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Chemical-by-chemical and cumulative risk assessment of residential indoor exposure to semivolatile organic compounds in France

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ABSTRACT

Background: The toxic effects of environmental exposure to chemicals are increasingly being studied and confirmed, notably for semivolatile organic compounds (SVOCs). These are found in many products and housing materials, from which they are emitted to indoor air, settled dust and other surfaces.
Objectives: The objective of this work is to assess the human health risk posed by residential indoor exposure to 32 SVOCs, assessed in previous nationwide studies.
Methods: A chemical-by-chemical risk assessment, using a hazard quotient (HQ) or excess risk (ER) method, was supplemented by a cumulative risk assessment (CRA). For CRA, a hazard index (HI) method, as well as higher tier approaches using relative potency factors (RPFs) or toxic equivalency factors (TEFs) were used for the following endpoints: neurotoxicity, reproductive toxicity, genotoxicity and immunotoxicity.
Results: HQs were above 1 for 50% of French children from birth to 2 years for BDE 47, and for 5% of children for lindane and dibutyl phthalate (DBP). Corresponding hazards are reprotoxic for BDE 47 and DBP, and immunotoxic for lindane. The CRA approach provided additional information of reprotoxic risks (HI > 1) that may occur for 95% of children and for 5% of the offspring for pregnant women's exposure. The SVOCs contributing most to these risks were PCB 101 and 118, BDE 47, and DBP. The higher tier CRA approaches showed that exposure to dwellings' SVOC mixtures were of concern for 95% of children for neurotoxic compounds having effects linked with neuronal death. To a lesser extent, effects mediated by the aryl hydrocarbon receptor (AhR) or by a decrease in testosterone levels may concern 5% of children and adults. Lastly, unacceptable immunotoxic risk related to exposure to 8 indoor PCBs was also observed for 5% of children.
Conclusions: In view of uncertainties related to compounds' toxicity for humans, these results justify the implementation of preventive measures, as well as the production of more standardized and comprehensive toxicological data for some compounds.

1. Introduction

People are exposed to an increasing number of chemicals, present in all media such as food, water, air, soil, and clothes. Exposure in residential indoor environments is of particular concern, due to their ubiquitous contamination and to the large amount of time people spent inside. Among chemicals found in dwellings, semivolatile organic compounds (SVOCs) represent a large class of organic compounds belonging to different chemical families and having a vapor pressure of between 10^{-14} and 10^{-4} atm (Weschler and Nazaroff, 2008). Because of their diverse properties - plasticizer, flame retardant, biocide, etc. (Mercier et al., 2011), they are used in a wide range of materials and products (wall materials, furniture, household cleaning products, etc.). Their particular physical-chemical properties render them capable of migrating from their sources and partitioning between indoor air, settled dust and other surfaces (Weschler and Nazaroff, 2010); people are thus exposed via inhalation, ingestion and dermal contact. A recent study has estimated aggregate exposure from measurement data for 32 SVOCs from different chemical families, frequently detected in French dwellings (Pelletier et al., 2017a): 6 phthalates, 4 polycyclic aromatic hydrocarbons (PAHs), 2 organophosphorus (OPs), 3 organochlorines (OCs), 2 polycyclic musks, 8 polychlorinated biphenyls (PCBs), and 7 polybromodiphenylethers (PBDEs).

Many of these SVOCs are suspected of having adverse health effects.

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Some exhibit an endocrine disruption mechanism, leading to potential effects on male reproduction. This is the case for phthalates, which have been studied extensively in human and other mammals. Specific effects on testosterone synthesis have also been shown following rodent exposure to PBDEs (BDE 99) and PAHs (benzo[*a*]pyrene) (Fournier et al., 2016). They are also known to be neurotoxic in experimental mammals, and numerous epidemiological studies suggest an association between early-life exposure to SVOCs (OCs, OPs, PCBs, PBDEs, PAHs, and phthalates) and behavioral impairment later in life (Fournier et al., 2017). PAHs (especially benzo[*a*]pyrene) and some OCs or OPs pesticides are also known to be carcinogenic compounds (IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, 2010; Inserm, 2013). Many SVOCs thus have common toxic effects, especially in early life, justifying cumulative risk assessment (CRA). For CRA we chose to focus i) on neurotoxicity, reproductive toxicity, and genotoxic carcinogenicity because these endpoints are related to systems which are particularly sensitive to chemical exposure during early life and ii) on SVOCs with mixture based toxicological data when available.

CRA addresses exposure from multiple compounds, based on defined criteria such as chemical structure, mechanism of action, target organ or toxic effect (EFSA, 2008; Boobis et al., 2008). These methods are usually based on the fundamental concept of additivity, and are described extensively elsewhere (Sarigiannis and Hansen, 2012; Fournier et al., 2014a). The CRA issue is a challenging one, and a consensus has been reached that hierarchical approaches should be adopted, with each tier being more refined - more certain and less cautious - than the previous one (Meek et al., 2011).

