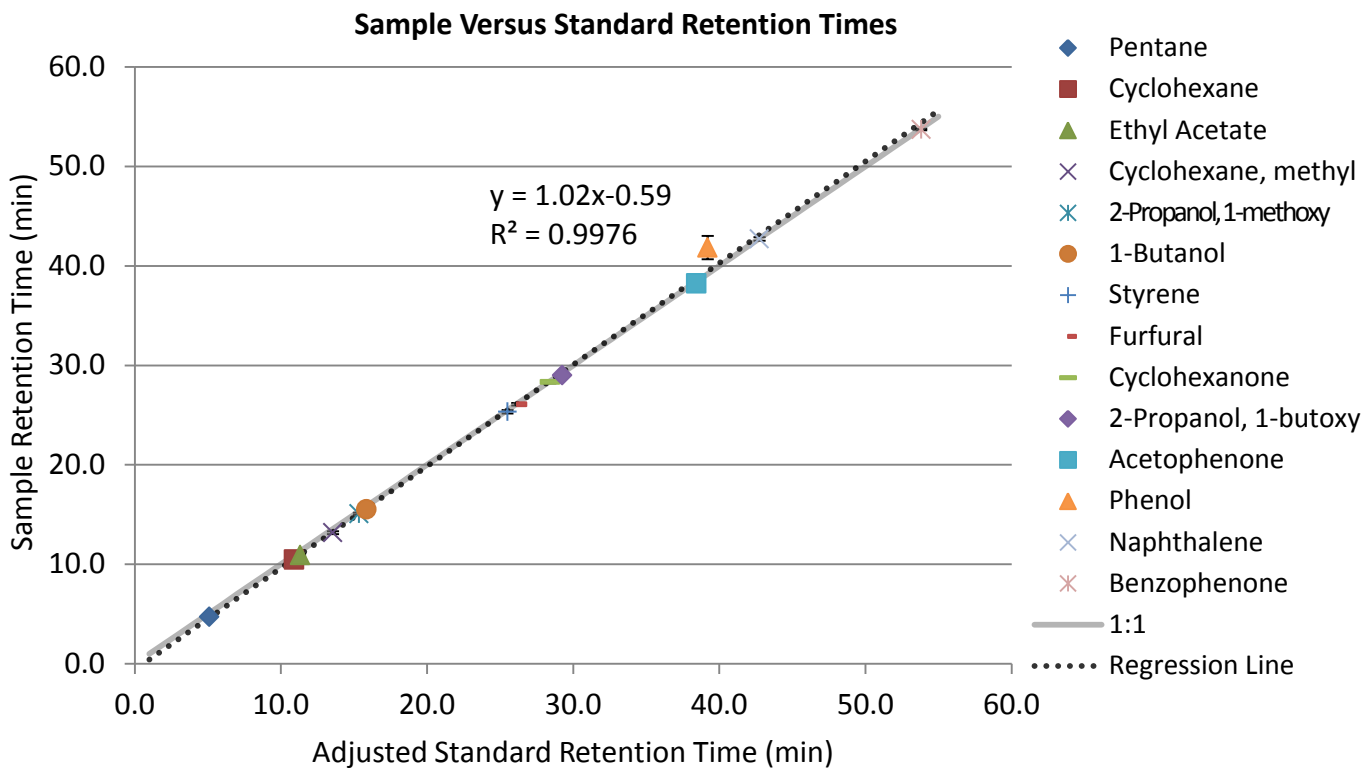


Figure 1. Relationship between the retention times of the adjusted pure standards versus retention times of the *a priori* target samples for 14 chemicals identified from the unknown chromatograph peaks.

Table 1. Probability-based Matching Results.[a]

STANDARDS	PBM (%)
Pentane	72
Cyclohexane	86
Ethyl acetate	83
Cyclohexane, methyl	93
2-Propanol, 1-methoxy	86
1-Butanol	78
Styrene	96
Furfural	90
Acetophenone	93
Phenol	94
Naphthalene	93
Benzophenone	96

[a] Cyclohexanone and 1-butoxy-2-propanol were not present in sufficient quantities for PBM sample analysis.

2.6.5 VOC Data Analysis

We first computed descriptive statistics for target and non-targeted analytes. Given uncertainties about the accuracy of quantified values for the non-targeted analytes, we limited analyses examining determinants of indoor VOCs to the targeted compounds only. For simplicity, we classified the targeted VOCs into two groups: (1) compounds with both indoor and mobile sources ("mixed and mobile sources" [MMS]) (n=15) and (2) compounds with primarily indoor sources ("household sources" [HS]) (n=23) (Table 7). The MMS VOCs (e.g., toluene) derive predominately from automotive exhaust or petroleum-based products like paints and adhesives.[97] The HS VOCs (e.g., d-limonene and 2-ethyl-1-hexanol) derive predominately from household products such as cleaning products, air fresheners, fragrances, or solvents.[98,99] Twelve of the HS VOCs are commonly used in fragrances. To verify these source groupings, we also examined Spearman correlation matrices to assess the relationships between VOCs within each group.

Potential determinants of targeted VOCs with detection frequencies >60% were examined in bivariate analyses. For both MMS and HS VOCs, we examined bivariate associations with license type (center/home-based), and building type (portable/non-portable). For MMS VOCs, we examined bivariate associations with season (summer/winter), gas appliances (present/absent), attached garages (present/absent), the use of glue (cement, epoxy or superglue) and permanent markers. For HS VOCs, we examined bivariate associations with reported use of air fresheners, "low-toxicity" cleaning products, and frequency of reported mopping. For MMS VOCs and specific non-fragrance HS VOCs, we also examined associations with the following building characteristics: carpet (present/absent), composite wood products (present/absent), vinyl floors (present/absent), occurrence of renovations within the last five years (yes/no), and installation of new floor coverings within the last year (yes/no). For these analyses, we used the non-parametric Wilcoxon rank-sum test. Due to the small sample size, multivariable statistical modeling was not appropriate.

We also computed indoor to outdoor (I/O) air concentration ratios of targeted VOCs for each facility with paired measurements (n=20) and used the Wilcoxon signed rank test to compare the levels. We evaluated Spearman rho correlations between the VOC levels and AER (hr^{-1}), RH (%), and temperature (°C). For MMS VOCs, we also evaluated correlations with length-adjusted traffic volumes (∑LATV) within a one kilometer (km) radius of the facility.[88]

2.7 Analysis software

All analyses were performed with STATA statistical software Version 13.0 (StataCorp, College Station, TX). Figures were produced in R Version 3.0.2 (The R Foundation for Statistical Computing, Vienna, Austria) and Microsoft Excel Version 2010.

2.8 Non-Cancer Risk Estimation

We conducted screening-level risk assessment was conducted to evaluate formaldehyde, acetaldehyde and VOC exposures in ECE facilities. Measured concentrations of indoor aldehydes and the 11 targeted and 6 non-targeted VOCs with available health benchmarks were compared with 8-hour, acute and chronic California OEHHA Reference Exposure Levels (RELs) and U.S. EPA Reference Concentrations (RfCs) listed in the Integrated Risk Information System (IRIS),[57,89,100,101,102] when available. If the ratios were greater than 1, the exposure exceeds the respective health-based exposure benchmark. Note, because the health-based

reference values include safety factors, exposures exceeding these levels are not necessarily likely to result in adverse health effects.

2.9 Cancer Risk Estimation

Under California's Proposition 65, OEHHA sets "Safe Harbor Levels" called No Significant Risk Levels (NSRLs) for carcinogenic substances, defined as the daily lifetime intake level posing a one in 100,000 (10^{-5}) excess risk of cancer over a lifetime.[103] Because NSRLs were developed for an adult weighing 70 kg, we computed age-adjusted NSRLs for VOCs that adjust for the difference in body weights (BW) between children and adults.[104] In addition, we used OEHHA's guidelines to define Safe Harbor Levels that account for the increased sensitivity of very young children, which incorporates an age sensitivity factor (ASF) of 10 for children <2 years old and of 3 for children between 2-6 years old.[103] Age-adjusted NSRLs were calculated for four age groups (i.e., birth to <1 year; 1 to <2 years; 2 to <3 years; and 3 to <6 years):

2.9.1 NSRL Calculations

$$NSRL_{\ child}\left(\frac{\mu g}{day}\right) = \frac{\frac{NSRL_{adult}\left(\frac{\mu g}{day}\right)}{BW_{\ adult}(70\ kg)} \times BW_{child}\ (Varies\ by\ Age\ Group, kg)}{ASF\ (Varies\ by\ Age\ Group)}$$

It should be noted that an age-adjusted NSRL is the estimated daily intake for that age range, which contributes 1/70th (assuming a 70-year lifespan) of the target lifetime cancer risk in that particular year of life. If the ratio of a child's aldehyde dose estimate (µg/day) to age-adjusted NSRL (µg/day) >1, the intake estimate exceeded the 10^{-5} cancer risk threshold for that year.

2.9.2 Exposure Dose Calculations

To compare with the age-adjusted NSRLs, child inhalation dose estimates were calculated based on the measured air formaldehyde, acetaldehyde and VOC concentrations and age-adjusted intake factors including inhalation rates (m^3/day), body weights (kg), and an exposure factor.[105] For age group birth to <1 year, the IR of 5.1 m^3/day[106] and BW of 6.8 kg[107] were derived from an average of three age groups (0-1, 3-5, and 6-11 months). For the respective age groups 1 to <2, 2 to <3, and 3 to <6 years, the IRs were 8.0, 9.5, and 10.9 m^3/day and the BWs were 11.4, 13.8, and 18.6 kg.[107] We divided daily IRs by three to obtain 8-hour IRs. See Appendix Table 28 for more information.

Since children are not present in ECE facilities every day, we assumed that children spend five days per week and 48 weeks per year (which accounts for four weeks away from child care for holidays and vacation) in child care. We assumed that alveolar absorption of these compounds was 100%, and that exposures occurred over one year.[105] Detailed information on the exposure dose calculations is presented in the following equations:

$$D_{child\ care} = \frac{C \times IR \times EF \times CF}{BW}$$

Where,

D=exposure dose received in child care assuming 8-hour day (mg/kg/8-hours)
C=contaminant concentration (mg/m³)
IR=inhalation rate (m³/8-hours)
EF=exposure factor
CF=conversion factor
BW=body weight (kg)

The EF is calculated[105]:

$$EF = \frac{F \times ED}{AT}$$

Where,

F = frequency of exposure (days/year)
ED = exposure duration (years)
AT = averaging time (ED x 365 days/year)

$$EF = \frac{\left(5\,\frac{days}{week}\right) \times \left(48\,\frac{weeks}{year}\right) \times (1\,year)}{1\,year\,\times\,365\frac{days}{year}} = 0.66$$

2.10 Hazard Assessment for Compounds without Non-Occupational Health-Based Exposure Benchmarks

Toxicological information for the VOCs were compiled from two main sources: (1) authoritative lists and reports from government agencies, NGOs, and other expert bodies and (2) a quantitative structure-activity relationship (QSAR) model.

Information sources used to complete the hazard assessment include:

- **ScoreCard**
  Maintained by the GoodGuide, ScoreCard[108] is an online program that identifies health hazards associated with chemicals. ScoreCard uses information from scientific sources and regulatory agencies to classify health hazards into two categories: recognized and suspected. ScoreCard has information on more than 11,200 chemicals but has not been updated since 2011.
- **Pharos Project**
  The Healthy Building Network curates the Pharos Project,[109] an online database compiling information on health hazards associated with chemicals used in consumer products and building materials. The Pharos Project compares chemical identifiers against 60 authoritative lists (including multiple international agencies such as the European Commission and Japan's Ministry of the Environment) and identifies associated health or environmental hazards. The Pharos Project contains more than 34,400 chemical profiles.

To address hazard identification data gaps, a well-recognized QSAR model was utilized to predict toxicity according to chemical structure:

- **Virtual models for Evaluating chemicals within a Global Architecture (VEGA)**
  The non-profit Istituto di Ricerche Farmacologiche "Mario Negri" in (Milan, Italy) created the VEGA[110] platform as an accessible and free QSAR tool for evaluating chemical safety. The QSAR program was developed with support from the European Union, and includes some overlapping models used in the Organization for Economic Co-operation and Development (OECD) QSAR Toolbox[111] program and outcomes included in the EPA TEST (Toxicity Estimation Software Tool) program. The VEGA platform focused on the following health endpoints : mutagenicity, carcinogenicity, developmental toxicity, and skin sensitization.[90,110,112] The IRCCS, Istituto di Ricerche Farmacologiche "Mario Negri"[113] assisted us with the use of VEGA. VEGA generates an applicability domain index (ADI) to assess the "fit" of its experimental data set to the chemical under investigation and the reliability of its predictions.[114] ADI scores >0.8 for mutagenicity models and >0.9 for the other models indicate good reliability. VEGA utilizes multiple models for some health endpoints and may yield contradictory predictions. When VEGA models produced contradictory predictions, we conservatively used the positive prediction for the health endpoint.[90]

We classified the compounds into potential hazard groups based on findings from VEGA, ScoreCard, and Pharos, including: potential carcinogen or mutagen (Group 1), developmental toxicants (Group 2), reproductive toxicants (Group 3), endocrine disrupting chemicals (Group 4), neurotoxicants (Group 5), immunotoxicants/sensitizers (Group 6), specific organ or acute toxicants (Group 7), irritants (Group 8), persistent or bioaccumulative chemicals (Group 9), and no information (Group 10). To quantify the breadth of hazard data, we allotted a binary score to each group according to the absence or presence (score=0 or 1) of positive toxicity data.[90] We summed the scores for each chemical, creating a cumulative "hazard score." We selected a hazard score of >3 to prioritize compounds for further review. We then evaluated chemical-specific information when available, including peer reviewed literature, summaries in the U.S. National Institute of Occupational (NIOSH) NIOSH Pocket Guide to Chemical Hazards (http://www.cdc.gov/niosh/npg/), Material Safety Data Sheets (MSDS), classification by the U.S. EPA Safer Choice Program (SCP), and independent reviews for final consideration of compounds warranting further study. For example, we excluded propylene glycol because it has been independently reviewed as a food additive.[115]

3 Results

3.1 ECE Facility and Child Characteristics

Building types included single family detached homes (37.5%), traditional school buildings (27.5%), portable school buildings (22.5%), office buildings (7.5%), and churches (5%). Half the facilities were in buildings constructed after 1970, with the oldest structure built in 1903 and the most recent built in 2008. Twenty-six (65%) facilities were in residential neighborhoods, eight (20.0%) were in commercial areas, five (12.5%) were adjacent to agricultural fields, and one (2.5%).

The 40 ECE facilities served a total of 1,764 children (average attendance=44 children; range=4-200). Seventy-six percent of the children were 3+ years, 19% were 2-3 years, and 5% were less than 2 years of age. Thirty-seven percent of children spent >8 hours per day in child care. See Appendix Table 29.

3.2 Air Temperature, Relative Humidity and Exchange Rates

Average indoor air temperature ranged from 16.0-24.6°C with a mean of 21.1±1.7°C. Average outdoor RH ranged from 21.6-74.7% with a mean of 49.4±12.0%. Average indoor RH ranged from 34.5-62.6% with a mean of 49.3±6.9%.

The 40 ECE facilities had an average AER of 2.0±1.4 hr^{-1} with a range of 0.28-5.63 hr^{-1}. Due to the moderate climate in Alameda and Monterey Counties, natural ventilation (such as opened windows) was often used, especially on warm and breezy afternoons. The AERs measured in ECE facilities were higher than rates reported in a study of California homes (median=1.41 versus 0.26 hr^{-1}, respectively)[60] However, thirty percent (12) of the facilities were below California ventilation guidelines for new construction (2.7 m^3/hour for each m^2 of floor space), with 3 facilities (7.5%) with very low ventilation ($\leq$1 m^3/hour/ m^2).[87] See Appendix Table 30 for more information.

3.3 Aldehydes

3.3.1 Aldehyde Concentrations in Air

Acetaldehyde and formaldehyde were detected in 100% of the ECE facilities measured.

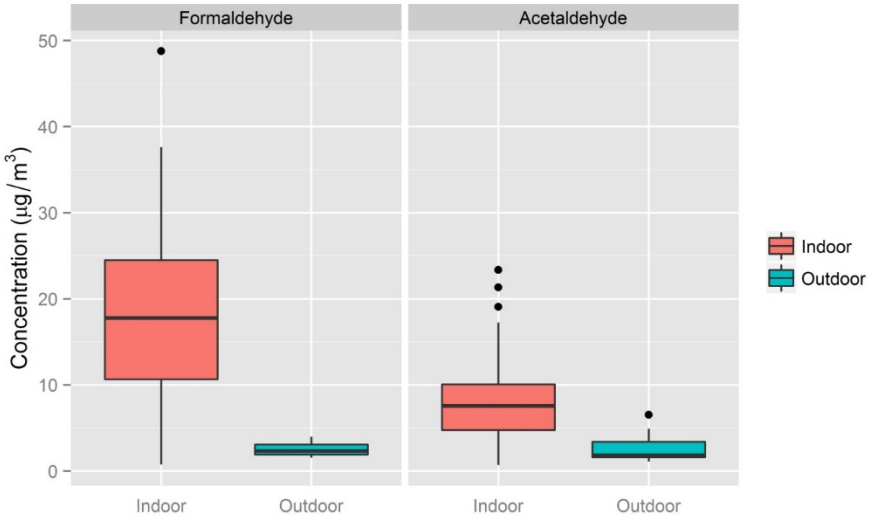
Table 2 summarizes results for indoor (n=40) and outdoor (n=19) measurements. The median (range) indoor formaldehyde and acetaldehyde concentrations were 17.8 µg/m^3 (0.7-48.8 µg/m^3) and 7.5 µg/m^3 (0.7-23.3 µg/m^3), respectively. The median (range) outdoor formaldehyde and acetaldehyde concentrations were 2.3 µg/m^3 (1.5-4.0 µg/m^3) and 1.8 µg/m^3 (1.1-6.5 µg/m^3), respectively. Overall, aldehyde levels were significantly higher indoors compared to outdoors ($p<0.05$; see Figure 2) indicating that indoor sources are primary contributors to indoor formaldehyde and acetaldehyde concentrations. Median (range) estimated emission rates were 59.2 µg/m²/h (8.1-152.7 µg/m²/h) for formaldehyde and 16.5 µg/m²/h (1.4-53.6 µg/m²/h) for acetaldehyde.

Table 2. Summary of Indoor (n=40) and Outdoor (n=19) Aldehyde Concentrations (µg/m³)[a]

Analyte[a]	GM (95% CI)	Arithmetic Mean±SD	Min	25th	50th	75th	90th	Max
Formaldehyde								
Indoor	15.9 (12.7, 19.9)	18.9±10.1	0.7	10.6	17.8	25.0	33.2	48.8
Outdoor	2.4 (2.1, 2.8)	2.5±0.8	1.5	1.9	2.3	3.1	3.9	4.0
Acetaldehyde								
Indoor	6.9 (5.5, 8.6)	8.5±5.4	0.7	4.7	7.5	10.5	17.1	23.3
Outdoor	2.2 (1.7, 2.8)	2.5±1.5	1.1	1.5	1.8	3.4	4.9	6.5

[a]All concentrations were detected above the MDL.

Figure 2. Box plots of indoor (n=40) vs. outdoor (n=19) formaldehyde and acetaldehyde concentrations.



3.3.2 Determinants of Aldehyde Concentrations

3.3.2.1 Formaldehyde

In bivariate analyses, formaldehyde levels were inversely associated with estimated AER in the room (r = -0.54; p-value<0.001), and weakly correlated with average RH (r=0.31, p=0.05) and average indoor temperature (r=0.22, p=0.17). Indoor formaldehyde concentrations were lower in the 35 ECE facilities with at least some composite wood products present (mean=17.5±8.0 µg/m^3) compared to five facilities with no composite wood products present (mean=28.6±17.7 µg/m^3) (p<0.05). Differences in AERs did not explain this finding, and given that most buildings and furnishings were older than 5 years it is likely that initial composite wood product sources had finished off-gassing. Formaldehyde levels were higher in the 12 home-based ECE facilities (mean=24.6±13.2 µg/m^3) compared to the 28 center-based ECE facilities (mean=16.4±7.4 µg/m^3) (p<0.05). In addition, use of "low-toxicity" cleaners was associated with lower formaldehyde levels (p-value<0.03).

Formaldehyde levels were not associated with season; location by county; building age; portable or manufactured buildings compared to all other building types; the presence of gas appliances; reported new flooring in the last year; reported renovations in the last 5 years; presence of carpet, or reported use of air freshener.[89]

Final multivariate regression model results for formaldehyde concentrations showed an inverse association between formaldehyde levels and AER (β=-3.52; p<0.001) and a positive association with average indoor temperature (β=2.51; p<0.01), RH (β=0.40; p<0.05), and home-based compared to center-based facilities (β=8.31; p<0.05; adjusted R^2=0.54) (Table 3).

Table 3. Results from Multiple Regression Analysis of Formaldehyde Levels (µg/m^3) and Predictors (n=40).[a]

	Coefficient	(95% CI)	p-value
Formaldehyde			
AER **(hr^{-1})**	-3.5	(-5.3, -1.8)	<0.001
Temperature **(°C)**	2.5	(0.9, 4.2)	0.004
RH **(%)**	0.4	(0.0, 0.8)	0.037
License Type (Home vs Center)	8.3	(1.6, 15.0)	0.016

[a]Adjusted R^2=0.54.

3.3.2.2 Acetaldehyde

In bivariate analyses, acetaldehyde levels were inversely associated with AER (r= -0.63; p-value<0.001) and weakly correlated with average indoor temperature (r=0.22, p=0.17). Indoor acetaldehyde levels were slightly lower in six ECE facilities with reported new floor coverings [Geometric mean (GM) (95% CI)=4.0 (1.4, 11.3) µg/m^3] compared to 34 facilities with no new floor coverings [GM (95% CI)=7.6 (6.1, 9.3) µg/m^3] (p<0.05), but this association did not persist in the multivariate models.

On a bivariate basis, acetaldehyde levels were not associated with season; location by county; license type (home-based versus center); building age; portable or manufactured buildings compared to all other building types; RH; the presence of composite wood products or gas appliances; reported renovations in the last 5 years; presence of carpet; or reported use of air freshener.

Final multivariate regression model results for acetaldehyde also showed an inverse association between acetaldehyde levels and AER (β=-0.34; p<0.001) and positive associations with RH (β=0.03; p<0.05) (adjusted R^2=0.50) (Table 4).

Table 4. Results from Multiple Regression Analysis of Log-Transformed Acetaldehyde Levels (µg/m^3) and Predictors (n=39).[a]

	Percent Change	(95% CI)	p-value
Acetaldehyde			
AER **(hr^{-1})**	-54.2	(-65.1, -40.0)	<0.001
Temperature **(°C)**	24.1	(-2.2, 57.5)	0.074
RH **(%)**	7.5	(1.6, 13.7)	0.013
Air Freshener Use (Yes/No)	100.0	(-6.8, 329.0)	0.074

[a] Adjusted R^2=0.50.

3.3.3 Aldehyde Emission Rates

We found no associations between formaldehyde or acetaldehyde emission rates and building age, temperature, RH, building type, renovations, new flooring, carpet, air freshener use, license type or presence of composite wood products. Acetaldehyde emission rates were slightly higher in facilities with air freshener use (median=17.8 vs 15.0 µg/m^2/h)(Mann-Whitney, p=0.08).

3.3.4 Aldehyde Health Risk Characterization

3.3.4.1 Non-cancer risk evaluation

We compared air concentrations of formaldehyde and acetaldehyde to the acute, 8-hour, and chronic RELs and RfC values, when available (Table 5).The 50th and 95th percentile formaldehyde air concentrations (17.8 and 37.3 µg/m^3, respectively) exceeded the 8-hour REL (9 µg/m^3) and chronic REL (9 µg/m^3).[116] The ratios comparing the formaldehyde 50th and 95th percentile concentrations to the 8-hour REL and chronic REL were 2.0 and 4.1, respectively. Formaldehyde levels exceeded the 8-hour REL and chronic REL in 87.5% of facilities. Acetaldehyde concentrations were lower than OEHHA RELs, but exceeded the U.S. EPA RfC in 30% of facilities. The ratios comparing the acetaldehyde 50th and 95th percentile concentrations to the RfC were 0.8 and 2.2, respectively.

The OEHHA 8-hour REL and chronic REL for formaldehyde are based on health effects including nasal obstruction and discomfort, lower airway discomfort, and eye irritation.[117] The U.S. EPA RfC for chronic acetaldehyde inhalation is based on degeneration of olfactory epithelium in two short-term rat inhalation studies.[57]

Table 5. Ratios of Indoor Aldehyde Air Concentrations to OEHHA Acute Reference Exposure Level (aREL), 8-hour REL, Chronic REL (cREL) and U.S. EPA Reference Concentration (RfC).

Analyte	Percentile (%)	Air Concentration (µg/m³)	aREL[a] (µg/m³)	Ratio[b] (aREL)	8-hr REL[a] (µg/m³)	Ratio[b] (8-hr REL)	cREL[a] (µg/m³)	Ratio[b] (cREL)	RfC[c] (µg/m³)	Ratio[b] (RfC)
Formaldehyde	50th	17.8	55	0.3	9	2	9	2	-[d]	NC
	95th	37.3		0.7		4.1		4.1		NC
Acetaldehyde	50th	7.5	470	0.02	300	0.03	140	0.05	9	0.8
	95th	20.2		0.04		0.07		0.1		2.2

Abbreviation
NC: not calculated

[a]OEHHA REL
[b]Ratio of air concentration to preceding exposure guideline REL or RfC.
[c]U.S. EPA RfC
[d]U.S. EPA RfC for formaldehyde has not been established

3.3.4.2 Cancer risk evaluation

We compared the 50th and 95th percentile inhalation dose estimates to the age-adjusted NSRL values by age group assessed (birth to <1 year; 1 to <2 years; 2 to <3 years; and 3 to <6 years) (Table 6). The 50th and 95th percentile dose estimates for formaldehyde and acetaldehyde exceeded the age-adjusted NSRL in all four age groups. The formaldehyde 50th and 95th percentile NSRL ratios for the four age groups were 51.7 and 108.4; 48.0 and 100.7; 14.1 and 29.6; and 12.0 and 25.2, respectively. The acetaldehyde 50th and 95th percentile NSRL ratios for the four age groups were 9.8 and 26.1; 9.1 and 24.3; 2.7 and 7.1; and 2.3 and 6.1, respectively. Child acetaldehyde and formaldehyde dose estimates exceeded age-adjusted NSRL benchmarks based on carcinogenicity in all of the facilities (Table 6).

Table 6. Aldehyde Inhalation Dose Estimates Compared to Age-adjusted NSRLs.

Age Group	50th% Dose Estimates (µg/day)	95th % Dose Estimates (µg/day)	$NSRL_{child}$ (µg/day)	50th % Ratio	95th % Ratio
Formaldehyde					
Birth to <1 year	19.9	41.8	0.39	51.7	108.4
1 to <2 years	31.3	65.6	0.65	48.0	100.7
2 to <3 years	37.1	77.9	2.6	14.1	29.6
3 to <6 years	42.6	89.4	3.5	12.0	25.2
Acetaldehyde					
Birth to <1 year	8.5	22.7	0.87	9.8	26.1
1 to <2 years	13.3	35.6	1.47	9.1	24.3
2 to <3 years	15.8	42.2	5.9	2.7	7.1
3 to <6 years	18.1	48.4	8.0	2.3	6.1

3.4 VOCs

3.4.1 Targeted VOC Levels in Air

3.4.1.1 Mixed Mobile Source VOCs

For the 15 MMS VOCs, the median indoor concentration ranged from 0.1 µg/m³ for 1,2,3-trimethylbenzene to 3.1 µg/m³ for toluene (Table 7). Seven compounds were detected in 100% of indoor samples – including toluene, ethylbenzene, and xylenes. Benzene was detected in 70.6% of samples.

Table 7. Distributions of Indoor Air Concentrations for 38 Targeted VOCs (µg/m³) (n=34 ECE facilities).[a]

Analyte	>MDL (%)	Geometric Mean±GSD	Arithmetic Mean±SD	25th %	Median	75th %	95th %	Max
Mixed and Mobile Sources (MMS)								
Benzene	70.6	0.8±0.5	0.9±0.5	<MDL	0.9	1.0	2.0	2.6
Butylbenzene	17.7	<MDL	<MDL	<MDL	<MDL	<MDL	0.1	0.2
n-Decaneb	90.9	0.6±0.9	0.8±0.9	0.4	0.6	1.0	3.0	4.5
n-Dodecane	91.2	0.8±0.9	1.1±1.1	0.4	0.7	1.6	2.8	5.0
Ethylbenzene	100.0	0.5±0.8	0.7±0.6	0.3	0.6	1.0	2.0	2.0
n-Heptane	100.0	1.5±1.2	3.0±4.1	0.5	1.5	3.5	10.9	19.8
n-Hexadecane	100.0	0.9±0.6	1.0±0.7	0.6	0.8	1.2	2.4	4.1
n-Hexane	58.8	0.7±0.8	0.9±0.9	<MDL	0.6	1.0	2.9	3.6
n-Octane	100.0	0.7±0.6	0.8±0.8	0.5	0.6	1.1	1.8	4.3
n-Tetradecane	100.0	2.1±0.9	3.1±3.3	1.1	1.9	4.0	7.7	17.3
Toluene	100.0	3.2±0.7	4.1±3.0	1.7	3.1	5.5	11.2	12.4
1,2,3-Trimethylbenzene	64.7	0.1±1.2	0.2±0.2	<MDL	0.1	0.3	0.7	1.0
1,2,4-Trimethylbenzene	97.1	0.5±0.9	0.7±0.6	0.3	0.5	0.9	2.3	2.7
n-Undecane	85.3	0.6±0.9	0.9±1.0	0.3	0.6	0.9	3.3	4.6
Xylenes	100.0	2.2±0.9	3.2±2.7	1.0	2.5	4.8	9.2	9.4
Household Sources (HS)								
Fragrances								
Benzaldehyde	100.0	2.7±0.5	3.0±1.7	2.0	2.4	3.8	5.7	9.4
Butanal	100.0	0.7±0.5	0.8±0.4	0.5	0.7	0.9	1.6	2.0
3-Carene	82.4	0.2±1.4	0.5±0.7	0.1	0.2	0.6	1.8	3.0
Decanal[f]	94.1	2.5±1.2	4.3±4.7	1.6	2.6	4.7	18.2	22.0
Heptanal	97.1	0.9±0.7	1.1±0.5	0.8	1.0	1.3	2.1	2.7
Hexanal[f]	100.0	6.3±0.6	7.7±5.4	3.9	5.7	10.0	20.9	22.5
d-Limonene	100.0	23.1±1.2	37.3±28.1	9.1	33.1	>68.7[c]	>74.9[c]	>81.5[c]
Nonanal	100.0	8.4±0.4	9.1±3.5	6.5	8.5	10.3	15.6	16.0

Table 7 Continued. Distributions of Indoor Air Concentrations for 38 Targeted VOCs (µg/m³) (n=34 ECE facilities).[a]

Analyte	>MDL (%)	Geometric Mean±GSD	Arithmetic Mean±SD	25th %	Median	75th %	95th %	Max
Octanal[f]	100.0	2.1±0.4	2.3±1.0	1.7	2.1	2.5	5.3	5.7
α-Pinene	100.0	3.7±1.0	6.4±10.0	1.7	3.6	6.4	19.9	57.7
α-Terpineol[g]	85.3	0.5±1.6	1.8±4.2	0.3	0.4	1.9	6.4	24.1
γ-Terpinene[f]	61.8	0.2±1.8	0.7±1.4	<MDL	0.3	0.4	4.8	7.1
Other household product sources								
2-Butoxyethanol	100.0	4.7±1.2	10.9±19.4	1.8	2.9	8.6	>64.0[c]	>92.4[c]
Carbon tetrachloride	2.9	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	2.1
Chloroform	38.2	0.6±1.0	1.3±2.6	<MDL	<MDL	0.8	7.7	12.6
Decamethylcyclopentasiloxane (D5)	100.0	34.0±0.9	46.4±28.2	17.4	51.4	>70.8[c]	>83.6[c]	>88.2[c]
2-Ethyl-1-hexanol	100.0	1.7±0.5	1.9±1.0	1.1	1.6	2.8	3.9	3.9
Hexamethylcyclotrisiloxane (D3)	50.0	2.3±0.7	3.0±2.3	<MDL	1.5	4.6	8.0	9.3
Methylene chloride	2.9	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	0.5
Octamethylcyclotetrasiloxane (D4)[b]	90.9	1.4±1.7	7.4±18.1	0.5	0.9	2.9	>70.9[c]	>78.5[c]
Tetrachloroethylene[b]	51.5	0.1±1.1	0.4±1.3	<MDL	0.1	0.2	1.0	7.8
Texanol[d]	100.0	5.0±1.0	8.7±12.0	2.4	4.6	8.6	32.7	60.7
TXIB[e]	100.0	4.6±0.9	7.7±13.8	2.3	4.7	7.9	14.1	82.8

[a] If indoor concentrations <MDL, values were imputed as MDL/√2.
[b] All VOCs were analyzed in 34 samples, except for decane, D4, and tetrachloroethylene (n=33 samples).
[c] Denotes when the highest calibration range was used as analyte mass to calculate sample concentration. Values underestimate the true air concentrations.
[d] Texanol: 2,2,4-trimethyl-1,3-pentanediol monoisobutyrate
[e] TXIB: 2,2,4-trimethyl-1,3-pentanediol diisobutyrate.
[f] U.S. EPA SCP "yellow triangle" rating: The chemical has met Safer Choice Criteria for its functional ingredient-class, but has some hazard profile issues.
[g] U.S. EPA SCP "green half-circle" rating: The chemical is expected to be of low concern based on experimental and modeled data.[118]

Many of the MMS VOCs were moderately to strongly correlated with each other (rho>0.35 ($p<0.05$); Table 8). For example, benzene was significantly correlated with all the MMS VOCs ($r=0.42$-0.84, $p<0.05$). The MMS VOCs were detected more frequently indoors than outdoors (Table 7, Table 10 and Appendix Table 31), and 93% had significantly higher levels indoors than outdoors (Table 10), with the mean I/O ratios ranging from 1.1 for benzene to 59.4 for n-tetradecane (Table 10), underscoring that some of these compounds also have indoor sources.

Table 8. Correlation Matrix for Mixed and Mobile Source (MMS) VOCs[a]

	Benzene	Decane	Dodecane	Ethyl-benzene	Heptane	Hexa-decane	Octane	Tetra-decane	Toluene	123-TMB	124-TMB	Undecane	Xylene
Benzene	1												
Decane	0.47*	1											
Dodecane	0.47*	0.51*	1										
Ethyl-benzene	0.78*	0.58*	0.35*	1									
Heptane	0.73*	0.35*	0.33	0.63*	1								
Hexa-decane	0.54*	0.19	0.23	0.31	0.69*	1							
Octane	0.74*	0.32	0.40*	0.58*	0.83*	0.54*	1						
Tetra-decane	0.48*	0.20	0.49*	0.32	0.47*	0.66*	0.40*	1					
Toluene	0.84*	0.37*	0.20	0.82*	0.74*	0.51*	0.73*	0.39*	1				
123-TMB	0.73*	0.58*	0.42*	0.84*	0.60*	0.34	0.55*	0.39*	0.72*	1			
124-TMB	0.84*	0.54*	0.31	0.93*	0.75*	0.39*	0.66*	0.30	0.88*	0.09	1		
Undecane	0.42*	0.71*	0.69*	0.45*	0.27	0.19	0.30	0.31	0.20	0.48*	0.33	1	
Xylene	0.79*	0.55*	0.34	0.99*	0.64*	0.32	0.59*	0.33	0.85*	0.86*	0.94*	0.43*	1

Abbreviations: 1,2,3-trimethylbenzene (1,2,3-TMB) and 1,2,4-trimethylbenzene (1,2,4-TMB).
[a]Spearman rho correlations. *$p<0.05$.

3.4.1.2 Household Source VOCs

For the 23 HS VOCs, the median indoor concentrations ranged from 0.1 for tetrachloroethylene to 51.4 µg/m³ for D5 (Table 7). The fragrance VOCs were frequently detected indoors with nine (of twelve) compounds detected in >90% of ECE facilities. D-limonene was detected in all facilities and had a median (range) of 33.1 µg/m3 (0.8-81.5 µg/m^3). Of the non-fragrance VOCs, D5 had the highest median concentration (51.4 µg/m³, range: 2.6-88.2 µg/m3). D4 also had a high detection frequency (90.9%) with a median concentration (range) of 0.9 µg/m^3 (0.1-78.5 µg/m^3). Many of the indoor HS VOC concentrations (Table 9) were also moderately correlated (rho>0.36, $p<0.05$), albeit less strongly than the MMS VOCs. HS VOCs were detected more frequently indoors than outdoors (n=20) (Table 7 and Table 10). The mean I/O ratios for HS VOCs ranged from 1.2 (carbon tetrachloride and methylene chloride) to 1,603.9 (d-limonene) and were higher than the MMS ratios, indicating that indoor sources were dominant for these compounds (Table 7); 91% of the 23 HS VOCs had significantly higher levels indoors than outdoors (Table 7).

Table 9. Correlation Matrix for Household Source (HS) VOCs.

	Benz-aldehyde	Butanal	3-Carene	Decanal	Heptanal	Hexanal	d-limonene	Nonanal	Octanal	α-Pinene	α-Terpineol	ɣ-Terpinene
Benz-aldehyde	1											
Butanal	0.52*	1										
3-Carene	0.41*	0.49*	1									
Decanal	0.06	0.08	-0.09	1								
Heptanal	0.43*	0.24	0.42*	0.02	1							
Hexanal	0.37*	0.64*	0.38*	0.26	0.48*	1						
d-limonene	0.10	0.37*	0.51*	-0.15	0.14	0.28	1					
Nonanal	0.15	-0.05	-0.05	0.23	0.62*	0.23	-0.18	1				
Octanal	0.60*	0.32	0.53*	0.22	0.77*	0.45*	0.33	0.51*	1			
a-Pinene	0.30	0.48*	0.66*	-0.24	0.27	0.30	0.39*	-0.11	0.31	1		
a-Terpineol	0.53*	0.54*	0.37*	0.08	0.34	0.58*	0.49*	0.00	0.43*	0.39*	1	
Terpinene	0.16	0.22	0.31	0.09	0.18	0.36*	0.49*	-0.07	0.28	0.38*	0.50*	1
2-Butoxy-ethanol	0.56*	0.57*	0.34	0.15	0.36*	0.34	0.26	0.30	0.40*	0.09	0.37*	0.14
D5	0.06	0.07	0.19	0.16	-0.04	0.05	0.32	-0.15	0.15	0.26	0.52*	0.22
2-Ethyl-1-hexanol	0.61*	0.70*	0.62*	0.04	0.37*	0.57*	0.56*	-0.06	0.52*	0.54*	0.72*	0.47*
D4	0.24	0.43*	0.32	-0.06	0.09	0.21	0.28	-0.16	0.06	0.37*	0.56*	0.07
Texanol	0.19	0.30	0.30	-0.32	0.40*	0.26	0.19	0.20	0.34	0.31	0.18	0.15
TXIB	0.20	0.06	0.44*	-0.31	0.25	0.22	0.24	-0.11	0.13	0.18	0.17	0.00

Abbreviations: decamethylcyclopentasiloxane (D5); octamethylcyclotetrasiloxane (D4); 2,2,4-trimethyl-1,3-pentanediol diisobutyrate (TXIB). [a]Pearson correlations. *p<0.05. **p<0.01.

Table 10. **Outdoor VOC Concentrations (µg/m^3) and Indoor-to-Outdoor (I/O) Ratios.**[a]

	Outdoor (n=20)		I/O Ratios	
Analyte	**>MDL (%)**	**Median**	**Mean Ratio±SD**	**Range**
Mixed and Mobile Sources				
Benzene	75.0	0.6	1.1±0.5	0.5-2.7
Butylbenzene	0.0	<MDL	1.4±1.3*	0.6-6.7
n-Decane	30.0	<MDL	9.0±11.5*	1.1-48.8
n-Dodecane	0.0	<MDL	7.7±8.2*	0.6-35.0
Ethylbenzene	65.0	0.1	6.7±7.1*	1.0-25.4
n-Heptane	85.0	0.4	4.2±4.3*	1.0-17.0
n-Hexadecane	5.0	<MDL	19.8±14.6*	5.2-62.2
n-Octane	60.0	0.1	8.2±6.1*	1.4-21.1
n-Tetradecane	10.0	<MDL	59.4±47.2*	17.5-164.9
Toluene	100.0	0.9	3.4±2.4*	1.3-9.7
1,2,3-Trimethylbenzene	25.0	<MDL	7.1±11.1*	0.3-37.6
1,2,4-Trimethylbenzene	60.0	0.1	5.5±4.5*	0.7-15.5
n-Undecane	5.0	<MDL	6.1±7.3*	0.6-29.1
Xylenes	100.0	0.6	4.9±6.0*	0.8-25.1
Household Sources				
Fragrances				
Benzaldehyde	100.0	2.3	1.3±0.6	0.3-2.5
Butanal	25.0	<MDL	13.6±9.6*	3.9-45.8
3-Carene	0.0	<MDL	24.8±31.5*	1.1-126.4
Decanal	55.0	0.1	39.3±35.3*	2.7-140.3
Heptanal	15.0	<MDL	26.0±10.2*	7.4-43.3
Hexanal	80.0	0.2	44.3±31.7*	9.3-119.1
d-Limonene	5.0	<MDL	1603.9±1481*	81.7-4015
Nonanal	95.0	.02	42.9±36.7*	5.6-167.8
Octanal	55.0	0.1	25.0±13.2*	8.8-54.1
α-Pinene	45.0	<MDL	59.9±62.8*	5.6-230.6
α-Terpineol	0.0	<MDL	34.3±51.1*	1.1-172.8
ɣ-Terpinene	0.0	<MDL	16.6±24.1*	0.9-84.0
Other household products				
2-Butoxyethanol	20.0	<MDL	88.4±85.7*	23.1-375.0
Carbon tetrachloride	0.0	<MDL	1.2±0.2*	0.6-1.4
Chloroform	0.0	<MDL	6.2±11.1*	0.9-38.1
Decamethylcyclopentasiloxane (D5)	95.0	0.3	159.8±129.9*	28.7-457.0
2-Ethyl-1-hexanol	5.0	<MDL	41.6±22.9*	15.0-101.2

Table 10 Continued. Outdoor VOC Concentrations (µg/m^3) and Indoor-to-Outdoor (I/O) Ratios.[a]

	Outdoor (n=20)		I/O Ratios	
Analyte	**>MDL (%)**	**Median**	**Mean Ratio±SD**	**Range**
Hexamethylcyclotrisiloxane (D3)	25.0	<MDL	1.4±1.1	0.4-5.3
Methylene chloride	0.0	<MDL	1.2±0.2*	0.6-1.4
Octamethylcyclotetrasiloxane (D4)	35.0	<MDL	67.3±177.6*	0.7-785.5
Tetrachloroethylene	30.0	<MDL	1.9±1.6*	0.4-6.5
Texanol	10.0	<MDL	278.7±435.8*	6.6-1,832
TXIB	10.0	<MDL	116.6±83.5*	11.2-324.5

[a]If VOC concentrations were <MDL, values were imputed as MDL/√2 and used for analyses.
*p<0.05 from Wilcoxon matched-pairs signed ranks test comparing indoor and outdoor VOC concentrations.

3.4.2 Determinants of Targeted VOC Air Concentrations

3.4.2.1 Mixed Mobile Source VOCs

Several indoor MMS VOC air concentrations (including benzene; n-heptane; n-hexadecane; n-tetradecane; toluene; and 1,2,4-trimethylbenzene) were inversely and significantly associated with AER (Spearman rho= -0.38 to -0.67, p<0.05). See Appendix Table 32. Three MMS VOCs were positively correlated with ΣLATV (including benzene, n-heptane, and n-hexadecane) (Spearman rho= 0.38-0.44, p<0.05). Five MMS VOCs were significantly lower (p<0.05) in centers compared to home-based facilities (ethylbenzene; n-octane; toluene; 1,2,4-trimethylbenzene; and xylenes). The presence/absence of gas appliances and attached garages were not significantly associated with these compounds (p<0.05) and does not explain the difference by license type. Reported glue use was significantly associated with indoor levels of xylenes (p<0.05;Table 11).

Table 11. Summary of Mixed and Mobile-Source (MMS) VOC Concentrations (µg/m^3) and Potential Indoor Determinants.[a]

	n-Hexadecane		n-Octane		Benzene		n-Heptane	
	n (%)	**Median**	**n (%)**	**Median**	**n (%)**	**Median**	**n (%)**	**Median**
License Type								
Center			23 (68)	0.5				
Home			11 (32)	0.9*				
Presence of CWPs[b]								
Yes			29 (85)	0.5	29 (85)	0.8		
No			5 (15)	1.3*	5 (15)	1.1*		
Presence of New Floors								
Yes					6 (18)	0.4	6 (18)	0.5
No					28 (82)	0.9*	28 (82)	1.9*
Use of Permanent Markers or Art Pens								
Yes	24 (71)	0.9*						
No	10 (29)	0.6						

	Ethylbenzene		1,2,4-Trimethylbenzene		Xylenes		Toluene	
	n (%)	**Median**	**n (%)**	**Median**	**n (%)**	**Median**	**n (%)**	**Median**
License Type								
Center	23 (68)	0.5	23 (68)	0.5	23 (68)	1.8	23 (68)	2.5
Home	11 (32)	1.0*	11 (32)	0.9*	11 (32)	4.8*	11 (32)	5.2*
Use of Glue								
Yes					6 (18)	4.0*		
No					28 (82)	1.8		

*p<0.05. [a]p-values from Wilcoxon rank-sum test of VOC air concentrations. [b]Composite Wood Products (CWPs).

3.4.2.2 Household Source VOCs

Butanal, hexanal, α-pinene, 2-ethyl-1-hexanol, and D4 were significantly and inversely associated with AER (Spearman rho= -0.42 to -0.62, $p<0.05$, See Appendix Table 33), indicating indoor sources of these chemicals. Indoor concentrations of VOCs found in fragrances (hexanal, decanal and D5) were significantly and positively correlated with reported air freshener use ($p<0.05$; Table 12). Levels of HS VOCs, including siloxanes, were similar in facilities that reported use/purchase of low-toxicity cleaners compared with those using traditional cleaners. However, D5 concentrations were significantly higher in facilities with higher mopping frequency, suggesting VOC emissions from the floor cleaner. Building type, vinyl flooring, carpet, and license type were not significantly associated with any HS VOCs.

Table 12. Summary of Household Source (HS) VOC Concentrations (µg/m^3) and Potential Indoor Determinants.[a]

	Decanal		Decamethylcyclo-pentasiloxane (D5)		Hexanal		2-Ethyl-1-hexanol	
	n (%)	Median	n (%)	Median	n (%)	Median	n (%)	Median
Use of Air Fresheners								
Yes	14 (41)	4.0*	14 (41)	70.7*	14 (41)	9.3*		
No	20 (59)	2.3	20 (59)	32.9	20 (59)	4.6		
Occurrence of Daily Mopping								
Yes			25 (74)	65.9*				
No			9 (26)	18.0				
Presence of New Floors								
Yes							6 (18)	1.1
No							28 (82)	1.9*

*$p<0.05$. [a]p-values from Wilcoxon rank-sum test of VOC air concentrations.

3.4.3 Non-targeted VOC Levels

Estimated levels of all 119 non-targeted VOC analytes are presented by chemical class in Table 13. For the 31 alkane compounds, the highest median concentrations were found for 3-methyl-hexane (275.3 ng/m^3) and methylcyclohexane (292.5 ng/m^3). For the 28 oxygenated hydrocarbon compounds, median concentrations ranged from 63.5 ng/m^3 for acetate-2-pentanol to 7357.4 ng/m^3 for propylene glycol. For the 15 aromatic compounds, median concentrations ranged from 105.2 ng/m^3 for 2-methoxynaphthalene to 1127.8 ng/m^3 for phenol. Naphthalene was detected in 96.9% of samples with a median concentration of 341.9 ng/m^3. Siloxane median concentrations were 1885.5 ng/m^3 for dodecamethylcyclohexasiloxane (D6) and 17.3 ng/m^3 for decamethyltetrasiloxane. For the 15 terpenes, median concentrations ranged from 65.5 ng/m^3 for 1-(2,6,6-trimethyl-2-cyclohexen-1-yl)-1-penten-3-one to 1,656.7 ng/m^3 for 2,6-dimethyl-7-octen-2-ol (Table 13).

