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Ranking Cancer Risks of Organic Hazardous Air Pollutants in the United States

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Abbreviations:

1,4-DCB = 1,4-dichlorobenzene

1,3-DCP = 1,3-dichloropropene

ASPEN = Assessment System for Population Exposure Nationwide

B[a]P = benzo[a]pyrene

ETS = environmental tobacco smoke

HAPs = Hazardous air pollutants

IRIS = Integrated Risk Information System

NATA = National Air Toxics Assessment

NHAPS = National Human Activity Patterns Survey

NHEXAS = National Human Exposure Assessment Survey

OEHHA = Office of Environmental Health Hazards Assessment (State of California)

PAH = Polycyclic aromatic hydrocarbon

PAH B2 = polycyclic aromatic hydrocarbons with more evidence of carcinogenicity

PAH CD = polycyclic aromatic hydrocarbons with less evidence of carcinogenicity

RIOPA = Relationship of Indoor, Outdoor, and Personal Air

TCDD = 2,3,7,8-tetrachlorodibenzo-*p*-dioxin

TEAM = Total Exposure Assessment Methodology

TEF = Toxicity equivalence factors

TEQ = Toxic equivalent

U.S. EPA = Environmental Protection Agency (U.S.)

VOC = Volatile organic compound

Outline of Section Headers

Abstract

Background: This study compares cancer risks from organic hazardous air pollutants (HAPs) based on total personal exposure summed across different microenvironments and exposure pathways. **Methods:** We developed distributions of personal exposure concentrations using field monitoring and modeling data for inhalation and, where relevant, ingestion pathways. We calculated risks for a non-occupationally exposed and non-smoking population using U.S. (U.S. EPA) and California Office of Environmental Health and Hazard Assessment (OEHHA) unit risks. The contribution to risk from indoor versus outdoor sources was determined using indoor/outdoor ratios for gaseous compounds and the infiltration factor for particle-bound compounds. **Results:** Using OEHHA's unit risks, the highest ranking compounds based on the population median are 1,3-butadiene, formaldehyde, benzene, and dioxin, with risks on the order of 10^{-4} – 10^{-5}. The highest risk compounds using the U.S. EPA unit risks were dioxin, benzene, formaldehyde, and chloroform, with risks on a similar order of magnitude. While indoor exposures are responsible for nearly 70% of risk using OEHHA's unit risks, when infiltration is accounted for, inhalation of outdoor sources contributed 50% to total risk, on average. Additionally, 15% of risk resulted from exposures through food, mainly due to dioxin. **Conclusions:** Most of the polycyclic aromatic hydrocarbon, benzene, acetaldehyde, and 1,3-butadiene risk came from outdoor sources, while indoor sources were primarily responsible for chloroform, formaldehyde, and naphthalene risks. The infiltration of outdoor pollution into buildings, emissions from indoor sources, and uptake through food are all important to consider in reducing overall personal risk to HAPs.

Introduction

The U.S. Clean Air Act designates hazardous air pollutants (HAPs) as those that "may reasonably be anticipated to be carcinogenic, mutagenic…." (CAAA 1990) and exhibit other adverse health effects. Effective reduction of exposures to HAPs requires determining the compounds, exposure pathways, and sources that contribute the most to human health risk.

Many prior risk assessments for HAPs have been limited by either including only indoor or outdoor concentrations or examination of a small subset of carcinogenic HAPs. The U.S. Environmental Protection Agency (U.S. EPA) assessed the nationwide risk from outdoor concentrations of most of the HAPs. Based on the Assessment System for Population Exposure Nationwide (ASPEN) model, the U.S. EPA found that almost half of total estimated lifetime cancer cases from HAPs could be attributed to volatile organic compounds (VOCs), with another 40% from polycyclic aromatic compounds (PAHs) (Woodruff et al. 2000). The median cancer risk was 17 cases out of every 100,000 people. An updated assessment finds a median risk of 4 in 100,000 (U.S. EPA 2006) accounting for changes in emissions estimates and lower cancer potency values for some of the larger contributors to risk (particularly 1,3-butadiene and formaldehyde). However, outdoor exposures account for only a portion of risk for many compounds.

In two older studies using indoor concentrations from homes and offices, one by Tancrede and another by McCann, calculated cancer potency factors with data from animal and human studies. Tancrede found annual mean risks from indoor air to be about 1 in 10,000 to 1 in 100,000 and McCann's risks are about an order of magnitude higher (McCann et al. 1986; Tancrede et al. 1987). Concentrations of many of these compounds, however, have changed since these studies were completed.

Personal exposure measurements from the Total Exposure Assessment Methodology (TEAM) studies provided estimates of individual cancer risks from benzene ranging from 1

in 10,000 for non-smokers to 7 in 10,000 for smokers (Wallace 1991a). More recently, Payne-Sturges et al. found risks from personal exposure over three times higher than those calculated using the ASPEN modeled outdoor concentrations (Payne-Sturges et al. 2004). Sax et al. also found risks from personal exposures of inner city teenagers to be on the order of 1 in 10,000 (Sax et al. 2006). Despite these studies, there has not been a broad analysis of cancer risk integrating total personal exposure to a wide range of organic HAPs in multiple microenvironments and across different exposure pathways. Also, two potentially high-risk classes of HAPs have not been included in previous personal exposure risk assessments – the dioxins and the polycyclic aromatic hydrocarbons.

Exposure to semi-volatile HAPs, such as dioxins/furans and polycyclic aromatic hydrocarbons (PAHs), can also come from non-inhalation pathways, especially food ingestion (Butler et al. 1993; Ramesh et al. 2004; U.S. EPA 2003). Although these compounds are primarily released to the air, some fraction is bound to particulate matter and then deposited onto vegetation or water bodies where they build up in the food chain. Multi-media sampling has been done previously (Butler et al. 1993; Chuang et al. 1999), but only for a specific compound or class of compounds, and the risks of multi-pathway exposures have not been analyzed or compared across compound groups.

To gain a wider perspective on population risks from organic HAPs, we estimated the cancer risks in the US by using calculated total personal exposure. We restricted ourselves to organic compounds that were responsible in aggregate for over 87% of the risk from Woodruff et al. (2000), along with several others with known indoor sources or for which ingestion is a main route of exposure. We chose to first model baseline exposures, defined as those not including specifically known and consistent high exposure scenarios. We also examine situations for some compounds where a particular and relatively constant high exposure scenario can be developed.

We developed a flexible modeling framework that integrates data from different sources. The modeled personal exposure distributions were multiplied by a measure of cancer potency to calculate risk distributions that were ranked relative to each other. Since there is significant uncertainty in the toxicity estimates, we compared the risks calculated using two different sets of cancer potencies – U.S. EPA's Integrated Risk Information System (IRIS) and the California Office of Environmental Health and Hazard Assessment (OEHHA). In addition, we compared the proportion of risk attributable to indoor, outdoor, and ingestion exposures with the proportion of risk attributable to indoor and outdoor sources.

