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Aggregating exposures & cumulating risk for semivolatile organic compounds: A review

Maud Pelletier[a,b], Nathalie Bonvallot[a,b], Philippe Glorennec[a,b,*]

[a] EHESP-School of Public Health, Sorbonne Paris Cité, Rennes, France
[b] INSERM-U1085, Irset-Research Institute for Environmental and Occupational Health, Rennes, France

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ABSTRACT

Increasingly, health risk assessment is addressing multiple pathway exposures to multiple contaminants. We reviewed aggregated exposure and cumulative risk approaches for contemporary and ubiquitous semivolatile organic compounds (SVOC). We identified 22 studies aggregating exposure pathways, and 31 cumulating risk. Exposure aggregation is based on the addition of pathway-specific doses, using kinetic modeling where it exists, and classic external dose equations otherwise. In most cases, exposure is dominated by a single route or source of exposure - mainly the oral pathway - via dietary or non-dietary exposure. Preferential routes and sources of exposure are influenced by SVOC physical-chemical properties such as vapor pressure. The cumulative risk approach for contaminants is based on dose addition. Simple sum of hazard quotient (Hazard Index: HI) is the most commonly used cumulative risk assessment approach, while Relative Potency Factor (RPF) appeared to the best suited – although this calls for a level of toxicological information that limits the number of compounds that can be studied simultaneously. Where both were performed, moving from HI to more refined approach produced similar results. In conclusion, both approaches - exposure aggregation and cumulative risk - rely on simple assumptions. Nevertheless, they allow uncertainty to be reduced, in comparison with source-by-source or chemical-by-chemical approaches.

1. Introduction

People are continuously and increasingly exposed to a multitude of organic chemicals (NHANES, 2015) from various sources (e.g. food, dust, cosmetics and personal care products (C & PCPs), textiles and materials) and media (e.g. air, water and soil), and by different routes of exposure such as inhalation, ingestion or dermal contact. Organic chemicals include a high number of compounds having various physical-chemical properties, and can be classified as volatile, semivolatile or non-volatile compounds. Semivolatile organic compounds (SVOCs) are defined as having a boiling point temperature of between 240 –and 400 °C (NF ISO 16000-6, 2006). This group includes a high number of organic molecules from different chemical families (e.g. phthalates, bisphenols, polycyclic aromatic hydrocarbons (PAHs), organophosphorus (OPs), organochlorines (OCs), synthetic musks, polychlorinated biphenyls (PCBs), polybromodiphenylethers (PBDEs)). The scientific community's growing interest in studying exposure to SVOCs is motivated by a rise in their use in consumer products as well as by improved analytical techniques that have shown their ubiquity, for example, in dwellings (Rudel et al., 2003; Weschler and Nazaroff, 2008). Moreover most are reprotoxic (Peretz et al., 2014; Kay et al., 2014), neurotoxic (Muñoz-Quezada et al., 2013; Costa et al., 2014), or carcinogenic compounds (Armstrong et al., 2004; IARC, 2015, 2015b), and have been found in human biological fluids (blood and urine).

When evaluating the impact of SVOC exposure on human health, exposures may be assessed using either external or internal doses. External dose is estimated from contamination data and human parameters such as body weight, inhalation and dust ingestion rate… Using a pharmacokinetic model or absorption factors, it can be converted to internal dose. Internal dose is preferentially assessed by biomonitoring. Biomonitoring data directly reflect internal aggregate exposures and could, with back calculation using pharmacokinetics models, inform as to the external dose attributable to each exposure pathway. However, using biomonitoring data does not inform on the source of exposure that is so useful for prevention strategies. Once exposure is assessed, the risk may be assessed by comparing exposures to a toxicological reference value. This value may be expressed as an external dose for a unique route of exposure, i.e. a reference dose or acceptable daily intake for ingestion (or a reference concentration for inhalation). They are usually estimated from an indicator of the dose-response

* Corresponding author at: INSERM-U1085, Irset-Research Institute for Environmental and Occupational Health, Rennes, France. EHESP-School of Public Health, Sorbonne Paris Cité, Rennes, France.
E-mail address: philippe.glorennec@ehesp.fr (P. Glorennec).