Table 13. Estimated Concentrations (ng/m³) of 119 Non-targeted Indoor VOCs in ECE Facilities (n=32).[a,b]

Analyte	>MDL (%)	Arithmetic Mean±SD	25th %	Median	75th %	95th %	Max
Alkanes							
Cyclododecane	31.3	203.8 ± 476.3	<MDL	<MDL	297.3	876.9	2466
Cyclohexane[c]	100.0	329.8 ± 356.1	96.8	221.0	403.9	1403	1515
Cyclohexane, methyl-	100.0	380.7 ± 454.5	95.0	292.5	410.8	1119	2372
Cyclooctane	28.1	243.0 ± 561.8	<MDL	<MDL	227.0	1266	2719
Decane, 3,7-dimethyl-	9.4	15.5 ± 70.0	<MDL	<MDL	<MDL	76.2	391.2
Decane, 2,2,4-trimethyl-	40.6	502.2 ± 1023	<MDL	<MDL	580.9	2614	4246
Decane, 2,2,6-trimethyl-	25.0	999.7 ± 2768	<MDL	<MDL	74.5	6331	12490
Decane, 2,2,7-trimethyl-	9.4	200.4 ± 1050	<MDL	<MDL	<MDL	319.8	5943
Decane, 2,2,8-trimethyl-	28.1	1069 ± 2344	<MDL	<MDL	565.7	6273	9453
Decane, 2,2,9-trimethyl-	6.3	11.4 ± 44.8	NC	NC	NC	NC	182.8
Dodecane, 5,8-diethyl-	25.0	865.1 ± 2389	<MDL	<MDL	56.6	5367	10750
Dodecane, 2,6,10-trimethyl-	9.4	120.6 ± 577.1	<MDL	<MDL	<MDL	477.4	3247
Dodecane, 2,7,10-trimethyl-	6.3	459.4 ±2571	NC	NC	NC	NC	14550
Hexadecane, 2,6,10,14-tetramethyl-	50.0	851.1 ± 2563	<MDL	83.1	343.7	8512	12260
Hexane, 2,4-dimethyl-	25.0	736.7 ± 2007	<MDL	<MDL	98.1	4569	9055
Hexane, 2-methyl-	100.0	430.8 ± 454.1	111.9	242.3	598.9	1532	1858
Hexane, 3-methyl-	96.9	464.0 ± 481.1	141.5	275.3	593.4	1725	1852
n-Nonadecane	100.0	182.4 ± 91.2	123.0	158.6	209.6	342.8	450.9
n-Nonane	100.0	328.1 ± 251.1	147.6	241.2	397.4	1017	1103
Nonane, 2-methyl-5-propyl-	21.9	502 ± 1172	<MDL	<MDL	<MDL	2398	5557
Octane, 2,6-dimethyl-	25.0	753.9 ± 2090	<MDL	<MDL	41.0	4752	9483
Octane, 2,3,6,7-tetramethyl-	12.5	144.7 ± 548.0	<MDL	<MDL	<MDL	1889	2527
Octane, 2,5,6-trimethyl-	46.9	1060± 3437	<MDL	<MDL	424.5	7675	18280
n-Pentadecane	31.3	797.6 ± 2005	<MDL	<MDL	1121	2550	10840
n-Pentane[d]	37.5	51.1 ± 104.0	<MDL	<MDL	49.7	394.0	417.8

Table 13 Continued. Estimated Concentrations (ng/m³) of 119 Non-targeted Indoor VOCs in ECE Facilities (n=32).[a,b]

Analyte	>MDL (%)	Arithmetic Mean±SD	25th %	Median	75th %	95th %	Max
Tetradecane, 2,2-dimethyl-	21.9	784.8 ± 2237	<MDL	<MDL	<MDL	5175	10300
Tridecane, 3-methyl-	6.3	9.2 ± 38.5	NC	NC	NC	NC	198.6
Tridecane, 2-methyl-2-phenyl-	12.5	36.1 ± 178.2	<MDL	<MDL	<MDL	61.3	1009
Undecane, 2,8-dimethyl-	15.6	62.5 ± 193.3	<MDL	<MDL	<MDL	314.0	1012
Undecane, 6,6-dimethyl-	21.9	1424 ± 4599	<MDL	<MDL	<MDL	11670	21930
Undecane, 6-ethyl-	15.6	118.6 ± 441.3	<MDL	<MDL	<MDL	512.1	2436
Oxygenated Hydrocarbons							
Acetic acid	87.5	1673 ± 2351	215.4	764.9	1954.4	7142	10550
Acetic acid, butyl ester[d]	96.9	941.3 ± 1608	245.8	389.4	777.2	6490	6997
Acetic acid, 2-methylpropyl ester[d]	75.0	249.9 ± 332.3	13.2	106.5	357.3	955.7	1492
Benzoic acid, 2-ethylhexyl ester	100.0	677.8 ± 1563	100.8	153.0	437.1	3610	8188
Benzoic acid, 2-hydroxy-, 3-methylbutyl	31.3	235.2 ± 577.0	<MDL	<MDL	275.8	1609	2867
1-Butanol[e]	100.0	1167 ± 915.4	638.3	847.5	1316	3505	3950
Cyclohexanol, 5-methyl-2-(1-methylethyl)	100.0	999.1 ± 1694	235.0	466.5	829.1	4529	8239
Cyclohexanone[e]	100.0	1039 ± 2101	366.5	517.1	868.0	2689	12200
Dipropylene glycol monomethyl ether[d]	93.7	1038 ± 2832	118.6	261.0	763.3	2543	16100
Ethanol	65.6	672.2 ± 1653	<MDL	105.1	434.9	3547	8538
Ethanol, 2-(2-butoxyethoxy)-	62.5	1138 ± 2335	<MDL	242.7	924.1	7119	10790
Ethanol, 2-(hexyloxy)-	75.0	955.2 ± 1700	25.9	214.6	1257	4000	8728
Ethyl acetate[e]	96.9	638.2 ± 940.3	143.3	250.5	628.7	3242	3412
1-Hexacosanol	9.4	103.0 ± 327.9	<MDL	<MDL	<MDL	1158	1223
Isopropyl alcohol[c]	100.0	17630 ± 85390	731.7	1552	3821	12670	485300
1,8-Nonanediol, 8-methyl-	31.3	115.8 ± 202.2	<MDL	<MDL	168.6	532.5	653.4
Octane, 1,1'-oxybis-	93.8	687.6 ± 655.3	191.0	511.8	891.7	1697	3106
1-Octanol	31.3	1479 ± 1479	<MDL	<MDL	2029	4535	4654
Octanol, 2-butyl-	12.5	33.5 ± 102.0	<MDL	<MDL	<MDL	252.8	489.2

Table 13 Continued. Estimated Concentrations (ng/m³) of 119 Non-targeted Indoor VOCs in ECE Facilities (n=32).[a,b]

Analyte	>MDL (%)	Arithmetic Mean±SD	25th %	Median	75th %	95th %	Max
1-Octanol, 2,2-dimethyl-	21.9	339.4 ± 1192	<MDL	<MDL	NC	3549	5881
3-Octanol, 3,7-dimethyl-, (±)-	65.6	506.8 ± 2017	<MDL	86.3	217.3	1334	11480
Pentanal	100.0	593.9 ± 613.2	331.8	410.9	581.8	1157	3698
2-Pentanol, acetate[d]	78.1	173.8 ± 210.0	23.3	63.5	292.4	622.1	744.6
2-Propanol, 1-butoxy-	78.1	893.7 ± 3030	28.1	121.4	510.9	3508	17090
2-Propanol, 1-methoxy-[c]	71.9	640.4 ± 2029	<MDL	131.3	319.7	2176	11420
2-Propanol, 1-(2-methoxy-1-methylethoxy)	90.6	513.2 ± 664.4	96.5	245.6	610.6	2363	2469
2-Propanol, 1-(2-methoxypropoxy)-	100.0	3276± 5211	603.0	1230	5517	11050	27620
1-Propanol, 2-(1-methylethoxy)-	25.0	25.9 ± 58.1	<MDL	<MDL	6.8	148.7	247.1
2-Propanol, 1-propoxy-	81.3	4448± 8626	77.7	266.8	7074	28160	31820
Propylene glycol	100.0	9535 ± 6581	4273	7357	15520	24010	25030
Tripropylene glycols	53.1	2791 ± 7214	<MDL	84.0	1260	23310	33230
Aromatics							
Acetic acid, phenylmethyl ester	100.0	831.9 ± 1432	188.3	366.4	897.3	4042	7525
Acetophenone[e]	100.0	1110 ± 319.9	971.4	1100	1162	1950	2144
Benzaldehyde, 4-methoxy-	21.9	119.2 ± 287.4	<MDL	<MDL	<MDL	565.4	1405
Benzene, (1-butylheptyl)-	87.5	456.1 ± 944.7	114.9	190.1	332.1	2745	4902
Benzene, (1-butylhexyl)-	87.5	164.6 ± 219.0	39.9	96.2	224.0	468.9	1172
Benzene, (1-butylnonyl)-	37.5	38.8 ± 132.3	<MDL	<MDL	14.5	222.8	727.9
Benzene, (1-butyloctyl)-	96.9	274.1 ± 815.5	54.4	80.1	138.1	1266	4584
Benzene, (1,1-dimethyldecyl)-	9.4	21.02 ± 113.9	<MDL	<MDL	<MDL	13.9	645.0
Benzene, (1,1-dimethylnonyl)-	31.3	35.8 ± 152.1	<MDL	<MDL	16.9	137.0	858.3
Benzene, (1-ethyldecyl)-	93.8	171.0 ± 484.9	27.5	57.8	93.6	989.3	2659
Benzene, 1-ethyl-3,5-dimethyl-	3.1	NC	<MDL	<MDL	<MDL	<MDL	172.0
Benzene, (1-ethylnonyl)-	100.0	269.5 ± 720.5	43.0	73.6	141.1	2387	3511
Benzene, (1-ethyloctyl)-	71.9	206.6 ± 528.7	<MDL	50.3	116.7	1104	2739

Table 13 Continued. Estimated Concentrations (ng/m³) of 119 Non-targeted Indoor VOCs in ECE Facilities (n=32).[a,b]

Analyte	>MDL (%)	Arithmetic Mean±SD	25th %	Median	75th %	95th %	Max
Benzene, (1-methyldecyl)-	96.9	475.7 ± 1315	73.0	114.0	207.7	4388	6357
Benzene, (1-methylnonyl)-	71.9	310.2 ± 954.2	<MDL	60.3	134.9	2277	5060
Benzene, (1-methylundecyl)-	28.1	133.9 ± 671.8	<MDL	<MDL	35.0	91.6	3812
Benzene, (1-pentylheptyl)-	100.0	274.9 ± 823.0	53.8	80.9	132.8	1266	4628
Benzene, (1-pentylhexyl)-	87.5	261.8 ± 477.2	32.1	102.0	251.5	1279	2426
Benzene, (1-pentyloctyl)-	56.3	68.4 ± 223.2	<MDL	17.7	44.1	220.0	1266
Benzene, (1-propylheptadecyl)-	78.1	114.2 ± 137.3	13.7	68.0	145.7	423.4	511.9
Benzene, (1-propylheptyl)-	81.3	223.7 ± 545.3	40.1	79.6	191.8	1186	2976
Benzene, (1-propylnonyl)-	96.9	227.0 ± 633.8	44.9	67.7	109.2	1172	3519
Benzene, (1-propyloctyl)-	90.6	293.5 ± 771.8	50.0	82.6	151.0	2322	3907
Benzophenone	100.0	965.5 ± 2681	246.1	362.4	796.1	1362	15530
Benzyl alcohol	100.0	850.4 ± 1269	285.4	483.3	894.2	3340	6853
Ethanol, 2-phenoxy-	68.8	1394 ± 2180	<MDL	465.4	1553.1	6789	8274
2-Ethylhexyl salicylate	100.0	778.9 ± 1162	207.0	359.5	679.9	2867	5697
Homosalate	93.8	449.8 ± 810.6	69.8	164.0	367.3	2610	3500
3-Methyl-4-isopropylphenol	15.6	38.6 ± 189.6	<MDL	<MDL	<MDL	81.1	1074
Naphthalene[c]	96.9	501.8 ± 659.7	212.5	341.9	572.0	1118	3833
Naphthalene, 2-methoxy-	100.0	174.5 ± 175.6	61.7	105.2	200.2	533.4	653.1
Phenol[c]	93.8	1550 ± 1554	588.9	1128	1843	3803	7588
2-Propenal, 3-phenyl-[d]	21.9	34.6 ± 80.5	<MDL	<MDL	<MDL	300.2	301.1
Styrene[c]	100.0	390.4 ± 338.2	144.8	300.9	568.4	1116	1328
Siloxanes and Silanol							
Cyclohexasiloxane, dodecamethyl- (D6)	100.0	2698 ± 3048	978.5	1886	3449	7166	16680
Heptasiloxane, hexadecamethyl-	96.9	431.2 ± 676.3	67.4	157.6	451.5	1729	3258
Hexasiloxane, tetradecamethyl-	93.8	636.2 ± 1777	64.1	181.7	508.4	1922	10080
Methyltris(trimethylsiloxy)silane	37.5	401 ± 1211	<MDL	<MDL	132.2	2916	6186

Table 13 Continued. Estimated Concentrations (ng/m³) of 119 Non-targeted Indoor VOCs in ECE Facilities (n=32).[a,b]

Analyte	>MDL (%)	Arithmetic Mean±SD	25th %	Median	75th %	95th %	Max
Pentasiloxane, dodecamethyl-	31.3	917.4 ± 4898	<MDL	<MDL	33.0	559.0	27750
Silanol, trimethyl-	100.0	270.6 ± 507.7	102.9	140.5	181.3	1775	2539
Tetrasiloxane, decamethyl	50.0	2524± 12120	<MDL	17.3	193.8	6186	68650
Trisiloxane, octamethyl-	43.8	2728.2 ± 14330	<MDL	<MDL	106.5	1874	81220
Terpenes							
Bicyclo[3.1.1]heptane, 6,6-dimethyl-2-me	100.0	3112 ± 4771	703.7	1602	3402	10210	25610
Camphor[d]	93.8	1139 ± 3900	188.6	338.8	696.0	1689	22410
Caryophyllene	15.6	21.9 ± 65.4	<MDL	<MDL	<MDL	258.6	263.2
1,4-Cyclohexadiene, 1-methyl-4-(1-methylethyl)	68.8	1116 ± 2385	<MDL	484.5	710.0	7612	11510
3-Cyclohexen-1-ol, 4-methyl-1-(1-methylethyl)	15.6	271.3 ± 851.1	<MDL	<MDL	<MDL	2394	3724
3-Cyclohexene-1-methanol, α	87.5	908.2 ± 1968	135.8	232.5	870.7	3468	10570
Eucalyptol	100.0	2733 ± 11740	158.6	327.9	1073	2670	66970
Furfural[e]	100.0	1027 ± 820.2	428.5	708.7	1378	3008	3258
5-Hepten-2-one, 6-methyl-	68.8	171.2 ± 247.6	<MDL	82.8	209.1	817.2	1062
β-Myrcene	90.6	1450 ± 1830	291.3	789.6	2148	6103	7877
7-Octen-2-ol, 2,6-dimethyl-	100.0	3034 ± 3824	637.9	1657	3214	11490	15500
1,3-Pentadiene, (Z)-	65.6	329.7 ± 401.5	<MDL	254.3	539.8	951.8	1960
1-Penten-3-one, 1-(2,6,6-trimethyl-2-cyclohexen-1-yl)	90.6	111.4 ± 121.9	36.5	65.5	130.6	408.2	506.8
α-Phellandrene	21.9	55.0 ± 136.7	<MDL	<MDL	<MDL	437.6	502.5
2-Propanol, 1-[1-methyl-2-(2-propenyloxy)-ethoxy]	12.5	340.3 ± 1906	<MDL	<MDL	<MDL	62.6	10780

Abbreviations: Not computable (NC).

[a]Method detection limit (MDL) was set as 5 ng toluene equivalent in chromatographs for unknown peaks using the mass spectral library search with the NIST08 database.

[b]Concentrations are presented for levels measured above the MDL only (i.e., the mean equals the mean of detectable values).
[c]Compounds with established U.S. EPA RfCs (cyclohexane; naphthalene; 2-propanol, 1-methoxy; styrene) and/or OEHHA chronic reference exposure levels (cRELs) (isopropyl alcohol; naphthalene; 2-propanol, 1-methoxy; phenol; styrene).
[d] Four compounds identified as warranting additional evaluation (i.e., Hazard score>3): 1) acetic acid, butyl ester; 2) camphor; 3) n-pentane; and 4) 3-phenyl-2-propenal. Three compounds with hazard scores>3 were not prioritized in our assessment: 1) acetate 2-pentanol; 2) dipropylene glycol monomethyl ether; and 3) 2-methylpropyl ester acetic acid.
[e]Compounds with established oral U.S. EPA RfDs but no RfC or REL (acetophenone; 1-butanol; cyclohexanone; ethyl acetate; furfural).

3.4.4 VOC Health Risk Characterizations

3.4.4.1 Non-cancer risk evaluation

Of the 10 targeted VOCs and six non-targeted VOCs with RELs or RfCs, none of the risk ratios exceeded one and were often much lower (Table 14 and Table 15).

Table 14. Ratios of Targeted VOC Air Concentrations to OEHHA Acute Reference Exposure Level (aREL) and Chronic REL (cREL), and U.S. EPA Reference Concentration (RfC).

Chemical[e]	Percentile (%)	Air Concentration (µg/m³)[a]	aREL[b] (µg/m³)	Ratio[c] (aREL)	cREL[b] (µg/m³)	Ratio[c] (cREL)	RfC[d] (µg/m³)	Ratio[c] (RfC)
2-Butoxyethanol	50th	2.9	14,000	0.0002	-	NC	1,600	0.002
	95th	64.0	14,000	0.005	-	NC	1,600	0.04
Benzene	50th	0.9	1,300	0.0007	60	0.01	30	0.03
	95th	2.0	1,300	0.001	60	0.03	30	0.07
Carbon tetrachloride	50th	<MDL	1,900	NC	40	NC	100	NC
	95th	<MDL	1,900	NC	40	NC	100	NC
Chloroform	50th	<MDL	150	NC	300	NC	-	NC
	95th	7.7	150	0.05	300	0.03	-	NC
Ethylbenzene	50th	0.6	-	NC	2,000	0.0003	1,000	0.0006
	95th	2.0	-	NC	2,000	0.003	1,000	0.002
n-Hexane	50th	0.6	-	NC	7,000	8E-05	700	0.0008
	95th	2.9	-	NC	7,000	0.0004	700	0.004
Methylene chloride	50th	<MDL	14,000	NC	400	NC	-	NC
	95th	<MDL	14,000	NC	400	NC	-	NC
Tetrachloroethylene	50th	0.1	20,000	4.0E-06	35	0.002	-	NC
	95th	1.0	20,000	4.9E-05	35	0.03	-	NC
Toluene	50th	3.1	37,000	8.2E-05	300	0.01	5,000	0.0006
	95th	11.2	37,000	0.0003	300	0.04	5,000	0.002
Xylenes	50th	2.5	22,000	0.0001	700	0.004	100	0.02
	95th	9.2	22,000	0.0004	700	0.01	100	0.09

Abbreviation: Not calculated (NC). [a]Concentrations averaged over school day (6-10 hours). [b]OEHHA REL. [c]Ratio of air concentration to preceding exposure guideline (REL or RfC). [d]U.S. EPA RfC.

Table 15. Ratios of Non-targeted VOC Air Concentrations to OEHHA Acute Reference Exposure Level (aREL) and Chronic REL (cREL), and U.S. EPA Reference Concentration (RfC).

Chemical	Percentile (%)	Air Concentration (µg/m³)[a]	aREL (µg/m^3)	Ratio[c] (aREL)	cREL[b] (µg/m^3)	Ratio[c] (cREL)	RfC[d] (µg/m^3)	Ratio[c] (RfC)
Cyclohexane	50th	0.22	-	NC	-	NC	6,000	3.68E-5
	95th	1.40	-	NC	-	NC	6,000	2.34E-4
Isopropyl alcohol	50th	1.55	3,200	4.85E-4	7,000	2.22E-4	-	NC
	95th	12.67	3,200	3.96E-3	7,000	1.81E-3	-	NC
Naphthalene	50th	0.34	-	NC	9	3.80E-2	3	1.14E-1
	95th	1.12	-	NC	9	1.24E-1	3	3.73E-1
Phenol	50th	1.13	5,800	1.94E-4	200	5.64E-3	-	NC
	95th	3.80	5,800	6.56E-4	200	1.90E-2	-	NC
2-Propanol, 1-methoxy-	50th	0.13	-	NC	7,000	1.88E-5	658,000	2.00E-7
	95th	2.18	-	NC	7,000	3.11E-4	658,000	3.31E-6
Styrene	50th	0.30	21,000	1.43E-5	900	3.34E-4	1,000	3.01E-4
	95th	1.12	21,000	5.54E-5	900	1.24E-3	1,000	1.12E-3

Abbreviation: Not calculated (NC). [a]Concentrations averaged over school day (6-10 hours). [b]OEHHA REL. [c]Ratio of air concentration to preceding exposure guideline (REL or RfC). [d]U.S. EPA RfC.

3.4.4.2 Cancer risk evaluation

Table 16 presents the 50th and 95th percentile inhalation dose estimates compared to the age-adjusted NSRL values by age group. The 50th and 95th percentile dose estimates for benzene exceeded the age-specific NSRL in all four age groups assessed (ratio range: 1.8-17.4). The 95th percentile dose estimates for chloroform exceeded the age-specific NSRL in all four age groups assessed (ratio range=5.2-22.5). The 95th percentile dose estimates for ethylbenzene exceeded the age-adjusted NSRL in the three youngest age groups (ratio range=1.2-4.2). The 50th percentile dose estimates for ethylbenzene exceeded the age-adjusted NSRL in the two youngest age groups (ratio range=1.2-1.3). Among the non-targeted VOCs, only naphthalene is listed as a carcinogen by OEHHA. Naphthalene NSRL ratios exceeded the age-specific NSRL in all age groups assessed (range: 1.6-22.4). If reflective of long-term averages, child dose estimates exceeded at least one age-adjusted NSRL benchmark for benzene, chloroform, ethylbenzene, and naphthalene in 71%, 38%, 56%, and 97% of facilities, respectively (Table 16).

Table 16. Inhalation VOC Dose Estimates Compared to $NSRL_{child\ (age\ group)}$.

Analyte	Age Group	Dose Estimates (µg/day) 50th %	Dose Estimates (µg/day) 95th %	$NSRL_{child}$ (µg/day)	Ratio 50th %	Ratio 95th %
Targeted						
Benzene	Birth to <1 year	1.0	2.3	0.1	7.4	17.4
	1 to <2 years	1.5	3.6	0.2	7.1	16.8
	2 to <3 years	1.8	4.2	0.9	2.1	4.9
	3 to <6 years	2.0	4.8	1.2	1.8	4.2
Chloroform	Birth to <1 year	NC	8.7	0.4	NC	22.5
	1 to <2 years	NC	13.6	0.7	NC	20.9
	2 to <3 years	NC	16.2	2.6	NC	6.1
	3 to <6 years	NC	18.5	3.5	NC	5.2
Ethylbenzene	Birth to <1 year	0. 7	2.2	0.5	1.3	4.2
	1 to <2 years	1.1	3.5	0.9	1.2	3.9
	2 to <3 years	1.3	4.1	3.5	0.4	1.2
	3 to <6 years	1.4	4.7	4.8	0.3	1.0
Non-targeted						
Naphthalene[a]	Birth to <1 year	0.38	1.3	0.06	6.9	22.4
	1 to <2 years	0.60	2.0	0.09	6.4	20.9
	2 to <3 years	0.83	2.7	0.38	2.2	7.2
	3 to <6 years	0.82	2.7	0.51	1.6	5.2

NC: not calculated. NSRLs are available for carbon tetrachloride and methylene chloride, but are not included here due to low detection frequencies (>MDL=3%).

[a] To measure naphthalene, we applied a modified toluene equivalent mass calibration to compute semi- quantitative estimates of its mass (see "*Identification and quantification of non-targeted VOCs*" above.)

3.4.5 Hazard Assessment and Prioritization for Future Study of Targeted VOCs

Of the targeted VOCs without non-occupational health-based exposure benchmarks, two were excluded due to low detection frequency (<60%). Table 17 shows the proportion of compounds with good VEGA reliability scores for each outcome. VEGA produced "good reliability" predictions for 92% of the chemicals for mutagenicity, 8% for carcinogenicity, 12% for developmental toxicity, and 56% for skin sensitization. VEGA positively predicted mutagenicity for 1,2,3-trimethylbenzene. For carcinogenicity, VEGA produced positive and negative predictions for 1,2,3-trimethylbenzene and 1,2,4-trimethylbenzene due to differences in toxicity data sources. VEGA identified 2-ethyl-1-hexanol, α-pinene, and a-terpineol as potential developmental toxicants. VEGA predicted 83% of the fragrance HS compounds as skin sensitizers, including d-limonene and α-pinene. Most of the fragrance HS compounds have been recognized as skin irritants.[109] Twenty-four of the 25 compounds had positive toxicological information cited by PHAROS, Scorecard or QSAR predictions (Table 18). The 24 VOCs were distributed into their respective hazard groups (Groups 1-9) as follows: 8% (n=2) for carcinogenicity or mutagenicity, 29% (n= 7) for developmental toxicity, 4% (n=1) for reproductive toxicity, 4% (n=1) for endocrine activity, 25% (n=6) for neurotoxicity, 58% (n=14) for immunotoxicity or sensitization, 71% (n=17) for specific organ or acute toxicity, 63% (n=15) for irritation, and 25% (n=6) for persistence or bioaccumulation. Each hazard group is not mutually exclusive. Seventeen compounds had hazard scores >0 and ≤3 (Table 19). We identified 7 compounds with hazard scores >3 for additional evaluation (Table 20): d-limonene; α-pinene; α-terpineol, 1,2,4-trimethylbenzene; D4; n-heptane; and heptanal. The persistent and bioaccumulative nature of cyclosiloxanes (D4 and D5) raises health concerns, especially given adverse reproductive effects reported in animals.[119] These compounds are also listed as priority chemicals for biomonitoring by the California Biomonitoring Program.[120] Thus, we recommend additional evaluation of D5 because of health concerns raised by OEHHA, and the high detection frequency and levels measured (Table 7).[120]

Table 17. Proportion of Targeted VOCs with Good VEGA Reliability Scores (n=25 analytes).

VEGA Endpoint	Proportion with "good reliability"
Mutagenicity[a]	92%
Carcinogencity[b]	8%
Developmental Toxicity[b]	12%
Skin Sensitization[b]	56%

[a]ADI>0.9. [b]ADI>0.8.

Table 18. Hazards Classification for 25 Targeted VOC Analytes.

Group No.	Criteria	Data Source[a]			No. of Chemicals[b]
		PHAROS	ScoreCard	VEGA	
1	Carcinogen or mutagen	0	0	2	2
2	Developmental toxicant	5	1	3	7
3	Reproductive toxicant	1	0		1
4	Endocrine-disrupting chemical	1	0		1
5	Neurotoxicant	2	6		6
6	Immunotoxicant or sensitizer	3	1	13	14
7	Specific organ or acute toxicants	17	6		17
8	Irritant	15			15
9	Persistent or bioaccumulative	6			6
10	No positive data	0	0	1[c]	1

[a]Grey boxes indicate that the data source does not have the specified health endpoint. [b]Total number of chemicals in each hazard group, which may be less than the summation of the data sources due to the non-exclusivity the hazard groups. [c]The one compound in Group 10, dodecane, was identified as a non-mutagen under VEGA QSAR model.

Table 19. Hazards Screening for 17 Targeted VOC Analytes (Hazard Score >0 and ≤3).[a,b]

Analyte	CAS No.	PHAROS[b]	ScoreCard[c]	VEGA[d]	Hazard Score
Mixed and Mobile Sources					
n-Decane	124-18-5	Irritant , Acute Toxicant	Data lacking	[Non-Mutagen]	2
n-Hexadecane	544-76-3	Irritant , Acute Toxicant	Data lacking	Non-Mutagen, Skin Sensitizer	3
n-Octane	111-65-9	Irritant, Neurotoxic, Respiratory Toxicant, Acute Toxicant	Neurotoxicity	Non-Mutagen	3
n-Tetradecane	629-59-4	Acute Toxicant	Data lacking	Non-Mutagen	1
1,2,3-Trimethylbenzene	526-73-8	Developmental Toxicant, Acute Toxicant	Data lacking	[Mutagen], Carcinogen	3
n-Undecane	1120-21-4	Acute Toxicant	Data lacking	[Non-Mutagen]	1
Household Sources					
Fragrances					
Butanal	123-72-8	Irritant, Acute Toxicant	Respiratory Toxicity, Skin or Sense Organ Toxicity	[Non-Mutagen]	2
3-Carene	13466-78-9	Asthmagen	Data lacking	Non-Mutagen, Sensitizer	1
Decanal[f]	112-31-2	Irritant, Acute Toxicant	Data lacking	Non-Mutagen, Skin Sensitizer	3
Hexanal[f]	66-25-1	Irritant	Data lacking	Non-Mutagen, Skin Sensitizer	2
Nonanal	124-19-6	Irritant	Data lacking	[Non-Mutagen], Skin Sensitizer	2
Octanal[f]	124-13-0	Irritant	Data lacking	Non-Mutagen, Skin Sensitizer	2
ɣ-Terpinene[f]	99-85-4	Data lacking	Data lacking	Non-Mutagen, Skin Sensitizer	1

Table 19 Continued. Hazards Screening for 17 Targeted VOC Analytes (Hazard Score >0 and ≤3).[a,b]

Analyte	CAS No.	PHAROS[b]	ScoreCard[c]	VEGA[d]	Hazard Score
Other household products					
2-Ethyl-1-hexanol	104-76-7	Developmental Toxicant, Irritant, Acute Toxicant	Developmental Toxicity, Gastrointestinal or Liver Toxicity	[Non-Mutagen], Developmental Toxicant	3
Texanol	25265-77-4	Acute Toxicant	Data lacking	Non-Mutagen, Skin Sensitizer	2
2,2,4-trimethyl-1,3-pentanediol diisobutyrate (TXIB)	6846-50-0	PBT	Data lacking	Non-Mutagen, Skin Sensitizer	2

Abbreviations: Persistent Bioaccumulative Toxicant (PBT).

[a]n-Dodecane was excluded from the hazard table due to the lack of positive toxicity data (i.e., Group 10; Hazard score=0). Compounds with health-based reference values were also excluded from the screening.
[b] Compounds identified as warranting additional evaluation (e.g., Hazard Score>3) are presented in the main paper (Table 20).
[c] "Acute Toxicant" is listed as "Toxic to Mammals" in PHAROS.
[d]Suspected effects.
[e]Brackets indicate experimental data.
[f] EPA SCP yellow triangle rating: The chemical has met Safer Choice Criteria for its functional ingredient-class, but has some hazard profile issues. Specifically, a chemical with this code is not associated with a low level of hazard concern for all human health and environmental endpoints. While it is a best-in-class chemical and among the safest available for a particular function, the function fulfilled by the chemical should be considered an area for safer chemistry innovation.[118]

Table 20. Summary of Potential Health Concerns for Targeted and Non-Targeted VOCs Warranting Additional Evaluation.[a]

Analyte	PHAROS[b]	ScoreCard[c]	VEGA[d]	Hazard Score
Mixed and Mobile Sources				
n-Heptane	Developmental Toxicant, Irritant, Neurotoxicant, Respiratory Toxicant, Acute Toxicant	Neurotoxicity	Non-Mutagen	5
n-Pentane	Acute Toxicant, Developmental Toxicant, Neurotoxicant, Persistent, Respiratory Toxicant, Specific Organ Toxicant	Neurotoxicity	Non-Mutagen	5
Household Sources				
Fragrances				
Acetic acid, butyl ester	Acute Toxicant, Developmental Toxicant, Neurotoxicant, Persistent, Specific Organ Toxicant	Gastrointestinal or Liver Toxicity, Neurotoxicity, Respiratory Toxicity, Skin or Sense Organ Toxicity	Non-Mutagen, Sensitizer	6
Heptanal	Irritant, Acute Toxicant	Neurotoxicity	[Non-Mutagen], Skin Sensitizer	4
d-Limonene	Developmental Toxicant, PBT, Skin Sensitizer, Suspected Asthmagen, Irritant (eye, skin), Acute Toxicant	Gastrointestinal or Liver Toxicity, Immunotoxicity, Kidney Toxicity, Neurotoxicity, Respiratory Toxicity, Skin or Sense Organ Toxicity	[Non-Mutagen], [Skin Sensitizer]	6
α-Pinene	Bioaccumulative, Irritant, Acute Toxicant	Neurotoxicity, Respiratory Toxicity, Skin or Sense Organ Toxicity	[Non-Mutagen], Developmental Toxicant, Skin Sensitizer	6

Table 20 Continued. Summary of Potential Health Concerns for Targeted and Non-Targeted VOCs Warranting Additional Evaluation.[a]

Analyte	PHAROS[b]	ScoreCard[c]	VEGA[d]	Hazard Score
2-Propenal, 3-phenyl-	Acute Toxicant, Developmental Toxicant, Reproductive Toxicant, Skin Sensitizer	Immunotoxicity, Neurotoxicity, Skin or Sense Organ Toxicity	[Non-Mutagen], Non-Carcinogen, [Sensitizer]	5
α-Terpineol[e]	Irritant, Acute Toxicant	Data lacking	[Non-Mutagen], Developmental Toxicant, Skin Sensitizer	4
1,2,4-Trimethylbenzene	Developmental Toxicant, Irritant (eye, skin, lungs), Acute Toxicant (inhalation)	Cardiovascular or Blood Toxicity, Neurotoxicity, Respiratory Toxicity	[Non-Mutagen], [Carcinogen], Sensitizer	6
Other household products				
Camphor	Acute Toxicant, Reproductive Toxicant, Specific Organ Toxicant	Gastrointestinal or Liver Toxicity, Neurotoxicity, Respiratory Toxicity, Skin or Sense Organ Toxicity	Sensitizer, [Developmental Toxicant]	5
Decamethylcyclopentasiloxane (D5)	PBT	Data lacking	Data lacking	1
Octamethylcyclotetrasiloxane (D4)	PBT (high priority), Reproductive Toxicant, EDC, Acute Toxicant	Gastrointestinal or Liver Toxicity	Data lacking	4

Abbreviations: Persistent Bioaccumulative Toxicant (PBT); Endocrine Disrupting Compound (EDC).

[a]Compounds with a hazard score >3, except for D5, which was prioritized due to potential health concerns raised by California OEHHA (OEHHA 2007) and high concentration measurements.
[b]Acute toxicant is listed as "Toxic to Mammals" in PHAROS.
[c]Suspected effects. [d]Brackets indicate experimental data.
[e]U.S. EPA SCP "green half circle" rating: The chemical is expected to be of low concern based on experimental and modeled data.[118]

3.4.6 Hazard Assessment and Prioritization for Future Study of Non-targeted VOCs

Table 21 shows the proportion of compounds with good VEGA reliability scores for each outcome. VEGA produced "good reliability" predictions for 90% of the chemicals for mutagenicity, 14% for carcinogenicity, 34% for developmental toxicity, and 57% for skin sensitization. 58 compounds had positive toxicological information cited by PHAROS, Scorecard or QSAR predictions (Table 22 and Table 23).

Applying the same methods described above to the 119 non-targeted VOCs with no non-occupational health-based exposure benchmarks, we identified 4 non-targeted VOCs with hazard scores >3 for further evaluation: butyl ester acetic acid; camphor; n-pentane; 2-propenal, 3-phenyl-.

Table 21. Proportion of Non-targeted VOCs with Good VEGA Reliability Scores (n=58 analytes).

VEGA Endpoint	Proportion with "good reliability"
Mutagenicity[a]	90%
Carcinogencity[b]	14%
Developmental Toxicity[b]	34%
Skin Sensitization[b]	57%

[a]ADI>0.9. [b]ADI>0.8.

Table 22. Hazards Classification for 107 Non-targeted VOC Analytes.

Group No.	Criteria	Data Source[a]			No. of Chemicals[b]
		PHAROS	ScoreCard	VEGA	
1	Carcinogen or mutagen	2	0	0	2
2	Developmental toxicant	9	1	17	23
3	Reproductive toxicant	6	5		10
4	Endocrine-disrupting chemical	2	1		2
5	Neurotoxicant	10	13		17
6	Immunotoxicant or sensitizer	2	2	31	32
7	Specific organ or acute toxicants	28	11		28
8	Irritant	9			9
9	Persistent or bioaccumulative	8			8
10	No positive health data				48

[a]Grey boxes indicate that the data source does not have the specified health endpoint.
[b]Total number of chemicals in each hazard group, which may be less than the summation of the data sources due to the non-exclusivity the hazard groups.

Table 23. Hazards Screening for 58 Non-targeted VOC Analytes.[a]

Analyte	CAS No.	PHAROS[b]	ScoreCard[c]	VEGA[d]	Hazard Score
Alkanes					
Cyclododecane	294-62-2	PBT	Data lacking	Non-Mutagen, Sensitizer	2
Cyclohexane, methyl-	108-87-2	Acute Toxicant, Developmental Toxicant, Neurotoxicant	Neurotoxicity	Non-Mutagen	3
Hexane, 2,4-dimethyl-	589-43-5	Acute Toxicant, Skin Irritant, Neurotoxicant	Data lacking	Non-Mutagen	2
Hexane, 2-methyl-	591-76-4	Acute Toxicant, Skin Irritant, Neurotoxicant	Data lacking	Non-Mutagen	2
Hexane, 3-methyl-	589-34-4	Acute Toxicant, Skin Irritant, Neurotoxicant	Data lacking	Non-Mutagen	3
n-Nonadecane	629-92-5	Data lacking	Data lacking	Non-Mutagen, Sensitizer	1
n-Nonane	111-84-2	Acute Toxicant, Neurotoxicant, Respiratory Toxicant, Specific Organ Toxicant	Neurotoxicity	[Non-Mutagen]	3
Pentadecane	629-62-9	Acute Toxicant	Data lacking	Non-Mutagen, Sensitizer	2

Table 23 Continued. Hazards Screening for 58 Non-targeted VOC Analytes.[a]

Analyte	CAS No.	PHAROS[b]	ScoreCard[c]	VEGA[d]	Hazard Score
n-Pentane[e]	109-66-0	Acute Toxicant, Developmental Toxicant, Neurotoxicant, Persistent, Respiratory Toxicant, Specific Organ Toxicant	Neurotoxicity	Non-Mutagen	5
Tetradecane, 2,2-dimethyl-	59222-86-5	Data lacking	Data lacking	Non-Mutagen, Sensitizer	1
Oxygenated Hydrocarbons					
Acetic acid[f]	64-19-7	Acute Toxicant, Developmental Toxicant, Neurotoxicant, Respiratory Toxicant	Cardiovascular or Blood Toxicity, Gastointestinal or Liver Toxicity, Respiratory Toxicity, Skin or Sense Organ Toxicity	[Non-Mutagen], Non-Sensitizer	3
Acetic acid, butyl ester[e]	123-86-4	Acute Toxicant, Developmental Toxicant, Neurotoxicant, Persistent, Specific Organ Toxicant	Gastrointestinal or Liver Toxicity, Neurotoxicity, Respiratory Toxicity, Skin or Sense Organ Toxicity	Non-Mutagen, Sensitizer	6
Acetic acid, 2-methylpropyl ester[e,g]	110-19-0	Acute Toxicant, Developmental Toxicant	Neurotoxicity	Non-Mutagen, Developmental Toxicant, Sensitizer	4

Table 23 Continued. Hazards Screening for 58 Non-targeted VOC Analytes.[a]

Analyte	CAS No.	PHAROS[b]	ScoreCard[c]	VEGA[d]	Hazard Score
Cyclohexanol, 5-methyl-2-(1-methylethyl)	15356-70-4	Data lacking	Data lacking	[Non-Mutagen], Developmental toxicant, Sensitizer	2
Dipropylene glycol monomethyl ether[e,f]	34590-94-8	Developmental Toxicant, Irritant, Neurotoxicant, Specific Organ Toxicant	Reproductive Toxicity, Neurotoxicity, Kidney Toxicity	Non- Mutagen, Developmental Toxicant,	5
Ethanol, 2-(2-butoxyethoxy)-[h]	112-34-5	Acute Toxicant, Developmental Toxicant, Specific Organ Toxicant	Reproductive Toxicity, Cardiovascular or Blood Toxicity, Kidney Toxicity, Neurotoxicity	Non-Mutagen, Developmental Toxicant,	3
Ethanol, 2-(hexyloxy)-	112-25-4	Acute Toxicant, Irritant	Gastrointestinal or Liver Toxicity, Respiratory Toxicity	Non-Mutagen	2
1-Hexacosanol	506-52-5	very low hazard-German	Data lacking	Non-Mutagen, Non-Carcinogen, Sensitizer	1
1,8-Nonanediol, 8-methyl-	54725-73-4	Data lacking	Data lacking	Non-Mutagen, Non-Carcinogen, Sensitizer	1

Table 23 Continued. Hazards Screening for 58 Non-targeted VOC Analytes.[a]

Analyte	CAS No.	PHAROS[b]	ScoreCard[c]	VEGA[d]	Hazard Score
Octane, 1,1'-oxybis-	629-82-3	low hazard to waters-German	Data lacking	Non-Mutagen, Non-Developmental Toxicant, Sensitizer	1
1-Octanol[h]	111-87-5	Acute Toxicant, Gene Mutation	Data lacking	Non-Mutagen	2
Octanol, 2-butyl-	3913-02-8	hazard to waters-German	Data lacking	Non-Mutagen, Developmental Toxicant, Sensitizer	2
1-Octanol, 2,2-dimethyl-	2370-14-1	Data lacking	Data lacking	Non-Mutagen, Sensitizer	1
3-Octanol, 3,7-dimethyl-, (±)-	57706-88-4	Data lacking	Data lacking	Non-Mutagen, Sensitizer	1
Pentanal	110-62-3	Acute Toxicant, Neurotoxicant	Data lacking	[Non-Mutagen], Sensitizer	3
2-Pentanol, acetate[e]	626-38-0	Irritant, Skin Sensitizer, Specific Organ Toxicant	Neurotoxicity, Respiratory Toxicity, Skin or Sense Organ Toxicity	Non-Mutagen, Sensitizer	4
2-Propanol, 1-butoxy-[f]	5131-66-8	Acute Toxicant, Irritant	Neurotoxicity	Non-Mutagen	3
2-Propanol, 1-(2-methoxy-1-methylethoxy)[f]	20324-32-7	U.S. EPA—low concern	Data lacking	Non-Mutagen, Developmental Toxicant	1

Table 23 Continued. Hazards Screening for 58 Non-targeted VOC Analytes.[a]

Analyte	CAS No.	PHAROS[b]	ScoreCard[c]	VEGA[d]	Hazard Score
2-Propanol, 1-(2-methoxypropoxy)-	13429-07-7	Acute Toxicant, Neurotoxicant	Data lacking	Non-Mutagen, Developmental Toxicant	3
1-Propanol, 2-(1-methylethoxy)-	3944-37-4	Data lacking	Data lacking	Non-Mutagen, Developmental Toxicant	1
2-Propanol, 1-propoxy-[f]	1569-01-3	Acute Toxicant	Data lacking	Non-Mutagen, Developmental Toxicant	2
Aromatic					
Acetic acid, phenylmethyl ester	140-11-4	Acute Toxicant, Specific Organ Toxicant	Gastrointestinal or Liver Toxicity, Kidney Toxicity, Neurotoxicity, Respiratory Toxicity	[Non-Mutagen], [Non-Carcinogen]	3
Benzaldehyde, 4-methoxy-	123-11-5	Acute Toxicant	Neurotoxicity	[Non-Mutagen], Non-Sensitizer	2
Benzene, 1-ethyl-3,5-dimethyl-	934-74-7	Data lacking	Data lacking	Non- Mutagen, Sensitizer	1
Benzophenone	119-61-9	Acute Toxicant, Carcinogen (possible), Endocrine Activity	Cardiovascular or Blood Toxicity, Endocrine Toxicity, Gastrointestinal or Liver Toxicity, Skin or Sense Organ Toxicity	[Non-Mutagen]	3

Table 23 Continued. Hazards Screening for 58 Non-targeted VOC Analytes.[a]

Analyte	CAS No.	PHAROS[b]	ScoreCard[c]	VEGA[d]	Hazard Score
Benzyl Alcohol	100-51-6	Acute Toxicant, Neurotoxicant	Gastrointestinal or Liver Toxicity, Immunotoxicity, Neurotoxicity, Skin or Sense Organ Toxicity	[Non-Mutagen], [Non-Carcinogen]	3
Ethanol, 2-phenoxy-[h]	122-99-6	Acute Toxicant, Developmental Toxicant, Reproductive Toxicant	Reproductive Toxicity, Developmental Toxicity	Non-Developmental Toxicant,	3
2-Ethylhexyl salicylate	118-60-5	Skin Irritant	Data lacking	Non-Mutagen, Non-Carcinogen, Non-Developmental Toxicant	1
Homosalate	118-56-9	Endocrine Activity, PBT	Data lacking	Non-Mutagen, Non-Carcinogen	2
3-Methyl-4-isopropylphenol	3228-02-2	Data lacking	Data lacking	Non-Mutagen, Non-Carcinogen, Developmental Toxicant	1
Naphthalene, 2-methoxy-[h]	93-04-9	Data lacking	Data lacking	Sensitizer	1
2-Propenal, 3-phenyl-[e]	104-55-2	Acute Toxicant, Developmental Toxicant, Reproductive Toxicant, Skin Sensitizer	Immunotoxicity, Neurotoxicity, Skin or Sense Organ Toxicity	[Non-Mutagen], Non-Carcinogen, [Sensitizer]	5

Table 23 Continued. Hazards Screening for 58 Non-targeted VOC Analytes.[a]

Analyte	CAS No.	PHAROS[b]	ScoreCard[c]	VEGA[d]	Hazard Score
Siloxanes					
Cyclohexasiloxane, dodecamethyl-	540-97-6	PBT	Data lacking	Data lacking	1
Decamethyl tetrasiloxane	141-62-8	PBT	Data lacking	Data lacking	1
Terpenes					
Bicyclo[3.1.1]heptane, 6,6-dimethyl-2-me	127-91-3	Acute Toxicant	Data Lacking	Non-Mutagen, Developmental Toxicant	2
Camphor[e]	76-22-2	Acute Toxicant, Reproductive Toxicant, Specific Organ Toxicant	Gastrointestinal or Liver Toxicity, Neurotoxicity, Respiratory Toxicity, Skin or Sense Organ Toxicity	Sensitizer, [Developmental Toxicant]	5
Caryophyllene	87-44-5	PBT	Data lacking	Non-Mutagen, Development Toxicant, Sensitizer	3
1,4-Cyclohexadiene, 1-methyl-4-(1-methylethyl)[h]	99-85-4	USEPA-medium hazard	Data lacking	Non-Mutagen, Sensitizer	1
3-Cyclohexen-1-ol, 4-methyl-1-(1-methylethyl)[g]	562-74-3	Hazard to waters-German	Data lacking	Non-Mutagen, Developmental Toxicant, Sensitizer	2
3-Cyclohexene-1-methanol, α	1679-51-2	Data lacking	Data lacking	Non-Mutagen, Developmental Toxicant, Sensitizer	2

Table 23 Continued. Hazards Screening for 58 Non-targeted VOC Analytes.[a]

Analyte	CAS No.	PHAROS[b]	ScoreCard[c]	VEGA[d]	Hazard Score
Eucalyptol[h]	470-82-6	Acute	Data lacking	[Non-Mutagen], Developmental Toxicant, Sensitizer	3
5-Hepten-2-one, 6-methyl-	110-93-0	Data lacking	Data lacking	Non-Mutagen, Sensitizer	1
β-Myrcene	123-35-3	Reproductive Toxicant (suspected), Irritant	Data lacking	Non-Mutagen, Sensitizer	3
7-Octen-2-ol, 2,6-dimethyl-[g]	18479-58-8	Data lacking	Data lacking	Non-Mutagen, Sensitizer	1
1,3-Pentadiene, (Z)-	1574-41-0	Data lacking	Data lacking	Sensitizer	1
1-Penten-3-one, 1-(2,6,6-trimethyl-2-cyclohexen-1-yl)[h]	7779-30-8	PBT	Data lacking	Non-Mutagen, Sensitizer	2
α-Phellandrene	99-83-2	Data lacking	Data lacking	Non-Mutagen, Sensitizer	1
2-Propanol, 1-[1-methyl-2-(2-propenyloxy)-ethoxy]	55956-25-7	Data lacking	Data lacking	Non-Mutagen, Developmental Toxicant, Sensitizer	2

Abbreviations: Persistent Bioaccumulative Toxicant (PBT).

[a]Compounds with health-based reference values were excluded, as well as compounds that lack positive toxicity data (i.e., Group 10; Hazard score = 0). [b]Acute Toxicant is listed as Toxic to Mammals in PHAROS. [c]Suspected effects.
[d]Brackets indicate experimental data.
[e]Four compounds identified as warranting additional evaluation (i.e., Hazard score>3): 1) acetic acid, butyl ester; 2) camphor; 3) n-pentane; and 4) 3-phenyl-2-propenal. Three compounds with hazard score>3 were not prioritized in our assessment: 1) acetate 2-pentanol; 2) dipropylene glycol monomethyl ether; and 3) 2-methylpropyl ester acetic acid.
[f]U.S. EPA SCP green circle rating: The chemical has been verified to be of low concern based on experimental and modeled data.[118]
[g]U.S. EPA SCP green half-circle: The chemical is expected to be of low concern based on experimental and modeled data.[118]
[h]U.S. EPA SCP yellow triangle: The chemical has met Safer Choice Criteria for its functional ingredient-class, but has some hazard profile issues.[118]

4 Discussion

4.1 Aldehydes

This is the first study to report indoor and outdoor air levels, emission rates and associated risks of formaldehyde, acetaldehyde and VOCs in U.S. child care environments. Formaldehyde and acetaldehyde were detected in 100% of the ECE facilities and in most cases exceed California or U.S. EPA health-based exposure benchmarks. Overall, the formaldehyde and acetaldehyde levels we observed (median=17.8 and 7.5 μg/m^3, respectively) were comparable to levels recently measured in homes and schools in the U.S. and in ECE facilities internationally, with median or mean values in ECE facilities ranging from 3 to 23 μg/m^3 for formaldehyde and from 5 to 18 μg/m^3 for acetaldehyde.[81,82,121] Our study detected aldehydes at much higher levels indoors compared to outdoors, confirming that primary sources of these contaminants are indoors.

Our finding that aldehyde concentrations were inversely associated with air exchange rates is consistent with other studies and underscores the importance of ventilation in reducing indoor concentrations for these compounds. We observed higher formaldehyde levels in home-based compared to center-based child care facilities. The lower AERs and presence of cooking activities in home-based facilities may explain this difference. The study sample size was too small to examine this finding in greater detail.

Child formaldehyde exposures in this study exceeded California OEHHA RELs in 87.5% of ECE facilities and child acetaldehyde exposures exceeded the U.S. EPA RfC in 30% of ECE facilities and both formaldehyde or acetaldehyde exposures exceeded age-adjusted OEHHA benchmarks based on carcinogenicity in all facilities.

