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Attributing population-scale human exposure to various source categories: Merging exposure models and biomonitoring data

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ABSTRACT

Information about the distribution of chemical-production mass with respect to use and release is a major and unavailable input for calculating population-scale exposure estimates. Based on exposure models and biomonitoring data, this study evaluates the distribution of total production volumes (and environmental releases if applicable) for a suite of organic compounds. We used Bayesian approaches that take the total intake from our exposure models as the prior intake distribution and the intake inferred from measured biomarker concentrations in the NHANES survey as the basis for updating. By carrying out a generalized sensitivity analysis, we separated the input parameters for which the modeled range of the total intake is within a factor of 2 of the intake inferred from biomonitoring data and those that result in a range greater than a factor of 2 of the intake. This analysis allows us to find the most sensitive (or important) parameters and the likelihood of emission rates for various source emission categories. Pie charts of contribution from each exposure pathway indicate that chemical properties are a primary determinant of the relative contribution of each exposure pathway within a given class of compounds. For compounds with relatively high octanol–water partition coefficients (K_{ow}) such as di-2-ethylhexyl phthalate (DEHP), pyrene, 2,2′,4,4′-tetrabromodiphenyl ether (PBDE-47), and 2,2′,4,4′,5,5′-hexabromodiphenyl ether (PBDE-153), more than 80% of exposure derives from outdoor food ingestion and/or indoor dust ingestion. In contrast, for diethyl phthalate (DEP), di-iso-butyl phthalate (DiBP), di-n-butyl phthalate (DnBP), butylbenzyl phthalate (BBP), and naphthalene, all relatively volatile compounds, either inhalation (indoor and outdoor) or dermal uptake from direct consumer use is the dominant exposure pathway. The approach of this study provides insights on confronting data gaps to improve population-scale exposure estimates used for high-throughput chemical prioritization.

1. Introduction

The environmental health community has growing concerns about many of the commercially available chemicals introduced into residential environments, resulting in exposure to these compounds and their transformation products. Information about potential exposure and adverse health effects in humans from residential uses is limited for most chemicals. Therefore, there has been a growing need for research to screen chemicals that may have potential health hazards, based on exposure and toxicity, among tens of thousands of available commercial chemicals (Cohen Hubal et al., 2010; Egeghy et al., 2011). Methods for conducting rapid toxicological assessments are currently being utilized to help evaluate potential hazards (Dix et al., 2007; Judson et al., 2011; Wetmore et al., 2012). Similar methods for estimating exposure levels for comparison with toxicity levels are needed to evaluate and prioritize large numbers of compounds in a rapid and efficient manner.

Three primary types of information are required to parameterize models used to estimate population-scale exposure levels: (1) chemical properties, (2) chemical emission rates and/or total production volumes, and (3) information about the mass of chemicals consumed in each use and release category. Chemical properties can be estimated using quantitative structure–activity (property) relationship (QSA(P)R) models. The U.S. Environmental Protection Agency (EPA) Estimation Program Interface Suite (EPI Suite™) is one of the publicly available software programs that allows one to compute chemical properties using a unique chemical abstracts service (CAS) registry number or simplified molecular-input line-entry system (SMILES) (U.S. EPA, 2014a). For chemical emission rates and total production volumes, three available databases of the U.S. EPA provide limited chemical emissions rates, including the National-Scale Air Toxics Assessments (NATA) (U.S. EPA, 2009), the Toxics Release Inventory (TRI) Program (U.S. EPA, 2014b), and the National Emissions Inventory (NEI) (U.S. EPA, 2014c). Total production volumes are available in the U.S. EPA's Inventory Update

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Reporting (IUR) (U.S. EPA, 2008) or Chemical Data Reporting (CDR) system (U.S. EPA, 2014d), but are rather uncertain as they are recorded in "bins", spanning several orders of magnitude for a given chemical. Also scarce are both information and databases about how chemicals are introduced to consumer products (e.g., food additives, personal care products, or pesticides) and environments (e.g., indoors or outdoors). This gap is a major impediment to generating exposure estimates for high-throughput screening (Arnot et al., 2012; Mitchell et al., 2013; Shin et al., 2012).

Accurate source inputs in high-throughput exposure models are critical for estimating population-scale exposure levels. One key need is the calculation of intake fraction (iF), the integrated intake of a compound per unit of emission, which varies by several orders of magnitude depending on the release scenario or the product use type (Bennett et al., 2002). For example, given the same amount of release, the intake rate of benzene from cigarette smoking is several orders of magnitude higher than that from outdoor inhalation due to releases from automobiles (Bennett et al., 2002). In addition, even with equivalent amounts of use, the magnitude of exposure to phthalates commonly used in both personal care products and vinyl flooring (e.g., di-n-butyl phthalate, di-iso-butyl phthalate) has also been shown to vary greatly depending on the product use type (Guo and Kannan, 2013). The information needed regarding the distribution of total production volumes to each use and release category was also addressed in evaluating the exposure to naphthalene inferred from measured concentrations in urine, finding that estimated exposure is primarily determined by the proportion of total production volumes emitted to the indoor environment, even though the estimated magnitude of indoor emissions is much smaller (0.3%) than that of outdoor emissions (99.7%) (Shin et al., 2013a; Wambaugh et al., 2013).

