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Maud Pelletier

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pour le grade de

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présentée par

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École des Hautes Études en Santé Publique
UFR Médecine

Expositions agrégées aux composés organiques semi-volatils dans l'habitat et risques sanitaires associés

Thèse soutenue à Rennes le 2 novembre 2017

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LISTE DES SIGLES ET ACRONYMES

AhR : Récepteur aux hydrocarbures aromatiques

AMM : Autorisation de mise sur le marché

Anses : Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail

BADGE : Diglycidyl ether de bisphénol-A

BBP : Phtalate de butyle et de benzyle

BDE : Bromodiphényléther

CG : Chromatographie gazeuse

CIRC : Centre international de recherche sur le cancer

CLP : Règlement relatif à la classification, à l'étiquetage et à l'emballage des substances chimiques et des mélanges

CMR : Cancérogène, mutagène et toxique pour la reproduction

COSV : Composé organique semi-volatil

COV : Composé organique volatil

CSTB : Centre scientifique et technique du bâtiment

DBP : Phtalate de dibutyle

DEHP : Phtalate de bis (2-éthylhexyle)

DEP : Phtalate de diéthyle

DiBP : Phtalate de di-isobutyle

DiNP : Phtalate de di-isononyle

DJE : Dose journalière d'exposition

DOHaD : Developmental origins of human adult diseases

DT : Désorption thermique

ECHA : Agence européenne des produits chimiques

ECOS-Habitat : Expositions cumulées aux composés organiques semi-volatils dans l'habitat

EHESP : École des hautes études en santé publique

ERI : Excès de risque individuel

ERS : Évaluation des risques sanitaires

ERSC : Évaluation des risques sanitaires cumulés

ERU : Excès de risque unitaire

HAP : Hydrocarbures aromatiques polycycliques

HBCD : Hexabromocyclododécane

HI : Hazard index

Ineris : Institut national de l'environnement industriel et des risques

Irset : Institut de recherche sur la santé, l'environnement et le travail

K_{oa} : Coefficient de partage entre l'octanol et l'air

K_{ow} : Coefficient de partage entre l'octanol et l'eau

LD : Limite de détection

LQ : Limite de quantification

LERES : Laboratoire d'études et de recherche en environnement et santé

OC : Organochlorés

OMS : Organisation mondiale de la santé

OP : Organophosphorés

OQAI : Observatoire de la qualité de l'air intérieur

PBDE : Polybromodiphényléthers

PBPK : Physiologically based pharmacokinetic

PBT : Persistante, bioaccumulable et toxique

PCB : Polychlorobiphényles

PM_{10} : Particules en suspension dans l'air d'un diamètre médian inférieur à 10 µm

PVC : Polychlorure de vinyle

QD : Quotient de danger

REACH : Règlement sur l'enregistrement, l'évaluation, l'autorisation et les restrictions des substances chimiques.

RFB : Retardateurs de flamme bromés

RoHS : Restriction of hazardous substances

RPF : Relative potency factors

SM : Spectrométrie de masse

TBP : Tributylphosphate

TBBPA : Tétrabromobisphénol-A

TEF : Toxic equivalency factor

UF : Facteur d'incertitude

US EPA : United States Environmental protection agency

VTR : Valeurs toxicologique de référence

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INTRODUCTION

Le 20ème siècle a connu le développement de l'industrie chimique avec l'emploi de composés de synthèse dans de nombreux domaines (énergie, construction, alimentation, santé, etc.). Cela a permis des avancées techniques et technologiques notables mais a également conduit à la contamination des milieux naturels (eau, air et sol) et des organismes vivants. Les substances chimiques organiques et inorganiques répertoriées par le *Chemical Abstract Service* représentent plus de 130 millions de composés au niveau mondial.[1] Au niveau européen, 145 000 substances chimiques produites à plus d'une tonne par an ont été préenregistrées en 2009 dans le cadre du règlement sur l'enregistrement, l'évaluation, l'autorisation et les restrictions des substances chimiques (REACH).

Certaines de ces substances chimiques ont des effets avérés ou suspectés sur la santé humaine à différents niveaux, allant de troubles du métabolisme à la perturbation de systèmes entiers du corps humain. L'augmentation de la présence des contaminants chimiques dans notre quotidien pourrait expliquer en partie l'augmentation des maladies chroniques telles que le diabète de type 2, l'obésité, les cancers, les maladies cardio-vasculaires, les stérilités, etc. Si la survenue d'une maladie chronique est également imputable à des facteurs « génétiques » individuels, ceux-ci ne représenteraient que 10% des causes (Manolio et al., 2009). La très grande majorité des causes (90 %) de ces maladies chroniques sont donc des facteurs environnementaux au sens large ou autrement dit « non-génétiques ». Ces derniers englobent les expositions aux divers contaminants environnementaux (chimiques, physiques et biologiques) mais aussi le mode de vie via l'alimentation, le

[1] CAS REGISTRY, *https://www.cas.org/content/chemical-substances*

surpoids, l'inactivité physique, le tabagisme, la consommation d'alcool, l'environnement social, etc. Ces facteurs environnementaux affectent « l'environnement chimique interne » par des phénomènes endogènes d'inflammations, de stress oxydant, d'infections, de perturbation endocriniennes ou encore en raison de maladies antérieures (Figure 1).

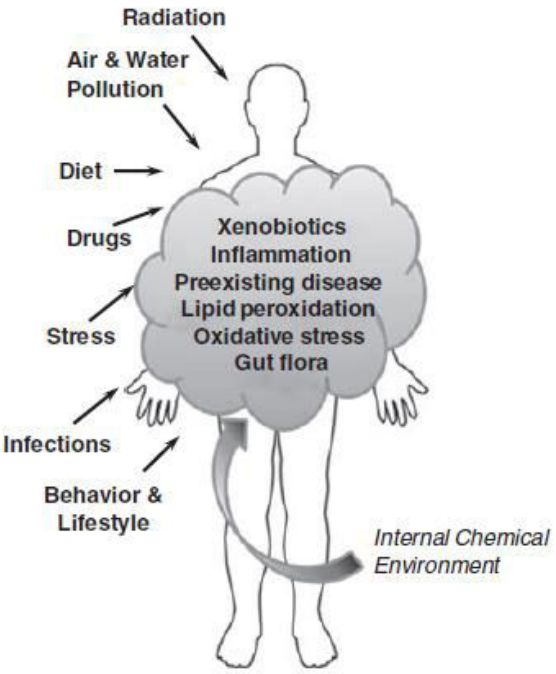

Figure 1 : Exposition environnementale aux composés chimiques issus de sources externes et internes (d'après Rappaport 2011).

Cette notion d'environnement chimique interne a été introduite par Rappaport et Smith (2010), et est reliée au concept « d'exposome » lui-même défini par Christopher Wild comme l'ensemble des expositions environnementales d'un organisme de sa période prénatale à la fin de sa vie (Wild 2005).

Dans le domaine des sciences de l'exposition, la caractérisation des exposomes peut se faire suivant deux approches dites « bottom-up » et « top-down » (Rappaport et Smith 2010). L'approche bottom-up estime la dose interne d'une substance à partir de données de contamination externes (concentration de la substance dans les

environnements extérieurs) (Figure 2). Cette approche permet de renseigner sur la contribution des sources et des voies d'exposition externes. A contrario, l'approche top-down se base sur des données de biomonitoring (concentrations dans les fluides corporels de la substance et/ou de ses métabolites) et permet ainsi de quantifier l'environnement chimique interne représentatif de l'ensemble (sources et voies) des expositions exo- et endogènes (Figure 2). Cependant cette approche ne permet pas, ou seulement dans de rares cas, de renseigner la contribution des différentes sources et voies d'exposition.

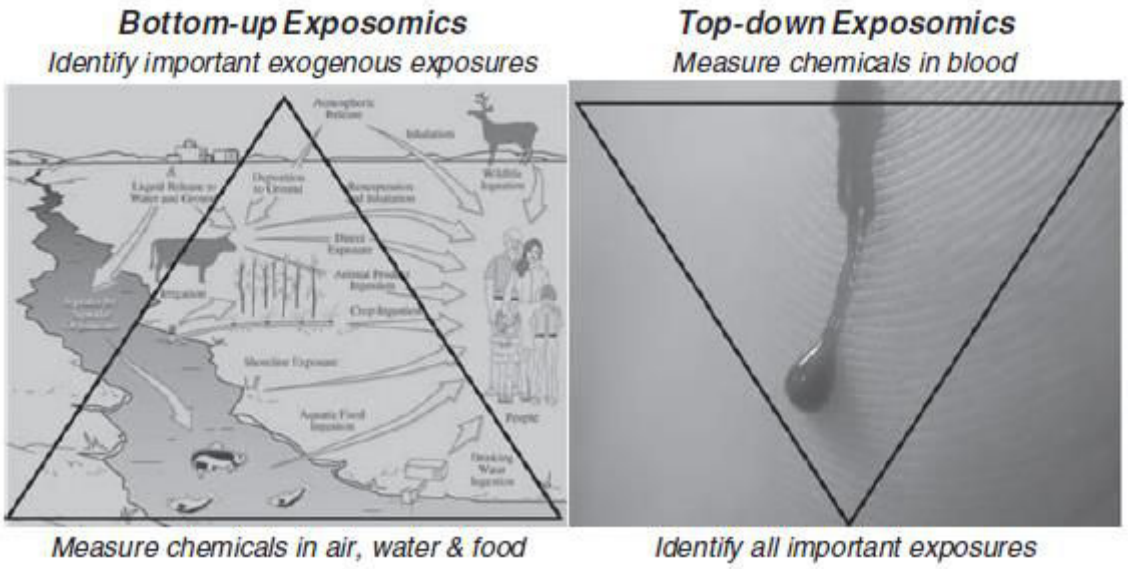

Figure 2 : Deux approches d'étude de l'exposome (d'après Rappaport 2011).

Si la notion de dose a longtemps été considérée comme le principal critère dans la survenue d'effets toxicologiques, la notion de fenêtre d'exposition, notamment illustrée par les effets toxiques des perturbateurs endocriniens, témoigne que des faibles doses peuvent être, selon la période d'exposition, plus délétères que des fortes doses. En effet, des expositions pré- et postnatales à certains polluants seraient susceptibles d'engendrer l'apparition de troubles ou de maladies pendant

l'enfance, l'adolescence et/ou l'âge adulte. Barker et al. (1989) ont ainsi introduit le concept du « DOHaD », *developmental origins of human adult diseases*, reposant sur le principe que le développement et la progression de maladies multifactorielles, comme les maladies cardiovasculaires, neurodégénératives (notamment les maladies d'Alzheimer, de Parkinson, de Huntington et la sclérose latérale amyotrophique) et métaboliques (notamment le diabète de type 2 et l'obésité) seraient entre autres expliqués par des phénomènes épigénétiques, induits par l'environnement et correspondant à des changements dans l'activité des gènes n'impliquant pas de modification de la séquence d'ADN et pouvant être transmis lors de divisions cellulaires.[2]

Les composés organiques peuvent être d'origine naturelle ou anthropique et sont constitués au moins de l'élément carbone et d'un ou plusieurs des éléments suivants : hydrogène, halogènes, oxygène, souffre, phosphore, silicium ou azote. Un classement selon leur degré de volatilité distingue les composés organiques volatils (COV), des semi-volatils (COSV) et des non volatils à température ambiante. Les COSV regroupent de nombreux contaminants issus de familles chimiques variées et utilisés pour leur propriétés de plastifiants, de retardateurs de flamme, de pesticides, etc. dans de nombreux matériaux de construction et de consommation. On les retrouve notamment dans les environnements intérieurs où ils sont détectés en très faibles concentrations depuis une quinzaine d'année du fait des progrès de la chimie analytique. Dans les habitats, l'Homme est exposé aux COSV par inhalation, ingestion et contact cutané. Des effets sanitaires néfastes sont rapportés pour certains d'entre eux ce qui en fait une préoccupation de santé publique.

[2] Dossier Inserm, février 2015, *https://www.inserm.fr/thematiques/genetique-genomique-et-bioinformatique/dossiers-d-information/epigenetique*

Se pose alors la question de l'impact de ces expositions aux multiples COSV sur la santé publique et, le cas échéant, de l'identification de priorités de prévention : quel(s) composé(s), quelle(s) source(s), quelle(s) voie(s) et quel(s) média(s) d'exposition considérer ?

Pour répondre à cette question, une démarche d'évaluation des risques sanitaires pour l'Homme a été initiée, reposant sur une approche « bottom-up » d'évaluation des expositions. Pour les COSV les plus préoccupants présents dans l'habitat français, le travail support de cette thèse visait dans un premier temps à en évaluer l'exposition en agrégeant les voies orale, respiratoire et cutanée ; et dans un second temps, à en évaluer les risques pour la santé humaine en considérant chaque composé individuellement mais également les risques cumulés liés à l'exposition simultanée à plusieurs composés.

Ce travail est la dernière partie du programme de recherche ECOS-Habitat « Exposition cumulées aux composés organiques semi-volatils dans l'habitat » initié en 2008 par l'École des hautes études en santé publiques (EHESP) et le Centre scientifique et technique du bâtiment (CSTB) en collaboration avec l'Institut national de l'environnement industriel et des risques (Ineris) (Glorennec et al., 2011). Il a ainsi bénéficié des résultats des travaux antérieurs ayant permis de caractériser :

- les expositions : avec la sélection des composés étudiés (Bonvallot et al., 2010), le développement de méthodes d'analyses multi-résidus (Mercier et al., 2012, 2014) et la quantification des COSV dans différents compartiments des logements français (Mandin et al., 2014, 2016 ; Blanchard et al., 2014) ;

- la toxicité : par le regroupement des composés selon leurs effets toxiques ainsi que la construction d'indicateurs de toxicité cumulée pour des effets neurotoxiques et reprotoxiques (Fournier et al., 2014, 2016, 2017).

Dans la suite de ce manuscrit sur publication sont présentés au chapitre 1 : le contexte scientifique et la présentation du sujet de thèse. Le chapitre 2 est consacré au travail de recherche bibliographique (Pelletier et al., 2017a) réalisé en amont des étapes d'évaluation des expositions et des risques. Dans le cadre spécifique de l'étude des COSV, ce travail a permis l'analyse critique des méthodes et des paramètres employés i) pour étudier l'exposition agrégée via différentes voies et ii) pour en évaluer les risques lors d'une exposition à plusieurs composés. Le chapitre 3 est consacré aux travaux menés pour évaluer les expositions agrégées aux COSV de l'habitat français (Pelletier et al., 2017b), incluant une étape préalable d'évaluation de l'exposition par voie cutanée (Pelletier et al., 2017c). Le chapitre 4 est consacré à l'évaluation des risques sanitaires, pour les expositions aux substances prises individuellement puis pour des expositions cumulées (soumis à *Environmental Health Perspectives*). Enfin, les chapitres 5 et 6 sont respectivement consacrés à la discussion générale de ce travail et aux perspectives qui s'en dégagent.

Chapitre 1 : Contexte scientifique

1.1. Les composés organiques semi-volatils

1.1.1. Définition

La définition d'un COSV repose à la fois sur des critères chimiques et physiques. Selon la Directive européenne n°1999/13/CE[3], un composé organique est une molécule contenant au moins l'élément carbone et un ou plusieurs des éléments suivants : hydrogène, halogènes, oxygène, soufre, phosphore, silicium ou azote. La norme NF ISO 16000-6 quant à elle, définit les composés organiques selon leur température d'ébullition et distingue, d'après la classification adoptée par l'organisation mondiale de la santé (OMS) en 1989, les composés organiques très volatils, volatils et semi-volatils. Ainsi les composés organiques ayant un point d'ébullition compris entre 240 et 400 °C sont dit semi-volatils.[4] Cette définition, parfois imprécise pour certains composés, peut être complétée par celle de la norme NF EN 13936, qui définit les COSV selon leur pression de vapeur saturante, comprise entre 0,001 et 100 Pa.[5]

1.1.2. Usages

Cette classification des composés organiques selon leurs paramètres physico-chimiques engendre une grande diversité chimique au sein des groupes formés. Ainsi les COSV englobent de nombreux composés issus de familles chimiques

[3] Directive n° 1999/13/CE du Conseil européen du 11 mars 1999 relative à la réduction des émissions de composés organiques volatils dues à l'utilisation de solvants organiques dans certaines activités et installations

[4] Environmental Protection Agency. Technical overview of volatile organic compounds, *https://www.epa.gov/indoor-air-quality-iaq/technical-overview-volatile-organic-compounds*

[5] Exposition sur les lieux de travail. Mesurage de l'agent chimique sous forme de mélange de particules aériennes et de vapeur. Exigences et méthodes d'essai. Norme NF EN 13936. La Plaine Saint Denis : AFNOR, (2014)

variées dont les phtalates, les retardateurs de flamme bromés (RFB) (comprenant notamment les polybromodiphényléthers (PBDE), le tétrabromobisphénol-A (TBBPA) et l'hexabromocyclododécane (HBCD)), les polychlorobiphényles (PCB), les organochlorés (OC), les organophosphorés (OP), les hydrocarbures aromatiques polycycliques (HAP), les pyréthrinoïdes, les muscs de synthèse, les bisphénols, les oxadiazolones, les parabènes, les organoétains, les perfluorés ou encore les dioxines (Weschler et Nazaroff, 2008 ; Mercier et al., 2011, 2012). Depuis les années 1950 les COSV sont utilisés pour leurs propriétés variées de plastifiants, de retardateurs de flamme, d'imperméabilisants, de surfactants, de désinfectants, de pesticides et biocides ou de conservateurs (Rudel et al., 2009 ; Mercier et al., 2011) (Tableau 1). Bien que de nombreuses molécules aient été interdites de production ou d'utilisation en France et en Europe (ex : les PCB, certains PBDE, pesticides, phtalates ou encore le bisphénol-A) elles peuvent être encore présentes du fait d'une « pseudo-persistance » liée au stock encore disponible (ex : les PBDE dans certains ordinateurs et les phtalates dans les matériaux en PVC), mais aussi du fait d'une biodégradation très lente (ex : les pesticides OC pour le traitement du bois et les PCB). De plus, les restrictions de mise sur le marché ont également engendré l'arrivée de nouvelles molécules de substitution (ex : les pyréthrinoïdes ont remplacé les pesticides OC et OP). À ceux-là s'ajoutent également des COSV issus des phénomènes de combustion comme les dioxines ou les HAP qui, entre autres, contaminent l'habitat.

Tableau 1 : Propriétés et usages des principaux COSV retrouvés dans les environnements intérieurs (adapté de Mercier et al. 2011).

Familles chimiques Propriétés	**Usages /Sources**
Alkylphénols Surfactants non ioniques (substitut des surfactants ioniques)	Utilisés dans les produits détergents et les produits d'entretien
Hydrocarbures aromatiques polycyliques (HAP) Résidus de combustion des matières organiques	Issus de la cuisson des aliments, du tabagisme, des fumées de l'encens et des bougies, du chauffage au bois ou au charbon, des feux de forêt, etc. Issus des émissions provenant du trafic, des industries, d'incinérateurs etc.
Muscs de synthèse Parfums (substitut des muscs naturels)	Utilisés dans les produits de soin et cosmétiques, les parfums, les produits de nettoyage
Pesticides organophosphorés (OP) et organochlorés (OC) Pesticides et biocides	Produits insecticides et biocides utilisés dans les domaines de l'agriculture, forestier et de santé publique (antiparasitaires). Également utilisés dans les constructions, les entrepôts et pour un usage domestiques (lutte contre les insectes, les parasites, protection des textiles etc.) (interdiction de nombreux produits pesticides OP et OC en France)
Pyréthrinoïdes Pesticides (substitut des pesticides OC et OP)	Produits insecticides et biocides utilisés dans les domaines de l'agriculture, forestier et de santé publique (antiparasitaires). Également utilisés dans les constructions, les entrepôts et pour un usage domestiques (lutte contre les insectes, les parasites, protection des textiles etc.)
Phtalates Plastifiants et agents fixateur	Utilisés dans les produits de soin et cosmétiques, les PVC souples (rideaux de douche, matériels médicaux, câbles électriques, etc.), les revêtements de sols ou des murs, les boîtiers et circuits imprimés
Retardateurs de flamme bromés (RFB)[1] Retardateurs de flamme	Utilisés dans les textiles, les mobiliers rembourrés (coussins, canapés, matelas, etc.), les plastiques, les matériaux électroniques (ordinateurs, télévisions, etc.)
Polychlorobiphényles (PCB) Retardateurs de flamme, stabilisateurs, isolant	Anciennement utilisés en France dans les câbles électriques comme isolant, dans les fluides caloporteurs des transformateurs et des condensateurs, dans les mobiliers rembourrés (coussins, canapés, matelas, etc.), les revêtements des sols et des murs (joints d'étanchéité, peintures, etc.)
Bisphénols Révélateurs chimique, synthèse de polymères, synthèse de résines époxydes	Utilisés dans les papiers thermiques, les plastiques (jouets, biberons, etc.), les contenants alimentaires (interdiction récente de l'utilisation du bisphénol-A en France)

[1] Comprennent les polybromodiphényléthers (PBDE), le tétrabromobisphénol-A (TBBPA) et l'hexabromocyclododécane (HBCD).

1.2. COSV dans l'habitat

1.2.1. Sources et comportement des COSV

Les propriétés variées des COSV amènent à les utiliser dans de nombreux matériaux ou produits (Tableau 1). Dans les logements on peut les retrouver dans les matériaux de construction (revêtements des sols et des murs), dans les matériaux électroniques (câbles électriques, ordinateurs), dans le mobilier (canapés, matelas), mais aussi dans des produits de consommation (cosmétiques, produits de nettoyage, désodorisants, emballages, textiles). La contamination de l'environnement intérieur se fait principalement par émission des COSV de leurs matériaux d'origine dans l'air intérieur. Ce phénomène de décharge est fonction des propriétés physico-chimiques des COSV mais aussi des conditions d'ambiance du logement (température, humidité). Les molécules émises par les multiples sources présentes dans l'habitat vont plus précisément se retrouver dans la phase gazeuse de l'air et être ainsi disponibles à la contamination d'autres milieux par des processus de sorption (adsorption et absorption) sur les différentes surfaces intérieures, incluant les particules en suspension dans l'air, les poussières sédimentées, les sols, le mobilier, les occupants ou encore leurs vêtements (Figure 3) (Xu et Little 2005 ; Weschler et Nazaroff, 2012). La sollicitation des matériaux, notamment par abrasion, va également enrichir les poussières. Les équilibres et répartitions entre la phase gazeuse et les différentes surfaces dans un environnement intérieur sont fonction des coefficients de partage spécifiques des composés (notamment le coefficient de partage entre l'octanol et l'air (Koa)) et des différents compartiments d'absorption cités ci-dessus, tels que les particules, les différentes surfaces, la peau, etc. (Finizio et al., 1997 ; Pankow, 1998 ; Weschler et Nazaroff, 2008). Ces phénomènes de

répartition des COSV associés à la persistance de certains contaminants, du fait d'une longue demi-vie (pouvant aller jusqu'à plusieurs années) et/ou d'un réservoir d'émission important, rendent les COSV pérennes dans l'habitat et pour certains même longtemps après que leurs matériaux d'origine aient été supprimés ou que leurs produits d'origine aient cessé d'être utilisés.

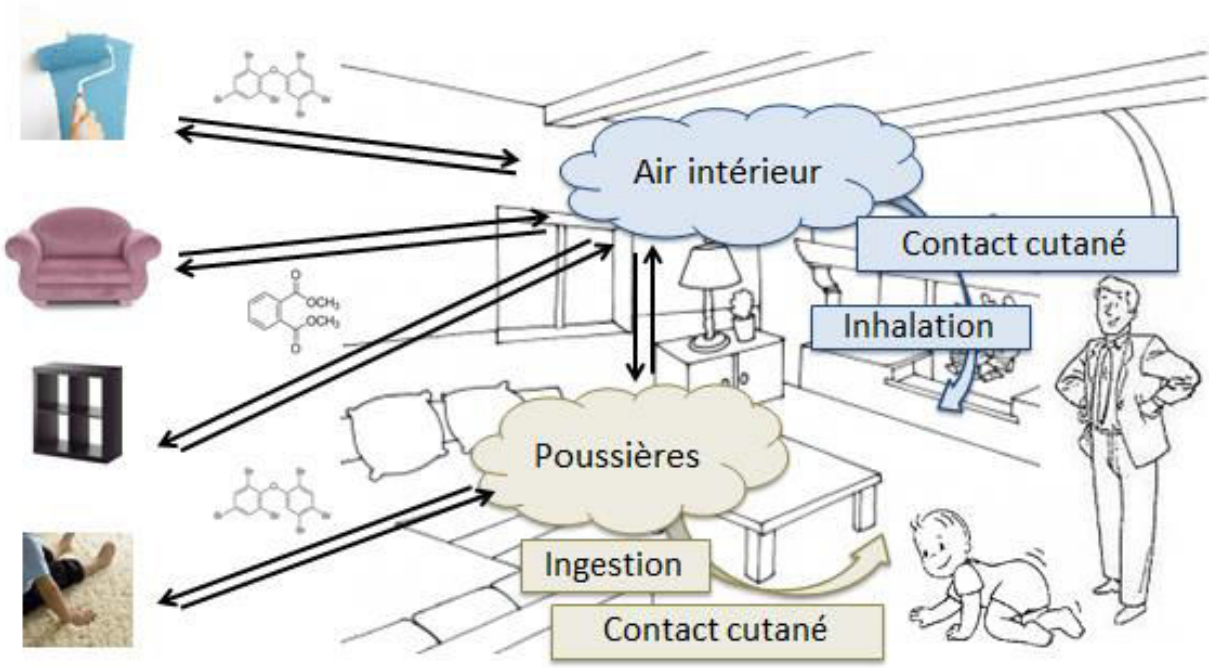

Figure 3 : Sources d'émission et voies d'exposition des COSV dans l'environnement intérieur.

1.2.2. Contaminations de l'habitat

La contamination des environnements intérieurs par les COSV fait l'objet de recherches scientifiques dans de nombreux pays d'Europe, d'Amérique du Nord et d'Asie principalement (Figure 4). Les PBDE et les pesticides sont les plus étudiés, viennent ensuite les phtalates, les HAP, les PCB et les perfluorés (Mercier et al., 2011). Les publications concernant leur quantification dans les milieux intérieurs est

en augmentation constante depuis plusieurs années : passant de 5 publications en 2003 à plus de 30 en 2014 (Mandin 2015). Ces publications concernent principalement les contaminations des poussières et des surfaces, devant la contamination de l'air intérieur, et se sont le plus souvent intéressées à l'habitat, devant les écoles, les bureaux et les voitures.

Figure 4 : Évolutions des publications sur les COSV depuis 2003 par milieu considéré (n=216) (d'après Mandin 2015).

Les taux de contaminations en COSV retrouvées dans l'habitat peuvent varier de plusieurs ordres de grandeur selon les pays du fait des usages, des périodes (changement de composition des produits, substitution), des règlementations mises en place et dans une moindre mesure selon les techniques analytiques utilisées pour les prélèvements, la préparation des échantillons et leurs analyses. Le tableau 2 présente les concentrations mesurées en France lors de deux campagnes de

mesures d'envergures nationales dans la phase particulaire de l'air et les poussières (Mandin et al., 2014, 2016) et celles mesurées dans d'autres pays pour les mêmes composés et par des techniques analytiques similaires. La contamination de la phase particulaire de l'air en France est comparable à celle quantifiée dans les autres pays, alors que la contamination des poussières au sol apparaît supérieure pour le DiBP, le bisphénol-A et la perméthrine.

Tableau 2 : Comparaison des concentrations médianes mesurées dans les poussières et la phase particulaire de l'air pour une sélection de COSV ayant des données disponibles dans les autres pays (d'après le Bulletin n°9 de l'OQAI)[6].

	Concentrations médianes dans les poussières au sol (µg/g)		**Concentrations médianes dans la phase particulaire de l'air (fraction PM_{10}) (ng/m^3)**	
	France	Autres pays	France	Autres pays[1]
DEHP	337	183 - 1050	46,2	12 (68 - 200)
DiBP	17	1,9 - 9,4	0,86	(75 - 270)
Benzo[a]pyrène	0,1	0,009 - 0,71	0,14	0,09 - 0,27
Bisphénol-A	4,2	0,24 - 3,7	< 1	(< 0,8 - 1,82)
Perméthrine	2,6	0,09 - 1,2	0,056	(< 0,4)
Galaxolide	1,1	0,04 - 0,99	< 0,042	(143 - 1130)
BDE 209	0.76	0.06 - 10	Non recherché	(0.001 - 0.29)

[1] Les chiffres entre parenthèses correspondent à des concentrations totales dans l'air (phase gazeuse et particulaire).