Concerns about the health effects of formaldehyde exposure resulted in a 2008 regulation to reduce formaldehyde emissions from composite wood products in California (CCR 17 §93120, 2008). The timing of our sample collection (2010-2011), however, does not reflect any impact of the California rules because they were phased in over several years and the buildings sampled in this study were all over 5 years of age.[9]

4.2 VOCs

This is the first study to report on a wide array of VOCs in U.S. early childhood and education environments. By applying novel automated mass spectral de-convolution and identification software combined with NIST mass spectral libraries, we were able to identify numerous chemicals not previously measured in ECE facilities or other indoor environments. In general, the VOC levels in the child care facilities were within the range of measurements in other child indoor environments.[9,60] For example, average indoor air concentrations of BTEX compounds ranged from 0.7 to 4.1 μg/m³ compared to mean levels in California classrooms that ranged from 0.41 to 6.32 μg/m³.[61] Overall, median indoor air levels of benzene, 2-butoxyethanol, chloroform, naphthalene and xylenes were similar to or slightly higher in the ECE facilities compared to those measured in new California homes.[60] In contrast, levels of d-limonene (median=33 μg/m^3) were higher than concentrations reported in new California homes (median=11 μg/m^3),[60] likely due to frequent cleaning in child care.[122] The D5 levels we observed (mean=46 μg/m^3) were also higher than measurements in U.S. office buildings (mean=3 μg/m^3).[123] D5 is frequently used as a solvent for blending fragrance oil, and is often

present in air fresheners and cleaning fluids.[119,124] Consistent with other studies, indoor levels were higher overall than outdoor levels, indicating that indoor sources predominated. For compounds with both indoor and outdoor sources (e.g. BTEX compounds), the I/O ratios were lower and several were associated with nearby traffic density, indicating that outdoor sources contributed to indoor contamination in some cases. For household source VOCs (with primarily indoor sources), we observed significant positive associations between D5, hexanal, and decanal with air fresheners, and D5 with mopping frequency, consistent with their use as fragrances and solvents in consumer products.[125] The I/O ratios for d-limonene and D5 were extremely high, underscoring the predominance of indoor sources.

Among the targeted and non-targeted VOCs with established non-cancer health-based inhalation benchmarks, there were no concentrations that exceeded acceptable thresholds. However, if reflective of long-term averages, the child dose estimates for benzene, chloroform, ethylbenzene, and/or naphthalene exceeded California Safe Harbor Levels for cancer (defined as > one in 100,000 [10^{-5}] excess risk of cancer over a lifetime) in 100% of the facilities. It is likely that our risk characterization underestimates total risk to the children since they are likely exposed to these chemicals in other indoor and outdoor environments.[60,126]

4.3 Hazard Assessment

In total, 12 compounds were identified for further review by the hazard analysis. Four of these– d-limonene, α-pinene, α-terpineol, and camphor– are terpenes. These products have natural sources, but are often concentrated in cleaning and other scented products and can be respiratory irritants. Levels of d-limonene were among the highest VOCs measured in the child care facilities, and several information sources suggest health concerns about this compound (Table 20).[127] The U.S. EPA Safer Choice Program (SCP) has classified limonene and pinene with yellow triangles, indicating they have "hazard profile" concerns.[118] Camphor is used in air fresheners and other consumer products and in concentrated forms as an insect repellant and pesticide; it is a known hazard that has been associated with child poisoning.[128] Terpenes can also react with ozone to form formaldehyde,[34] a known carcinogen, and ultrafine particles.[129] Given the high formaldehyde levels previously reported in these facilities,[89] additional research on terpenes is needed to assess overall exposure and health risks and determine whether these compounds are significantly contributing to formaldehyde exposure.

The remaining 8 compounds identified for further review include: acetic acid, butyl ester; D4; D5; n-heptane; heptanal; n-pentane; 3-phenyl-2-propenal; 1,2,4-trimethylbenzene. European agencies have set occupational exposure standards for 1,2,4-trimethylbenzene and n-heptane based on adverse developmental effects, and they both affect the respiratory and central nervous systems.[130,131] Heptanal is one of several fragrance-related compounds we measured and is identified as a respiratory irritant in occupational settings with high exposures.[98] Butyl ester acetic acid (Table 23; CAS #123-86-4) has natural sources and is used in air fresheners, cleaners, as a synthetic flavoring in foods, and in floor sealants and finishes.[109] Although the hazard score for this compound was relatively high (6), aggregated information summarized in PHAROS and ScoreCard generally indicate only moderate hazards, and the median estimated levels were < 1 μg/m^3. However, its use in air fresheners and cleaners suggest the potential for widespread exposure as mixtures of fragrance-related compounds. Fragrances have been associated with reductions in lung function and other respiratory symptoms.[132] Thus, additional research on low level exposure and chronic toxicities for these fragrance-related compounds is needed.

There are three compounds with hazard scores >3 that we did not prioritize in our assessment (dipropylene glycol monomethyl ether; 2-methylpropyl ester acetic acid; and acetate 2-pentanol). 2-Methylpropyl ester acetic acid (Table 23; CAS #110-19-0) is a solvent used in a variety of coatings and also as a flavoring agent.[109,133] Although the hazard score from our analysis was >3, aggregated information summarized in PHAROS and ScoreCard indicate only moderate hazards, and the U.S. EPA SCP classified this compound as a "green half-circle", indicating low concern but missing data.[118] Similarly, aggregated information for dipropylene glycol monomethyl ether (DGME) (Table 23; CAS #34590-94-8), a solvent used in coatings and flooring, suggests some moderate hazards and contradicts the classification as a "green circle", or of low concern, by the U.S. EPA SCP.[118] However, according to a 2001 review by U.S. EPA, one DGME isomer is a reproductive toxicant, but adverse effects were noted at exposures in animals at 1818 mg/m^3 to 2424 mg/m^3, with No Observed Adverse Effect Levels (NOAELs) from > 303 mg/m^3 to 1212 mg/m^3.[134] Applying uncertainty factors to these NOAELs would result in health-based exposure thresholds significantly higher than the levels we measured. Thus, we did not prioritize this compound for further research.

Levels of acetate 2-pentanol (CAS #626-38-0) were very low (<1 µg/m^3) and this substance is listed as a food ingredient by the U.S. Food and Drug Administration.[135] At very high exposures effects on skin, the respiratory system, and central nervous system are noted,[131] but at many orders of magnitude above the levels we estimated (median=0.06 µg/m^3 versus a NIOSH REL of 650 mg/m^3.[131] Thus, we also did not prioritize this compound for further research.

In summary, this screening identified 12 VOCs without non-occupational health-based exposure benchmarks in these ECE facilities that warrant additional exposure and hazard assessment. Recommendations for follow-up of these and other measured VOCs are discussed below.

4.4 Limitations

Although this study is the largest to date reporting on a wide variety of VOCs in U.S. ECE facilities, the sample size of 40 limited our statistical power for statistical analyses. In particular, initial analytical problems with interference by alcohols from hand sanitizers reduced the final sample size for VOCs to 34, further limiting our power to build multivariable models and draw inferences. The samples were also collected during a single day and may not reflect long-term levels. Finally, the sources of indoor air contaminants are ubiquitous and difficult to disentangle, and thus may not have been fully captured in our questionnaire and inspection data.

The lack of toxicological information for many of the chemicals we measured is another limitation. For example, QSAR programs are constrained by the availability of adequate toxicological data for reference chemicals to make accurate hazard predictions. Insufficient VEGA reliability scores limited our capacity to judge whether some compounds pose health hazards and warrant additional study. Similarly, the databases we used that aggregate toxicological information may not be complete, and may not consider proprietary information or government or other reports that are not published in the peer-reviewed literature.[108,109]

5 Summary and Conclusions

Approximately 1.1 million California children ages 0-5 and 146,000 staff spend 40 or more hours per week in child care centers or preschools. Although VOCs and other environmental

exposures have been documented in schools and other indoor environments where children spend time, there is virtually no information available on environmental exposures to volatile organic compounds (VOCs) in California child care, collectively known as Early Childhood Education (ECE) facilities. These chemicals can exacerbate asthma and other respiratory illnesses or impair neurocognitive functioning in children and some are known carcinogens. As part of the parent study to this supplement (Agreement Number 08-305), we measured formaldehyde, acetaldehyde, and 38 targeted VOCs in 40 ECE facilities. We also tentatively identified and quantified 119 additional, non-targeted VOCs indicated by the instrument chromatograms, showing exposures to a much broader array of chemicals. For this supplement to the parent study, we conducted additional analyses examining aldehyde exposures and risk and prepared journal articles reporting these findings to the larger scientific community. We also completed additional laboratory analyses confirming that we had correctly identified the non-targeted VOCs and conducted a screening risk assessment to evaluate chemicals with available health-based reference values. However, more than 70% of the VOCs we had studied lacked benchmarks to assess potential health risks. To address this data gap, we completed an extensive literature review and applied quantitative structural-activity relationship (QSAR) models to identify potential health concerns and prioritize compounds for additional exposure and health evaluation.

5.1 Formaldehyde and Acetaldehyde

This is the first study to evaluate formaldehyde and acetaldehyde levels in U.S. child care environments. Formaldehyde and acetaldehyde were detected in 100% of the ECE facilities at much higher levels indoors compared with outdoors. Overall, the formaldehyde and acetaldehyde levels we observed were comparable to levels recently measured in homes and schools in the U.S. and in ECE facilities internationally. Child formaldehyde exposures in this study exceeded California 8-hour and Chronic OEHHA Reference Exposure Levels in 87.5% of ECE facilities and child acetaldehyde exposures exceeded the U.S. EPA RfC in 30% of ECE facilities and both formaldehyde or acetaldehyde exposures exceeded age-adjusted OEHHA benchmarks based on carcinogenicity in all facilities. Concerns about the health effects of formaldehyde exposure resulted in a 2008 regulation to reduce formaldehyde emissions from composite wood products in California (CCR 17 §93120, 2008). The timing of our sample collection (2010-2011), however, does not reflect any impact of the California rules because they were phased in over several years and the buildings sampled in this study were all over 5 years of age.

5.2 VOCs

This is also the first study to report on a wide array of VOCs in U.S. early childhood and education environments. By applying novel automated mass spectral de-convolution and identification software (AMDIS) combined with NIST mass spectral libraries, we were able to identify numerous chemicals not previously measured in ECE facilities or other indoor environments. In general, the VOC levels in the child care facilities were within the range of measurements in other child indoor environments, however levels of d-limonene were higher than concentrations reported in new California homes, likely due to frequent cleaning in child care. The D5 levels we observed were also higher than measurements in U.S. office buildings. D5 is frequently used as a solvent for blending fragrance oil, and is often present in air fresheners and cleaning fluids. Consistent with other studies, overall, indoor VOC levels were higher than outdoor levels, indicating that indoor sources predominated. The indoor/outdoor

concentration ratios for d-limonene and D5 were extremely high, underscoring the predominance of indoor sources.

The large number of unknown peaks - up to 120 - on the instrument chromatogram underscored that children are exposed to many different chemicals that had never been measured in indoor environments. The use of NIST spectral libraries and the application of automated mass spectral de-convolution and identification (AMDIS) software to identity these compounds, with additional confirmation by comparison to select pure standards, greatly increased our ability to examine children's exposures and guide further analyses to target compounds with potential health concerns requiring additional study.

Based on measurements of the targeted VOCs and estimated levels of naphthalene, intake rates of benzene, chloroform, ethylbenzene, and/or naphthalene exceeded California Safe Harbor Levels for cancer in in 71%, 38%, 56%, and 97% of the facilities, respectively. While exposures to 17 of the VOC compounds we measured were below non-cancer health benchmarks, more than 70% of the compounds lacked any health-based exposure standards that could be used to characterize potential risks. Through review of databases aggregating toxicological information and the application of QSAR modeling methods, we identified 12 chemicals that warrant additional exposure and health evaluation due to the potential for carcinogenic, neurologic, or other health effects (acetic acid, butyl ester; camphor; D4; D5; n-heptane; heptanal; d-limonene; n-pentane; 3-phenyl-2-propenal; α-pinene; α-terpineol; 1,2,4-trimethylbenzene). These chemicals include commonly used terpenes and fragrance-related compounds, which have been associated with respiratory or other health problems.

6 Recommendations

The research team recommends the following, based on the parent study (Agreement Number 08-305) and the additional work conducted for this supplement:

a. The use of automated mass spectral de-convolution and identification software (AMDIS) combined with matching to mass spectral libraries and follow-up confirmation with pure standards is an effective tool to identify unknown VOCs in indoor environments. Future indoor air quality studies should consider these methods to identify significant unknown chemicals beyond the a priori list of target analytes, allowing a broader assessment of exposures and potential health risks. The library of chemicals identified in this study provide guidance on the choice of target analytes for future studies of indoor air quality in child care.

b. More research is needed to determine the relative contribution of composite wood products versus other sources (i.e., other building materials and furnishings, cleaning materials, personal care products, etc.) to indoor formaldehyde contamination in new and older buildings serving child care.

c. Additional studies determining sources and health impacts of VOC compounds where levels exceeded exposure benchmarks based on carcinogenicity should be a high priority, including benzene, chloroform, ethylbenzene, and naphthalene.

d. Based on extensive toxicological review and the application of QSAR models, the following 12 chemicals should be prioritized for additional exposure and health evaluation due to their potential for carcinogenic, neurologic, respiratory, or other health effects: acetic acid, butyl ester; camphor; D4; D5; n-heptane; heptanal; d-limonene; n-pentane; 3-phenyl-2-propenal; α-pinene; α-terpineol; 1,2,4-trimethylbenzene). These

include chemicals commonly used terpenes and fragrance-related compounds, which have been associated with respiratory symptoms, common problems among children in child care.

e. The lack of toxicological information for many of the chemicals we measured is a basic limitation, and even QSAR programs are constrained by the availability of adequate toxicological data for reference chemicals to make accurate hazard predictions. Additional toxicological evaluations are needed for many of the chemicals we identified to fully inform health risk assessments of these exposures.

f. While the chemicals we identified are not uniquely found in child care, the seriousness of the health risks associated with the VOC levels observed in ECE environments demonstrate that potentially harmful exposures are occurring and indicate that more research is needed to fully assess potential health risks and identify sources of indoor air contamination. If warranted, restrictions on the use of some compounds should be considered as well as outreach to child care providers on strategies to improve indoor air quality, such as ensuring proper ventilation, to mitigate these exposures.

7 References

1. Breysse P, Farr N, Galke W, Lanphear B, Morley R, Bergofsky L. The relationship between housing and health: children at risk. Environ Health Perspect 2004;112:1583-8.
2. EPA US. Exposure Factors Handbook Edition (Final) EPA/600/R-09/052F. Washington, DC. 2011.
3. Wiley JA, Cheng YT, Robinson JP, Piazza T, Stork L, Pladsen K. Study of Children's Activity Patterns, final report to the ARB contract no. A733-149; 1991 http://www.arb.ca.gov/research/single-project.php?row_id=64944
4. CPSC. Staff Study of Safety Hazards in Child Care Settings. 1999. (Accessed July 2, 2008, at www.cpsc.gov/library/ccstudy.html) 1999.
5. Tulve NS, Jones PA, Nishioka MG, et al. Pesticide measurements from the First National Environmental Health Survey of Child Care Centers using a multi-residue GC/MS analysis method. Environ Sci Technol 2006;40:6269-74.
6. Lopez E, de Cos P. Preschool and Childcare Enrollment in California (Prepared for Assemblywoman W. Chan): California Research Bureau; . 2004.
7. U. S. GAO. Child Care: State Efforts to Enforce Safety and Health Requirements. Washington, D.C.; . 2004.
8. Goveia M, Shaikh N, Windham G, Bembom O, Feldman K, Kreutzer R. Pediatric Asthma-Related Environmental Practices and Asthma Awareness in California Child Care Centers. Asthma, Allergy & Immunology 2005;18:12-24. 2005.
9. Bradman A, Gaspar F, Castorina R, Maddalena R, Tong-Lin E, McKone TE. Environmental Exposures in Early Childhood Education Environments, Final Report to California Air Resources Board; Sacramento, CA. Contract Number 08-305. 2012. http://www.arb.ca.gov/research/single-project.php?row_id=64830.
10. Cummins SK, Jackson RJ. The built environment and children's health. Pediatr Clin North Am 2001;48:1241-52.
11. Ehrlich RI, Du Toit D, Jordaan E, et al. Risk factors for childhood asthma and wheezing. Importance of maternal and household smoking. Am J Respir Crit Care Med 1996;154:681-8.
12. Honicky RE, Osborne JS, 3rd. Respiratory effects of wood heat: clinical observations and epidemiologic assessment. Environ Health Perspect 1991;95:105-9.
13. Krieger J, Higgins DL. Housing and health: time again for public health action. Am J Public Health 2002;92:758-68.
14. Licorish K, Novey HS, Kozak P, Fairshter RD, Wilson AF. Role of Alternaria and Penicillium spores in the pathogenesis of asthma. J Allergy Clin Immunol 1985;76:819-25.
15. Lindgren S, Belin L, Dreborg S, Einarsson R, Pahlman I. Breed-specific dog-dandruff allergens. J Allergy Clin Immunol 1988;82:196-204.
16. Luczynska CM, Li Y, Chapman MD, Platts-Mills TA. Airborne concentrations and particle size distribution of allergen derived from domestic cats (Felis domesticus). Measurements using cascade impactor, liquid impinger, and a two-site monoclonal antibody assay for Fel d I. Am Rev Respir Dis 1990;141:361-7.
17. Martinez FD, Cline M, Burrows B. Increased incidence of asthma in children of smoking mothers. Pediatrics 1992;89:21-6.
18. Molfino NA, Nannini LJ, Martelli AN, Slutsky AS. Respiratory arrest in near-fatal asthma. N Engl J Med 1991;324:285-8.
19. Morris K, Morgenlander M, Coulehan JL, Gahagen S, Arena VC. Wood-burning stoves and lower respiratory tract infection in American Indian children. Am J Dis Child 1990;144:105-8.

20. Norback D, Bjornsson E, Janson C, Widstrom J, Boman G. Asthmatic symptoms and volatile organic compounds, formaldehyde, and carbon dioxide in dwellings. Occup Environ Med 1995;52:388-95.
21. Rosenstreich DL, Eggleston P, Kattan M, et al. The role of cockroach allergy and exposure to cockroach allergen in causing morbidity among inner-city children with asthma. N Engl J Med 1997;336:1356-63.
22. Strachan DP, Flannigan B, McCabe EM, McGarry F. Quantification of airborne moulds in the homes of children with and without wheeze. Thorax 1990;45:382-7.
23. Targonski PV, Persky VW, Ramekrishnan V. Effect of environmental molds on risk of death from asthma during the pollen season. J Allergy Clin Immunol 1995;95:955-61.
24. Verhoeff AP, van Strien RT, van Wijnen JH, Brunekreef B. Damp housing and childhood respiratory symptoms: the role of sensitization to dust mites and molds. Am J Epidemiol 1995;141:103-10.
25. Weitzman M, Gortmaker S, Walker DK, Sobol A. Maternal smoking and childhood asthma. Pediatrics 1990;85:505-11.
26. Wieslander G, Norback D, Bjornsson E. Asthma and the indoor environment: the significance of emission of formaldehyde and volatile organic compounds from newly painted indoor surfaces. Int Arch Occup Environ Health 1997;69:115-24.
27. Rumchev KS, J.; Bulsara, M.; Phillips, M.; Stick, S. Association of domestic exposure to volatile organic compounds with asthma in young children. Thorax 2004;59:746-51.
28. Ware JH, Spengler JD, Neas LM, et al. Respiratory and irritant health effects of ambient volatile organic compounds. The Kanawha County Health Study. Am J Epidemiol 1993;137:1287-301.
29. Harving H, Dahl R, Molhave L. Lung function and bronchial reactivity in asthmatics during exposure to volatile organic compounds. Am Rev Respir Dis 1991;143:751-4.
30. Koren HS, Graham DE, Devlin RB. Exposure of humans to a volatile organic mixture. III. Inflammatory response. Arch Environ Health 1992;47:39-44.
31. ATSDR. Interaction Profile for: Benzene, Toluene, Ethylbenzene, and Xylenes (BTEX): Agency for Toxic Substances and Disease Registry; 2004.
32. Choi H, Schmidbauer N, Sundell J, Hasselgren M, Spengler J, Bornehag CG. Common household chemicals and the allergy risks in pre-school age children. PloS one 2010;5:e13423.
33. Choi H, Schmidbauer N, Spengler J, Bornehag CG. Sources of propylene glycol and glycol ethers in air at home. International journal of environmental research and public health 2010;7:4213-37.
34. Wolkoff P, Clausen PA, Wilkins CK, Nielsen GD. Formation of Strong Airway Irritants in Terpene/Ozone Mixtures. Indoor Air 2000;10:82-91.
35. U.S. EPA. Formaldehyde (CASRN 50-00-0). In. Cincinatti, OH: Office of Research and Development, National Center for Environmental Assessment, Environmental Criteria and Assessment Office; 1991.
36. International Agency for Research on Cancer (IARC). IARC Monographs on the Evaluation of Carcinogenic Risks to Humans; Formaldehyde, 2-Butoxyethanol and 1-tert-Butoxypropan-2-ol. Lyon; 2006.
37. U.S. EPA. Acetaldehyde (CASRN 75-07-0). In. Cincinatti, OH: Office of Research and Development, National Center for Environmental Assessment, Environmental Criteria and Assessment Office; 1991.
38. International Agency for Research on Cancer (IARC). IARC Monographs on the Evaluation of Carcinogenic Risks to Humans; Re-evaluation of Some Organic Chemicals, Hydrazine and Hydrogen Peroxide. Lyon; 1999.

39. Woutersen RA, Appelman LM, Feron VJ, Van der Heijden CA. Inhalation toxicity of acetaldehyde in rats. II. Carcinogenicity study: interim results after 15 months. Toxicology 1984;31:123-33.
40. Woutersen RA, Appelman LM, Van Garderen-Hoetmer A, Feron VJ. Inhalation toxicity of acetaldehyde in rats. III. Carcinogenicity study. Toxicology 1986;41:213-31.
41. Albert RE, Sellakumar AR, Laskin S, Kuschner M, Nelson N, Snyder CA. Gaseous formaldehyde and hydrogen chloride induction of nasal cancer in the rat. J Natl Cancer Inst 1982;68:597-603.
42. Kerns WD, Pavkov KL, Donofrio DJ, Gralla EJ, Swenberg JA. Carcinogenicity of formaldehyde in rats and mice after long-term inhalation exposure. Cancer Res 1983;43:4382-92.
43. Liebling T, Rosenman KD, Pastides H, Griffith RG, Lemeshow S. Cancer mortality among workers exposed to formaldehyde. Am J Ind Med 1984;5:423-8.
44. Stayner L, Smith AB, Reeve G, et al. Proportionate mortality study of workers in the garment industry exposed to formaldehyde. Am J Ind Med 1985;8:75-6.
45. Gardner MJ, Pannett B, Winter PD, Cruddas AM. A cohort study of workers exposed to formaldehyde in the British chemical industry: an update. Br J Ind Med 1993;50:827-34.
46. Rumchev KB, Spickett JT, Bulsara MK, Phillips MR, Stick SM. Domestic exposure to formaldehyde significantly increases the risk of asthma in young children. Eur Respir J 2002;20:403-8.
47. Quackenboss JL, M.; Michaud, J.; Bronnimann, D. Formaldehyde exposure and acute health effects study. Environmental International 1989;15:169-76.
48. Offermann FJ. Ventilation and Indoor Air Quality in New Homes: California Air Resources Board and California Energy Commission; 2009.
49. Jenkins P. Relevance of Asa Bradman's Proposal to Regulations: Additional Information (Personal Communication to Asa Bradman). In; 2008.
50. California Air Resources Board (CARB). California Portable Classrooms Study. Report to the Legislature. Sacramento, CA: California Air Resources Board Research Division; 2004.
51. Rumchev K, Spickett J, Bulsara M, Phillips M, Stick S. Association of domestic exposure to volatile organic compounds with asthma in young children. Thorax 2004;59:746-51.
52. Wieslander G, Norback D, Bjornsson E, Janson C, Boman G. Asthma and the indoor environment: the significance of emission of formaldehyde and volatile organic compounds from newly painted indoor surfaces. Int Arch Occup Environ Health 1997;69:115-24.
53. Hauptmann M, Lubin JH, Stewart PA, Hayes RB, Blair A. Mortality from solid cancers among workers in formaldehyde industries. Am J Epidemiol 2004;159:1117-30.
54. Pinkerton LE, Hein MJ, Stayner LT. Mortality among a cohort of garment workers exposed to formaldehyde: an update. Occup Environ Med 2004;61:193-200.
55. IARC. Formaldehyde, 2-butoxyethanol and 1-tert-butoxypropan-2-ol: International Agency for Research on Cancer; 2006.
56. NTP. Report on Carcinogens. Twelfth Edition. In: National Toxicology Program, ed. Research Triangle Park, NC; 2011.
57. U.S. EPA. Acetaldehyde (CASRN 75-07-0). In: U.S. Environmental Protection Agency, ed.; 2012.
58. U.S. EPA. Formaldehyde (CASRN 50-00-0). In: U.S. Environmental Protection Agency, ed.; 2012.
59. CARB. Environmental Health Conditions in California's Portable Classrooms. Report to the California Legislature. In: California Air Resources Board, ed. Sacramento, CA; 2004.

60. Offermann FJ. Ventilation and Indoor Air Quality in New Homes. PIER Collaborative Report. In. Sacramento, CA; 2009.
61. Whitmore R. California Portable Classrooms Study Phase II: Main Study, Final Report, Vol II. In. Sacramento, CA; 2003.
62. CARB. Composite Wood Products ATCM. In: California Air Resources Board, ed. Current Regulation(s); 2014.
63. U.S. EPA. Formaldehyde Emission Standards for Composite Wood Products. Proposed Rules. . In: Fed Regist, ed.; 2013.
64. U.S. EPA. Child-Specific Exposure Factors Handbook. Washington, D.C.: National Center for Environmental Assessment; 2002 September. Report No.: EPA-600-P-00-002B.
65. Bearer CF. How are children different from adults? Environ Health Perspect 1995;103 Suppl 6:7-12.
66. Cohen Hubal EA, Sheldon LS, Burke JM, et al. Children's exposure assessment: a review of factors influencing children's exposure, and the data available to characterize and assess that exposure. Environ Health Perspect 2000;108:475-86.
67. Lo B, O'Connell M, eds. Ethical Considerations for Research on Housing-Related Health Hazards Involving Children. Washington, DC: The National Academies Press; 2005.
68. Goveia M, Shaikh, N, Windham, G, Bembom, O, Feldman, K, and Kreutzer, R. Pediatric Asthma-Related Environmental Practices and Asthma Awareness in California Child Care Centers. Asthma, Allergy & Immunology 2005;18:12-24.
69. Sutton R. Greener School Cleaning Supplies = Fresh Air + Healthier Kids. Washington, DC; 2009.
70. Volatile Organic Compounds (VOCs). U.S. Environmnetal Protection Agency, 2012. (Accessed accessed Nov 20, 2013, at http://www.epa.gov/iaq/voc.html.)
71. Salthammer T, Mentese S, Marutzky R. Formaldehyde in the indoor environment. Chemical reviews 2010;110:2536-72.
72. Kelly TJ, Smith DL, Satola J. Emission rates of formaldehyde from materials and consumer products found in California homes. Environmental Science & Technology 1999;33:81-8.
73. CARB. Indoor Air Pollution in California: Report to the California Legislature. In. Sacramento, CA: California Air Resources Board; 2005.
74. CARB. Acetaldehyde as a Toxic Air Contaminant. In. Sacramento, CA: California Air Resources Board; 1993.
75. Kelly TJ. Determination of Formaldehyde and Toulene Diisocyanate Emissions from Indoor Residential Sources. In. Sacramento, CA; 1996.
76. Zhang J, Lioy PJ, He Q. Characteristics of aldehydes: concentrations, sources, and exposures for indoor and outdoor residential microenvironments. Environ Sci Technol 1994;28:146-52.
77. Destaillats H, Lunden MM, Singer BC, et al. Indoor secondary pollutants from household product emissions in the presence of ozone: a bench-scale chamber study. Environ Sci Technol 2006;40:4421-8.
78. Kabir E, Kim KH, Sohn J, Kweon B, Shin J. Indoor air quality assessment in child care and medical facilities in Korea. Environ Monit Assess 2012;184:6395-409.
79. Roda C, Barral S, Ravelomanantsoa H, et al. Assessment of indoor environment in Paris child day care centers. Environ Res 2011;111:1010-7.
80. Ruotsalainen R, Jaakkola N, Jaakkola JJK. Ventilation and indoor air quality in Finnish daycare centers. Environ Int 1993;19:109-19.
81. St-Jean M, St-Amand A, Gilbert NL, et al. Indoor air quality in Montréal area day-care centres, Canada. Environ Res 2012;118:1-7.

82. Zuraimi MS, Tham KW. Effects of child care center ventilation strategies on volatile organic compounds of indoor and outdoor origins. Environ Sci Technol 2008;42:2054-9.
83. CCLD Facility Search Form. Community Care Licensing Division, 2010. (Accessed accessed Jan 10, 2010, at http://www.ccld.ca.gov/docs/ccld_search/ccld_search.aspx.)
84. Bartlett KH, Martinez M, Bert J. Modeling of occupant-generated CO2 dynamics in naturally ventilated classrooms. J Occup Environ Hyg 2004;1:139 - 48.
85. Bekö G, Lund T, Nors F, Toftum J, Clausen G. Ventilation rates in the bedrooms of 500 Danish children. Build Environ 2010;45:2289-95.
86. Persily A. Evaluating building IAQ and ventilation with indoor carbon dioxide. ASHRAE Transactions 1997;103:1-12,193.
87. 120.1 C. Title 24, Part 6, Building Energy Efficiency Standards for Residental and Nonresidential Buildings, Section 120.1. In: California Energy Commission 2013.
88. California Department of Public Health, Environmental Health Investigation Branch, CEHTP Traffic Linkage Service Demonstration. 2007. (Accessed at http://www.ehib.org/traffic_tool.jsp#sol.)
89. Bradman A, Gaspar F, Castorina R, et al. Formaldehyde and Acetaldehyde Exposure and Risk Characterization in California Early Childhood Education Environments. Indoor Air 2016; Jan 25. DOI 10.1111/ina.12283. [Epub ahead of print].
90. Hoang T, Castorina R, Gaspar F, et al. VOC Exposures in California Early Childhood Education Environments. Indoor Air (Submitted) 2016.
91. U.S. EPA. Determination of Formaldehyde in Ambient Air Using Adsorbent Cartridge Followed by High Performance Liquid Chromatography (HPLC) [Active Sampling Methodology]. In: Center for Environmental Research Information, ed. Compendium of Methods for the Determination of Toxic Organic Compounds in Ambient Air. Cincinatti, OH; 1999.
92. U.S. EPA. Determination of Volatile Organic Compounds in Ambient Air Using Active Sampling Onto Sorbent Tubes. Cincinatti: Center for Environmental Research Information, Office of Research and Development,; 1999.
93. Hornung RW, Reed LD. Estimation of average concentration in the presence of nondetectable values. Appl Occup Environ Hyg 1990;5:46-51.
94. Linstrom P, Mirokhin Y, Tchekhovskoi D, Yang X. NIST/EPA/NIH Mass Spectral Library and NIST Mass Spectral Search Program. In. 2.2 ed. Gaithersburg, MD: The NIST Mass Spectrometry Data Center; 2014.
95. Hodgson AT. A Review and a Limited Comparison of Methods for Measuring Total Volatile Organic Compounds in Indoor Air. Indoor Air 1995;5:247-57.
96. McLafferty FW, Turecek F. Interpretation of Mass Spectra. 4 ed. Sausalito, CA: University Science Books; 1993.
97. U.S. EPA. Toxicological Review of Toluene (CAS No. 108-88-3): US Environmental Protection Agency; 2005.
98. U.S. National Library of Medicine. Hazardous Substances Data Bank (HSDB), Bethesda, MD., 2013. (Accessed accessed Nov 13, 2013, at http://toxnet.nlm.nih.gov/newtoxnet/hsdb.htm.)
99. Cooper SD, Raymer JH, Pellizzari ED, Thomas KW. The identification of polar organic compounds found in consumer products and their toxicological properties. J Expo Anal Environ Epidemiol 1995;5:57-75.
100. Integrated Risk Information System (IRIS). 2015. (Accessed accessed Nov 13, 2013, at http://www.epa.gov/IRIS/.)

101. All OEHHA Acute, 8-hour and Chronic Reference Exposure Levels (chRELs) as of June 2014. California Office of Environmental Health Hazard Assessment, 2014. (Accessed accessed Nov 13, 2014, at http://www.oehha.ca.gov/air/Allrels.html.)
102. OEHHA. Proposition 65: No Significant Risk Levels (NSRLs) for Carcinogens and Maximum Allowable Dose Levels (MADLs) for Chemicals Causing Reproductive Toxicity. In. Sacramento, CA; 2013.
103. OEHHA. Proposition 65: Process for Developing Safe Harbor Numbers. In: Office of Environmental Health Hazard Assessment, ed. Sacramento, CA; 2001.
104. U.S. EPA. Exposure Factors Handbook 2011 Edition (Final). Washington, DC: U.S. Environmental Protection Agency; 2011. Report No.: EPA/600/R-09/052F.
105. ATSDR. Public Health Assessment Guidance Manual. In. Atlanta, GA; 2005.
106. Arcus-Arth A, Blaisdell RJ. Statistical distributions of daily breathing rates for narrow age groups of infants and children. Risk analysis : an official publication of the Society for Risk Analysis 2007;27:97-110.
107. U.S. EPA. Child-Specific Exposure Factors Handbook (Final Report). In. Washington DC; 2008.
108. Chemical Profiles. 2011. (Accessed accessed Nov 13, 2013, at http://scorecard.goodguide.com/chemical-profiles/.)
109. PharosProject. 2014. (Accessed accessed Feb 12, 2014, at https://www.pharosproject.net/.)
110. Istituto di Ricerche Farmacologiche Mario Negri. Virtual models for property Evaluation of chemicals within a Global Architecture (VEGA). 2014. (Accessed June 2, 2014, at http://www.vega-qsar.eu/.)
111. QSAR Toolbox. 2012. (Accessed at http://www.qsartoolbox.org/.)
112. Nendza M, Gabbert S, Kuhne R, et al. A comparative survey of chemistry-driven in silico methods to identify hazardous substances under REACH. Regul Toxicol Pharm 2013;66:301-14.
113. Istituto di Ricerche Farmacologiche Mario Negri. (Accessed at http://www.marionegri.it/en_US/home.)
114. IRCCS. Istituto di Ricerche Farmacologiche Mario Negri. Guidelines for the VEGA models (version 2.1.1).
115. ATSDR. Agency for Toxic Substances and Disease Registry. Toxicological profile for Propylene Glycol. In: U.S. Department of Health & Human Services, ed. Atlanta, GA; 1997.
116. All OEHHA Acute, 8-hour and Chronic Reference Exposure Levels (RELs). California Office of Environmental Health Hazard Assessment, 2013. (Accessed Nov 25, 2013, at http://oehha.ca.gov/air/allrels.html.)
117. OEHHA. Appendix D. Individual Acute, 8-Hour, and Chronic Reference Exposure Level Summaries. In. Sacramento, CA; 2008.
118. U.S. EPA. Safer Choice. Safer Chemical Ingredient's List (SCIL). http://www.epa.gov/saferchoice/safer-ingredients#scil (accessed December 12, 2015).
119. Cyclosiloxanes. 2008. (Accessed accessed Jan 10, 2015, at http://www.biomonitoring.ca.gov/sites/default/files/downloads/1208cyclosiloxanes.pdf.)
120. Priority Chemicals. 2014. (Accessed accessed Nov 30, 2015, at http://www.biomonitoring.ca.gov/chemicals/priority-chemicals.)
121. Roda C, Kousignian I, Guihenneuc-Jouyaux C, et al. Formaldehyde exposure and lower respiratory infections in infants: findings from the PARIS cohort study. Environ Health Perspect 2011;119:1653-8.
122. Steinemann AC. Fragranced consumer products and undisclosed ingredients. Environ Impact Asses 2009;29:32-8.

123. Yucuis RA, Stanier CO, Hornbuckle KC. Cyclic siloxanes in air, including identification of high levels in Chicago and distinct diurnal variation. Chemosphere 2013;92:905-10.
124. Maddalena RL, McKone TE, Destaillats H, Russell M, Hodgson AT, Perino C. Quantifying pollution emissions from office equipment: a concern in energy-efficient buildings. In. Sacramento, CA; 2011.
125. Marsili R. Flavor, Fragrance, and Odor Analysis. Boca Raton, FL: CRC Press; 2001.
126. Jia C, Batterman S, Godwin C. VOCs in industrial, urban and suburban neighborhoods, Part 1: Indoor and outdoor concentrations, variation, and risk drivers. Atmospheric Environment 2008;42:2083-100.
127. Kim YW, Kim MJ, Chung BY, et al. Safety evaluation and risk assessment of d-Limonene. Journal of toxicology and environmental health Part B, Critical reviews 2013;16:17-38.
128. Khine H, Weiss D, Graber N, Hoffman RS, Esteban-Cruciani N, Avner JR. A cluster of children with seizures caused by camphor poisoning. Pediatrics 2009;123:1269-72.
129. Rohr AC, Weschler CJ, Koutrakis P, Spengler JD. Generation and quantification of ultrafine particles through terpene/ozone reaction in a chamber setting. Aerosol Sci Tech 2003;37:65-78.
130. Deutsche Forschungsgemeinschaft. List of MAK and BAT Values 2012. Weinheim, Germany: Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area; 2012. Report No.: 48.
131. CDC. Centers for Disease Control and Prevention. NIOSH Pocket Guide to Chemical Hazards. National Institue for Occupational Safety and Health. 2010. http://www.cdc.gov/niosh/npg/ [Accessed 12 December 2015].
132. Dales RE, Cakmak S, Leech J, Liu L. The association between personal care products and lung function. Annals of epidemiology 2013;23:49-53.
133. NIH. National Institutes of Health. National Center for Biotechnology Information. PubChem. http://pubchem.ncbi.nlm.nih.gov/compound/8038#section=Top [Accessed 10 December 2015].
134. UNEP. United National Environment Program. Organisation for Economic Co-operation and Development (OECD). Screening Information Dataset (SIDS). Dipropylene glycol methyl ether. SIDS Initial Assessment Report for 12th SIAM (Paris, France, 27-29 June 2001). http://www.inchem.org/documents/sids/sids/34590-94-8.pdf.
135. U.S. FDA. Food and Drug Administration. Substance Registration System. Unique identifier. UNII B570113U4Q. http://fdasis.nlm.nih.gov/srs/ [accessed December 12, 2015].
136. Baptista FJ, Bailey BJ, Randall JM, Meneses JF. Greenhouse ventilation rate: theory and measurement with tracer gas techniques. Journal of Agricultural Engineering Research 1999;72:363-74.
137. Murray DM, Burmaster DE. Residential air exchange rates in the United States: empirical and estimated parametric distributions by season and climatic region. Risk Analysis 1995;15:459-65.
138. Maddalena R, Li N, Hodgson A, Offermann F, Singer B. Maximizing Information from Residential Measurements of Volatile Organic Compounds. In: Ernest Orlando Lawrence Berkeley National Laboratory, ed.; 2013.
139. Maddalena R, Russell M, Sullivan DP, Apte MG. Formaldehyde and other volatile organic chemical emissions in four FEMA temporary housing units. Environ Sci Technol 2009;43:5626-32.

8 Appendix

Air Exchange Rate Computations

Given the highly fluctuating indoor environment, we used mass balance and tracer gas methods to calculate air exchange rates (AERs). We selected carbon dioxide (CO_2) as the tracer gas due to its low toxicity and acceptability to ECE directors. When children were not present, we added medical-grade CO_2 until levels were ~2500 ppm. Based on the CO_2 decay rates, we computed AERs and compared them to those obtained from the continuous mass-balance model. The CO_2 decay method uses the following equation[86,136]:

$$C_t - C_{input} = \left[C_{orig} - C_{input}\right] e^{(-Qt/V_r)}$$

Where,

e^x=exponential function

C_t=Concentration of tracer at elapsed time, ppm

C_{input}=Concentration of tracer from inlet air and occupant emissions, ppm

C_{orig}=Concentration of tracer at start of test, ppm

Q=Effective ventilation rate, m^3/hour

t=Time of test duration, hour

V_r=Volume of child care room, liters

Our model accounted for CO_2 input from outdoors and occupant emissions. Total CO_2 input into the room was calculated using:

$$E_{total} = \frac{C_{out}}{1{,}000{,}000} * V_r * AER + E_{occ}$$

Where,

E_{total}=Total volumetric CO_2 ER into room, $\left(\frac{L}{h}\right)$

C_{out}=Average outdoor CO_2 concentration, ppm

V_r=Volume of room, liters

E_{occ}=Volumetric ER of CO_2 from room occupants, $\left(\frac{L}{h}\right)$

CO_2 input from room occupants was calculated using per person emission rates (ERs).[86] Occupancy logs recorded minute-by-minute changes of three different age groups. Children <5 years old were assumed to have a CO_2 ER of 10.44 L/h and adults a rate of 18.72 L/h.[86] Adult ERs were used for child occupants between ages of 5-18 years.

$$E_{occ} = \left[\varepsilon_{0-5} * 10.44 \frac{l}{h}\right] + \left[\varepsilon_{5-18} * 18.74 \frac{l}{h}\right] + \left[\varepsilon_{adults} * 18.74 \frac{l}{h}\right]$$

Where,

ε_{0-5}=Number of children <5 years old

ε_{5-18}=Number of children between ages 5-18 years

ε_{adults}=Number of adults

The emission profile and measured indoor and outdoor CO_2 concentrations were used to fit mass-balance models to the data by optimizing the estimated AER. QTrak indoor CO_2 concentrations, ventilation, and occupancy logs were matched using minute-by-minute time measurements. Ventilation logs recorded minute-by-minute changes in ventilation (including the openings of doors/windows). An observed change in the indoor environment denoted a separate AER for that time period. Since outdoor CO_2 concentration variability was low (mean CV=3.8%) and an average daily AER was computed, we used average daily outdoor CO_2 in the models. When the occupancy changed, the mass-balance equation was calculated with a new CO_2 input (L/h) and predicted CO_2 before occupancy change was used as C_{orig}. Predicted CO_2 was calculated using an adapted equation:

$$C_{pred} = C_{Pred,Occ\,\Delta} * e^{[-AER*(t_i - t_{AER})]} + \left[\frac{\frac{E_{total}}{V_r}}{AER} * 1{,}000{,}000\right] * \left[1 - e^{[-AER*(t_i - t_{AER})]}\right]$$

Where,

C_{pred}=Predicted CO_2 from model, ppm

$C_{Pred,Occ\,\Delta}$=Predicted CO_2 before occupancy change, ppm

t_i=Elapsed time, hours

t_{AER}=Elapsed time at start of new AER, hours

Initial "predicted CO_2" concentrations were based on the QTrak CO_2 measurements. When the tracer gas CO_2 was released, the predicted CO_2 concentration was the peak QTrak measurement for the corresponding minute. To produce the best fit between the predicted and QTrak-generated CO_2 concentrations, we used the "Solver" function in Microsoft Excel to minimize mean squared error (MSE) between the model and QTrak-generated values by changing the AER for each time period based on the ventilation logs. Solver adequately reduced MSE in most instances, but diminished the AER to zero for occasional periods. We designated 0.15 hour^{-1} as the AER lower limit, which was the 5th percentile from a study of U.S. residences.[137] This optimization approach provided AERs during distinct time periods when ventilation would differ (open versus closed windows), which were time-weighted to calculate a daily average AER. While the use of CO_2 measurements to estimate AER is a standard approach, because CO_2 has natural sources (occupants, outdoor air) these methods may result in higher uncertainty compared to perfluorocarbon tracer (PFT) gas measurements. However, most ECE directors opposed the use of PFT gas (an unnatural substance) in their facilities. To compensate for the uncertainty with using CO_2, we compared real-time CO_2 measurements to ventilation logs (noting room occupancy and door/window use), which combined with the use of medical grade CO_2, improved the precision of our AER estimates.

Emission Rate Calculation

Differences in AERs and room size among ECE facilities will contribute to variability in aldehyde air concentrations. To normalize VOC air levels so they could be compared across

facilities, we calculated pollutant emission rates per unit area over time (μg/m²/h) [138] using the following equation:

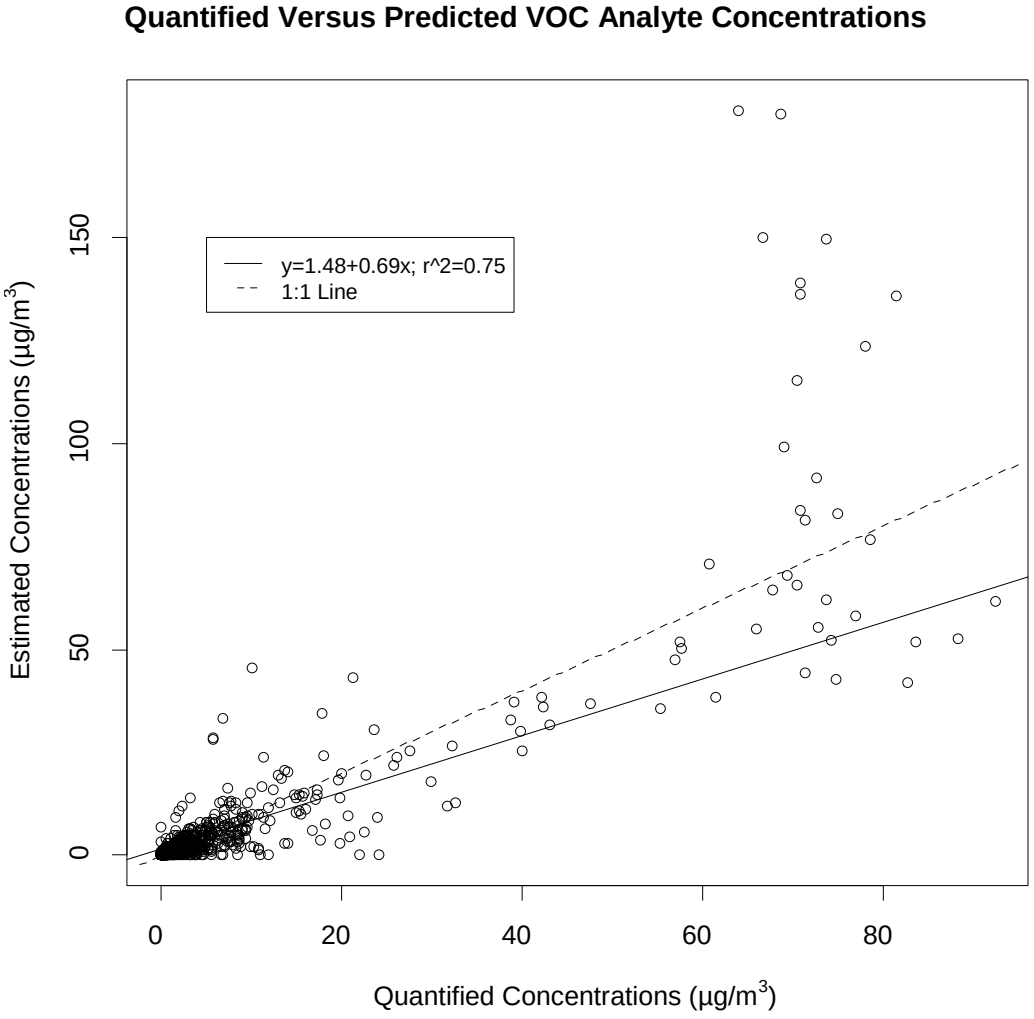
$$ER = AER \times h \times \Phi \times (\mathrm{C} - \mathrm{C}_0)$$

Where,

ER=Emission Rate (μg/m^2/h)
h=Height (m)
Φ=Correction factor for non-ventilated space
C=Steady-state indoor aldehyde concentration (μg/m^3)
C_0=Outdoor aldehyde concentration (μg/m^3)

ER calculations assumed pseudo steady-state and well-mixed room conditions. We applied a correction factor (0.9) for non-ventilated space.[139] For facilities without outdoor measurements, we substituted average outdoor concentration for C_0 (2.5 μg/m³ for both aldehydes). Since most indoor concentrations greatly exceeded outdoor levels, this substitution did not introduce uncertainty.

Figure 3. Relationship between VOC analyte concentrations measured with standard calibration curves versus estimated concentrations from semi-quantitative method. Lines in graph are the linear regression and one to one slope.



Method Detection Limits and Calibration Ranges for VOC Analytes

Calibration standards were prepared from liquid standards. Calibration ranges are the low and high masses from laboratory prepared standards. Method detection limits (MDLs) and low/high calibration masses are converted to µg/m³ by dividing the mass by the average sample volume collected in this study for indoor VOC measurements (~7 liters). VOC MDLs ranged from 0.03 µg/m³ to 1.80 µg/m³. See Appendix Table 24 below. VOC high mass calibrations ranged from 56 to 92 µg/m³ and low mass calibrations ranged from 0.5 to 1 µg/m³. For four compounds (D4 and D5 siloxanes, d-limonene, and 2-butoxyethanol) in 29 cases, the VOC levels were above the calibration high mass. In those cases, the mass above the range was substituted with the high calibration mass.