Methods

In this analysis, we 1) develop personal exposure distributions; 2) calculate and compare baseline risks; 3) examine the influence of alternative scenarios in exposure patterns and uncertainties in toxicity estimates on the results of the baseline assessment; 4) determine the relative contribution of the ingestion pathway and the various inhalation microenvironments to the baseline risk; and 5) disaggregate risk into indoor and outdoor source components.

Our baseline model represents a non-specified population of office-working and non-employed adults between the ages of 18-65, which are assumed to be a relatively "low exposure" population. We do not include smokers or manufacturing workers in the baseline because these populations are expected to have higher exposures from sources for which characterization was beyond the scope of this assessment. We classified compounds based on the availability of concentration data, emissions sources, and the primary route of exposure.

- *Group 1 compounds* are VOCs expected to come only from outdoor sources and include vinyl chloride, carbon tetrachloride, 1,3-dichloropropene, ethylene dibromide, and

ethylene dichloride. Measured ambient concentrations are not readily available for most of these compounds.

- *Group 2 compounds* are VOCs with indoor and outdoor sources, and available data on concentrations in the home and other microenvironments. Group 2 includes benzene, formaldehyde, chloroform, 1,4-dichlorobenzene, methylene chloride, trichloroethylene, perchloroethylene, 1,3-butadiene, and acetaldehyde.
- *Group 3 compounds* are semi-volatile, with a substantial amount of exposure from ingestion, and include PAHs and dioxins.

Since the results are dependent on the assumptions and choices for the input parameters, we conducted several analyses to examine the effect of variability in exposure and uncertainty in cancer potency values. We quantified exposure parameter variability associated with the baseline distribution, assuming that the higher percentiles of the distribution will encompass highly exposed individuals, except for cases where there is evidence of a bi-modal distribution. In the latter case, there may be specific instances with additional indoor or outdoor sources, leading to a separate exposure distribution from the general population and, consequently, a different risk ranking. Regarding toxicity, cancer potency factors have not previously encompassed heterogeneity across the population; however, we examined uncertainty by comparing the results from 2 different sets of cancer potency factors.

Exposure Model. Figure 1 illustrates the overall model used in this analysis. Exposure was calculated using Monte Carlo simulations in Crystal Ball (Decisioneering) according to equation 1:

$$E = \frac{1}{T}\sum_{i=1}^{k} C_i t_i \qquad [1]$$

E = the exposure to an individual of pollutant X (summed over k microenvironments)

C_i = the concentration in the ith microenvironment

t_i = the time spent in the microenvironment

T = the total amount of time

Distributions for the time spent in each microenvironment were taken from the National Human Activity Patterns Survey (NHAPS) (Graham and McCurdy 2004; Kleipeis et al. 2001; McCurdy and Graham 2003). The model population consisted of 4 types of people, sampled according to the percentage of the population that they represent in the 2000 Census (Clark and Weismantle 2003) - non-working males (11%), working males (38%), non-working females (17%), and working females (33%). Since NHAPS only provides cross-sectional 24-hour data, each working person has the same weekday 5 days of the week and the same weekend day for two days. Non-working individuals have the same day seven days a week. The workday data came from people surveyed on a day they went to work, and weekend data came from working people surveyed on a day they did not go to work. In order to preserve the relationship between time in each microenvironment, we sampled from the NHAPS individuals' diary-days directly. For the risk calculation we assume that these week-long exposures are representative of lifetime exposures.

Concentration distributions were derived by evaluating and combining data reported in several studies. We searched the peer-reviewed literature for studies that measured the compounds of interest in each microenvironment, giving preference to studies conducted in the US and after 1995, to reflect more recent emission sources. Most of the data used were published prior to 2006. A small subset was obtained directly from the study investigators.

For Group 1 compounds, we derived ambient concentration distributions from ASPEN model results. These concentrations were used as personal exposure concentrations, since we assume no indoor sources for these compounds. ASPEN estimates ambient concentrations of HAPs for each census tract in the US and includes emissions from point, area, and mobile sources, as well as secondary formation, decay, and deposition.

ASPEN is the most comprehensive and spatially representative source of information for all outdoor HAPs concentrations. We used ambient concentrations for all census tracts based on 1996 emissions data, the most recent data available at the time this analysis was conducted (U.S. EPA 1996b) (Table 1).

For Group 2 compounds, we compared each study's reported parameters (usually the arithmetic mean and standard deviation, and median and 90th percentiles), the percentage of detectable samples, and the limits of detection, where reported. When deriving the final input distributions, we combined studies by weighting each city/geographic region equally. If multiple studies were conducted in an area, each study was given equal weight to determine the distribution in that city/geographic region. We assumed lognormal distributions for all studies where raw data were not available to us and fit the reported parameters in Crystal Ball (Table 2).

In-home and outdoor concentrations were derived from studies conducted in a range of urban and suburban communities, ranging from both coasts of the United States and the Midwest and southwest, and including various ethnic groups and neighborhood sources (see Table 2). If more than 50% of the values were under the detection limit, and the detection limit was deemed to be high compared with other studies, we chose not to use those data. In all other cases of low detects, we did not discard the study, as these values indicate a low environmental concentration level. We compared the studies qualitatively to assess whether a particular one appeared to indicate a higher or lower distribution than other studies, or if there appeared to be a subpopulation with a distinctly different concentration distribution. Outdoor distributions were similarly developed.

Studies where the mean exceeded the 90th percentile (a highly skewed distribution) were not included in the baseline. Indoor data excluded were from Sax et al. from New York City in their summer sampling for 1,4-dichlorobenzene, and NHEXAS

trichloroethylene data from U.S. EPA's Region 5. We also did not include any studies where the 90th percentile for 1,4-dichlorobenzene exceeded 100 μg/m^3, which was over 100 times the median. Such a large tail indicated several homes from a few studies with extremely high concentrations, bringing the means to be almost 10 times the means of other studies (Adgate et al. 2004b; Sax et al. 2004).

Data for transportation, shopping, dining, and office workplaces were taken from various studies listed in Table 2. The miscellaneous "other" microenvironment was assigned the same concentration distributions as the outdoors.

Group 3 compounds consist of congeners that are weighted by a toxicity equivalence factor (TEF) relative to a reference congener (benzo[a]pyrene (B[a]P) for PAHs and for 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) for dioxins). We summed the TEF-weighted exposure concentrations for each congener to arrive at a total toxic equivalent (TEQ) concentration.

The PAHs were divided into two groups based on the evidence available for carcinogenic effects. The first group (benzo[a]anthracene, benzo[b]fluoranthene, benzo[a]pyrene, chrysene, dibenzo[a,h]anthracene, indeno[1,2,3-cd]pyrene) have evidence of carcinogenicity from animal studies, and we refer to them as PAH B2. Concentrations in air and food were available for these compounds. The second group (anthracene, benzo[g,h,i]perylene, phenanthrene, pyrene, fluoranthene) are less certain to be carcinogens and are named PAH CD. We only consider the inhalation pathway for the PAH CD compounds, as most of these compounds have not been as successfully quantified in food and have much smaller contributions to the total TEF weighted food exposure than the PAH-B2 compounds. Naphthalene is treated separately because it has TEF weighted concentrations that are at least an order of magnitude higher than other PAHs.