[6] Bulletin n°9 de l'Observatoire de la Qualité de l'Air Intérieur (OQAI) : Premier état de la contamination des logements français en composés organiques semi-volatils : pesticides, phtalates, retardateurs de flamme, etc. (2015)

1.3. Expositions, effets sanitaires et aspects règlementaires

1.3.1. Voies d'exposition

Lorsque l'on s'intéresse aux contaminations environnementales, il existe trois voies d'exposition humaine majoritaires : la voie respiratoire, la voie orale et la voie cutanée. Outre l'alimentation et le contact direct avec les matériaux et produits, l'Homme est en permanence exposé dans les logements à deux milieux contaminés : l'air intérieur et les poussières (au sol et sur le mobilier). Dans le cas des COSV, les expositions sont donc l'inhalation d'air, l'ingestion de poussières et le contact cutané avec les COSV présent dans l'air et sur les poussières (Figure 1). L'air est composé de deux phases : la phase gazeuse où les COSV sont directement disponibles à l'absorption et la phase particulaire où les COSV ne sont disponibles qu'après un phénomène de désorption des particules (Weschler et Nazaroff 2010). Si l'ingestion de poussières et l'inhalation d'air (phase gazeuse et phase particulaire) sont des voies d'exposition aux contaminants chimiques clairement identifiées et documentées dans la littérature, la voie cutanée, pour les COSV, l'était beaucoup moins. Cependant des travaux récents ont démontré que le contact cutané avec la phase gazeuse de l'air aurait une part non négligeable dans l'exposition totale à certains COSV présents dans l'habitat (Weschler et Nazaroff, 2014). Ces résultats ont ensuite été confirmés par des études expérimentales menée chez l'Homme pour certains phtalates (Weschler et al., 2015 ; Morrison et al., 2016).

1.3.2. Usages, effets sanitaires et règlementations relatifs aux principales familles chimiques de COSV

La toxicité et les effets sanitaires des COSV ont fait l'objet de nombreuses recherches toxicologiques et épidémiologiques. Des effets sur différents systèmes ont été rapportés, notamment sur les systèmes nerveux et reproducteur (Fournier et al., 2014), l'appareil respiratoire (asthme, bronchite, etc.) ou encore le système immunitaire (Inserm 2013 ; Bamai et al., 2014). De par leur capacité à interagir avec les fonctions endocriniennes de l'organisme et à en perturber les fonctions métaboliques, reproductrices ou encore neurologiques, un grand nombre de COSV sont également considérés comme perturbateurs endocriniens (Inserm 2008).[7,8,9] De plus le centre international de recherche sur le cancer (CIRC) a documenté et classé cancérigènes plusieurs COSV selon leur niveau de danger.[10]

1.3.2.1. Les hydrocarbures aromatiques polycycliques

La famille des HAP regroupe plusieurs centaines de molécules organiques constituées d'au moins deux cycles aromatiques benzéniques. Ils sont générés lors d'une combustion incomplète de la matière organique par des phénomènes naturels (feux de forêt, éruptions volcaniques) ou plus majoritairement anthropiques (émissions domestiques et industrielles) (voir Tableau 1). Seulement certains HAP

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[7] Towards the establishment of a priority list of substances for further evaluation of their role in endocrine disruption. Commission Européenne (2000) *http://ec.europa.eu/environment/archives/docum/pdf/bkh_main.pdf*

[8] Communication sur la mise en œuvre de la stratégie communautaire concernant les perturbateurs endocriniens. Commission des communautés européennes (2001)

[9] Defining criteria for identifying endocrine disruptors in the context of the implementation of the plant protection products regulation and biocidal products regulation. Commission Européenne (2016), *https://ec.europa.eu/health/sites/health/files/endocrine_disruptors/docs/2016_impact_assessment_en.pdf*

[10] Monographies du CIRC, volumes 1-119 (2017), *http://monographs.iarc.fr/FR/Classification/*

ont fait l'objet d'études toxicologiques chez l'animal. Ces études ont rapporté des effets systémiques hématopoïétiques, hépatiques, immunologiques et pulmonaires, ainsi que des effets cancérigènes après exposition orale, pulmonaire et cutanée. Chez les rongeurs des effets sur la reproduction sont rapportés pour le benzo[a]pyrène (ATSDR 1995). Le benzo[a]pyrène est également classé comme cancérogène avéré (groupe 1) par le CIRC, trois autres HAP sont classés cancérogènes probables (groupe 2a) et onze autres sont classés cancérogènes possibles (groupe 2b).

D'un point de vue réglementaire, seul le benzo[a]pyrène est classé comme CMR de catégorie 1b (règlement relatif à la classification, à l'étiquetage et à l'emballage des substances chimiques et des mélanges (CLP)), pour ses effets suspectés cancérigènes, mutagènes et toxiques pour la reproduction chez l'homme. Le règlement CLP a été mis en place par l'Union européenne afin que les dangers soient clairement communiqués aux travailleurs et aux consommateurs.

1.3.2.2. Les muscs de synthèse

Les muscs de synthèse se substituent aux muscs naturels et sont utilisés pour leurs propriétés odorantes dans les produits cosmétiques, les parfums et les produits ménagers (voir Tableau 1). Ils se divisent en plusieurs catégories selon leur structure chimiques : 1) les nitrés dont la production et l'utilisation ont fortement diminué en Europe en raison de leur lente biodégradation dans l'environnement et d'effets neurotoxiques et phototoxiques de certains composés; 2) les polycycliques qui sont majoritairement utilisés aujourd'hui bien que des effets sur la santé humaine soient

suspectés; et 3) les macrocycliques dont l'utilisation est limitée du fait d'un coût élevé de production. En termes de production européenne, 95 % du marché est représenté par deux muscs nitrés (xylène et cétone) et deux muscs polycycliques (le galaxolide et le tonalide) (OSPAR 2004). Concernant les muscs xylène et cétone, des associations entre des effets gynécologiques et leurs présences dans le sang de femmes ont été rapportés bien qu'aucune relation de causalité définitive n'ait encore été établie (Eisenhardt et al., 2001).

Les muscs nitrés sont reconnus comme substances dangereuses et ont été évalués dans le cadre de la règlementation REACH. Ils ont été identifiés par la Commission européenne en 2011[11] comme substances très persistantes et bioaccumulables (substances « vPvB »). Depuis leur production a été progressivement remplacée par les muscs polycycliques. Ces derniers ont été enregistrés dans le cadre de REACH. Depuis, la Commission européenne a conclu à un risque négligeable pour la santé humaine pour le galaxolide et le tonalide. En effet, des études *in vitro* sur cellules humaines rapportent une faible activité œstrogénique pour ces deux composés (Seinen et al., 1999 ; Schreurs et al., 2004).

1.3.2.3. Les pesticides

Les pesticides peuvent être regroupés selon leurs usages et notamment selon l'organisme nuisible à éliminer. On retrouve principalement les insecticides, qui ciblent les insectes, les herbicides, qui ciblent les végétaux, et les fongicides, qui ciblent les moisissures et les microchampignons. Il existe aussi les rodonticides,

[11] Règlement (CE) n°143/2011

contre les rongeurs, les acaricides, contre les acariens, les nématicides, contre les vers, et les molluscicides, contre les mollusques. On peut également distinguer les produits phytosanitaires (pour le traitement des végétaux), des biocides (pour la désinfection des surfaces et environnements) et des produits antiparasitaires humains et vétérinaires. Par ailleurs, les usages non agricoles représentent 10 % de la consommation annuelle des pesticides en France[12], avec entre autres les usages domestiques d'insecticides. Les insecticides regroupent différentes familles chimiques, dont les OC, les OP, les carbamates et les pyrethrinoïdes.

Ces insecticides ont des propriétés neurotoxiques à « fortes » doses largement documentées, à la fois chez l'animal et chez l'Homme, et notamment par inhibition de l'activité de l'acétylcholinestérase pour les OP et les carbamates et par perturbation des canaux sodiques pour les OC et les pyréthrinoïdes (He 2000 ; Thany et al., 2013). Leurs effets sur les fonctions cognitives, après une exposition chronique, engendrent des troubles neurocomportementaux du type troubles de l'attention sélective, de la concentration, de la mémoire associative et de la parole, ainsi qu'une diminution du quotient intellectuel et des difficultés scolaires chez l'enfant (Kamel et Hoppin 2004 ; González-Alzaga et al., 2014 ; Quirós-Alcalá et al., 2014). Dans le cas des maladies neurodégénératives, les OC seraient impliqués dans l'induction de la maladie de Parkinson (Weisskopf et al., 2010 ; Moisan et al., 2015) et les OP semblent l'être dans l'induction de la maladie d'Alzheimer (Zaganas et al., 2013). Le développement des OP est en partie lié à l'interdiction des OC du fait leur bioaccumulation dans les graisses de l'organisme. Cependant, du fait de leur lente biodégradabilité, les OC sont encore retrouvés dans les environnements extérieurs et

[12] Rapport parlementaire sur Pesticides et Santé de l'Opecst, Claude Gatignol et Jean-Claude Étienne, 29 avril 2010

intérieurs. Il est à noter que les OP ne sont pas bioaccumulables, de même que les pyréthrinoïdes (insecticides de troisième génération) qui entrent notamment dans la composition des produits vétérinaires et domestiques (ATSDR 2003). De nombreux insecticides ont des effets de perturbation endocrinienne (McKinlay et al., 2008) entraînant des troubles de la reproduction et de la fertilité (Radwan et al., 2014 ; Chiu et al., 2015 ; Guo et al., 2017), mais aussi des troubles métaboliques favorisant la survenue de pathologies métaboliques, notamment l'obésité, le syndrome métabolique, voire le diabète (Montgomery et al., 2008 ; Inserm 2013).

De nombreuses pathologies cancéreuses sont également plus ou moins associées à l'exposition aux pesticides : des lymphomes non hodgkiniens, des myélomes multiples, les tumeurs cérébrales chez l'enfant, le cancer de la prostate, le cancer du testicule, les mélanomes malins, des leucémies et la maladie de Hodgkin (Inserm 2013). Le CIRC a notamment classé le lindane comme cancérogène avéré (groupe 1), le diazinon, le 4,4-DDT et la dieldrine comme cancérogènes probables (groupe 2a), le dichlorvos comme cancérogène possible (groupe 2b) et la perméthrine comme probablement non cancérogène (groupe 3).

La réglementation française concernant les produits phytosanitaires visait à diminuer de moitié leur utilisation à l'horizon 2018 via le plan « Ecophyto I » établit en 2008, suite au Grenelle de l'environnement de 2007. Le plan « Ecophyto II » remplace le précédent depuis octobre 2015. Il vise toujours une réduction de moitié de l'utilisation des produits phytosanitaires bien que cet objectif ait été reculé à l'horizon 2025 et soit dorénavant organisé en deux temps : 25 % d'ici à 2020 (par la généralisation et l'optimisation des techniques actuellement disponibles) et 25 % supplémentaire d'ici

à 2025 (par des mutations profondes des systèmes de production)[13]. Les objectifs de ce plan s'inscrivent dans le cadre Européen de 2009[14]. Concernant les usages non agricoles, la « loi Labbé » n° 2014-110 vise à mieux encadrer l'utilisation des produits phytosanitaires au niveau national. Elle est complétée par la loi n°2015-992 relative à la transition énergétique pour la croissance verte. Cette dernière interdit l'utilisation des pesticides de synthèse depuis le 1er janvier 2017 dans les espaces verts appartenant à l'État, aux collectivités locales et aux établissements publics. Elle prévoit leur interdiction de vente, d'usage et de détention par les particuliers au 1er janvier 2019.

Concernant les biocides, le règlement européen n°528-2012 est appliqué et vise à harmoniser la mise sur le marché et l'utilisation de ces produits en Europe. En France, depuis 2016, c'est l'Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (Anses) qui est chargée de coordonner l'évaluation des dangers, des risques et de l'efficacité des substances actives et des produits biocides en vue de délivrer ou non leurs autorisations de mise sur le marché (AMM).[15]

1.3.2.4. Les phtalates

Les phtalates sont majoritairement utilisés dans les plastiques afin de les rendre souples et flexibles, et dans les cosmétiques comme agents fixateurs (Tableau 1). Les effets sur la santé humaine varient d'un composé à l'autre et touchent pour certains la reproduction et le développement (Heudorf et al., 2007 ; Sharpe and

[13] « Plan Ecophyto II », *http://agriculture.gouv.fr/plan-ecophyto-2015*

[14] Directive 2009/128/CE

[15] Lignes directrices pour la délivrance des décisions relatives à la mise à disposition sur le marché des produits biocides, *https://www.anses.fr/fr/system/files/LIGNES-DIRECTRICES-Biocides.pdf*

Skakkebaek 2008 ; Dodson et al., 2012 ; Le Moal et al., 2015). Des effets immunotoxiques entraînant des allergies ou de l'asthme ont également été observés (Braun et al., 2013 ; Hoppin et al., 2013 ; Bamai et al., 2014), ainsi que des corrélations entre l'exposition aux phtalates et l'incidence du diabète et de l'obésité (Stahlhut et al., 2007 ; Buser et al., 2014).

Certains phtalates ont été classés reprotoxiques selon la classification CLP, pour leurs effets sur la fertilité et sur le développement. Cela a conduit à l'introduction progressive de mesures de prévention et de restriction. Ainsi pour les jouets ou les articles de puériculture destinés aux enfants de moins de 3 ans, la limite supérieure a été fixée à 0,1 % de la masse de matière plastifiée pour le DEHP, le BBP, le DBP, le DiNP, le DiBP ou le DnOP.[16] De même pour les matériaux et objet réutilisables en contact avec les aliments non gras pour le DEHP, le BBP et le DBP.[17] L'utilisation de certains phtalates est même interdite dans les matériaux et objet réutilisables en contact avec les aliments gras (DEHP et DBP)[3] et dans la composition des cosmétiques (DEHP, DBP et DMEP)[18].

1.3.2.5. Les retardateurs de flamme bromés

Les RFB sont utilisés pour ignifuger une grande variété de produits (Tableau 1). De par leurs propriétés physico-chimiques ils sont également lipophiles et bioaccumulables. D'un point de vue commercial les plus utilisés sont : le TBBPA, les

[16] Directive 2005/84/CE

[17] Directive 2007/19/CE

[18] Directive 2004/93/CE

PBDE, et l'HBCD.[19] Le TBBPA est produit par bromation du bisphénol-A, et est utilisé en tant que réactif ou additif dans les matériaux. La famille des PBDE regroupe 209 congénères que l'on peut classer selon le nombre d'atome de brome portés par la molécule (mono-, di-, tri-, tétra-, penta-, hexa-, hepta-, octa-, nona- et déca-BDE), mais aussi selon leur position sur les cycles benzéniques (BDE 1 à BDE 209). On les retrouve principalement sous la forme de 3 mélanges commerciaux : le penta-BDE (ou mélange DE-71), l'octa-BDE et le déca-BDE (BDE 209) (en fonction du type de congénère majoritaire). L'HBCD est utilisé sous forme d'un mélange de trois diastéréoisomères α, β et γ.

Si certains congénères des PBDE ont fait l'objet de plusieurs études chez l'animal et chez l'Homme (Martin et al., 2017), il est à noter un manque d'informations scientifiques concernant les potentiels toxiques du TBPPA et de l'HBCD. Des effets neurologiques (changement neurocomportementaux, hyperactivité, etc.) ont été observés chez l'animal adulte après des expositions pré- et post-natales aux PBDE (EFSA 2011 ; ATSDR 2017). Chez l'Homme, des études épidémiologiques ont démontré une diminution du quotient intellectuel et des troubles de l'apprentissage chez les enfants nés de mères ayant une charge plus élevée en PBDE pendant leur grossesse (Eskenazi et al., 2013). De nombreuses études ont démontré que les PBDE pouvaient interagir avec le système endocrinien, bien que les effets en résultant ne soient pas cohérents (ATSDR 2017). Les résultats de la plupart des études épidémiologiques sur l'homéostasie thyroïdienne suggèrent une association entre l'exposition aux PBDE et une modification de la régulation de la fonction thyroïdienne (Kim et al., 2014). Des effets indirects pourraient avoir un impact sur les

[19] Les retardateurs de flammes bromés, EFSA, *https://www.efsa.europa.eu/fr/topics/topic/brominated-flame-retardants*

fonctions de la reproduction (notamment la maturation sexuelle), les fonctions neurocomportementales, sur le développement embryonnaire et sur le développement cognitif des jeunes enfants (EFSA 2011). Le déca-BDE a été classé comme possiblement cancérigène pour l'Homme (classe C) par l'US EPA sur la base d'une augmentation significative du nombre de nodules, et des carcinomes ou adénomes hépatiques chez les rongeurs (US EPA 2006).

En raison de leurs effets sanitaires et de leurs propriétés de bioaccumulation et de persistance dans l'environnement, le penta-BDE et l'octa-BDE ont été interdits en Europe en 2003[20]. En 2005, un amendement de la directive « RoHS »[21], *restriction of hazardous substances*, sur la restriction des substances chimiques dangereuses dans les équipements électriques et électroniques limitait la concentration maximale des PBDE à 0,1 % en masse. Le déca-BDE, enregistré dans le cadre du règlement REACH en 2010, a été récemment ajouté à l'annexe XVII dudit règlement en 2017[22]. Cette nouvelle restriction entrainera à compter du 2 mars 2019 une interdiction de fabrication ou de mise sur le marché du déca-BDE en tant que tel et une interdiction d'utilisation pour la production ou la mise sur le marché comme constituant d'autres produits dans une concentration égale ou supérieure à 0,1 % en masse. Cependant des exceptions sont prévues pour certaines utilisations et notamment dans les équipements électriques et électroniques.

[20] Directive 2003/11/CE

[21] Directive 2005/747/CE

[22] Règlement (UE) 2017/227 de la Commission du 9 février 2017

L'HBCD a été enregistré comme substance persistante, bioaccumulable et toxique (PBT) extrêmement préoccupante dans le cadre de la règlementation REACH (ECHA 2008). Il a ensuite été inclus dans la liste des substances soumises à autorisation (Annexe XIV du règlement REACH) en 2011, entrainant son interdiction d'utilisation pour la production ou la mise sur le marché après août 2015 dans l'ensemble de l'Union européenne. Contrairement à l'HBCD, le TBBPA n'est pas produit en Europe, mais il est importé à hauteur de 1 000 à 10 000 tonnes par an et a été préenregistré en 2010 dans le cadre de la règlementation REACH.

Face à ces restrictions d'usage des nouveaux RFB (NRFB) ont été produits et une dizaine de substances ont été mises sur le marché (Covaci et al., 2011). D'autres substances chimiques sont également utilisées pour leur propriétés ignifuges, et notamment un composé organophosphoré : le tributylphosphate (TBP), classé comme CMR de catégorie 2 (règlement CLP), pour ses effets suspectés cancérigènes.

1.3.2.6. Les polychlorobiphényles

La famille des PCB regroupe 209 congénères dérivés du biphényle que l'on peut classer selon leur degré de chloration (allant du monochloro- au décachloro-biphényle), mais aussi selon leur position sur les cycles phényliques (PCB 1 à PCB 209). Leurs propriétés d'isolant électrique et d'ininflammabilité ont conduit à les utiliser en mélange dans de nombreux produits en tant que fluide caloporteur ou d'additifs (Tableau 1). De par leurs propriétés physico-chimiques, les PCB sont des composés peu biodégradables et très lipophiles. Ces propriétés les rendent bioaccumulables et persistants dans l'environnement, mais aussi dans les tissus gras humains, dont le lait maternel et les lipides sanguins. Les PCB ont été massivement

utilisés en France des années 1930 à 1980. Bien qu'ils aient été interdits et que leurs émissions dans l'environnement aient beaucoup diminué, les PCB sont encore présents dans les environnements extérieurs (notamment les sédiments marins ou de rivières) et intérieurs, même longtemps après que leurs sources d'origine aient été supprimées. On les retrouve encore également dans les tissus humains (Fréry et al., 2013) en raison de leur accumulation au fur et à mesure de la chaîne alimentaire et notamment dans les poissons gras (Anses 2016).

Les principaux effets des PCB sur la santé humaine sont neurotoxiques. De nombreuses études, chez le jeune enfant exposé durant la grossesse et l'allaitement, ont rapportés des effets neurocomportementaux (ATSDR 2000 ; Ribas-Fito et al., 2001 ; Gray et al., 2005). Les PCB sont également connus pour affecter le système endocrinien. Ces effets peuvent ensuite entraîner des altérations du développement neurologique, de la reproduction et induire des tumeurs hormono-dépendantes (ATSDR 2000). Les PCB sont classés comme cancérogène avéré (groupe 1) par le CIRC.

En France, leur fabrication et la mise sur le marché de produits ou d'appareils les contenant est totalement interdite depuis 1987. Depuis 2001, un inventaire national des appareils contenant des PCB a été constitué afin de les décontaminer et de les éliminer. Au niveau international, la convention de Stockholm de 2011 sur les polluants organiques persistants, vise à interdire la production et l'utilisation des PCB par tous les pays signataires d'ici 2025.

1.3.2.7. Les bisphénols

Les bisphénols regroupent plusieurs molécules ayant une structure chimique commune portant deux groupes phénol. Ils sont utilisés pour la fabrication de plastique et de résines mais aussi comme révélateurs dans l'impression thermique (Tableau 1). Le bisphénol-A est le plus étudié et règlementé d'entre eux. Le rapport d'expertise collective publié par l'Anses en 2011[23], relatif aux effets sanitaires du bisphénol-A, rapporte des effets confirmés chez l'animal sur le développement cérébral et sur la glande mammaire, ainsi que des effets suspectés sur la thyroïde. Chez l'Homme, des effets sont suspectés sur le système cardiovasculaire et sur le système métabolique (diabète) (Melzer et al., 2010).

Le bisphénol-A a été classé « présumé toxique pour la reproduction » (catégorie 1B) par l'Europe en juillet 2016, et a été identifié comme substance extrêmement préoccupante par l'Anses et par l'agence européenne des produits chimiques (ECHA) pour ses propriétés reprotoxiques en décembre 2016, et pour ses propriétés de perturbateur endocrinien en juin 2017. Ces effets concernent des perturbations du cycle menstruel, du développement pubertaire, de la croissance et du maintien ultérieur des caractères physiques féminins.

L'utilisation du bisphénol-A fait l'objet d'un encadrement juridique croissant en France. Il est interdit dans les biberons depuis juin 2010 et dans les conditionnements, contenants ou ustensiles destinés à entrer en contact avec les aliments depuis décembre 2012. Au niveau Européen, une limite de migration dans

[23] Connaissances relatives aux usages du bisphénol A (Anses, septembre 2011)

les jouets sera applicable à partir de 2018[24] et son utilisation sera limitée à 0,02 % en masse dans les papiers thermiques en 2020.[25]

L'Anses recommande également de porter une attention particulière lors de l'utilisation du bisphénol-M, du bisphénol-B et du diglycidyl ether de bisphénol-A (BADGE). Les travaux de l'agence, relatifs à l'utilisation des potentiels substituts du bisphénol-A (les bisphénols-S, -F, -AF et -AP), concluent sur le fait qu'une évaluation des risques sanitaires ne peut être conduite au vu de l'insuffisance des données toxicologiques disponibles et des données de contaminations environnementales potentielles.[26]

En conclusion de cette revue des principales familles chimiques de COSV, il est important de rappeler que l'exposition aux composés présents dans l'habitat est chronique et multiple, et que la population peut être considérée comme particulièrement vulnérable à certain moment de la vie, en particulier lors de la grossesse (femmes enceintes, fœtus) et lors de l'enfance. En effet, l'exposition de la femme enceinte même à des faibles doses de contaminants chimiques pourrait être responsable d'effets à long terme sur le développement du fœtus et de l'enfant (Grandjean et al., 2008). Le jeune enfant, de par son comportement (évolution au sol, contacts plus fréquents avec les poussières déposées, portage des mains et objets à la bouche) est plus exposé que le reste de la population aux COSV, mais également plus vulnérable en terme d'effet compte tenu du développement des

[24] Directive 2009/48/CE

[25] Modification par la Commission Européenne de l'Annexe XVII du Règlement REACH (12 décembre 2016)

[26] Substances reprotoxiques et perturbateurs endocriniens. Composés de la famille des bisphénols : bisphénols M, S, B, AP, AF, F et BADGE (Anses, mars 2013)

systèmes neurologique, reproducteur, pulmonaire et immunitaire qui se poursuit après la naissance.

1.4. Présentation du sujet de thèse

C'est dans ce contexte général de contamination de l'environnement intérieur par les COSV, associée à des effets sanitaires suspectés ou avérés pour certains, que le projet ECOS-Habitat a été initié en 2008. L'objectif du projet était d'apprécier l'importance du problème de santé publique posé par les diverses expositions aux COSV présents dans l'habitat français (Glorennec et al., 2011, 2014). Pour y répondre, de nombreux travaux ont été menés en amont de cette thèse afin d'améliorer la connaissance de la contamination de l'habitat français. Ces travaux, représentés dans la Figure 5, ont permis dans l'ordre de :

1) hiérarchiser les COSV sur la base de données toxicologiques et de données de contamination rapportées dans les environnements intérieurs (Bonvallot et al., 2010) ;

2) mettre au point des méthodes d'analyse multi résidus de certains de ces composés dans les environnements intérieurs (Mercier et al., 2012, 2014) ;

3) mesurer ces composés dans la phase particulaire de l'air et les poussières (Mandin et al., 2014, 2016) pour une estimation représentative de la contamination des logements en France ;

4) mesurer simultanément ces composés dans les phases gazeuse et particulaire de l'air, et les poussières, afin de modéliser la concentration en phase gazeuse à partir de données de contaminations de la phase particulaire ou des poussières (Blanchard et al., 2014 ; Wei et al., 2017) ;

et 5) construire des indicateurs de toxicité cumulée pour des groupes de COSV ayant des effets neuro- ou reprotoxiques communs (Fournier et al., 2014, 2016, 2017).

La dernière étape du projet, constituant ce travail de thèse, est l'évaluation des expositions et des risques sanitaires cumulés (ERSC) aux COSV présents dans l'habitat français.

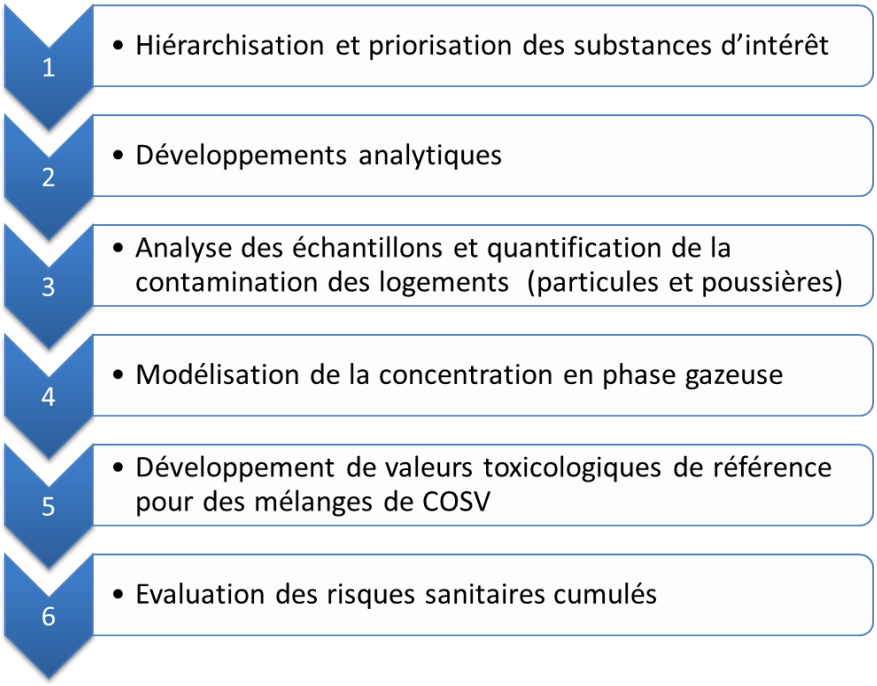

Figure 5 : Les principales étapes du projet ECOS-Habitat.

Ce travail de thèse clôture ainsi le projet ECOS-Habitat et a pour objectif de répondre à la question de recherche posée initialement : « **Les expositions cumulées aux multiples COSV présents dans les logements français posent-elles un problème de santé publique ?** ».

Dans une perspective d'aide à la décision, une démarche d'ERSC a été conduite en plus d'une ERS classique, afin de cerner l'importance du problème de santé publique que peuvent représenter ces expositions, et d'identifier les composés, médias et voies d'exposition les plus contributifs aux risques. L'hypothèse de recherche est que les expositions cumulées aux COSV présents dans l'environnement intérieur, même à faibles doses ou à des doses non toxiques individuellement, pourraient conduire à un impact sanitaire.

Une approche « bottom-up », ou indirecte, a été privilégiée pour identifier les voies et sources les plus contributives à l'exposition et au risque. La méthode a été établie sur la base des résultats obtenus par une analyse de l'état de l'art des méthodes d'agrégation des expositions et de cumul des risques pour les COSV, présentée sous forme d'article dans le chapitre 2 (Pelletier et al., 2017a).