In this study, we compared exposures inferred from biomarkers to exposures estimated from fate and transport models to explore the uncertainties associated with modeled iF and our lack of knowledge regarding the distribution of total production volumes to each use and release category for a suite of organic compounds. The exposure pathways for the modeled exposures include dermal uptake from direct consumer use, indoor inhalation, indoor dermal uptake, indoor dust ingestion, outdoor inhalation, and outdoor food ingestion. We assumed that the total production volumes are distributed to direct dermal application (e.g., fragrance, cosmetics), indoor residential consumer use resulting in indoor emissions (e.g., couch, vinyl flooring), and outdoor emissions. We then compared modeled exposure with estimated exposure inferred from biomarkers collected in the National Health and Nutrition Examination Survey (NHANES) (CDC, 2005, 2009). We identified critical uncertainties of model inputs (i.e., individual modeled iF and the distribution of total production volumes) via a generalized sensitivity analysis (Guven and Howard, 2007; Spear and Hornberger, 1980). This analysis addresses the critical need to obtain accurate information of source emission distribution in generating exposure estimates for high-throughput screening.

The objective of this study is to understand the importance of chemical properties and the distribution of total production volumes among different use and release categories on the magnitude of resulting human exposures. In addition, we explain how source inputs can be disaggregated to compute population-scale human exposure using exposure models and biomonitoring data and how critical input parameters can be identified via a generalized sensitivity analysis.

2. Materials and methods

2.1. Overview

The overall approach involves four steps to develop and evaluate our modeling methods. We first outline the information available for each domain of the model including biomarkers. Second, we describe how we modeled exposure levels for each exposure pathway. Third, we explain how a generalized sensitivity analysis is applied to identify critical inputs of modeled exposures. Last, we revise and evaluate the likelihood of emission rates for various source emission categories. The overview of source-to-exposure models used in this study is also depicted in Fig. 1.

Population-scale exposure levels or intake rates can be calculated in two ways. For each release environment, we can use standard exposure models that account for cumulative intake based on human exposure factors (e.g., inhalation/ingestion rates and time spent in microenvironments) to estimate iF. Then, the mass introduced to a specific mode of entry can be multiplied by iF for each release compartment and the total intake then obtained by summing the intake from all possible release compartments. Another method is to back-calculate the intake rate from biomonitoring data as the concentrations in biological media are likely to reflect actual body burden (Asimakopoulos et al., 2013; Guo et al., 2013; Lorber and Egeghy, 2011; Ma et al., 2013; Shin et al., 2013a). The intake rates from two approaches allow determining the likely source emission distribution using Bayesian principles that take the intake from our exposure models as the prior estimate of iF and the intake from measured concentrations in the NHANES survey as the updating datum.

2.2. Data sources

2.2.1. Selected compounds

We selected nine organic compounds for analysis based on the availability of both biomarker data in the NHANES survey and emissions/total production data in the EPA databases during the period of 2001–2004. The selected compounds include one phthalate [diethyl phthalate (DEP)] primarily associated with direct consumer use such as fragrance or cosmetics, one phthalate [di-iso-butyl phthalate (DiBP)] often used in both polyvinyl chloride (PVC) products and personal care products, three phthalates [di-n-butyl phthalate (DnBP), butylbenzyl phthalate (BBP), di-2-ethylhexyl phthalate (DEHP)] with emissions from vinyl flooring and PVC plastics directly to the air compartment of the indoor environment (Dodson et al., 2012; Hauser and Calafat, 2005; Heudorf et al., 2007), two polycyclic aromatic hydrocarbons (PAHs) [naphthalene (Nap), pyrene (Pyr)] with both indoor and outdoor emission sources (Jia and Batterman, 2010; U.S. EPA, 2014e), and two polybrominated diphenyl ethers (PBDEs) [2,2′,4,4′-tetrabromodiphenyl ether (PBDE-47), 2,2′,4,4′,5,5′-hexabromodiphenyl ether (PBDE-153)] used as flame retardants resulting in continuous emissions to the home (Rahman et al., 2001). The selected compounds represent a range of chemical properties, spanning from relatively volatile compounds (e.g. DEP, Nap) to those with a high affinity for organic materials and thus likely to exhibit bioaccumulation (e.g. DEHP, PBDE-153). Chemical properties for these nine studied compounds are listed in Table A1 in the Appendix.

2.2.2. Total production volumes and outdoor emissions

For five phthalates and two PAHs, we obtained total production volume data from the U.S. EPA's 2002 IUR system (U.S. EPA, 2008). The production data in the IUR system are reported as a range, with maximum values being 2 to 50 times greater than minimum values. To address this variance, we used the geometric mean of the end points of the range to model exposures. For DnBP, DEHP, Nap, and Pyr, we obtained additional emission rate estimates from the 2002 NATA database (U.S. EPA, 2009).

For PBDE-47 and PBDE-153, neither total production volumes nor outdoor emission rates are available in the EPA databases. Thus, we used the reported production volume of PentaBDE and OctaBDE along with percent mass composition of PBDEs in PentaBDE and OctaBDE products to estimate the total production volumes of PBDE-47 and PBDE-153. PBDE-47 is a major PBDE-congener in PentaBDE and PBDE-153 is used in both PentaBDE and OctaBDE products. Based on market demand, the estimate of PentaBDE total production volume in the Americas (i.e., North, Central, and South America) is 7100 metric tons in 2001 (Birnbaum and Staskal, 2004; UNEP, 2007a). The global production for OctaBDE was