Home indoor and outdoor air PAH concentrations came from the Relationship of Indoor, Outdoor, and Personal Air (RIOPA) study in Los Angeles, California; Houston, Texas; and Elizabeth, New Jersey (Naumova et al. 2002). We combined reported gas- and particulate-phase PAH congener distributions to arrive at a total concentration distribution for each congener (Table 3). Naphthalene was not included in the above study; therefore, we used indoor data from other, smaller studies (Jia et al. 2005; Van Winkle and Scheff 2001). Several studies were excluded because there were a greater percentage of below-detection limit values, due to high detection limits, or because the measurements were taken from studies that were much earlier than our time criteria. We included correlations in the indoors and outdoors for non-smoking homes to avoid artificially lowering the variability of the ultimate distribution, since many congeners have similar sources. Most studies did not report correlations between compounds, so we had to use a study conducted too early to be included in our overall distributions (Mitra and Ray 1995).

Since PAH concentrations decrease sharply within less than a hundred meters from the road (Levy et al. 2003; Zhu et al. 2002), it is preferable, in the absence of commuter exposure data, to use roadside data to represent transportation microenvironments. Concentrations of specific congeners of PAHs in US transportation microenvironments were not found in our literature search at the time of model development, therefore we used data from a roadside study in Denmark (Nielsen 1996). For congeners not reported in this study, we substituted the outdoor concentration (see Table 3). Because little information on PAH concentrations exists for other microenvironments, except for naphthalene in offices, we used the outdoor concentration instead.

PAH ingestion exposures were derived from a study of B[a]P in food in the US (Kazerouni et al. 2001) (Table 3). Since no other congeners were reported, we determined the contribution of B[a]P to total PAH in food by taking the ratio of each TEF-weighted PAH

to B[a]P from several studies in Europe (Devos et al. 1990; Falco et al. 2003; Lodovici et al. 1995; Thomson and Muller 1998). We found that B[a]P is responsible for 30-80% of the TEF weighted mixture, with a mean value of 58%. We divided the B[a]P exposure in Kazerouni's U.S. study by this percentage.

Exposure to dioxins and dioxin-like compounds is dominated by ingestion, therefore inhalation exposures for dioxin were not included (Safe 1998; U.S. EPA 2003). We used the U.S. EPA evaluation of ingestion from surveys of dioxin concentrations in different foods and geographic areas and estimated intake rates from the Exposure Factors Handbook (U.S. EPA 2003) (Table 3).

Industrial areas. Heavily industrial areas that are sources of Group 1 compounds may not be adequately reflected in the tails of the general population exposure distributions. About 1% of all counties had median concentrations significantly higher than the medians of all other counties. A lognormal concentration distribution was fit based on the NATA median and 95th percentile values for these counties (Table 1). We included compounds for which the ratio of the mean concentration of the top 1% counties to the baseline was greater than 2 (vinyl chloride and 1,3-dichloropropene) in the alternative scenario.

1,4-Dichlorobenzene. Homes with high levels of 1,4-dichlorobenzene in several studies were associated with users of moth repellants and/or deodorizers, representing a subset of the population with a separate 1,4-dichlorobenzene distribution and modeled as an alternative high exposure scenario (Table 2).

Smoking. We derived the incremental exposure from environmental tobacco smoke (ETS) from Nazaroff and Singer (Nazaroff and Singer 2004), who calculated a daily time-averaged concentration of for acetaldehyde, formaldehyde, benzene, and 1,3-butadiene attributed to ETS. For PAHs, we calculated the difference between smoking and non-smoking home mean concentrations of PAHs (Mitra and Ray 1995).

Risk calculation. Risks were calculated by multiplying the intake of a substance by the cancer potency factor. The cancer potency factor has historically been a linear extrapolation from the high-dose animal or human studies to the low doses of environmental exposure using either a maximum likelihood estimate (for epidemiology) or the upper 95th percent confidence limit (for animal studies) on the dose-response. Baseline risk was calculated using OEHHA values, because these include compounds for which the U.S. EPA IRIS database does not have listed inhalation unit risks (Table 4). The TEQ exposures for Group 3 compounds were multiplied by the cancer potency factor for the reference compound.

Indoor and outdoor source contribution. To obtain the source contributions to exposure, we subtract out the contribution to indoor concentrations from infiltration from the outdoors, and add this latter amount to the outdoor contribution. Exposure to Group 1 VOCs was assumed to be the same indoors as outdoors, due to a lack of indoor sources and a penetration efficiency for gases of 1 (Lewis and Zweidinger 1992). Dioxins were assumed to have outdoor sources only. Microenvironments with indoor sources were home, work (office), shopping, and dining. Microenvironments classified with only outdoor source contributions were travel, the outdoors, and the other non-defined microenvironments, and ingestion.

For gas-phase pollutants, the indoor-outdoor ratio was used to determine the indoor and outdoor contribution of each pollutant to the indoor concentrations. We calculated the fraction from indoor sources for the gas-phase and particle-phase PAHs separately. We used the phase distributions for each congener reported from the RIOPA study (Naumova et al. 2003) and assumed 100% infiltration efficiency for the gas phase portion and an infiltration factor of 0.69 for the particle phase, from Meng et al. for the RIOPA data (Meng et al. 2005).

Results

Baseline risks. Figure 2 shows the baseline risk ranking using OEHHA unit risks or cancer potency factors, along with the median risk calculated using the U.S. EPA potency factors. Compounds with median risks falling near 1 x 10^{-4} are 1,3-butadiene, benzene, formaldehyde and dioxin through food. Compounds with risks between 1 x 10^{-4} and 1 x 10^{-6} include carbon tetrachloride, acetaldehyde, PAHs through food, 1,4-dichlorobenzene, naphthalene, perchloroethylene, chloroform, and ethylene dichloride. For formaldehyde, dioxin, chloroform, and ethylene dibromide, calculation of risk using U.S. EPA's potency factors resulted in higher values.

Alternate exposure scenarios. Figure 2 also shows the median risk when using the alternative exposure scenarios for 1) high ambient levels of 1,3-dichloropropene (1,3-DCP) and vinyl chloride; 2) exposure to ETS at home for 1,3-butadiene, formaldehyde, benzene, acetaldehyde, naphthalene, and other PAHs; and 3) homes with extensive use of 1,4-dichlorobenzene (1,4-DCB) products. For each of these cases, the additional risk was about an order of magnitude or less.

Alternate toxicity. A comparison of the mean risks by pathway and selected compounds using the OEHHA and U.S. EPA cancer potency factors is shown in Figure 3. Total risk using the OEHHA values is 6 x 10^{-4}, compared with 1 x 10^{-3} using U.S. EPA values. Inhalation accounts for 83% and ingestion for 17% of total risk if the OEHHA values are used. Using U.S. EPA values, inhalation is assigned 41% of risk and 59% goes to ingestion, with dioxin responsible for 58% of total risk.