La première étape (chapitre 3) a consisté à évaluer l'exposition agrégée de la population française aux COSV détectés dans les trois compartiments étudiés : les phases gazeuse et particulaire de l'air, et les poussières. Les doses d'exposition ont été estimées pour chaque voie d'absorption (inhalation, ingestion et voie cutanée) avant d'être agrégées par sommation. Une démarche probabiliste par simulations de Monte Carlo en deux dimensions a été conduite afin de tenir compte de l'incertitude et de la variabilité associées aux paramètres d'entrée et ainsi aboutir à une distribution des doses par composé. Ce travail a été conduit pour 11 tranches d'âge allant de la naissance à 30 ans et est présenté sous forme d'article (Pelletier et al., 2017b). Un travail préalable sur la modélisation de l'exposition par voie cutanée a été mené, notamment pour identifier les paramètres importants. Il est présenté sous forme d'article (Pelletier et al., 2017c).

La deuxième étape (chapitre 4) a consisté à évaluer quantitativement les risques sanitaires sur la base des expositions agrégées estimées préalablement. Les risques ont été évalués pour chaque composé de manière individuelle, puis pour des mélanges de COSV ayant des effets toxiques communs, à une échelle biologique plus ou moins fine (organes/systèmes cibles puis mécanismes d'action ou conséquences cellulaire). Le travail est présenté sous forme d'un dernier article (soumis à *Environmental Health Perspectives*).

La discussion générale des principales limites de ce travail et des perspectives qui s'en dégagent font l'objet des chapitres 5 et 6 respectivement.

Chapitre 2 : État de l’art des méthodes d’agrégation des expositions et de cumul des risques pour les COSV

Afin d'analyser les méthodes employées pour évaluer les risques liés aux expositions multiples aux COSV, une revue de la littérature a été conduite. Celle-ci a permis de recenser les méthodes et les paramètres employés i) pour étudier l'exposition agrégée via différentes voies par une approche « bottom-up » et ii) pour en évaluer les risques cumulés d'une exposition à plusieurs composés.

Vingt-deux études relatives à l'exposition à un ou plusieurs COSV et agrégeant au minimum deux voies d'expositions ont été recensées. L'agrégation des expositions est fondée sur l'addition de doses externes ou internes. L'estimation des doses externes est majoritairement conduite par l'emploi d'équations de doses journalières d'exposition (DJE). Dans certains cas, l'emploi de modèles pharmacocinétiques a permis d'estimer les doses internes des contaminants, voire de leurs métabolites, et de prendre en compte les phénomènes d'absorption, de métabolisme et de dégradation. Cependant ces modèles ne sont disponibles que pour certaines familles chimiques et ne sont donc pas systématiquement utilisés. Dans la plupart des cas, l'exposition est dominée par une seule voie ou une seule source. On retrouve fréquemment la voie orale comme majoritaire, que ce soit pour des expositions alimentaires et non alimentaires (ingestion de poussière). Cette prédominance n'est pas systématique et cela confirme donc l'intérêt d'une approche agrégée.

Concernant l'ERSC, 31 études se sont intéressées à évaluer les risques liés aux expositions à plus d'un COSV. L'estimation de « Hazard Indexes » (HI) et l'emploi de « Relative Potency Factors » (RPF) sont les méthodes les plus employées. L'estimation de HI apparaît comme l'approche la plus simple à conduire et permet de prendre en compte un plus grand nombre de composés. La construction et l'emploi de RPF nécessite de disposer d'un niveau d'informations toxicologiques plus précis

pour chaque composé, ce qui peut en limiter le nombre pouvant être étudiés simultanément.

En conclusion, les approches d'agrégation des expositions et d'ERSC reposent sur des hypothèses simples d'additivités, mais permettent néanmoins de réduire l'incertitude en comparaison des approches composé par composé ou encore source par source, qui *de facto* reposent sur des hypothèses de voies d'expositions négligeables et d'absence d'effets communs.

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

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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

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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

(continued on next page)

Table 1 *(continued)*

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	
			Indoor air Indoor dust Soil							
Von Goetz et al. (2010)	Phenols (1)	Dietary Residential	Food Breast milk Indoor air Indoor dust Dental sealings	Ingestion Inhalation	External dose equation	Absorption factors	Deterministic	Internal	Average individual	Yes
Linares et al. (2010)	PAHs (16) PCBs (7) PCNs (5)	Dietary Occupational (petrochemistry)	Food Drinking water Air Soil	Dermal Ingestion Inhalation	External dose equation	Dermal absorption factor	Probabilistic	External (ingestion, inhalation) Internal (dermal)	Average individual	No
Lu et al. (2010)	OPs (1)	Dietary Residential	Food Drinking water Indoor air Indoor dust Toy surfaces Soil	Ingestion Inhalation	PBPK model		Deterministic	Internal	Individual	Yes
Lorber (2007)	PBDEs (9)	Dietary Residential	Food Indoor air Indoor dust Soil	Dermal Ingestion Inhalation	Simple one-compartment PK model		Deterministic	Internal	Average individual	Yes
Wormuth et al. (2006)	Phthalates (8)	Dietary Residential Personal care products	Food Indoor air Outdoor air Indoor dust Clothing Personal care products	Dermal Ingestion Inhalation	External dose equation	Absorption factors	Deterministic	Internal	Average individual	Yes
Duggan et al. (2003)	OPs (31)	Dietary Residential	Food Drinking water Non-dietary	Dermal Ingestion Inhalation	External dose equation	Dermal absorption factor	Deterministic	External (ingestion, inhalation) Internal (dermal)	Average individual	Yes
Wilson et al. (2003)	OCs (9) OPs (2) PAHs (20) PCBs (18) Phenols (3) Phthalates (2)	Dietary Residential	Food Indoor air Outdoor air Indoor dust Soil	Ingestion Inhalation	External dose equation	No	Deterministic	External	Individual	Yes
Shurdut et al. (1998)	OPs (1)	Dietary Residential	Food Indoor air Indoor surfaces	Dermal Ingestion Inhalation	External dose equation	Dermal absorption factor	Probabilistic	External (ingestion, inhalation) Internal (dermal)	Average individual	Yes

OCs = Organochlorines; OPs = Organophosphorus; PACEM = Probabilistic aggregate consumer exposure model; PAHs = Polycyclic aromatic hydrocarbons; PBDEs = Polybrominated diphenyl ethers; PCBs = Polychlorinated biphenyls; PCNs = Polychlorinated naphthalenes; PFAAs = Perfluoroalkyl acids; RFRs = Replacement flame retardants; SHEDS-multimedia = Stochastic human exposure and dose simulation model for multimedia.

relationship in laboratory mammals to which uncertainty factors are applied to take into account inter/intra-species differences (Dybing et al., 2002). For some chemicals, internal reference dose are proposed such as biomonitoring equivalent which are estimates of the concentration of the substance (or a metabolite) in blood or urine that is consistent with the reference dose (Hays and Aylward, 2009).

In the case of indoor SVOCs, exposure occurs via different sources and media and concerns many compounds simultaneously. Multiple exposure to mixtures is now widely recognized and addressed, notably by international and national institutions in charge of risk assessment. In the WHO/IPCS Framework for Risk Assessment of Combined Exposures to Multiple Chemicals, aggregate exposure is defined as exposure to the same substance from multiple sources, via multiple pathways, and routes (Meek et al., 2011). Cumulative risk assessment linked to co-exposure to different substances is also recommended when feasible (Meek et al., 2011).

The objective of this study is to review the methods employed in the literature regarding (1) exposure aggregation to an SVOC excluding biomonitoring and (2) cumulative risk assessment for a mixture of SVOCs.

2. Methods

The search covered the period from 1985 until 2016. Publications were selected in line with the following criteria: addressing SVOC human exposure, aggregating at least two routes of exposure for one SVOC or assessing cumulative risk to at least two SVOCs. Because they do not provide methods for the aggregation of several routes of exposure; publications that considered exposures to an SVOC from different sources (e.g. foodstuff) but via a single exposure route (e.g. ingestion) were discarded, even though aggregation was the mentioned terminology. Using the Web Of Knowledge™ website (Thomson Reuters, www.webofknowledge.com), publications were selected primarily by searching in the field "topic" (title, abstract and key words): ((exposure AND (assessment OR evaluation) AND (cumulat* OR aggregat*) AND (chemicals OR products OR substances OR compounds OR pollutants) AND health) OR (PBPK AND (SVOC OR pesticide OR phthalate OR flame retardant OR plasticizer OR PCB OR musk OR PAH OR organochlor* OR organophosph* OR pyrethroid) NOT (rat* OR mice OR mouse OR bear). Secondly, selected publications were screened on the basis of the subject-title match. Thirdly, those publications remaining were subjected to an exhaustive abstract reading in order to remove those which did not address the research subject and to separate publications performing exposure aggregation from those dealing with cumulative risk assessment (CRA). Publications identified in the reference list of others were added. Since the objective was to review methods, publications' results are presented only where they allow the comparison of different methods.

Regarding publications that aggregated exposure, the following items were retrieved: references, chemical class, exposure characteristics (source, media, and route of exposure), exposure modeling (type of approach: deterministic or probabilistic, type of aggregated dose, and the doses aggregation level: external or internal), and whether comparison with biomonitoring data was made. Regarding publications that cumulated risks, the following items were retrieved: references, number of chemical cumulated, SVOC selection criteria (related to occurrence and toxicity), CRA characteristics (grouping by chemical class or not, the dose calculation basis, and the method employed), and toxicity indicators characteristics (type, source, point of departure, and type of toxicological endpoint).

3. Results and discussion

This search identified 22 publications that carried out an exposure aggregation from at least two routes of exposure to an SVOC and 31 publications that carried out a CRA to at least two SVOCs.

3.1. Aggregate exposure assessment

Twenty-two publications carrying out SVOC exposure aggregation were identified, and these are presented in Table 1. This may seem few, given the high number of compounds concerned, yet assessments are often focused on exposure to a compound from various sources but via a single exposure route. The oldest dates back to 1998 and from 2010 to 2016, one to five publications per year were retrieved from the literature.

Seven publications aggregated exposure to OPs, six to phthalates, four to pyrethroids, three to PAHs, three to PBDEs, three to phenols, two to PCBs, two to parabens, one to musks, one to OCs, one to polychlorinated naphthalenes (PCNs), one to perfluoroalkyl acids (PFAAs) and one to replacement flame retardants (RFRs). Residential exposure was studied most (18 publications), addressing exposure to air (n = 16), dust (n = 13), surfaces (n = 7), soil (n = 6) and dental sealing (n = 1). Fourteen of the publications addressed dietary exposure: all were interested in solid food exposure, four took drinking water into account and three were also interested in breast milk exposure. Three publications addressed occupational source with exposures to air (n = 2) or to air and soil (n = 1). Two publications addressed exposure to C & PCPs.

Human exposure to these various sources and media could occur via three pathways: inhalation, ingestion or dermal contact. Of the 22 publications selected, a majority (n = 14) aggregated exposure by three pathways, whereas the rest did so by two pathways. As an example, Gosens et al. (2014) aggregated exposure to four parabens contained in C & PCPs by dermal and ingestion pathways. The reason put forward for not studying exposure by inhalation was that none of the investigated C & PCPs applied by spray contained parabens. Another reason for not studying a route of exposure is negligible absorption, in comparison with the other pathway. For instance, Wilson et al. (2003) assessed the aggregated exposure by ingestion and inhalation of 37 SVOCs present in several media (indoor and outdoor air, indoor dust, soil and food) rather than by dermal absorption because this was considered negligible in comparison. Because of recent advances in dermal exposure importance (Weschler and Nazaroff, 2012) and modeling (Gong et al., 2014; Shi and Zhao, 2014; Morrison et al., 2016), this pathway is expected to be more systematically considered in the future. Indeed human experiments with exposure to phthalates have proven this pathway to be significant for some SVOCs (Weschler et al., 2015).

Aggregation of exposure was always conducted by estimating exposure for each route individually, then summing them. These exposures were often assessed by employing classic external dose equations (e.g. U.S. EPA, 1992) combining human parameters (such as weight, body surface area, inhalation rate, amount of ingested dust and frequency of use) with media or product contamination (e.g. SVOC concentration in the media or product). Thirteen publications have used this method. An alternative could be the employment of pharmacokinetic (PK) and/or pharmacodynamics (PD) models to aggregate exposure to individual SVOCs by several routes, and provide an absorbed dose. The physiologically-based pharmacokinetic model (PBPK), describes the physiological, biochemical, and physical-chemical processes governing the absorption, distribution, metabolism, and excretion of a xenobiotic in the body. It consists of a series of compartments receiving the xenobiotic via systemic circulation. These models could also incorporate a pharmacodynamic dimension (PBPK/PD) relating to processes leading to a critical health outcome (e.g. acetylcholinesterase inhibition). PK and PD models require the same parameters as for external dose equations, with the addition of physiological, physiochemical (e.g. partition coefficient) and biochemical (e.g. metabolic rate constant) parameters. Eight publications have used PK models: four used a PBPK model, two a one-compartment PK model and one a PBPK/PD model. The four PBPK models were developed for three different chemical families (PAHs, pyrethroids and OPs), the two one-compartment PK models for PBDE compounds and for PAH compounds, whereas the PBPK/PD model was only developed for OP compounds –

chlorpyrifos, to be precise. When PK and/or PD models were available these appeared to be the preferred method for assessment of overall exposure to an SVOC. However, because these are available only for certain specific SVOCs, and because their construction entails high consumption of both data and resources, they are not systematically used. In order to estimate and aggregate exposures to an SVOC, some publications have also used specific exposure models, which include PK modeling components, such as the Stochastic Human Exposure and Dose Simulation model for multimedia (SHEDS-Multimedia) which was developed by the U.S. EPA's Office of Research and Development to simulate aggregate exposure via dietary and residential routes (inhalation and dermal contact) to a variety of environmental chemicals such as pesticides, metals and persistent organic pollutants 〈https://www.epa.gov/chemical-research/stochastic-human-exposure-and-dose-simulation-sheds-estimate-human-exposure〉. Three publications used SHEDS-Multimedia to assess exposure to pyrethroid and OP compounds. Another specific model is the Probabilistic Aggregate Consumer Exposure Model (PACEM), first used by Gosens et al. (2014) to facilitate aggregate exposure assessment of parabens compounds present in C & PCPs. However, though these are more adaptable to various SVOCs than are PK and/or PD models, they could be limited by the use of predefined scenarios (e.g. residential pesticide use scenarios using SHEDS-Multimedia, such as indoor flying insect killer, pet treatment, vegetable patch, etc.) or data (e.g. Dutch C & PCPs use data for PACEM). Compared to classical external dose modeling, most of the time achieved with a deterministic approach, these models use distributions for the human parameters inputs and contamination data in order to allow a probabilistic approach.

Exposure assessment to a contaminant could be expressed as an external or internal dose, the latter reflecting contaminant uptake after crossing absorption barriers. Only Wilson et al. (2003) and Roosens et al. (2010) expressed results as external doses for each route of exposure. Fifteen other publications estimated internal doses for each route of exposure, and five estimated internal dose only for the dermal pathway. Of these, nine publications used a PK approach to convert external exposure into organ, tissue or fluid concentrations. Eleven other publications converted external exposure into internal exposure by applying absorption factors retrieved from the literature or considered a default value of 100%. For the dermal pathway the authors used dermal absorption fraction (Shurdut et al., 1998; Duggan et al., 2003; Linares et al., 2010; Gosens et al., 2014) or a transdermal permeability coefficient (Beko et al., 2013). Transdermal permeability coefficients are more precise, because they take into account partition through the different layers of the skin to the dermal capillaries, and these were recently available in the literature for several SVOCs (Weschler and Nazaroff, 2012). This explains why their use has increased since 2013 (in comparison with 1998) for dermal absorption factors. Internal dose appears as the logical metric when considering aggregation of exposure. The most sophisticated approach is PBPK modeling, followed by PK modeling, use of absorption factor, or default 100% absorption. Using external doses (most often observed for inhalation and ingestion) actually consists in considering that there is no differential absorption between exposure routes. This should at least deserve an uncertainty analysis with reported values for bioavailability.

Both external and internal exposure assessments require input parameters (such as human parameters, media or product contamination data and specific parameters of SVOCs). With regard to these parameters, single values could be used to conduct a deterministic approach. A conservative choice of parameters is considered as a lower tier approach by several authors (Delmaar and van Engelen, 2006; Sarigiannis et al., 2013), and was indeed employed in ten publications. A higher tier approach could be conducted by probabilistic analyses with Monte Carlo simulation by introducing distributions rather than single values, and this was employed by twelve authors. Both approaches were used and compared by Gosens et al. (2014) to estimate aggregate exposure, by ingestion and dermal contact, to four parabens. Although exposure assessment results were comparable in both approaches, internal exposures estimated by the higher tier approach were always below those estimated by the lower tier approach for each paraben. This result confirmed that a deterministic approach gave a good conservative starting point for exposure assessment but that a probabilistic approach gave a more realistic and more informative exposure assessment where enough data were available (by, for example, allowing estimation of the proportion of population above the reference dose, and enabling sensitivity analysis).

Most of the studies (n = 16) aggregated exposures for an average individual using representative data from a population, e.g. a specific age group. Six studies aggregated exposures for specific individuals with their own data.

Most studies (n = 16) compared their estimations of aggregate exposure to human biomonitoring data (e.g. NHANES), and eleven of these found consistent results. A reason for the discrepancies could be for instance the non-inclusion of a major pathway, such as diet for phthalates (Beko et al., 2013).

It is noteworthy that the authors discussed the contribution made to exposure by each pathway, source or media. The major route of exposure depends on: the studied compounds; the conditions of exposure to these compounds (e.g. residential or occupational), the routes of exposure assessed, and whether the population of interest included children more susceptible to dust ingestion (Beamer et al., 2012; Wason et al., 2012; Gaspar et al., 2014; Mitro et al., 2016). Some authors investigated influent parameters such as SVOC physical-chemical parameters with molecular weight (Beko et al., 2013), and vapor pressure (Wilson et al., 2003), which are related to their partitioning among various media (e.g. indoor air, dust), leading to a preferential route of exposure. As an example, Beko et al. (2013) found the dermal pathway to be the major route of exposure for two phthalates (DnBP and DiBP). Xue et al. (2014) studied exposure to seven pyrethroids when using, or not using, pesticide at home. These authors found ingestion to be the major route of exposure in both cases, with dietary exposure being the most contributive for the population not using pesticides, and non-dietary exposure for the population that does use them. Zartarian et al. (2012) found the same results regarding children's aggregate (dietary and non-dietary) residential exposure to permethrin. The circumstance of exposure also has an influence. For example Wei et al. (2013) studied global exposure to a pyrethroid during and after aircraft disinfection treatments, finding inhalation to be the major route of exposure during the pre-flight spray, and dermal pathway to be the major route of exposure for the residual treatment scenario. The dominant pathway may change depending on exposure level. For example Trudel et al. (2011) found ingestion of food to be the dominant pathway for several PBDEs up to about the 60th quantile of the total dose, while oral and dermal uptake of dust dominated above the 60th quantile, because of a larger variability of concentration and dust ingestion rate. Because few studies (n = 6) addressed global exposure to SVOCs via ingestion, inhalation and dermal contact to at least food, air, dust or soil and objects (such as toys, clothing or indoor surfaces), it is difficult to determine a general dominant pathway trend in global exposure assessment to SVOC. However, as observed by Wilson et al. (2003), on the basis of 54 SVOCs, ingestion was found to be the main route of exposure for the less volatile compounds, whereas inhalation was the most significant for the more volatile compounds.

To summarize, choice of method depends strongly on research objectives. A PK and/or PD model seemed preferential when assessing total exposure to an SVOC. However, because they are available only for certain SVOCs, and because their construction involves high data and resource consumption, a lower tier approach - such as employing external dose equation - appeared to be more adequate (at least as a first step) and provided consistent estimations. Inclusion of an uncertainty analysis in exposure assessment appears essential in this situation.

Lastly, even where exposure to an SVOC is governed by a major

Table 2
Publications performing cumulative risk assessment (CRA) on semivolatile organic compounds.

References (year of publication)	Number of chemicals cumulated	SVOCs selection criteria		CRA			Toxicity indicators			
		Occurrence	Toxicity	Grouping by chemical class	Dose calculation basis	Method	Type	Source	Type of toxicological endpoint	POD
Li et al. (2016)	Pyrethroids (7)	Dietary contamination	AChE inhibitors	Yes	Contamination data	HI	ADI RfD	na	na	na
Lozowicka et al. (2016)	CBs (1) OPs (3) Pyrethroids (3)	Dietary contamination	AChE inhibitors Sodium channel modulators	Yes	Contamination data	HI	ADI	EFSA	na	na
Quijano et al. (2016)	CBs (7) OPs (12) Pyrethroids (7)	Dietary contamination	AChE inhibitors	Yes	Contamination data	RPF ADI	RPF	U.S. EPA	AChE activity	NOAEL BMD
Zentai et al. (2016)	OPs (24)	Dietary contamination	AChE inhibitors	Yes	Contamination data	RPF	RPF RfD	Boon et al. (2008) Caldas et al. (2006) JMPR	AChE activity	NOAEL BMD_{10}
Gao et al. (2016)	Phthalates (3)	Urinary measurement	Multiple Anti-androgenic	Yes	Biomonitoring data	HI	TDI RfD	EFSA Kortenkamp and Faust (2010)	Effects on reproduction and development Anti-Androgenic	NOAEL LOAEL BMD
Ogbeide et al. (2016)	OCs (13)	Water, sediment and biota contamination	-	Yes	Contamination data	HI	RfD	U.S. EPA	na	na
Jensen et al. (2015)	Different classes of pesticides (20)	Dietary contamination	Multiple	No	Contamination data	HI	ADI	EC EFSA JMPR	na	na
Blaznik et al. (2015)	CBs (4) OPs (10)	Dietary contamination	AChE inhibitors	No	Contamination data	RPF	RPF RfD	Boon et al. (2008) European commission	AChE activity	NOAEL LOAEL BMD_{10}
Kranich et al. (2014)	Phthalates (5)	-	Anti-androgenic	Yes	Biomonitoring data	HI	TDI RfD	EFSA Kortenkamp and Faust (2010)	Effects on reproduction and development Anti-Androgenic	NOAEL LOAEL BMD
Peluso et al. (2014)	OCs (9)	Water contamination	Multiple	Yes	Contamination data	HI	RfD	U.S. EPA IRIS	na	na
Xue et al. (2014)	Pyrethroids (7)	Residential (consumer use) Urinary measurement	-	Yes	Contamination data	RPF	RPF RfD	U.S. EPA	na	na
Chang et al. (2014)	Phthalates (7)	-	Anti-androgenic	Yes	Contamination data	HI	TDI RfD	EFSA WHO U.S. EPA	Hepatotoxicity Anti-Androgenic	na
Dewalque et al. (2014)	Phthalates (4)	Urinary measurement	Anti-androgenic	Yes	Biomonitoring data	HI	TDI RfD	EFSA Kortenkamp and Faust (2010)	Effects on reproduction and development Anti-Androgenic	NOAEL LOAEL BMD
Christensen et al. (2014)	Phthalates (5)	Dietary contamination Urinary measurement	Anti-androgenic	Yes	Biomonitoring data	HI	TDI RfD	EFSA Denmark EPA	Effects on reproduction and development Anti-Androgenic	NOAEL LOAEL
Jardim et al. (2014)	OPs (7) Pyrethroids (4)	Dietary contamination	Multiple	Yes	Contamination data	RPF	RPF RfD	Caldas et al. (2006) U.S. EPA JMPR U.S. EPA	AChE activity	NOAEL BMD
Leeman et al. (2013)	CBs (7) OPs (26) Phthalates (6)	Dietary contamination	AChE inhibitors AChE inhibitors Anti-androgenic	Yes	Contamination data	RPF	RPF ADIRfD	Calculated EU Pesticide Database	na	na
Borg et al. (2013)	PFASs (17)	Dietary contamination Urinary measurement	Multiple	Yes	Biomonitoring data	HI	RfD	Calculated	Hepatotoxicity Reproductive toxicity	NOAEL LOAEL

(continued on next page)

Table 2 *(continued)*

References (year of publication)	Number of chemicals cumulated	SVOCs selection criteria		CRA			Toxicity indicators			
		Occurrence	Toxicity	Grouping by chemical class	Dose calculation basis	Method	Type	Source	Type of toxicological endpoint	POD
Beko et al. (2013)	Phthalates (3)	Residential (dust contamination) Urinary measurement	Anti-androgenic	Yes	Biomonitoring data Contamination data	HI	TDI	EFSA	Effects on reproduction and development	BMD NOAEL LOAEL
Kalantari et al. (2013)	PCBs (5)	Dietary contamination	Reduction of hepatic retinoid	Yes	Contamination data	RPF CombinedMOE	RPF RfD	Kalantari et al. (2012) Calculated	Hepatic retinoids Body/liver weights	na BMD_{05}
Beamer et al. (2012)	OPs (2)	Dietary contamination Residential (media contamination)	AChE inhibitors	Yes	Contamination data	RPF HI	RPF RfD	U.S. EPA	ChE inhibition (plasma, RBC) ChE inhibition (brain)	BMD_{10} NOAEL
Søeborg et al. (2012)	Phthalates (4)	Urinary measurement	Anti-androgenic	Yes	Biomonitoring data	HI	TDI RfD	EFSA Kortenkamp and Faust (2010)	Effects on reproduction and development Anti-Androgenic	NOAEL LOAEL
Ragas et al. (2011)	CBs (1) Neonicotinoids (1) OCs (1) OPs (2) Pyrethroids (1)	Dietary contamination	Nervous system Liver	Yes	Contamination data	HI	ADI	EC WHO	na	na
Koch et al. (2011)	Phthalates (3)	Urinary measurement	Anti-androgenic	Yes	Biomonitoring data	HI	TDI	EFSA	Effects on reproduction and development	NOAEL LOAEL
Kortenkamp and Faust (2010)	OCs (1) OPs (1) Parabens (2) Phenols (1) Phthalates (5) PBDEs (1) Other classes of pesticides (4)	-	Anti-androgenic	No	Contamination data	HI	RfD ADI	Calculated EFSA	Anti-androgenic	NOAEL LOAEL BMDL
Linares et al. (2010)	PAHs (3)	Chemical and petrochemical industries emissions	-	Yes	Contamination data	HI	RfD	U.S. EPA	na	na
Bosgra et al. (2009)	OPs (31)	Dietary contamination	AChE inhibitors	Yes	Contamination data	RPF Combine d MOE	RPF	Calculated	AChE activity	BMD_{20}
Benson (2009)	Phthalates (5)	-	Anti-androgenic	Yes	Biomonitoring data	RPF HI	RfD	Calculated	Anti-Androgenic	NOAEL LOAEL BMDL
Boon et al. (2008)	OPs (26) CBs (8)	Dietary contamination	AChE inhibitors	Yes	Contamination data	RPF	RPF RfD	Calculated JMPR	AChE activity	NOAEL BMD_{10}
Durmusoglu et al. (2007)	Phenols (1) PAHs (4)	Tire industries emissions	Respiratory irritation	No	Contamination data	HI	RfD	U.S. EPA	Not specific	na
Caldas et al. (2006)	OPs (22) CBs (3)	Dietary contamination	AChE inhibitors	No	Contamination data	RPF	RPF RfD	Calculated JMPR	AChE activity	NOAEL BMD_{10}
Castorina et al. (2003)	OPs (11)	OPs commonly applied that metabolize dialkyl compounds	AChE inhibitors	Yes	Biomonitoring data	RPF Combined MOE	RPF	Calculated	AChE activity	BMD_{10}

AChE = acetylcholinesterase; ADI = Acceptable daily intake; CBs = Carbamates; DNEL = Derived no effect level; EC = European Commission; HI = Hazard index; HQ = Hazard quotient; JMPR = Joint FAO/WHO Meeting on Pesticide Residues; MOE = margin of exposure; na = not available; OCs = Organochlorines; OPs = Organophosphorus; PAHs = Polycyclic aromatic hydrocarbons; PCBs = Polychlorinated biphenyls; PFAs = Perfluoroalkoxy alkanes; POD = Point of departure; POPs = Persistent organic pollutants; RBC = Red blood cell; RfD = Reference dose.

route, aggregating exposure provides useful information regarding exposure characteristics such as influent media, or variation between compounds of the same chemical family. Aggregation of all routes of exposure to an SVOC appears essential, especially when performing a risk assessment in a second step.

3.2. Cumulative risk assessment

Thirty-one publications conducting SVOC CRA were identified for inclusion in this review, and these are presented in Table 2. The oldest dates back to 2003, and since 2009, from one to seven publications per year were retrieved from the literature.