Table 24. MDL and Calibration Ranges for VOC Analytes[a]

Analyte	Mass MDL (ng)	Concentration MDL (µg/m³)	Low Mass Calibration (µg/m³)	High Mass Calibration (µg/m³)
Benzaldehyde	1.90	0.27	0.5	74
Benzene	4.08	0.58	0.9	56
Butanal	0.45	0.06	0.5	74
2-Butoxyethanol	0.52	0.07	0.5	76
Butylbenzene	0.26	0.04	0.5	73
Carbon tetrachloride	5.04	0.72	1.1	69
3-Carene	0.23	0.03	0.5	71
Chloroform	3.22	0.46	1.1	64
Decamethylcyclopentasiloxane	0.44	0.06	0.5	73
Decanal	0.62	0.09	0.5	76
n-Decane	0.89	0.13	0.5	71
n-Dodecane	1.47	0.21	0.5	73
2-Ethyl-1-hexanol	0.45	0.06	0.5	71
Ethylbenzene	0.30	0.04	0.5	73
Heptanal	0.43	0.06	0.5	72
n-Heptane	0.46	0.07	0.5	71
n-Hexadecane	0.49	0.07	0.5	71
Hexamethylcyclotrisiloxane	12.62	1.8	0.6	92
Hexanal	0.48	0.07	0.5	74
n-Hexane	3.10	0.44	0.9	57
d-Limonene	0.24	0.03	0.5	71
Methylene chloride	2.53	0.36	1.0	57
Nonanal	0.60	0.09	0.5	73
Octamethylcyclotetrasiloxane	1.27	0.18	0.5	73
Octanal	0.65	0.09	0.5	75
n-Octane	0.31	0.04	0.5	74
a-Pinene	0.32	0.05	0.5	73

Table 24 Continued. MDL and Calibration Ranges for VOC Analytes[a]

Analyte	Mass MDL (ng)	Concentration MDL (µg/m³)	Low Mass Calibration (µg/m³)	High Mass Calibration (µg/m³)
a-Terpineol	0.36	0.05	0.5	72
g-Terpinene	0.24	0.03	0.5	70
Tetrachloroethylene	0.50	0.07	0.5	80
n-Tetradecane	0.43	0.06	0.5	70
Texanol	0.37	0.05	0.5	74
Toluene	0.38	0.05	0.5	74
Trimethylbenzene (1,2,3)	0.28	0.04	0.5	75
Trimethylbenzene (1,2,4)	0.36	0.05	0.5	75
TXIB	0.51	0.07	0.5	70
n-Undecane	1.55	0.22	0.5	73
m/p-Xylene[b]	0.57	0.08	0.5	73
o-Xylene[b]	0.47	0.07	0.5	73

[a] Analysis used mass MDL and calibration ranges. Mass MDL and calibration ranges were converted to concentrations assuming typical sample volume of 7 liters. [b]Detection frequencies were determined for xylene isomers, then combined for total xylene detection ("xylenes").

Surrogate Compounds and EI/TI Conversion Factors

To provide a first estimate of the mass of the compounds we started by assigning each compound to a chemical class. The relationship between the extracted ion for the particular chemical class and that of toluene was determined using surrogate compounds from the calibration data collected over the course of the project. For each calibration data file, we determined the area of the extracted ion (EI_x) and the total ion (TI_x) for each chemical (x) and for toluene. This was only done when the TIC peaks were separated from other peaks. The chemical class, surrogate compounds, individual EI_x/TI_x ratios and overall surrogate specific class EI_s/TI_s ratio are presented in Appendix Table 25. We assume that the TIC response for the surrogate compound (toluene) is equal to the TIC response for all chemicals in the analysis. With this assumption, the extracted ion response for toluene ($EI_{toluene}$) was transformed to surrogate category response (EIs) and assigned to each chemical (EI_x) by,

$$EI_{toluene} \times \frac{TI}{EI_{toluene}} \times \frac{EI_s}{TI} = EI_x$$

The EI_x values were then used to quantify the estimated mass of individual chemicals based on the chemical class assignment and the conversion factor determined by the five-point toluene calibration curve. Using the final quantification method, each data file was analyzed a final time including a careful review of peak identification and integration. There was no attempt to distinguish between isomers or confirm the NIST identification with pure standards beyond what was included with the initial set of target chemicals.

Table 25. Surrogate Compounds and EI/TI Conversion Factors.

Class[1]	Surrogate compound[2]	EI_x/TI_x[3]		EI_s/TI_s
		Average	St. Dev	
Aldehydes	Butanal	0.33	0.12	0.19
	Hexanal	0.22	0.05	
	Heptanal	0.16	0.03	
	Octanal	0.11	0.02	
	Nonanal	0.15	0.02	
	Decanal	0.11	0.02	
Alkanes	Octane	0.20	0.05	0.26
	Undecane	0.29	0.06	
	Dodecane	0.29	0.06	
	Tetradecane	0.27	0.05	
	Hexadecane	0.25	0.04	
Alkoxy	2-Butoxyethanol	0.43	0.05	0.36
	2-Ethyl-1-hexanol	0.36	0.06	
	Texanol	0.26	0.04	
	TXIB	0.24	0.03	
Aromatics	Benzene	0.48	0.11	0.39
	Toluene	0.45	0.04	
	Ethylbenzene	0.43	0.03	
	m/p-Xylene	0.47	0.02	
	o-Xylene	0.38	0.01	
	1,2,4-Trimethylbenzene	0.27	0.10	
	1,2,3-Trimethylbenzene	0.38	0.01	
	Butylbenzene	0.39	0.01	
Halogenated	Tetrachloroethylene	0.38	0.01	0.17
Siloxane	D3	0.62	0.04	0.36
	D4	0.52	0.02	
	D5	0.33	0.09	
Terpene	3-Carene	0.27	0.02	0.19
	d-Limonene	0.23	0.02	
	a-Terpineol	0.16	0.01	
Toluene	Toluene			0.43

[1] Dominant classes of chemicals identified in the indoor air. Each chemical was assigned to one of these classes.

[2] Chemicals included in the standard calibration method for the project that were selected as surrogates for the specific class.

[3] The average (and standard deviation) of all conversion factors for the given chemical across all calibration runs preformed during the project.

Table 26. Spearman Rank Correlation Test Results for VOC Analyte Concentrations Between Quantified and Semi-quantified Analysis Methods.

Analyte	Spearman's rho	p-value	Analyte	Spearman's rho	p-value
Benzaldehyde	0.79	<0.005	Nonanal	0.98	<0.005
Benzene	0.91	<0.005	Octamethylcyclotetra-siloxane (D4)	0.99	<0.005
Butanal	0.84	<0.005	Octanal	0.86	<0.005
2-Butoxyethanol	0.97	<0.005	n-Octane	0.95	<0.005
Butylbenzene	0.27	0.13	a-Pinene	0.93	<0.005
3-Carene	0.98	<0.005	a-Terpineol	-0.52	0.12
Decamethylcyclopenta-siloxane (D5)	0.89	<0.005	g-Terpinene	0.52	0.002
Decanal	0.18	0.31	Tetrachloroethylene	0.9	<0.005
n-Dodecane	0.91	<0.005	n-Tetradecane	0.72	<0.005
2-Ethyl-1-hexanol	0.29	0.11	Texanol	0.63	<0.005
Ethylbenzene	0.99	<0.005	Toluene	1.00	<0.005
Heptanal	0.97	<0.005	1,2,3-Trimethylbenzene	0.82	<0.005
n-Heptane	0.94	<0.005	1,2,4-Trimethylbenzene	0.58	<0.005
Hexadecane	0.39	0.03	TXIB	0.88	<0.005
Hexamethylcyclotri-siloxane (D3)	0.71	<0.005	n-Undecane	0.92	<0.005
Hexanal	0.73	<0.005	m/p-Xylene	0.99	<0.005
n-Hexane	0.92	<0.005	o-Xylene	0.99	<0.005
d-Limonene	0.96	<0.005			

Probability-based matching (PBM) was also performed to compare the mass spectra of the standards to the mass spectra of the samples (See Appendix Table 27 below) The PBM logarithm provided further confirmation of VOC identification. All PBM mass spectra were selected from ECE 32 sample results, except for acetophenone and phenol, which were selected from ECE 19 due to higher detectable masses. Of the VOCs detected, seven had a PBM score above 90% and all were above 70% (Range 72-96%), affirming a high quality of accuracy in VOC identification. The PBM test could not detect cyclohexanone and 1-butoxy-2-propanol in the selected samples due to their low masses.

Table 27. Probability-based Matching Results.[a]

STANDARDS	PBM (%)
Pentane	72
Cyclohexane	86
Ethyl acetate	83
Cyclohexane, methyl	93
2-Propanol, 1-methoxy	86
1-Butanol	78
Styrene	96
Furfural	90
Acetophenone	93
Phenol	94
Naphthalene	93
Benzophenone	96

[a] Cyclohexanone and 1-butoxy-2-propanol were not present in sufficient quantities for PBM sample analysis.

Table 28. Inhalation Rates and Body Weights Used for Dose Calculations by Age Group.[a]

	Inhalation Daily Volume		Body Weight
	(m^3/day)	(m^3/8-hour)	(kg)
Birth to <1 year	5.10	1.70	6.8[b]
1 to <2 years	8.00	2.67	11.4
2 to <3 years	9.50	3.17	13.8
3 to <6 years	10.90	3.63	18.6

[a] Inhalation rates and body weights are mean values recommended in the U.S. EPA's Exposure Factors Handbook.[107]

[b] Value based on average of three age groups (birth to <1 month, 2 to <6 months, and 6 to <12 months) from Arcus-Arth and Blaisdell, 2007.[106]

Table 29. Age Distribution of Children in 34 ECE Facilities and Time Spent Indoor/Outdoor (n=1431 children).[a]

Age	Number of Children (%)
<2 years	86 (6)
2-3 years	229 (16)
3-6 years	1116 (78)
Time Indoors	
<5 hours	339 (24)
5-8 hours	455 (32)
>8 hours	637 (45)
Time Outdoors	**Number of Facilities (%)**
<1 hour	2 (6)
1-2 hours	12 (35)
3-4 hours	19 (56)
5-6 hours	1 (3)

[a] Four - 200 children per facility, average 43.

Table 30. Temperature, Relative Humidity, and AER.

Indoor	Mean±SD	Range
Average air temp	21.1±1.7	16.0-24.6 °C
Average RH	48.3±6.8%	34.5-60.0%
Average AER	1.7±1.3 hr^{-1}	0.3-5.6 hr^{-1}
Outdoor		
Average RH	49.4±12.0%	21.6-74.7%

Table 31. Summary of Outdoor VOC Analyte Concentrations (µg/m³) (n=20).[a,b]

Analyte	>MDL (%)	Geometric Mean±GSD	Arithmetic Mean±SD	25th %	Median	75th %	95th %	Max
Mixed and Mobile Sources								
Benzene	75.0	0.6±0.4	0.7±0.3	<MDL	0.6	0.9	1.2	1.2
n-Decane	30.0	0.1±0.6	0.2±0.1	<MDL	<MDL	0.2	0.4	0.4
Ethylbenzene	65.0	0.1±1.2	0.2±0.3	<MDL	0.1	0.3	0.8	0.9
n-Heptane	85.0	0.4±1.1	0.6±0.6	0.2	0.4	0.9	1.8	1.9
n-Hexane	25.0	0.4±0.5	<MDL	<MDL	<MDL	<MDL	1.0	1.3
n-Octane	60.0	0.1±1.1	0.2±0.1	<MDL	0.1	0.2	0.5	0.5
Toluene	100.0	1.1±0.8	1.5±1.2	0.7	0.9	2.1	4.1	4.1
1,2,3-Trimethylbenzene	25.0	0.0±1.0	0.1±0.2	<MDL	<MDL	0.1	0.5	0.7
1,2,4-Trimethylbenzene	60.0	0.1±1.2	0.2±0.3	<MDL	0.1	0.3	1.0	1.3
Xylenes	100	0.8±1.0	1.2±1.4	0.4	0.6	1.5	4.3	5.4
Household Sources								
Fragrances								
Benzaldehyde	100.0	2.3±0.4	2.4±1.1	1.8	2.3	2.7	4.8	6.3
Butanal	25.0	0.1±0.6	0.1±0.1	<MDL	<MDL	0.1	0.2	0.2
Decanal	55.0	0.1±0.7	0.1±0.1	<MDL	0.1	0.2	0.4	0.5
Heptanal	15.0	0.0±0.5	0.1±0.0	<MDL	<MDL	<MDL	0.1	0.2
Hexanal	80.0	0.1±0.7	0.2±0.1	0.1	0.2	0.2	0.5	0.6
Nonanal	95.0	0.3±0.7	0.4±0.3	0.2	0.2	0.5	0.9	1.2
Octanal	55.0	0.1±0.6	0.1±0.1	<MDL	0.1	0.2	0.3	0.3
a-Pinene	45.0	0.1±1.3	0.2±0.3	<MDL	<MDL	0.3	0.9	1.1
Other household products								
2-Butoxyethanol	20.0	0.1±0.8	0.1±0.1	<MDL	<MDL	<MDL	0.4	0.5
Decamethylcyclopentasiloxane (D5)	95.0	0.3±0.8	0.4±0.4	0.2	0.3	0.6	1.2	1.3
Hexamethylcyclotrisiloxane (D3)	25.0	1.4±0.4	<MDL	<MDL	<MDL	<MDL	3.9	4.6

Table 31 Continued. Summary of Outdoor VOC Analyte Concentrations (µg/m³) (n=20).[a,b]

Analyte	>MDL (%)	Geometric Mean±GSD	Arithmetic Mean±SD	25th %	Median	75th %	95th %	Max
Octamethylcyclotetrasiloxane (D4)	35.0	0.1±0.3	0.2±0.1	<MDL	<MDL	0.2	0.3	0.3
Tetrachloroethylene	30.0	0.1±0.6	0.1±0.1	<MDL	<MDL	0.1	0.3	0.4
Texanol	15.0	0.0±0.6	0.1±0.1	<MDL	<MDL	<MDL	0.2	0.2
TXIB	15.0	0.1±0.7	0.1±0.2	<MDL	<MDL	<MDL	0.5	0.9

[a] Compounds detected in <10% of facilities were removed: butylbenzene, carbon tetrachloride, 3-carene, chloroform, n-dodecane, 2-ethyl-1-hexanol, n-hexadecane, d-limonene, methylene chloride, a-terpineol, g-terpinene, n-tetradecane, and n-undecane. [b] If outdoor concentrations <MDL, values were imputed as MDL/√2.

Table 32. Correlations Between Mixed and Mobile Source (MMS) VOCs and Continuous Environmental Parameters.[a,b]

		Benzene	n-Decane	n-Dodecane	Ethylbenzene	n-Heptane	n-Hexadecane
	Mean±SD	Correlation					
AER (hr^{-1})	1.7±1.3 hr^{-1}	-0.41*	0.05	-0.02	-0.24	-0.54**	-0.67**
Temperature (°C)	21.1±1.7°C	0.19	0.30	0.34†	0.09	0.14	0.34†
Relative Humidity (%)	48.3±6.8%	0.32	0.01	0.03	0.26	0.29	0.16
ΣLATV (vehicle-km/hr)	11,126.7± 11,643.0 vehicle-km/hr	0.39*	0.16	-0.07	0.24	0.38*	0.44*

	n-Octane	n-Tetradecane	Toluene	1,2,3-Trimethyl-benzene	1,2,4-Trimethyl-benzene	n-Undecane	Xylenes
	Correlation						
AER (hr-1)	-0.29	-0.38*	-0.48**	-0.26	-0.40*	0.11	-0.28
Temperature (°C)	0.14	0.34†	0.02	0.09	0.00	0.27	0.08
Relative Humidity (%)	0.34†	0.17	0.31	0.25	0.28	0.08	0.27
ΣLATV (vehicle-km/hr)	0.23	0.07	0.25	0.25	0.34†	-0.01	0.24

†p=0.05. *p<0.05. **p<0.01. [a]Spearman's rho correlations. [b]Sample size=34, except for n-decane (n=33).

Table 33. Correlations between Household Source (HS) VOCs and Continuous Environmental Parameters.[a,b,c,d]

		Benzaldehyde	Butanal	3-Carene	Decanal	Heptanal	Hexanal	d-Limonene
	Mean±SD	Correlation						
AER (hr-1)	1.7±1.3 hr^{-1}	-0.13	-0.62**	-0.22	-0.03	-0.11	-0.42*	-0.34
Temperature (°C)	21.1±1.7 °C	0.15	0.21	0.30	-0.15	0.15	0.32	0.25
Relative Humidity (%)	48.3±6.8 %	0.33	0.11	-0.03	-0.11	0.14	0.15	-0.04

	Nonanal	Octanal	α-Pinene	α-Terpineol	ɣ-Terpinene	2-Butoxy-ethanol	D5	2-Ethyl-1-hexanol
	Correlation							
AER (hr-1)	0.14	-0.09	-0.50**	-0.30	-0.30	-0.24	-0.08	-0.53**
Temperature (°C)	0.11	0.23	0.08	0.51**	0.20	0.08	0.08	0.43*
Relative Humidity (%)	0.02	0.16	0.22	0.21	0.21	0.05	-0.02	0.12

	D4	Texanol	TXIB
	Correlation		
AER (hr-1)	-0.43*	-0.02	-0.16
Temperature (°C)	0.16	0.08	0.16
Relative Humidity (%)	-0.05	-0.07	0.19

*p<0.05. **p<0.01. [a]Spearman's rho correlations. [b]If indoor VOC concentrations <MDL, values were imputed as MDL/√2. [c]Abbreviations: decamethylcyclopentasiloxane (D5); octamethylcyclotetrasiloxane (D4); 2,2,4-trimethyl-1,3-pentanediol diisobutyrate (TXIB). [d]Sample size=34, except for D4 (n=33).

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Formaldehyde and acetaldehyde exposure and risk characterization in California early childhood education environments

Abstract Little information is available about air quality in early childhood education (ECE) facilities. We collected single-day air samples in 2010–2011 from 40 ECE facilities serving children ≤6 years old in California and applied new methods to evaluate cancer risk in young children. Formaldehyde and acetaldehyde were detected in 100% of samples. The median (max) indoor formaldehyde and acetaldehyde levels ($\mu g/m^3$) were 17.8 (48.8) and 7.5 (23.3), respectively, and were comparable to other California schools and homes. Formaldehyde and acetaldehyde concentrations were inversely associated with air exchange rates (Pearson $r = -0.54$ and -0.63, respectively; $P < 0.001$). The buildings and furnishings were generally >5 years old, suggesting other indoor sources. Formaldehyde levels exceeded California 8-h and chronic Reference Exposure Levels (both 9 $\mu g/m^3$) for non-cancer effects in 87.5% of facilities. Acetaldehyde levels exceeded the U.S. EPA Reference Concentration in 30% of facilities. If reflective of long-term averages, estimated exposures would exceed age-adjusted 'safe harbor levels' based on California's Proposition 65 guidelines (10^{-5} lifetime cancer risk). Additional research is needed to identify sources of formaldehyde and acetaldehyde and strategies to reduce indoor air levels. The impact of recent California and proposed U.S. EPA regulations to reduce formaldehyde levels in future construction should be assessed.

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Key words: Child care; Children; Air; Exposure; Formaldehyde; Acetaldehyde.

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Practical Implications

This is the first study to report indoor and outdoor air levels of formaldehyde and acetaldehyde in U.S. child care environments. These compounds were detected in 100% of the samples, with much higher levels indoors compared to outdoors. Formaldehyde levels exceeded California reference exposure levels (RELs) in 87.5% of the ECE facilities, and acetaldehyde exposures exceeded the U.S. EPA RfC in 30% of the facilities, while exposures to both compounds exceeded age-adjusted benchmarks based on carcinogenicity in all facilities. We expect that California and proposed U.S. EPA rules will reduce formaldehyde emissions from new composite wood products; however, additional research is needed to determine the relative contributions of different sources in existing day care centers and to identify additional measures that would be most effective for protecting public health. Given that current exposures exceed health benchmarks, outreach to child care providers is warranted to reduce indoor exposures of young children.

Introduction

Nationally, about 61% (12.5 million) of all U.S. children <5 years old are enrolled in some type of regular child care (Laughlin, 2013). Many infants and young children spend as much as 10 h per day, 5 days per week, in child care and preschool. These facilities are located in a variety of building types, including houses, schools, commercial buildings, and portable classrooms.

Volatile organic compounds (VOCs) are emitted from building materials, and furnishings and are often

found at higher concentrations indoors than outdoors (U.S. EPA, 2012a). Aldehydes (including formaldehyde and acetaldehyde), a subset of VOCs, are ubiquitous in indoor environments. Formaldehyde is emitted from a variety of materials and consumer products (Salthammer et al., 2010). Composite wood products (CWPs) containing urea-formaldehyde (UF) resin have been identified as a significant contributor to indoor formaldehyde (Hun et al., 2010; Kelly et al., 1999). Other sources include wallpaper; paints; permanent press fabrics; acid-catalyzed UF coatings on shelving, paneling, and furniture; cosmetic products; cigarette smoke; and other combustion sources such as fuel burning appliances (CARB, 2005). Indoor sources of acetaldehyde include CWPs made with formaldehyde-based adhesives, rigid polyurethane foams, adhesives, coatings, lubricants, and inks (Frey et al., 2014; Kelly, 1996; Singer et al., 2006; Wu et al., 2011). Formaldehyde and acetaldehyde are also formed from chemical reactions between ozone and VOCs emitted from household items such as carpets, art supplies, cleaning products, disinfectants, and air fresheners (Destaillats et al., 2006; Zhang et al., 1994).

A large body of research has raised concerns about the health effects of aldehyde exposure in children (McGwin et al., 2010; Mendell, 2007). Exposure to these compounds has been associated with increased risk of pediatric asthma and respiratory symptoms including decreased lung function, inflammation, and airway obstruction (Hulin et al., 2010; Norback et al., 1995; Roda et al., 2011; Wieslander et al., 1997). Numerous rodent studies have reported adenocarcinomas and squamous cell carcinomas subsequent to aldehyde exposure (Kerns et al., 1983; Woutersen et al., 1986); while occupational cohort studies have reported associations between formaldehyde exposure and genotoxic effects, nasopharyngeal cancer, and myeloid leukemia mortality (Costa et al., 2015; Hauptmann et al., 2004; Pinkerton et al., 2004). The International Agency for Research on Cancer (IARC) and the U.S. National Toxicology Program (NTP) identified formaldehyde as a known human carcinogen in 2006 and 2011, respectively (IARC, 2012; NTP, 2011). The U.S. Environmental Protection Agency (EPA) classifies both formaldehyde and acetaldehyde as probable human carcinogens (U.S. EPA, 2012b,c).

Recent studies have shown poor indoor air quality in schools and residences and have documented elevated levels of formaldehyde and acetaldehyde above established cancer and non-cancer health benchmark levels (Frey et al., 2014; Offermann, 2009; Weisel et al., 2005; Whitmore, 2003). Reflecting concerns about the health effects of formaldehyde exposure, the California Air Resources Board (CARB) finalized new rules in 2008 to reduce formaldehyde emissions from CWPs (CCR 17 §93120, 2008). The U.S. EPA proposed similar standards in May 2013 and is currently reviewing comments received in May 2014 (CFR 40 §770, 2014). Thus, national regulation of formaldehyde emissions from CWPs is still pending.

Very limited information is available about formaldehyde in U.S. ECE facilities. As part of a broader study of environmental contaminants in 40 California facilities (CARB, 2012), we measured indoor and outdoor formaldehyde and acetaldehyde in air. In this study, we report new information about formaldehyde and acetaldehyde air levels in these facilities and estimate child exposures. We also apply new methods developed by the California Office of Environmental Health Hazard Assessment (OEHHA) to evaluate potential cancer risk from aldehyde exposures among children (Bradman et al., 2014).

Methods

Recruitment

We enrolled 40 ECE facilities located in two northern California counties [Monterey (n = 20) and Alameda (n = 20)] in this study (CARB, 2012). Monterey County, CA, is largely rural and agricultural, while Alameda County, CA, is predominantly urban or suburban. To recruit a diverse sample, we geographically coded center and large home-based licensed (>8 children) ECE facilities by zip code using publicly available databases (Community Care Licensing Division, 2010). We ultimately recruited and obtained measurements in 28 child care centers and 12 home-based facilities between May 2010 and May 2011. All procedures were reviewed by the UC Berkeley Committee for the Protection of Human Subjects and written informed consent was obtained from each director or a senior administrator.

Questionnaire and site visit

Upon enrollment of a facility into the study, field technicians administered a questionnaire to a site supervisor and conducted a facility inspection (CARB, 2012). The inspection focused on the primary child care room where air samples were collected, cooking areas, and the bathroom. Information obtained included building type (home, school, or office and if portable or manufactured), building age and condition, ECE type (home vs. center), building materials, renovations (within the last 5 years), new flooring (within the last year), air freshener and cleaning product use, natural ventilation, and the presence of CWP furniture.

Environmental sampling and analysis

Indoor air samples were collected in the primary child care room over a single day at each of the 40 ECE facilities (CARB, 2012). All indoor samples

were collected from a single location in the room where children spent most of their indoor time. Aldehyde samplers, consisted of silica gel cartridges coated with 2,4-dinitrophenyl-hydrazine (Sep-Pak XPoSure™; Waters corporation, Millford, MA, USA.) with ozone scrubbers (P/N WAT054420; Waters) upstream, were deployed around the height of a child's breathing zone (~1 m) and were protected by a 'kiddie-corral' made of unfinished solid wood. The air sampling system used a single rotary vane pump to provide vacuum for multiple sampling lines used during monitoring. The pump was installed in a stainless steel box lined with sound insulating foil-faced formaldehyde-free fiberglass. Air was pulled through each formaldehyde sampling line at approximately 0.25 liters per minute (LPM) and regulated by inline taper flowmeters. Calibration curves were determined for each flowmeter using a Gilibrator® airflow calibrator (Sensidyne, St. Petersburg, FL, USA). Calibration curves were checked after sampling was completed and were consistent with prior results. Outdoor air samples were collected from a subset of ECE facilities (n = 19), concurrent with the indoor air samples. All aldehyde samples were analyzed following U.S. EPA Method TO-11A (U.S. EPA, 1999). Cartridges were extracted by eluting with 2 ml of high-purity acetonitrile and analyzed by high-performance liquid chromatography (1200 Series; Agilent Technologies, Santa Clara, CA, USA) using a C_{18} reverse phase column with 65:35 H_2O:acetonitrile mobile phase at 0.35 ml/min and UV detection at 360 nm. Multipoint calibrations were prepared for the target aldehydes using commercially available hydrazone derivatives of formaldehyde and acetaldehyde. The method detection limit (MDL) for formaldehyde and acetaldehyde was 10 and 1.0 ng, respectively. Using the average total collected air volume (0.12 m^3), formaldehyde and acetaldehyde MDLs as a concentration were 0.08 and 0.008 $\mu g/m^3$, respectively. Quality assurance and quality control (QA/QC) samples included analytical blanks (n = 8), field blanks (n = 9), and indoor duplicate samples (n = 12). The median formaldehyde and acetaldehyde levels in analytical blanks were 0.12 and 0.21 $\mu g/m^3$ and 0.34 and 0.30 $\mu g/m^3$ in field blanks, respectively. The mean relative percent differences (RPDs) between duplicate field aldehyde samples were 6.4 ± 6.1% for formaldehyde and 5.7 ± 4.5% for acetaldehyde, indicating good precision for field duplicates. (See Supporting Information (SI), Tables S1 and S2 for more information.)

Real-time measurements of carbon dioxide (CO_2), relative humidity (RH), and temperature were recorded at 60-second intervals over the entire school day using Q-Trak™ IAQ Monitors (model 8554, TSI Inc., Shoreview, MN, USA). The CO_2 analyzer uses non-dispersive infrared and has a range of 0–5000 ppm. The accuracy is ± (3% of reading + 50 ppm) at 25°C with a resolution of 1 ppm. The temperature sensor is a thermistor with a range of 0–50°C. A thin-film capacitive sensor measures humidity with a range of 5–95% RH (TSI, 2006). All IAQ monitors were calibrated in the spring of 2010 by the manufacturer.

Air exchange and emission rate calculations

Differences in air exchange rates (AER) and room size among ECE facilities will contribute to variability in aldehyde air concentrations across facilities for a given source strength. To normalize formaldehyde and acetaldehyde air concentrations for comparison across facilities, we calculated pollutant emission rates per unit floor area ($\mu g/m^2/h$) (Hodgson et al., 2000; Maddalena et al., 2009) based on the estimated AER during the day of sampling and the size of the room corrected to represent the available well mixed space in the room where monitoring occurred. (See SI, Equations S1, S2 and Table S3.)

The AER were estimated using two approaches. The first approach used a mass balance of continuously measured indoor CO_2 concentrations and occupant-based CO_2 emissions to calculated AER for various observed conditions (windows, interior doors and/or exterior doors open/closed) during the sampling day. We recorded minute-by-minute occupancy to estimate CO_2 emissions and recorded changes in the room that might impact AER. Most occupants during the monitoring day were either preschool children (age < 5) or adults (age > 18) so we assumed that the two age groups had per person CO_2 emission rates of 0.0029 l/s and 0.0052 l/s, respectively (Persily, 1997). The dynamic mass balance was solved for AER to minimize the sum of the squared errors between modeled and measured CO_2 concentrations for each period when conditions in the room were consistent. The second AER estimation method used a tracer decay test conducted midday when children were out of the room using a bulk release of medical grade CO_2 (Praxair, Part Number CD M-10) (Bartlett et al., 2004; Bekö et al., 2010). We elected to use CO_2 (both biogenic and augmented) as the tracer gas to estimate AER because it was more acceptable to the ECE directors than releasing other chemical tracers into the room. (See SI, Equation S1, Figure S1, and Table S3 for more detailed information.)

Data analysis

For facilities with duplicate aldehyde measurements (n = 12), the average of the two measurements was used for data analysis. We first computed descriptive

statistics for formaldehyde and acetaldehyde air concentrations and emission rates. We then examined predictors of indoor air formaldehyde and acetaldehyde air concentrations. Based on visual inspection of quantile–quantile plots of the concentration data and the Shapiro–Wilk test ($P > 0.05$), we determined that untransformed formaldehyde concentrations and log-transformed acetaldehyde concentrations approximated normal distributions. For statistical analyses, we used untransformed formaldehyde and log-transformed acetaldehyde data. We used a *t*-test to examine bivariate associations between indoor aldehyde air concentrations with potential determinants including location (Alameda vs. Monterey County); presence of CWP furniture (yes/no); air freshener use (yes/no); use/purchase of 'low-toxicity' cleaner (yes/no); presence of carpets (yes/no); the presence of gas appliances (yes/no); occurrence of renovations within the last 5 years (yes/no); reported installation of new floor coverings within the last year (yes/no); building type (portable or manufactured/non-portable or non-manufactured); season (winter vs. non-winter months); and license type (center- vs. home-based). Pearson's correlations were used to examine associations of aldehyde levels with building age (in years), AER (per hour), RH (%), and temperature (°C). We then used multivariate linear regression models to examine associations between indoor aldehyde levels and all potential determinants identified *a priori*. All potential determinant variables were initially included in the model and then eliminated in a stepwise fashion if *P*-value >0.1.

Because formaldehyde and acetaldehyde emission rates were not normally distributed, we used the non-parametric Mann–Whitney rank sum test and Spearman's rank correlation test to evaluate bivariate associations between the emission rates and the potential determinants described above.

Finally, we compared average AERs to the California Residential Code for ventilation (CCR 24 §R120.1, 2013) although we note that the AERs were calculated only for the room where monitoring occurred and not for the entire facility.

Stata software version 13 (StataCorp LP, College Station, TX, USA) was used for descriptive statistics and tests of association, while figures were produced in R Version 3.0.2 (The R Foundation for Statistical Computing, Vienna, Austria) and Microsoft Excel Version 2010.

Non-cancer risk evaluation

A screening-level risk assessment was conducted to evaluate formaldehyde and acetaldehyde exposures in ECE facilities. Measured concentrations of indoor aldehydes were compared to California EPA Office of Environmental Health Hazard Assessment (OEHHA) Reference Exposure Levels (RELs) and U.S. EPA Reference Concentrations (RfCs), when available. Formaldehyde and acetaldehyde concentrations were compared to the acute, 8 h, and chronic RELs (OEHHA, 2013a), while acetaldehyde concentrations were also compared with its RfC (U.S. EPA, 2012c). If the ratios were greater than 1, the exposure exceeds the respective health-based exposure benchmark. However, because the health-based reference values include safety factors, exposures exceeding these levels are not necessarily expected to result in adverse health effects.

No significant risk levels for cancer

Under California's Proposition 65, OEHHA sets 'Safe Harbor Levels' called No Significant Risk Levels (NSRLs) for carcinogenic substances, defined as the daily intake level posing a one in 100,000 (10^{-5}) excess risk of cancer over a lifetime (OEHHA, 2001). The NSRL for formaldehyde is 40 μg/day and acetaldehyde is 90 μg/day (OEHHA, 2013b). Because NSRLs were developed for an adult weighing 70 kg, we computed age-adjusted NSRLs for formaldehyde and acetaldehyde that adjust for the difference in body weights (BW) between children and adults (U.S. EPA, 2011). In addition, we applied OEHHA's guidelines to account for the increased sensitivity of very young children, which incorporates an age sensitivity factor (ASF) of 10 for children <2 years old and of three for children between 2 and 6 years old (OEHHA, 2001). Following methods we applied to evaluate flame retardant exposures in this population (Bradman et al., 2014), age-adjusted NSRLs were calculated for four age groups (i.e., birth to <1 year; 1 to <2 years; 2 to <3 years; and 3 to <6 years):

$$\mathrm{NSRL}_{\mathrm{child}}\left(\frac{\mu\mathrm{g}}{\mathrm{day}}\right) = \frac{\dfrac{\mathrm{NSRL}_{\mathrm{adult}}\left(\dfrac{\mu\mathrm{g}}{\mathrm{day}}\right)}{\mathrm{BW}_{\mathrm{adult}(70\,\mathrm{kg})}} \times \mathrm{BW}_{\mathrm{child}}(\text{Varies by Age Group, kg})}{\mathrm{ASF}(\text{Varies by Age Group})}$$

In summary, the $\mathrm{NSRL}_{\mathrm{child\ (0\ to\ <1\ year)}}$ is the estimated daily intake for that age range which contributes 1/70th (assuming a 70-year lifespan) of the target lifetime cancer risk in that particular year of life. If the ratio of a child's aldehyde dose estimate (μg/day) to

the age-adjusted NSRL (μg/day) >1, the dose estimate exceeded the 10^{-5} cancer risk threshold.

Child inhalation dose estimates were calculated based on the measured air formaldehyde and acetaldehyde concentrations. Using a standard inhalation dose equation, we combined aldehyde concentrations with age-adjusted intake factors including inhalation rates (m^3/day), body weights (kg), and an exposure factor (ATSDR, 2005). As children are not present in ECE facilities every day, we calculated the exposure factor assuming a child spends 5 days per week and 48 weeks per year (which accounts for 4 weeks away from child care for holidays and vacation). We assumed that absorption of these compounds was 100% and that exposures occurred over 1 year (ATSDR, 2005). Detailed information on the calculations is presented in the SI, Equation S3.

Results

ECE facility and child characteristics

The 40 ECE facilities served a total of 1764 children. Building types included single family detached homes (37.5%), traditional school buildings (27.5%), portable school buildings (22.5%), office buildings (7.5%), and churches (5%). Half the facilities were in buildings constructed after 1970, with the oldest structure built in 1903 and the most recent built in 2008. Twenty-six (65%) facilities were in residential neighborhoods, eight (20.0%) were in commercial areas, five (12.5%) were adjacent to agricultural fields, and one (2.5%) was in a rural/ranch area.

The average attendance per facility was 44 children (range = 4–200). The majority of children (76%) were 3–6 years old, 19% were 2–3 years, and 5% were less than 2 years of age; 95% of the children spent at least 1–2 h outside each day, with some spending up to 6 h outside, depending on the weather. Thirty-seven percent of children spent >8 h per day in child care, 41% spent 5–8 h, and 22% spent <5 h.

Air temperature, relative humidity, and exchange rates

Average outdoor air temperature ranged from 11.0 to 31.7°C with a mean of 19.0 ± 6.0°C.

Average indoor air temperature ranged from 16.0 to 24.6°C with a mean of 21.1 ± 1.7°C. Average outdoor RH ranged from 21.6 to 74.7% with a mean of 49.4 ± 12.0%. Average indoor RH ranged from 34.5 to 62.6% with a mean of 49.3 ± 6.9%.

The 40 ECE facilities had an average AER of 2.0 ± 1.4 per hour as measured in the primary room where children spent most of their indoor time with a range of 0.28–5.63 per hour. Due to the moderate climate in Alameda and Monterey Counties, natural ventilation (such as opened windows) was often used, especially on warm and breezy afternoons. As expected, the AERs measured in ECE facilities were higher than rates reported in a study of California homes (median = 1.41 vs. 0.26 per hour, respectively) (Offermann, 2009). However, thirty percent (12) of the facilities were below California ventilation guidelines for new construction (2.7 m^3/h for each m^2 of floor space), with three facilities (7.5%) with very low ventilation (≤1 $m^3/h/m^2$) (CCR, 2013).

Aldehyde concentrations in air

Acetaldehyde and formaldehyde were detected in 100% of the ECE facilities measured. Table 1 summarizes results for indoor (n = 40) and outdoor (n = 19) measurements. The median (range) indoor formaldehyde and acetaldehyde concentrations were 17.8 $\mu g/m^3$ (0.7–48.8 $\mu g/m^3$) and 7.5 $\mu g/m^3$ (0.7–23.3 $\mu g/m^3$), respectively. The median (range) outdoor formaldehyde and acetaldehyde concentrations were 2.3 $\mu g/m^3$ (1.5–4.0 $\mu g/m^3$) and 1.8 $\mu g/m^3$ (1.1–6.5 $\mu g/m^3$), respectively. Overall, aldehyde levels were higher indoors compared to outdoors ($P < 0.05$; see Figure 1 and all measurements in SI Table S5), indicating that indoor sources are primary contributors to indoor formaldehyde and acetaldehyde concentrations.

Determinants of formaldehyde concentrations

In bivariate analyses, formaldehyde levels were inversely associated with estimated AER in the room ($r = -0.54$; P-value<0.001), and weakly correlated with average RH ($r = 0.31$, $P = 0.05$) and average indoor temperature ($r = 0.22$, $P = 0.17$). Indoor formaldehyde concentrations were lower in the 35

Table 1 Summary of indoor (n = 40) and outdoor (n = 19) aldehyde concentrations ($\mu g/m^3$)[a]

Analyte[a]	GM (95% CI)	Arithmetic Mean ± s.d.	Min	25th %	Median	75th %	90th %	Max
Formaldehyde								
Indoor	15.9 (12.7, 19.9)	18.9 ± 10.1	0.7	10.6	17.8	25.0	33.2	48.8
Outdoor	2.4 (2.1, 2.8)	2.5 ± 0.8	1.5	1.9	2.3	3.1	3.9	4.0
Acetaldehyde								
Indoor	6.9 (5.5, 8.6)	8.5 ± 5.4	0.7	4.7	7.5	10.5	17.1	23.3
Outdoor	2.2 (1.7, 2.8)	2.5 ± 1.5	1.1	1.5	1.8	3.4	4.9	6.5

[a]All concentrations were detected above the MDL.

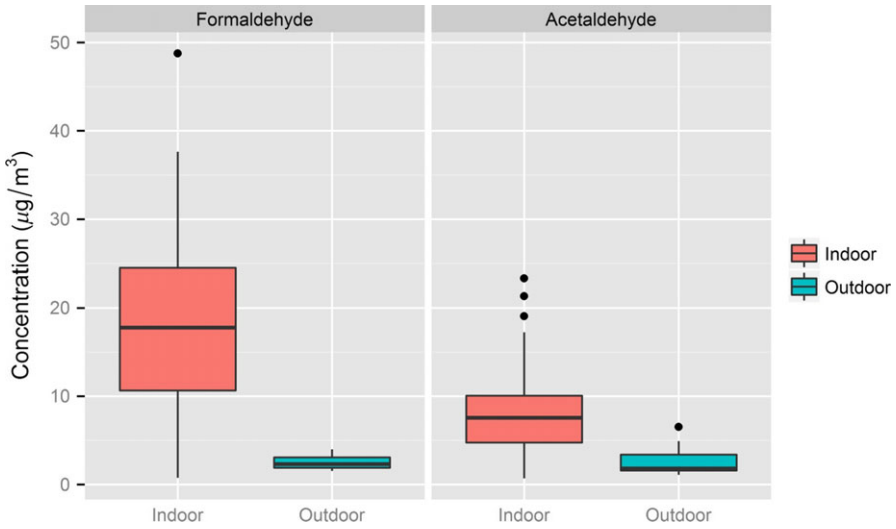

Fig. 1 Box plots of indoor (n = 40) vs. outdoor (n = 19) formaldehyde and acetaldehyde concentrations

ECE facilities with at least some CWP furniture present (mean = 17.5 ± 8.0 $\mu g/m^3$) compared to five facilities with no CWP furniture present (mean = 28.6 ± 17.7 $\mu g/m^3$) ($P < 0.05$). Differences in AERs did not explain this finding, and given that most buildings and furnishings were older than 5 years, it is likely that initial CWP sources had finished off-gassing. Formaldehyde levels were higher in the 12 home-based ECE facilities (mean = 24.6 ± 13.2 $\mu g/m^3$) compared to the 28 center-based ECE facilities (mean = 16.4 ± 7.4 $\mu g/m^3$) ($P < 0.05$). In addition, reported use of 'low-toxicity' cleaners was associated with lower formaldehyde levels (P-value <0.03).

Formaldehyde levels were not associated with season; location by county; building age; portable or manufactured buildings compared to all other building types; the presence of gas appliances; reported new flooring in the last year; reported renovations in the last 5 years; presence of carpet, or reported use of air freshener. (See SI, Table S6 for detailed information on bivariate analyses.)

Final multivariate regression model results for formaldehyde concentrations showed an inverse association between formaldehyde levels and AER ($\beta = -3.52$; $P < 0.001$) and a positive association with average indoor temperature ($\beta = 2.51$; $P < 0.01$), RH ($\beta = 0.40$; $P < 0.05$), and home-based compared to center-based facilities ($\beta = 8.31$; $P < 0.05$) (adjusted $R^2 = 0.54$) (SI Table S7).

Determinants of acetaldehyde concentrations

In bivariate analyses, acetaldehyde levels were inversely associated with AER ($r = -0.63$; P-value <0.001) and weakly correlated with average indoor temperature ($r = 0.22$, $P = 0.17$). Indoor acetaldehyde levels were slightly lower in six ECE facilities with reported new floor coverings [Geometric mean (GM) (95% CI) = 4.0 (1.4, 11.3) $\mu g/m^3$] compared to 34 facilities with no new floor coverings [GM (95% CI) = 7.6 (6.1, 9.3) $\mu g/m^3$] ($P < 0.05$), but this association did not persist in the multivariate models.

On a bivariate basis, acetaldehyde levels were not associated with season; location by county; license type (home-based vs. center); building age; portable or manufactured buildings compared to all other building types; RH; the presence of CWP or gas appliances; reported renovations in the last 5 years; presence of carpet; or reported use of air freshener. (See SI, Table S6 for detailed information on bivariate analyses.)

Final multivariate regression model results for acetaldehyde also showed an inverse association between acetaldehyde levels and AER ($\beta = -0.34$; $P < 0.001$) and positive associations with RH ($\beta = 0.03$; $P < 0.05$) (adjusted $R^2 = 0.50$) (SI Table S8).

Aldehyde emission rates

Median (range) estimated emission rates were 59.2 $\mu g/m^2/h$ (8.1–152.7 $\mu g/m^2/h$) for formaldehyde and 16.5 $\mu g/m^2/h$ (1.4–53.6 $\mu g/m^2/h$) for acetaldehyde (SI Table S4). These emission rates were similar to estimates for 11 new, unfurnished, and unoccupied homes in the U.S. (formaldehyde = 45–31 $\mu g/m^2/h$ and acetaldehyde = 17–25 $\mu g/m^2/h$) (Hodgson et al., 2000). We found no associations between formaldehyde or acetaldehyde emission rates and potential determinants (SI Table S9). Consistent with the higher formaldehyde levels in home-based ECE facilities (see above), formaldehyde emission rates were somewhat higher in home-based compared to center-based facilities (median = 68.2 vs. 57.9 $\mu g/m^2/h$). Acetaldehyde emission rates were slightly higher in facilities with air freshener use (median = 17.8 vs. 15.0 $\mu g/m^2/h$) (Mann–Whitney, $P = 0.08$).

Aldehyde health risk characterization

We compared air concentrations of formaldehyde and acetaldehyde to the acute, 8 h, and chronic RELs and RfC values, when available (see Table 2). The 50th and 95th percentile formaldehyde air concentrations (17.8 and 37.3 $\mu g/m^3$, respectively) exceeded the 8-h REL and chronic REL (both 9 $\mu g/m^3$) (OEHHA, 2013a), with ratios of 2.0 and 4.1, respectively. Formaldehyde levels exceeded the 8-h REL and chronic REL in 87.5% of facilities. Acetaldehyde concentrations were lower than OEHHA RELs, but exceeded the U.S. EPA RfC in 30% of facilities, with ratios of 0.8 and 2.2 at the 50th and 95th percentiles, respectively.

The OEHHA 8-h REL and chronic REL for formaldehyde are based on health effects including nasal obstruction and discomfort, lower airway discomfort, and eye irritation (OEHHA, 2008). The U.S. EPA RfC for chronic acetaldehyde inhalation is based on degeneration of olfactory epithelium in two short-term rat inhalation studies (U.S. EPA, 2012c).

Table 3 presents the ratios of the 50th and 95th percentile inhalation dose estimates to the age-adjusted NSRL values by age group (birth to <1 year; 1 to <2 years; 2 to <3 years; and 3 to <6 years). The 50th and 95th percentile dose estimates for formaldehyde and acetaldehyde exceeded the age-adjusted NSRL in all four age groups (range of ratios = 12.0–51.7 and 2.3–9.8 for median formaldehyde and acetaldehyde levels, respectively). Child acetaldehyde or formaldehyde dose estimates exceeded age-adjusted NSRL benchmarks based on carcinogenicity in 97.5% and 100% of the facilities, respectively.

Table 3 Aldehyde inhalation dose estimates compared to age-adjusted NSRLs

Age group	50th % dose estimates (μg/day)	95th % dose estimates (μg/day)	$NSRL_{child}$ (μg/day)	50th % ratio	95th % ratio
Formaldehyde					
Birth to <1 year	19.9	41.8	0.39	51.7	108.4
1 to <2 years	31.3	65.6	0.65	48.0	100.7
2 to <3 years	37.1	77.9	2.6	14.1	29.6
3 to <6 years	42.6	89.4	3.5	12.0	25.2
Acetaldehyde					
Birth to <1 year	8.5	22.7	0.87	9.8	26.1
1 to <2 years	13.3	35.6	1.5	9.1	24.3
2 to <3 years	15.8	42.2	5.9	2.7	7.1
3 to <6 years	18.1	48.4	8.0	2.3	6.1

Discussion

This is the first study to report indoor and outdoor air levels, emission rates and associated risks of formaldehyde and acetaldehyde in dedicated U.S. child care environments. These chemicals were detected in 100% of the ECE facilities and in most cases exceed California or U.S. EPA health-based exposure benchmarks. Overall, the formaldehyde and acetaldehyde levels we observed (median = 17.8 and 7.5 $\mu g/m^3$, respectively) were within range of levels recently measured in homes and schools in the U.S. and in ECE facilities internationally, with median or mean values in ECE facilities ranging from 3 to 23 $\mu g/m^3$ for formaldehyde and from 5 to 18 $\mu g/m^3$ for acetaldehyde (Roda et al., 2011; St-Jean et al., 2012; Zuraimi and Tham, 2008). (See SI Table S10 for more detailed information on levels measured in other studies.)

Overall, our study detected aldehydes at much higher levels indoors compared to outdoors, confirming that primary sources of these contaminants are indoors. In contrast to previous studies, we did not observe seasonal variations in indoor aldehyde concentrations (Rehwagen et al., 2003; Wallace et al., 1991), possibly due to the study area's mild climate with natural ventilation use throughout the year and the relatively small sample size.

Our finding that aldehyde concentrations were inversely associated with air exchange rates is consistent with other studies and underscores the importance of ventilation in reducing indoor concentrations for these compounds. For example, California researchers also reported higher formaldehyde and acetaldehyde concentrations in houses with lower outdoor air exchange rates (Offermann, 2009) and several international studies have documented inverse association between AERs and aldehyde levels inside child care centers (St-Jean et al., 2012; Zuraimi and Tham, 2008).

Table 2 Ratios of indoor aldehyde air concentrations to OEHHA acute reference exposure level (aREL), 8-h REL, chronic REL (cREL), and U.S. EPA reference concentration (RfC)

Analyte	Percentile (%)	Air concentration ($\mu g/m^3$)	aREL[a] ($\mu g/m^3$)	Ratio[b] (aREL)	8-h REL[a] ($\mu g/m^3$)	Ratio[b] (8-h REL)	cREL[a] ($\mu g/m^3$)	Ratio[b] (cREL)	RfC[c] ($\mu g/m^3$)	Ratio[b] (RfC)
Formaldehyde	50th	17.8	55	0.3	9	2	9	2	–[d]	NC
	95th	37.3		0.7		4.1		4.1		NC
Acetaldehyde	50th	7.5	470	0.02	300	0.03	140	0.05	9	0.8
	95th	20.2		0.04		0.07		0.1		2.2

NC, not calculated.

[a]OEHHA REL.

[b]Ratio of air concentration to preceding exposure guideline REL or RfC.

[c]U.S. EPA RfC.

[d]U.S. EPA RfC for formaldehyde has not been established.

We observed higher formaldehyde levels in home-based compared to center-based child care facilities. The lower AERs and presence of cooking activities in home-based facilities may explain this difference. Additionally, homes typically may have more potential formaldehyde sources such as composite wood construction and cabinetry, carpeting, draperies, gas cooking facilities, and personal care and cleaning products. The study sample size was too small to examine this finding in greater detail.

An important finding of this study is that child formaldehyde exposures exceeded California OEHHA RELs in 87.5% of the ECE facilities and child acetaldehyde exposures exceeded the U.S. EPA RfC in 30% and that 100% of the formaldehyde exposures and 97.5% of the acetaldehyde exposures exceeded age-adjusted OEHHA benchmarks based on carcinogenicity. This is of special concern because, in general, children are more vulnerable to toxic substances in their environment because they have higher exposures per kilogram of body weight (Selevan et al., 2000) and are less developed immunologically, physiologically, and neurologically (Cohen Hubal et al., 2000; Lo and O'Connell, 2005). Additionally, these elevated exposures were found in buildings built at least 5 years ago, indicating that there are major contributions from sources other than composite wood products. Further, only limited indoor concentration reductions are expected in such locations due to current and proposed composite wood product regulations because those regulations apply primarily to new construction and furnishings. While other studies have found elevated formaldehyde levels in homes and businesses, particularly in newer buildings, our study indicates that elevated levels are present in nearly all of the dedicated environments where younger children spend their time.