Sources of exposure. If we compare the baseline mean risks from an exposure perspective, 69% of total risk comes from exposures occurring indoors (52% in the home), 9% from outdoors, 7% from travel time, and 15% from food. From a source rather than

time-activity perspective, the distribution changes, where 35% of risk comes from indoor sources (27% in the home), 50% from outdoor sources, including mobile sources, and 15% from food. If we consider exposures from the PAHs and dioxin in food to come from either mobile or industrial sources, then the outdoor source contribution to risk becomes 65%.

We also examined source contributions to inhalation exposure for the Group 2 VOCs and the PAHs. While Group 2 VOCs and naphthalene had higher contributions from indoor exposures than outdoor exposures, the source contribution profiles differed depending on the compound (Table 5). Figure 4 shows more detail for benzene, formaldehyde, and PAH-B2. For benzene, exposures indoors at home and in other indoor microenvironments (work, shopping, dining) compose more than 50% of exposure, on average. Benzene sources, however, are shown to be primarily (median of 80%) from the outdoors. Formaldehyde sources tend to be indoors, but outdoor sources are responsible for a median of 30% of formaldehyde exposure. For PAH-B2, transportation is responsible for the highest percentage of exposure, and the median contribution from outdoor sources is about 90%.

Discussion

Average total lifetime cancer risk from organic hazardous air pollutants is about 6 in 10,000 when estimated using cancer potency factors determined by California. The U.S. EPA's factors lead to a risk estimate of about 1 in 1,000. Among the top-ranking compounds in both analyses are 1,3-butadiene, formaldehyde, benzene, and dioxin. Outdoor and indoor emissions as well as people's diet are all important contributors to total risk. By using cancer potency factors, our estimates likely represent upper bound risks, but the internal consistency of our methodology allows us to compare between compounds and with other published studies.

Comparison with other studies. We first place our findings in context by comparing our results to previous risk assessments. If we look at median risks from our study using U.S. EPA cancer potencies and the 1996 NATA (U.S. EPA 1996b), for most compounds we calculated higher risks. We saw increases for compounds with indoor sources, such as formaldehyde and chloroform, as well as for some compounds with primarily outdoor sources, such as acetaldehyde, benzene and 1,3-butadiene. Formaldehyde and acetaldehyde demonstrated the greatest differences in risk between personal and ASPEN exposure values. Some of the differences between the studies may be due to the tendency of ASPEN to underestimate concentrations when compared with ambient monitors (U.S. EPA 1996a). Compared with an earlier risk study by McCann et al. we find that our median risks are lower, possibly because McCann's data were from more than twenty years ago (McCann et al. 1986), when some chemicals were used more widely, resulting in higher concentrations

A risk assessment using personal exposures measured for inner-city teenagers in Los Angeles and New York City provides a more direct comparison to our results for Group 2 compounds. Sax et al. found that of the VOCs, formaldehyde and 1,4-dichlorobenzene were the primary risk drivers (Sax et al. 2006). Their study had several high 1,4-dichlorobenzene homes, explaining the importance of this compound in this population. Our inclusion of high 1,4-dichlorobenzene homes shows a similar result, with this compound increasing in the risk ranking (Figure 2). Sax et al. also did an indoor/outdoor source apportionment using a mass balance model, producing similar percentage contributions to personal risks from indoor and outdoor sources from all matched compounds between our studies, Figure 4. These study similarities may partially be due to the fact that Sax et al. was a primary source for the indoor/outdoor ratios we used, but our concentration inputs and time activity were for a much broader population than in Sax et al. Our analysis found about the same mean percentage from indoor home sources and a higher percentage from outdoor sources, but we included

additional indoor and outdoor microenvironments not distinguished in Sax et al. Our risks are also similar to those calculated by Payne-Sturges using personal monitoring data in Baltimore.

Uncertainties in cancer potency. While we attempted to explore uncertainty in cancer potency factors by using OEHHA and U.S. EPA values, actual uncertainty in these values greatly exceeds the differences in the values used by these agencies. Some assumptions may systematically bias risk upwards across all compounds. For example, the unit risk assumes a standard body weight (70 kg) and average breathing rate (20 m^3/day), both of which do not reflect the variability of the population at large (U.S. EPA 1997). Assumptions such as these may bias our estimates but would not change the ranking of compounds.

On the other hand, other assumptions could dramatically influence the risk estimates for individual compounds. In particular, for compounds for which the cancer-causing potential is due to cell death and proliferation, rather than genotoxiciy, the linear at low dose assumption may not be applicable. Evidence for some compounds indicates a "threshold" rather than linear dose-response, which implies that short-term high exposures could be important because of the cellular damage that could lead to cancer. Our analysis addresses only long-term chronic exposures, which is appropriate under the current linear framework for cancer potency estimation but may need to be re-evaluated in the future.

The U.S. EPA is currently re-assessing formaldehyde (U.S. EPA 2007) based on studies that show that formaldehyde may follow a hockey or J-shaped dose response (Conolly et al. 2003, 2004). This is supported by the finding of a lack of increased formaldehyde in blood of the metabolized DNA protein cross-links in exposed rats (Heck and Casanova 2004). Also, some analyses have called into question the effect found in the occupational studies used to derive the formaldehyde risk (Heck and Casanova 2004; Marsh et al. 1992).

Based on some of these arguments, the 1999 NATA uses a lower unit risk (three orders of magnitude less then the IRIS value) for formaldehyde. Using this unit risk value, the formaldehyde risk, based on the median personal exposure in our model, drops to 9×10^{-8} from 2×10^{-4} (using the U.S. EPA risk) or 9×10^{-5} (using the OEHHA risk). While the U.S. EPA considered formaldehyde a probably human carcinogen, in 2004, the International Agency for Research on Cancer (IARC) deemed that there was sufficient evidence to consider formaldehyde a human carcinogen based on the epidemiology for nasopharyngeal cancer, in particular (International Agency for Research on Cancer 2004). This clearly demonstrates that there are potentially large uncertainties associated with interpretation of similar evidence, as well as ongoing changes in cancer potency estimation, making our risk rankings far from static.

Also being reassessed is chloroform, which has been found to be cytotoxic, rather than genotoxic (Golden et al. 1997; Tan et al. 2003). Dioxin is also likely to be a tumor promoter, rather than an initiator (Popp et al. 2006; Schwarz and Appel 2005). Questions regarding the main epidemiological studies used in assessing dioxin risk relate to the method and difficulty of measuring and reconstructing exposure, the high levels of exposure, and the lack of quantification of potential exposure to other highly toxic compounds (Crump et al. 2003; Starr 2003).

Another interesting point with regard to toxicity is the difference in estimates for benzene provided by the US EPA. The risks differ by almost a factor of 4 due to the difference in dose-response predicted by two different exposure assessments of the same cohort. Benzene is the compound with the strongest human evidence for carcinogenicity, such that human epidemiology can be used to derive the cancer potency. However, we see that the estimated potency factor can depend on assumptions within the analysis, and is far

from a defined quantity. Future work would benefit from the ability to better characterize the uncertainty surrounding model choices in the development of cancer potency factors.