For each study, SVOCs were included in a CRA on the basis of their occurrence and/or a similar pattern of toxicity. Firstly, regarding occurrence, dietary contamination was the most used criterion (n = 16), followed by the occurrence of SVOC metabolites in humans (n = 8). In addition, two studies chose on the basis of their presence in industrial emissions, three on their presence in the residential environment, one on their presence in drinking water, one on their presence in the water, sediment and biota of a specific river and lastly, four studies provided no explanation regarding occurrence for the selection of compounds. Secondly, regarding toxicity patterns for compound selection, having an anti-androgenic mechanism of action (n = 11), or inhibiting the acetylcholinesterase (AChE) mechanism (n = 11) were the most studied effects. In addition, sodium channel modulators, toxic effects on the nervous system, toxic effects on the liver, the reduction of hepatic retinoid, and respiratory irritation were also studied. Finally, five publications based their compound selection on multiple toxic effects. Chemical classes investigated were: carbamates (CBs), OPs, OCs, PAHs, parabens, PBDEs, PCBs, phenols, phthalates, polyfluoroalkylated substances (PFASs) and pyrethroids. In fact, 12 publications studied OP compounds, 11 phthalate compounds, 7 carbamate compounds and 6 pyrethroid compounds. The scientific community's growing interest in OPs and phthalates is driven by suspicion of toxic health effects, such as the anti-androgenic effects of some phthalates on the male reproductive system (Joensen et al., 2012), or the neurotoxic effects of some OPs (Mileson et al., 1998), their ubiquitous occurrence in various media (Rudel et al., 2003; Blanchard et al., 2014), and the acknowledged presence of these compounds and their metabolites in human biological fluids (NHANES, 2015), as well as - specifically for OPs - the availability of relative potency factors (RPF) published by governmental agencies (U.S. EPA 2006). Finally the review reveals that a majority of the publications (n = 26) performed CRA for SVOCs coming from the same chemical class and only five encompassed compounds from different families.

A CRA can be performed using several methods that have been developed and used for decades now, notably for regulatory purposes on polluted sites (U.S. EPA, 1989). Most of these are based on the following additivity assumptions, notably with the “Incremental Lifetime Cancer Risk”, a sum of cancer risks commonly used in regulatory risk assessment. “Dose additivity” assumes that each compound of a mixture is supposed to contribute to the overall observed effect in proportion to its concentration (dose), with the assumption that “toxicants in a mixture act upon similar biological systems and contribute to a common response in proportion to their respective potencies” (Calabrese, 1990). On the other hand, “response additivity” assumes that each compound of a mixture is supposed to contribute to the overall observed effect in proportion to its effect (response), with the assumption that “toxicants in a mixture act upon dissimilar biological systems and act independently” (Calabrese, 1990). This notion does not take into account the possibility of such toxicological interaction as antagonism or potentiation and could lead to biased estimation of the risk. For example, Boon et al. (2008) have highlighted an overestimation when conducting a CRA to OPs and carbamates exposures. Even though these are known for their common AChE inhibiting activity, their specific mechanisms of action are different - indeed AChE receptor binding is mostly irreversible regarding OPs whereas it is reversible regarding carbamates. However, toxicological interaction (i.e. antagonism or potentiation) is mostly based on the saturation phenomena of metabolic systems, which can be considered as never being achieved regarding low, even sometimes very low (e.g. up to ng/m3 in indoor air regarding several SVOCs) (Blanchard et al., 2014) compound concentrations in the exposure media (ATSDR 2004). Nevertheless, an empirical analysis of low-dose synergy, by Boobis et al. (2011) revealed results of low magnitude 1.5–3.5). Furthermore, the principal purpose of risk assessments is to help regulatory or policy-making organizations make decisions and to develop operative strategies regarding the control of human exposure to environmental, residential and occupational pollutants, leading to consideration of the additivity assumptions as operational.

Several CRA methods exist and the most commonly used in the literature are, from the lowest to the highest tier, the Hazard Index (HI) method, the Point of Departure Index (PODI) and the RPF approaches, described extensively elsewhere (U.S. EPA, 2000; Sarigiannis and Hansen, 2012; Fournier et al., 2014a). Briefly, the HI method is based on the sum of hazard quotients (HQ) for substances affecting the same target organ or system. For each substance involved, the HQ is calculated by dividing exposure by reference dose (i.e. the level at which no adverse effects are expected in humans) (U.S. EPA, 2000). This method was used in 20 publications. Although it provides a transparent and comprehensive result (HI < 1 indicates that there is little likelihood that an adverse effect might be observed from chronic exposure) this method is also a lower tier approach, because the reference doses are not necessarily constructed with regard to the same target organ, and can sometimes be imprecise with regard to the compounds' mechanism of action. However, it does allow the study of compounds from different chemical classes, but affecting the same target organ or system. Four publications are concerned in this review; all the others studied compounds from a single class (n = 16). In order to quantify interaction effects in a mixture, Ragas et al. (2011) followed the interaction-based HI approach developed by the U.S. EPA (2000). This method assumes that interactions among compounds in a complex mixture are dependent on those of all possible binary combinations of the individual mixture components. The HI is multiplied by a weight factor reflecting the significance of these interactions. The authors observed interaction effects in two groups (with, for instance, four and two pesticides respectively) and found that the interaction-based HI was always higher than the conventional one. However, because of weak scientific evidence regarding the calculation procedure, and a weak empirical basis regarding parameter values, the authors have warned that these interaction-based HIs should be used with caution (Ragas et al., 2011).

The PODI approach differs from the HI in that the sum of exposures to each compound is expressed as a fraction of its respective and comparable point of departure (POD) for effects of toxicological relevance (for example, a benchmark dose) rather than a fraction of the reference dose – inducing less uncertainty. The reciprocal of the PODI is the combined margin of exposure (MOE) based on the sum of individual MOEs. For each compound involved, the MOE is calculated by dividing its POD to human exposure (EFSA, 2008). Three of the publications used a combined MOE approach.

The RPF approach assumes similarity of mechanisms of action between individual compounds and uses toxicity data for an index compound to normalize the potencies of each other compound in a mixture. Usually the potencies are POD derived from dose-response curves. The combined toxicity of the mixture corresponds to the sum of the potency normalized doses to yield total equivalent exposure, expressed as index compound equivalents, which is then compared to the reference dose of the index compound (EFSA, 2008). This method was used in 13 publications. Seven publications studied compounds from the same chemical class - mostly OPs (n = 4) - whereas the others studied compounds from different classes (n = 6). Four of them applied a RPF approach class by class, whereas Caldas et al. (2006) and Blaznik et al.

(2015) performed a RPF approach to OP and CB compounds having the same mechanism of action.

Several publications compared CRA methods. Three publications used both a RPF and a combined MOE approach. One of these is interested in cumulating risks linked to exposure to five PCBs, and although the authors found similar results with respect to estimates of median MOE values, they pointed out that the advantage of the RPF approach is that it is more easily implemented in practice, and accounts quantitatively for both variability and the various uncertainties involved (Kalantari et al., 2013). Furthermore, RPF data published by the U.S. EPA are available for the OPs (U.S. EPA 2006), CBs (U.S. EPA 2007), and pyrethroids (U.S. EPA 2011). Benson (2009) and Beamer et al. (2012) found similar results when using both a RPF and an HI approach. Beamer et al. (2012) did not assess the potential added value of a RPF approach to an HI approach, yet Benson (2009) suggested using the less complex HI approach for future CRA to simultaneous phthalates.

The reference doses employed by the authors could differ for a single SVOC according to: the toxicological endpoint studied and the type of POD chosen (no observed adverse effect level (NOAEL), lowest observed adverse effect level (LOAEL) or Benchmark Dose (BMD)); the value of the uncertainty factor applied, and the date of construction, depending on the organization producing these values (e.g. acceptable/tolerable daily intakes (A/TDI) from EFSA or WHO, and reference doses (RfD) from U.S. EPA). Dewalque et al. (2014) and Gao et al. (2016) both calculated HI to several phthalates using two different reference values, (1) TDI from EFSA based on effects on reproduction and development and (2) reference dose from Kortenkamp and Faust (2010) based on anti-androgenic effects. Each author found different results, attesting to the fact that cumulative assessment is dependent on the reference value taken into account.

Dose calculation for exposure estimation was based on contamination data alone in 21 publications and on both contamination and biomonitoring data in 9. Only Beko et al. (2013) estimated daily intakes from both media phthalates compound contaminations (with the exception of foodstuffs) and urinary concentrations of their metabolites before conducting a CRA using an HI approach. The authors found an HI from urinary concentrations to be twice as high as from media contaminations.

Following a tiered approach when conducting a CRA is now recognized by institutions such as the EFSA's Scientific Panel on Plant Protection products and their Residues (PPR) which recommends the use of tiered approaches when assessing risks of chronic exposure to pesticide residues (EFSA, 2008). Several authors of this review have confirmed the pertinence of this recommendation for conducting a CRA on SVOC exposure. A lower tier method (such as the HI approach) could be used as a first step, with recourse to a higher tier method (such as the RPF approach) being justified where the outcome suggests further refinement is called for.

4. Conclusions and perspectives

Aggregate exposures and cumulative risks need to be taken into consideration in addressing total SVOC exposure and the overall risk they pose. In particular, the dermal pathway has proven to be significant in the recent years. This literature review has revealed that relatively simple approaches based on the sum of exposures, doses or effects can be useful, at least in a first tier. However, these first-tier approaches carry their own uncertainties and should be accompanied by an uncertainty analysis of simplifying assumptions. It is however important to keep in mind that not choosing to aggregate exposures or cumulate risks creates more uncertainty because of the implicit assumption of independence of exposures and effects.

This review has highlighted that, because they consider differential absorption rates related to the different routes of exposure, as well as metabolism phenomena, pharmacokinetic models are useful tools for aggregating exposure. Because these are currently available only for certain SVOCs, there is a need for development of generic models for those SVOCs sharing common toxicological effects (e.g. a PBPK model for reprotoxic SVOC). They could also be used for reverse dosimetry using biomonitoring data.

When assessing cumulative risks to several compounds (e.g. in order to build a RPF), a compromise needs to be reached between the exhaustiveness of the compounds list and the required precision of the toxicity estimates for each substance involved in the mixture. A great progress towards putting cumulative risk assessment into practice would be to generate comparable toxicity data in order to build RPF. This may be achieved, for instance, with the use of standardized high-throughput assays as developed last years by the US EPA (Kavlock et al., 2012), associated with the development of omics strategies (i.e. proteomics or transcriptomics). Recent works in these topics are very promising (Hannas et al., 2011; Thomas et al., 2010, 2012; Van Ravenzwaay et al., 2014; Chauhan et al., 2016; Labib et al., 2016).

Both PBPK building and toxicity testing is time and resources consuming and a proposal would be to focus efforts on ubiquitous compounds sharing, or suspected to share, the same mechanism of action. A next step would be to identify compounds the populations are frequently exposed to, and then define corresponding cumulative assessment groups, such it has already be done for certain environments (Fournier et al., 2014b), or regulatory processes (Boobis et al., 2008).

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Chapitre 3 : Estimation des expositions agrégées aux COSV présents dans les logements français

3.1. Cas particulier de la voie cutanée

La voie cutanée a longtemps été considérée comme négligeable dans l'exposition totale aux contaminants environnementaux (hormis les contacts cutanés avec les liquides en milieux professionnels et les contacts cutanés avec les crèmes et les liquides pour les usages médicaux et cosmétiques). Depuis plusieurs années de nombreuses études se sont intéressées au passage transcutané et à la modélisation de son absorption, notamment concernant l'exposition aux COSV présents dans les environnements intérieurs (Weschler et Nazaroff 2012 ; Gong et al., 2014). Plusieurs études ont par la suite démontré l'importance de l'exposition par contact cutané, notamment aux COSV présents dans la phase gazeuse de l'air intérieur, dans l'exposition globale (Bekö et al., 2013 ; Weschler et Nazaroff 2014 ; Weschler et al., 2015 ; Morrison et al., 2016). L'exposition par contact cutané avec les poussières est quant à elle la plupart du temps négligée (Mitro et al., 2016), notamment en raison d'une contribution minime quand elle est prise en compte dans l'estimation de l'exposition totale (Bekö et al., 2013).

Les modèles à l'équilibre, adaptés aux COSV par Weschler et Nazaroff (2012), permettent d'estimer l'absorption cutanée et requièrent, entre autres, l'estimation d'un coefficient de perméabilité, le $k_{p\text{-}g}$, représentant l'absorption d'un COSV à partir de la phase gazeuse de l'air jusqu'aux capillaires dermiques et ainsi à son passage dans la circulation sanguine générale. Ce coefficient est ensuite retrouvé dans les équations de DJE afin d'estimer une dose interne.

Au total, de nombreux paramètres sont requis pour l'estimation de l'exposition par passage cutané : des données de contamination de la phase gazeuse et de l'air total

(phases gazeuse et particulaire), des paramètres physico-chimiques (la constante de Henry, les coefficients de partage octanol-eau et octanol-air), des variables humaines d'exposition (le poids, la surface cutanée, le temps passé dans le logement) et des paramètres d'exposition (le transfert de masse d'un COSV de l'air intérieur à la couche d'air superficielle de la peau, la concentration des particules totales en suspension, la fraction volumique de matière organique associée aux particules en suspension et la densité particulaire). La variabilité et l'incertitude associées à ces paramètres d'entrée peuvent entraîner des variations non négligeables sur les estimations des expositions et Salthammer et Schripp (2015) recommandent leur prise en compte dans les modèles de prédiction.

Afin d'évaluer et de quantifier l'impact de l'incertitude et de la variabilité de ces paramètres d'entrée, une analyse de sensibilité probabiliste, par simulations de Monte Carlo, a été conduite pour évaluer les modèles à l'équilibre d'estimation du $k_{p\text{-}g}$, de la contamination en phase gazeuse et pour finir de la DJE. Cette analyse de sensibilité a été conduite pour 8 COSV, de volatilités variables, et issues de 8 familles chimiques différentes : phtalates, bisphénols, HAP, OP, OC, muscs polycycliques, PCB et PBDE. La méthodologie mise en place ainsi que les résultats obtenus ont fait l'objet d'une publication dans *Environment International* et sont présentés sous forme d'article dans la suite de ce chapitre 3.1.

L'analyse de sensibilité a révélé que la variation des résultats de DJE obtenus été majoritairement influencée par la variabilité des données de contaminations de l'air intérieur, dans un premier temps, puis par l'incertitude associée aux paramètres physico-chimiques dans un second temps. L'incertitude et la variabilité associées aux

variables humaines et aux paramètres d'exposition ont quant à elles une influence négligeable, voire nulle, sur la variation des résultats pour une tranche d'âge donnée.

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Dermal absorption of semivolatile organic compounds from the gas phase: Sensitivity of exposure assessment by steady state modeling to key parameters

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ABSTRACT

Recent research has demonstrated the importance of dermal exposure for some semivolatile organic compounds (SVOCs) present in the gas phase of indoor air. Though models for estimating dermal intake from gaseous SVOCs exist, their predictions can be subject to variations in input parameters, which can lead to large variation in exposure estimations. In this sensitivity analysis for a steady state model, we aimed to assess these variations and their determinants using probabilistic Monte Carlo sampling for 8 SVOCs from different chemical families: phthalates, bisphenols, polycyclic aromatic hydrocarbons (PAHs), organophosphorus (OPs), organochlorines (OCs), synthetic musks, polychlorinated biphenyls (PCBs) and polybromodiphenylethers (PBDEs). Indoor SVOC concentrations were found to be the most influential parameters. Both Henry's law constant (H) and octanol/water partition coefficient (K_{ow}) uncertainty also had significant influence. While exposure media properties such as volume fraction of organic matter in the particle phase ($f_{om\text{-}part}$), particle density (ρ_{part}), concentration ([TSP]) and transport coefficient (χ_d) had a slight influence for some compounds, human parameters such as body weight (W), body surface area (A) and daily exposure (t) make a marginal or null contribution to the variance of dermal intake for a given age group. Inclusion of a parameter sensitivity analysis appears essential to reporting uncertainties in dermal exposure assessment.

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1. Introduction

People spend >80% of their time in enclosed spaces, largely in dwellings in which they are exposed to an increasing number of chemicals from various sources and via different exposure routes. In addition to other pollutants found in indoor environments (radon, carbon monoxide, formaldehyde and other volatile organic compounds), semivolatile organic compounds (SVOCs) have received a great deal of attention, due to a rise in their use in consumer products as well as improved analytical techniques that have shown their ubiquity in dwellings (Rudel et al., 2003; Weschler and Nazaroff, 2008).

SVOCs include organic molecules from many different chemical families (phthalates, bisphenols, polycyclic aromatic hydrocarbons (PAHs), organophosphorus (OPs), organochlorines (OCs), synthetic musks, polychlorinated biphenyls (PCBs), polybromodiphenylethers (PBDEs), etc.). They are emitted from multiple household sources: flooring and wall materials, furniture, cosmetics, cleaning products, combustion products, packaging, etc. Due to their physical-chemical properties, they are able to migrate to, and partition between, different indoor

Abbreviations: A, Body surface area (m^2); C_a, SVOC total concentration in indoor air ($C_g + F$) (ng/m^3); C_g, SVOC concentration in the gas phase (ng/m^3); $DI_{dermal\text{-}gas}$, Daily intake by dermal exposure through the gas phase (micrograms per kilogram of body weight per day, μg/kg-bw/d); F, SVOC concentration in the particulate phase (ng/m^3 of air); $f_{om\text{-}part}$, Volume fraction of organic matter associated with airborne particles; H, Henry's law constant ($Pa \cdot m^3/mol$); K_{oa}, Octanol/air partition coefficient; K_{ow}, Octanol/water partition coefficient; K_p, Gas/particle distribution coefficient ($m^3/\mu g$); $k_{p\text{-}g}$, Indoor air transdermal permeability coefficient, describing the transport of a gas phase SVOC from bulk indoor air to dermal capillaries, through the boundary layer adjacent to skin, the stratum corneum and viable epidermis composite (m/h); MW, SVOC molecular weight (g/mol); P_s, SVOC vapor pressure (Pa); R, Ideal gas constant ($=8.314\ Pa \cdot m^3/mol \cdot K$); ρ_{part}, Density of airborne particles (g/m^3); SVOC, Semivolatile organic compound; t, Daily exposure duration (h/d); T, Temperature (K); [TSP], Total suspended particle concentration ($\mu g/m^3$); W, Body weight (kg); χ_d, Coefficient describing the external transport of a gas phase SVOC from the bulk indoor air to the boundary layer adjacent to the skin (m/h).

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compartments, including gas phase and airborne particles and settled dust (Weschler and Nazaroff, 2008), as well as other available surfaces such as walls, ceiling and flooring materials – or human skin and clothing. The scientific community's growing interest in studying exposure to these compounds is motivated by suspicion of reprotoxic, (Rubin, 2011; Moreau-Guigon and Chevreuil, 2014), neurotoxic (Baldi et al., 2001; Elbaz et al., 2009; Blanc-Lapierre et al., 2012; Zaganas et al., 2013) and carcinogenic (Armstrong et al., 2004; IARC, 2015a, b) health effects, as well as the acknowledged presence of these compounds and their metabolites in human biological fluids (blood and urine) (NHANES, 2015). This interest is even more pronounced with regard to pregnant women and young children, considered more sensitive to these toxic effects (Grandjean et al., 2008).

At home, in addition to food ingestion (the main exposure pathway for many SVOCs), people are exposed through a variety of pathways: direct contact with the SVOC source, inhalation and contact with indoor air (gaseous and particulate phases), ingestion and contact with settled dust (on floor and furniture). Young children are more exposed than the rest of the population due to their more frequent contact with the ground and deposited dust, carrying objects in their mouths, etc. Though dust ingestion and inhalation of gaseous and particulate phases are the two best-documented exposure pathways in the literature, dermal absorption is rarely assessed in the course of environmental exposure assessments, because it is presumed to be negligible. Nevertheless, recent research has hypothesized the significance of dermal exposure (Weschler and Nazaroff, 2012; Gong et al. 2014) and more recently Weschler et al. (2015) and Morrison et al. (2016a) have corroborated these findings via experimental human dermal exposure to two gaseous phthalates: diethyl phthalate (DEP) and di-*n*-butyl phthalate (DnBP). The results confirm that transdermal uptake directly from air can be a meaningful exposure pathway for DEP and DnBP, and that direct dermal absorption from air is also expected to be significant for other SVOCs, where the molecular weight and K_{ow} are in a similar range. Beko et al. (2013) estimated daily intakes resulting from four different indoor exposure pathways: dust ingestion, inhalation and dermal exposure through gas phase and through dust adhering to skin, based on phthalates' metabolites levels in urine samples of DEP, DnBP, di(isobutyl) phthalate (DiBP), butyl benzyl phthalate (BBzP) and di(2-ethylhexyl) phthalate (DEHP) and their concentration in dust samples collected at the same time. They found that gas phase dermal absorption was the major exposure pathway for the more volatile compounds, in comparison with the other pathways involved. They also found that intake through dermal contact with dust contributed only very slightly to total intake for all studied phthalates. In order to assess SVOC gas phase dermal exposure, some authors have adapted and used a model based on mass-transfer resistance to calculate an indoor air transdermal permeability coefficient k_{p-g} (Weschler and Nazaroff, 2012; Beko et al., 2013). This mass-transfer model describes the transport of a gas phase SVOC from bulk indoor air to dermal capillaries, through the boundary layer adjacent to skin, the stratum corneum and the viable epidermis composite.

At equilibrium and due to their physical-chemical properties, especially K_{oa}, SVOCs partition between the gas and particle phases of indoor air (Finizio et al., 1997; Pankow, 1998; Weschler and Nazaroff, 2008). When assessing gaseous SVOC dermal exposure, concentration in the gas phase (C_g) is required and could be either measured or modeled from total concentration in indoor air (C_a) - which is the sum of gas and particulate (F) phases ($C_g + F = C_a$). Salthammer and Schripp (2015) have highlighted the importance of taking parameter uncertainty and variability into account when assessing SVOC partitioning and exposure. Weschler and Nazaroff (2014) have already assessed the sensitivity of k_{p-g} and other partitioning coefficient calculations, such as K_p, to the octanol/water partition coefficient (K_{ow}), the octanol/air partition coefficient (K_{oa}) and Henry's law constant (H) uncertainties. We would like to continue this work here by evaluating the sensitivity of dermal intake, i.e. the mass of pollutant entering the body per kg of body weight and unit of time, to these parameters using a steady-state model.

The objective of this sensitivity analysis is to evaluate dermal intake variation caused by the uncertainty and variability of input parameters when using the model described by Weschler and Nazaroff (2012) for dermal absorption of gas phase SVOCs. We chose the study by Blanchard et al. (2014), in which 57 indoor SVOCs of health interest (Bonvallot et al., 2010) were measured with separation of their gas phase and airborne particle concentrations, as a starting study. We selected eight compounds from different chemical families having varied K_{oa} and volatility to represent contrasting situations: dimethyl phthalate (DMP), phenanthrene, galaxolide (HHCB), PCB 105, diazinon, permethrin, bisphenol A (BPA) and BDE 154.

2. Methods

2.1. Equation tested for dermal intake modeling

For a given human, chronic daily intake of gas phase SVOC via the dermal pathway, $DI_{dermal-gas}$, can be estimated in steady-state conditions using the following equation adapted by Beko et al. (2013).

$$DI_{dermal-gas} = \frac{\frac{C_g \times k_{p-g} \times A \times t}{1000}}{W} \tag{1}$$

where C_g is the SVOC gas phase concentration (ng/m^3), A is the body surface area (m^2), t is the daily duration of exposure (h/d), W is the body weight (kg), k_{p-g} is the SVOC transdermal permeability coefficient (m/h) and $DI_{dermal-gas}$ is expressed in μg/kg-bw/d.

The indoor air transdermal permeability coefficient (k_{p-g}) can be estimated using the steady-state model adapted by Weschler and Nazaroff (2012, 2014), (see supplementary material for the intermediate equations used to derive Eq. (2)):

$$k_{p-g} = 1/\left(\frac{1}{\gamma_d} + \left(\frac{H}{RT}/\frac{10^{(0.7\times \log(K_{ow}) - 0.0722\times MW^{2/3} - 5.252)} \times 3600 \times 10^{-2}}{1 + \left(10^{(0.7\times \log(K_{ow}) - 0.0722\times MW^{2/3} - 5.252)} \times MW^{0.5} \times 3600/2.6\right)}\right)\right) \tag{2}$$

where K_{ow} is the SVOC octanol-water partition coefficient, MW is the SVOC molecular weight (g/mol), H is the Henry's law constant (Pa·m^3/mol), R is the ideal gas constant (8.314 Pa·m^3/mol·K), T is the air temperature (K) and γ_d is the coefficient that describes the external transport of an SVOC from the gas phase in the core of a room through the boundary layer adjacent to the skin (m/h).

When estimating dermal intake from the gas phase (see Eqs. (1) and (2)), exposure assessors may face two situations which can be distinguished in terms of availability of the C_g value: A) C_g is measured experimentally or B) C_g is calculated from total indoor air concentration (C_a). Assuming that SVOCs are in equilibrium between gas and particulate phases, C_g can be estimated from C_a using the partitioning model proposed by Weschler and Nazaroff (2010) and can be expressed as follows (see supplementary material for the detailed calculation):

$$C_g = \frac{C_a}{1 + \left([TSP] \times \frac{f_{om-part} \times K_{ow} \times R \times T}{\rho_{part} \times 10^6 \times H}\right)} \tag{3}$$

where [TSP] is the total suspended particle concentration (μg/m^3), $f_{om-part}$ is the volume fraction of organic matter associated with airborne particles and ρ_{part} is the density of airborne particles.

2.2. Parameter estimation

The impact of uncertainty or variability of equation parameters on $DI_{dermal-gas}$ variability was assessed. Parameter distributions were

Table 1
Parameter distributions used in the dermal intake sensitivity analysis from gas phase for 8 SVOCs.

Parameter	DMP	Phenanthrene	HHCB	Permethrin	Diazinon	PCB105	BPA	BDE154	Sources
Log (K_{ow})[a]	Log-normal min = 1.35 μ = 1.65 σ = 0.14	Logistic μ = 4.50 scale = 0.09	Triangular min = 3.42 μ = 5.23 max = 6.26	Minimum extreme likeliest = 6.51 scale = 0.73	Minimum extreme likeliest = 3.74 scale = 0.37	Minimum extreme likeliest = 6.72 scale = 0.35	Triangular min = 3.32 μ = 3.48 max = 4.04	Triangular min = 6.86 μ = 7.89 max = 8.83	Internet databases[c], Chemexper, ACD/Labs calculators, EPI Suite software (US EPA, v4.1), Mackay et al., 2010a, b, c, d.
H[a] (Pa·m^3/mol)	Triangular min = 6.20E-3 μ = 3.60E-2 max = 1.11E-1	Triangular min = 2.38 μ = 3.74 max = 5.55	Uniform min = 7.66E-2 max = 1.34E + 1	Triangular min = 2.33E-6 μ = 5.34E-2 max = 1.89E-1	Triangular min = 7.00E-3 μ = 4.25E-2 max = 1.44E-1	Triangular min = 2.43 μ = 2.24E + 1 max = 8.36E + 1	Triangular min = 9.28E-7 μ = 2.49E-6 max = 4.05E-6	Triangular min = 4.77E-2 μ = 1.46E-1 max = 2.40E-1	
C_g (ng/m^3)	Log-normal min = 0 μ_g = 8.57 σ_g = 2.23	Log-normal min = 4.16 μ_g = 3.88 σ_g = 2.98	Log-normal min = 0 μ_g = 6.67E + 1 σ_g = 2.57	Uniform [0–0.6(LOQ)]	Discrete (p = 0.03) 2.45 Uniform (p = 0.97) [0–0.6(LOQ)]	Discrete (p = 0.03) 0.4 Uniform (p = 0.97) [0–0.25(LOQ)]	Uniform [0–0.6(LOQ)]	Uniform [0–0.6(LOQ)]	Blanchard et al., 2014.
C_a (ng/m^3)	Log-normal μ = 1.18E + 3 p50 = 4.36E + 2 p95 = 4.65E + 3	Log-normal μ = 6.1 p50 = 1.10E + 1 p95 = 2.90E + 1	Log-normal μ = 1.19E + 2 p50 = 1.01E + 2 p95 = 2.45E + 2	Uniform (p = 0.92) [0–0.3(LOQ)] Uniform (p = 0.08) [0.3(LOQ)–2]	Uniform (p = 0.98) [0–0.3 (LOQ)] Uniform (p = 0.02) [0.3(LOQ)–3.1E + 1]	Uniform (p = 0.88) [0–0.3 (LOQ)] Uniform (p = 0.12) [0.3(LOQ)–1.2]	Uniform (p = 0.84) [0–0.8(LOQ)] Uniform (p = 0.16) [0.8(LOQ)–2.2E + 1]	Triangular min = 0 μ = 6.20E-4 max = 1.09E-2	Rudel et al., 2010 (phen, per, diaz, PCB105, BPA), Fromme et al., 2004 (DMP, HHCB), Fromme et al., 2009 (BDE154).
γ_d (m/h)	Triangular min = 5, likeliest = 6, max = 10								Tamas et al., 2006; Pandrangi and Morrison, 2008; Weschler and Nazaroff, 2008.
[TSP] (μg/m^3)	Log-normal, μ_g = 37.34, σ_g = 2.17, p95 = 182								Ramalho et al. (2012).
$f_{om-part}$	Normal, μ = 0.35, σ = 0.2								Salthammer and Schripp, 2015.
ρ_{part} (g/m^3)	Normal, μ = 1.6E + 6, σ = 0.5E + 6								Pitz et al., 2003.
W[b] (kg)	Log-normal, μlnx = 2.68, σlnx = 0.17, p95 = 22.0								Tanguy et al., 2007.
A[b] (m^2)	Log-normal, μ = −0.28, σ = 0.12, p95 = 0.94								Sabaterie et al., 2013.
T (h/d)	Normal, μ = 17.17, σ = 0.63								Zeghnoun and Dor, 2010.