The California 8-h and chronic formaldehyde RELs (both 9 $\mu g/m^3$, or about 0.007 ppm) used as the relevant health benchmarks for this analysis are similar to the U. S. Agency for Toxic Substances and Disease Registry's Minimal Risk Levels of 0.008 ppm for chronic exposures (1 year or longer) that is set as a screening level to protect the general public (ATSDR, 1999). While the California RELs tend to be lower than international benchmarks, which range from 30 to 120 $\mu g/m^3$ for 8-h exposure, France has established a long-term exposure benchmark of 10 $\mu g/m^3$, almost identical to the OEHHA chronic REL (Kaden et al., 2010; Salthammer et al., 2010). The World Health Organization has published a 30-min standard of 100 $\mu g/m^3$ based on sensory irritation and also judged to protect against cancer, which some investigators believe are more appropriate than the OEHHA benchmarks (Kaden et al., 2010; Nielsen et al. 2013; Golden 2011).

This study has several limitations. The sample size of 40 ECE facilities limited our statistical power to draw inferences. Further, this was a cross-sectional study and data collection at each site occurred over the course of just 1 day. Therefore, concentration results may not reflect long-term averages or seasonal differences related to changing patterns of window use with outdoor temperatures. The majority of the buildings were older than 5 years, so few would be expected to have substantial off-gassing from the original building materials or furnishings. During the inspections, we could not identify the materials used in renovations for 23 facilities (57.5%) and there are many other sources of formaldehyde that we were not able to assess, such as treated fabrics and personal care products. Accordingly, we were not able to identify associations between indoor air levels and such potential sources. Another limitation was the use of CO_2 measurements to estimate AERs because the use of perfluorocarbon tracer (PFT) gas was unacceptable to the ECE directors. While the use of CO_2 as a tracer is a common method (Bartlett et al., 2004; Bekö et al., 2010), this method and our modified approach (see Methods Section and SI) may result in higher uncertainty compared to PFT gas measurements. We were able to track room occupancy and door and window use in all facilities, and our use of a concentration decay test with medical grade CO_2 allowed more precise estimates that could be compared to patterns over the full day and improved the accuracy of our AER estimates. Finally, the participation rate was less than 5% of those contacted, possibly resulting in selection bias. However, the participating ECE facilities reflected a diverse cross-section of northern California, including center and home-based facilities, Head Start programs and school districts, private and non-profit providers, middle class families, and low income and immigrant communities.

Concerns about the health effects of formaldehyde exposure resulted in a 2008 regulation to reduce formaldehyde emissions from CWP in California (CCR, 2008). The U.S. EPA proposed similar national regulations in 2013, which are currently under review (CFR, 2014). The timing of our sample collection (2010–2011), however, does not reflect any impact of the California rules because they were phased in over several years (CARB, 2014) and the buildings sampled in this study were all over 5 years of age. Given the potential health risks associated with the formaldehyde levels observed in indoor environments where young children spend time, additional assessment is needed to determine the extent to which these regulations will reduce exposure in future newly constructed day care centers and identify measures that can be taken to reduce exposures in existing dedicated child care facilities.

Conclusion

Child formaldehyde exposures in this study exceeded California RELs in 87.5% of the ECE facilities tested and acetaldehyde exposures exceeded the U.S. EPA

RfC in 30%. Exposures also exceeded age-adjusted benchmarks based on carcinogenicity in 100% of the facilities. Our findings demonstrate that potentially harmful formaldehyde and acetaldehyde exposures are occurring in dedicated ECE environments. More research is needed to identify the additional major sources of formaldehyde in ECE centers. Additionally, the efficacy of California and newly proposed federal regulations to reduce formaldehyde exposure below levels of concern should be evaluated. If warranted, new formaldehyde-use restrictions should be considered as well as outreach to child care providers on strategies to improve indoor air quality, such as ensuring proper ventilation, to mitigate these exposures.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:
Appendix S1. This includes: QA/QC information, ventilation calculation steps, emission rate calculation steps, exposure dose calculations steps, and summary results for potential determinants using Pearson correlation tests, bivariate *t*-tests and multiple linear regression analyses.

References

ATSDR (1999) *Toxicological Profile for Formaldehyde*, Atlanta, GA, Agency for Toxic Substances and Disease Registry.

ATSDR (2005) *Public Health Assessment Guidance Manual*, Atlanta, GA, Agency for Toxic Substances and Disease Registry.

Bartlett, K.H., Martinez, M. and Bert, J. (2004) Modeling of occupant-generated CO2 dynamics in naturally ventilated classrooms, *J. Occup. Environ. Hyg.*, **1**, 139–148.

Bekö, G., Lund, T., Nors, F., Toftum, J. and Clausen, G. (2010) Ventilation rates in the bedrooms of 500 Danish children, *Build. Environ.*, **45**, 2289–2295.

Bradman, A., Castorina, R., Gaspar, F., Nishioka, M., Colon, M., Weathers, W., Egeghy, P.P., Maddalena, R., Williams, J., Jenkins, P.L. and McKone, T.E. (2014) Flame retardant exposures in California early childhood education environments, *Chemosphere*, **116**, 61–66.

CARB (2005) *Indoor Air Pollution in California: Report to the California Legislature*, Sacramento, CA, California Air Resources Board. http://www.arb.ca.gov/research/indoor/ab1173/rpt0705.pdf.

CARB (2012) *Environmental Exposures in Early Childhood Education Environments*, Sacramento, CA, California Air Resources Board (08-305). http://www.arb.ca.gov/research/single-project.php?row_id = 64830.

CARB (2014) *Composite Wood Products ATCM*, California Air Resources Board. http://www.arb.ca.gov/toxics/compwood/compwood.htm.

CCLD (2010) CCLD Facility Search Form, Jan 10 2010. Community Care Licensing Division. http://www.ccld.ca.gov/docs/ccld_search/ccld_search.aspx.

CCR (2008) Title 17. California Code of Regulations, Sections 93120-93120.12. *Airborne Toxic Control Measure to Reduce Formaldehyde Emissions from Composite Wood*.

CCR (2013) Title 24, Part 6. California Energy Commission, Section R120.1. *Building Energy Efficiency Standards for Residential and Nonresidential Buildings*.

CFR (2014) Title 40. Code of Federal Regulations, Section 770. *Formaldehyde Emission Standards for Composite Wood Products*. Proposed Rules, U.S. Environmental Protection Agency.

Cohen Hubal, E.A., Sheldon, L.S., Burke, J.M., Mccurdy, T.R., Berry, M.R., Rigas, M.L., Zartarian, V.G. and Freeman, N.C. (2000) Children's exposure assessment: a review of factors influencing children's exposure, and the data available to characterize and assess that exposure, *Environ. Health Perspect.*, **108**, 475–486.

Costa, S., Carvalho, S., Costa, C., Coelho, P., Silva, S., Santos, L.S., Gaspar, J.F., Porto, B., Laffon, B. and Teixeira, J.P. (2015) Increased levels of chromosomal aberrations and DNA damage in a group of workers exposed to formaldehyde, *Mutagenesis*, **30**, 463–473.

Destaillats, H., Lunden, M.M., Singer, B.C., Coleman, B.K., Hodgson, A.T., Weschler, C.J. and Nazaroff, W.W. (2006) Indoor secondary pollutants from household product emissions in the presence of ozone: a bench-scale chamber study, *Environ. Sci. Technol.*, **40**, 4421–4428.

Frey, S.E., Destaillats, H., Cohn, S., Ahrentzen, S. and Fraser, M.P. (2014) Characterization of indoor air quality and resident health in an Arizona senior housing apartment building, *J. Air Waste Manage. Assoc.*, **64**, 1251–1259.

Golden, R. (2011) Identifying an indoor air exposure limit for formaldehyde considering both irritation and cancer hazards, *Critical Reviews in Toxicology*, **41**, 672–721.

Hauptmann, M., Lubin, J.H., Stewart, P.A., Hayes, R.B. and Blair, A. (2004) Mortality from solid cancers among workers in formaldehyde industries, *Am. J. Epidemiol.*, **159**, 1117–1130.

Hodgson, A.T., Rudd, A.F., Beal, D. and Chandra, S. (2000) Volatile organic compound concentrations and emission rates in new manufactured and site-built houses, *Indoor Air*, **10**, 178–192.

Hulin, M., Caillaud, D. and Annesi-Maesano, I. (2010) Indoor air pollution and childhood asthma: variations between urban and rural areas, *Indoor Air*, **20**, 502–514.

Hun, D.E., Corsi, R.L., Morandi, M.T. and Siegel, J.A. (2010) Formaldehyde in residences: long-term indoor concentrations and influencing factors, *Indoor Air*, **20**, 196–203.

IARC (2012) *Chemical Agents and Related Occupations: A Review of Human Carcinogens*, Vol. 100F, Lyon, International Agency for Research on Cancer.

Kaden, D.A., Madin, C., Nielsen, G.D. and Wolkoff, P. (2010) *Formaldehyde, WHO Guidelines for Indoor Air Quality:*

Selected Pollutants, Geneva, World Health Organization.

Kelly, T.J. (1996) *Determination of Formaldehyde and Toulene Diisocyanate Emissions from Indoor Residential Sources*, Sacramento, CA, California Air Resources Board (Contract No. 93–315).

Kelly, T.J., Smith, D.L. and Satola, J. (1999) Emission rates of formaldehyde from materials and consumer products found in California homes, *Environ. Sci. Technol.*, **33**, 81–88.

Kerns, W.D., Pavkov, K.L., Donofrio, D.J., Gralla, E.J. and Swenberg, J.A. (1983) Carcinogenicity of formaldehyde in rats and mice after long-term inhalation exposure, *Cancer Res.*, **43**, 4382–4392.

Laughlin, L. (2013) *Who's Minding the Kids? Child Care Arrangements: Spring 2011*, Washington, DC, U.S. Census Bureau (P70-135).

Lo, B. and O'Connell, M. (eds) (2005) *Ethical Considerations for Research on Housing-Related Health Hazards Involving Children*, *National Research Council and Institute of Medicine of the National Academies*, Washington, DC, The National Academies Press.

Maddalena, R., Russell, M., Sullivan, D.P. and Apte, M.G. (2009) Formaldehyde and other volatile organic chemical emissions in four FEMA temporary housing units, *Environ. Sci. Technol.*, **43**, 5626–5632.

McGwin, G., Lienert, J. and Kennedy, J.I. (2010) Formaldehyde exposure and asthma in children: a systematic review, *Environ. Health Perspect.*, **118**, 313–317.

Mendell, M.J. (2007) Indoor residential chemical emissions as risk factors for respiratory and allergic effects in children: a review, *Indoor Air*, **17**, 259–277.

Nielsen, G.D., Søren, T.L. and Wolkoff, P. (2013) Recent trend in risk assessment of formaldehyde exposures from indoor air, *Arch. Toxicol.*, **87**, 73–98.

Norback, D., Bjornsson, E., Janson, C., Widstrom, J. and Boman, G. (1995) Asthmatic symptoms and volatile organic compounds, formaldehyde, and carbon dioxide in dwellings, *Occup. Environ. Med.*, **52**, 388–395.

NTP (2011) *Report on Carcinogens*, 12th edn, Research Triangle Park, NC, National Toxicology Program, U.S. Department of Health and Human Services.

OEHHA (2001) *Proposition 65: Process for Developing Safe Harbor Numbers*, Sacramento, CA, California Office of Environmental Health Hazard Assessment.

OEHHA (2008) *Appendix D. Individual Acute, 8-Hour, and Chronic Reference Exposure Level Summaries*, Sacramento, CA, California Office of Environmental Health Hazard Assessment.

OEHHA (2013a) *All OEHHA Acute, 8-hour and Chronic Reference Exposure Levels (RELs)*, Nov 25, 2013. California Office of Environmental Health Hazard Assessment. http://oehha.ca.gov/air/allrels.html.

OEHHA (2013b) *Proposition 65: No Significant Risk Levels (NSRLs) for Carcinogens and Maximum Allowable Dose Levels (MADLs) for Chemicals Causing Reproductive Toxicity*, Sacramento, CA, California Office of Environmental Health Hazard Assessment.

Offermann, F.J. (2009) *Ventilation and Indoor Air Quality in New Homes. PIER Collaborative Report*, Sacramento, CA, California Air Resources Board and California Energy Commission (CEC-500-2009-085).

Persily, A. (1997) Evaluating building IAQ and ventilation with indoor carbon dioxide, *ASHRAE Trans.*, **103**, 1–12, 193.

Pinkerton, L.E., Hein, M.J. and Stayner, L.T. (2004) Mortality among a cohort of garment workers exposed to formaldehyde: an update, *Occup. Environ. Med.*, **61**, 193–200.

Rehwagen, M., Schlink, U. and Herbarth, O. (2003) Seasonal cycle of VOCs in apartments, *Indoor Air*, **13**, 283–291.

Roda, C., Kousignian, I., Guihenneuc-Jouyaux, C., Dassonville, C., Nicolis, I., Just, J. and Momas, I. (2011) Formaldehyde exposure and lower respiratory infections in infants: findings from the PARIS cohort study, *Environ. Health Perspect.*, **119**, 1653–1658.

Salthammer, T., Mentese, S. and Marutzky, R. (2010) Formaldehyde in the indoor environment, *Chem. Rev.*, **110**, 2536–2572.

Selevan, S.G., Kimmel, C.A. and Mendola, P. (2000) Identifying critical windows of exposure for children's health, *Environ. Health Perspect.*, **108**(Suppl 3), 451–455.

Singer, B.C., Coleman, B.K., Destaillats, H., Hodgson, A.T., Lunden, M.M., Weschler, C.J. and Nazaroff, W.W. (2006) Indoor secondary pollutants from cleaning product and air freshener use in the presence of ozone, *Atmos. Environ.*, **40**, 6696–6710.

St-Jean, M., St-Amand, A., Gilbert, N.L., Soto, J.C., Guay, M., Davis, K. and Gyorkos, T.W. (2012) Indoor air quality in Montréal area day-care centres, Canada, *Environ. Res.*, **118**, 1–7.

TSI (2006) *Model 8552/8554 Q-Trak Plus IAQ Monitor: Operation and Service Manual*, Shoreview, MN, TSI.

U.S. EPA (1999) *Determination of Formaldehyde in Ambient Air Using Adsorbent Cartridge Followed by High Performance Liquid Chromatography (HPLC) [Active Sampling Methodology]*, Cincinatti, OH, U.S. Environmental Protection Agency (EPA/625/R-96/010b), Center for Environmental Research Information.

U.S. EPA (2011) *Exposure Factors Handbook 2011 Edition (Final)*, Washington, DC, U.S. Environmental Protection Agency.

U.S. EPA (2012a) *Volatile Organic Compounds (VOCs)*, Nov 20, 2013. U.S. Environmental Protection Agency. http://www.epa.gov/iaq/voc.html.

U.S. EPA (2012b) *Formaldehyde (CASRN 50–00-0)*, Integrated Risk Information System (IRIS), U.S. Environmental Protection Agency.Washington, DC. http://www.epa.gov/iris.

U.S. EPA (2012c) *Acetaldehyde (CASRN 75–07-0)*, Integrated Risk Information System (IRIS), U.S. Environmental Protection Agency. Washington, DC. http://www.epa.gov/iris.

Wallace, L., Nelson, W., Ziegenfus, R., Pellizzari, E., Michael, L., Whitmore, R., Zelon, H., Hartwell, T., Perritt, R. and Westerdahl, D. (1991) The Los Angeles TEAM Study: personal exposures, indoor-outdoor air concentrations, and breadth concentrations of 25 volatile organic compounds, *J. Expo. Anal. Environ. Epidemiol.*, **1**, 157–192.

Weisel, C.P., Zhang, J., Turpin, B.J., Morandi, M.T., Colome, S., Stock, T.H. and Spektor, D.M. (2005) *Relationship of Indoor, Outdoor, and Personal Air (RIOPA)*, Boston, MA, Health Effects Institute.

Whitmore, R. (2003) *California Portable Classrooms Study Phase II: Main Study, Final Report*, Vol. II, Sacramento, CA, California Air Resources Control Board, California Department of Health Services, and RTI International (Contract No. 00-317).

Wieslander, G., Norback, D., Bjornsson, E., Janson, C. and Boman, G. (1997) Asthma and the indoor environment: the significance of emission of formaldehyde and volatile organic compounds from newly painted indoor surfaces, *Int. Arch. Occup. Environ. Health*, **69**, 115–124.

Woutersen, R.A., Appelman, L.M., Van Garderen-Hoetmer, A. and Feron, V.J. (1986) Inhalation toxicity of acetaldehyde in rats. III. Carcinogenicity study, *Toxicology*, **41**, 213–231.

Wu, X.M., Apte, M.G., Maddalena, R. and Bennett, D.H. (2011) Volatile organic compounds in small- and medium-sized commercial buildings in California, *Environ. Sci. Technol.*, **45**, 9075–9083.

Zhang, J., Lioy, P.J. and He, Q. (1994) Characteristics of aldehydes: concentrations, sources, and exposures for indoor and outdoor residential microenvironments, *Environ. Sci. Technol.*, **28**, 146–152.

Zuraimi, M.S. and Tham, K.W. (2008) Effects of child care center ventilation strategies on volatile organic compounds of indoor and outdoor origins, *Environ. Sci. Technol.*, **42**, 2054–2059.

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Formaldehyde and Acetaldehyde Exposure and Risk Characterization in California Early Childhood Education Environments

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QA/QC: Aldehydes

Analytical and field blanks (Table S1) consisted of unused Xposure sampler cartridges. The aldehyde masses measured in field blanks somewhat exceed those in analytical blanks and, when converted to concentration, only constitute a small percentage of the field sample concentrations.

Table S1. Summary Statistics of Analytical Blanks (n=8) and Field Blanks (n=9)

Summary Statistics	**Formaldehyde Mass (ng)**	**Formaldehyde Concentration[a] (μg/m^3)**	**Acetaldehyde Mass (ng)**	**Acetaldehyde Concentration[a] (μg/m^3)**
Analytical Blanks				
Mean	16.62	0.14[b]	27.50	0.23
Median	14.33	0.12[b]	25.64	0.21
SD	18.46	0.15	6.37	0.05
Minimum	<MDL	<MDL	22.13	0.18
Maximum	51.80	0.43	42.73	0.36
Field Blanks				
Mean	48.8	0.41	51.9	0.43
Median	40.6	0.34	36.6	0.30
SD	18.8	0.16	28.6	0.24
Minimum	30.7	0.26	28.8	0.24
Maximum	89.7	0.75	114.6	0.96

[a] Assuming 120 L sample volume
[b] <LOQ

Side-by-side duplicate indoor aldehyde samples (n=12) were assessed for precision. The mean relative percent differences (RPDs) between field and duplicate aldehyde samples were 6.4±6.1% for formaldehyde and 5.7±4.5% for acetaldehyde, indicating good precision for field duplicates (Table S2).

Table S2. Duplicate Indoor Aldehyde Summary Statistics (n=12)

	Formaldehyde Field (µg/m³)	**Formaldehyde Duplicate (µg/m³)**	**Formaldehyde RPD (%)**	**Acetaldehyde Field (µg/m³)**	**Acetaldehyde Duplicate (µg/m³)**	**Acetaldehyde RPD (%)**
Mean	18.1	18.3	6.4	7.5	7.4	5.7
Median	12.2	12.4	5.0	6.4	6.3	4.6
Std.Deviation	12.7	13.6	6.1	4.6	4.6	4.5

Equation S1. Air Exchange Rate Computations

Difference in the fresh air dilution rates and the room size at each facility contribute to variability in exposure concentrations for a given emission source. To facilitate the comparison of results across facilities, we normalized the measured concentration to a floor-area based emission rate ($\mu g/m^2/h$) for each target compound as described in Equation S2 below. The main input to the calculation of area-based emission rates are the room volume and AER. Room volume is measured directly and reduced by 10% to account for unmixed space in the room (i.e., closed cabinets, furniture and other room contents). The estimation of AER is described below.

Given the highly fluctuating indoor environment in child care facilities, we used a dynamic mass balance tracer gas method to calculate air exchange rates (AERs) over the course of a sampling day then estimated the time-averaged AER from the modeling results. We selected carbon dioxide (CO_2) as the tracer gas due to its low toxicity, acceptability to ECE directors and opportunity to use continuous CO_2 emissions from room occupants rather than inject tracer chemical into the room. While the use of CO_2 measurements to estimate AER is a standard approach, because CO_2 has natural sources (occupants, outdoor air) these methods may result in higher uncertainty compared to perfluorocarbon tracer (PFT) gas measurements. However, most ECE directors opposed the use of PFT gas (an unnatural substance) in their facilities.

To reduce uncertainty in the AERs estimated from the dynamic CO_2 mass balance approach, when children were not present, we added medical-grade CO_2 to the room until concentrations were ~2500 ppm and computed the AER using the CO_2 decay rate.The decay rate AERs determined when the room was unoccupied were compared to the time-averaged AER obtained from the continuous mass-balance model.

The dynamic mass balance accounts for changes in room conditions that might impact ventilation rate and the time dependant tracer input which includes both intake from outdoors and biogenic emission from occupants. Total CO_2 tracer input into the room was calculated as:

$$E_{total} = \frac{C_{out}}{1{,}000{,}000} * V_r * AER + E_{occ}$$

Where,

E_{total}=Total volumetric CO_2 ER into room, $\left(\frac{L}{h}\right)$

C_{out}=Average outdoor CO_2 concentration, ppm

V_r=Available mixing volume of room, liters

AER= Air exchange rate in the room, $\left(\frac{1}{h}\right)$

E_{occ}=Volumetric ER of CO_2 from room occupants, $\left(\frac{L}{h}\right)$

Since outdoor CO_2 concentration variability was low (mean CV=3.8%) and an average daily AER was ultimately computed from the dynamic mass balance, we used average daily outdoor CO_2 concentration across all time periods in the model. CO_2 emission rate from room occupants was calculated using per person emission rates (ERs) (Persily, 1997). Occupancy logs recorded minute-by-minute changes in occupancy. The CO_2 biogenic per-person emission rate is a

function of the rate of oxygen consumption by the individual and oxygen consumption is a function of the indivual body surface area, the metabolic activity of the person and a respiratory quotient that converst the oxygen consumed to the CO_2 emitted (Persily, 1997). Most of the occupants in the room were either children (age ≤ 5) or adults (age > 18) so we used the conditions for an average sized adult engaged in office work and a typical child as reported by Persily (1997). Children ≤5 years old were assumed to have a CO_2 ER of 0.0029 L/s (10.44 L/h) and occupants > 6 years of age were assumed to have a rate of 0.0052 L/s) (18.72 L/h) (Persily, 1997).

$$E_{occ} = \left[\varepsilon_{0-5} * 10.44\frac{L}{h}\right] + \left[\varepsilon_{>5} * 18.72\frac{L}{h}\right]$$

Where,

ε_{0-5}=Number of children ≤5 years old

$\varepsilon_{>5}$=Number of occupants ages > 5 years

QTrak indoor CO_2 concentration measurements, the room condition, and the occupancy logs were matched using minute-by-minute time measurements and the room condition logs recorded minute-by-minute changes in conditions that might impact ventilation (including the openings of doors/windows). An observed change in the indoor condition denoted a separate AER for that time period. The estimated AER over each period when conditions and occupancy were unchanging was used to fit the model to the emission profile and measured indoor and outdoor CO_2 concentrations. When the occupancy changed, a new CO_2 input (L/h) was used without a changing the AER. When ventilation conditions changed in the room then a new AER was estimated for the period until the next ventilation contition change. The dynamic CO_2 mass balance was calculated using the following equation:

$$C_{pred} = C_{Pred,Occ\,\Delta} \times e^{[-AER\times(t_i - t_{AER})]} + \left[\frac{E_{total}/V_r}{AER} \times 1{,}000{,}000\right] \times \left[1 - e^{[-AER\times(t_i - t_{AER})]}\right]$$

Where,

C_{pred}=Predicted CO_2 from model, ppm

$C_{Pred,Occ\,\Delta}$=Predicted CO_2 at start of period following occupancy/ventilation change, ppm

t_i=Elapsed time from start of constant occupancy/ventilation period, hours

t_{AER}=Time at start of new occupancy/ventilation period, hours

Initial "predicted CO_2" concentrations were based on the QTrak CO_2 measurements at the beginning of the monitoring period. The best fit between the model and measurements was determined by optimizing the AER to minimize the mean squared error (MSE) between the predicted and the measured CO_2 for each constant occupancy/ventalition period. We designated 0.15 hour^{-1} as the AER lower limit, which was the 5th percentile from a study of U.S. residences (Murray and Burmaster, 1995) to facilitate the model solution.

The solution to the dynamic mass balance provides AERs for each period of constant occupancy/ventilation and the time-weighted average of each AER were used to calculate a daily average AER.

Given the uncertainaty in the dynamic mass balance, we augmented the estimate of AER using a standard decay model by adding medical grade CO_2 to the room when children were outside. The CO_2 decay method is based on the following equation (Persily, 1997, Baptista et. al. , 1999):

$$C_t - C_{input} = \left[C_{orig} - C_{input}\right] e^{(-Qt/V_r)}$$

Where,

e^x=exponential function

C_t=Concentration of tracer at elapsed time, ppm

C_{input}=Concentration of tracer ventilation air and occupant emissions, ppm

C_{orig}=Concentration of tracer at start of log-linear decay period, ppm

Q=Effective ventilation rate, m^3/hour

t=Elapsed time from start of log-liner decay period, hour

V_r=Volume of child care room, liters

We note that Q/V_r is equal to the AER and that C_{input} is negligible when the augmentated concentration starts at a factor of 5 – 10 greater than the outdoor concentration. With these assumptions, the above equation reduces to

$$\ln(C_t) = -AER \times t + \ln(C_{orig})$$

Such that the negative slope of the log-linear regression of C_t (determined from the CO_2 measurements) and elapsed time fromteh start of the log-linear period, t (h) is equal to the average AER for the period over which the decay is monitored.

AER Calculation Example

Figure S1 and Table S3 present AER calculations for ECE 29, which had four distinct ventilation condition time periods marking changes in indoor environment (opened door) with a number of changes in occupancy. Period-specific AERs were calculated by minimizing the MSE between predicted and measured CO_2 concentrations. The time-weighted average AER was calculated over the full sampling period.

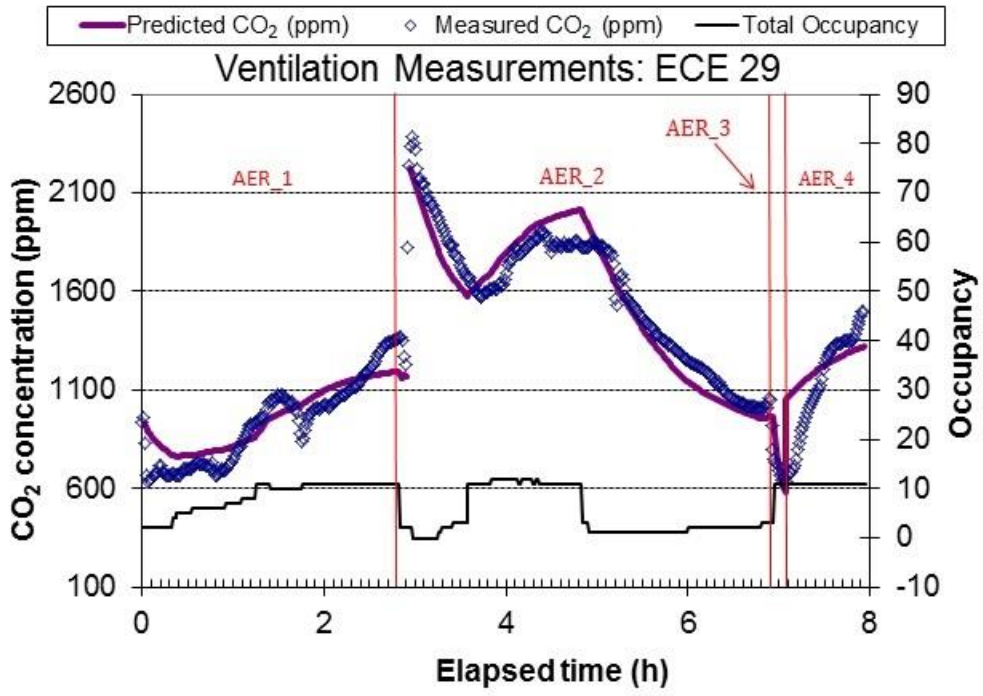

Figure S1. Predicted and measured CO_2 concentrations at ECE 29.

By fitting predicted with measured CO_2 levels, AERs were calculated for four different time periods representing different ventilation conditions in the indoor environment (opened window/door).

Table S3. Calculated AERs at ECE 29

Time Period	AER (h^{-1})	Ventilation Notes
AER_1	1.83	One passage door open
AER_2	0.87	CO_2 release, one passage door open
AER_3	13.05	One entry and passage door open
AER_4	1.48	One passage door open
AER_{TWA}	1.49	Time-Weighted Average

Equation S2. Emission Rate Calculation

To normalize the aldehyde measurements and account for differences in AER and room size, we computed aldehyde ERs per unit of area over time (Maddalena et. al. , 2009).

$$ER = AER \times h \times \Phi \times (\mathrm{C} - \mathrm{C_0})$$

Where,

ER=Emission Rate ($\mu g/m^2/h$)
h=Height (m)
Φ=Correction factor for non-ventilated space
C=Steady-state indoor aldehyde concentration ($\mu g/m^3$)
C_0=Outdoor aldehyde concentration ($\mu g/m^3$)

ER calculations assumed pseudo steady-state and well-mixed room conditions. We applied a correction factor (0.9) for non-ventilated space (Maddalena et. al., 2009). For facilities without outdoor measurements, we substituted average outdoor concentration for C_0 (2.5 $\mu g/m^3$ for both aldehydes). Since most indoor concentrations greatly exceeded outdoor levels, this substitution did not introduce uncertainty.

Table S4. Summary of Estimated Aldehyde Emission Rates ($\mu g/m^2/h$)

Emission Rate	**N**	**Min**	**25th %**	**Median**	**75th %**	**Max**
Formaldehyde	39	8.1	34.8	59.2	100.4	152.7
Acetaldehyde	38	1.4	11.2	16.5	27.7	53.6

Equation S3. Exposure Dose Calculations

Using a standard inhalation dose equation (ATSDR, 2005), we combined aldehyde concentrations with age-specific intake factors including inhalation rate (IR), body weight (BW), and exposure factor (EF). For age group birth to <1 year, the IR of 5.1 m^3/day (Arcus-Arth and Blaisdell, 2007) and BW of 6.8 kg (U.S. EPA, 2008) were derived from an average of three age groups (0-1, 3-5, and 6-11 months). For the respective age groups 1 to <2, 2 to <3, and 3 to <6 years, the IRs were 8.0, 9.5, and 10.9 m^3/day and the BWs were 11.4, 13.8, and 18.6 kg (U.S. EPA, 2008). We divided daily IRs by three to obtain 8-hour IRs.

$$D_{child\ care} = \frac{C \times IR \times EF \times CF}{BW}$$

Where,

D=exposure dose received in child care assuming 8-hour day (mg/kg/8-hours)
C=contaminant concentration (mg/m^3)
IR=inhalation rate (m^3/8-hours)
EF=exposure factor
CF=conversion factor
BW=body weight (kg)

The EF is calculated (ATSDR, 2005):

$$EF = \frac{F \times ED}{AT}$$

Where,

F = frequency of exposure (days/year)
ED = exposure duration (years)
AT = averaging time (ED x 365 days/year)

We assumed that a child spends five days/week and 48 weeks/year (accounting for holidays/vacation) in child care. We assumed AT as one year.

$$EF = \frac{\left(5\,\frac{days}{week}\right) \times \left(48\,\frac{weeks}{year}\right) \times (1\,year)}{1\,year\ \times\ 365\,\frac{days}{year}} = 0.66$$

Table S5. Acetaldehyde and formaldehyde concentrations and air exchange rates (AER) by ECE facility (n=40).

ECE #	Indoor Acetaldehyde ($\mu g/m^3$)	Outdoor Acetaldehyde ($\mu g/m^3$)	Indoor Formaldehyde ($\mu g/m^3$)	Outdoor Formaldehyde ($\mu g/m^3$)	AER (hr^{-1})
1	3.19	-	7.42	-	3.75
2	3.06	-	9.16	-	3.54
3	2.81	-	7.57	-	3.45
4	9.65	-	28.40	-	1.56
5	4.76	-	9.12	-	2.83
6	2.64	-	8.38	-	4.92
7	3.98	-	10.30	-	4.96
8	19.07	4.90	29.33	3.76	0.54
9	5.49	-	18.18	-	1.29
10	12.38	-	36.91	-	1.06
11	7.83	1.13	13.32	1.53	1.23
12	7.50	-	10.59	-	1.18
13	17.24	-	26.95	-	0.28
14	17.03	-	48.77	-	1.14
15	7.18	-	14.02	-	0.87
16	12.27	-	17.17	-	0.53
17	5.06	-	16.37	-	2.50
18	8.35	-	24.06	-	0.94
19	5.59	-	22.00	-	1.40
20	15.58	1.65	18.58	1.84	1.49
21	8.22	1.63	20.86	1.90	0.83
22	14.68	1.81	21.39	2.30	1.25
23	23.34	3.36	30.28	3.94	0.29
24	8.37	2.01	15.75	2.26	0.28
25	9.41	-	19.39	-	0.90
26	7.84	3.42	25.86	2.71	1.80
27	7.59	1.74	12.83	2.02	2.27
28	0.69	2.31	0.74	3.03	1.34
29	5.99	4.31	14.04	3.10	2.41
30	21.34	-	37.63	-	0.69
31	6.15	-	32.31	-	0.86
32	11.25	6.52	19.27	3.53	2.38
32	3.06	3.67	8.29	1.87	3.65
34	5.71	-	11.37	-	1.46
35	4.71	1.63	19.49	2.54	4.19
36	8.69	1.54	34.14	2.00	1.37
37	4.68	1.55	18.31	2.55	3.40
38	8.33	1.96	17.34	3.97	3.06
39	5.00	1.09	10.66	1.57	2.86
40	2.63	1.45	9.54	1.80	5.63

Table S6. Summary of Aldehyde Air Levels (μg/m^3) and Potential Determinants[a] (n=40).

Determinant	n (%)	Formaldehyde Mean±SD or Correlation[b]	Acetaldehyde Mean±SD or Correlation[b]	Acetaldehyde GM (95% CI) or Correlation[c]
Presence of composite wood furniture				
Yes	35 (87.5)	17.5±8.0	7.9±5.0	6.5 (5.1, 8.2)
No	5 (12.5)	28.6±17.7*	12.3±7.3	10.1 (3.9, 26.3)
Temperature (°C)				
Pearson r (Mean±SD=21.1±1.7°C)	40 (100)	0.22	0.23	0.22
AER (hr^{-1})				
Pearson r (Mean±SD=2.0±1.4 hr^{-1})	40 (100)	-0.54**	-0.64**	-0.63**
Indoor relative humidity (%)				
Pearson r (Mean±SD=49.3±6.9%)	40 (100)	0.31	0.11	0.13
Age of building (years)				
Pearson r (Mean±SD=43.0±29.1 years)	31 (77.5)	0.12	-0.03	-0.04
Building type				
Portable	9 (22.5)	19.8±8.4	10.3±7.2	8.2 (4.7, 14.4)
Non-portable	31 (77.5)	18.6±10.6	7.9±4.8	6.5 (5.0, 8.4)
Occurrence of renovations within the last five years				
Yes	23 (57.5)	17.6±10.7	8.0±5.5	6.3 (4.5, 8.7)
No	17 (42.5)	20.7±9.1	9.1±5.5	7.7 (5.7, 10.5)
Installation of new floor coverings within last year				
Yes	6 (15)	12.6±7.2	5.4±3.8	4.0 (1.4, 11.3)
No	34 (85)	20.0±10.2	9.0±5.5*	7.6 (6.1, 9.3)*
Presence of carpet				
Yes	12 (30)	20.8±8.5	9.7±5.8	8.4 (5.8, 12.1)
No	28 (70)	18.1±10.7	7.9±5.3	6.3 (4.7, 8.4)
Air freshener use				
Yes	17 (42.5)	18.3±10.0	9.0±5.1	7.7 (5.8, 10.3)
No	22 (55)	18.9±10.4	8.0±5.9	6.2 (4.3, 8.8)
License Type				
Center	28 (70)	16.4±7.4	7.9±5.6	6.2 (4.6, 8.3)
Home	12 (30)	24.6±13.2*	9.8±5.1	8.7 (6.3, 12.0)

Table S6 (Continued). Summary of Aldehyde Air Levels (µg/m^3) and Potential Determinants[a] (n=40).

Determinant	n (%)	Formaldehyde Mean±SD or Correlation[b]	Acetaldehyde Mean±SD or Correlation[b]	Acetaldehyde GM (95% CI) or Correlation[c]
Season				
Spring	11 (27.5)	19.6±10.7	7.2±5.4	5.9 (3.9, 9.0)
Summer	7 (17.5)	18.6±12.5	7.9±6.1	6.1 (3.0, 12.5)
Fall	10 (25)	21.1±10.9	9.4±4.6	8.5 (6.2, 11.7)
Winter	12 (30)	16.6±8.0	9.2±6.1	7.0 (4.0, 12.5)
Winter Season				
Winter	12 (30)	16.6±8.0	9.2±6.1	7.0 (4.0, 12.5)
Spring/summer/fall	28 (70)	19.9±10.9	8.1±5.2	6.8 (5.4, 8.6)
Reported use/purchase of low-toxicity cleaner				
Yes	13 (32.5)	13.6±6.7	6.4±4.4	5.4 (3.8, 7.7)
No	24 (60)	21.5±11.2*	9.4±5.9	7.6 (5.5, 10.4)
County				
Alameda	20 (50)	19.5±12.7	8.5±6.2	6.4 (4.3, 9.4)
Monterey	20 (50)	18.3±6.8	8.5±4.7	7.4 (5.7, 9.5)
Presence of gas appliances				
Yes	33 (82.5)	18.7±1.8		
No	6 (15)	19.4±4.5		

*p-value<0.05. **p-value<0.01.

[a] p-values from Pearson correlations or t-tests of aldehyde air levels.
[b] Arithmetic mean±SD except when Pearson coefficient is presented. Pearson calculations used untransformed acetaldehyde data.
[c] Geometric mean and 95% CI except when Pearson coefficient is presented. Pearson calculations used log-transformed acetaldehyde data.

Table S7. Results from Multiple Regression Analysis of Formaldehyde Levels (μg/m^3) and Predictors (n=40).[a]

	Coefficient	**(95% CI)**	**p-value**
Formaldehyde			
AER **(**hr^{-1}**)**	-3.5	(-5.3, -1.8)	<0.001
Temperature **(°C)**	2.5	(0.9, 4.2)	0.004
RH **(%)**	0.4	(0.0, 0.8)	0.037
License Type (Home vs Center)	8.3	(1.6, 15.0)	0.016

[a]Adjusted R^2=0.54.

Table S8. Results from Multiple Regression Analysis of Log-Transformed Acetaldehyde Levels (μg/m^3) and Predictors (n=39).[a]

	Percent Change	**(95% CI)**	**p-value**
Acetaldehyde			
AER **(**hr^{-1}**)**	-54.2	(-65.1, -40.0)	<0.001
Temperature **(°C)**	24.1	(-2.2, 57.5)	0.074
RH **(%)**	7.5	(1.6, 13.7)	0.013
Air Freshener Use (Yes/No)	100.0	(-6.8, 329.0)	0.074

[a] Adjusted R^2=0.50.

Table S9. Summary of Aldehyde Emission Rates (μg/m^3/hr) and Potential Determinants.[a]

	Formaldehyde ER[b]		Acetaldehyde ER[c]	
Determinant	**n (%)**	**Median or Correlation[d]**	**n (%)**	**Median or Correlation[d]**
Presence of composite wood furniture				
Yes	34 (87.2)	59.2	33 (86.8)	16.5
No	5 (12.8)	59.2	5 (13.2)	23.5
Temperature (°C)				
Spearman rho (Mean±SD=21.1±1.7°C)	39 (100)	0.01	38 (100)	0.20
Indoor relative humidity (%)				
Spearman rho (Mean±SD=49.3±6.9%)	39 (100)	0.12	38 (100)	-0.14
Age of building (years)				
Spearman rho (Mean±SD=43.0±29.1 years)	31 (79.5)	-0.06	30 (78.9)	-0.09
Building type				
Portable	9 (23.1)	50.3	9 (23.7)	17.2
Non-portable	30 (76.9)	60.4	29 (76.3)	16.5
Occurrence of renovations within the last five years				
Yes	22 (56.4)	59.6	21 (55.3)	19.1
No	17 (43.6)	55.7	17 (44.7)	16.1
Installation of new floor coverings within last year				
Yes	5 (12.8)	90.9	5 (13.2)	25.2
No	34 (87.2)	58.5	33 (86.8)	16.5
Presence of carpet				
Yes	12 (30.8)	57.8	12 (31.6)	16.1
No	27 (69.2)	60.9	26 (68.4)	16.9
Air freshener use				
Yes	17 (43.6)	58.4	17 (44.7)	17.8
No	21 (53.8)	59.2	20 (52.6)	15.0
License Type				
Center	27 (69.2)	57.9	26 (68.4)	16.3
Home	12 (30.8)	68.2	12 (31.6)	21.5

Table S9 (Continued). Summary of Aldehyde Emission Rates (μg/m^3/hr) and Potential Determinants.[a]

	Formaldehyde ER[b]		Acetaldehyde ER[c]	
Determinant	**n (%)**	**Median or Correlation[d]**	**n (%)**	**Median or Correlation[d]**
Season				
Spring	11 (28.2)	90.9	11 (28.9)	25.2
Summer	7 (17.9)	62.8	7 (18.4)	17.8
Fall	10 (25.6)	51.0	10 (26.3)	15.9
Winter	11 (28.2)	55.7	10 (26.3)	14.1
Winter Season				
Winter	11 (28.2)	55.7	10 (26.3)	14.1
Spring/summer/fall	28 (71.8)	60.0	28 (73.7)	16.9
Reported use/purchase of low-toxicity cleaner				
Yes	13 (33.3)	14.1	13 (34.2)	16.1
No	23 (59.0)	60.9	22 (57.9)	21.5
Use of natural ventilation				
Yes	35 (89.7)	58.4	34 (89.5)	16.7
No	4 (10.3)	80.6	4 (10.5)	16.5
County				
Alameda	19 (48.7)	50.3	18 (47.4)	15.9
County	20 (51.3)	62.4	20 (52.6)	20.5
Presence of gas appliances				
Yes	32 (82.1)	59.6		
No	6 (15.4)	70.4		

Abbreviation: ER: Emission rate

[a]No Spearman rank correlation or Mann-Whitney tests of aldehyde emission rates and potential determinants achieved statistical significance ($p<0.05$).
[b]Formaldehyde ER: n=39.
[c]Acetaldehyde ER: n=38.
[d]Medians except when Spearman rank coefficient is presented.

Table S10. Selected Formaldehyde and Acetaldehyde Concentrations (µg/m^3) in United States Homes and Schools and International ECE Facilities.[a,b]

Country/State	Building Type	Formaldehyde (µg/m^3)	Acetaldehyde (µg/m^3)	Reference
California, US	New Homes	Median=36	Median=20	(Offermann, 2009)
California, US	Los Angeles Homes	Median=23.4	Median=9.2	(Weisel et. al. , 2005)
California, US	Portable Classrooms	Median=17.8	Median=11.2	(Whitmore, 2003)
California, US	Traditional Classrooms	Median=14.3	Median=11.0	(Whitmore, 2003)
California, US	Commercial Buildings	GM=16.4	GM=8.9	(Wu et. al. , 2011)
US (nationwide)	Homes	Median=20.1	Median=18.6	(Liu et. al. , 2006)
US (eastern and southeastern)	Manufactured & Site-Built Homes	GM=42-44	GM=18-36	(Hodgson et. al. , 2000)
Finland	ECE Facilities	Mean=15	N/A	(Ruotsalainen et. al. , 1993)
Korea	ECE Facilities	Mean=23	N/A	(Kabir et. al. , 2012)
Canada	ECE Facilities	Mean=23	Mean=18.2	(St-Jean et. al. , 2012)
France	ECE Facilities	GM=9.9-15.2	GM=5.0-5.6	(Roda et. al. , 2011)
Singapore	ECE Facilities	GM=3.0-11.5	GM=5.7-14.4	(Zuraimi and Tham, 2008)

[a]N/A: not available.[b]GM: geometric mean.

References

Arcus-Arth, A. and Blaisdell, R.J. (2007) Statistical distributions of daily breathing rates for narrow age groups of infants and children, *Risk analysis : an official publication of the Society for Risk Analysis*, **27**, 97-110.

ATSDR (2005) *Public Health Assessment Guidance Manual*, Atlanta, GA, Agency for Toxic Substances and Disease Registry.

Baptista, F.J., Bailey, B.J., Randall, J.M. and Meneses, J.F. (1999) Greenhouse ventilation rate: theory and measurement with tracer gas techniques, *Journal of Agricultural Engineering Research*, **72**, 363-374.

Hodgson, A.T., Rudd, A.F., Beal, D. and Chandra, S. (2000) Volatile Organic Compound Concentrations and Emission Rates in New Manufactured and Site-Built Houses, *Indoor Air*, **10**, 178-192.

Kabir, E., Kim, K.H., Sohn, J., Kweon, B. and Shin, J. (2012) Indoor air quality assessment in child care and medical facilities in Korea, *Environ Monit Assess*, **184**, 6395-6409.

Liu, W., Zhang, J., Zhang, L., Turpin, B.J., Weisel, C.P., Morandi, M.T., Stock, T.H., Colome, S. and Korn, L.R. (2006) Estimating contributions of indoor and outdoor sources to indoor carbonyl concentrations in three urban areas of the United States, *Atmospheric Environment*, **40**, 2202-2214.

Maddalena, R., Russell, M., Sullivan, D.P. and Apte, M.G. (2009) Formaldehyde and other volatile organic chemical emissions in four FEMA temporary housing units, *Environ Sci Technol*, **43**, 5626-5632.

Murray, D.M. and Burmaster, D.E. (1995) Residential air exchange rates in the United States: empirical and estimated parametric distributions by season and climatic region, *Risk Analysis*, **15**, 459-465.

Offermann, F.J. (2009) Ventilation and Indoor Air Quality in New Homes. PIER Collaborative Report., Sacramento, CA.

Persily, A. (1997) Evaluating building IAQ and ventilation with indoor carbon dioxide, *ASHRAE Transactions*, **103**, 1-12,193.

Roda, C., Barral, S., Ravelomanantsoa, H., Dusséaux, M., Tribout, M., Le Moullec, Y. and Momas, I. (2011) Assessment of indoor environment in Paris child day care centers, *Environ Res*, **111**, 1010-1017.

Ruotsalainen, R., Jaakkola, N. and Jaakkola, J.J.K. (1993) Ventilation and indoor air quality in Finnish daycare centers, *Environ Int*, **19**, 109-119.

St-Jean, M., St-Amand, A., Gilbert, N.L., Soto, J.C., Guay, M., Davis, K. and Gyorkos, T.W. (2012) Indoor air quality in Montréal area day-care centres, Canada, *Environ Res*, **118**, 1-7.

U.S. EPA (2008) *Child-Specific Exposure Factors Handbook (Final Report)*, Washington DC, U.S. Environmental Protection Agency.

Weisel, C.P., Zhang, J., Turpin, B.J., Morandi, M.T., Colome, S., Stock, T.H. and Spektor, D.M. (2005) Relationship of Indoor, Outdoor, and Personal Air (RIOPA), Health Effects Institute.

Whitmore, R. (2003) *California Portable Classrooms Study Phase II: Main Study, Final Report, Vol II*, Sacramento, CA, California Air Resources Control Board, California Department of Health Services, and RTI International (Contract No. 00-317).

Wu, X.M., Apte, M.G., Maddalena, R. and Bennett, D.H. (2011) Volatile Organic Compounds in Small- and Medium-Sized Commercial Buildings in California, *Environmental Science & Technology*, **45**, 9075-9083.

Zuraimi, M.S. and Tham, K.W. (2008) Effects of child care center ventilation strategies on volatile organic compounds of indoor and outdoor origins, *Environ Sci Technol*, **42**, 2054-2059.

VOC Exposures in California Early Childhood Education Environments

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Running head:

VOC Levels in Child Care

ABSTRACT

Little information exists about exposures to volatile organic compounds (VOCs) in early childhood education (ECE) environments. We measured 38 VOCs in single-day air samples collected in 2010-2011 from 34 ECE facilities serving California children and evaluated potential health risks. We also examined unknown peaks in the GC/MS chromatographs for indoor samples and identified 119 of these compounds using mass spectral libraries. VOCs found in cleaning products had the highest indoor concentrations (d-limonene and decamethylcyclopentasiloxane [D5] medians: 33.1 and 51.4 μg/m³, respectively). If reflective of long-term averages, child exposures to benzene, chloroform, ethylbenzene, and/or naphthalene exceeded age-adjusted "safe harbor levels" based on California's Proposition 65 guidelines (10^{-5} lifetime cancer risk) in 71%, 38%, 56%, and 97% of facilities, respectively. For VOCs without health benchmarks, we used information from toxicological databases and quantitative structure-activity relationship (QSAR) models to assess potential health concerns and identified 12 VOCs that warrant additional evaluation, including a number of terpenes and fragrance compounds. While VOC levels in ECE facilities resemble those in school and home environments, mitigation strategies are warranted to reduce exposures. More research is needed to identify sources and health risks of many VOCs and to support outreach to improve air quality in ECE facilities.