Uncertainties in exposure. Concentration data are lacking for non-home microenvironments for many compounds, especially in workplaces and other indoor microenvironments, leading to greater uncertainty in these distributions. For example, while air risk from PAHs was not high in our risk ranking, we found that travel exposures may be important for this group. We were unable to find on-road or in-vehicle PAH congener data at the time of our analysis, therefore we used a Danish study. However, since diesel passenger cars are used more commonly in Europe, the U.S. PAH air mixture from mobile sources is probably different, particularly since diesel has been found to emit more of the lower-weight PAHs (Marr et al. 1999; Rogge et al. 1993; Shah et al. 2005; Westerholm and Hang 1994).

Group 1 compound concentrations were modeled, and therefore we do not have ambient or in-microenvironment data for these compounds. We are assuming that ASPEN is providing a reasonable estimate of the potential exposures to Group 1, and the high ends of these compounds' distribution were still relatively low. Measurement data, however, would validate whether or not ASPEN is under-predicting concentrations for these compounds.

We were also limited by a small number of VOC studies in other microenvironments. Despite this, because the contribution to total exposure from the home drives risk for the baseline population, this data scarcity should not add a disproportionate amount of uncertainty for non-industrial workers.

Uncertainties in PAH ingestion arise from the use of B[a]P intake values for the US to extrapolate to total PAH food intake. We found that B[a]P exposure values in the US, compared to several European countries, are about two to four times less. The variability of exposure through food can also be influenced by the distribution of foodstuffs, which can

result in ingestion far from the source of environmental contamination; some types of cooking, particularly grilling meat (Kazerouni et al. 2001), which increases PAH concentration; and differences in intake rates.

The baseline exposure may not include specific groups of the population that may have a separate and much higher exposure distribution, such as people who are exposed to chemicals at work, live in a highly industrial region, or have large contributions from sources in their homes. In some cases, such as the Group 1 compounds, even the counties with the highest 1% of modeled outdoor concentrations did not result in significant contributions to total risk. It is possible that we have underestimated exposure to Group 1 compounds, however, the risk is so low from these compounds that the actual concentrations would have to be much higher for most of the Group 1 compounds to confer high risks. In contrast, the subset of homes with a separate exposure distribution to 1,4-dichlorobenzene was highly exposed enough that it becomes a major risk driver for these households.

A key question is therefore what percentage the population would fall into these high risk categories. According to an analysis of the National Health and Nutrition Examination Survey III (NHANES III) about 4% of a subsample of 982 subjects reported using mothballs, 9% reported toilet bowl deodorizer use, and 32% air freshener use. The first two products are the most likely sources of 1,4-dichlorobenzene, although some air freshener products may contain it. This study also found a higher probability of 1,4-dichlorobenzene product usage with non-whites (Churchill et al. 2001), supported by findings from the TEAM studies in Los Angeles (Wallace 1991b) as well as studies finding higher 1,4-dichlorobenzene exposures among non-white participants (Adgate et al. 2004; Sax et al. 2004). These percentages of the population may not be large, but the 1,4-dichlorobenzene risk becomes a significant risk driver. We note that there may also be higher naphthalene exposures among mothball users, but sufficient data to estimate this potential impact were not available. Non-smokers living

with smokers, which amounts to about 17% of households as of 1991 (U.S. Department of Health and Human Services 2006), also have elevated risks, particularly from 1,3-butadiene. For the high exposure Group 1 scenarios, the 1% of counties with the highest average concentrations includes high population counties, such that about 10-15% of the population live in these counties.

Other exposure assessment uncertainties pertain to the data for input distributions. Study methods can also influence the measurement of concentrations. Many studies (RIOPA, Minnesota, and NHEXAS) used passive charcoal badges, which have been shown to have high detection limits, and a negative bias in comparison to active sampling methods (Chung et al. 1999; Gordon et al. 1999). While we did not notice large differences between studies with different methods (except for the percentage of non-detects), it is possible that there is some bias due to measurement methods.

Another uncertainty is that the concentrations in the model for Group 2 compounds came from predominantly urban studies, with limited suburban data, and may not be representative of non-urban areas. Additionally, compounds from common sources, for example, mobile sources, would exhibit high correlations, and therefore their concentrations would be expected to be related. We were able to incorporate correlations between PAH congeners, however, we could not do so for other compounds.

One possibly high risk HAP that was not included in our analysis is diesel exhaust. Diesel particulate matter is a significant exclusion from our HAPs list. A sample calculation using the 1999 NATA ambient concentrations for diesel PM and a recommended inhalation unit risk from OEHHA gives us a risk of 2.7×10^{-4}, which is on the order of the dioxin risk. The difficulty with diesel PM is that it is more difficult to quantify in measurement studies, as usually elemental carbon is used but only as a proxy, thus we chose to exclude it.

Additional uncertainties about the exposure assessment arise from the time-activity estimates and population assumptions. The time activity and exposures are calculated for 18-65 year-olds and extrapolated to a lifetime. We do not expect the differences for childhood and old age to be much greater than these adult exposures, although these omissions may create some bias in the results. We have tried to preserve the relationship between activities in broad categories across a day, however we are unable to create an accurate representation of long term time activity patterns. Our risks are based on the assumption that people's week-long activities will not vary on average over time. On an individual level, this would misstate a person's variability in time activity (i.e., by considering shopping/dining to either occur every day or no days). When incorporated across the population, however, we would still be able to capture the population variability in activity patterns and therefore personal exposures. While we do not expect that day-to-day behavior would exhibit large differences over time, future exposure modeling would benefit from the inclusion of longitudinal patterns of time use.

Conclusions. In conclusion, this analysis has attempted to estimate cancer risk from exposure to hazardous air pollutants to a general population, as well as high risk scenarios for certain compounds. The risk to the general population is two orders of magnitude larger than the EPA acceptable risk level. Including risks from highly exposed and susceptible subpopulations would increase this risk. Because regulatory decisions are based on risk evaluations, it is important to know where exposures are coming from and to include as much of the current toxicological information as possible. Our analyses provide insight not only about the high-risk compounds, but also about the predominant sources of exposure for those compounds, which will allow for more effective means of exposure reduction. Future research should focus on refining toxicity evidence for the high-risk compounds in our

analysis and on filling some identified microenvironmental exposure gaps, to further reduce uncertainties in decisions regarding prioritization among HAPs control measures.