A: body surface area; BPA: bisphenol A; C_a: SVOC total concentration in indoor air; C_g: SVOC concentration in the gas phase; diaz: diazinon; DMP: dimethyl phthalate; $f_{om-part}$: volume fraction of organic matter associated with airborne particles; γ_d: coefficient describing the external transport of a gas phase SVOC from the bulk indoor air to the boundary layer adjacent to the skin; H: Henry's law constant; HHCB: galaxolide; K_{ow}: octanol/water partition coefficient; μ: arithmetic mean; μ_g: geometric mean; per: permethrin; phe: phenanthrene; ρ_{part}: density of airborne particles; σ: standard deviation; σ_g: geometric standard deviation; t: daily exposure duration; [TSP]: total suspended particle concentration; W: body weight. Distribution parameters may be different for a same distribution law because of diversity of reporting data in the literature.

[a] Measured or estimated at 25 °C.

[b] Spearman's rank correlation between mass and body surface area is 0.99 for a 4-year-old male child (Sabaterie et al., 2013).

[c] Hazardous Substances Data Bank (HSBD), ChemIDplus, Chemspider, Chemicalize and the French toxicological and environmental data sheets from INERIS.

constructed or retrieved from the literature as detailed below. For a given group of occupants in a given indoor setting, some of these parameters will be the same for all SVOCs (γ_d, [TSP], $f_{om-part}$, ρ_{part}, W, A and t) while others will vary from one compound to another (K_{ow}, H, C_g and C_a).

2.2.1. Physical-chemical parameters

For each SVOC, measured or estimated values of log (K_{ow}) and Henry's law constant (H) at 25 °C were retrieved from: online databases - Hazardous Substances Data Bank (HSBD) and ChemIDplus (http://toxnet.nlm.nih.gov/), Chemspider (http://www.chemspider.com/), and Chemicalize (http://www.chemicalize.org/); toxicological and environmental data sheets from the French National Competence Centre for Industrial Safety and Environmental Protection (INERIS) (http://www.ineris.fr/substances/fr/page/21); online calculators - Chemexper (https://www.chemexper.com/) and ACD/Labs (http://www.acdlabs.com/); EPI Suite software (US EPA, v4.1) and the Handbook of Physical-Chemical Properties and Environment Fate for Organic Chemicals (Mackay et al., 2010a, b, c, d). Only values at 25 °C (reference temperature) were selected, in order to be consistent and to estimate $DI_{dermal-gas}$ at a constant temperature. For each SVOC, where at least 15 values for their log (K_{ow}) and H were retrieved from the sources mentioned above, distributions were fitted – and otherwise we used triangular distributions (between minimum, average and maximum values). Corresponding distributions are displayed in Table 1.

2.2.2. Contamination data

In situation A (C_g measured): SVOC gas phase concentration values (C_g) were retrieved from Blanchard et al. (2014). When 100% (i.e. in 30 out of 30 dwellings) of the data were > the limit of quantification (LOQ), log-normal distributions were fitted. When 100% of the values were <LOQ, uniform distributions between 0 and LOQ were used. Lastly when single values were >LOQ, custom distributions were constructed, related to their probabilities of occurrence, with continuous range between 0 and LOQ and discrete ranges for the values > LOQ. In situation B (C_g measured from C_a): SVOC indoor air concentration values (C_a) were retrieved from the literature (Fromme et al., 2004; Fromme et al., 2009 and Rudel et al., 2010). Log-normal distributions were fitted where possible; otherwise custom distributions were constructed, related to their probabilities of occurrence, with continuous ranges from 0 to LOQ and from LOQ to maximum value, or triangular distributions between minimum, average and maximum values. Corresponding distributions are displayed in Table 1.

2.2.3. Human parameters

We considered a 4-year-old male child to be representative of the sensitive population in terms of the identified toxicological effects and exposure behavior. As an example we searched literature for body weight (W), surface area (A), and time spent in dwellings (t) for a child living in France. Log-normal distributions were used for weight and body surface area. Normal distribution was used for the space-time-budget. Corresponding distributions are displayed in Table 1.

2.2.4. Exposure media properties

The assessment of gas phase SVOC dermal transfer requires the use of exposure media properties such as γ_d, [TSP], $f_{om-part}$ and ρ_{part}. Triangular distribution was used for γ_d, using the minimum and maximum values found in the literature and the generally-assumed 6 m/h as the most likely value to occur. Log-normal distribution was used for [TSP] and $f_{om-part}$. Normal distribution was used for ρ_{part}. Corresponding distributions are displayed in Table 1.

3. Simulation

Dermal intake sensitivity analysis (Eq. (1)) was performed using Crystal Ball® software (Oracle©, version 11.1.1.3.00). For each SVOC and for each of the two situations regarding C_g (A: C_g measured, B: C_g modeled), Latin Hypercube one-dimensional simulations were carried out with 10^5 runs.

4. Results and discussion

4.1. Daily dermal intake variation

Daily dermal intake variations are presented in Table 2.

The relative interdecile range of $DI_{dermal-gas}$, when C_g value is measured (situation A), ranged from 1.2 for BPA to 6.3 for galaxolide (HHCB). When C_g is estimated from C_a (situation B), $DI_{dermal-gas}$ variation was highest for BPA having a relative interdecile range of 17.8 and lowest for phenanthrene, at 1.4. The following sensitivity analysis results allow us to interpret $DI_{dermal-gas}$ variation, particularly for compounds having high relative interdecile ranges.

4.2. Sensitivity to model parameters

Results of the sensitivity analysis are presented in Fig. 1 as tornado charts, showing relative contributions to total variation of gas phase SVOC daily dermal intakes (μg/kg-bw/d) according to key parameters. Parameters having a relative contribution that is always lower than 5% are not shown in Fig. 1, that is, each of the human parameters: W, A and t (situation A and B) and γ_d (only for situation B).

The sensitivity analysis of $DI_{dermal-gas}$ calculation, when C_g is measured (situation A), reveals that for the studied compounds the most influential parameters are: C_g, H and log (K_{ow}). $DI_{dermal-gas}$ estimation is mainly driven by variability in C_g.

When C_g is estimated from C_a (situation B), $DI_{dermal-gas}$ variation is dominated by variability in C_a, with the exception of HHCB and BDE 154 for which it is mainly driven by uncertainty in log (K_{ow}). For permethrin and BDE 154, uncertainties in $f_{om-part}$, ρ_{part} and [TSP] are also significant, though less influential in $DI_{dermal-gas}$ calculation.

For a given age group in both situations, the following parameters make a marginal or null contribution to $DI_{dermal-gas}$ variation for all of the studied SVOCs: t, W, A, and γ_d - with the exception of BPA in situation A, for which γ_d makes a significant contribution.

4.3. Variability and uncertainty in C_g and C_a measurements

Indoor air SVOCs concentrations can be variable and/or uncertain. Variabilities in indoor air concentrations (C_g and C_a) are high due to several conditions, such as differences in occupant habits, variety of sources, and dwelling characteristics. For example, Clausen et al.

Table 2
Variations in daily dermal intake ($DI_{dermal-gas}$), expressed as the relative interdecile range, for each SVOC and for each of the two situations regarding gas phase concentration (A: C_g measured, B: C_g modeled).

Situation	SVOC	Relative interdecile range $= \frac{d90-d10}{d50}$
A	Dimethyl phthalate (DMP)	3.1
	Phenanthrene	1.9
	Galaxolide (HHCB)	6.3
	Permethrin	2.2
	Diazinon	3.1
	PCB 105	2.8
	Bisphenol A (BPA)	1.2
	BDE 154	1.6
B	Dimethyl phthalate (DMP)	6.2
	Phenanthrene	1.4
	Galaxolide (HHCB)	2.8
	Permethrin	3.6
	Diazinon	3.1
	PCB 105	3.7
	Bisphenol A (BPA)	17.8
	BDE 154	7.3

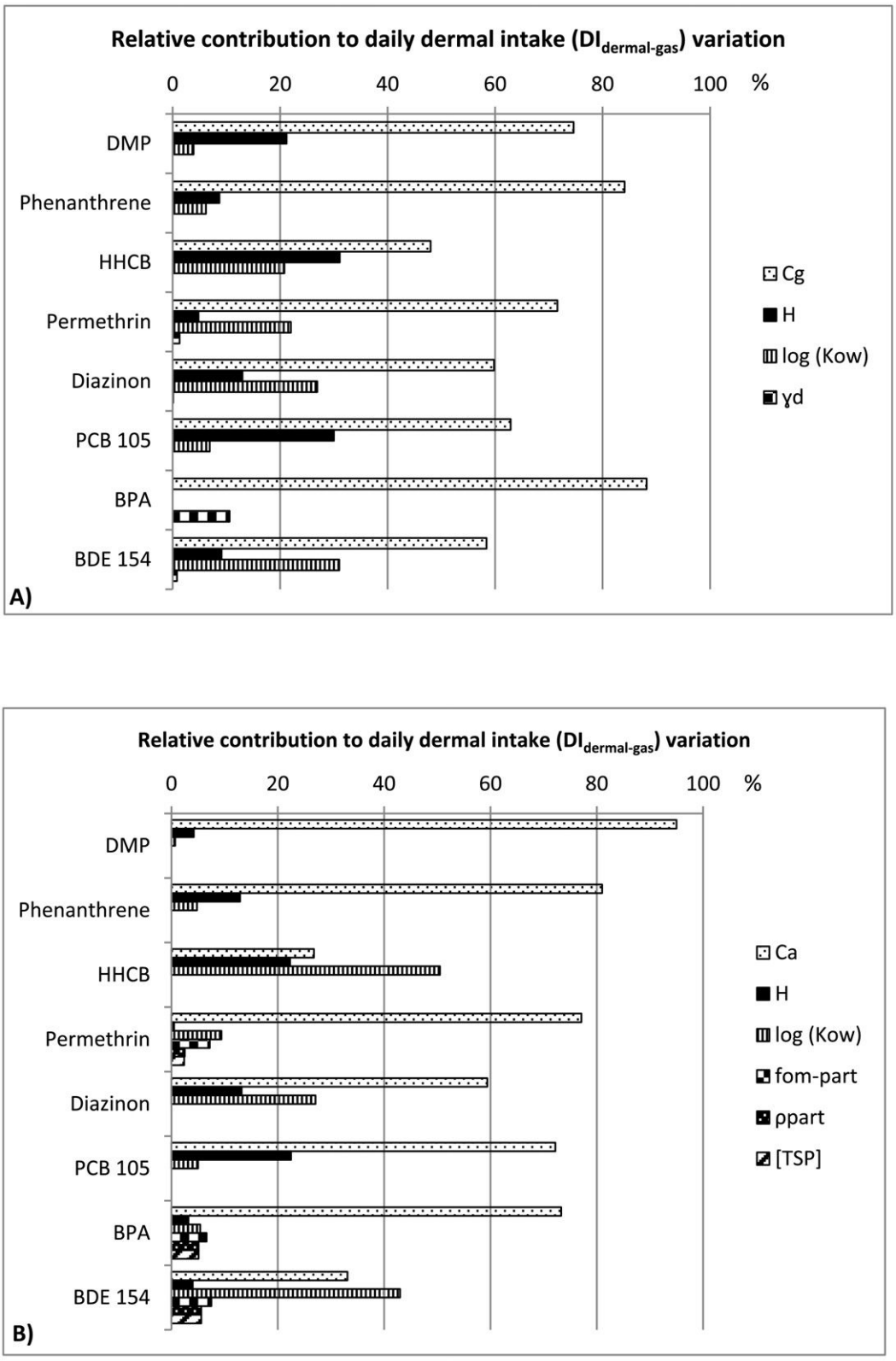

Fig. 1. Relative contribution (%) to total variation of gaseous SVOC daily dermal intakes (μg/kg-bw/d) according to key parameters: C_g, C_a, log (K_{ow}), H, γ_d, $f_{om-part}$, ρ_{part}, and [TSP] for both situations: A) C_g is measured and B) C_g is estimated from C_a.

(2012) found that indoor temperature has a significant influence on DEHP air concentrations: this increases by a factor of about 10 with an increase of 12 °C in indoor temperature. Furthermore, these concentrations may vary considerably from one country to another depending, for example, on national regulations regarding the use of specific SVOCs (Weschler and Nazaroff, 2008). In this sensitivity analysis, C_g and C_a were retrieved from studies (Fromme et al., 2004; Fromme et al., 2009; Rudel et al., 2010 and Blanchard et al., 2014) having measured

these concentrations at various indoor temperatures and in different countries. But C_g and C_a are also uncertain, especially when all or most values are below the LOQ. When C_g and C_a values were below the LOQ (permethrin, diazinon, PCB 105, BPA and BDE 154), the applied distribution shape (custom, triangular and uniform) also brings uncertainty to these unknown values. In order to assess the impact of the distribution on C_g and C_a uncertainty, triangular distributions (between 0, LOQ/2 and LOQ) were also tested in place of uniform distributions (data not shown). The same results were found, providing evidence that distribution shape does not influence the relative contribution of C_g and C_a uncertainty in $DI_{dermal\text{-}gas}$ result variation.

Moreover, some LOQs used as maxima in uniform distribution regarding C_g (permethrin, BPA and BDE 154) are open to discussion because they are high in comparison with other studies in which fewer compounds were measured at the same time. This uncertainty can lead to discrepancy between the two situations regarding the distribution we used, especially for BDE 154 concentrations in indoor air (see Table 1) where C_g maximum value (0.6 = LOQ) is larger than C_a maximum (0.01). This unrealistic situation is the only one in our study - but it is important to bear in mind that the objective here is a sensitivity analysis linked to information availability, rather than an exposure assessment.

4.4. Uncertainty in physical-chemical parameter values

Physical-chemical parameters can either be measured experimentally or calculated using other chemical properties. Depending on which of these methods is used, it follows that values vary by one order of magnitude or more (Finizio et al., 1997) - and these uncertainties will be propagated in the calculation of k_{p-g}, C_g and $DI_{dermal-gas}$. On this topic, Weschler and Nazaroff (2008) warned that H, K_{ow} and K_{oa} values, calculated using the SPARC Online Calculator v4.0 (Hilal et al., 2003, 2004), sometimes vary substantially from experimentally derived values. For the same parameters, Schossler et al. (2011) demonstrated that values vary by one order of magnitude or more between the results obtained using software tools such as EPI Suite (US EPA, 2013) or the SPARC Online Calculator v4.6. In this study, log (K_{ow}) and H values were collected from several databases, online calculators and literature sources at 25 °C, and for each SVOC (see Table 1). The wide intervals obtained for certain compounds -such as H for HHCB - corroborate the relatively high level of uncertainty for these parameters.

When assessing gas/particle SVOC distribution (see Eq. (8) in the supplementary material for the detailed calculation), Salthammer and Schripp (2015) assumed normal distributions for H and log (K_{ow}). Due to the lack of data (as discussed above) the authors calculated mean and standard deviation, in order to build normal distribution using just two values for certain compounds. In our study, where at least 15 values for these parameters were retrieved from literature, log-normal distributions were fitted - otherwise we used triangular, minimum extreme or logistic distributions (see Table 1). However, in order to assess the impact of distribution, other distributions, such as uniform, were also tested and the same parameters were found to be most sensitive regarding $DI_{dermal-gas}$ variability, providing evidence that choice of distribution shape does not influence the relative contribution made by H and log (K_{ow}) in $DI_{dermal-gas}$ result variation.

In each situation (A and B), H and log (K_{ow}) have a significant influence on $DI_{dermal-gas}$ variability, depending on the range of H and log (K_{ow}) values. For example, H values for HHCB range from [7.66E-2 to 13.4], which logically leads to this parameter having a greater influence on $DI_{dermal-gas}$ variability (see Fig. 1). These results are consistent with previous studies: Weschler and Nazaroff (2014) assessed k_{p-g} sensitivity (see Eq. (2)) to the same key parameters and also found that the permeability coefficient was more sensitive to H. In the same way, Salthammer and Schripp (2015) assessed the sensitivity of K_p (see Eqs. (8) and (9) in the supplementary material for the detailed calculation) and found that the error margin in K_p calculation was dominated by H uncertainty. Because log (K_{ow}) and H are two of the most influential parameters on $DI_{dermal-gas}$ variation for every SVOC and in both situations, reducing their uncertainties could significantly reduce variation on $DI_{dermal-gas}$ and uncertainty in exposure analysis.

4.5. Uncertainty in exposure media properties

In earlier studies, default values were used for $f_{om-part}$, ρ_{part}, [TSP] and γ_d. Regarding the volume fraction of organic matter associated with airborne particles, $f_{om-part}$, we assumed the same normal distribution parameters as Salthammer and Schripp (2015). Regarding particle density, ρ_{part}, several values are found in the literature and 1.10^6 g/m^3 is often assumed, as a default value (Turpin and Lim, 2001). In order to assess $DI_{dermal-gas}$ sensitivity to this parameter, normal distribution was used rather than a single value (Pitz et al., 2003). Regarding total suspended particle concentration, [TSP], a default value of 20 μg/m^3 was assumed by Weschler and Nazaroff (2008). More recently, Salthammer and Schripp (2015) found that [TSP] strongly influenced gas/particle partitioning, and we decided to build a log-normal distribution for this parameter using data on indoor PM_{10} concentrations (Ramalho et al., 2012). These data are weekly-averaged, and cover different climate zones and seasons. Regarding γ_d, a value of 6 m/h is assumed for the coefficient describing the external transport of a gas phase SVOC from bulk indoor air to the boundary layer adjacent to the skin (Weschler and Nazaroff, 2012). The authors have previously estimated this parameter to range between 5 and 10 m/h (Weschler and Nazaroff, 2008). In this study, triangular distribution was built between these three values. This parameter variation's influence on $DI_{dermal-gas}$ variation was insignificant, with the exception of BPA in situation A (see Fig. 1, A). Nevertheless, Weschler and Nazaroff (2008) also proposed an estimate of 3 m/h for the mass-transfer coefficient. In order to provide a comprehensive sensitivity analysis we assessed different distribution shapes: triangular with a minimum of 3, a likeliest value of 6 and a maximum of 10 and uniform between 3 and 10. The results (not shown) were identical and γ_d did not become an influential parameter.

While exposure media properties such as $f_{om-part}$, ρ_{part}, [TSP] and γ_d have a slight influence (<10%, see Fig. 1) for some compounds (permethrin, BPA and BDE 154), they make a marginal or null contribution (<5%) to the variance of dermal intake for a given age group, for the other SVOCs and in both situations.

4.6. Variability in human parameters

Human parameters such as body weight (W), body surface area (A) and daily exposure (t) make a marginal or null contribution (<5%) to the variance of dermal intake for a given age group, for each SVOC and in each situation. However, one has to bear in mind that we ran the model for a given age group and that these parameters would have a larger impact when applied on a more diverse population. Regarding the role of clothing in dermal exposure, Piotrowski (1971) assessed the exposed body surface area (A) and found little difference in dermal absorption between clothed and naked people exposed to phenol vapor. More recently Morrison et al. (2016a, b) assessed the influence of clothing on the dermal uptake of two phthalates (DEP and DnBP). The authors found that clean clothes were protective against air pollutants; whereas worn clothes, because they have adsorbed air pollutants, increased dermal intake. Because only clean clothes could be considered protective, we decided to not take into account the role of clothing in this sensitivity analysis, and to assume total body surface area exposed to indoor air when calculating $DI_{dermal-gas}$. However, the fact that we found A to make a marginal or null contribution (<5%) to the variance of dermal intake, does not mean that clothing should not, when possible, be taken into account in assessing dermal exposure. In this case the proportion of exposed body surface area has to be taken into account.

In addition to the important role of clothing, other parameters not included in this model are suspected of influencing or playing a role in dermal exposure were not taken into account in this sensitivity analysis: skin temperature, metabolic processes on (e.g. ionization) or in the skin, the effects of bathing on SVOC levels in skin-surface lipids, etc.

Furthermore, it is important to bear in mind that we did not assess model uncertainty - only parametric uncertainty when using this model. A first source of uncertainty is model boundaries. Indeed our model relies partly on equation of Mitragotri (2002) that may lead to greater uncertainty when MW is higher than 400, which is the case for BDE 154. In addition, more sophisticated, and recent, models exist taking into account the dynamics of aerosols and/or the clothing effect. Regarding the dynamics of aerosols, Shi and Zhao (2015) showed that, in their model, air exchange rate and surfaces cleaning frequency were influential parameters, while density of settled dust and its organic fraction were important media properties. Also, the transient model proposed by Gong et al. (2014), addresses the rapidly changing conditions and concentrations and considers a convective mass transfer resistance in the boundary air layer adjacent to the skin, and leads to lower estimates of dermal uptake. Morrison et al. (2016a, b) improved this model taking clothing effect modeling, and showed that bathing frequency and change of clothes frequency were influential. Also, the introduction of a skin surface lipid film in the models and its interactions with clothing may affect the results, so do the corresponding additional parameters, such as for instance the thickness of this lipidic film.

5. Conclusion

When assessing dermal absorption of gas phase SVOCs, variation of dermal intake estimation is driven firstly by variability and uncertainty in indoor air concentration (C_g or C_a), and secondly by uncertainty in SVOC physical-chemical parameters: log (K_{ow}) and H. While exposure media properties such as volume fraction of organic matter in the particle phase ($f_{om\text{-}part}$), particle density (ρ_{part}), concentration ([TSP]) and transport coefficient (γ_d) do have a slight influence (<10%) for some compounds, human parameters such as body weight (W), body surface area (A) and daily exposure (t) make a marginal or null contribution (<5%) to the variance of dermal intake for a given age group.

Considering that $DI_{dermal-gas}$ variation can be high for some compounds, exposure assessors aiming to assess SVOC $DI_{dermal-gas}$ using the k_{p-g}, or to estimate C_g from C_a, must pay particular attention to the determination, estimation, and selection of the following SVOC-specific parameters: concentration in gas phase (C_g) or indoor air (C_a), K_{ow} and H.

It is however important to remain aware, when analyzing these results, that exposure to an SVOC is strongly dependent on its partition between gas phase and particulate phase. When an SVOC is more abundant in the gas phase, dermal absorption will be greater than dust ingestion, and conversely, when a SVOC is more present in the particulate phase, dust ingestion is likely to be greater than dermal absorption (Weschler and Nazaroff, 2012). Therefore, less volatile SVOCs ($P_s < 10^{-6}$ Pa), which are more present in the particulate phase and have a low predicted dermal absorption, do not require the same caution in estimation of dermal intake in order to assess their total exposure to indoor SVOC.

In general, inclusion of an uncertainty analysis in exposure assessment appears to be essential. In view of these sensitivity analysis results, reducing log (K_{ow}) and H uncertainties could significantly reduce uncertainties in $DI_{dermal-gas}$ assessment.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.envint.2017.02.005.

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SUPPLEMENTARY MATERIAL

Dermal absorption of semivolatile organic compounds from the gas phase: sensitivity of exposure assessment to key parameters

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Contents

Intermediate equations used to derive the SVOC transdermal permeability coefficient and to estimate the gas phase concentration from its concentration in total indoor air.

Transdermal permeability coefficient

The transdermal permeability coefficient, $k_{p\text{-}g}$ (m/h), is calculated using a resistors-in-series approach proposed by Weschler and Nazaroff (2012):

$$\frac{1}{k_{p-g}} = \frac{1}{\gamma_d} + \frac{1}{k_{p-b}} \tag{1}$$

Where γ_d is the coefficient that describes the external transport of an SVOC from the gas phase in the core of a room through the boundary layer adjacent to the skin (m/h) and $k_{p\text{-}b}$ is the compound's permeability coefficient which describes the SVOC's transport from the gas phase at the skin surface through the epidermis to the dermal capillaries (m/h) and is estimated as follows:

$$k_{p-b} = \frac{k_{p-w}}{K_{gw}} \tag{2}$$

Where K_{gw} is the equilibrium partition coefficient for the SVOC between the gas phase and water and can be estimated as follows (Meylan and Howard, 1991):

$$K_{gw} = \frac{H}{RT} \tag{3}$$

Where H is the Henry's law constant (Pa.m^3/mol), R is the gas constant (8.314 Pa.m^3/mol.K) and T is temperature (K).

In Equation 2, $k_{p\text{-}w}$ is the compound's permeability coefficient through the stratum corneum/viable epidermis when the vehicle in contact with skin is water (cm/h) and is estimated as follows:

$$k_{p-w} = \frac{k_{p-cw}}{1+B} \tag{4}$$

Where $k_{p\text{-}cw}$ is the compound's permeability coefficient through the stratum corneum when the vehicle in contact with the skin is water (cm/s) and is estimated using Equation 5 (Mitragotri, 2002):

$$\log(k_{p-cw}) = 0.7 \times \log(K_{ow}) - 0.0722 \times MW^{\frac{2}{3}} - 5.252 \tag{5}$$

Where K_{ow} is the species octanol-water partition coefficient and MW is the molecular weight of the compound (g/mol).

In Equation 4, B is the ratio of the stratum corneum permeability ($k_{p\text{-}cw}$) to the viable epidermis permeability for the selected compound and is estimated using Equation 6 (Bunge et al., 1995):

$$B = \frac{k_{p-cw} \times MW^{0.5}}{2.6} \tag{6}$$

Where $k_{p\text{-}cw}$ is expressed in cm/h.

SVOC gas phase concentration

SVOC gas phase concentration (C_g) can be estimated from its concentration in total indoor air (C_a) using a partitioning model proposed by Weschler and Nazaroff (2010):

$$C_g = \frac{C_a}{1 + ([TSP] \times K_p)} \tag{7}$$

Where [TSP] is the total suspended particle concentration (µg/m^3) and K_p is the gas/particle distribution coefficient (m^3/µg). K_p can be estimated according to Equation 8 (Weschler and Nazaroff, 2010):

$$K_p = \frac{f_{om-part} \times K_{oa}}{\rho_{part} \times 10^6} \tag{8}$$

Where $f_{om\text{-}part}$ is the volume fraction of organic matter associated with airborne particles, ρ_{part} is the density of airborne particles (g/m^3) and K_{oa} is the octanol/air partition coefficient. K_{oa} can be estimated according to Equation 9:

$$K_{oa} = \frac{K_{ow} \times R \times T}{H} \tag{9}$$

Where K_{ow} is the octanol/water distribution coefficient, H is the Henry's law constant (Pa.m^3/mol), R is the gas constant (8.314 Pa.m^3/mol.K) and T is temperature (K).

We combined these equations to express and estimate C_g from C_a as follows:

$$C_g = \frac{C_a}{1 + ([TSP] \times \frac{f_{om-part} \times K_{ow} \times R \times T}{\rho_{part} \times 10^6 \times H})} \tag{10}$$

When using these models we made the implicit assumption that SVOC are in equilibrium between gas and particulate phases.

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3.2. Choix des composés pour l'estimation des expositions

La sélection des composés finalement étudiés dans ce travail découle de nombreux choix effectués à plusieurs étapes du projet ECOS-Habitat. La Figure 6 propose un schéma récapitulatif de ces étapes, elles-mêmes détaillées ci-après.

254	Liste initiale des COSV identifiés comme pouvant être présents dans l'habitat .
↓ 66	COSV hiérarchisés sur la base de données de contamination et de toxicité (Bonvallot et al., 2010).
↙ ↓ ↘ 48 66 57	COSV analysables par une approche multi résidus (Mercier et al., 2012, 2014) recherchés respectivement dans les échantillons de poussières (Mandin et al., 2016), et dans les phases particulaire (Mandin et al., 2014) et gazeuse de l'air (Blanchard et al., 2014) des habitats français.
40	COSV dont les données de contamination étaient disponibles dans les trois médias étudiés.
↓ 32	COSV disposant de données de contamination permettant l'estimation des expositions.

Figure 6 : Sélection des COSV étudiés pour l'estimation des expositions.