Key words: child care, children, exposure, volatile organic compounds, VOCs, risk characterization, QSAR

Practical Implications

This is the first study to report on a wide array of VOCs in U.S. early childhood and education environments. VOCs found in cleaning products had the highest indoor concentrations (d-limonene and decamethylcyclopentasiloxane [D5] medians: 33.1 and 51.4 μg/m³, respectively). If

reflective of long-term averages, child exposures to benzene, chloroform, ethylbenzene, and/or naphthalene exceeded age-adjusted "safe harbor levels" based on California's Proposition 65 guidelines (10^{-5} lifetime cancer risk) in 71%, 38%, 56%, and 97% of facilities, respectively. Our findings demonstrate that potentially harmful VOC exposures are occurring in ECE environments, and indicate that more research is needed to fully assess the potential health risks to young children and adult staff and identify major sources of VOCs present in ECE centers. Given that current exposures exceed health benchmarks, outreach to child care providers is warranted to reduce indoor exposures of young children.

INTRODUCTION

Many infants and young children spend as much as ten hours per day, five days per week, in early childhood education (ECE) facilities, which includes child care facilities and preschools. Nationally, about 61% (13 million) of all U.S. children under 5 years old are enrolled in child care (Laughlin 2013). ECE facilities are varied and include family child care providers, private centers, and programs run by schools and government agencies. These facilities are located in a variety of building types including houses, schools, commercial buildings, and portable classrooms. Studies of early life exposures have primarily focused on homes or classrooms, but few studies have examined exposures in ECE facilities (FIFCFS 2013; Seltenrich 2013).

Recent studies indicate that ECE environments may contain environmental contaminants hazardous to children's health, including volatile organic compounds (VOCs) (Breysse et al. 2004). VOCs are ubiquitous in indoor environments, with sources including building materials and furnishings, consumer products (cleaning and art supplies), personal care products, and outdoor infiltration from traffic and industrial emissions (U.S. EPA 2011a). Exposures to benzene, toluene, ethyl benzene, and xylenes (collectively, BTEX), a subset of VOCs commonly found in vehicular exhaust, can cause neurological, developmental, and respiratory health effects (ATSDR 2004).

Glycol ethers (e.g., 2-butoxyethanol) are frequently used as solvents in household products such as paints, and have been associated with increased risk of asthma, rhinitis, and eczema (Choi et al. 2010). Terpenes (e.g., d-limonene), frequently used in cleaning products, may react with ozone to produce hazardous secondary pollutants such as formaldehyde and ultrafine particles (Destaillats et al. 2006; Rohr et al. 2003). Compared to adults, children are more vulnerable to the adverse effects of environmental contaminants because they are less developed immunologically, physiologically, and neurologically than adults (Bearer 1995). They also breathe more air per kg of body weight compared with adults and are thus more highly exposed when contaminants are present.

While a few international studies have examined VOC levels in child care facilities (Mendes et al. 2014; St-Jean et al. 2012; Zuraimi and Tham 2008), scarce information is available about U.S. facilities. As part of a broader study of environmental contaminants in 40 California ECE facilities, we measured indoor and outdoor air concentrations of VOCs (Bradman et al. 2012). In this paper, we report indoor and outdoor levels of 38 VOCs, including 15 compounds with predominantly mobile sources and 23 with non-mobile sources, and evaluate potential determinants of exposure. In addition to the targeted VOCs, we also detected numerous peaks in the gas chromatography/mass spectrometry (GC/MS) chromatographs indicating the presence of many other VOCs in these environments. We used automated deconvolution information software (AMDIS) and National Institute of Standards and Technology spectral libraries (Linstrom et al. 2014) to identify 119 non-targeted VOCs and then estimated concentrations using a toluene model. For all compounds, we compared exposure levels to health-based reference values when available, and, for a subset of compounds identified as carcinogens, we applied new methods developed by the California Office of Environmental Health Hazard Assessment (OEHHA) to evaluate potential cancer risk among children (Bradman et al. 2016). Finally, for VOCs without established health benchmarks, we conducted a hazard assessment using information from toxicological databases and quantitative

structure-activity relationship (QSAR) models to identify and prioritize chemicals that warrant additional exposure and health evaluation.

MATERIALS AND METHODS

Study population, questionnaires, and study visits

The procedures for participant recruitment, ECE site inspections, and sample collection have been described previously (Bradman et al. 2016). Briefly, we enrolled 40 ECE facilities located in two northern California counties [Monterey (n=20) and Alameda (n=20)]. Questionnaire and inspection forms were administered to assess environmental quality in the facilities. Information obtained included building type (home, school, or office and if portable or manufactured), ECE type (home vs. center), building materials, renovations (within the last five years), new flooring (within the last year), air freshener and cleaning product use, ventilation, and the presence of composite wood products (CWPs). Site visits occurred from May 2010 to May 2011. All study protocols were approved by the University of California, Berkeley Committee for the Protection of Human Subjects and informed written consent was obtained from each ECE facility program director or senior administrator.

Building and Environmental Parameters

We used Q-TRAK™ IAQ Monitors (model 8554, TSI Inc.) to measure real-time indoor carbon dioxide (CO_2), relative humidity (RH), and temperature at 60-second intervals in all facilities. TSI calibrated the monitors in the spring of 2010. To address concerns by the ECE facility directors about perfluorocarbon tracer (PFT) gases, as previously described (Bradman et al. 2016), we used continuous indoor CO_2 measurements to estimate air exchange rates (AERs) (Bartlett et al. 2004; Bekö et al. 2010). To improve the precision of the estimates, we also released medical grade CO_2 (Praxair, Part Number CD M-10, United States Pharmacopeia grade) as a tracer gas in each facility when children were not present (and no air sampling was being conducted) to temporarily

increase indoor CO_2 levels and use the subsequent decay curve to validate the estimated AER (Bartlett et al. 2004; Bekö et al. 2010; Bradman et al. 2016).

VOC air sampling

Indoor air samples were collected in the main child care room during a single day at each facility (Bradman et al. 2012). VOC samplers were deployed at the height of a child's breathing zone (~1 meter) and were protected by a "kiddie-corral" made of untreated wood. The air sampling system used a rotary vane pump to provide vacuum for multiple sampling lines used during monitoring. The pump was placed in a stainless steel box lined with sound-insulating foil-faced fiberglass; the exhaust system included a muffler to reduce noise and a HEPA and carbon filter to eliminate possible emissions by the pump. Air was pulled at approximately 0.015 liters per minute (LPM) and regulated by inline taper flowmeters. Outdoor air samples were collected from a random subset of ECE facilities (n=20) using SKC AirChek 2000 pumps. Flow rates for both the inline flowmeters and AirChek pumps were calibrated using a Gilibrator® air flow calibrator.

Initial VOC samplers used glass sorbent tubes containing Tenax-TA® backed with Carbosieve™. However, alcohols released by hand sanitizers produced large interferent peaks in chromatograms, rendering samples from six facilities unusable. To resolve these problems, final protocols used separate Tenax-TA® and CarboTrap™ sorbent glass tubes (P/N 012347-005-00; Gerstel or equivalent) to sample VOCs. In one facility without alcohol interference, VOC levels were collected on a Tenax-TA with a Carbosieve sorbent glass tube. In summary, we report valid indoor VOC measurements for a total of 34 ECE facilities, including 20 with outdoor measurements.

Laboratory analyses

The samples were analyzed at Lawrence Berkeley National Laboratory (LBNL) following U.S. EPA Method TO-17 (U.S. EPA 1999). Multipoint calibrations were prepared from standards to quantify 38 target analytes. All standards and analytes were referenced to an internal

standard (~120 ng) of 1-bromo-4-fluorobenzene. See Supporting Information (SI) for more details. All compounds over the method detection limit (MDL) (< 1 to several ng) were evaluated using the NIST spectral library followed by comparison to reference standards. On a mass/volume basis, the MDLs ranged from 0.03–1.80 μg/m³ (See SI Table S1 for MDL values). VOC levels below the MDL were imputed to MDL/√2 (Hornung and Reed 1990). Decamethylcyclopentasiloxane (D5), d-limonene, and octamethylcyclotetrasiloxane (D4) masses exceeded the highest calibration standard in 15 (44%), 11 (32%), and 2 (6%) of the ECE facilities, respectively. The analytical methods did not allow for reanalysis of these samples because the entire sample was consumed during the analyses. For these samples, the calibration high mass was used to calculate air concentration (using the sample-specific volume, which averaged ~7 liters).

For three duplicate VOC samples, the mean relative percent difference (RPD) was 15.2±4.8%, showing good precision overall. Seventeen travel blanks were analyzed for possible contamination. Of the 38 analytes measured, only two had median blank masses above the method detection limit: hexamethylcyclotrisiloxane (4.1 ng) and benzaldehyde (1.5 ng). Three Tenax travel spikes were used to quantify recovery. For all 38 analytes, average recovery for the travel spikes was 96.0% (SD=8.0). See SI for additional QA/QC results. Note, when duplicate samples were collected, the average was used for final analyses.

Identification and quantification of non-targeted VOCs

For 32 facilities, we identified unknown peaks on the chromatograms from indoor air samples by conducting a mass spectral library search with the National Institute of Science and Technology (NIST) NIST08 database (Linstrom et al. 2014). This approach utilizes automated deconvolution information software (AMDIS), which improves resolution of complex chromatograms with large numbers of unresolved or partially resolved peaks. For especially complex chromatograms, we used a dominant and/or unique fragment ion chromatogram in the mass spectra, referred to here as the extracted ion chromatogram (EIC). The chemical name and

retention time for each peak was recorded if the match quality was >80% as determined by the Chemstation software. This approach resulted in the identification of 151 chemicals, including overlap with the previously reported *a priori* target analytes (where standard calibration curves were used). As additional verification, we ran pure standards for 14 selected chemicals identified with the spectral libraries diluted to levels comparable to our estimated concentrations and compared the retention times. The retention times matched almost perfectly (R^2=0.998), confirming the accuracy of our prior identification based on the spectral libraries. We also assessed probability-based matching (PBM) based on the pure standards and measurements in two of the ECE facilities (McLafferty and Turecek 1993). Seven had a PBM score above 90% and all were above 70% (Range 72-96%), affirming the accuracy of the VOC identification. See SI for more information.

We applied a modified toluene equivalent mass calibration to compute semi-quantitative estimates of the mass of each VOC identified with the spectral libraries. Toluene equivalent mass has long been used in reporting total volatile organic compounds (TVOC) for unidentified chemicals, and is optimal for total ion chromatographs (TIC) with well-resolved peaks (Hodgson 1995). We report values for each VOC if the peaks were >5 ng toluene equivalent in the chromatographs. In total, 119 additional VOC analytes were identified and quantified. To assess the quality of the estimated values, we compared levels of the 38 VOCs quantified *a priori* with the standard calibration curve versus estimated values from the toluene equivalent mode. The R^2 of the regression was 0.75, indicating reasonable estimation, with a tendency to underestimate true values with the toluene model (see SI Figure S1).

Overall, these results indicate that we correctly identified the non-targeted VOCs and the estimated values are a good indicator of the likely concentrations.

Data analysis

We first computed descriptive statistics for target and non-targeted analytes. For simplicity, we classified the targeted VOCs into two groups: (1) compounds with both indoor and mobile

sources ("mixed and mobile sources" [MMS]) (n=15), and (2) compounds with primarily indoor sources ("household sources" [HS]) (n=23) (Table 1). The MMS VOCs (e.g., toluene) derive predominately from automotive exhaust and petroleum-based products like paints and adhesives (U.S. EPA 2005). The HS VOCs (e.g., d-limonene and 2-ethyl-1-hexanol) derive predominately from household products such as cleaning products, air fresheners, fragrances, or solvents (Cooper et al. 1995; HSDB 2013). To verify these source groupings, we also examined Spearman correlation matrices to assess the relationships between VOCs within each group.

Potential determinants of targeted VOCs with detection frequencies >60% were examined in bivariate analyses. For both MMS and HS VOCs, we examined bivariate associations with license type (center/home-based), and building type (portable/non-portable). For MMS VOCs, we examined bivariate associations with season (summer/winter), gas appliances (present/absent), attached garages (present/absent), the use of glue (cement, epoxy or superglue) and permanent markers. For HS VOCs, we examined bivariate associations with reported use of air fresheners, "low-toxicity" cleaning products, and frequency of reported mopping. For MMS VOCs and specific non-fragrance HS VOCs, we also examined associations with the following building characteristics: carpet (present/absent), composite wood products (present/absent), vinyl floors (present/absent), occurrence of renovations within the last five years (yes/no), and installation of new floor coverings within the last year (yes/no). For these analyses, we used the non-parametric Wilcoxon rank-sum test. Due to the small sample size, multivariable statistical modeling was not appropriate.

We computed indoor to outdoor (I/O) air concentration ratios of targeted VOCs for each facility with paired measurements (n=20) and used the Wilcoxon signed rank test to compare the levels. We evaluated Spearman rho correlations between the VOC levels and AER (hr^{-1}), RH (%), and temperature (°C). For MMS VOCs, we also evaluated correlations with length-adjusted traffic volumes (∑LATV) within a one kilometer (km) radius of the facility (CDPH 2007).

All analyses were performed with STATA statistical software Version 13.0 (StataCorp, College Station, TX).

Health risk characterization

Non-Cancer Risk Estimation: Among the 157 compounds evaluated, 10 targeted and 6 non-targeted VOCs had OEHHA Reference Exposure Levels (RELs) and/or U.S. EPA Reference Concentrations (RfCs) (OEHHA 2014; U.S. EPA 2013). We compared indoor VOCs concentrations to these inhalation benchmarks. An additional 6 compounds had EPA oral reference doses (RfDs). However, because of differences in risk across exposure routes, we did not compare estimated inhalation exposures to the oral RfDs.

Cancer Risk Estimation: Among the 157 compounds evaluated, four (benzene, chloroform, ethylbenzene, and naphthalene) have been identified as carcinogens under California's Proposition 65 and have "Safe Harbor Levels," called No Significant Risk Levels (NSRLs) (OEHHA 2013), defined by OEHHA as the daily dose posing a one in 100,000 (10^{-5}) excess risk of cancer over a lifetime (OEHHA 2001). We computed child-specific NSRLs for these VOCs based on standard child body weights and respiration and adjusted for OEHHA age-specific sensitivity factors (ASF) of 10 for children < two years of age and 3 for children between the ages of two and six years (ATSDR 2005; Bradman et al. 2016; OEHHA 2001; U.S. EPA 2011b). Age-adjusted NSRLs were computed for four age groups: birth to <1 year; 1 to <2 years; 2 to <3 years; and 3 to <6 years. An age-adjusted NSRL is the estimated daily intake which contributes $1/70^{th}$ (assuming a 70-year lifetime) of the target lifetime cancer risk in that particular year of life. We then estimated children's daily dose estimates assuming the measurement was representative of exposure over one year, that a child spends five days per week and 48 weeks per year in childcare, and 100% absorption of the inhaled VOCs (ATSDR 2005). If the ratio of a child's VOC dose estimate (µg/day) to the age-adjusted NSRL (µg/day) is greater than 1, the dose estimate exceeded the 10^{-5} threshold. See SI Equations S1-S2 and Table S5 for more information.

Hazard Assessment for compounds without non-occupational health-based exposure benchmarks

For compounds that lacked non-occupational health-based exposure benchmarks (REL, RfC, or RfD) and had detection frequencies >60%, we reviewed information from online databases which aggregate information on chemical hazards from a broader set of authoritative lists, GoodGuide's ScoreCard and the Healthy Building Network's Pharos Project (Healthy Building Network 2014; ScoreCard 2011). We also applied quantitative structure-activity relationship (QSAR) models (Virtual models for property Evaluation of chemicals within a Global Architecture [VEGA]) to predict potential toxicity for mutagenicity, carcinogenicity, developmental toxicity, and skin sensitization for all compounds with good reliability scores (IRCCS 2014; Nendza et al. 2013) (See SI Hazard Assessment for further details). VEGA utilizes multiple models for some health endpoints and may yield contradictory predictions. When VEGA models produced contradictory predictions, we conservatively used the positive prediction for the health endpoint.

We classified the compounds into potential hazard groups based on findings from VEGA, ScoreCard, and Pharos, including: potential carcinogen or mutagen (Group 1), developmental toxicants (Group 2), reproductive toxicants (Group 3), endocrine disrupting chemicals (Group 4), neurotoxicants (Group 5), immunotoxicants/sensitizers (Group 6), specific organ or acute toxicants (Group 7), irritants (Group 8), persistent or bioaccumulative chemicals (Group 9), and no information (Group 10). To quantify the breadth of hazard data, we allotted a binary score to each group according to the presence or absence (score=1 or 0) of positive toxicity data. We summed the scores for each chemical, creating a cumulative "hazard score." We selected a hazard score of >3 to prioritize compounds for further review. We then evaluated chemical-specific information when available, including peer reviewed literature, summaries in the U.S. National Institute of Occupational (NIOSH) NIOSH Pocket Guide to Chemical Hazards (http://www.cdc.gov/niosh/npg/), Material Safety Data Sheets (MSDS), classification by the U.S. EPA Safer Choice Program (SCP), and independent reviews for final consideration of compounds

warranting further study. For example, we excluded propylene glycol because it has been independently reviewed as a food additive (ATSDR 1997).

RESULTS

ECE facility characteristics

Detailed ECE facility and child characteristics for this study have been published previously (Bradman et al. 2016). The programs served 1,764 children, with an average of 44 children per facility. Average outdoor and indoor air temperature (mean) ranged from 11.0-31.7°C (19.0) to 16.0-24.6°C (21.1), respectively. Average outdoor and indoor RH (mean) ranged from 21.6-74.7% (49.4) to 34.5-62.6% (49.3), respectively. See SI Tables S6–S8 for further information. The ECE facilities had an average AER of 1.7±1.3 hr^{-1} with a range of 0.3-5.6 hr^{-1}. Due to the moderate climate in California, natural ventilation (i.e. open windows) was often used. The AERs measured in this study were higher than rates reported in new California homes (median=1.31 versus 0.26 hr^{-1}, respectively) (Offermann 2009).

Targeted VOC Levels in Air

MMS VOCs: For the 15 MMS VOCs, the median indoor concentration ranged from 0.1 μg/m³ for 1,2,3-trimethylbenzene to 3.1 μg/m³ for toluene (Table 1). Seven compounds were detected in 100% of indoor samples – including toluene, ethylbenzene, and xylenes. Benzene was detected in 70.6% of samples. Many of the MMS VOCs were moderately to strongly correlated with each other (rho>0.35-0.84; SI Table S9). For example, benzene was significantly correlated with all the MMS VOCs ($r=0.42-0.84$, $p<0.05$). The MMS VOCs were detected more frequently indoors than outdoors (Tables 1 & 2 and SI Table S10), and 93% had significantly higher levels indoors than outdoors, with the mean I/O ratios ranging from 1.1 for benzene to 7.1 for 1,2,3-trimethylbenzene (Table 2), underscoring that several of these compounds also have indoor sources.

HS VOCs: For the 23 HS VOCs, the median indoor concentrations ranged from 0.1 for tetrachloroethylene to 51.4 μg/m³ for D5 (Table 1). The fragrance VOCs were frequently detected indoors with nine (of twelve) compounds detected in >90% of ECE facilities. D-limonene was detected in all facilities and had a median (range) of 33.1 $\mu g/m^3$ (0.8-81.5 $\mu g/m^3$). D5 had the highest median concentration (51.4 μg/m³, range: 2.6-88.2 $\mu g/m^3$). D4 also had a high detection frequency (90.9%) with a median concentration (range) of 0.9 $\mu g/m^3$ (0.1-78.5 $\mu g/m^3$). Many of the indoor HS VOC concentrations (SI Table S11) were also moderately correlated (rho>0.36), albeit less strongly than the MMS VOCs. HS VOCs were detected more frequently indoors than outdoors (n=20) (Tables 1 & 2). The mean I/O ratios for HS VOCs ranged from 1.3 (benzaldehyde) to 1,603.9 (d-limonene) and were higher than the MMS ratios, indicating that indoor sources were dominant for these compounds; 91% of the 23 HS VOCs had significantly higher levels indoors than outdoors (Table 2).

Determinants of targeted VOCs

MMS VOCs: Several indoor MMS VOC air concentrations (including benzene; n-heptane; n-hexadecane; n-tetradecane; toluene; and 1,2,4-trimethylbenzene) were inversely and significantly associated with AER (Spearman rho= -0.38 to -0.67, $p<0.05$, see SI Table S12). Three MMS VOCs, benzene, n-heptane, and n-hexadecane, were positively correlated with proximity to traffic (ΣLATV) (Spearman rho= 0.38-0.44, $p<0.05$). Five MMS VOCs were significantly lower ($p<0.05$) in centers compared to home-based facilities (ethylbenzene; n-octane; toluene; 1,2,4-trimethylbenzene; and xylenes). The presence/absence of gas appliances and attached garages in home-based facilities was not significantly associated with these compounds ($p<0.05$) and does not explain the difference by license type. Reported glue use was significantly associated with indoor levels of xylenes ($p<0.05$; Table S13).

HS VOCs: Butanal, hexanal, α-pinene, 2-ethyl-1-hexanol, and D4 were significantly and inversely associated with AER (Spearman rho= -0.42 to -0.62, $p<0.05$, See SI Table S14),

indicating indoor sources of these chemicals. Indoor concentrations of analytes found in fragrances (hexanal, decanal and D5) were significantly and positively correlated with reported air freshener use ($p<0.05$; SI Table S15). Levels of HS VOCs, including siloxanes, were similar in facilities that reported use/purchase of low-toxicity cleaners compared with those using traditional cleaners. However, D5 concentrations were significantly higher in facilities with higher mopping frequency, suggesting VOC emissions from the floor cleaners. Building type, vinyl flooring, carpet, and license type were not significantly associated with any HS VOCs.

Non-targeted VOC Levels in Air

Estimated levels of all 119 non-targeted VOC analytes are presented by chemical class in the SI (Table S16). For the 31 alkane compounds, median concentrations ranged from < MDL to 0.29 $\mu g/m^3$ for methylcyclohexane. For the 31 oxygenated hydrocarbon compounds, median concentrations ranged from <MDL to 7.36 $\mu g/m^3$ for propylene glycol. For the 34 aromatic compounds, median concentrations ranged from <MDL to 1.13 $\mu g/m^3$ for phenol. Naphthalene, a possible carcinogen, was detected in 96.9% of samples with a median concentration of 0.34 $\mu g/m^3$. Siloxane median concentrations ranged from <MDL to 1.89 $\mu g/m^3$ for dodecamethyl-cyclohexasiloxane (D6). For the 15 terpenes, median concentrations ranged from <MDL to 1.66 $\mu g/m^3$ for 2,6-dimethyl-7-octen-2-ol.

Health Risk Characterization

Non-cancer risk evaluation: Of the 10 targeted VOCs and six non-targeted VOCs with RELs or RfCs, none of the risk ratios exceeded one and were often much lower (see SI Tables S17 and S18).

Cancer risk evaluation: Table 3 presents the 50^{th} and 95^{th} percentile inhalation dose estimates compared to the age-adjusted NSRL values by age group. The 50^{th} and 95^{th} percentile dose estimates for benzene exceeded the age-specific NSRL in all four age groups assessed (ratio range: 1.8-17.4). The 95^{th} percentile dose estimates for chloroform exceeded the age-specific

NSRL in all four age groups assessed (ratio range=5.2-22.5). The 95th percentile dose estimates for ethylbenzene exceeded the age-adjusted NSRL in the three youngest age groups (ratio range=1.2-4.2). The 50th percentile dose estimates for ethylbenzene exceeded the age-adjusted NSRL in the two youngest age groups (ratio range=1.2-1.3). Among the non-targeted VOCs, only naphthalene is listed as a carcinogen by OEHHA (OEHHA 2013). Naphthalene NSRL ratios exceeded the age-specific NSRL in all age groups assessed (range: 1.6-22.4) (Table 3). If reflective of long-term averages, child dose estimates exceeded age-adjusted NSRL benchmarks for benzene, chloroform, ethylbenzene, and naphthalene in 71%, 38%, 56%, and 97% of facilities, with all facilities having exposures to at least one compound exceeding the respective NSRL.

Hazard Assessment and Prioritization for Future Study

Of the targeted VOCs without non-occupational health-based exposure benchmarks, two were excluded from detailed review due to lower detection frequency (<60%). Twenty-four of the remaining 25 compounds had positive toxicological information cited by PHAROS, Scorecard or QSAR predictions (See SI Tables S19 and S20). The 24 VOCs were distributed into respective hazard groups (Groups 1-9) as follows: 8% (n=2) for carcinogenicity or mutagenicity, 29% (n= 7) for developmental toxicity, 4% (n=1) for reproductive toxicity, 4% (n=1) for endocrine activity, 25% (n=6) for neurotoxicity, 58% (n=14) for immunotoxicity or sensitization, 71% (n=17) for specific organ or acute toxicity, 63% (n=15) for irritation, and 25% (n=6) for persistence or bioaccumulation (See SI Tables S19 and S21). Each hazard group is not mutually exclusive. We identified 7 compounds with hazard scores >3 for additional evaluation (Table 4): d-limonene; α-pinene; α-terpineol, 1,2,4-trimethylbenzene; D4; n-heptane; and heptanal. The persistent and bioaccumulative nature of cyclosiloxanes (D4 and D5) raises health concerns, especially given adverse reproductive effects reported in animals (Biomonitoring California 2008). These compounds are also listed as priority chemicals for biomonitoring by the California Biomonitoring Program (Biomonitoring California 2014). Thus, we recommend additional evaluation of D5

because of health concerns raised by OEHHA, and the high detection frequency and levels measured (Table 1) (OEHHA 2007).

Applying the same methods to the 119 non-targeted VOCs with no non-occupational health-based exposure benchmarks (SI Tables S22 & S23), we identified 4 additional compounds with hazard scores >3 for further evaluation: butyl ester acetic acid; camphor; n-pentane; 2-propenal, 3-phenyl- (see Table 4 and SI Table S24 for detailed hazard information).

In total, 12 compounds were identified for further review by the hazard analysis. Four of these– d-limonene, α-pinene, α-terpineol, and camphor– are terpenes. These products have natural sources, but are often concentrated in cleaning and other scented products. Levels of d-limonene were among the highest VOCs measured in the childcare facilities, and several information sources suggest health concerns about this compound (Table 4) (Kim et al. 2013). The U.S. EPA Safer Choice Program (SCP) has classified limonene and pinene with yellow triangles, indicating they have "hazard profile" concerns (U.S. EPA 2015). Camphor is used in air fresheners and other consumer products and in concentrated forms as an insect repellant and pesticide; it is a known hazard that has been associated with child poisoning (Khine et al. 2009). Terpenes can also react with ozone to form formaldehyde (Wolkoff et al. 2000), a known carcinogen, and ultrafine particles (Rohr et al. 2003), Given the high formaldehyde levels previously reported in these facilities (Bradman et al. 2016), additional research on the relative contributions of terpenes and other formaldehyde sources in daycare centers is needed to assess overall exposure and health risks and determine whether these compounds are significantly contributing to formaldehyde exposure.

The remaining 8 compounds identified for further review include: acetic acid, butyl ester; D4; D5; n-heptane; heptanal; n-pentane; 3-phenyl-2-propenal; and 1,2,4-trimethylbenzene. European agencies have set occupational exposure standards for 1,2,4-trimethylbenzene and n-heptane based on adverse developmental effects, and they both affect the respiratory and central nervous systems (Deutsche Forschungsgemeinschaft 2012). Heptanal is one of several fragrance-

related compounds we measured and is identified as a respiratory irritant in occupational settings with high exposures (HSDB 2013). Butyl ester acetic acid (SI Table S24; CAS #123-86-4) has natural sources and is used in air fresheners, cleaners, as a synthetic flavoring in foods, and in floor sealants and finishes (Healthy Building Network 2014). Although the hazard score for this compound was relatively high (6), aggregated information summarized in PHAROS and ScoreCard generally indicate only moderate hazards, and the median estimated levels were < 1 $\mu g/m^3$. However, its use in air fresheners and cleaners suggest the potential for widespread exposure as mixtures of fragrance-related compounds. Fragrances have been associated with reductions in lung function and other respiratory symptoms (Dales et al. 2013). Thus, additional research on low level exposure and chronic toxicities for these fragrance-related compounds is needed.

There are three compounds with hazard scores >3 that we did not prioritize in our assessment (dipropylene glycol monomethyl ether and 2-methylpropyl ester acetic acid, acetate 2-pentanol). 2-Methylpropyl ester acetic acid (SI Table S24; CAS #110-19-0) is a solvent used in a variety of coatings and also as a flavoring agent (Healthy Building Network 2014). Although the hazard score from our analysis was >3, aggregated information summarized in PHAROS and ScoreCard indicate only moderate hazards, and the U.S. EPA SCP classified this compound as a "green half-circle", indicating low concern but missing data. Similarly, aggregated information for dipropylene glycol monomethyl ether (DGME) (SI Table S24; CAS #34590-94-8), a solvent used in coatings and flooring, suggests some moderate hazards and contradicts the classification as a "green circle", or of low concern, by the U.S. EPA SCP. According to a 2001 review by the United Nations Environment Program (UNEP), one DGME isomer is a reproductive toxicant, but adverse effects were noted at exposures in animals at 1818 mg/m^3 to 2424 mg/m^3, with No Observed Adverse Effect Levels (NOAELs) from > 303 mg/m^3 to 1212 mg/m^3 (UNEP 2001). Applying uncertainty factors to these NOAELs would result in health-based exposure thresholds significantly higher than the levels we measured. Thus, we did not prioritize this compound for further research.

Levels of acetate 2-pentanol (CAS #626-38-0) were very low (<1 μg/m^3) and this substance is listed as a food ingredient by the U.S. Food and Drug Administration. At very high exposures, effects on skin, the respiratory system, and central nervous system are noted, but at many orders of magnitude above the levels we estimated (median=0.06 μg/m^3 versus a NIOSH REL of 650 mg/m^3). Thus, we also did not prioritize this compound for further research.

In summary, this initial screening identified 12 VOCs without non-occupational health-based exposure benchmarks in these ECE facilities that warrant additional exposure and hazard assessment. Recommendations for follow-up of these and other measured VOCs are discussed below.

DISCUSSION

This is the first study to report on a wide array of VOCs in U.S. early childhood and education environments. Among the chemicals with established non-cancer health-based inhalation benchmarks, there were no concentrations that exceeded acceptable thresholds. However, if reflective of long-term averages, child dose estimates exceeded age-adjusted NSRL benchmarks for benzene, chloroform, ethylbenzene, and naphthalene in 71%, 38%, 56%, and 97% of facilities, respectively. All facilities had exposures to at least one compound exceeding the respective NSRL. It is likely that our risk characterization underestimates total risk to the children since they are likely exposed to these chemicals in other indoor and outdoor environments (Jia et al. 2008; Offermann 2009).

A strength of this study was the successful application of AMDIS software combined with NIST mass spectral libraries to identify numerous chemicals not previously measured in ECE facilities or other indoor environments. Among all the compounds we initially targeted or subsequently identified, the vast majority did not have non-occupational health-based exposure benchmarks relevant to young children. However, based on the application of QSAR models and

extensive review of aggregated health information for all VOCs measured, we identified 12 compounds that warrant additional research on exposure and health risks (acetic acid, butyl ester; camphor; D4; D5; n-heptane; heptanal; d-limonene; n-pentane; 3-phenyl-2-propenal; α-pinene; α-terpineol; 1,2,4-trimethylbenzene). These include commonly used terpenes and fragrance-related compounds, which have been associated with respiratory or other health problems (Dales et al. 2013; HSDB 2013; Khine et al. 2009; Kim et al. 2013; Wolkoff et al. 2000). Future studies examining VOC exposures in ECE facilities should target these compounds, as well as other compounds where exposures exceeded exposure benchmarks based on carcinogenicity (benzene, chloroform, ethylbenzene, and naphthalene).

Consistent with other studies, overall, indoor levels were higher than outdoor levels, indicating that indoor sources predominated. For compounds with both indoor and outdoor sources (e.g. BTEX compounds), the I/O ratios were relatively low and several were associated with nearby traffic density, indicating that outdoor sources contributed to indoor contamination in some cases. We also observed a significant positive association between xylenes and reported use of cement glue, epoxy, or super glue, consistent with xylene's use in adhesives (McLafferty and Turecek 1993). For household source VOCs (with primarily indoor sources), we observed significant positive associations between D5, hexanal, and decanal with air fresheners, and D5 with mopping frequency, consistent with their use as fragrances and solvents in consumer products (Marsili 2001).

In general, the VOC levels in the child care facilities were within the range of measurements in other child indoor environments (Offermann 2009). For example, average indoor air concentrations of BTEX compounds ranged from 0.7 to 4.1 μg/m³ compared to mean levels in California classrooms that ranged from 0.41 to 6.32 μg/m³ (Whitmore 2003). Overall, median indoor air levels of benzene, 2-butoxyethanol, chloroform, naphthalene and xylenes were similar to or slightly higher in the ECE facilities compared to those measured in new California homes (Offermann 2009). In contrast, levels of d-limonene (median=33 $\mu g/m^3$) were higher than

concentrations reported in new California homes (median=11 μg/m^3) (Offermann 2009), likely due to frequent cleaning in child care (Steinemann 2009). The D5 levels we observed (mean=46 μg/m^3) were also higher than measurements in U.S. office buildings (mean=3 μg/m^3) (Yucuis et al. 2013). D5 is frequently used as a solvent for blending fragrance oil, and is often present in air fresheners and cleaning fluids (Biomonitoring California 2008; Maddalena et al. 2011). The I/O ratios for d-limonene and D5 were extremely high, underscoring the predominance of indoor sources.

Limitations of this study include the sample size and the 8-hour sample collection period. Although it is the largest study to date reporting on a wide variety of VOCs in U.S. ECE facilities, our original sample size of 40 facilities was reduced to 34 for most measurements due to analytical challenges, limiting our statistical power to build multivariable models and draw inferences. Also, the samples were collected during a single day and may not reflect long-term levels. Limitations related to our use of CO_2 as a tracer gas to estimate AERs (Bartlett et al. 2004; Bekö et al. 2010) has been described previously (Bradman et al. 2016). Further, the sources of indoor air contaminants are ubiquitous and difficult to disentangle, and thus may not have been fully captured in our questionnaire and inspection data.

The lack of toxicological information for many of the chemicals we measured is another limitation. For example, QSAR programs are constrained by the availability of toxicological data for reference chemicals adequate to making accurate hazard predictions. Insufficient VEGA reliability scores limited our capacity to judge whether some compounds pose health hazards and warrant additional study. Similarly, the databases we used that aggregate toxicological information may not be complete, and may not consider proprietary information or government or other reports that are not published in the peer-reviewed literature (Healthy Building Network 2014; ScoreCard 2011).

In summary, child exposures for benzene, chloroform, ethylbenzene, and/or naphthalene exceeded California Safe Harbor Levels for cancer in all of the ECE facilities tested. More exposure

research is needed on these compounds to clarify the long-term risks to children. While exposures to 16 of the VOC compounds we measured were below non-cancer health benchmarks, more than 70% of the compounds lacked any health-based exposure standards that could be used to characterize potential risks. Based on databases aggregating toxicological information and the application of QSAR modeling methods, we identified 12 chemicals without health benchmarks that warrant additional exposure and health evaluation due to the potential for carcinogenic or neurologic effects and other health effects. Our findings demonstrate that potentially harmful VOC exposures are occurring in ECE environments, and indicate that more research is needed to fully assess the potential health risks to young children and adult staff and identify major sources of VOCs present in ECE centers. If warranted, restrictions on the use of some compounds should be considered as well as outreach to child care providers on strategies to improve indoor air quality, such as ensuring proper ventilation, to mitigate these exposures.

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Table 1. Distributions of Indoor Air Concentrations for 38 Targeted VOCs (μg/m³) (n=34 ECE facilities).[a]

Analyte	>MDL (%)	Geometric Mean±GSD	Arithmetic Mean±SD	25th %	Median	75th %	95th %	Max
Mixed and Mobile Sources								
Benzene	70.6	0.8±0.5	0.9±0.5	<MDL	0.9	1.0	2.0	2.6
Butylbenzene	17.7	<MDL	<MDL	<MDL	<MDL	<MDL	0.1	0.2
n-Decane[b]	90.9	0.6±0.9	0.8±0.9	0.4	0.6	1.0	3.0	4.5
n-Dodecane	91.2	0.8±0.9	1.1±1.1	0.4	0.7	1.6	2.8	5.0
Ethylbenzene	100.0	0.5±0.8	0.7±0.6	0.3	0.6	1.0	2.0	2.0
n-Heptane	100.0	1.5±1.2	3.0±4.1	0.5	1.5	3.5	10.9	19.8
n-Hexadecane	100.0	0.9±0.6	1.0±0.7	0.6	0.8	1.2	2.4	4.1
n-Hexane	58.8	0.7±0.8	0.9±0.9	<MDL	0.6	1.0	2.9	3.6
n-Octane	100.0	0.7±0.6	0.8±0.8	0.5	0.6	1.1	1.8	4.3
n-Tetradecane	100.0	2.1±0.9	3.1±3.3	1.1	1.9	4.0	7.7	17.3
Toluene	100.0	3.2±0.7	4.1±3.0	1.7	3.1	5.5	11.2	12.4
1,2,3-Trimethylbenzene	64.7	0.1±1.2	0.2±0.2	<MDL	0.1	0.3	0.7	1.0
1,2,4-Trimethylbenzene	97.1	0.5±0.9	0.7±0.6	0.3	0.5	0.9	2.3	2.7
n-Undecane	85.3	0.6±0.9	0.9±1.0	0.3	0.6	0.9	3.3	4.6
Xylenes	100.0	2.2±0.9	3.2±2.7	1.0	2.5	4.8	9.2	9.4
Household Sources								
Fragrances								
Benzaldehyde	100.0	2.7±0.5	3.0±1.7	2.0	2.4	3.8	5.7	9.4
Butanal	100.0	0.7±0.5	0.8±0.4	0.5	0.7	0.9	1.6	2.0
3-Carene	82.4	0.2±1.4	0.5±0.7	0.1	0.2	0.6	1.8	3.0
Decanal[f]	94.1	2.5±1.2	4.3±4.7	1.6	2.6	4.7	18.2	22.0
Heptanal	97.1	0.9±0.7	1.1±0.5	0.8	1.0	1.3	2.1	2.7
Hexanal[f]	100.0	6.3±0.6	7.7±5.4	3.9	5.7	10.0	20.9	22.5
d-Limonene	100.0	23.1±1.2	37.3±28.1	9.1	33.1	>68.7[c]	>74.9[c]	>81.5[c]
Nonanal	100.0	8.4±0.4	9.1±3.5	6.5	8.5	10.3	15.6	16.0

Table 1 (cont.) Distributions of Indoor Air Concentrations for 38 Targeted VOCs (μg/m³) (n=34 ECE facilities).[a]

Analyte	>MDL (%)	Geometric Mean±GSD	Arithmetic Mean±SD	25th %	Median	75th %	95th %	Max
Octanal[f]	100.0	2.1±0.4	2.3±1.0	1.7	2.1	2.5	5.3	5.7
α-Pinene	100.0	3.7±1.0	6.4±10.0	1.7	3.6	6.4	19.9	57.7
α-Terpineol[g]	85.3	0.5±1.6	1.8±4.2	0.3	0.4	1.9	6.4	24.1
ɣ-Terpinene[f]	61.8	0.2±1.8	0.7±1.4	<MDL	0.3	0.4	4.8	7.1
Other household sources								
2-Butoxyethanol	100.0	4.7±1.2	10.9±19.4	1.8	2.9	8.6	>64.0[c]	>92.4[c]
Carbon tetrachloride	2.9	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	2.1
Chloroform	38.2	0.6±1.0	1.3±2.6	<MDL	<MDL	0.8	7.7	12.6
Decamethylcyclopentasiloxane (D5)	100.0	34.0±0.9	46.4±28.2	17.4	51.4	>70.8[c]	>83.6[c]	>88.2[c]
2-Ethyl-1-hexanol	100.0	1.7±0.5	1.9±1.0	1.1	1.6	2.8	3.9	3.9
Hexamethylcyclotrisiloxane (D3)	50.0	2.3±0.7	3.0±2.3	<MDL	1.5	4.6	8.0	9.3
Methylene chloride	2.9	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	0.5
Octamethylcyclotetrasiloxane (D4)[b]	90.9	1.4±1.7	7.4±18.1	0.5	0.9	2.9	>70.9[c]	>78.5[c]
Tetrachloroethylene[b]	51.5	0.1±1.1	0.4±1.3	<MDL	0.1	0.2	1.0	7.8
Texanol[d]	100.0	5.0±1.0	8.7±12.0	2.4	4.6	8.6	32.7	60.7
TXIB[e]	100.0	4.6±0.9	7.7±13.8	2.3	4.7	7.9	14.1	82.8

[a] If indoor concentrations <MDL, values were inputed as MDL/√2.
[b] All VOCs were analyzed in 34 samples, except for decane, D4, and terachloroethylene (n=33 samples).
[c] Denotes when the highest calibration range was used as analyte mass to calculate sample concentration. Values underestimate the true air concentrations.
[d] Texanol: 2,2,4-trimethyl-1,3-pentanediol monoisobutyrate
[e] TXIB: 2,2,4-trimethyl-1,3-pentanediol diisobutyrate.
[f] U.S. EPA SCP "yellow triangle" rating: The chemical has met Safer Choice Criteria for its functional ingredient-class, but has some hazard profile issues.
[g] U.S. EPA SCP "green half-circle" rating: The chemical is expected to be of low concern based on experimental and modeled data (U.S. EPA 2015).

Table 2. Outdoor VOC Concentrations (µg/m^3) and Indoor-to-Outdoor (I/O) Ratios.[a]

	Outdoor (n=20)		I/O Ratios	
Analyte	**>MDL (%)**	**Median**	**Mean Ratio±SD**	**Range**
Mixed and Mobile Sources				
Benzene	75.0	0.6	1.1±0.5	0.5-2.7
Butylbenzene	0.0	<MDL	1.4±1.3*	0.6-6.7
n-Decane	30.0	<MDL	9.0±11.5*	1.1-48.8
n-Dodecane	0.0	<MDL	7.7±8.2*	0.6-35.0
Ethylbenzene	65.0	0.1	6.7±7.1*	1.0-25.4
n-Heptane	85.0	0.4	4.2±4.3*	1.0-17.0
n-Hexadecane	5.0	<MDL	19.8±14.6*	5.2-62.2
n-Octane	60.0	0.1	8.2±6.1*	1.4-21.1
n-Tetradecane	10.0	<MDL	59.4±47.2*	17.5-164.9
Toluene	100.0	0.9	3.4±2.4*	1.3-9.7
1,2,3-Trimethylbenzene	25.0	<MDL	7.1±11.1*	0.3-37.6
1,2,4-Trimethylbenzene	60.0	0.1	5.5±4.5*	0.7-15.5
n-Undecane	5.0	<MDL	6.1±7.3*	0.6-29.1
Xylenes	100.0	0.6	4.9±6.0*	0.8-25.1
Household Sources				
Fragrances				
Benzaldehyde	100.0	2.3	1.3±0.6	0.3-2.5
Butanal	25.0	<MDL	13.6±9.6*	3.9-45.8
3-Carene	0.0	<MDL	24.8±31.5*	1.1-126.4
Decanal	55.0	0.1	39.3±35.3*	2.7-140.3
Heptanal	15.0	<MDL	26.0±10.2*	7.4-43.3
Hexanal	80.0	0.2	44.3±31.7*	9.3-119.1
d-Limonene	5.0	<MDL	1603.9±1481*	81.7-4015
Nonanal	95.0	.02	42.9±36.7*	5.6-167.8
Octanal	55.0	0.1	25.0±13.2*	8.8-54.1
α-Pinene	45.0	<MDL	59.9±62.8*	5.6-230.6
α-Terpineol	0.0	<MDL	34.3±51.1*	1.1-172.8
ɣ-Terpinene	0.0	<MDL	16.6±24.1*	0.9-84.0

Table 2 (cont.) Outdoor VOC Concentrations (µg/m^3) and Indoor-to-Outdoor (I/O) Ratios.[a]

	Outdoor (n=20)		I/O Ratios	
Analyte	**>MDL (%)**	**Median**	**Mean Ratio±SD**	**Range**
Other household sources				
2-Butoxyethanol	20.0	<MDL	88.4±85.7*	23.1-375.0
Carbon tetrachloride	0.0	<MDL	1.2±0.2*	0.6-1.4
Chloroform	0.0	<MDL	6.2±11.1*	0.9-38.1
Decamethylcyclopentasiloxane (D5)	95.0	0.3	159.8±129.9*	28.7-457.0
2-Ethyl-1-hexanol	5.0	<MDL	41.6±22.9*	15.0-101.2
Hexamethylcyclotrisiloxane (D3)	25.0	<MDL	1.4±1.1	0.4-5.3
Methylene chloride	0.0	<MDL	1.2±0.2*	0.6-1.4
Octamethylcyclotetrasiloxane (D4)	35.0	<MDL	67.3±177.6*	0.7-785.5
Tetrachloroethylene	30.0	<MDL	1.9±1.6*	0.4-6.5
Texanol	10.0	<MDL	278.7±435.8*	6.6-1,832
TXIB	10.0	<MDL	116.6±83.5*	11.2-324.5

*p<0.05 from Wilcoxon matched-pairs signed ranks test comparing indoor and outdoor VOC concentrations.

[a]If VOC concentrations were <MDL, values were imputed as MDL/√2 and used for analyses.

Table 3. Inhalation VOC Dose Estimates Compared to $NSRL_{child\ (age\ group)}$.

Analyte	Age Group	Dose Estimates (µg/day) Median	Dose Estimates (µg/day) 95th %	$NSRL_{child}$ (µg/day)	Ratio Median	Ratio 95th %
Targeted						
Benzene	Birth to <1 year	1.0	2.3	0.1	7.4	17.4
	1 to <2 years	1.5	3.6	0.2	7.1	16.8
	2 to <3 years	1.8	4.2	0.9	2.1	4.9
	3 to <6 years	2.0	4.8	1.2	1.8	4.2
Chloroform	Birth to <1 year	NC	8.7	0.4	NC	22.5
	1 to <2 years	NC	13.6	0.7	NC	20.9
	2 to <3 years	NC	16.2	2.6	NC	6.1
	3 to <6 years	NC	18.5	3.5	NC	5.2
Ethylbenzene	Birth to <1 year	0. 7	2.2	0.5	1.3	4.2
	1 to <2 years	1.1	3.5	0.9	1.2	3.9
	2 to <3 years	1.3	4.1	3.5	0.4	1.2
	3 to <6 years	1.4	4.7	4.8	0.3	1.0
Non-targeted						
Naphthalene[a]	Birth to <1 year	0.38	1.3	0.06	6.9	22.4
	1 to <2 years	0.60	2.0	0.09	6.4	20.9
	2 to <3 years	0.83	2.7	0.38	2.2	7.2
	3 to <6 years	0.82	2.7	0.51	1.6	5.2

NC: not calculated.
NSRLs are available for carbon tetrachloride and methylene chloride, but are not included here due to low detection frequencies (>MDL=3%).

[a] To measure naphthalene, we applied a modified toluene equivalent mass calibration to compute semi- quantitative estimates of its mass (see "*Identification and quantification of unknown VOCs*" above.)

Table 4. Summary of Potential Health Concerns for VOCs Warranting Additional Evaluation.[a]

Analyte	PHAROS[b]	ScoreCard[c]	VEGA[d]	Hazard Score
Mixed and Mobile Sources				
n-Heptane	Developmental Toxicant, Irritant, Neurotoxicant, Respiratory Toxicant, Acute Toxicant	Neurotoxicity	Non-Mutagen	5
n-Pentane	Acute Toxicant, Developmental Toxicant, Neurotoxicant, Persistent, Respiratory Toxicant, Specific Organ Toxicant	Neurotoxicity	Non-Mutagen	5
Household Sources				
Fragrances				
Acetic acid, butyl ester	Acute Toxicant, Developmental Toxicant, Neurotoxicant, Persistent, Specific Organ Toxicant	Gastrointestinal or Liver Toxicity, Neurotoxicity, Respiratory Toxicity, Skin or Sense Organ Toxicity	Non-Mutagen, Sensitizer	6
Heptanal	Irritant, Acute Toxicant	Neurotoxicity	[Non-Mutagen], Skin Sensitizer	4
d-Limonene	Developmental Toxicant, PBT, Skin Sensitizer, Suspected Asthmagen, Irritant (eye, skin), Acute Toxicant	Gastrointestinal or Liver Toxicity, Immunotoxicity, Kidney Toxicity, Neurotoxicity, Respiratory Toxicity, Skin or Sense Organ Toxicity	[Non-Mutagen], [Skin Sensitizer]	6
α-Pinene	Bioaccumulative, Irritant, Acute Toxicant	Neurotoxicity, Respiratory Toxicity, Skin or Sense Organ Toxicity	[Non-Mutagen], Developmental Toxicant, Skin Sensitizer	6
2-Propenal, 3-phenyl-	Acute Toxicant, Developmental Toxicant, Reproductive Toxicant, Skin Sensitizer	Immunotoxicity, Neurotoxicity, Skin or Sense Organ Toxicity	[Non-Mutagen], Non-Carcinogen, [Sensitizer]	5
α-Terpineol[e]	Irritant, Acute Toxicant	Data lacking	[Non-Mutagen], Developmental Toxicant, Skin Sensitizer	4

Table 4 (Cont.) Summary of Potential Health Concerns for Targeted VOCs Warranting Additional Evaluation.[a]

Analyte	PHAROS[b]	ScoreCard[c]	VEGA[d]	Hazard Score
1,2,4-Trimethylbenzene	Developmental Toxicant, Irritant (eye, skin, lungs), Acute Toxicant (inhalation)	Cardiovascular or Blood Toxicity, Neurotoxicity, Respiratory Toxicity	[Non-Mutagen], [Carcinogen], Sensitizer	6
Other household products				
Camphor	Acute Toxicant, Reproductive Toxicant, Specific Organ Toxicant	Gastrointestinal or Liver Toxicity, Neurotoxicity, Respiratory Toxicity, Skin or Sense Organ Toxicity	Sensitizer, [Developmental Toxicant]	5
Decamethylcyclopentasiloxane (D5)	PBT	Data lacking	Data lacking	1
Octamethylcyclotetrasiloxane (D4)	PBT (high priority), Reproductive Toxicant, EDC, Acute Toxicant	Gastrointestinal or Liver Toxicity	Data lacking	4

Abbreviations: Persistent Bioaccumulative Toxicant (PBT); Endocrine Disrupting Compound (EDC).