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Table 1: Exposure distributions for Group 1 compounds (all lognormal)

Compound ($\mu g/m^3$)[a]	GM	GSD
1,3-dichloropropene	0.067	2.609
High 1,3-dichloropropene	0.23	1.13
Carbon tetrachloride	0.880	1.002
Ethylene dibromide	0.008	1.002
Ethylene dichloride	0.061	1.057
Vinyl chloride	0.001	4.966
High vinyl chloride	0.02	2.37

[a] All compound concentrations from (U.S. EPA 1996b)

Table 2: Distributions of concentration inputs in μg/m^3 for Group 2 compounds

Compound	Home (LogN)	Office[l] (LogN)	Commute (LogN)	Dining	Grocery (LogN)	Non-grocery (LogN)	Outdoor/Other (LogN)
	GM, GSD	GM, GSD	GM, GSD	Distribution	GM, GSD	GM, GSD	GM, GSD
Formaldehyde	18, 2[a, b, c, d]	15,1.5[e]	11, 1.5[f, g]	Bet (1.4, 7.3)[f]	14, 1.5 [f]	21, 2.7[f]	2.5, 3.0[a, b, d]
Acetaldehyde	9, 2[a, c]	7.0, 1.6[e]	4.3, 1.4[f, g]	Gam (39, 0.9)[f]	21, 2.1[f]	10, 2.4[f]	4.7, 1.4[a, b, c, d]
1,3-Butadiene	0.3, 3.7[a, d]	0.2, 3.4[e]	1.5, 2.1[f, g]	LogN (1.0, 6.3)[f]	0.2, 3.4[f,]	0.2, 3.4[f]	0.1, 3.6[a]
Benzene	2.1, 3.1[a, d, h, i, j, k, l, m, n]	3.5, 1.8[e]	6.3, 1.9[f, g, o]	LogN (3.1, 2.1)[f]	1.7, 1.6 [f]	1.7, 2.1[f]	1.8, 1.9[a, d, i, j, k, m]
Methylene chloride	0.8, 5.8[a, i, j, m]	0.7, 6.7[e]	1.4, 2.0[f, o]	LogN (1.4, 5)[f]	1.1, 2.7[f]	2.1, 5.8[f]	0.4, 3.5[a, d, i, j, m]
Chloroform	1.2, 2.8[a, d, h, i, j, k, l, m]	0.3, 3.0[e]	0.4, 2.4[f]	Gam (1.9, 0.9)[f]	1.2, 2.3[f]	0.4, 3.7[f]	0.2, 3.5[a, d, i, j, l., m]
Trichloroethylene	0.2, 4.1[a, h, i, j, m]	0.3, 4.0[e]	0.3, 2.4[f, o]	LogN (0.3, 5.2)[f]	0.3, 2.1[f]	0.4, 5.0[f]	0.2, 2.5[a, d, i, j, l, m]
Perchloroethylene	0.9, 4.3[a, d, h, i , l, m]	2.0, 3.1[e]	0.4, 2.5[f, o]	LogN (2.1, 5.6)[f]	0.9, 2.5[f]	1.4, 3.4[f]	0.4, 4.2[a, d, i, j, k, l, m]
1,4-Dichlorobenzene	0.4, 6.9[h, k, l, m]	0.9, 4.5[e]	0.5, 2.6[f]	LogN (1.5, 5.9)[f]	2.7, 3.3[f]	1.7, 7.7[f]	0.1, 6.2[a, d, l, m]
High 1,4-DCB	18, 4.5[a, i]						

Studies: [a](Sax et al. 2004), [b](Reiss et al. 1995), [c](Zhang et al. 1994), [d](Weisel et al. 2005), [e]BASE study data (Environmental Health and Engineering 2002; Girman et al. 1999), [f](Loh et al. 2006), [g](Rodes et al. 1998), [h](Van Winkle and Scheff 2001), [i](Adgate et al. 2004b), [j](Payne-Sturges et al. 2004), [k](Clayton et al. 1999), [l](Adgate et al. 2004a), [m](Sexton et al. 2004), [n](Gordon et al. 1999), [o](Batterman et al. 2002); NOTE: For offices and grocery stores, the non-grocery distribution was used for 1,3-butadiene; Distribution parameters: Lognormal = LogN (geo mean, geo std dev), Gamma = Gam (scale, shape), Beta = Bet (alpha, beta)

Table 3: Group 3 concentrations and TEFs

All Lognormal µg/m3	Home GM, GSD	Commute GM, GSD	Outdoor GM, GSD	TEF
PAH B2				
benzo[a] anthracene	3E-05, 3.8[a]	8E-05, 2.5[a]	8E-05, 2.5[a]	0.1[b]
benzo[b] fluoranthene	1E-04, 3.2[a]	3E-04, 2.1[a]	3E-04, 2.1[a]	0.1[b]
Benzo[a] pyrene	6E-05, 2.8[a]	2E-03, 2.0[c,d]	9E-05, 2.4[a]	1[b]
Chrysene/Iso-Chrysene	2E-04, 2.5[a]	3E-04, 2.1[a]	3E-04, 2.1[a]	0.001[b]
Dibenz[a,h]anthracene	8E-06, 3.4[a]	2E-05, 1.9[a]	2E-05, 1.9[a]	1[b]
Indeno (1,2,3-cd)pyrene	1E-04, 4.7[a]	2E-03, 2.1[c,d]	3E-04, 2.4[a]	0.1[b]
PAH CD				
Anthracene	1E-03, 2.6[a]	8E-04, 2.0[a]	8E-04, 2.0[a]	0.0005[e]
Benzo[ghi] perylene	2E-04, 3.7[a]	4E-03, 1.8[c,d]	3E-04, 2.5[a]	0.02[e]
Phenanthrene	3E-02, 2.7[a]	1E-03, 1.8[c,d]	2E-02, 1.8[a]	0.0005[e]
Pyrene	2E-03, 2.8[a]	2E-03, 1.8[a]	2E-03, 2.1[a]	0.001[e]
Fluoranthene	3E-03, 2.3[a]	2E-03, 1.7[a]	3E-03, 2.2[a]	0.05[e]
Naphthalene	9E-01, 4.9[f, g]	2E-01, 3.0[f, g]	1E-01, 2.3[f, g]	0.031[b]

Ingestion

mg/kg-d (TEF weighted)	GM, GSD
PAH	1.26E-06, 1.54[h]
Dioxin	5.36E-10, 1.55[i]

[a](Naumova et al. 2002)
[b](California EPA 2005)
[c](Nielsen 1996)
[d](Lim et al. 1999)
[e](Larsen and Larsen 1998)
[f](Van Winkle and Scheff 2001)
[g](Jia et al. 2005)
[h](Kazerouni et al. 2001)
[i](U.S. EPA 2003)

Table 4: Cancer unit risks and potency factors

	U.S. EPA (per ug/m3)	CA (OEHHA) (per ug/m3)
1,3-Butadiene	3.00E-05	1.70E-04
Methylene Chloride	4.70E-07	1.00E-06
Chloroform	2.30E-05	5.30E-06
Benzene (high/low for U.S. EPA)	7.8[a]/2.20E-06	2.90E-05
Carbon tetrachloride	1.50E-05	4.20E-05
Trichloroethylene	N/A	2.00E-06
Perchloroethylene	N/A	5.90E-06
1,4-Dichlorobenzene	N/A	1.10E-05
Formaldehyde	1.30E-05	6.00E-06
Acetaldehyde	2.20E-06	2.70E-06
1,3-dichloropropene	4.00E-06	N/A
Ethylene Dibromide (central/high for U.S. EPA)	3.00/6.00E-04[b]	7.10E-05
Ethylene Dichloride	2.60E-05	2.10E-05
Vinyl Chloride (continuous adult)	4.40E-06	N/A
Vinyl Chloride (continuous from birth)	8.80E-06[c]	7.80E-05
B(a)P (inhalation)	N/A	1.10E-03
B(a)P (oral slope factor in (mg/kg/day)-1)	7.3	12
Dioxin (oral slope factor in (pg/kg/day)-1)	1.00E-03	1.30E-04

[a]Used higher estimate for comparisons
[b]Used upper bound estimate for comparisons
[c]Used continuous from birth for comparisons

Table 5: Median indoor source contributions to HAPs risk from inhalation exposure.