Une première étape de hiérarchisation des substances, sur la base de données de contamination et de toxicité, avait conduit à sélectionner 66 composés parmi une liste initiale de 254 substances identifiées comme pouvant être présentes dans l'habitat (Bonvallot et al., 2010). Dans un second temps, les composés qui étaient analysables par une approche multi résidus (en chromatographie en phase gazeuse couplée à la spectrométrie de masse en tandem) (Mercier et al., 2012, 2014) ont été recherchés parmi ces 66 dans les échantillons de poussières (Mandin et al., 2016), et dans les phases particulaire (Mandin et al., 2014) et gazeuse de l'air (Blanchard et al., 2014) des habitats français, soit 48, 66 et 57 composés respectivement.

Enfin, l'étape d'évaluation des expositions par inhalation d'air, par ingestion de poussières et par contact cutané avec les COSV présents dans la phase gazeuse de l'air nécessitait de disposer de données de contamination dans les trois médias étudiés pour chaque composé. Cette étape a conduit à la sélection des 40 composés remplissant cette condition (en rouge dans le Tableau 3). Parmi ces composés, une recherche dans la littérature a été conduite pour ceux pour lesquels la détection était trop faible dans l'un ou plus des trois médias étudiés (lorsque 99 % ou plus de leurs données de contamination étaient inférieures à la limite de détection (LD)), afin d'identifier d'autres études les ayant mesurés (de préférence européennes, postérieures à 2000 et dont la méthode de prélèvement et la taille de l'échantillon étaient rapportées). Vingt et un composés étaient concernés par cette recherche et en grande majorité pour leurs concentrations en phase gazeuse. Les études ont été sélectionnées si elles employaient des LD plus faibles que celles des études de Mandin et al. (2014, 2016) et Blanchard et al. (2014). Au final, sur ces 21 COSV, 8 ont été exclus car aucune autre étude, employant une LD plus faible, n'a été trouvée dans la littérature. Cela concerne : le diazinon, l'endrine, l'alpha-endosulfan, la perméthrine, le BDE 119, le PCB 77, le PCB 126 et le bisphénol-A. Ainsi, l'estimation des expositions agrégées concernent 32 COSV au total (en rouge et en gras dans le Tableau 3).

Cette méthode a été appliquée afin d'éviter la surestimation de l'exposition par une modélisation trop incertaine de leur contamination, notamment en phase gazeuse.

Tableau 3 : COSV ayant été recherchés dans les médias étudiés dans les logements français (2003 à 2011).

Familles chimiques	COSV[1]	Poussières (n=48)[2]	Phase particulaire (n=66)[3]	Phase gazeuse (n=57)[4]
Alkylphénols	4-tert-butylphénol		X	
	4-tert-octylphénol		X	
	4-n-nonylphénol		X	
Hydrocarbures aromatiques polycyliques	Acépnaphtène	X		X
	Anthracène	X	X	X
	Benzo[a]pyrène	X	X	X
	Fluorène	X	X	X
	Phénanthrène	X	X	X
	Fluoranthène		X	X
	Pyrène		X	X
	Benzo[a]anthracène		X	
	Chrysène		X	
	Benzo[b]fluoranthène		X	
	Benzo[k]fluoranthène		X	
	Dibenzo[a,h]anthracène		X	
	Indéno[1,2,3-c,d]pyrène		X	
	Benzo[g,h,i]pérylène		X	
Muscs polycycliques	**Galaxolide**	X	X	X
	Tonalide	X	X	X
Pesticides organophosphorés	Dichlorvos	X		X
	Chlorpyrifos	X	X	X
	Diazinon	X	X	X
Pesticides organochlorés	**Aldrine**	X	X	X
	Atrazine		X	
	Dieldrine	X	X	X
	Endrine	X	X	X
	Alpha-HCH		X	X
	Gamma-HCH (Lindane)	X	X	X
	Oxadiazon	X	X	
	4,4'-DDE	X	X	
	4,4'-DDT		X	X
	Alpha-endosulfan	X	X	X
	Cis-chlordane		X	X
	Trans-chlordane		X	X
	Heptachlore		X	X
	Métolachlore		X	
Phtalates	**BBP**	X	X	X
	DBP	X	X	X
	DEHP	X	X	X
	DEP	X	X	X
	DiBP	X	X	X
	DiNP	X	X	X
	DMP		X	X
	DMEP		X	X
	DOP		X	
Pyréthrinoïdes	Cyfluthrine	X		
	Cyperméthrine	X		X
	Deltaméthrine	X		
	Perméthrine	X	X	X
	Tetraméthrine			X
Polybromodiphényléthers	Congénères **28**, **47**, **85**, **99**, **100**, 119, **153**, **154** et 209	X	X (sauf 209)	X
Polychlorobiphényles	Congénères **28**, **31**, **52**, 77, **101**, **105**, **118**, 126, **138**, **153** et 180	X (sauf 180)	X	X
Bisphénols	Bisphénol-A	X	X	X
	Bisphénol-M			X
	Diglycidyl ether de bisphénol-A (BADGE)			X
Autres composés	Triclosan		X	
	Tributylphosphate	X	X	X

[1] Les COSV en rouge sont ceux ayant été recherchés dans les trois médias et en gras ceux pour lesquels l'estimation des expositions agrégées a été conduite.

2 Mandin et al., 2014. [3] Mandin et al., 2016. [4] Blanchard et al., 2014.

3.3. Estimation des expositions agrégées

Les expositions par inhalation d'air (phases gazeuse et particulaire), par ingestion de poussières et par contact cutané avec les COSV présents dans la phase gazeuse de l'air, ont été estimées pour chacun des 32 COSV par l'utilisation d'équations de DJE. Les DJE sont exprimées en doses internes par la prise en compte de la biodisponibilité pulmonaire pour l'exposition par inhalation, de la biodisponibilité orale et de la bioaccessibilité des composés dans les poussières pour l'exposition par ingestion et par l'estimation du coefficient de perméabilité pour l'exposition cutanée. Ces DJE ont ensuite été sommées afin d'estimer l'exposition agrégée pour chaque composé et ce pour plusieurs tranches d'âge allant de la naissance à 30 ans. La variabilité diminue entre les tranches d'âge au-delà de 30 ans. Pour cette raison, les DJE estimées pour la tranche d'âge des 21-30 ans peuvent être considérées comme valables pour les adultes de plus de 30 ans.

Une démarche probabiliste, par simulations de Monte Carlo en deux dimensions, a été conduite afin de tenir compte séparément de l'incertitude et de la variabilité associée aux paramètres d'entrée. Cette estimation des expositions a fait l'objet d'une publication dans *Environment International* et est présentée sous forme d'article dans la suite de ce chapitre 3.3.

Au vu du nombre de résultats, il a été choisi de présenter dans cet article ceux obtenus pour la tranche d'âge des 2-3 ans car une des plus exposées (évolution au sol, contacts main-bouche plus fréquents, fréquence respiratoire élevée) et une des plus sensibles en terme d'effets (par le développement des principaux systèmes organiques continuant après la naissance). Le détail des résultats obtenus par

tranche d'âge est présenté en matériel supplémentaire. Les DJE agrégées estimées pour les 32 COSV pour un enfant de 2-3 ans couvrent plusieurs ordres de grandeur, avec des valeurs médianes allant de 8,7 pg/kg/j pour le BDE 85 à 1,3 µg/kg/j pour le DiBP. La part de chaque voie dans l'exposition varie selon les composés et liée à leur degré de volatilité. Cependant, l'air apparaît comme le média dominant pour 28 des 32 COSV avec une contribution de l'inhalation d'air et du contact cutané avec la phase gazeuse supérieure à 50 %.

L'analyse de sensibilité a révélé que la variation des résultats de DJE était majoritairement influencée par la variabilité des données de contaminations dans un premier temps, puis par l'incertitude associée aux paramètres physico-chimiques dans un second temps.

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Indoor residential exposure to semivolatile organic compounds in France

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ABSTRACT

Multiple chemicals are emitted in residential accommodation. Aggregate Daily Doses (ADD) (ng/kg-bw/d) were estimated for 32 semivolatile organic compounds (SVOCs) of different chemical families that are frequently detected in French dwellings in both air and settled dust. Daily doses were determined using steady-state models for the population, categorized into 11 age groups covering birth to age 30. Three routes of exposure were taken into account: dust ingestion, inhalation (gaseous and particulate phases) and dermal contact with the gaseous phase of air. Contamination levels were preferentially retrieved from large, nationwide representative datasets. A two-dimensional probabilistic approach was used to assess parametric uncertainty and identify the most influential factors. For children aged 2 to 3 years, ADD estimates spanned orders of magnitude, with median values ranging from 8.7 pg/kg-bw/d for 2,2′,3,4,4′-pentabromodiphenylether (BDE 85) to 1.3 μg/kg-bw/d for di-isobutyl phthalate (DiBP). Inhalation, ingestion and dermal pathway contributed at varying levels, and depending on compound, air was the dominant medium for 28 of the 32 compounds (either by inhalation or dermal contact). Indoor exposure estimate variance was mainly driven by indoor contamination variability, and secondarily by uncertainty in physical and chemical parameters. These findings lend support to the call for cumulative risk assessment of indoor SVOCs.

1. Introduction

Both consumer product use and the production of chemicals have been rising constantly since the mid-20th century, and many of these chemicals are semivolatile organic compounds (SVOCs). SVOCs include compounds from various chemical families: phthalates, bisphenols, polycyclic aromatic hydrocarbons (PAHs), organophosphorus (OPs), organochlorines (OCs), synthetic musks, polychlorinated biphenyls (PCBs) and polybromodiphenylethers (PBDEs).

The health effects of SVOCs have been assessed by numerous studies on both humans and animals; some are suspected of having reprotoxic (Casas et al., 2013; Rubin, 2011), neurotoxic (Baldi et al., 2001; Blanc-Lapierre et al., 2012; Elbaz et al., 2009; Zaganas et al., 2013) or carcinogenic effects (Armstrong et al., 2004; IARC, 2015a, 2015b).

SVOCs are emitted by volatilization from their source materials and contaminate other compartments; in some cases, they can also migrate directly from source (Sukiene et al., 2017). In the indoor environment, they are found in the gas phase, airborne particles, settled dust (Weschler and Nazaroff, 2008) and on any other available surfaces such as walls, ceiling and flooring – as well as on human skin and clothing. In addition to dietary exposure and dermal contact with consumer products, humans are continuously exposed to these chemicals through various pathways, including inhalation of indoor air (gaseous and particulate phases), ingestion of settled dust and dermal contact with indoor air and settled dust (on floor and other surfaces). Many authors have assessed indoor exposure to certain families of SVOCs (phthalates, PBDEs, etc.), taking into account one or more exposure media via oral, respiratory (and sometimes dermal) pathways (Bekö et al., 2013; Gaspar et al., 2014; Linares et al., 2010; Mitro et al., 2016; Roosens et al., 2010; Trudel et al., 2011; Wilson et al., 2003). Mitro et al. (2016) recently estimated indoor exposures based on US dust surveys and an air contamination model. Here, we seek to use measurement data to assess the exposure of a large population and estimate the associated uncertainty.

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The objective of this study was to estimate the indoor exposure of people of various age groups, to 32 SVOCs from different chemical families frequently detected in French dwellings (Blanchard et al., 2014; Mandin et al., 2014, 2016). Three routes of exposure were taken into account: dust ingestion, inhalation of air (gaseous and particulate phases) and dermal contact with the gaseous phase of air. Contamination levels were preferentially retrieved from large, representative datasets. A two-dimensional probabilistic approach was used to assess the uncertainty associated with the different parameters, and identify the most impacting factors.

2. Methods

2.1. Target population

To address exposure across a broad section of the population, we estimated exposures for 11 age groups from birth to age 30 (as an example of an adult), following the U.S. Environmental Protection Agency (U.S. EPA, 2005) recommendations as to which age groups should be considered within a health risk assessment.

2.2. Compounds selection

32 SVOCs were selected on the basis of their health interest (Bonvallot et al., 2010), and because they were detected in both the air and the settled dust of French dwellings (Blanchard et al., 2014; Mandin et al., 2014, 2016).

2.3. Exposure model

The Aggregate Daily Doses (ADD) (ng/kg-bw/d) were assessed by summing internal (uptake) daily doses from dust ingestion ($DD_{ing\text{-}dust}$), inhalation of air (both gaseous and particulate phases) ($DD_{inh\text{-}air}$) and dermal contact with gas phase ($DD_{derm\text{-}gas}$).

Very few studies included the dermal exposure to dust pathway when assessing aggregate exposures to SVOCs. Trudel et al. (2011) studied dermal exposure to 8 PBDEs in dust. Even though they overestimated this pathway using in vitro experimental data with acetone as carrier vehicle (Roper et al., 2006), they found the contribution of dermal exposure to dust to be consistently < 20%, even for the most contaminated region, and for every age group (below 1 year to 65 years of age). Bekö et al. (2013) estimated indoor exposure to five phthalates and found a very low (< 1%) contribution of dermal exposure to dust, in comparison to other pathways. Since this pathway is typically found to be minor and required uptake parameters are ill-suited to dust exposure even when available, dermal exposure to dust was not addressed in this work.

2.4. Equations for exposure dose estimation

Daily Doses (DD) can be estimated in steady-state conditions using the following equations. These were adapted from relationships developed by Bekö et al. (2013) and Weschler and Nazaroff (2012, 2014).

Ingestion of settled dust:

$$DD_{ing\text{-}dust} = \frac{C_{dust} \times DI \times f_{oral} \times f_{dust} \times t}{BW} \quad (1)$$

where C_{dust} is the SVOC concentration in settled dust (ng/g), DI is the amount of dust ingested by an individual per day (g/d), f_{oral} is the oral bioavailability of the SVOC (−), f_{dust} is the bioaccessibility of the SVOC from the dust (−), t is the fraction of time spent in dwellings (−), BW is the body weight (kg), and $DD_{ing\text{-}dust}$ is expressed in ng/kg-bw/d.

Inhalation of indoor air:

$$DD_{inh\text{-}air} = \frac{(C_{part} + C_{gas}) \times IR \times f_{pulm} \times t}{BW} \quad (2)$$

where C_{part} is the SVOC particulate phase concentration (ng/m^3), C_{gas} is the SVOC gas phase concentration (ng/m^3), IR is the inhalation rate for an individual per day (m^3/d), f_{pulm} is the pulmonary bioavailability of the SVOC (−), t is the fraction of time spent in dwellings (−), BW is the body weight (kg), and $DD_{inh\text{-}air}$ is expressed in ng/kg-bw/d.

Dermal contact with the gas phase:

$$DD_{derm\text{-}gas} = \frac{C_{gas} \times k_{p\text{-}g} \times BSA \times t}{BW} \quad (3)$$

where C_{gas} is the SVOC gas phase concentration (ng/m^3), $k_{p\text{-}g}$ is the SVOC transdermal permeability coefficient (m/h), BSA is the body surface area (m^2), t is the daily duration exposure (h/d), BW is the body weight (kg), and $DD_{derm\text{-}gas}$ is expressed in ng/kg-bw/d. The steady-state model adapted by Weschler and Nazaroff (2012, 2014) used to estimate $k_{p\text{-}g}$ is described in more detail in Supplemental Material (see S1). This requires use of the SVOC octanol/water partition coefficients (log (K_{ow})), Henry's law constants (H) and coefficients describing the external transport of a gaseous SVOC from the bulk indoor air to the boundary layer adjacent to the skin (γ_d).

The ADD for a single SVOC for an individual was then calculated by summing the previous doses according to the following equation, and expressed in ng/kg-bw/d:

$$ADD = DD_{ing\text{-}dust} + DD_{inh\text{-}air} + DD_{derm\text{-}gas} \quad (4)$$

2.5. Parameter estimation for exposure model

Parameter distributions were constructed or retrieved from the literature as detailed below. Some of these parameters will be the same for all SVOCs (γ_d, BW, BSA, IR, DI and t) while others will vary from one compound to another (f_{oral}, f_{dust}, f_{pulm}, log (K_{ow}), H, C_{dust}, C_{part} and C_{gas}).

2.5.1. Physical and chemical parameters

For each SVOC, measured or estimated values of log (K_{ow}) and H at 25 °C were retrieved from: online databases - Hazardous Substances Data Bank (HSBD) and ChemIDplus (http://toxnet.nlm.nih.gov/), Chemspider (http://www.chemspider.com/), and Chemicalize (http://www.chemicalize.org/); toxicological and environmental data sheets from the French National Competence Center for Industrial Safety and Environmental Protection (INERIS) (http://www.ineris.fr/substances/fr/page/21); online calculators - Chemexper (https://www.chemexper.com/) and ACD/Labs (http://www.acdlabs.com/); EPI Suite software (U.S. EPA, 2013, v4.1) and the Handbook of Physical-Chemical Properties and Environment Fate for Organic Chemicals (Mackay et al., 2010a, 2010b, 2010c, 2010d). Particular attention was paid to avoiding duplicates (EPI Suite software, HSBD and ChemIDplus often used the same sources for these parameters). Furthermore, only values at the reference temperature of 25 °C were selected, in order to obtain comparable data between compounds and estimate DD at a constant temperature. At least two values were available for each SVOC. Where at least 15 values for log (K_{ow}) and H were available, distributions were fitted. Otherwise, we used either triangular distributions having at least three values (minimum, average and maximum), or uniform distributions for two retrieved values. See Table S1 for corresponding distributions and input parameters for each SVOC.

2.5.2. Contamination data

Contamination data were provided from measurements taken in recent French housing surveys. Concentration levels in settled dust collected from vacuum cleaner bags were retrieved from a national survey covering the 3.6 million French dwellings that were home to at least one child aged 6 months to 6 years in 2008–2009, using 145 samples (Mandin et al., 2014). Concentration levels in airborne Particulate Matter (PM) of 10 μm in diameter were retrieved from a national survey covering the 24.7 million French main residences, using 285

samples (Mandin et al., 2016). PM samples were collected from each living room over a period of one week, and assumed to be representative of each dwelling as a whole. SVOC gas phase concentrations were not available at national scale; data from 30 French dwellings (Blanchard et al., 2014) were used as a surrogate.

Modeling was established regarding the percentage of samples above the limit of detection (LOD) or the limit of quantification (LOQ) for the retrieved studies. For settled dust and PM measurements, lognormal distributions were fitted using summary statistics when > 75% of data were above LOD (Burmaster and Hull, 1997). This concerns 20 and 14 compounds, for settled dust and PM measurements respectively. Where detection frequency ranged from 20 to 75%, the maximum-likelihood estimation (MLE) was used to estimate lognormal distributions (Helsel, 2011; Helsel and Hirsch, 1992). This statistical method could be used to estimate the undetected data in the studies of Mandin et al. (2014, 2016), because sample sizes were large enough - with 145 and 285 samples for dust and PM respectively. The number of compounds concerned was 7 for settled dust and 11 for PM measurements. Where detection frequency ranged from 1 to 20%, custom distribution was modeled with discrete probability for the quantified values, and continuous uniform probability from 0 to LOD and from LOD to LOQ. The number of compounds concerned was 5 for settled dust and 7 for PM measurements. For the gas phase measurements, the Blanchard et al. (2014) sample size (n = 30) was too small to use MLE. So, where detection frequency ranged from 1 to 99%, custom distribution was modeled using continuous uniform probability from 0 to LOQ and discrete probability for the quantified values. For all three media, a literature survey was conducted to retrieve specific data when detection frequency was < 1%. Publications were selected in the following order of preference: conducted in Europe, post-2000 and providing sample size, measurement method, LOD and/or LOQ values and percentage of samples above the LOD and/or LOQ. Where a lower LOD or LOQ was used, other contamination information was used instead of the initially-selected data (Blanchard et al., 2014; Mandin et al., 2014, 2016). See Table S2 for corresponding distributions and input parameters for each SVOC in each medium.

2.5.3. Exposure media properties

Assessment of $DD_{derm\text{-}gas}$ (Eq. 3) requires use of a transdermal permeability coefficient, $k_{p\text{-}g}$, estimated using the specific physical and chemical parameters of each SVOC, and a non-specific mass transport coefficient, γ_d. This last describes the external transport of an SVOC from the gas phase in the core of a room through the boundary layer adjacent to the skin, see Eq. 1 (Supplemental Material). A triangular distribution was modeled for γ_d, using the minimum and maximum values found in the literature and the generally assumed value of 6 m/h as most likely (Pandrangi and Morrison, 2008; Tamas et al., 2006; Weschler and Nazaroff, 2008). See Table S3 for corresponding distribution and input parameters.

2.5.4. Bioaccessibility and bioavailabilities

Bioaccessibility in dust (f_{dust}) is the fraction of pollutant released from settled dust into the gastrointestinal tract and available for absorption (Rostami and Juhasz, 2011). For each SVOC, f_{dust} was retrieved from the literature survey performed by Raffy et al. (2016). Oral bioavailability (f_{oral}) is the fraction of a contaminant reaching the digestive system and absorbed into systemic circulation (Rostami and Juhasz, 2011). Pulmonary bioavailability (f_{pulm}) is the fraction of a contaminant reaching the alveolar system and absorbed into systemic circulation. For each SVOC, f_{oral} and f_{pulm} were retrieved from the following online databases: the HSBD (https://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB) and the Agency for Toxic Substances and Disease Registry (ATSDR) (https://www.atsdr.cdc.gov/). For each compound displaying at least three available values, triangular distributions were modeled (minimum, average and maximum values). Where only two values were retrieved, uniform distributions were modeled (minimum and maximum). Where only a single value was available, triangular distributions were modeled between this value (as the likeliest), and the minimum and the maximum values retrieved from other compounds belonging to the same chemical family. Finally, if no value was found for an SVOC, a uniform distribution was modeled between the minimum and the maximum values found for the other compounds from the same chemical family - or from the entire studied chemical families taken together if no other compound from the same chemical family was assessed. See Table S4 for corresponding distributions and input parameters for each SVOC.

2.5.5. Human body parameters

The World Health Organization (WHO, 2006) has identified and suggested common critical life stages for use in exposure and risk assessment. Because these were not available for every parameter and age group for populations living in France, we used the U.S. EPA Exposure Factors Handbook (U.S. EPA, 2011). The potential influence of this is covered in the discussion section. We compiled the distribution of human body weight (BW), body surface area (BSA), dust ingestion (DI), inhalation rate (IR) and time spent in dwellings (t). Lognormal distributions were used for BW, BSA and DI. Normal distributions were used for IR and t. See Table S5 for corresponding distributions and input parameters.

2.6. Simulation

DD from all three routes of exposure (Eqs. (1) to (3)) and ADD (Eq. (4)) were estimated using Crystal Ball® software (Oracle©, version 11.1.1.3.00). Latin Hypercube two-dimensional simulations were carried out with 500,000 runs for each SVOC, and each age group. Two-dimensional simulations take into account both the uncertainty (lack of knowledge about a parameter) and the variability (heterogeneity of a parameter in a population) of the input parameters. The following parameters were considered variable (i.e. high variability in relation to uncertainty): C_{dust}, C_{part}, C_{gas}, γ_d, BW, BSA, IR and t, whereas log (K_{ow}), H, f_{oral}, f_{dust} and f_{pulm}, were considered uncertain. DI was considered both uncertain and variable. Sensitivity analysis was performed in a one-dimensional simulation by assessing the contribution of each input parameter to ADD variance (the output), using linear regression.

3. Results

ADD (ng/kg-bw/d) estimates for the 32 SVOCs for children aged 2 to 3 years are shown in Fig. 1. We are presenting results for this specific segment because young children are more vulnerable than the rest of the population in terms of exposure to contaminants (due to more frequent contact with the ground and deposited dust, carrying objects in their mouths, higher inhalation rates, etc.) and more sensitive in terms of effects (due to ongoing development of the main organ systems, which continues after birth). Detailed results for ADD and the three DD from each exposure route for all 11 age groups (birth to age 30) are shown in Tables S8 to S18. ADD estimations spanned orders of magnitude, with median values ranging from 8.7 pg/kg-bw/d for 2,2′,3,4,4′-pentabromodiphenylether (BDE 85) to 1.3 μg/kg-bw/d for diisobutyl phthalate (DiBP) for children aged 2 to 3 years. Variability of ADD (relative interpercentile range, see Table S6) ranged from 1.2 for 2,2′,4,4′,5-pentabromodiphenylether (BDE 99) to 12 for 2,3,3′,4,4′-pentachlorobiphenyl (PCB 105), with a median value of 4. The median uncertainty on the mean was 40%, ranging from 11% for the benzo[*a*]pyrene to 230% for 2,3′,4,4′,5-pentachlorobiphenyl (PCB 118) (see detailed relative errors in Table S13).

The relative contribution of exposure pathways to aggregated median exposure is presented in Fig. 1 (bottom panel) for children aged 2 to 3 years. The relative contributions made by each route of exposure to total indoor estimates differ by compound, and could be related to their degree of volatility. For the most volatile SVOCs - that is those

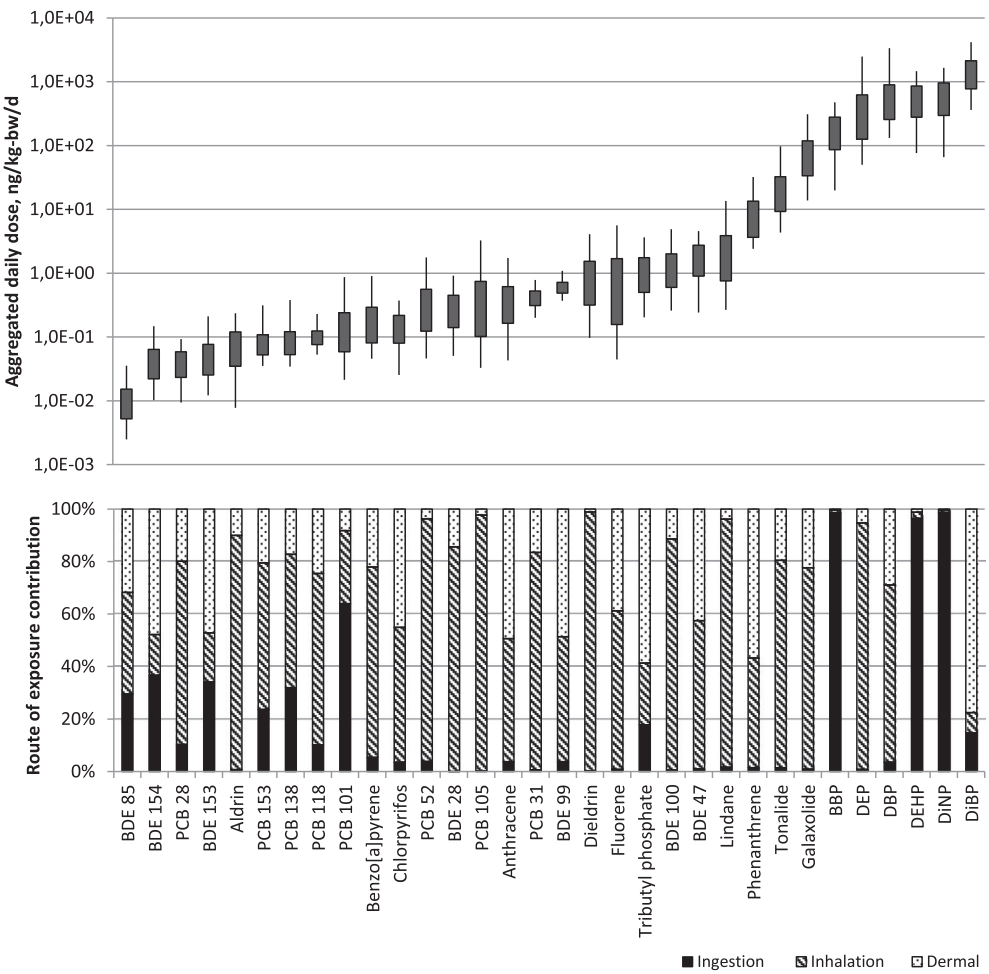

Fig. 1. Top panel of the graph shows Aggregate daily dose of each SVOC for a child aged 2 to 3 years (ng/kg-bw/d), percentiles 5th, 25th, 75th and 95th are presented in box plot format. The bottom panel of the graph shows the contribution made by each route of exposure (ingestion, inhalation and dermal exposure from air) to total indoor exposure, based on the median value estimated for each SVOC for children aged 2 to 3 years (ng/kg-bw/d).

compounds having an octanol-air partition coefficient (log (K_{oa})) value of 9 or less (see Table S1) and expected to be primarily gaseous (Weschler and Nazaroff, 2012), inhalation and dermal contact with the gas phase were the dominant routes of exposure: fluorene, anthracene, aldrin, dieldrin, tonalide, galaxolide, tributylphosphate, diethyl phthalate (DEP), dibutyl phthalate (DBP), DiBP and 2,4,4′-trichlorobiphenyl (PCB 28), 2,4′,5-trichlorobiphenyl (PCB 31) and 2,2′,5,5′-tetrachlorobiphenyl (PCB 52). For less volatile SVOCs - that is those compounds having a log (K_{oa}) value of 13 or greater (see Table S1) and expected to be primarily in the particle phase (Weschler and Nazaroff, 2012), dust ingestion was the dominant route of exposure: diethylhexyl phthalate (DEHP), di-isononyl phthalate (DiNP) and 2,2′,4,4′,5,6′-hexabromodiphenylether (BDE 154). The contribution made by different pathways was more contrasted for SVOCs having a log (K_{oa}) value of between 9 and 13 (see Table S1). On the whole, air was the dominant exposure medium (sum of inhalation and dermal contact > 50% of ADD) for 28 compounds out of 32, while dust was the major contributor for DEHP, DiNP, benzyl butyl phthalate (BBP) and 2,2′,4,5,5′-pentachlorobiphenyl (PCB 101). Overall, dust ingestion is more contributive to exposure for less volatile chemicals, although this is not the case with BBP and PCB 101, both of which are found in relatively high concentrations in dust.