The objective of this study, conducted within the framework of the ECOS project (Glorennec et al., 2011), was to assess the public health risk posed by 32 SVOCs. Briefly the ECOS project aimed to develop multi-residue analytical methods appropriate to indoor contamination (Mercier et al., 2012, 2014), as well as to measure indoor contamination in France (Mandin et al., 2016; Blanchard et al., 2014), group compounds on the basis of common toxicity (Fournier et al., 2014b), and develop mixture toxicity indicators (Fournier et al., 2016, 2017). Using nationwide measurements, we assessed exposure (by inhalation, contact and ingestion) to 32 indoor SVOCs on a population basis, that is, the distributions of exposure are representative of those of the population living in France (Pelletier et al., 2017b). A chemical-by-chemical risk assessment was completed using lower to higher tier CRA, as recommended by Meek et al. (2011), based on reference doses from risk assessment databases and mixture toxicity indicators from the literature.

2. Methods

2.1. Chemical-by-chemical risk assessment

For non-carcinogenic SVOCs, hazard quotients (HQ, unitless) were calculated as follows:

$$HQ = \frac{ADD}{RfD \times f_{oral}} \quad (1)$$

With
ADD: Aggregate daily dose (mg/kg-bw/day)
RfD: Reference dose (mg/kg-bw/day)
f_{oral}: Oral bioavailability

ADDs were retrieved from a previous exposure study encompassing air inhalation, dust ingestion, and dermal contact and are expressed as internal doses; 32 SVOCs were selected on the basis of their health interest and because they were detected in both the air and the settled dust of French dwellings (Pelletier et al., 2017b). Briefly, in this previous study, ADDs were simulated on the basis on nationwide representative measurements (Mandin et al., 2014, 2016) in airborne particulate matter and dust for most compounds, which were combined with a static partitioning model and human exposure factors. This two-dimensional Monte Carlo simulation revealed that the exposure variance was mainly driven by the contamination variability rather than by the uncertainty in modeling parameters.

RfD is an estimate of a daily oral exposure that is likely to be without an appreciable risk of deleterious effects during a lifetime (US EPA, 2002). For this risk assessment, RfDs based on oral exposure were preferred because they were available for most SVOCs. We retrieved RfDs, or their equivalents (minimal risk levels or acceptable daily intakes), from the following online databases: the Integrated Risk Information System (IRIS) from US EPA (https://www.epa.gov/iris), the toxicological profiles from Agency for Toxic Substances and Disease Registry (ATSDR) (https://www.atsdr.cdc.gov/), the Joint Meeting on Pesticide Residues (JMPR) from the WHO (http://apps.who.int/pesticide-residues-jmpr-database/Home/Range/A-C), the Joint FAO/WHO Expert Committee on Food Additives (JECFA) (http://apps.who.int/food-additives-contaminants-jecfa-database/search.aspx), the Office of Environmental Health Hazard Assessment (OEHHA) (http://oehha.ca.gov/chemicals), Health Canada (https://www.canada.ca/en/health-canada.html), the French agency for food, environment and occupational safety (ANSES) (https://www.anses.fr/fr), and the EU pesticide database from European Commission (http://www.efsa.europa.eu/). RfDs were selected according to the following criteria: i) status = final (non-provisional), ii) methods = derived from classical dose-response data, and iii) update = not the oldest value. Finally, where previous criteria were met for several RfDs, the most conservative was chosen (see Table S1). Where no RfDs were available for individual PCBs or PBDEs compounds, we made the assumption of similar toxic potency between congeners having the same molecular formula (same number of halogenated atoms) and used the RfD of the known congener. Because ADDs are internal doses, RfDs were converted into internal doses using oral bioavailability coefficients (f_{oral}). These are the fraction of a contaminant reaching the digestive system and absorbed into the systemic circulation (Rostami and Juhasz, 2011). See Table S2 for corresponding f_{oral} coefficient for each compound. Where RfDs were based on studies using adult mammals, the risk was assessed for the exposure of both an adult (aged 21 to 30 years, as an example) and a child (from birth to the age of 2 years, as an example) because the uncertainty factors applied for intra-species variability are supposed to take into account differences in the sensitivity of responses within a species (US EPA, 2008). Given that early-life (pre- and postnatal periods) is considered as a very vulnerable period, where RfDs were based on prenatal studies, the risk was assessed only for the exposure of a pregnant woman (aged 21–30 years, as an example). And where RfDs were based on postnatal studies, the risk was assessed only for the exposure of a child (from birth to the age of 2 years, as an example). Lastly, HQs were calculated for median and high uptake estimates (ADD 50th and 95th percentiles, respectively).

For genotoxic carcinogen SVOCs, excess risks (ER, unitless) were calculated as follows for an adult continuously exposed from birth to the age of 30 years:

$$ER = \text{ADD} \times (\text{CSF} \times f_{oral}) \times \frac{ED}{LD} \quad (2)$$

With
CSF: Cancer slope factor $(\text{mg/kg-bw/day})^{-1}$
ED: Exposure duration (30 years)
LD: Life duration (70 years)

CSF is an estimate of the increased cancer risk from oral exposure to a dose of 1 mg/kg/day over a lifetime (US EPA, 2005). CSFs were retrieved from literature using the same method as for RfDs (see Table S1). Finally, ERs were calculated for median and high uptake estimates (ADD 50th and 95th percentiles, respectively).

2.2. Cumulative risk assessment

CRA methods are based on the assumption that additivity is