	Indoor Sources
Acetaldehyde	15%
Formaldehyde	70%
1,3-Butadiene	10%
Benzene	20%
Chloroform	70%
Methylene Chloride	45%
1,4-Dichlorobenzene	35%
Perchloroethylene	30%
Trichloroethylene	25%
PAH B2	10%
PAH CD	20%
Naphthalene	60%

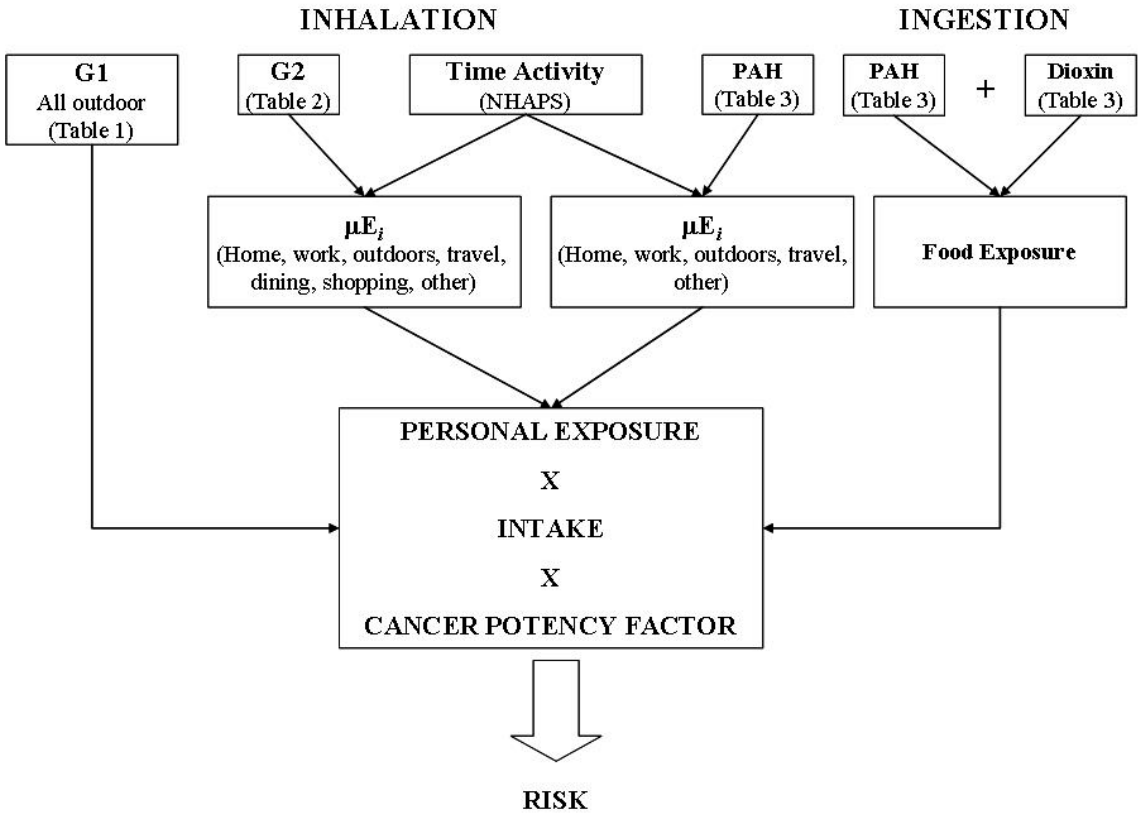
Figure Legends

Figure 1: Representation of personal exposure and risk model. Refer to tables for compound concentrations. G1 = Group 1 VOCs, G2 = Group 2 VOCs, NHAPS = National Human Activity Patterns Survey, PAH = polycyclic aromatic hydrocarbons, μE_i = exposure in microenvironment *i.*

Figure 2: Baseline risk ranking using OEHHA toxicity estimates. 1,3-Dichloropropene does not have a unit risk value from OEHHA, therefore the U.S. EPA risk estimate was used. ● indicates the distribution medians if the U.S. EPA risk estimates were used (where available). Benzene risk uses unit risk of 2.2 e-6 $(\mu g/m^3)^{-1}$. ▲ indicates the risk using the unit risk of 7.8 e-6 $(\mu g/m^3)^{-1}$. **X** indicates the median of the distributions of the high exposure scenarios. Smoking home exposure accounts for the high exposure for benzene, formaldehyde, 1,3-butadiene, acetaldehyde, naphthalene, and PAH CD and PAH B2. High home exposure from mothballs and associated products account for 1,4-dichlorobenzene. The top 1% emission counties are the high scenarios for 1,3-dichloropropene and vinyl chloride. Bars represent 5^{th}, and 95^{th} percentiles. Boxes represent the 25^{th}, 50^{th}, and 75^{th} percentiles.

Figure 3: Risk from ingestion and inhalation. Figure 3a shows the mean total risk calculated with OEHHA's cancer potency values (6×10^{-4}) and Figure 3b shows the median total risk using the federal U.S. EPA's values (1×10^{-3}). The inhalation fraction is further broken down into several of the higher risk compounds.

Figure 4: The contribution of exposure in microenvironments compared to indoor (home and other) and outdoor source contribution to inhalation risk for benzene, formaldehyde, and the TEF-weighted exposures to PAH B2. Other indoor includes work in offices, shops, and restaurants. Trans = transportation microenvironment. Bars represent 5^{th}, and 95^{th} percentiles. Boxes represent the 25^{th}, 50^{th}, and 75^{th} percentiles.