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Table 1
Publications including exposure aggregation on semivolatile organic compounds.

References (year of publication)	Chemical class (nb. of publications)	Exposure pathways			Exposure modeling		Aggregation			Comparison with biomonitoring data
		Source	Media	Route	Source-to-external dose	External-to-internal dose	Approach	Type of aggregated dose	Aggregation level	
Ginsberg and Foos (2016)	Phthalates (1)	Dietary Residential	Food Breast milk Drinking water Indoor air Indoor dust Indoor objects Clothing	Dermal Ingestion Inhalation	External dose equation	Absorption factors	Deterministic	Internal	Average individual	Yes
Mitro et al. (2016)	Musks (1) Parabens (3) PFAAs (11) Phenols (7) Phthalates (8) RFRs (15)	Residential	Indoor air Indoor dust	Dermal Ingestion Inhalation	External dose equation	Dermal absorption factors	Deterministic	External (ingestion, inhalation) Internal (dermal)	Average individual	No
Gosens et al. (2014)	Parabens (4)	Personal care products	Personal care products	Dermal Ingestion	External dose equation and PACEM	Absorption factors	Deterministic Probabilistic	Internal	Individual	No
Gaspar et al. (2014)	Phthalates (2)	Residential	Indoor air Indoor dust	Dermal Ingestion Inhalation	External dose equation	Dermal absorption factors	Probabilistic	Internal	Average individual	No
Poet et al. (2014)	OPs (1)	Residential	Indoor air Indoor surface (carpet treated)	Dermal Inhalation	PBPK/PD model		Deterministic	Internal	Individual	Yes
Ortiz et al. (2014)	PAHs (1)	Occupational	Indoor air	Dermal Inhalation	PBPK model and simple one-compartment PK model		Deterministic	Internal	Individual	Yes
Xue et al. (2014)	Pyrethroids (7)	Dietary Residential	Food Indoor air	Dermal Ingestion Inhalation	SHEDS-Multimedia	PK model	Probabilistic	Internal	Average individual	Yes
Beko et al. (2013)	Phthalates (5)	Residential	Gas phase Particle phase Indoor dust	Dermal Ingestion Inhalation	External dose equation	Dermal absorption factor	Probabilistic	External (ingestion, inhalation) Internal (dermal)	Average individual	Yes
Wei et al. (2013)	Pyrethroids (1)	Occupational (aircraft disinfection)	Indoor air	Dermal Ingestion Inhalation	PBPK model		Probabilistic	Internal	Average individual	Yes
Wason et al. (2013)	Pyrethroids (3) OPs (2)	Residential	Indoor dust Indoor surfaces Soil	Dermal Ingestion	SHEDS-Multimedia		Probabilistic	Internal	Average individual	No
Beamer et al. (2012)	OPs (2)	Dietary Residential	Food Indoor air Indoor dust Indoor surfaces and toy	Dermal Ingestion Inhalation	PBPK model		Probabilistic	Internal	Individual	Yes
Zartarian et al. (2012)	Pyrethroids (1)	Dietary Residential	Food Indoor air	Dermal Ingestion Inhalation	SHEDS-Multimedia	PK model	Probabilistic	Internal	Average individual	Yes
Trudel et al. (2011)	PBDEs (8)	Dietary Residential	Food Indoor air Indoor dust Indoor surfaces Soil	Dermal Ingestion Inhalation	External dose equation	Absorption factors	Probabilistic	Internal	Average individual	Yes
Roosens et al. (2010)	PBDEs (6)	Dietary Residential	Food Breast milk	Ingestion Inhalation	External dose equation	No	Probabilistic	External	Average individual	No

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