[a]Compounds with a hazard score >3, except for D5, which was prioritized due to potential health concerns raised by California OEHHA (OEHHA 2007) and high concentration measurements.
[b]Acute toxicant is listed as "Toxic to Mammals" in PHAROS.
[c]Suspected effects.
[d]Brackets indicate experimental data.
[e]U.S. EPA SCP "green half circle" rating: The chemical is expected to be of low concern based on experimental and modeled data (U.S. EPA 2015).

REFERENCES

ATSDR. 1997. Agency for Toxic Substances and Disease Registry. Toxicological profile for Propylene Glycol. Atlanta, GA.

ATSDR. 2004. Interaction Profile for: Benzene, Toluene, Ethylbenzene, and Xylenes (BTEX).Agency for Toxic Substances and Disease Registry. Atlanta, GA.

ATSDR. 2005. Public Health Assessment Guidance Manual. Agency for Toxic Substances and Disease Registry. Atlanta, GA.

Bartlett KH, Martinez M, Bert J. 2004. Modeling of occupant-generated CO2 dynamics in naturally ventilated classrooms. J Occup Environ Hyg 1(3): 139-148.

Bearer CF. 1995. How are children different from adults? Environ Health Perspect 103 Suppl 6: 7-12.

Bekö G, Lund T, Nors F, Toftum J, Clausen G. 2010. Ventilation rates in the bedrooms of 500 Danish children. Build Environ 45(10): 2289-2295.

Biomonitoring California. 2008. Cyclosiloxanes. Available: http://www.biomonitoring.ca.gov/sites/default/files/downloads/1208cyclosiloxanes.pdf [accessed accessed Jan 10, 2015].

Biomonitoring California. 2014. Priority Chemicals. Available: http://www.biomonitoring.ca.gov/chemicals/priority-chemicals [accessed Nov 30, 2015].

Bradman A, Gaspar F, Castorina R, Maddalena R, Tong-Lin E, McKone TE. Environmental Exposures in Early Childhood Education Environments, Final Report to California Air Resources Board; Sacramento, CA. Contract Number 08-305. 2012. http://www.arb.ca.gov/research/single-project.php?row_id=64830.

Bradman A, Gaspar F, Castorina R, Williams J, Hoang T, Jenkins P, et al. 2016. Formaldehyde and Acetaldehyde Exposure and Risk Characterization in California Early Childhood Education Environments. Indoor Air Jan 25. DOI 10.1111/ina.12283. [Epub ahead of print].

Breysse P, Farr N, Galke W, Lanphear B, Morley R, Bergofsky L. 2004. The relationship between housing and health: children at risk. Environ Health Perspect 112(15): 1583-1588.

CDC. Centers for Disease Control and Prevention. NIOSH Pocket Guide to Chemical Hazards. National Institue for Occupational Safety and Health. 2010. http://www.cdc.gov/niosh/npg/ [Accessed 12 December 2015].

CDPH. 2007. California Department of Public Health, Environmental Health Investigation Branch, CEHTP Traffic Linkage Service Demonstration. Available: http://www.ehib.org/traffic_tool.jsp#sol.

Choi H, Schmidbauer N, Sundell J, Hasselgren M, Spengler J, Bornehag CG. 2010. Common household chemicals and the allergy risks in pre-school age children. PloS one 5(10): e13423.

Cooper SD, Raymer JH, Pellizzari ED, Thomas KW. 1995. The identification of polar organic compounds found in consumer products and their toxicological properties. J Expo Anal Environ Epidemiol 5(1): 57-75.

Dales RE, Cakmak S, Leech J, Liu L. 2013. The association between personal care products and lung function. Annals of epidemiology 23(2): 49-53.

Destaillats H, Lunden MM, Singer BC, Coleman BK, Hodgson AT, Weschler CJ, et al. 2006. Indoor secondary pollutants from household product emissions in the presence of ozone: a bench-scale chamber study. Environ Sci Technol 40(14): 4421-4428.

Deutsche Forschungsgemeinschaft. 2012. List of MAK and BAT Values 2012. (Maximum Concentrations and Biological Tolerance Values at the Workplace). 48. Weinheim, Germany:Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area.

FIFCFS. 2013. Federal Interagency Forum on Child and Family Statistics. America's Children: Key National Indicators of Well-being: Child Care. Available: http://www.childstats.gov/ [accessed accessed Feb 7, 2015.
Healthy Building Network. 2014. PharosProject. Available: https://www.pharosproject.net/ [accessed accessed Feb 12, 2014.
Hodgson AT. 1995. A Review and a Limited Comparison of Methods for Measuring Total Volatile Organic Compounds in Indoor Air. Indoor Air 5(4): 247-257.
Hornung RW, Reed LD. 1990. Estimation of average concentration in the presence of nondetectable values. Appl Occup Environ Hyg 5: 46-51.
HSDB. 2013. U.S. National Library of Medicine. Hazardous Substances Data Bank (HSDB), Bethesda, MD. Available: http://toxnet.nlm.nih.gov/newtoxnet/hsdb.htm [accessed accessed Nov 13, 2013.
IRCCS. 2014. Istituto di Ricerche Farmacologiche Mario Negri. Virtual models for property Evaluation of chemicals within a Global Architecture (VEGA). Available: http://www.vega-qsar.eu/ [accessed accessed June 2, 2014.
Jia C, Batterman S, Godwin C. 2008. VOCs in industrial, urban and suburban neighborhoods, Part 1: Indoor and outdoor concentrations, variation, and risk drivers. Atmospheric Environment 42(9): 2083-2100.
Khine H, Weiss D, Graber N, Hoffman RS, Esteban-Cruciani N, Avner JR. 2009. A cluster of children with seizures caused by camphor poisoning. Pediatrics 123(5): 1269-1272.
Kim YW, Kim MJ, Chung BY, Bang du Y, Lim SK, Choi SM, et al. 2013. Safety evaluation and risk assessment of d-Limonene. Journal of toxicology and environmental health Part B, Critical reviews 16(1): 17-38.
Laughlin L. 2013. Who's Minding the Kids? Child Care Arrangements: Spring 2011. P70-135. Washington, DC.
Linstrom P, Mirokhin Y, Tchekhovskoi D, Yang X. 2014. NIST/EPA/NIH Mass Spectral Library and NIST Mass Spectral Search Program. Gaithersburg, MD: The NIST Mass Spectrometry Data Center.
Maddalena RL, McKone TE, Destaillats H, Russell M, Hodgson AT, Perino C. 2011. Quantifying pollution emissions from office equipment: a concern in energy-efficient buildings. CEC-500-2011-046. Sacramento, CA:California Air Resources Control Board, California Department of Health Services, and RTI International.
Marsili R. 2001. Flavor, Fragrance, and Odor Analysis. Boca Raton, FL: CRC Press.
McLafferty FW, Turecek F. 1993. Interpretation of Mass Spectra. 4 ed. Sausalito, CA: University Science Books.
Mendes A, Aelenei D, Papoila AL, Carreiro-Martins P, Aguiar L, Pereira C, et al. 2014. Environmental and ventilation assessment in Child Day Care Centers in Porto: the ENVIRH Project. Journal of toxicology and environmental health Part A 77(14-16): 931-943.
Nendza M, Gabbert S, Kuhne R, Lombardo A, Roncaglioni A, Benfenati E, et al. 2013. A comparative survey of chemistry-driven in silico methods to identify hazardous substances under REACH. Regul Toxicol Pharm 66(3): 301-314.
OEHHA. 2001. Proposition 65: Process for Developing Safe Harbor Numbers. California Office of Environmental Health Hazard Assessment. Sacramento, CA.
OEHHA. 2007. Toxicity Data Review: Decamethylcyclopentasiloxane (D5). California Office of Environmental Health Hazard Assessment. Sacramento, CA.
OEHHA. 2013. Proposition 65: No Significant Risk Levels (NSRLs) for Carcinogens and Maximum Allowable Dose Levels (MADLs) for Chemicals Causing Reproductive Toxicity. California Office of Environmental Health Hazard Assessment. Sacramento, CA.
OEHHA. 2014. All OEHHA Acute, 8-hour and Chronic Reference Exposure Levels (chRELs) as of June 2014. Available: http://www.oehha.ca.gov/air/Allrels.html [accessed accessed Nov 13, 2014.

Offermann FJ. 2009. Ventilation and Indoor Air Quality in New Homes. PIER Collaborative Report. CEC-500-2009-085. Sacramento, CA:California Air Resources Board and California Energy Commission.
Rohr AC, Weschler CJ, Koutrakis P, Spengler JD. 2003. Generation and quantification of ultrafine particles through terpene/ozone reaction in a chamber setting. Aerosol Sci Tech 37(1): 65-78.
ScoreCard. 2011. Chemical Profiles. Available: http://scorecard.goodguide.com/chemical-profiles/ [accessed accessed Nov 13, 2013.
Seltenrich N. 2013. Environmental exposures in the context of child care. Environ Health Perspect 121(5): a160-165.
St-Jean M, St-Amand A, Gilbert NL, Soto JC, Guay M, Davis K, et al. 2012. Indoor air quality in Montréal area day-care centres, Canada. Environ Res 118(0): 1-7.
Steinemann AC. 2009. Fragranced consumer products and undisclosed ingredients. Environ Impact Asses 29(1): 32-38.
NIH. National Institutes of Health. National Center for Biotechnology Information. PubChem. http://pubchem.ncbi.nlm.nih.gov/compound/8038#section=Top [Accessed 10 December 2015].
U.S. EPA. 1999. Determination of Volatile Organic Compounds in Ambient Air Using Active Sampling Onto Sorbent Tubes. (Compendium of Methods for the Determination of Toxic Organic Compounds in Ambient Air). Cincinatti:Center for Environmental Research Information, Office of Research and Development,.
U.S. EPA. 2005. Toxicological Review of Toluene (CAS No. 108-88-3). (In Surpport of Summary Information on the Integrated Risk Information system (IRIS)).US Environmental Protection Agency.
U.S. EPA. 2011a. Background Indoor Air Concentrations of Volatile Organic Compounds in North American Residences (1990-2005): A Compilation of Statistics for Assessing Vapor Intrusion. EPA 530-R-10-001. Washington DC.
U.S. EPA. 2011b. Exposure Factors Handbook 2011 Edition (Final). EPA/600/R-09/052F. Washington, DC:U.S. Environmental Protection Agency.
U.S. EPA. 2013. Integrated Risk Information System (IRIS). Available: http://www.epa.gov/IRIS/ [accessed accessed Nov 13, 2013.
U.S. EPA. 2015. Safer Choice. Safer Chemical Ingredient's List (SCIL). http://www.epa.gov/saferchoice/safer-ingredients#scil (accessed December 12, 2015).
U.S. FDA. Food and Drug Administration. Substance Registration System. Unique identifier. UNII B570113U4Q. http://fdasis.nlm.nih.gov/srs/ [accessed December 12, 2015].
UNEP. United National Environment Program. Organisation for Economic Co-operation and Development (OECD). Screening Information Dataset (SIDS). Dipropylene glycol methyl ether. SIDS Initial Assessment Report for 12th SIAM (Paris, France, 27-29 June 2001). http://www.inchem.org/documents/sids/sids/34590-94-8.pdf.
Whitmore R. 2003. California Portable Classrooms Study Phase II: Main Study, Final Report, Vol II. Contract No. 00-317. Sacramento, CA:California Air Resources Control Board, California Department of Health Services, and RTI International.
Wolkoff P, Clausen PA, Wilkins CK, Nielsen GD. 2000. Formation of Strong Airway Irritants in Terpene/Ozone Mixtures. Indoor Air 10(2): 82-91.
Yucuis RA, Stanier CO, Hornbuckle KC. 2013. Cyclic siloxanes in air, including identification of high levels in Chicago and distinct diurnal variation. Chemosphere 92(8): 905-910.
Zuraimi MS, Tham KW. 2008. Effects of child care center ventilation strategies on volatile organic compounds of indoor and outdoor origins. Environ Sci Technol 42(6): 2054-2059.

Supporting Information

VOC Exposures in California Early Childhood Education Environments

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LABORATORY ANALYSES

Glass sorbent tubes were thermally desorbed for analysis by gas chromatography (GC)/mass spectrometry (MS) using a thermodesorption auto-sampler (Model TDSA2; Gerstel), thermodesorption oven (Model TDS3, Gerstel), and cooled injection system (Model CIS4; Gerstel) fitted with a Tenax-packed glass liner (P/N 013247-005-00; Gerstel). Desorption temperatures of 25°C with a 0.5-minute delay followed by a 60°C/min ramp to 250°C and a 4-minute hold time were used. The cryogenic trap is held at -10°C and then heated within 0.2 minutes to 270°C at a rate of 12°C/s, followed by a 3-minute hold time. Analytes were resolved on a GC (Series 6890Plus; Agilent Technologies) equipped with a 30 meter HP-1701 14% Cyanopropyl Phenyl Methyl polysiloxane column (Model 19091U-233; Agilent Technologies) at an initial temperature of 1°C for 0.5 minutes then ramped to 40°C at 25°C/min, to 115°C at 3°C/min and finally to 250°C at 10°C/min, holding for 10 minutes. The resolved analytes were detected using an electron impact MS system (5973; Agilent Technologies) operated in scan mode.

Method Detection Limits and Calibration Ranges for VOC Analytes

Calibration standards were prepared from liquid standars. Calibration ranges are the low and high masses from laboratory prepared standards. Method detection limits (MDLs) and low/high calibration masses are converted to μg/m³ by dividing the mass by the average sample volume collected in this study for indoor VOC measurements (~7 liters). VOC MDLs ranged from 0.03 μg/m³ to 1.80 μg/m³. See Table S1 below. VOC high mass calibrations ranged from 56 to 92 μg/m³ and low mass calibrations ranged from 0.5 to 1 μg/m³. For four compounds (D4 and D5 siloxanes, d-limonene, and 2-butoxyethanol) in 29 cases, the VOC levels were above the calibration high mass. In those cases, the mass above the range was substituted with the high calibration mass.

Table S1. MDL and calibration ranges for VOC analytes[a]

Analyte	Mass MDL (ng)	Concentration MDL (µg/m³)	Low Mass Calibration (µg/m³)	High Mass Calibration (µg/m³)
Benzaldehyde	1.90	0.27	0.5	74
Benzene	4.08	0.58	0.9	56
Butanal	0.45	0.06	0.5	74
2-Butoxyethanol	0.52	0.07	0.5	76
Butylbenzene	0.26	0.04	0.5	73
Carbon tetrachloride	5.04	0.72	1.1	69
3-Carene	0.23	0.03	0.5	71
Chloroform	3.22	0.46	1.1	64
Decamethylcyclopentasiloxane	0.44	0.06	0.5	73
Decanal	0.62	0.09	0.5	76
n-Decane	0.89	0.13	0.5	71
n-Dodecane	1.47	0.21	0.5	73
2-Ethyl-1-hexanol	0.45	0.06	0.5	71
Ethylbenzene	0.30	0.04	0.5	73
Heptanal	0.43	0.06	0.5	72
n-Heptane	0.46	0.07	0.5	71
n-Hexadecane	0.49	0.07	0.5	71
Hexamethylcyclotrisiloxane	12.62	1.8	0.6	92
Hexanal	0.48	0.07	0.5	74
n-Hexane	3.10	0.44	0.9	57
d-Limonene	0.24	0.03	0.5	71
Methylene chloride	2.53	0.36	1.0	57
Nonanal	0.60	0.09	0.5	73
Octamethylcyclotetrasiloxane	1.27	0.18	0.5	73
Octanal	0.65	0.09	0.5	75
n-Octane	0.31	0.04	0.5	74
a-Pinene	0.32	0.05	0.5	73

Table S1 (Continued). MDL and calibration ranges for VOC analytes[a]

Analyte	Mass MDL (ng)	Concentration MDL (µg/m³)	Low Mass Calibration (µg/m³)	High Mass Calibration (µg/m³)
a-Terpineol	0.36	0.05	0.5	72
g-Terpinene	0.24	0.03	0.5	70
Tetrachloroethylene	0.50	0.07	0.5	80
n-Tetradecane	0.43	0.06	0.5	70
Texanol	0.37	0.05	0.5	74
Toluene	0.38	0.05	0.5	74
Trimethylbenzene (1,2,3)	0.28	0.04	0.5	75
Trimethylbenzene (1,2,4)	0.36	0.05	0.5	75
TXIB	0.51	0.07	0.5	70
n-Undecane	1.55	0.22	0.5	73
m/p-Xylene[b]	0.57	0.08	0.5	73
o-Xylene[b]	0.47	0.07	0.5	73

[a] Analysis used mass MDL and calibration ranges. Mass MDL and calibration ranges were converted to concentrations assuming typical sample volume of 7 liters. [b]Detection frequencies were determined for xylene isomers, then combined for total xylene detection ("xylenes").

VOC QUALITY ASSURANCE/QUALITY CONTROL

VOC Duplicate, Blank, Spike, and Breakthrough Samples

Three duplicate VOC samples were collected. In one facility, duplicate samples utilized sample tubes with Tenax backed by CarboTrap; at the other two, duplicate samples utilized Tenax-only sample tubes. For all VOC analytes, the mean relative percent difference (RPD) was 15.1±4.8%, showing a relatively small error between measurements. VOC mean RPDs ranged from 3.7±3.7% to 23.9±5.6%. Seventeen travel blanks were analyzed to quantify possible contamination. Results show little contamination during travel and analysis. Of the 38 analytes measured, only two had median blank masses above the method detection limit: hexamethylcyclotrisiloxane (4.1 ng) and benzaldehyde (1.5 ng). Three Tenax travel spikes were prepared with a Level 4 calibration standard (~100 ng) in 1 µL of methanol then purged with 2L of He. Travel spikes were prepared and brought into the field and returned to the laboratory to quantify recovery. For all 38 analytes, average recovery for the travel spikes was 96.0±8.0%. All VOC average recoveries were within ±15% of 96.2%, except for TXIB, which had an average recovery of 69.2%.

At five facilities, a second Tenax-TA tube was placed "downstream" from the field sample to quantify the amount of an analyte that passes through one Tenax tube, referred to as breakthrough. For breakthrough concentrations, the vast majority of VOCs (77.4% of 195 measurements) were not detectable. Overall, average breakthrough was minimal. For four facilities, only five VOCs showed breakthrough concentrations (range = 0.1-0.8 ng/m³). In one

sample (ECE 28), the measured VOCs on the breakthrough tube were significant: 29 VOCs with breakthrough ranges of 0.2-89.1 ng/m³. For ECE 28, the breakthrough to field sample ratio ranged from 0.1-5.6. Breakthrough is a function of both contaminant concentration and sample volume and occurs when the absorption capacity of a media is exceeded.[1] We ruled out breakthrough because the breakthrough tube concentrations did not coincide with the primary tube concentrations (in some cases the contaminants were higher on the breakthrough tube than the primary tube and some chemicals were present on the breakthrough tube that were not on the primary tube which is impossible if breakthrough occurred). The tube was used after facility 28 and the results for subsequent uses were valid (including one breakthrough experiment, one indoor measurement and one trip spike). We also ruled out contamination of the tube from the home or from another facility. Except for D3, the majority of the contaminants on the tube in question are of higher molecular weight so they were not likely taken up by diffusion. The elevated D3 relative to the other two siloxanes is unusual for an environmental sample and the chromatogram had a number of other higher order siloxanes not quantified in the sample. This was the first time this tube was used in the field; however, when Tenax sorbent tubes are purchased they are pre-conditioned, plus all new tubes were conditioned in the lab before deployment. From the evidence presented, the elevated breakthrough was either because the tube was not originally purged or contaminated by contact with a substance like silicone grease. We believe this anomaly does not invalidate any other sample results.

Identification and Quantification of Non-targeted VOCs

To identify compounds for quantification, we first reviewed a chromatograph from each ECE facility. To get an initial estimate of the different chemical classes present in the samples, we screened the samples for five ions generally related to a specific chemical class. These included siloxanes (m/z = 73), terpenes (m/z = 93), alkyl-aromatics (m/z = 91), alkoxy (m/z = 45) and alkanes (m/z = 57). Using this information, we selected several samples with a wide variety of chemical classes represented to develop the compound list for the method.

For each of the selected chromatograms, each peak was identified using a mass spectral library search with the NIST08 database. The chemical name and retention time for each peak with a match quality greater than ~80% was added to the compound list in the quantification method and used to quantify the next data file. After the next file was quantified and each identified peak reviewed to confirm that it was a good match, the chromatogram was carefully reviewed for additional unidentified peaks. The mass spectrum from each remaining unidentified peak was searched using the NIST08 database and if a good quality match was found, the additional chemical was added to the compound list in the method along with the associated retention time. This process was repeated with each data file until all peaks greater than about 5 ng toluene equivalent were identified. The approach resulted in the identification of 151 unique chemicals, including overlap with the *a priori* target analytes where standard calibration curves were used.

To provide a first estimate of the mass of the compounds we started by assigning each compound to a chemical class. The relationship between the extracted ion for the particular chemical class and that of toluene was determined using surrogate compounds from the calibration data collected over the course of the project. For each calibration data file, we determined the area of the extracted ion (EI_x) and the total ion (TI_x) for each chemical (x) and for toluene. This was only done when the TIC peaks were separated from other peaks. The chemical class, surrogate compounds, individual EI_x/TI_x ratios and overall surrogate specific class EI_s/TI_s ratio are presented in Table S2. We assume that the TIC response for the surrogate compound (toluene) is equal to the TIC response for all chemicals in the analysis. With this assumption, the extracted ion response for toluene ($EI_{toluene}$) was transformed to surrogate category response (EI_s) and assigned to each chemical (EI_x) by,

$$EI_{toluene} \times \frac{TI}{EI_{toluene}} \times \frac{EI_s}{TI} = EI_x$$

The EI_x values were then used to quantify the estimated mass of individual chemicals based on the chemical class assignment and the conversion factor determined by the five-point toluene calibration curve. Using the final quantification method, each data file was analyzed a final time including a careful review of peak identification and integration.

Table S2. Surrogate compounds and EI/TI conversion factors.

Class[1]	Surrogate compound[2]	EI_x/TI_x[3]		EI_s/TI_s
		Average	St. Dev	
Aldehydes	Butanal	0.33	0.12	0.19
	Hexanal	0.22	0.05	
	Heptanal	0.16	0.03	
	Octanal	0.11	0.02	
	Nonanal	0.15	0.02	
	Decanal	0.11	0.02	
Alkanes	Octane	0.20	0.05	0.26
	Undecane	0.29	0.06	
	Dodecane	0.29	0.06	
	Tetradecane	0.27	0.05	
	Hexadecane	0.25	0.04	
Alkoxy	2-Butoxyethanol	0.43	0.05	0.36
	2-Ethyl-1-hexanol	0.36	0.06	
	Texanol	0.26	0.04	
	TXIB	0.24	0.03	
Aromatics	Benzene	0.48	0.11	0.39
	Toluene	0.45	0.04	
	Ethylbenzene	0.43	0.03	
	m/p-Xylene	0.47	0.02	
	o-Xylene	0.38	0.01	
	1,2,4-Trimethylbenzene	0.27	0.10	
	1,2,3-Trimethylbenzene	0.38	0.01	
	Butylbenzene	0.39	0.01	
Halogenated	Tetrachloroethylene	0.38	0.01	0.17
Siloxane	D3	0.62	0.04	0.36
	D4	0.52	0.02	
	D5	0.33	0.09	
Terpene	3-Carene	0.27	0.02	0.19
	d-Limonene	0.23	0.02	
	a-Terpineol	0.16	0.01	
Toluene	Toluene			0.43

[1] Dominant classes of chemicals identified in the indoor air. Each chemical was assigned to one of these classes.

[2] Chemicals included in the standard calibration method for the project that were selected as surrogates for the specific class.

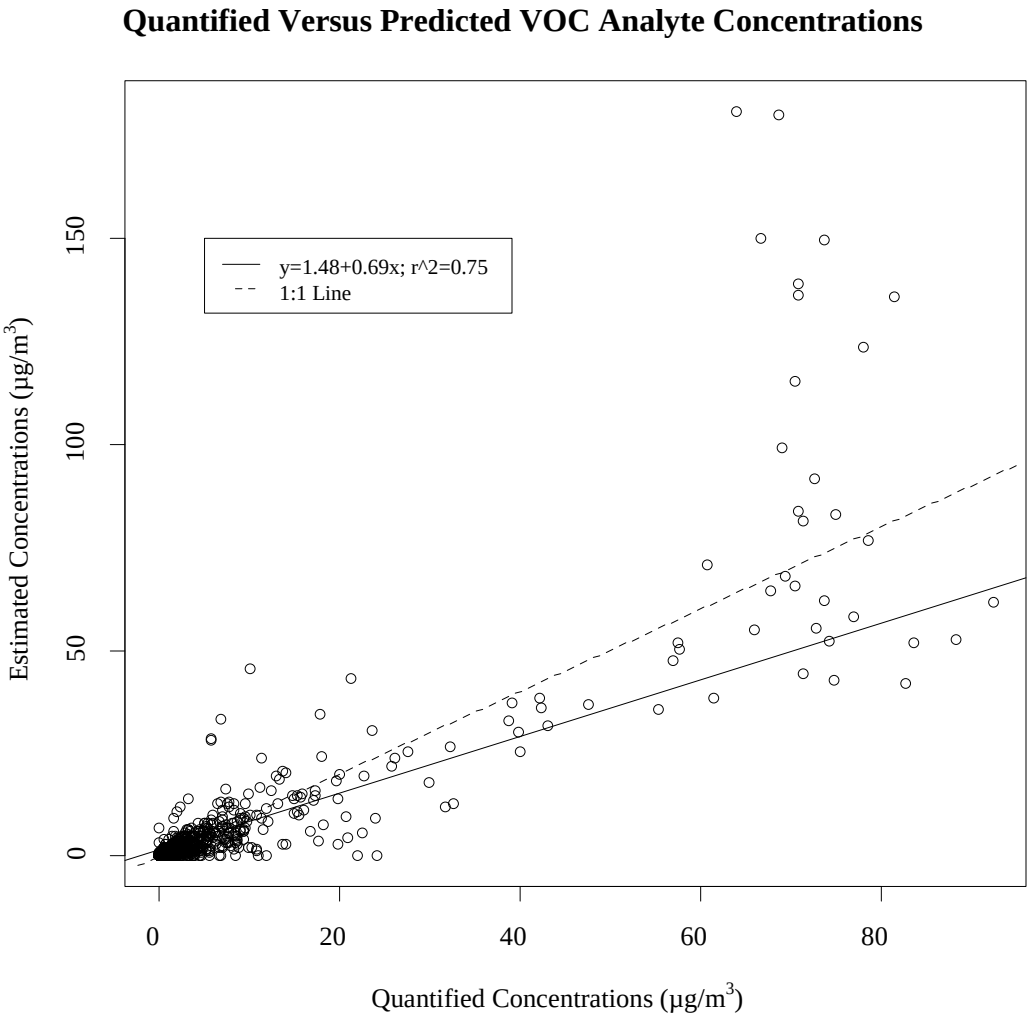
[3] The average (and standard deviation) of all conversion factors for the given chemical across all calibration runs preformed during the project.

To assess the quality of the estimated values, we examined the association of the measured versus estimated values for those compounds that were included *a priori* in the standard calibration curve (See Table S3). The measured and estimated values for all compounds were strongly correlated (R^2=0.75, p<0.05) (Figure S1). More than 60% of the individual compounds had a Spearman correlation >0.8 and more than 70% had a Spearman correlation >0.7 (Table S3). The semi-quantitative model generally underestimated VOC analytes (slope=0.69) (Figure S1).

Table S3. Spearman rank correlation test results for VOC analyte concentrations between quantified and semi-quantified analysis methods.

Analyte	Spearman's rho	p-value	Analyte	Spearman's rho	p-value
Benzaldehyde	0.79	<0.005	Nonanal	0.98	<0.005
Benzene	0.91	<0.005	Octamethylcyclotetra-siloxane (D4)	0.99	<0.005
Butanal	0.84	<0.005	Octanal	0.86	<0.005
2-Butoxyethanol	0.97	<0.005	n-Octane	0.95	<0.005
Butylbenzene	0.27	0.13	a-Pinene	0.93	<0.005
3-Carene	0.98	<0.005	a-Terpineol	-0.52	0.12
Decamethylcyclopenta-siloxane (D5)	0.89	<0.005	g-Terpinene	0.52	0.002
Decanal	0.18	0.31	Tetrachloroethylene	0.9	<0.005
n-Dodecane	0.91	<0.005	n-Tetradecane	0.72	<0.005
2-Ethyl-1-hexanol	0.29	0.11	Texanol	0.63	<0.005
Ethylbenzene	0.99	<0.005	Toluene	1.00	<0.005
Heptanal	0.97	<0.005	1,2,3-Trimethylbenzene	0.82	<0.005
n-Heptane	0.94	<0.005	1,2,4-Trimethylbenzene	0.58	<0.005
Hexadecane	0.39	0.03	TXIB	0.88	<0.005
Hexamethylcyclotri-siloxane (D3)	0.71	<0.005	n-Undecane	0.92	<0.005
Hexanal	0.73	<0.005	m/p-Xylene	0.99	<0.005
n-Hexane	0.92	<0.005	o-Xylene	0.99	<0.005
d-Limonene	0.96	<0.005			

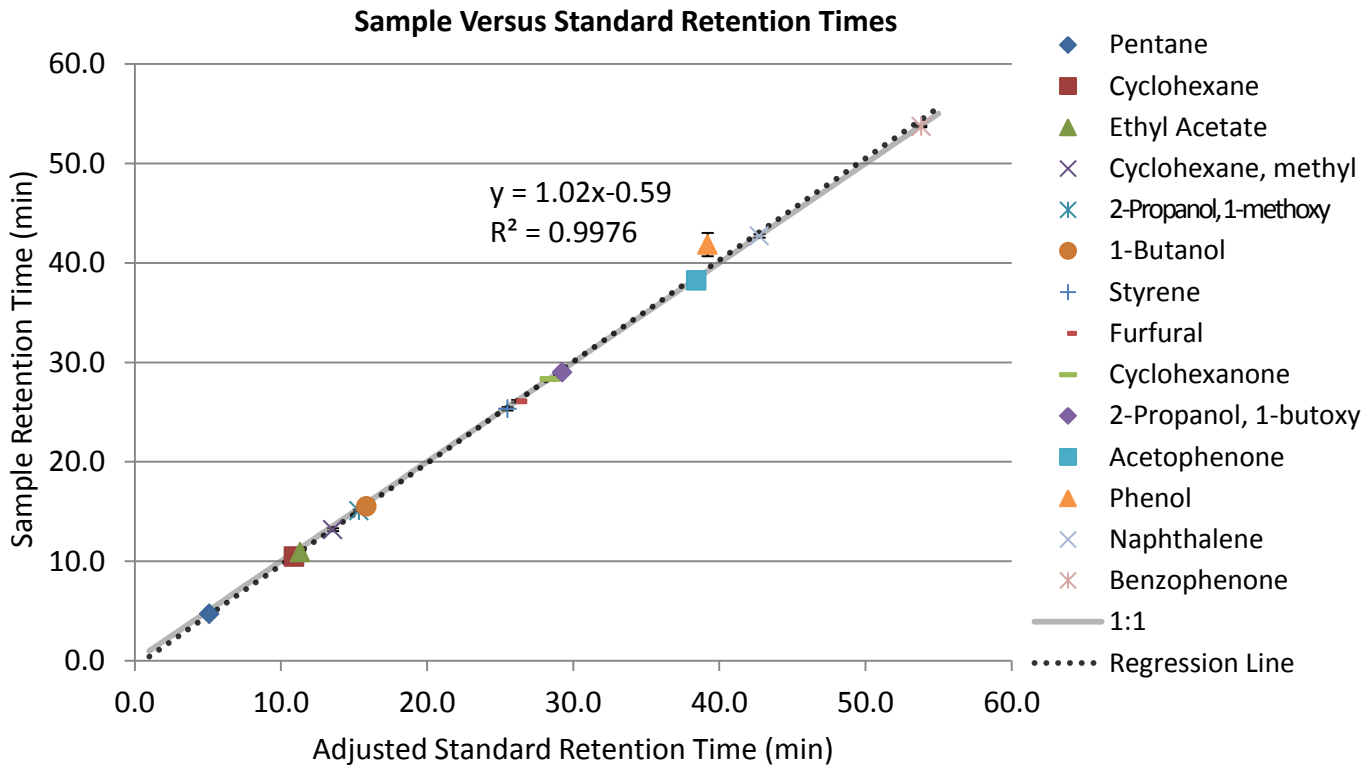
Figure S1. Relationship between VOC analyte concentrations measured with standard calibration curves versus estimated concentrations from semi-quantitative method. Lines in graph are the linear regression and one to one slope.



PURE STANDARDS

Pure standards were measured for 14 chemicals (identified from the unknown chromatograph peaks) under the same conditions as the initial VOC analysis of the *a priori* target analytes. The TD-GC/MS instrument currently contains a new, replacement column from the the *a priori* target analysis (but the same part number: Agilent DB-1701), resulting in slightly different retention times. The average retention time shift was calculated to adjust the standards' retention time under the *a priori* target conditions. Figure S2 compares the adjusted retention times from the 14 standards to the retention times obtained from the original VOC sample analysis. The high R^2 value indicates accurate identification of VOCs (R^2>0.99).

Figure S2. Relationship between the retention times of the adjusted pure standards versus retention times of the *a priori* target samples for 14 chemicals identified from the unknown chromatograph peaks.



Probability-based matching (PBM) was also performed to compare the mass spectra of the standards to the mass spectra of the samples (See Table S4 below) The PBM logarithm provided further confirmation of VOC identification. All PBM mass spectra were selected from ECE 32 sample results, except for acetophenone and phenol, which were selected from ECE 19 due to higher detectable masses. Of the VOCs detected, seven had a PBM score above 90% and all were above 70% (Range 72-96%), affirming a high quality of accuracy in VOC identification. The PBM test could not detect cyclohexanone and 1-butoxy-2-propanol in the selected samples due to their low masses.

Table S4. Probability-based matching results.[a]

STANDARDS	PBM (%)
Pentane	72
Cyclohexane	86
Ethyl acetate	83
Cyclohexane, methyl	93
2-Propanol, 1-methoxy	86
1-Butanol	78
Styrene	96
Furfural	90
Acetophenone	93
Phenol	94
Naphthalene	93
Benzophenone	96

[a] Cyclohexanone and 1-butoxy-2-propanol were not present in sufficient quantities for PBM sample analysis.

Equation S1. NSRL Calculations

The age-specific No Significant Risk Level (NSRL) calculations were based on the following equation:

$$NSRL_{\ child}\left(\frac{\mu g}{day}\right) = \frac{\frac{NSRL_{adult}\left(\frac{\mu g}{day}\right)}{BW_{\ adult}(70\ kg)} \times BW_{child}\ (Varies\ by\ Age\ Group, kg)}{ASF\ (Varies\ by\ Age\ Group)}$$

The age-specific NSRL, such as the $NSRL_{child\ (0\ to\ <1\ year)}$, is the estimated daily intake for that age range, which contributes $1/70^{th}$ (assuming a 70-year lifetime) of the target lifetime cancer risk in that particular year of life. If the ratio of a child's VOC dose estimate (µg/day) to age-adjusted NSRL (µg/day) is greater than 1, the exposure dose estimate exceeded the 10^{-5} threshold.

To compare with the age-adjusted NSRLs, child inhalation dose estimates were calculated based on the measured VOC air concentrations. Estimates assume exposure duration of 8 hours per day, 5 days per week, 48 weeks per year. Age-specific breathing rates on a body weight basis and an age sensitivity factor (ASF) are also used in the calculation. Using a standard inhalation dose equation, we combined VOC concentrations with age-specific intake factors including inhalation rates (m^3/day), body weights (kg), and an exposure factor (see **Equation S2** and **Table S5** below).[2] Since children are not present in ECE facilities every day, we calculated the exposure factor assuming a child spends five days per week and 48 weeks per year (which accounts for four weeks away from child care for holidays and vacation). We assumed that alveolar absorption of these compounds was 100%, and that exposures occurred over one year. [2]

Equation S2. Exposure Dose Calculations

Using a standard inhalation dose equation, we combined concentrations of VOCs with age-specific intake factors including inhalation rates (m^3/day), body weights (kg), and an exposure factor.[2] We assumed that alveolar absorption of these compounds was 100% and exposures occurred over one year. The inhalation rates and child body weight estimates are presented in **Table S5**.

$$D_{child\ care} = \frac{C \times IR \times EF \times CF}{BW}$$

Where,

D=exposure dose received in child care assuming 8 hour day (mg/kg/8 hours)
C=contaminant concentration (mg/m³)
IR=inhalation rate (m³/8 hours)
EF=exposure factor
CF=conversion factor
BW=body weight (kg)

The EF is calculated[1]:

$$EF = \frac{F \times ED}{AT}$$

Where,

EF = exposure factor
F = frequency of exposure (days/year)
ED = exposure duration (years)
AT = averaging time (ED x 365 days/year)

We calculated EF assuming that a child spends five days per week and 48 weeks per year (which accounts for four weeks away from day care for holidays and vacation) in child care. The averaging time will depend on how many years the child is in child care but is assumed to be one year in our calculations.

$$EF = \frac{\left(5\,\frac{days}{week}\right) \times \left(48\,\frac{weeks}{year}\right) \times (1\,year)}{1\,year\ \times\ 365\,\frac{days}{year}} = 0.66$$

Table S5. Inhalation rates and body weights used for dose calculations by age group.[a]

	Inhalation Daily Volume		Body Weight
	(m^3/day)	**(m^3/8-hour)**	**(kg)**
Birth to <1 year	5.10	1.70	6.8[b]
1 to <2 years	8.00	2.67	11.4
2 to <3 years	9.50	3.17	13.8
3 to <6 years	10.90	3.63	18.6

[a] Inhalation rates and body weights are mean values recommended in the U.S. EPA's Exposure Factors Handbook.[3]

[b] Value based on average of three age groups (birth to <1 month, 2 to <6 months, and 6 to <12 months) from Arcus-Arth and Blaisdell, 2007.[4]

Table S6. ECE facility building and neighborhood types (n=34).

Building Type	**Number of Facilities (%)**
Single family detached homes	14 (41.2)
Traditional school buildings	9 (26.5)
Portable school buildings	7 (20.6)
Office buildings	2 (5.9)
Churches	2 (5.9)
Neighborhood Type	
Residential	23 (67.6)
Commercial	6 (17.6)
Near agricultural fields	4 (11.8)
Rural/ranch area	1 (2.9)

Table S7. Age distribution of children in 34 ECE facilities and time spent indoor/outdoor (n=1431 children).[a]

Age	**Number of Children (%)**
<2 years	86 (6)
2-3 years	229 (16)
3-6 years	1116 (78)
Time Indoors	
<5 hours	339 (24)
5-8 hours	455 (32)
>8 hours	637 (45)
Time Outdoors	**Number of Facilities (%)**
<1 hour	2 (6)
1-2 hours	12 (35)
3-4 hours	19 (56)
5-6 hours	1 (3)

[a] Four - 200 children per facility, average 43.

Table S8. Temperature, relative humidity, and AER.

Indoor	**Mean±SD**	**Range**
Average air temp	21.1±1.7	16.0-24.6 °C
Average RH	48.3±6.8%	34.5-60.0%
Average AER	1.7±1.3 hr^{-1}	0.3-5.6 hr^{-1}
Outdoor		
Average RH	49.4±12.0%	21.6-74.7%

Table S9. Correlation Matrix for Mixed and Mobile Source (MMS) VOCs[a]

	Benzene	Decane	Dodecane	Ethyl-benzene	Heptane	Hexa-decane	Octane	Tetra-decane	Toluene	123-TMB	124-TMB	Undecane	Xylene
Benzene	1												
Decane	0.47*	1											
Dodecane	0.47*	0.51*	1										
Ethyl-benzene	0.78*	0.58*	0.35*	1									
Heptane	0.73*	0.35*	0.33	0.63*	1								
Hexa-decane	0.54*	0.19	0.23	0.31	0.69*	1							
Octane	0.74*	0.32	0.40*	0.58*	0.83*	0.54*	1						
Tetra-decane	0.48*	0.20	0.49*	0.32	0.47*	0.66*	0.40*	1					
Toluene	0.84*	0.37*	0.20	0.82*	0.74*	0.51*	0.73*	0.39*	1				
123-TMB	0.73*	0.58*	0.42*	0.84*	0.60*	0.34	0.55*	0.39*	0.72*	1			
124-TMB	0.84*	0.54*	0.31	0.93*	0.75*	0.39*	0.66*	0.30	0.88*	0.09	1		
Undecane	0.42*	0.71*	0.69*	0.45*	0.27	0.19	0.30	0.31	0.20	0.48*	0.33	1	
Xylene	0.79*	0.55*	0.34	0.99*	0.64*	0.32	0.59*	0.33	0.85*	0.86*	0.94*	0.43*	1

Abbreviations: 1,2,3-trimethylbenzene (123-TMB) and 1,2,4-trimethylbenzene (1,2,4-TMB).

[a]Spearman rho correlations. *$p<0.05$.

Table S10. Summary of outdoor VOC analyte concentrations (μg/m³) (n=20).[a,b]

Analyte	>MDL (%)	Geometric Mean±GSD	Arithmetic Mean±SD	25th %	Median	75th %	95th %	Max
Mixed and Mobile Sources								
Benzene	75.0	0.6±0.4	0.7±0.3	<MDL	0.6	0.9	1.2	1.2
n-Decane	30.0	0.1±0.6	0.2±0.1	<MDL	<MDL	0.2	0.4	0.4
Ethylbenzene	65.0	0.1±1.2	0.2±0.3	<MDL	0.1	0.3	0.8	0.9
n-Heptane	85.0	0.4±1.1	0.6±0.6	0.2	0.4	0.9	1.8	1.9
n-Hexane	25.0	0.4±0.5	<MDL	<MDL	<MDL	<MDL	1.0	1.3
n-Octane	60.0	0.1±1.1	0.2±0.1	<MDL	0.1	0.2	0.5	0.5
Toluene	100.0	1.1±0.8	1.5±1.2	0.7	0.9	2.1	4.1	4.1
1,2,3-Trimethylbenzene	25.0	0.0±1.0	0.1±0.2	<MDL	<MDL	0.1	0.5	0.7
1,2,4-Trimethylbenzene	60.0	0.1±1.2	0.2±0.3	<MDL	0.1	0.3	1.0	1.3
Xylenes	100	0.8±1.0	1.2±1.4	0.4	0.6	1.5	4.3	5.4
Household Sources								
Fragrances								
Benzaldehyde	100.0	2.3±0.4	2.4±1.1	1.8	2.3	2.7	4.8	6.3
Butanal	25.0	0.1±0.6	0.1±0.1	<MDL	<MDL	0.1	0.2	0.2
Decanal	55.0	0.1±0.7	0.1±0.1	<MDL	0.1	0.2	0.4	0.5
Heptanal	15.0	0.0±0.5	0.1±0.0	<MDL	<MDL	<MDL	0.1	0.2
Hexanal	80.0	0.1±0.7	0.2±0.1	0.1	0.2	0.2	0.5	0.6
Nonanal	95.0	0.3±0.7	0.4±0.3	0.2	0.2	0.5	0.9	1.2
Octanal	55.0	0.1±0.6	0.1±0.1	<MDL	0.1	0.2	0.3	0.3
a-Pinene	45.0	0.1±1.3	0.2±0.3	<MDL	<MDL	0.3	0.9	1.1
Other household products								
2-Butoxyethanol	20.0	0.1±0.8	0.1±0.1	<MDL	<MDL	<MDL	0.4	0.5
Decamethylcyclopentasiloxane (D5)	95.0	0.3±0.8	0.4±0.4	0.2	0.3	0.6	1.2	1.3
Hexamethylcyclotrisiloxane (D3)	25.0	1.4±0.4	<MDL	<MDL	<MDL	<MDL	3.9	4.6

Table S10 (Continued). Summary of outdoor VOC analyte concentrations (μg/m³) (n=20).[a,b]

Analyte	>MDL (%)	Geometric Mean±GSD	Arithmetic Mean±SD	25th %	Median	75th %	95th %	Max
Octamethylcyclotetrasiloxane (D4)	35.0	0.1±0.3	0.2±0.1	<MDL	<MDL	0.2	0.3	0.3
Tetrachloroethylene	30.0	0.1±0.6	0.1±0.1	<MDL	<MDL	0.1	0.3	0.4
Texanol	15.0	0.0±0.6	0.1±0.1	<MDL	<MDL	<MDL	0.2	0.2
TXIB	15.0	0.1±0.7	0.1±0.2	<MDL	<MDL	<MDL	0.5	0.9

[a] Compounds detected in <10% of facilities were removed: butylbenzene, carbon tetrachloride, 3-carene, chloroform, n-dodecane, 2-ethyl-1-hexanol, n-hexadecane, d-limonene, methylene chloride, a-terpineol, g-terpinene, n-tetradecane, and n-undecane. [b] If outdoor concentrations <MDL, values were imputed as MDL/√2.

Table S11. Correlation Matrix for Household Source (HS) VOCs.

	Benz-aldehyde	Butanal	3-Carene	Decanal	Heptanal	Hexanal	d-limonene	Nonanal	Octanal	α-Pinene	α-Terpineol	ɣ-Terpinene
Benz-aldehyde	1											
Butanal	0.52*	1										
3-Carene	0.41*	0.49*	1									
Decanal	0.06	0.08	-0.09	1								
Heptanal	0.43*	0.24	0.42*	0.02	1							
Hexanal	0.37*	0.64*	0.38*	0.26	0.48*	1						
d-limonene	0.10	0.37*	0.51*	-0.15	0.14	0.28	1					
Nonanal	0.15	-0.05	-0.05	0.23	0.62*	0.23	-0.18	1				
Octanal	0.60*	0.32	0.53*	0.22	0.77*	0.45*	0.33	0.51*	1			
a-Pinene	0.30	0.48*	0.66*	-0.24	0.27	0.30	0.39*	-0.11	0.31	1		
a-Terpineol	0.53*	0.54*	0.37*	0.08	0.34	0.58*	0.49*	0.00	0.43*	0.39*	1	
Terpinene	0.16	0.22	0.31	0.09	0.18	0.36*	0.49*	-0.07	0.28	0.38*	0.50*	1
2-Butoxy-ethanol	0.56*	0.57*	0.34	0.15	0.36*	0.34	0.26	0.30	0.40*	0.09	0.37*	0.14
D5	0.06	0.07	0.19	0.16	-0.04	0.05	0.32	-0.15	0.15	0.26	0.52*	0.22
2-Ethyl-1-hexanol	0.61*	0.70*	0.62*	0.04	0.37*	0.57*	0.56*	-0.06	0.52*	0.54*	0.72*	0.47*
D4	0.24	0.43*	0.32	-0.06	0.09	0.21	0.28	-0.16	0.06	0.37*	0.56*	0.07
Texanol	0.19	0.30	0.30	-0.32	0.40*	0.26	0.19	0.20	0.34	0.31	0.18	0.15
TXIB	0.20	0.06	0.44*	-0.31	0.25	0.22	0.24	-0.11	0.13	0.18	0.17	0.00

Abbreviations: decamethylcyclopentasiloxane (D5); octamethylcyclotetrasiloxane (D4); 2,2,4-trimethyl-1,3-pentanediol diisobutyrate (TXIB). [a]Pearson correlations. *p<0.05. **p<0.01.

Table S12. Correlations between Mixed and Mobile Source (MMS) VOCs and continuous environmental parameters.[a,b]

		Benzene	n-Decane	n-Dodecane	Ethylbenzene	n-Heptane	n-Hexadecane
	Mean±SD	**Correlation**					
AER (hr^{-1})	1.7±1.3 hr^{-1}	-0.41*	0.05	-0.02	-0.24	-0.54**	-0.67**
Temperature (°C)	21.1±1.7°C	0.19	0.30	0.34†	0.09	0.14	0.34†
Relative Humidity (%)	48.3±6.8%	0.32	0.01	0.03	0.26	0.29	0.16
ΣLATV (vehicle-km/hr)	11,126.7± 11,643.0 vehicle-km/hr	0.39*	0.16	-0.07	0.24	0.38*	0.44*

	n-Octane	n-Tetradecane	Toluene	1,2,3-Trimethyl-benzene	1,2,4-Trimethyl-benzene	n-Undecane	Xylenes
	Correlation						
AER (hr-1)	-0.29	-0.38*	-0.48**	-0.26	-0.40*	0.11	-0.28
Temperature (°C)	0.14	0.34†	0.02	0.09	0.00	0.27	0.08
Relative Humidity (%)	0.34†	0.17	0.31	0.25	0.28	0.08	0.27
ΣLATV (vehicle-km/hr)	0.23	0.07	0.25	0.25	0.34†	-0.01	0.24

†p=0.05. *p<0.05. **p<0.01. [a]Spearman's rho correlations. [b]Sample size=34, except for n-decane (n=33).

Table S13. Summary of Mixed and Mobile-Source (MMS) VOC concentrations (μg/m^3) and potential determinants.[a]

	n-Hexadecane		n-Octane		Benzene		n-Heptane	
	n (%)	**Median**	**n (%)**	**Median**	**n (%)**	**Median**	**n (%)**	**Median**
License Type								
Center			23 (68)	0.5				
Home			11 (32)	0.9*				
Presence of CWPs[b]								
Yes			29 (85)	0.5	29 (85)	0.8		
No			5 (15)	1.3*	5 (15)	1.1*		
Presence of New Floors								
Yes					6 (18)	0.4	6 (18)	0.5
No					28 (82)	0.9*	28 (82)	1.9*
Use of Permanent Markers or Art Pens								
Yes	24 (71)	0.9*						
No	10 (29)	0.6						

	Ethylbenzene		1,2,4-Trimethylbenzene		Xylenes		Toluene	
	n (%)	**Median**	**n (%)**	**Median**	**n (%)**	**Median**	**n (%)**	**Median**
License Type								
Center	23 (68)	0.5	23 (68)	0.5	23 (68)	1.8	23 (68)	2.5
Home	11 (32)	1.0*	11 (32)	0.9*	11 (32)	4.8*	11 (32)	5.2*
Use of Glue								
Yes					6 (18)	4.0*		
No					28 (82)	1.8		

*$p<0.05$. [a]p-values from Wilcoxon rank-sum test of VOC air concentrations. [b]Composite Wood Products (CWPs).