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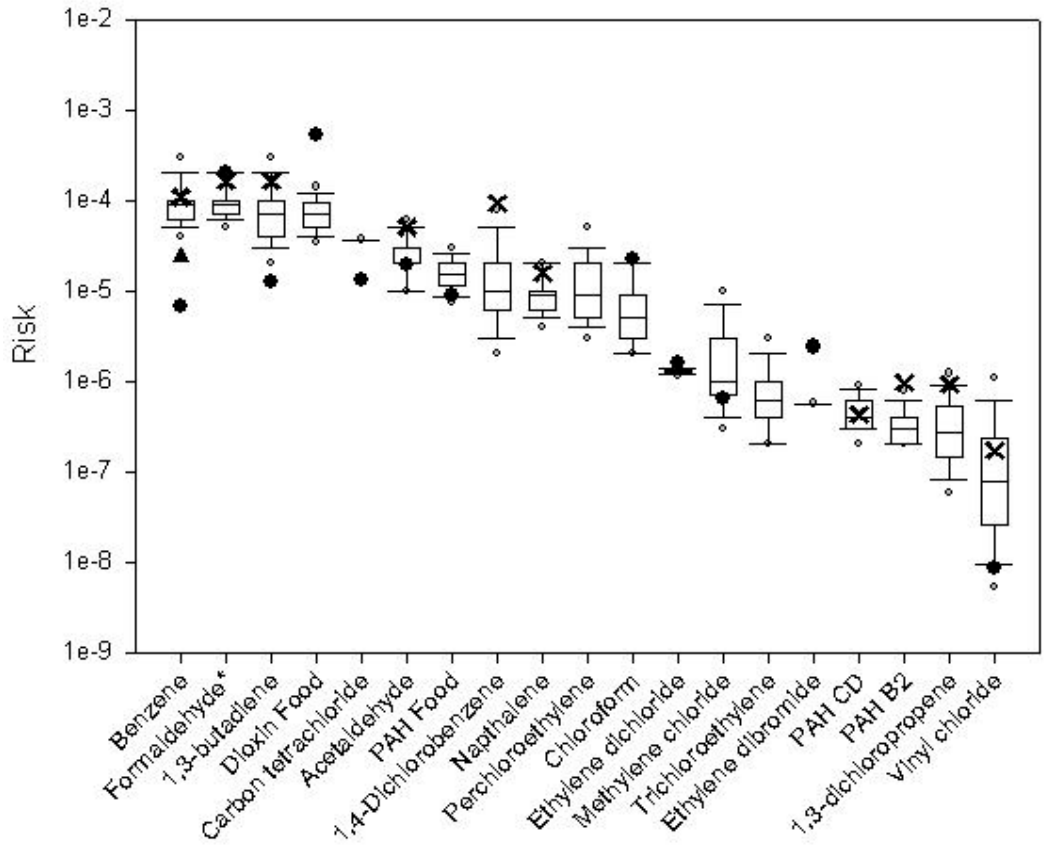

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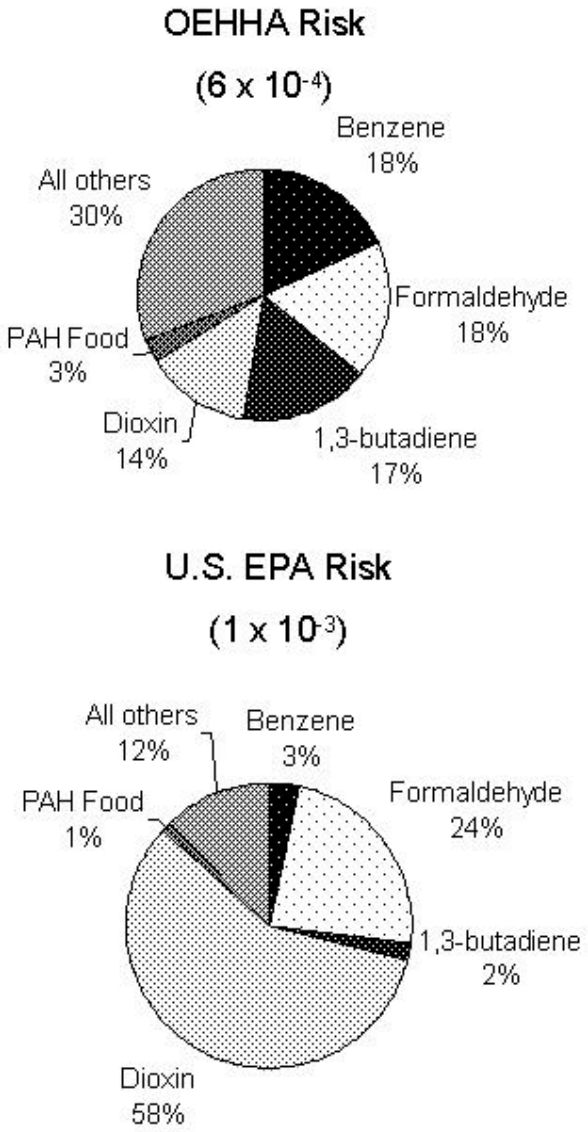
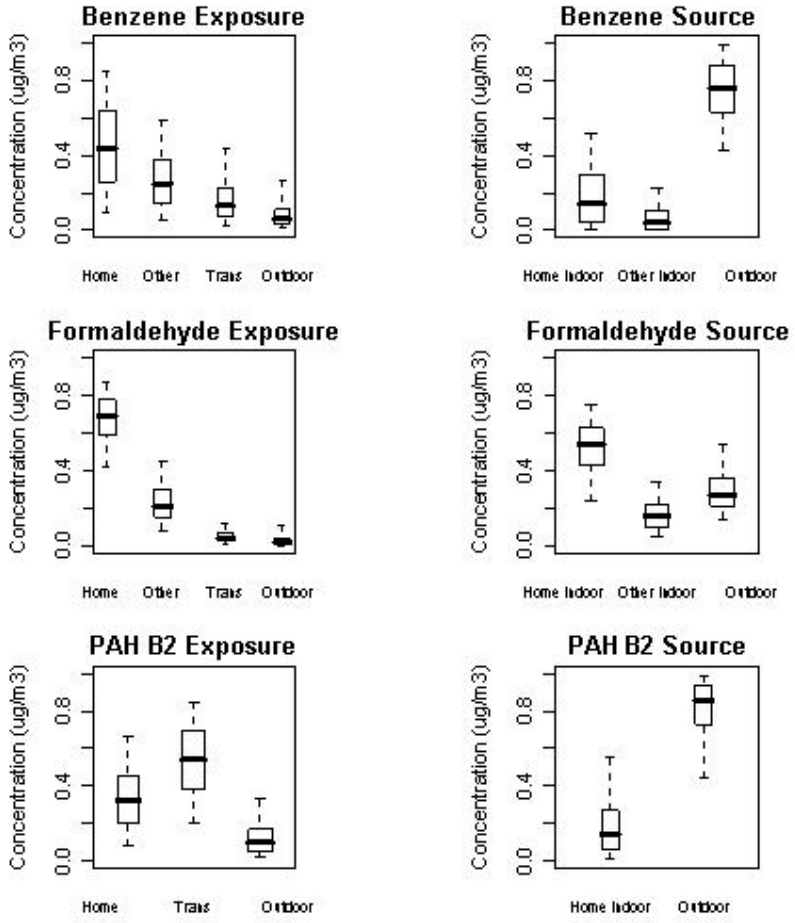


Figure 3: Risk from ingestion and inhalation. The first figure shows the mean total risk calculated with OEHHA's cancer potency values (6×10^{-4}) and the second figure shows the median total risk using the federal U.S. EPA's values (1×10^{-3}). The inhalation fraction is further broken down into several of the higher risk compounds.



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