Relative contributions of exposure pathways for P95 values were similar to median values. Notable exceptions were that higher contributions from dust ingestion were found for PCB 118, 2,2′,3,4,4′,5′-hexachlorobiphenyl (PCB 138) and 2,2′,4,4′,5,5′-hexachlorobiphenyl (PCB 153), and higher contributions from inhalation were found for benzo[*a*]pyrene and DBP.

The main sensitivity analysis results are shown in Fig. 2 (see Table S7 for detailed results). These reveal that contamination parameters are most influential: C_{gas}, C_{part} and C_{dust}, the only exception being H for BDE 99. Their relative contributions to ADD variance ranged from 30% for galaxolide (C_{part}) and BDE 99 (H) to 89% for fluorene (C_{gas}). For most compounds, the other influential parameters (having contributions higher than 10%) are the other contamination parameters: C_{gas}, C_{part} and C_{dust}, and also f_{pulm}. For some compounds, other influential parameters are f_{dust} (DEHP and DiNP) alongside physical and chemical parameters: log (K_{ow}) and H (lindane and BDE 99). Furthermore, compounds have been ranked by volatility in Fig. 2 (based on their log (K_{oa}) values), from most volatile (fluorene) to least volatile (DiNP). Among the most volatile SVOCs, C_{gas} tended to be the more influential parameter, while C_{dust} and C_{part} appeared influential for the least volatile. Lastly, we note that within each age group, human parameters were not influential.

ADD (ng/kg-bw/d) estimates for the 32 SVOCs for four age groups are shown in Fig. 3: infants aged 0 to 1 months, infants aged 1 to 3 months, children aged 2 to 3 years and adults aged 21 to 30 years. As expected, ADD decreases with age because of increasing BW - except within the [0–1 month] category where the dust ingestion rate equals 0 mg, and ADD may be lower in comparison with other groups. This is true in particular of compounds making a major contribution to dust ingestion (PCB 101, BBP, DEHP and DiNP). Detailed results for ADD across all 11 age groups (birth to age 30) are shown in Tables S8 to S18.

4. Discussion

Indoor exposure to 32 SVOCs was modeled using contamination measurements from dwellings and human body parameters. ADD

SVOC	Relative contribution (%)							
	[10-20]	[20-30]	[30-40]	[40-50]	[50-60]	[60-70]	[70-80]	[80-90]
Fluorene								**Cgas**
DEP	Cdust	fpulm			**Cgas**			
Anthracene								**Cgas**
Phenanthrene	Cdust						**Cgas**	
PCB 28			fpulm	**Cgas**				
PCB 31		fpulm			**Cgas**			
Tonalide		fpulm		**Cpart**				
Aldrin			fpulm		**Cgas**			
Dieldrin			fpulm		**Cpart**			
Galaxolide		fpulm Cgas	**Cpart**					
Tributylphosphate							**Cgas**	
DiBP		Cdust				**Cgas**		
PCB 52	Cdust	fpulm			**Cpart**			
DBP		fpulm			**Cpart**			
Lindane	fpulm H	Cpart	**Cgas**					
Chlorpyrifos		fpulm			**Cgas**			
BBP	Cpart				**Cdust**			
PCB 101	Cgas					**Cdust**		
BDE 28	fpulm	Cpart		**Cgas**				
PCB 138		Cgas				**Cdust**		
PCB 153			Cgas	**Cdust**				
PCB 118		Cdust			**Cgas**			
PCB 105	fpulm					**Cpart**		
BDE 47								**Cgas**
Benzo[a]pyrene								**Cpart**
BDE 99		Kow	**H**					
BDE 85							**Cgas**	
BDE 100	fpulm					**Cpart**		
BDE 153	Cdust					**Cgas**		
DEHP	fdust					**Cdust**		
BDE 154		Cdust				**Cgas**		
DiNP			fdust	**Cdust**				

Fig. 2. Relative contribution (%) of key parameters (C_{gas}, C_{part}, C_{dust}, f_{pulm}, f_{dust}, log (K_{ow}) and H) to total variation of Aggregate daily doses from exposures to 32 indoor SVOCs (ng/kg-bw/d) for children aged 2 to 3 years. Only relative contributions above 10% are represented. Bold font indicates the more influential parameter for each SVOC. Compounds are ranked according to their volatility (based on their log (K_{oa}) values) from the most volatile (fluorene) to the least volatile (DiNP).

spanned orders of magnitude from 8.7 pg/kg-bw/d to 1.3 μg/kg-bw/d. Inhalation, ingestion and dermal pathway all contributed, though differently across compounds. Indoor exposure estimations were influenced more by variability in indoor concentrations (C_{gas}, C_{part} and C_{dust}) than by uncertainty in physical and chemical parameters.

Study strengths include: 1) estimation of indoor exposure to numerous SVOCs from different chemical families via gas- and particle-phase inhalation, dermal contact with gas phase, and ingestion of settled dust; 2) use of field measurements in dust, particulate and gaseous phases; 3) use, when available, of large and nationwide representative datasets; 4) choice of a two-dimensional probabilistic approach, and 5) consideration of many age groups.

Study limitations include: 1) use of an exposure model that neglects dynamic conditions; 2) use of different data sets for different exposure media, and 3) uncertainty analysis being restricted to parameter uncertainty.

We used steady-state models to estimate indoor exposure to SVOCs. Because indoor air measurements were performed over a period of one week, and settled dust being collected in a vacuum cleaner, we assumed that equilibrium had been reached. Because we frequently move from one environment into another, or between rooms having different concentrations, equilibrium is rarely achieved for the transfer from air to skin. A transient model developed by Gong et al. (2014) considered convective mass transfer resistance in the boundary air layer adjacent

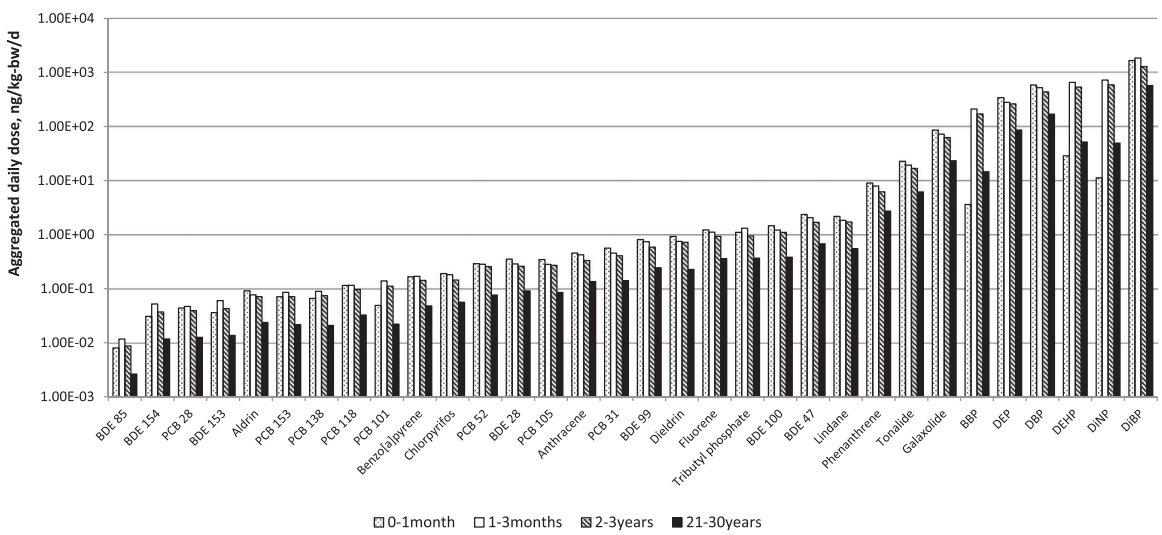

Fig. 3. Aggregate daily dose of each SVOC for four age groups (ng/kg-bw/d).

to the skin. Morrison et al. (2016) have recently improved this model by including skin surface lipids, which increase overall resistance to SVOC uptake from air. However, because these models require parameters that are not available for all compounds, default parameters are employed - rendering a probabilistic assessment difficult.

For contamination data in the three media when the detection frequency was < 1% (Blanchard et al., 2014; Mandin et al., 2014, 2016) a literature survey was conducted to retrieve other contamination information, which was then employed (instead of the initially-targeted data) where a lower LOD or LOQ was used by the authors (see Table S2). This concerned settled dust and gas phase concentrations for the 2,4,4′-tribromodiphenylether (BDE 28), and gas phase concentration alone for 12 other SVOCs: benzo[*a*]pyrene, PCB 31, PCB 105, PCB 118, PCB 138, PCB 153, BDE 47, BDE 85, BDE 99, 2,2′,4,4′,6-pentabromodiphenylether (BDE 100), 2,2′,4,4′,5,5′-hexabromodiphenylether (BDE 153) and BDE 154.

To put our results into perspective, this indoor aggregate multimedia and multipathway exposure assessment was compared to the few other studies investigating the same exposure pathways, namely: Bekö et al. (2013), Gaspar et al. (2014) and Mitro et al. (2016), who investigated phthalates and galaxolide for children aged 3 to 6 years in Denmark, California (US) and 14 states of the US, respectively. Our ADD estimated median values for children aged 3 to 6 years (see Table S14) were compared to: estimated median values for DBP and DEHP (Bekö et al., 2013; Gaspar et al., 2014); estimated median values for DiBP, BBP and DEP (Bekö et al., 2013), and estimated average values for DBP, DEHP, DiBP, BBP, DEP and galaxolide (Mitro et al., 2016). Similar results were found for DBP, DEHP and DEP. For DiBP, we found a median value equal to 1.1 μg/kg-bw/d, consistent with the 1.5 μg/kg-bw/d found by Bekö et al. (2013). Using a dust contamination level for this compound that was seven times lower, Mitro et al. (2016) found a lower exposure level equal to 0.1 μg/kg-bw/d. This difference in concentration data between French and US samples may also reflect a shift in the use of phthalates as a result of changes to the formulation of plasticizers. For BBP, we found a median value equal to 0.1 μg/kg-bw/d, consistent with the 0.2 μg/kg-bw/d of Mitro et al. (2016). Using a dust contamination level for this compound that was four times lower, Bekö et al. (2013) found a lower exposure level equal to 0.01 μg/kg-bw/d. Regarding galaxolide, our exposure level of 0.05 μg/kg-bw/d is consistent with Mitro et al. (2016) who found 0.1 μg/kg-bw/d - in line with dust contamination that was twice as high as ours.

Pathway contributions were found to be similar to Mitro et al. (2016) for DBP, DEP and galaxolide, with inhalation as the main route of exposure (> 50%), followed by dermal absorption from the gas phase and dust ingestion. Pathway contribution estimates from Bekö et al. (2013) for DiBP, BBP and DEHP are also similar to our findings, with total uptake dominated by dermal absorption from the gas phase for DiBP, and dust ingestion for BBP and DEHP. The results of the present study were also comparable to Gaspar et al. (2014), with dust ingestion dominating total uptake of DEHP.

In addition to the indoor exposure in dwellings assessed by this study, other sources of exposure (e.g. diet and personal care products) and other indoor environments (e.g. schools and offices) for many of these compounds contribute to total exposure, as well as direct dermal contact with surfaces. The use of personal care products, directly applied to skin or inhaled from aerosols, could have a non-negligible contribution to total exposure for some compounds, e.g., for certain phthalates (Romero-Franco et al., 2011) and musks (Zhang et al., 2017). Most of the studies addressing SVOC exposure assessment also looked at dietary ingestion (Beamer et al., 2012; Duggan et al., 2003; Lorber, 2007; Roosens et al., 2010; Trudel et al., 2011; Wilson et al., 2003; Wormuth et al., 2006). This could naturally lead to higher ADD estimates and different pathway contributions. Diet has been shown to be an important source of exposure for certain compounds: e.g. some PBDEs (Trudel et al., 2011) and some phthalates (Wilson et al., 2003). However, several authors who have performed exposure assessments on both indoor and diet exposure found that dietary ingestion was not the main route of exposure for chlorpyrifos (Beamer et al., 2012; Duggan et al., 2003), DEP, BBP and DiNP (Wormuth et al., 2006), some PBDEs (Lorber, 2007), some PCBs and some OCs (Wilson et al., 2003). For certain compounds, exposure via dietary ingestion could also equal exposure via non-dietary ingestion: e.g. DEHP (Wormuth et al., 2006), and anthracene, phenanthrene, benzo[*a*]pyrene and fluorene (Wilson et al., 2003). To put our results in perspective, we compared them to those of the French infant total diet study (ANSES, 2016a, 2016b). We compared to lower bound (LB) and upper bound (UB) median estimates for children aged 2 to 3 years. For 6 PCBs (sum of PCB 28, 52, 101, 138, 153 and 2,2′,3,4,4′,5,5′-heptachlorobiphenyl (PCB 180)) our median residential indoor ADDs were about one order of magnitude lower than dietary exposure estimates (LB and UB). For 7 PBDEs (sum of BDE 28, 47, 99, 100, 153, 154 and 2,2′,3,4,4′,5′,6-heptabromodiphenylether (BDE 183)) they were about one order of magnitude higher (LB and UB). For DEHP they were of the same order of magnitude (LB and UB). For DiNP and lindane they were of the same order of magnitude as the LB estimates and about one order of magnitude lower than the UB. For BBP, DEP and DBP they were of the order of magnitude of UB estimates, and one order of magnitude higher than the LB. For DiBP they were about one or two orders of magnitude higher than UB and LB respectively. For chlorpyrifos, dieldrin and aldrin they were of the same order of magnitude, in comparison with the LB estimates, and about two orders of magnitude lower, in comparison with the UB.

Compared to more traditional deterministic approaches, probabilistic methods (e.g. Monte Carlo simulations) have the main advantage of addressing input parameters featuring both uncertainty and variability. ADD estimations were mainly dependent on variability in indoor concentrations (C_{gas}, C_{part} and C_{dust}), and secondarily by uncertainty in f_{pulm} and physical and chemical parameters. Uncertainty of parameters is related to lack of total knowledge, whereas data variability refers to true heterogeneity. An interesting finding is that although input parameter uncertainty has been accused of causing broad uncertainty in exposure estimates (Pelletier et al., 2017; Salthammer and Schripp, 2015), it appeared to contribute less to total variance of ADD than did variability. For every compound but one, variability of a concentration explains at least 40% of ADD variance; in half of all cases, this exceeded 60%. Concentrations of a chemical within dwellings span orders of magnitude, especially as a result of the presence (or absence) of a source in the dwelling. Physical and chemical parameters can either be measured experimentally or calculated using other chemical properties. Depending on which of these methods is used, it follows that values vary by one order of magnitude or more (Finizio et al., 1997) - and these uncertainties are propagated in the calculation of $DD_{derm\text{-}gas}$ and then ADD. Up to 34% of ADD variation for aldrin could be explained by uncertainty in f_{pulm} (see Table S7) because data for most of the SVOCs were unavailable. Indeed, data were available for just two compounds: 2,2′,4,4′-tetrabromodiphenylether (BDE 47) and benzo[*a*]pyrene, leading to modeling of uniform distribution between 0 and 100% for most compounds (see Table S4) and to potential overestimation of inhalation exposure. The same limit was encountered for the other uptake fractions (f_{oral} and f_{dust}), though to a lesser extent. For most SVOCs, in respect of f_{oral}, even where pharmacokinetics studies were available and provided qualitative evidence that the SVOC was absorbed following oral exposure, no quantitative data describing in vivo oral absorption were available in the literature. Moreover, in laboratory animals, absorption of a compound can also depend strongly on experimental parameters, such as the carrier vehicle employed (Huwe et al., 2008). For example, gastrointestinal lindane bioavailability in rats ranged from 6% when the compound was suspended in water to 99% when given in oil. A further aspect is that we used PM_{10} measurements, whereas a smaller sampling fraction would have been more representative of respirable particles - this may result in an overestimation of the inhalation pathway for those SVOCs mainly present in the particulate phase (BDE 47, BDE 99, benzo[*a*]pyrene, PCB 118, PCB 138 and PCB 153). Human

body parameters (BW, BSA, IR, DI and t) are highly variable and, to a lesser extent, uncertain. Özkaynak et al. (2011) found significant uncertainty on DI, and this result led us to consider both uncertainty and variability for this parameter in our study. Nevertheless, we found that human body parameters made a marginal or null contribution (see Table S7) to the variance of ADD for a child aged 2 to 3 years, for each SVOC. It is however important to bear in mind both that we ran the model age-group by age-group, and that these parameters can have a broader impact when applied to a more diverse population.

Recent studies have investigated and modeled the clothing effect. Morrison et al. (2016) have shown that frequency of bathing and changing clothes were influential in terms of dermal uptake. In addition, introduction to the model of a skin surface lipid film, and its interactions with clothing, may affect results. The authors assessed the influence of clothing on the dermal uptake of two phthalates (DEP and DBP). They found that clean clothes were protective against air pollutants, whereas worn clothes, because they had adsorbed air pollutants, increased dermal uptake. Because only clean clothes could be considered protective, we decided to not take into account the role of clothing in this study, making the assumption that the total body surface area was exposed to the gaseous phase.

5. Conclusions

This indoor aggregate multimedia and pathway exposure assessment considered a wide range of pollutants, across a broad population. It reveals that exposure spanned orders of magnitude, from pg/kg-bw/d to μg/kg-bw/d and was mainly dependent on indoor SVOC contaminations. Within the boundaries of the conceptual model we used, exposure variability overwhelmed its uncertainty. Air was the dominant medium for most compounds, either by inhalation or dermal contact. Along with evidence of these compounds causing similar toxic effects (Fournier et al., 2014; Mitro et al., 2016), these findings lend support to the call for cumulative risk assessment of indoor SVOCs.

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The authors declare having no competing financial interests.

Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.envint.2017.08.024.

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SUPPLEMENTAL MATERIAL

Indoor exposure to semivolatile organic compounds in France

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References

S1. Calculating transdermal permeability coefficient

The transdermal permeability coefficient, $k_{p\text{-}g}$ (m/h), is calculated using a resistors-in-series approach proposed by Weschler and Nazaroff (2012):

$$\frac{1}{k_{p-g}} = \frac{1}{\gamma_d} + \frac{1}{k_{p-b}} \tag{1}$$

Where γ_d is the coefficient that describes the external transport of an SVOC from the gas phase in the core of a room through the boundary layer adjacent to the skin (m/h) and $k_{p\text{-}b}$ is the compound's permeability coefficient which describes the SVOC's transport from the gas phase at the skin surface through the epidermis to the dermal capillaries (m/h) and is estimated as follows:

$$k_{p-b} = \frac{k_{p-w}}{K_{gw}} \tag{2}$$

Where K_{gw} is the equilibrium partition coefficient for the SVOC between the gas phase and water and can be estimated as follows (Meylan and Howard, 1991):

$$K_{gw} = \frac{H}{RT} \tag{3}$$

Where H is the Henry's law constant (Pa.m^3/mol), R is the gas constant (8.314 Pa.m^3/mol.K) and T is temperature (K).

In Equation 2, $k_{p\text{-}w}$ is the compound's permeability coefficient through the stratum corneum/viable epidermis when the vehicle in contact with skin is water (cm/h) and is estimated as follows:

$$k_{p-w} = \frac{k_{p-cw}}{1+B} \tag{4}$$

Where $k_{p\text{-}cw}$ is the compound's permeability coefficient through the stratum corneum when the vehicle in contact with the skin is water (cm/s) and is estimated using Equation 5 (Mitragotri, 2002):

$$\log(k_{p-cw}) = 0.7 \times \log(K_{ow}) - 0.0722 \times MW^{\frac{2}{3}} - 5.252 \tag{5}$$

Where K_{ow} is the species octanol-water partition coefficient and MW is the molecular weight of the compound (g/mol).

In Equation 4, B is the ratio of the stratum corneum permeability ($k_{p\text{-}cw}$) to the viable epidermis permeability for the selected compound and is estimated using Equation 6 (Bunge et al., 1995):

$$B = \frac{k_{p-cw} \times MW^{0.5}}{2.6} \tag{6}$$

Where $k_{p\text{-}cw}$ is expressed in cm/h.

Table S1: Distribution shapes and input parameters of SVOC physical and chemical parameters: molecular weight (MW), octanol/water partition coefficient (K_{ow}) and Henry's law constant (H), used for the dose estimation regarding the number of values retrieved from literature. Octanol/air partition coefficient (K_{oa}) employed to classify SVOC regarding their volatility degree are also displayed

SVOCs	CAS number	Log K_{oa}[1]	MW (g/mol)[1]	Log K_{ow}[1,2,3]			H (Pa.m^3/mol)[1,2,3]		
				Number of values	Distribution shape	Parameters	Number of values	Distribution shape	Parameters
Aldrin	309-00-2	8.08	364.92	22	Logistic	scale=0.55 mean=5.97 max=7.5	11	Triangular	min=1.42 likeliest=33.58 max=91.23
Anthracene	120-12-7	7.55	178.24	32	Logistic	scale=0.2 mean=4.48 max=5.34	10	Triangular	min=1.96 likeliest=5.11 max=8.68
BBP	85-68-7	9.02	312.37	20	Logistic	scale=0.3 mean=4.63 max=5.08	10	Triangular	min=0.00022 likeliest=0.25 max=0.84
BDE100	189084-64-8	11.98	564.69	10	Triangular	min=6.51 likeliest =7.02 max=8.03	4	Triangular	min=0.07 likeliest=0.23 max=0.38
BDE153	000006-01-7	12.15	643.59	10	Triangular	min=6.86 likeliest =7.47 max=8.55	4	Triangular	min=0.05 likeliest=0.15 max=0.34
BDE154	207122-15-4	13.27	643.59	9	Triangular	min=6.86 likeliest =7.76 max=8.83	3	Triangular	min=0.048 likeliest=0.15 max=0.24
BDE28	41318-75-6	9.5	406.9	11	Triangular	min=5.47 likeliest =5.8 max=6.7	5	Triangular	min=0.75 likeliest=2.13 max=5.1
BDE47	5436-43-1	10.53	485.8	13	Triangular	min=5.87 likeliest =6.31 max=7.39	5	Triangular	min=0.3 likeliest=0.93 max=1.5
BDE85	182346-21-0	11.66	564.69	10	Triangular	min=6.64 likeliest =7.1 max=8.02	4	Triangular	min=0.11 likeliest=0.65 max=2.03
BDE99	60348-60-9	11.31	564.69	13	Triangular	min=6.61 likeliest =7.03 max=8.19	5	Triangular	min=0.12 likeliest=0.65 max=2.03
Benzo[a]pyrene	50-32-8	10.86	252.32	28	Logistic	scale=0.29 mean=6.28 max=7.99	6	Triangular	min=0.021 likeliest=0.051 max=0.082
Chlorpyrifos	2921-88-2	8.88	350.59	23	Min Extreme	scale=0.27 likeliest=5.03 max=5.27	13	Triangular	min=0.0041 likeliest=1.36 max=7.9
DBP	84-74-2	8.63	278.35	26	Weibull	min=3.23 mean=4.48 max=5.2	12	Triangular	min=0.028 likeliest=0.17 max=0.46
DEHP	117-81-7	12.56	390.57	27	Min Extreme	scale=1.33 likeliest=7.9 max=9.68	16	Beta	min=0.0041 alpha=0.33 beta=1.03 max=5.04
DEP	84-66-2	7.02	222.24	18	Logistic	scale=0.21 mean=2.57 max=3.22	9	Triangular	min=0.002 likeliest=0.56 max=4.71
DiBP	84-69-5	8.41	278.35	13	Triangular	min=4.11 likeliest =4.32 max=4.47	4	Triangular	min=6.43E-07 likeliest=0.069 max=0.133
Dieldrin	60-57-1	8.13	380.91	27	Logistic	scale=0.46 mean=4.85 max=6.2	14	Triangular	min=0.02 likeliest=1.71 max=5.88

DiNP	28553-12-0	13.59	418.62	7	Triangular	min=8.6 likeliest =9.04 max=9.4	5	Triangular	min=0.15 likeliest=11 max=41.4
Fluorene	86-73-7	6.79	166.22	22	Min Extreme	scale=0.17 likeliest=4.2 max=4.51	11	Triangular	min=3.5 likeliest=9.16 max=16.92
Lindane	58-89-9	8.84	290.83	34	Logistic	scale=0.2 mean=3.68 max=5.32	26	Lognormal	location=0.0019 mean=1.88 SD=14.38
Galaxolide	1222-05-5	8.17	258.41	6	Triangular	min=3.42 likeliest =5.41 max=6.26	2	Uniform	min=0.077 max=13.37
PCB101	37680-73-2	9.06	326.44	33	Logistic	scale=0.3 mean=6.44 max=7.64	14	Triangular	min=9.12 likeliest=25.59 max=47.19
PCB105	32598-14-4	10	326.44	18	Min Extreme	scale=0.35 likeliest=6.72 max=7.14	11	Triangular	min=2.43 likeliest=22.43 max=83.59
PCB118	31508-00-6	9.82	326.44	16	Max Extreme	scale=0.24 likeliest=6.59 max=7.42	10	Triangular	min=3.94 likeliest=20.96 max=40.8
PCB138	35065-28-2	9.51	360.88	20	Lognormal	location=5.99 mean=7.01 SD=0.38	11	Triangular	min=2.6 likeliest=4.05 max=5.09
PCB153	35065-27-1	9.73	360.88	36	Lognormal	location=5.96 mean=7.05 SD=0.44	19	Lognormal	location=0.01 mean=21.47 SD=22.79
PCB28	7012-37-5	7.71	257.55	17	Min Extreme	scale=0.13 likeliest=5.67 max=5.81	10	Triangular	min=17.02 likeliest=29.22 max=38.51
PCB31	16606-02-3	7.92	257.55	20	Max Extreme	scale=0.23 likeliest=5.67 max=6.33	12	Triangular	min=17.02 likeliest=30.95 max=94.13
PCB52	35693-99-3	8.47	291.99	22	Min Extreme	scale=0.23 likeliest=6.03 max=6.34	24	Max Extreme	scale=14.31 likeliest=25.72 max=94.15
Phenanthrene	85-01-8	7.57	178.24	39	Logistic	scale=0.11 mean=4.49 max=5.15	11	Triangular	min=2.38 likeliest=3.83 max=5.55
Tonalide	21145-77-7	7.95	258.41	5	Triangular	min=3.98 likeliest =5.47 max=6.37	3	Triangular	min=1.1 likeliest=6.49 max=14.08
Tributyl phosphate	126-73-8	8.24	266.32	12	Triangular	min=2.5 likeliest =3.86 max=4.26	4	Triangular	min=0.14 likeliest=0.28 max=0.53

[1]EPI Suite software (US EPA, v4.1)

[2]Online databases (Hazardous substances data bank (HSBD), ChemIDplus, Chemspider, Chemicalize and INERIS); Chemexper; ACD/Labs calculators; Mackay et al. (2010a; 2010b; 2010c; 2010d)

[3]Measured or estimated values were retrieved at 25°C

Table S2: Distribution shapes and input parameters of SVOC concentration in settled dust, particulate and gaseous phases used for the dose estimation regarding the percent of data above LOD or LOQ (from Mandin et al. 2014; Mandin et al. 2016; Blanchard et al. 2014)