Table S14. Correlations between Household Source (HS) VOCs and continuous environmental parameters.[a,b,c,d]

		Benzaldehyde	Butanal	3-Carene	Decanal	Heptanal	Hexanal	d-Limonene
	Mean±SD	**Correlation**						
AER (hr-1)	1.7±1.3 hr^{-1}	-0.13	-0.62**	-0.22	-0.03	-0.11	-0.42*	-0.34
Temperature (°C)	21.1±1.7 °C	0.15	0.21	0.30	-0.15	0.15	0.32	0.25
Relative Humidity (%)	48.3±6.8 %	0.33	0.11	-0.03	-0.11	0.14	0.15	-0.04

	Nonanal	Octanal	α-Pinene	α-Terpineol	ɣ-Terpinene	2-Butoxy-ethanol	D5	2-Ethyl-1-hexanol
	Correlation							
AER (hr-1)	0.14	-0.09	-0.50**	-0.30	-0.30	-0.24	-0.08	-0.53**
Temperature (°C)	0.11	0.23	0.08	0.51**	0.20	0.08	0.08	0.43*
Relative Humidity (%)	0.02	0.16	0.22	0.21	0.21	0.05	-0.02	0.12

	D4	Texanol	TXIB
	Correlation		
AER (hr-1)	-0.43*	-0.02	-0.16
Temperature (°C)	0.16	0.08	0.16
Relative Humidity (%)	-0.05	-0.07	0.19

*p<0.05. **p<0.01. [a]Spearman's rho correlations. [b]If indoor VOC concentrations <MDL, values were inputed as MDL/√2. [c]Abbreviations: decamethylcyclopentasiloxane (D5); octamethylcyclotetrasiloxane (D4); 2,2,4-trimethyl-1,3-pentanediol diisobutyrate (TXIB). [d]Sample size=34, except for D4 (n=33).

Table S15. Summary of Household Source (HS) VOC concentrations (μg/m^3) and potential indoor determinants[a]

	Decanal		**Decamethylcyclo-pentasiloxane (D5)**		**Hexanal**		**2-Ethyl-1-hexanol**	
	n (%)	**Median**	**n (%)**	**Median**	**n (%)**	**Median**	**n (%)**	**Median**
Use of Air Fresheners								
Yes	14 (41)	4.0*	14 (41)	70.7*	14 (41)	9.3*		
No	20 (59)	2.3	20 (59)	32.9	20 (59)	4.6		
Occurrence of Daily Mopping								
Yes			25 (74)	65.9*				
No			9 (26)	18.0				
Presence of New Floors								
Yes							6 (18)	1.1
No							28 (82)	1.9*

*$p<0.05$. [a]p-values from Wilcoxon rank-sum test of VOC air concentrations.

Table S16 Estimated concentrations (ng/m³) of 119 non-targeted indoor VOCs in ECE facilities (n=32)**.**[a,b]

Analyte	>MDL (%)	Arithmetic Mean±SD	25th %	Median	75th %	95th %	Max
Alkanes							
Cyclododecane	31.3	203.8 ± 476.3	<MDL	<MDL	297.3	876.9	2466
Cyclohexane[c]	100.0	329.8 ± 356.1	96.8	221.0	403.9	1403	1515
Cyclohexane, methyl-	100.0	380.7 ± 454.5	95.0	292.5	410.8	1119	2372
Cyclooctane	28.1	243.0 ± 561.8	<MDL	<MDL	227.0	1266	2719
Decane, 3,7-dimethyl-	9.4	15.5 ± 70.0	<MDL	<MDL	<MDL	76.2	391.2
Decane, 2,2,4-trimethyl-	40.6	502.2 ± 1023	<MDL	<MDL	580.9	2614	4246
Decane, 2,2,6-trimethyl-	25.0	999.7 ± 2768	<MDL	<MDL	74.5	6331	12490
Decane, 2,2,7-trimethyl-	9.4	200.4 ± 1050	<MDL	<MDL	<MDL	319.8	5943
Decane, 2,2,8-trimethyl-	28.1	1069 ± 2344	<MDL	<MDL	565.7	6273	9453
Decane, 2,2,9-trimethyl-	6.3	11.4 ± 44.8	NC	NC	NC	NC	182.8
Dodecane, 5,8-diethyl-	25.0	865.1 ± 2389	<MDL	<MDL	56.6	5367	10750
Dodecane, 2,6,10-trimethyl-	9.4	120.6 ± 577.1	<MDL	<MDL	<MDL	477.4	3247
Dodecane, 2,7,10-trimethyl-	6.3	459.4 ±2571	NC	NC	NC	NC	14550
Hexadecane, 2,6,10,14-tetramethyl-	50.0	851.1 ± 2563	<MDL	83.1	343.7	8512	12260
Hexane, 2,4-dimethyl-	25.0	736.7 ± 2007	<MDL	<MDL	98.1	4569	9055
Hexane, 2-methyl-	100.0	430.8 ± 454.1	111.9	242.3	598.9	1532	1858
Hexane, 3-methyl-	96.9	464.0 ± 481.1	141.5	275.3	593.4	1725	1852
n-Nonadecane	100.0	182.4 ± 91.2	123.0	158.6	209.6	342.8	450.9
n-Nonane	100.0	328.1 ± 251.1	147.6	241.2	397.4	1017	1103
Nonane, 2-methyl-5-propyl-	21.9	502 ± 1172	<MDL	<MDL	<MDL	2398	5557
Octane, 2,6-dimethyl-	25.0	753.9 ± 2090	<MDL	<MDL	41.0	4752	9483
Octane, 2,3,6,7-tetramethyl-	12.5	144.7 ± 548.0	<MDL	<MDL	<MDL	1889	2527
Octane, 2,5,6-trimethyl-	46.9	1060± 3437	<MDL	<MDL	424.5	7675	18280
n-Pentadecane	31.3	797.6 ± 2005	<MDL	<MDL	1121	2550	10840
n-Pentane[d]	37.5	51.1 ± 104.0	<MDL	<MDL	49.7	394.0	417.8

Table S16 (cont.) Estimated concentrations (ng/m³) of 119 non-targeted indoor VOCs in ECE facilities (n=32)**.**[a,b]

Analyte	>MDL (%)	Arithmetic Mean±SD	25th %	Median	75th %	95th %	Max
Tetradecane, 2,2-dimethyl-	21.9	784.8 ± 2237	<MDL	<MDL	<MDL	5175	10300
Tridecane, 3-methyl-	6.3	9.2 ± 38.5	NC	NC	NC	NC	198.6
Tridecane, 2-methyl-2-phenyl-	12.5	36.1 ± 178.2	<MDL	<MDL	<MDL	61.3	1009
Undecane, 2,8-dimethyl-	15.6	62.5 ± 193.3	<MDL	<MDL	<MDL	314.0	1012
Undecane, 6,6-dimethyl-	21.9	1424 ± 4599	<MDL	<MDL	<MDL	11670	21930
Undecane, 6-ethyl-	15.6	118.6 ± 441.3	<MDL	<MDL	<MDL	512.1	2436
Oxygenated Hydrocarbons							
Acetic acid	87.5	1673 ± 2351	215.4	764.9	1954.4	7142	10550
Acetic acid, butyl ester[d]	96.9	941.3 ± 1608	245.8	389.4	777.2	6490	6997
Acetic acid, 2-methylpropyl ester[d]	75.0	249.9 ± 332.3	13.2	106.5	357.3	955.7	1492
Benzoic acid, 2-ethylhexyl ester	100.0	677.8 ± 1563	100.8	153.0	437.1	3610	8188
Benzoic acid, 2-hydroxy-, 3-methylbutyl	31.3	235.2 ± 577.0	<MDL	<MDL	275.8	1609	2867
1-Butanol[e]	100.0	1167 ± 915.4	638.3	847.5	1316	3505	3950
Cyclohexanol, 5-methyl-2-(1-methylethyl)	100.0	999.1 ± 1694	235.0	466.5	829.1	4529	8239
Cyclohexanone[e]	100.0	1039 ± 2101	366.5	517.1	868.0	2689	12200
Dipropylene glycol monomethyl ether[d]	93.7	1038 ± 2832	118.6	261.0	763.3	2543	16100
Ethanol	65.6	672.2 ± 1653	<MDL	105.1	434.9	3547	8538
Ethanol, 2-(2-butoxyethoxy)-	62.5	1138 ± 2335	<MDL	242.7	924.1	7119	10790
Ethanol, 2-(hexyloxy)-	75.0	955.2 ± 1700	25.9	214.6	1257	4000	8728
Ethyl acetate[e]	96.9	638.2 ± 940.3	143.3	250.5	628.7	3242	3412
1-Hexacosanol	9.4	103.0 ± 327.9	<MDL	<MDL	<MDL	1158	1223
Isopropyl alcohol[c]	100.0	17630 ± 85390	731.7	1552	3821	12670	485300
1,8-Nonanediol, 8-methyl-	31.3	115.8 ± 202.2	<MDL	<MDL	168.6	532.5	653.4
Octane, 1,1'-oxybis-	93.8	687.6 ± 655.3	191.0	511.8	891.7	1697	3106
1-Octanol	31.3	1479 ± 1479	<MDL	<MDL	2029	4535	4654

Table S16 (cont.) Estimated concentrations (ng/m³) of 119 non-targeted indoor VOCs in ECE facilities (n=32).[a,b]

Analyte	>MDL (%)	Arithmetic Mean±SD	25th %	Median	75th %	95th %	Max
Octanol, 2-butyl-	12.5	33.5 ± 102.0	<MDL	<MDL	<MDL	252.8	489.2
1-Octanol, 2,2-dimethyl-	21.9	339.4 ± 1192	<MDL	<MDL	NC	3549	5881
3-Octanol, 3,7-dimethyl-, (±)-	65.6	506.8 ± 2017	<MDL	86.3	217.3	1334	11480
Pentanal	100.0	593.9 ± 613.2	331.8	410.9	581.8	1157	3698
2-Pentanol, acetate[d]	78.1	173.8 ± 210.0	23.3	63.5	292.4	622.1	744.6
2-Propanol, 1-butoxy-	78.1	893.7 ± 3030	28.1	121.4	510.9	3508	17090
2-Propanol, 1-methoxy-[c]	71.9	640.4 ± 2029	<MDL	131.3	319.7	2176	11420
2-Propanol, 1-(2-methoxy-1-methylethoxy)	90.6	513.2 ± 664.4	96.5	245.6	610.6	2363	2469
2-Propanol, 1-(2-methoxypropoxy)-	100.0	3276± 5211	603.0	1230	5517	11050	27620
1-Propanol, 2-(1-methylethoxy)-	25.0	25.9 ± 58.1	<MDL	<MDL	6.8	148.7	247.1
2-Propanol, 1-propoxy-	81.3	4448± 8626	77.7	266.8	7074	28160	31820
Propylene glycol	100.0	9535 ± 6581	4273	7357	15520	24010	25030
Tripropylene glycols	53.1	2791 ± 7214	<MDL	84.0	1260	23310	33230
Aromatics							
Acetic acid, phenylmethyl ester	100.0	831.9 ± 1432	188.3	366.4	897.3	4042	7525
Acetophenone[e]	100.0	1110 ± 319.9	971.4	1100	1162	1950	2144
Benzaldehyde, 4-methoxy-	21.9	119.2 ± 287.4	<MDL	<MDL	<MDL	565.4	1405
Benzene, (1-butylheptyl)-	87.5	456.1 ± 944.7	114.9	190.1	332.1	2745	4902
Benzene, (1-butylhexyl)-	87.5	164.6 ± 219.0	39.9	96.2	224.0	468.9	1172
Benzene, (1-butylnonyl)-	37.5	38.8 ± 132.3	<MDL	<MDL	14.5	222.8	727.9
Benzene, (1-butyloctyl)-	96.9	274.1 ± 815.5	54.4	80.1	138.1	1266	4584
Benzene, (1,1-dimethyldecyl)-	9.4	21.02 ± 113.9	<MDL	<MDL	<MDL	13.9	645.0
Benzene, (1,1-dimethylnonyl)-	31.3	35.8 ± 152.1	<MDL	<MDL	16.9	137.0	858.3
Benzene, (1-ethyldecyl)-	93.8	171.0 ± 484.9	27.5	57.8	93.6	989.3	2659
Benzene, 1-ethyl-3,5-dimethyl-	3.1	NC	<MDL	<MDL	<MDL	<MDL	172.0
Benzene, (1-ethylnonyl)-	100.0	269.5 ± 720.5	43.0	73.6	141.1	2387	3511

Table S16 (cont.) Estimated concentrations (ng/m³) of 119 non-targeted indoor VOCs in ECE facilities (n=32).[a,b]

Analyte	>MDL (%)	Arithmetic Mean±SD	25th %	Median	75th %	95th %	Max
Benzene, (1-ethyloctyl)-	71.9	206.6 ± 528.7	<MDL	50.3	116.7	1104	2739
Benzene, (1-methyldecyl)-	96.9	475.7 ± 1315	73.0	114.0	207.7	4388	6357
Benzene, (1-methylnonyl)-	71.9	310.2 ± 954.2	<MDL	60.3	134.9	2277	5060
Benzene, (1-methylundecyl)-	28.1	133.9 ± 671.8	<MDL	<MDL	35.0	91.6	3812
Benzene, (1-pentylheptyl)-	100.0	274.9 ± 823.0	53.8	80.9	132.8	1266	4628
Benzene, (1-pentylhexyl)-	87.5	261.8 ± 477.2	32.1	102.0	251.5	1279	2426
Benzene, (1-pentyloctyl)-	56.3	68.4 ± 223.2	<MDL	17.7	44.1	220.0	1266
Benzene, (1-propylheptadecyl)-	78.1	114.2 ± 137.3	13.7	68.0	145.7	423.4	511.9
Benzene, (1-propylheptyl)-	81.3	223.7 ± 545.3	40.1	79.6	191.8	1186	2976
Benzene, (1-propylnonyl)-	96.9	227.0 ± 633.8	44.9	67.7	109.2	1172	3519
Benzene, (1-propyloctyl)-	90.6	293.5 ± 771.8	50.0	82.6	151.0	2322	3907
Benzophenone	100.0	965.5 ± 2681	246.1	362.4	796.1	1362	15530
Benzyl alcohol	100.0	850.4 ± 1269	285.4	483.3	894.2	3340	6853
Ethanol, 2-phenoxy-	68.8	1394 ± 2180	<MDL	465.4	1553.1	6789	8274
2-Ethylhexyl salicylate	100.0	778.9 ± 1162	207.0	359.5	679.9	2867	5697
Homosalate	93.8	449.8 ± 810.6	69.8	164.0	367.3	2610	3500
3-Methyl-4-isopropylphenol	15.6	38.6 ± 189.6	<MDL	<MDL	<MDL	81.1	1074
Naphthalene[c]	96.9	501.8 ± 659.7	212.5	341.9	572.0	1118	3833
Naphthalene, 2-methoxy-	100.0	174.5 ± 175.6	61.7	105.2	200.2	533.4	653.1
Phenol[c]	93.8	1550 ± 1554	588.9	1128	1843	3803	7588
2-Propenal, 3-phenyl-[d]	21.9	34.6 ± 80.5	<MDL	<MDL	<MDL	300.2	301.1
Styrene[c]	100.0	390.4 ± 338.2	144.8	300.9	568.4	1116	1328
Siloxanes and Silanol							
Cyclohexasiloxane, dodecamethyl- (D6)	100.0	2698 ± 3048	978.5	1886	3449	7166	16680
Heptasiloxane, hexadecamethyl-	96.9	431.2 ± 676.3	67.4	157.6	451.5	1729	3258
Hexasiloxane, tetradecamethyl-	93.8	636.2 ± 1777	64.1	181.7	508.4	1922	10080

Table S16 (cont.) Estimated concentrations (ng/m³) of 119 non-targeted indoor VOCs in ECE facilities (n=32).[a,b]

Analyte	>MDL (%)	Arithmetic Mean±SD	25th %	Median	75th %	95th %	Max
Methyltris(trimethylsiloxy)silane	37.5	401 ± 1211	<MDL	<MDL	132.2	2916	6186
Pentasiloxane, dodecamethyl-	31.3	917.4 ± 4898	<MDL	<MDL	33.0	559.0	27750
Silanol, trimethyl-	100.0	270.6 ± 507.7	102.9	140.5	181.3	1775	2539
Tetrasiloxane, decamethyl	50.0	2524± 12120	<MDL	17.3	193.8	6186	68650
Trisiloxane, octamethyl-	43.8	2728.2 ± 14330	<MDL	<MDL	106.5	1874	81220
Terpenes							
Bicyclo[3.1.1]heptane, 6,6-dimethyl-2-me	100.0	3112 ± 4771	703.7	1602	3402	10210	25610
Camphor[d]	93.8	1139 ± 3900	188.6	338.8	696.0	1689	22410
Caryophyllene	15.6	21.9 ± 65.4	<MDL	<MDL	<MDL	258.6	263.2
1,4-Cyclohexadiene, 1-methyl-4-(1-methylethyl)	68.8	1116 ± 2385	<MDL	484.5	710.0	7612	11510
3-Cyclohexen-1-ol, 4-methyl-1-(1-methylethyl)	15.6	271.3 ± 851.1	<MDL	<MDL	<MDL	2394	3724
3-Cyclohexene-1-methanol, α	87.5	908.2 ± 1968	135.8	232.5	870.7	3468	10570
Eucalyptol	100.0	2733 ± 11740	158.6	327.9	1073	2670	66970
Furfural[e]	100.0	1027 ± 820.2	428.5	708.7	1378	3008	3258
5-Hepten-2-one, 6-methyl-	68.8	171.2 ± 247.6	<MDL	82.8	209.1	817.2	1062
β-Myrcene	90.6	1450 ± 1830	291.3	789.6	2148	6103	7877
7-Octen-2-ol, 2,6-dimethyl-	100.0	3034 ± 3824	637.9	1657	3214	11490	15500
1,3-Pentadiene, (Z)-	65.6	329.7 ± 401.5	<MDL	254.3	539.8	951.8	1960
1-Penten-3-one, 1-(2,6,6-trimethyl-2-cyclohexen-1-yl)	90.6	111.4 ± 121.9	36.5	65.5	130.6	408.2	506.8
α-Phellandrene	21.9	55.0 ± 136.7	<MDL	<MDL	<MDL	437.6	502.5
2-Propanol, 1-[1-methyl-2-(2-propenyloxy)-ethoxy]	12.5	340.3 ± 1906	<MDL	<MDL	<MDL	62.6	10780

Abbreviations: Not computable (NC).

[a]Method detection limit (MDL) was set as 5 ng toluene equivalent in chromatographs for unknown peaks using the mass spectral library search with the NIST08 database.
[b]Concentrations are presented for levels measured above the MDL only (i.e., the mean equals the mean of detectable values).
[c]Compounds with established U.S. EPA RfCs (cyclohexane; naphthalene; 2-propanol, 1-methoxy; styrene) and/or OEHHA chronic reference exposure levels (cRELs) (isopropyl alcohol; naphthalene; 2-propanol, 1-methoxy; phenol; styrene).
[d] Four compounds identified as warranting additional evaluation (i.e., Hazard score>3): 1) acetic acid, butyl ester; 2) camphor; 3) n-pentane; and 4) 3-phenyl-2-propenal. Three compounds with hazard scores>3 were not prioritized in our assessment (SEE RESULTS): 1) acetate 2-pentanol; 2) dipropylene glycol monomethyl ether; and 3) 2-methylpropyl ester acetic acid.
[e]Compounds with established oral U.S. EPA RfDs but no RfC or REL (acetophenone; 1-butanol; cyclohexanone; ethyl acetate; furfural).

Table S17. Ratios of targeted VOC air concentrations to OEHHA acute Reference Exposure Level (aREL) and chronic REL (cREL), and U.S. EPA Reference Concentration (RfC).

Chemical[e]	Percentile (%)	Air Concentration (µg/m³)[a]	aREL[b] (µg/m³)	Ratio[c] (aREL)	cREL[b] (µg/m³)	Ratio[c] (cREL)	RfC[d] (µg/m³)	Ratio[c] (RfC)
2-Butoxyethanol	50th	2.9	14,000	0.0002	-	NC	1,600	0.002
	95th	64.0	14,000	0.005	-	NC	1,600	0.04
Benzene	50th	0.9	1,300	0.0007	60	0.01	30	0.03
	95th	2.0	1,300	0.001	60	0.03	30	0.07
Carbon tetrachloride	50th	<MDL	1,900	NC	40	NC	100	NC
	95th	<MDL	1,900	NC	40	NC	100	NC
Chloroform	50th	<MDL	150	NC	300	NC	-	NC
	95th	7.7	150	0.05	300	0.03	-	NC
Ethylbenzene	50th	0.6	-	NC	2,000	0.0003	1,000	0.0006
	95th	2.0	-	NC	2,000	0.003	1,000	0.002
n-Hexane	50th	0.6	-	NC	7,000	8E-05	700	0.0008
	95th	2.9	-	NC	7,000	0.0004	700	0.004
Methylene chloride	50th	<MDL	14,000	NC	400	NC	-	NC
	95th	<MDL	14,000	NC	400	NC	-	NC
Tetrachloroethylene	50th	0.1	20,000	4.0E-06	35	0.002	-	NC
	95th	1.0	20,000	4.9E-05	35	0.03	-	NC
Toluene	50th	3.1	37,000	8.2E-05	300	0.01	5,000	0.0006
	95th	11.2	37,000	0.0003	300	0.04	5,000	0.002
Xylenes	50th	2.5	22,000	0.0001	700	0.004	100	0.02
	95th	9.2	22,000	0.0004	700	0.01	100	0.09

Abbreviation: Not calculated (NC). [a]Concentrations averaged over school day (6-10 hours). [b]OEHHA REL. [c]Ratio of air concentration to preceding exposure guideline (REL or RfC). [d]U.S. EPA RfC.

Table S18. Ratios of non-targeted VOC air concentrations to OEHHA acute reference exposure level (aREL) and chronic REL (cREL), and U.S. EPA Reference Concentration (RfC).

Chemical	Percentile (%)	Air Concentration (µg/m³)[a]	aREL (µg/m³)	Ratio[c] (aREL)	cREL[b] (µg/m³)	Ratio[c] (cREL)	RfC[d] (µg/m³)	Ratio[c] (RfC)
Cyclohexane	50th	0.22	-	NC	-	NC	6,000	3.68E-5
	95th	1.40	-	NC	-	NC	6,000	2.34E-4
Isopropyl alcohol	50th	1.55	3,200	4.85E-4	7,000	2.22E-4	-	NC
	95th	12.67	3,200	3.96E-3	7,000	1.81E-3	-	NC
Naphthalene	50th	0.34	-	NC	9	3.80E-2	3	1.14E-1
	95th	1.12	-	NC	9	1.24E-1	3	3.73E-1
Phenol	50th	1.13	5,800	1.94E-4	200	5.64E-3	-	NC
	95th	3.80	5,800	6.56E-4	200	1.90E-2	-	NC
2-Propanol, 1-methoxy-	50th	0.13	-	NC	7,000	1.88E-5	658,000	2.00E-7
	95th	2.18	-	NC	7,000	3.11E-4	658,000	3.31E-6
Styrene	50th	0.30	21,000	1.43E-5	900	3.34E-4	1,000	3.01E-4
	95th	1.12	21,000	5.54E-5	900	1.24E-3	1,000	1.12E-3

Abbreviation: Not calculable (NC). [a]Concentrations averaged over school day (6-10 hours). [b]OEHHA REL. [c]Ratio of air concentration to preceding exposure guideline (REL or RfC). [d]U.S. EPA RfC.

TOXICOLOGICAL REVIEW

Toxicological information for the VOCs were compiled from two main sources: (1) authoritative lists and reports from government agencies, NGOs, and other expert bodies and (2) a quantitative structure-activity relationship (QSAR) model.

Information sources used to complete the hazard assessment include:

- **EPA Integrated Risk Information System (IRIS)**
  If available, health-based reference concentrations (RfCs) were obtained from theIRIS database.[5] If RfCs were not available, the reference doses (RfDs) were recorded if available.
- **California OEHHA**
  When available, OEHHA Reference Exposure Levels (RELs)[6] were obtained for both acute and chronic exposure. The chemicals were also checked against OEHHA Proposition 65 (Prop65)[7] listings for known cancer or reproductive toxicity.
- **ScoreCard**
  Maintained by the GoodGuide, ScoreCard[8] is an online program that identifies health hazards associated with chemicals. ScoreCard uses information from scientific sources and regulatory agencies to classify health hazards into two categories: recognized and suspected. Due to overlap between ScoreCard's "recognized" health effects with the toxicity data from preceding sources, ScoreCard's "suspected" health effects provided more insight into potential hazards and were recorded. ScoreCard has information on more than 11,200 chemicals and has not been updated since 2011.
- **Pharos Project**
  The Healthy Building Network curates the Pharos Project,[9] an online database compiling information on health hazards associated with chemicals used in consumer products and building materials. The Pharos Project compares chemical identifiers against 60 authoritative lists (including multiple international agencies such as the European Commission and Japan's Ministry of the Environment) and identifies associated health or environmental hazards. The Pharos Project characterizes 22 health and environmental hazard endpoints and contains more than 34,400 chemical profiles. The Pharos results provided qualitative information on the health hazards of the target chemicals.

To address hazard identification data gaps, a well-recognized QSAR model was utilized to predict toxicity according to chemical structure:

- **Virtual models for Evalulating chemicals within a Global Architecture (VEGA)**
  The non-profit Istituto di Ricerche Farmacologiche "Mario Negri" in (Milan, Italy) created the VEGA[10] platform as an accessible and free QSAR tool for evaluating chemical safety. The QSAR program was developed with support from the European Union, and includes some overlapping models used in the Organisation for Economic Co-operation and Development (OECD) QSAR Toolbox[11] program and outcomes included in the EPA TEST (Toxicity Estimation Software Tool) program. The VEGA platform focused on the following health endpoints : mutagenicity, carcinogenicity, developmental toxicity, and skin sensitization. The Istituto di Ricerche Farmacologiche "Mario Negri"[12] assisted us with the use of VEGA for our chemicals. The hazards assessment only recorded prediction results that had "good reliability" scores, indicating

that the model predicted results within the applicability domain index (ADI). VEGA generates ADIs to assess the "fit" of its experimental data set to the chemical under investigation and the reliability of its predictions. ADI scores >0.8 for mutagenicity models and >0.9 for the other models indicate good reliability

The ADI ranges from 0 (worst case) to 1 (best case) and incorporates several other indices, including: similar molecules with known experimental value, accuracy of prediction for similar molecules, concordance for similar molecules, atom centered fragments similarity check, and model descriptors range check.[13] Taking into account all the previous indices, the final ADI gives a general global assessment on the applicability domain for the predicted compound. The predicted substance is in the applicability domain of the model ("good reliability") if the final ADI>0.9 for the mutagenicity model and >0.8 for the carcinogenicity, developmental toxicity, and skin sensitization models. VEGA's mutagenicity models contain more refined training sets and can achieve a higher precision ADI.

HAZARD ASSESSMENT

Ranking & Prioritization

For the 25 targeted VOCs without health-based benchmarks, we used information from authoritative lists and QSAR models (described above) to classify the chemicals into 10 hazard groups. **Table S19** shows the hazard grouping criteria, data source, and number of chemicals in each group. Group classifications are not mutally exclusive.

Table S19. Hazards classification table for 25 targeted VOC analytes.

Group No.	Criteria	Data Source[a]			No. of Chemicals[b]
		PHAROS	ScoreCard	VEGA	
1	Carcinogen or mutagen	0	0	2	2
2	Developmental toxicant	5	1	3	7
3	Reproductive toxicant	1	0		1
4	Endocrine-disrupting chemical	1	0		1
5	Neurotoxicant	2	6		6
6	Immunotoxicant or sensitizer	3	1	13	14
7	Specific organ or acute toxicants	17	6		17
8	Irritant	15			15
9	Persistent or bioaccumulative	6			6
10	No positive data	0	0	1[c]	1

[a]Grey boxes indicate that the data source does not have the specified health endpoint. [b]Total number of chemicals in each hazard group, which may be less than the summation of the data sources due to the non-exclusivity the hazard groups. [c]The one compound in Group 10, n-dodecane, was identified as a non-mutagen under VEGA QSAR model.

VEGA was used to assess the 25 targeted VOCs that lacked health-based reference values. Table S20 shows the proportion of compounds with good reliability scores for each outcome. VEGA produced "good reliability" predictions for 92% for mutagenicity, 8% for carcinogenicity, 12% for developmental toxicity, and 56% for skin sensitization. VEGA positively predicted mutagenicity for 1,2,3-trimethylbenzene. For carcinogenicity, VEGA produced positive and negative predictions for 1,2,3-trimethylbenzene and 1,2,4-trimethylbenzene due to differences in toxicity data sources. VEGA identified 2-ethyl-1-hexanol, α-pinene, and a-terpineol as potential developmental toxicants. VEGA predicted 83% of the fragrance HS compounds as skin sensitizers, including d-limonene and α-pinene. Most of the fragrance HS compounds have been recognized as skin irritants.[9]

Table S20. Proportion of targeted VOCs with good VEGA reliability scores (n=25 analytes).

VEGA Endpoint	**Proportion with "good reliability"**
Mutagenicity[a]	92%
Carcinogencity[b]	8%
Developmental Toxicity[b]	12%
Skin Sensitization[b]	56%

[a]ADI>0.9. [b]ADI>0.8.

Table S21. Hazards screening for 17 targeted VOC analytes (Hazard Score >0 and ≤3).[a,b]

Analyte	CAS No.	PHAROS[c]	ScoreCard[d]	VEGA[e]	Hazard Score
Mixed and Mobile Sources					
n-Decane	124-18-5	Irritant , Acute Toxicant	Data lacking	[Non-Mutagen]	2
n-Hexadecane	544-76-3	Irritant , Acute Toxicant	Data lacking	Non-Mutagen, Skin Sensitizer	3
n-Octane	111-65-9	Irritant, Neurotoxic, Respiratory Toxicant, Acute Toxicant	Neurotoxicity	Non-Mutagen	3
n-Tetradecane	629-59-4	Acute Toxicant	Data lacking	Non-Mutagen	1
1,2,3-Trimethylbenzene	526-73-8	Developmental Toxocant, Acute Toxicant	Data lacking	[Mutagen], Carcinogen	3
n-Undecane	1120-21-4	Acute Toxicant	Data lacking	[Non-Mutagen]	1
Household Sources					
Fragrances					
Butanal	123-72-8	Irritant, Acute Toxicant	Respiratory Toxicity, Skin or Sense Organ Toxicity	[Non-Mutagen]	2
3-Carene	13466-78-9	Asthmagen	Data lacking	Non-Mutagen, Sensitizer	1
Decanal[f]	112-31-2	Irritant, Acute Toxicant	Data lacking	Non-Mutagen, Skin Sensitizer	3
Hexanal[f]	66-25-1	Irritant	Data lacking	Non-Mutagen, Skin Sensitizer	2
Nonanal	124-19-6	Irritant	Data lacking	[Non-Mutagen], Skin Sensitizer	2
Octanal[f]	124-13-0	Irritant	Data lacking	Non-Mutagen, Skin Sensitizer	2
ɣ-Terpinene[f]	99-85-4	Data lacking	Data lacking	Non-Mutagen, Skin Sensitizer	1
Other household products					
2-Ethyl-1-hexanol	104-76-7	Developmental Toxicant, Irritant, Acute Toxicant	Developmental Toxicity, Gastrointestinal or Liver Toxicity	[Non-Mutagen], Developmental Toxicant	3

Table S21 (cont.) Hazards screening for 17 targeted VOC analytes (Hazard Score >0 and ≤3).[a,b]

Analyte	CAS No.	PHAROS[c]	ScoreCard[d]	VEGA[e]	Hazard Score
Texanol	25265-77-4	Acute Toxicant	Data lacking	Non-Mutagen, Skin Sensitizer	2
2,2,4-trimethyl-1,3-pentanediol diisobutyrate (TXIB)	6846-50-0	PBT	Data lacking	Non-Mutagen, Skin Sensitizer	2

[a]n-Dodecane was excluded from the hazard table due to the lack of positive toxicity data (i.e., Group 10; Hazard score=0). Compounds with health-based reference values were also excluded from the screening.
[b] Compounds identified as warranting additional evaluation (e.g., Hazard Score>3) are presented in the main paper (Table 4).
[c] "Acute Toxicant" is listed as "Toxic to Mammals" in PHAROS.
[d]Suspected effects.
[e]Brackets indicate experimental data.
[f] EPA SCP yellow triangle rating: The chemical has met Safer Choice Criteria for its functional ingredient-class, but has some hazard profile issues. Specifically, a chemical with this code is not associated with a low level of hazard concern for all human health and environmental endpoints. While it is a best-in-class chemical and among the safest available for a particular function, the function fulfilled by the chemical should be considered an area for safer chemistry innovation.[14]

Abbreviations: Persistent Bioaccumulative Toxicant (PBT)

For the 107 non-targeted VOCs without health-based benchmarks, we used information from authoritative lists and QSAR models to classify the chemicals into 10 hazard groups. Table S21 shows the hazard grouping criteria, data source, and number of chemicals in each group. Group classifications are not mutally exclusive.

Table S22. Hazards classification table for 107 non-targeted VOC analytes.

Group No.	Criteria	Data Source[a]			No. of Chemicals[b]
		PHAROS	ScoreCard	VEGA	
1	Carcinogen or mutagen	2	0	0	2
2	Developmental toxicant	9	1	17	23
3	Reproductive toxicant	6	5		10
4	Endocrine-disrupting chemical	2	1		2
5	Neurotoxicant	10	13		17
6	Immunotoxicant or sensitizer	2	2	31	32
7	Specific organ or acute toxicants	28	11		28
8	Irritant	9			9
9	Persistent or bioaccumulative	8			8
10	No positive health data				48

[a]Grey boxes indicate that the data source does not have the specified health endpoint. [b]Total number of chemicals in each hazard group, which may be less than the summation of the data sources due to the non-exclusivity the hazard groups.

VEGA was used to assess the non-targeted VOCs that lacked health-based reference values (n=58 analytes). Table S22 shows the proportion of compounds with good reliability scores for each outcome.

Table S23. Proportion of non-targeted VOCs with good VEGA reliability scores (n=58 analytes).

VEGA Endpoint	Proportion with "good reliability"
Mutagenicity[a]	90%
Carcinogencity[b]	14%
Developmental Toxicity[b]	34%
Skin Sensitization[b]	57%

[a]ADI>0.9. [b]ADI>0.8.

Table S24. Hazards screening for 58 non-targeted VOC analytes.[a]

Analyte	CAS No.	PHAROS[b]	ScoreCard[c]	VEGA[d]	Hazard Score
Alkanes					
Cyclododecane	294-62-2	PBT	Data lacking	Non-Mutagen, Sensitizer	2
Cyclohexane, methyl-	108-87-2	Acute Toxicant, Developmental Toxicant, Neurotoxicant	Neurotoxicity	Non-Mutagen	3
Hexane, 2,4-dimethyl-	589-43-5	Acute Toxicant, Skin Irritant, Neurotoxicant	Data lacking	Non-Mutagen	2
Hexane, 2-methyl-	591-76-4	Acute Toxicant, Skin Irritant, Neurotoxicant	Data lacking	Non-Mutagen	2
Hexane, 3-methyl-	589-34-4	Acute Toxicant, Skin Irritant, Neurotoxicant	Data lacking	Non-Mutagen	3
n-Nonadecane	629-92-5	Data lacking	Data lacking	Non-Mutagen, Sensitizer	1
n-Nonane	111-84-2	Acute Toxicant, Neurotoxicant, Respiratory Toxicant, Specific Organ Toxicant	Neurotoxicity	[Non-Mutagen]	3
Pentadecane	629-62-9	Acute Toxicant	Data lacking	Non-Mutagen, Sensitizer	2
n-Pentane[e]	109-66-0	Acute Toxicant, Developmental Toxicant, Neurotoxicant, Persistent, Respiratory Toxicant, Specific Organ Toxicant	Neurotoxicity	Non-Mutagen	5
Tetradecane, 2,2-dimethyl-	59222-86-5	Data lacking	Data lacking	Non-Mutagen, Sensitizer	1

Table S24 (cont.) Hazards screening for 58 non-targeted VOC analytes.[a]

Analyte	CAS No.	PHAROS[b]	ScoreCard[c]	VEGA[d]	Hazard Score
Oxygenated Hydrocarbons					
Acetic acid[f]	64-19-7	Acute Toxicant, Developmental Toxicant, Neurotoxicant, Respiratory Toxicant	Cardiovascular or Blood Toxicity, Gastointestinal or Liver Toxicity, Respiratory Toxicity, Skin or Sense Organ Toxicity	[Non-Mutagen], Non-Sensitizer	3
Acetic acid, butyl ester[e]	123-86-4	Acute Toxicant, Developmental Toxicant, Neurotoxicant, Persistent, Specific Organ Toxicant	Gastrointestinal or Liver Toxicity, Neurotoxicity, Respiratory Toxicity, Skin or Sense Organ Toxicity	Non-Mutagen, Sensitizer	6
Acetic acid, 2-methylpropyl ester[e,g]	110-19-0	Acute Toxicant, Developmental Toxicant	Neurotoxicity	Non-Mutagen, Developmental Toxicant, Sensitizer	4
Cyclohexanol, 5-methyl-2-(1-methylethyl)	15356-70-4	Data lacking	Data lacking	[Non-Mutagen], Developmental toxicant, Sensitizer	2
Dipropylene glycol monomethyl ether[e,f]	34590-94-8	Developmental Toxicant, Irritant, Neurotoxicant, Specific Organ Toxicant	Reproductive Toxicity, Neurotoxicity, Kidney Toxicity	Non- Mutagen, Developmental Toxicant,	5
Ethanol, 2-(2-butoxyethoxy)-[h]	112-34-5	Acute Toxicant, Developmental Toxicant, Specific Organ Toxicant	Reproductive Toxicity, Cardiovascular or Blood Toxicity, Kidney Toxicity, Neurotoxicity	Non-Mutagen, Developmental Toxicant,	3
Ethanol, 2-(hexyloxy)-	112-25-4	Acute Toxicant, Irritant	Gastrointestinal or Liver Toxicity, Respiratory Toxicity	Non-Mutagen	2

Table S24 (cont.) Hazards screening for 58 non-targeted VOC analytes.[a]

Analyte	CAS No.	PHAROS[b]	ScoreCard[c]	VEGA[d]	Hazard Score
1-Hexacosanol	506-52-5	very low hazard-german	Data lacking	Non-Mutagen, Non-Carcinogen, Sensitizer	1
1,8-Nonanediol, 8-methyl-	54725-73-4	Data lacking	Data lacking	Non-Mutagen, Non-Carcinogen, Sensitizer	1
Octane, 1,1'-oxybis-	629-82-3	low hazard to waters-German	Data lacking	Non-Mutagen, Non-Developmental Toxicant, Sensitizer	1
1-Octanol[h]	111-87-5	Acute Toxicant, Gene Mutation	Data lacking	Non-Mutagen	2
Octanol, 2-butyl-	3913-02-8	hazard to waters-German	Data lacking	Non-Mutagen, Developmental Toxicant, Sensitizer	2
1-Octanol, 2,2-dimethyl-	2370-14-1	Data lacking	Data lacking	Non-Mutagen, Sensitizer	1
3-Octanol, 3,7-dimethyl-, (±)-	57706-88-4	Data lacking	Data lacking	Non-Mutagen, Sensitizer	1
Pentanal	110-62-3	Acute Toxicant, Neurotoxicant	Data lacking	[Non-Mutagen], Sensitizer	3
2-Pentanol, acetate[e]	626-38-0	Irritant, Skin Sensitizer, Specific Organ Toxicant	Neurotoxicity, Respiratory Toxicity, Skin or Sense Organ Toxicity	Non-Mutagen, Sensitizer	4
2-Propanol, 1-butoxy-[f]	5131-66-8	Acute Toxicant, Irritant	Neurotoxicity	Non-Mutagen	3
2-Propanol, 1-(2-methoxy-1-methylethoxy)[f]	20324-32-7	U.S. EPA—low concern	Data lacking	Non-Mutagen, Developmental Toxicant	1

Table S24 (cont.) Hazards screening for 58 non-targeted VOC analytes.[a]

Analyte	CAS No.	PHAROS[b]	ScoreCard[c]	VEGA[d]	Hazard Score
2-Propanol, 1-(2-methoxypropoxy)-	13429-07-7	Acute Toxicant, Neurotoxicant	Data lacking	Non-Mutagen, Developmental Toxicant	3
1-Propanol, 2-(1-methylethoxy)-	3944-37-4	Data lacking	Data lacking	Non-Mutagen, Developmental Toxicant	1
2-Propanol, 1-propoxy-[f]	1569-01-3	Acute Toxicant	Data lacking	Non-Mutagen, Developmental Toxicant	2
Aromatic					
Acetic acid, phenylmethyl ester	140-11-4	Acute Toxicant, Specific Organ Toxicant	Gastrointestinal or Liver Toxicity, Kidney Toxicity, Neurotoxicity, Respiratory Toxicity	[Non-Mutagen], [Non-Carcinogen]	3
Benzaldehyde, 4-methoxy-	123-11-5	Acute Toxicant	Neurotoxicity	[Non-Mutagen], Non-Sensitizer	2
Benzene, 1-ethyl-3,5-dimethyl-	934-74-7	Data lacking	Data lacking	Non- Mutagen, Sensitizer	1
Benzophenone	119-61-9	Acute Toxicant, Carcinogen (possible), Endocrine Activity	Cardiovascular or Blood Toxicity, Endocrine Toxicity, Gastrointestinal or Liver Toxicity, Skin or Sense Organ Toxicity	[Non-Mutagen]	3
Benzyl Alcohol	100-51-6	Acute Toxicant, Neurotoxicant	Gastrointestinal or Liver Toxicity, Immunotoxicity, Neurotoxicity, Skin or Sense Organ Toxicity	[Non-Mutagen], [Non-Carcinogen]	3
Ethanol, 2-phenoxy-[h]	122-99-6	Acute Toxicant, Developmental Toxicant, Reproductive Toxicant	Reproductive Toxicity, Developmental Toxicity	Non-Developmental Toxicant,	3

Table S24 (cont.) Hazards screening for 58 non-targeted VOC analytes.[a]

Analyte	CAS No.	PHAROS[b]	ScoreCard[c]	VEGA[d]	Hazard Score
2-Ethylhexyl salicylate	118-60-5	Skin Irritant	Data lacking	Non-Mutagen, Non-Carcinogen, Non-Developmental Toxicant	1
Homosalate	118-56-9	Endocrine Activity, PBT	Data lacking	Non-Mutagen, Non-Carcinogen	2
3-Methyl-4-isopropylphenol	3228-02-2	Data lacking	Data lacking	Non-Mutagen, Non-Carcinogen, Developmental Toxicant	1
Naphthalene, 2-methoxy-[h]	93-04-9	Data lacking	Data lacking	Sensitizer	1
2-Propenal, 3-phenyl-[e]	104-55-2	Acute Toxicant, Developmental Toxicant, Reproductive Toxicant, Skin Sensitizer	Immunotoxicity, Neurotoxicity, Skin or Sense Organ Toxicity	[Non-Mutagen], Non-Carcinogen, [Sensitizer]	5
Siloxanes					
Cyclohexasiloxane, dodecamethyl-	540-97-6	PBT	Data lacking	Data lacking	1
Decamethyl tetrasiloxane	141-62-8	PBT	Data lacking	Data lacking	1
Terpenes					
Bicyclo[3.1.1]heptane, 6,6-dimethyl-2-me	127-91-3	Acute Toxicant	Data Lacking	Non-Mutagen, Developmental Toxicant	2
Camphor[e]	76-22-2	Acute Toxicant, Reproductive Toxicant, Specific Organ Toxicant	Gastrointestinal or Liver Toxicity, Neurotoxicity, Respiratory Toxicity, Skin or Sense Organ Toxicity	Sensitizer, [Developmental Toxicant]	5

Table S24 (cont.) Hazards screening for 58 non-targeted VOC analytes.[a]

Analyte	CAS No.	PHAROS[b]	ScoreCard[c]	VEGA[d]	Hazard Score
Caryophyllene	87-44-5	PBT	Data lacking	Non-Mutagen, Development Toxicant, Sensitizer	3
1,4-Cyclohexadiene, 1-methyl-4-(1-methylethyl)[h]	99-85-4	USEPA-medium hazard	Data lacking	Non-Mutagen, Sensitizer	1
3-Cyclohexen-1-ol, 4-methyl-1-(1-methylethyl)[g]	562-74-3	Hazard to waters-German	Data lacking	Non-Mutagen, Developmental Toxicant, Sensitizer	2
3-Cyclohexene-1-methanol, α	1679-51-2	Data lacking	Data lacking	Non-Mutagen, Developmental Toxicant, Sensitizer	2
Eucalyptol[h]	470-82-6	Acute	Data lacking	[Non-Mutagen], Developmental Toxicant, Sensitizer	3
5-Hepten-2-one, 6-methyl-	110-93-0	Data lacking	Data lacking	Non-Mutagen, Sensitizer	1
β-Myrcene	123-35-3	Reproductive Toxicant (suspected), Irritant	Data lacking	Non-Mutagen, Sensitizer	3
7-Octen-2-ol, 2,6-dimethyl-[g]	18479-58-8	Data lacking	Data lacking	Non-Mutagen, Sensitizer	1
1,3-Pentadiene, (Z)-	1574-41-0	Data lacking	Data lacking	Sensitizer	1
1-Penten-3-one, 1-(2,6,6-trimethyl-2-cyclohexen-1-yl)[h]	7779-30-8	PBT	Data lacking	Non-Mutagen, Sensitizer	2
α-Phellandrene	99-83-2	Data lacking	Data lacking	Non-Mutagen, Sensitizer	1
2-Propanol, 1-[1-methyl-2-(2-propenyloxy)-ethoxy]	55956-25-7	Data lacking	Data lacking	Non-Mutagen, Developmental Toxicant, Sensitizer	2

[a]Compounds with health-based reference values were excluded, as well as compounds that lack positive toxicity data (i.e., Group 10; Hazard score = 0).
[b]Acute Toxicant is listed as Toxic to Mammals in PHAROS.
[c]Suspected effects.

[d]Brackets indicate experimental data.
[e]Four compounds identified as warranting additional evaluation (i.e., Hazard score>3): 1) acetic acid, butyl ester; 2) camphor; 3) n-pentane; and 4) 3-phenyl-2-propenal. Three compounds with hazard score>3 were not prioritized in our assessment (SEE RESULTS): 1) acetate 2-pentanol; 2) dipropylene glycol monomethyl ether; and 3) 2-methylpropyl ester acetic acid.
[f]U.S. EPA SCP green circle rating: The chemical has been verified to be of low concern based on experimental and modeled data.[14]
[g]U.S. EPA SCP green half-circle: The chemical is expected to be of low concern based on experimental and modeled data.[14]
[h]U.S. EPA SCP yellow triangle: The chemical has met Safer Choice Criteria for its functional ingredient-class, but has some hazard profile issues.[14]

Abbreviations: Persistent Bioaccumulative Toxicant (PBT).

REFERENCES

1. Massachusetts Department of Environmental Protection. *Indoor Air Sampling and Evaluation Guide*; 2002.
2. ATSDR. *Public Health Assessment Guidance Manual*; Agency for Toxic Substances and Disease Registry, Atlanta, GA, 2005.
3. U.S. EPA. *Child-Specific Exposure Factors Handbook (Final Report)*; U.S. Environmental Protection Agency, Washington DC, 2008.
4. Arcus-Arth, A.; Blaisdell, R. J., Statistical distributions of daily breathing rates for narrow age groups of infants and children. *Risk analysis : an official publication of the Society for Risk Analysis* **2007,** *27*, (1), 97-110.
5. U.S. EPA. *Integrated Risk Information System (IRIS).* http://www.epa.gov/IRIS/ (accessed Nov 13, 2013).
6. OEHHA. *All OEHHA Acute, 8-hour and Chronic Reference Exposure Levels (chRELs) as of June 2014.* California Office of Environmental Health Hazard Assessment. http://www.oehha.ca.gov/air/Allrels.html (accessed Nov 13, 2014).
7. OEHHA. *Proposition 65: No Significant Risk Levels (NSRLs) for Carcinogens and Maximum Allowable Dose Levels (MADLs) for Chemicals Causing Reproductive Toxicity*; California Office of Environmental Health Hazard Assessment, Sacramento, CA, 2013. http://oehha.ca.gov/prop65/getNSRLs.html (accessed August 7, 2015).
8. ScoreCard. *Chemical Profiles.* http://scorecard.goodguide.com/chemical-profiles/ (accessed Nov 13, 2013).
9. Healthy Building Network. *PharosProject.* https://www.pharosproject.net/ (accessed Feb 12, 2014).
10. Istituto di Ricerche Farmacologiche Mario Negri. *Virtual models for property Evaluation of chemicals within a Global Architecture (VEGA).* http://www.vega-qsar.eu/ (accessed June 2, 2014).
11. Organisation for Economic Co-operation and Development (OECD). *QSAR Toolbox.* http://www.qsartoolbox.org/
12. Istituto di Ricerche Farmacologiche Mario Negri. *Istituto di Ricerche Farmacologiche Mario Negri.* http://www.marionegri.it/en_US/home
13. Istituto di Ricerche Farmacologiche Mario Negri. *Guidelines for the VEGA models (version 2.1.1).* http://www.vega-qsar.eu/guidelines.html
14. U.S. EPA. Safer Choice. Safer Chemical Ingredient's List (SCIL). http://www.epa.gov/saferchoice/safer-ingredients#scil [accessed December 12, 2015].