SVOCs	C_{dust} (ng/g)			C_{part} (ng/m³)			C_{gas} (ng/m³)		
	% > LOD	Distribution shape	Parameters	% > LOD	Distribution shape	Parameters	% > LOQ	Distribution shape	Parameters
Aldrin	7	Custom	[0-5.3]=93% [5.3-13.2]=4% max=1834.5	1	Custom	[0-0.002]=99% [0.002-0.004]=0% max =0.02	7	Custom	[0-0.6]=93% max=1.2
Anthracene	92	Lognormal	p50=49.5 p75=111.4 p95=289.2	98	Lognormal	GM=0.01 GSD=0.003 p95=0.05	47	Custom	[0-0.6]=53% max=5.5
BBP	100	Lognormal	GM=15470 GSD=5002 p95=439300	98	Lognormal	GM=2 GSD=5 p95=31.9	20	Custom	[0-1.3]=80% max=6.5
BDE100	38	Lognormal	GM=7.1 GSD=2.8 p75=13	47	Lognormal	GM=2.7 GSD=2.3 P75=4.3	0	Lognormal[2]	AM=0.2 SD=0.2 p75=0.2
BDE153	19	Custom	[0-21.1]=80% [21.1-52.6]=17% max =222.5	7	Custom	[0-0.004]=93% [0.004-0.008]=4% max =0.1	0	Lognormal[2]	AM=0.03 SD=0.06 p75=0.02
BDE154	19	Custom	[0-21.1]=80% [21.1-52.6]=17% max =160.5	3	Custom	[0-0.004]=97% [0.004-0.008]=2% max =0.1	0	Lognormal[2]	AM=0.02 SD=0.03 p75=0.01
BDE28	7	Lognormal[1]	GM=0.6 p50=0.3 p95=1.7	22	Lognormal	GM=0.4 GSD=2 P75=0.4	0	Lognormal[2]	AM=0.3 SD=0.4 p75=0.4
BDE47	86	Lognormal	p50=17.4 p75=36.7 p95=122.6	88	Lognormal	p50=0.01 p75=0.03 p95=0.1	0	Lognormal[2]	AM=2.5 SD=2.4 p75=3.9
BDE85	13	Custom	[0-5.3]=87% [5.3-13.2]=10% max =103	1	Custom	[0-0.004]=99% [0.004-0.008]=0.4% max =0.09	0	Lognormal[2]	AM=0.01 SD=0.02 p75=0.008
BDE99	90	Lognormal	p50=24.5 p75=41.5 p95=161.7	87	Lognormal	p50=0.009 p75=0.02 p95=0.06	0	Lognormal[2]	AM=0.76 SD=1.1 p75=0.7
Benzo[a]pyrene	99	Lognormal	GM=102.6 p25=32.6 p95=637.2	100	Lognormal	GM=0.1 GSD=4.9 p95=1.1	0	Triangular[3]	min=0.004 GM=0.007 max=0.01
Chlorpyrifos	67	Lognormal	GM=7.5 GSD=4 p75=11.5	10	Custom	[0-0.04]=90% [0.04-0.08]=7% max =0.5	7	Custom	[0-0.6]=93% max=1.2
DBP	100	Lognormal	GM=13890 GSD=2204 p95=55040	72	Lognormal	GM=1145.3 GSD=4.6 P75=3289.8	100	Lognormal	AM=94.6 SD=51 location=-44.1
DEHP	100	Lognormal	GM=299800 GSD=2293 p95=1171000	100	Lognormal	GM=52.57 p25=22.34 p95=389.4	7	Custom	[0-10]=93% max=20.2
DEP	98	Lognormal	p50=3239 p75=5322 p95=27800	62	Lognormal	GM=960.4 GSD=4.3 P75=2557.6	100	Lognormal	AM=204.1 SD=164.2 location=9.9
DiBP	100	Lognormal	GM=25300 GSD=2755 p95=176900	96	Lognormal	p50=0.9 p75=2.8 p95=22.9	100	Lognormal	AM=649.7 SD=620.4 location=7.7
Dieldrin	53	Lognormal	GM=8 GSD=2.9 p75=13	23	Lognormal	GM=4.1 GSD=2.4 P75=4.1	10	Custom	[0-0.6]=90% max=5.5
DiNP	100	Lognormal	GM=159900 GSD=2761 p95=906700	99	Lognormal	GM=8.7 GSD=3 p95=50.1	10	Custom	[0-25]=90% max=35.6
Fluorene	99	Lognormal	GM=41.5 p25=31.7 p95=93.8	99	Lognormal	GM=0.03 p25=0.01 p95=0.2	33	Custom	[0-0.6]=67% max=33.5
Lindane	94	Lognormal	p50=24.7 p75=43.2 p95=252.7	56	Lognormal	GM=3.7 GSD=3.4 P75=6.4	83	Custom	[0-0.6]=17% max=66.1
Galaxolide	100	Lognormal	GM=901.1	47	Lognormal	GM=65	100	Lognormal	AM=104.2

			p25=401.1 p95=3492			GSD=4.4 P75=122.5			SD=125.3 location=0
PCB101	80	Lognormal	p50=7.7 p75=75.2 p95=425.1	89	Lognormal	p50=0.001 p75=0.005 p95=0.03	7	Custom	[0-0.3]=93% max=2.2
PCB105	54	Lognormal	GM=6.1 GSD=7.2 P75=21.5	61	Lognormal	GM=1 GSD=4.6 P75=2.6	1	Lognormal[4]	AM=0.1 SD=1.6 location=0.002
PCB118	74	Lognormal	GM=11.4 GSD=8.9 p75=65.5	86	Lognormal	p50=0.002 p75=0.006 p95=0.05	1	Lognormal[4]	AM=0.4 SD=2.8 location=0.01
PCB138	82	Lognormal	p50=6.3 p75=54.4 p95=385	89	Lognormal	p50=0.002 p75=0.008 p95=0.05	1	Lognormal[4]	AM=0.2 SD=1.5 location=0.003
PCB153	79	Lognormal	p50=7.3 p75=52.7 p95=388.7	89	Lognormal	p50=0.002 p75=0.008 p95=0.04	1	Lognormal[4]	AM=0.4 SD=7.4 location=0.003
PCB28	45	Lognormal	GM=3.3 GSD=2.7 P75=6	18	Custom	[0-0.0004]=82% [0.0004-0.001]=10% max =0.009	3	Custom	[0-0.3]=97% max=0.3
PCB31	48	Lognormal	GM=3.2 GSD=3 P75=5.5	23	Lognormal	GM=0.4 GSD=2 P75=0.4	1	Lognormal[4]	AM=1.4 SD=2.6 location=0
PCB52	78	Lognormal	p50=3.7 p75=26.29 p95=219.8	58	Lognormal	GM=0.8 GSD=3.6 P75=1.9	13	Custom	[0-0.3]=87% max=0.5
Phenanthrene	100	Lognormal	GM=354.9 p25=177 p95=1625	100	Lognormal	GM=0.06 p25=0.03 p95=0.3	100	Lognormal	AM=11.2 SD=10.7 location=4.2
Tonalide	99	Lognormal	GM=309.5 p25=204.3 p95=1021	58	Lognormal	GM=21.6 GSD=4.5 P75=41	100	Lognormal	AM=20.2 SD=19.4 location=2.7
Tributylphosphate	99	Lognormal	p50=218.7 p75=325.8 p95=646.7	12	Custom	[0-0.04]=88% [0.04-0.08]=4% max =1.5	63	Custom	[0-0.6]=37% max=5.4

AM: arithmetic mean; GM: geometric mean; GSD: geometric standard deviation; p: percentile; SD: standard deviation

[1]Fromme et al. (2009)

[2]Batterman et al. (2009)

[3]Naumova et al. (2002)

[4]Zhang et al. (2011)

Table S3: Distribution shape and input parameters of the mass transport coefficient (γ_d), describing the external transport of an SVOC from the gas phase in the core of a room through the boundary layer adjacent to the skin

	Distribution shape	Parameters	Sources
γ_d (m/h)	Triangular	min=5 likeliest=6 max=10	Tamas et al. (2006) Pandrangi and Morrison (2008) Weschler and Nazaroff (2008)

Table S4: Distribution shapes and input parameters of SVOC oral and pulmonary bioavailabilities (f_{oral} and f_{pulm}), and dust bioaccessibility (f_{dust}) used for the dose estimation regarding the number of values retrieved from literature

SVOCs	f_{oral} (-)[1]			f_{pulm} (-)[1]			f_{dust} (-)[2]		
	Number of values	Distribution shape	Parameters	Number of values	Distribution shape	Parameters	Number of values	Distribution shape	Parameters
Aldrin	0	Uniform	min=6 max=99	0	Uniform	min=0 max=100	1	Triangular	min=12 likeliest=12 max=52
Anthracene	4	Triangular	min=53 likeliest=68 max=75	0	Uniform	min=50 max=70	0	Uniform	min=2 max=17
BBP	0	Uniform	min=50 max=100	0	Uniform	min=0 max=100	4	Triangular	min=5 likeliest=13 max=17
BDE100	5	Triangular	min=70 likeliest=84 max=92	0	Triangular	min=0 likeliest=91 max=100	12	Triangular	min=20 likeliest=41 max=68
BDE153	5	Triangular	min=70 likeliest=85 max=95	0	Triangular	min=0 likeliest=91 max=100	12	Triangular	min=26 likeliest=40 max=55
BDE154	6	Triangular	min=70 likeliest=83 max=95	0	Triangular	min=0 likeliest=91 max=100	12	Triangular	min=26 likeliest=38 max=58
BDE28	0	Uniform	min=70 max=95	0	Triangular	min=0 likeliest=91 max=100	8	Triangular	min=29 likeliest=37 max=50
BDE47	8	Triangular	min=70 likeliest=85 max=95	1	Triangular	min=0 likeliest=91 max=100	12	Triangular	min=22 likeliest=39 max=71
BDE85	1	Triangular	min=44 likeliest=44 max=95	0	Triangular	min=0 likeliest=91 max=100	9	Triangular	min=19 likeliest=40 max=50
BDE99	5	Triangular	min=70 likeliest=82 max=92	0	Triangular	min=0 likeliest=91 max=100	12	Triangular	min=16 likeliest=33 max=71
Benzo[a]pyrene	7	Triangular	min=23 likeliest=43 max=80	4	Triangular	min=50 likeliest=59 max=70	7	Triangular	min=2 likeliest=5 max=9
Chlorpyrifos	3	Triangular	min=70 likeliest=83 max=90	0	Uniform	min=0 max=100	2	Uniform	min=13 max=41
DBP	0	Uniform	min=50 max=100	0	Uniform	min=0 max=100	4	Triangular	min=3 likeliest=9 max=15
DEHP	2	Uniform	min=50 max=100	0	Uniform	min=0 max=100	4	Triangular	min=1 likeliest=8 max=16
DEP	0	Uniform	min=50 max=100	0	Uniform	min=0 max=100	3	Triangular	min=20 likeliest=25 max=30
DiBP	0	Uniform	min=50 max=100	0	Uniform	min=0 max=100	3	Triangular	min=13 likeliest=13 max=17
Dieldrin	0	Uniform	min=6 max=99	0	Uniform	min=0 max=100	1	Triangular	min=12 likeliest=12 max=52
DiNP	0	Uniform	min=50	0	Uniform	min=0	0	Uniform	min=1

			max=100			max=100			max=81
Fluorene	0	Uniform	min=23 max=97	0	Uniform	min=50 max=70	0	Uniform	min=2 max=17
Lindane	3	Triangular	min=6 likeliest=80 max=99	0	Uniform	min=0 max=100	2	Uniform	min=31 max=52
Galaxolide	0	Uniform	min=0 max=100	0	Uniform	min=0 max=100	0	Uniform	min=1 max=92
PCB101	2	Uniform	min=48 max=92	0	Uniform	min=0 max=100	3	Triangular	min=3 likeliest=50 max=76
PCB105	2	Uniform	min=61 max=99	0	Uniform	min=0 max=100	1	Triangular	min=3 likeliest=3 max=76
PCB118	0	Uniform	min=27 max=100	0	Uniform	min=0 max=100	2	Uniform	min=10 max=23
PCB138	6	Triangular	min=70 likeliest=89 max=100	0	Uniform	min=0 max=100	3	Triangular	min=19 likeliest=22 max=47
PCB153	8	Triangular	min=27 likeliest=72 max=100	0	Uniform	min=0 max=100	3	Triangular	min=16 likeliest=24 max=41
PCB28	4	Triangular	min=60 likeliest=78 max=98	0	Uniform	min=0 max=100	4	Triangular	min=36 likeliest=54 max=74
PCB31	2	Uniform	min=60 max=98	0	Uniform	min=0 max=100	0	Uniform	min=3 max=76
PCB52	2	Uniform	min=73 max=93	0	Uniform	min=0 max=100	1	Triangular	min=3 likeliest=22 max=76
Phenanthrene	3	Triangular	min=86 likeliest=93 max=97	0	Uniform	min=50 max=70	0	Uniform	min=2 max=17
Tonalide	0	Uniform	min=0 max=100	0	Uniform	min=0 max=100	0	Uniform	min=1 max=92
Tributyl phosphate	1	Triangular	min=0 likeliest=50 max=100	0	Uniform	min=0 max=100	0	Uniform	min=1 max=92

[1]Online databases (Agency for toxic substances and disease registry (ATSDR); Hazardous substances data bank (HSBD))

[2] Yu et al. (2011 ; 2012 ; 2013); Abdallah et al. (2012); Ertl et al. (2012); Kang et al. (2012 ; 2013); Wang et al. (2013); Fang et al. (2014); He et al. (2015)

Table S5: Distribution shapes and input values of human body parameters: body weight (BW), body surface area (BSA), inhalation rate (IR), amount of dust ingested (DI), and time spent in dwellings (t) for an individual in a day, used for the dose estimation for eleven age groups

	BW (kg)	**BSA** (m^2)	**IR** (m^3/d)	**DI** (mg/j)	**t** (h/d)
General source	U.S. EPA Exposure Factors Handbook (U.S. EPA 2011)				
Specific source(s)	U.S. EPA Analysis of NHANES, 1999-2006 data		Arcus-Arth and Blaisdell (2007); Brochu et al. (2006); U.S. EPA (2009); Stifelman (2007)	Hogan et al. (1998)	U.S. EPA re-analysis of source data from U.S. EPA (1996)
Distribution shape	Lognormal	Lognormal	Normal	Lognormal	Normal
Parameters	AM, p5, p10, p15, p25, p50, p75, p85, p90, p95		AM, p95	Central tendency, upper percentile	AM, p95

AM: arithmetic mean; p: percentile

For DI we modelled lognormal distributions using the central tendency and the upper percentile recommended by the U.S. EPA Exposure Factors Handbook. We also made the following assumptions suitable to the U.S. EPA Exposure Factors Handbook:

- Before 6 weeks the DI is considered equal to 0 mg/d.
- Until 6 weeks to 30years old we considered an upper percentile of 100 mg/d.
- For the age group of [3-6years] we considered a central tendency of 60 mg/d.

Table S6: Variations in aggregated daily doses (ng/kg-bw/d), expressed as the relative interpercentile range, for 2 to 3 years old children and for each SVOC

SVOCs	p5	p50	p95	Relative interpercentile range $= \frac{p95 - p5}{p50}$
Aldrin	7,8E-03	7,1E-02	2,4E-01	3,2
Dieldrin	9,7E-02	7,2E-01	4,1E+00	5,5
Lindane	2,7E-01	1,7E+00	1,4E+01	7,7
Chlorpyrifos	2,5E-02	1,4E-01	3,7E-01	2,4
Tributylphosphate	2,0E-01	9,4E-01	3,6E+00	3,7
Galaxolide	1,4E+01	6,3E+01	3,1E+02	4,7
Tonalide	4,3E+00	1,7E+01	9,7E+01	5,5
Anthracene	4,3E-02	3,3E-01	1,7E+00	5,1
Benzo[a]pyrene	4,6E-02	1,4E-01	9,0E-01	6,0
Fluorene	4,5E-02	9,3E-01	5,6E+00	6,0
Phenanthrene	2,4E+00	6,2E+00	3,2E+01	4,8
PCB 28	9,4E-03	3,9E-02	9,3E-02	2,1
PCB 31	2,0E-01	4,1E-01	7,8E-01	1,4
PCB 52	4,6E-02	2,6E-01	1,8E+00	6,7
PCB 101	2,1E-02	1,1E-01	8,7E-01	7,7
PCB 105	3,3E-02	2,7E-01	3,3E+00	12,0
PCB 118	5,3E-02	9,7E-02	2,3E-01	1,8
PCB 138	3,4E-02	7,4E-02	3,8E-01	4,7
PCB 153	3,5E-02	7,1E-02	3,1E-01	3,9
BBP	2,0E+01	1,7E+02	4,8E+02	2,7
DBP	1,3E+02	4,4E+02	3,4E+03	7,4
DEHP	7,6E+01	5,4E+02	1,5E+03	2,6
DEP	5,0E+01	2,6E+02	2,5E+03	9,3
DiBP	3,6E+02	1,3E+03	4,2E+03	3,0
DiNP	6,6E+01	5,9E+02	1,6E+03	2,7
BDE 28	5,1E-02	2,6E-01	9,1E-01	3,3
BDE 47	2,4E-01	1,7E+00	4,6E+00	2,6
BDE 85	2,5E-03	8,7E-03	3,6E-02	3,8
BDE 99	3,7E-01	5,9E-01	1,1E+00	1,2
BDE 100	2,6E-01	1,1E+00	4,9E+00	4,2
BDE 153	1,2E-02	4,3E-02	2,1E-01	4,7
BDE 154	1,0E-02	3,7E-02	1,5E-01	3,7

Table S7: Relative contribution (%) to total variation of aggregated daily doses from exposures to 32 SVOC (ng/kg-bw/d) according to 15 inputs parameters for 2 to 3 years old children

SVOCs	Cpart	Cgas	Cdust	foral	fdust	fpulm	H	logKow	BW	BSA	IR	t (-)	t (h)	DI	ɣd
Aldrin	0	52	0	0	0	34	1	1	2	2	7	2	0	0	0
Dieldrin	54	3	0	0	0	32	0	0	1	1	6	2	0	0	0
Lindane	21	38	7	0	0	11	16	1	1	1	2	1	0	0	0
Chlorpyrifos	1	54	2	0	0	23	5	2	2	2	5	3	0	0	0
Tributylphosphate	1	71	6	2	3	4	1	6	1	1	1	1	1	1	0
Galaxolide	30	24	7	0	0	22	6	2	1	1	5	2	0	0	0
Tonalide	44	13	2	0	0	27	1	1	2	2	6	2	0	0	0
Anthracene	1	83	9	0	0	0	1	1	1	1	2	1	1	0	0
Benzo[a]pyrene	81	0	2	0	0	0	0	0	2	2	6	3	0	1	0
Fluorene	0	89	3	0	0	0	1	0	1	1	3	1	0	0	0
Phenanthrene	0	78	11	0	0	0	1	1	1	1	3	1	2	0	0
PCB 28	0	48	0	0	0	33	0	0	3	3	7	4	0	1	0
PCB 31	6	52	3	0	0	28	0	0	1	1	6	2	0	0	0
PCB 52	53	2	11	0	0	24	0	0	1	1	5	2	0	0	0
PCB 101	1	17	63	1	4	4	0	0	2	2	1	3	0	2	0
PCB 105	68	1	5	0	0	19	0	0	1	1	4	1	0	0	0
PCB 118	2	58	26	1	1	5	0	0	1	1	1	2	0	1	0
PCB 138	2	26	63	0	1	2	0	0	1	1	0	2	0	2	0
PCB 153	6	39	46	2	1	2	1	0	1	1	0	1	0	1	0
BBP	15	1	58	4	5	0	0	0	2	2	0	4	0	9	0
DBP	59	5	0	0	0	23	2	2	2	2	5	2	1	0	0
DEHP	0	0	65	5	19	0	0	0	3	3	0	6	0	0	0
DEP	53	6	10	0	0	22	1	1	1	1	4	1	0	0	0
DiBP	3	61	26	0	0	0	4	0	1	1	0	0	3	0	0
DiNP	4	1	42	3	38	0	0	0	2	2	0	3	0	6	0
BDE 28	23	49	0	0	0	11	1	1	2	2	8	3	0	0	0
BDE 47	0	80	0	0	0	3	3	6	1	1	3	1	2	0	0
BDE 85	0	73	6	1	1	2	3	2	2	2	2	3	1	2	0
BDE 99	0	7	2	0	0	9	30	23	6	5	7	4	6	0	0
BDE 100	64	5	2	0	0	12	1	1	2	2	8	3	0	0	0
BDE 153	1	67	15	0	1	0	2	4	2	2	0	2	2	2	0
BDE 154	0	62	22	0	1	0	1	4	2	2	0	2	2	3	0

Table S8: Daily doses (DD) from each route of exposure (ingestion of dust, inhalation and dermal contact with the gas phase) and aggregated daily doses (ADD) estimated (ng/kg-bw/d) for 32 SVOCs for the age group of [0-1 month]

SVOCs	Estimated daily doses[1]	p5	p25	p50	p75	p95	Uncertainty on the mean (%)
Aldrin	DDing-dust	0	0	0	0	0	-
	DDinh-air	5,40E-03	3,30E-02	7,92E-02	1,51E-01	3,13E-01	59
	DDderm-gas	1,11E-03	5,56E-03	1,11E-02	1,71E-02	2,90E-02	122
	ADD	8,11E-03	4,06E-02	9,12E-02	1,67E-01	3,37E-01	51
Dieldrin	DDing-dust	0	0	0	0	0	-
	DDinh-air	8,14E-02	3,57E-01	9,04E-01	2,08E+00	5,99E+00	56
	DDderm-gas	1,32E-03	6,60E-03	1,33E-02	2,05E-02	1,07E-01	166
	ADD	9,32E-02	3,73E-01	9,27E-01	2,11E+00	6,04E+00	55
Lindane	DDing-dust	0	0	0	0	0	-
	DDinh-air	1,86E-01	7,84E-01	1,97E+00	4,85E+00	1,73E+01	59
	DDderm-gas	1,28E-02	5,73E-02	9,77E-02	2,67E-01	1,77E+00	126
	ADD	2,53E-01	8,98E-01	2,18E+00	5,28E+00	1,89E+01	68
Chlorpyrifos	DDing-dust	0	0	0	0	0	-
	DDinh-air	8,98E-03	3,95E-02	8,76E-02	1,62E-01	3,28E-01	58
	DDderm-gas	9,48E-03	4,71E-02	9,44E-02	1,45E-01	2,29E-01	104
	ADD	2,48E-02	9,85E-02	1,90E-01	3,02E-01	5,32E-01	49
Tributylphosphate	DDing-dust	0	0	0	0	0	-
	DDinh-air	1,85E-02	9,94E-02	2,61E-01	5,97E-01	1,50E+00	56
	DDderm-gas	6,75E-02	3,41E-01	7,99E-01	1,72E+00	3,82E+00	55
	ADD	1,01E-01	4,77E-01	1,10E+00	2,34E+00	5,14E+00	37
Galaxolide	DDing-dust	0	0	0	0	0	-
	DDinh-air	6,88E+00	2,58E+01	5,74E+01	1,24E+02	3,96E+02	56
	DDderm-gas	4,09E+00	1,05E+01	2,01E+01	3,82E+01	9,30E+01	140
	ADD	1,70E+01	4,44E+01	8,60E+01	1,66E+02	4,50E+02	64
Tonalide	DDing-dust	0	0	0	0	0	-
	DDinh-air	2,01E+00	7,16E+00	1,60E+01	3,63E+01	1,31E+02	56
	DDderm-gas	1,66E+00	2,94E+00	4,74E+00	8,05E+00	1,81E+01	65
	ADD	5,29E+00	1,21E+01	2,27E+01	4,52E+01	1,40E+02	46
Anthracene	DDing-dust	0	0	0	0	0	-
	DDinh-air	1,46E-02	7,70E-02	1,91E-01	4,13E-01	1,26E+00	9
	DDderm-gas	2,29E-02	1,17E-01	2,45E-01	4,65E-01	1,34E+00	40
	ADD	4,68E-02	2,15E-01	4,57E-01	8,81E-01	2,56E+00	21
Benzo[a]pyrene	DDing-dust	0	0	0	0	0	-
	DDinh-air	6,59E-03	3,94E-02	1,21E-01	3,35E-01	1,23E+00	10
	DDderm-gas	3,15E-02	3,96E-02	4,54E-02	5,13E-02	6,01E-02	21
	ADD	5,06E-02	8,53E-02	1,66E-01	3,81E-01	1,28E+00	11
Fluorene	DDing-dust	0	0	0	0	0	-
	DDinh-air	2,37E-02	1,25E-01	5,58E-01	1,59E+00	5,26E+00	10
	DDderm-gas	1,52E-02	7,58E-02	5,36E-01	8,82E-01	2,87E+00	38
	ADD	5,02E-02	2,11E-01	1,22E+00	2,48E+00	8,30E+00	16

Phenanthrene	DDing-dust	0	0	0	0	0	-
	DDinh-air	5,92E-01	1,80E+00	3,42E+00	7,50E+00	2,15E+01	10
	DDderm-gas	2,17E+00	3,17E+00	5,42E+00	1,20E+01	2,85E+01	23
	ADD	3,37E+00	5,28E+00	9,03E+00	1,99E+01	4,80E+01	14
PCB 28	DDing-dust	0	0	0	0	0	-
	DDinh-air	2,18E-03	1,33E-02	3,17E-02	5,95E-02	1,14E-01	56
	DDderm-gas	1,11E-03	5,60E-03	1,12E-02	1,71E-02	2,48E-02	21
	ADD	4,24E-03	2,09E-02	4,38E-02	7,56E-02	1,35E-01	37
PCB 31	DDing-dust	0	0	0	0	0	-
	DDinh-air	9,25E-02	2,82E-01	4,58E-01	6,79E-01	1,12E+00	118
	DDderm-gas	7,30E-02	9,19E-02	1,05E-01	1,19E-01	1,39E-01	120
	ADD	1,96E-01	3,86E-01	5,63E-01	7,85E-01	1,23E+00	112
PCB 52	DDing-dust	0	0	0	0	0	-
	DDinh-air	2,73E-02	1,12E-01	2,71E-01	6,64E-01	2,40E+00	56
	DDderm-gas	1,37E-03	6,82E-03	1,37E-02	2,13E-02	4,53E-02	112
	ADD	3,79E-02	1,27E-01	2,90E-01	6,89E-01	2,42E+00	48
PCB 101	DDing-dust	0	0	0	0	0	-
	DDinh-air	2,81E-03	1,51E-02	3,52E-02	6,68E-02	1,61E-01	60
	DDderm-gas	1,27E-03	6,37E-03	1,28E-02	1,96E-02	3,93E-02	43
	ADD	5,44E-03	2,38E-02	4,89E-02	8,51E-02	1,94E-01	36
PCB 105	DDing-dust	0	0	0	0	0	-
	DDinh-air	2,56E-02	1,13E-01	3,36E-01	9,93E-01	4,60E+00	61
	DDderm-gas	6,67E-03	8,39E-03	9,60E-03	1,09E-02	1,27E-02	370
	ADD	3,51E-02	1,22E-01	3,45E-01	1,00E+00	4,61E+00	55
PCB 118	DDing-dust	0	0	0	0	0	-
	DDinh-air	1,64E-02	4,98E-02	8,01E-02	1,16E-01	1,80E-01	288
	DDderm-gas	2,41E-02	3,03E-02	3,47E-02	3,92E-02	4,60E-02	272
	ADD	5,03E-02	8,42E-02	1,15E-01	1,51E-01	2,16E-01	230
PCB 138	DDing-dust	0	0	0	0	0	-
	DDinh-air	9,75E-03	2,95E-02	4,75E-02	6,91E-02	1,09E-01	227
	DDderm-gas	1,28E-02	1,61E-02	1,85E-02	2,09E-02	2,45E-02	284
	ADD	2,79E-02	4,78E-02	6,61E-02	8,79E-02	1,29E-01	132
PCB 153	DDing-dust	0	0	0	0	0	-
	DDinh-air	1,02E-02	3,10E-02	4,99E-02	7,22E-02	1,13E-01	228
	DDderm-gas	1,47E-02	1,85E-02	2,11E-02	2,39E-02	2,80E-02	250
	ADD	3,09E-02	5,19E-02	7,10E-02	9,37E-02	1,35E-01	173
BBP	DDing-dust	0	0	0	0	0	-
	DDinh-air	4,44E-01	1,34E+00	2,30E+00	3,92E+00	1,11E+01	57
	DDderm-gas	1,06E-01	5,31E-01	1,07E+00	1,72E+00	4,90E+00	75
	ADD	1,13E+00	2,33E+00	3,61E+00	5,84E+00	1,44E+01	41
DBP	DDing-dust	0	0	0	0	0	-
	DDinh-air	4,08E+01	1,44E+02	3,60E+02	9,91E+02	4,52E+03	56
	DDderm-gas	5,96E+01	1,24E+02	1,87E+02	2,69E+02	4,20E+02	47
	ADD	1,68E+02	3,40E+02	5,87E+02	1,22E+03	4,75E+03	39

DEHP	DDing-dust	0	0	0	0	0	-
	DDinh-air	2,09E+00	7,35E+00	1,65E+01	3,82E+01	1,33E+02	57
	DDderm-gas	9,97E-01	4,98E+00	9,94E+00	1,52E+01	2,38E+01	84
	ADD	7,24E+00	1,74E+01	2,88E+01	5,16E+01	1,45E+02	51
DEP	DDing-dust	0	0	0	0	0	-
	DDinh-air	3,44E+01	1,30E+02	3,14E+02	8,11E+02	3,50E+03	60
	DDderm-gas	7,01E+00	1,33E+01	2,13E+01	3,42E+01	6,48E+01	88
	ADD	5,29E+01	1,54E+02	3,43E+02	8,40E+02	3,52E+03	47
DiBP	DDing-dust	0	0	0	0	0	-
	DDinh-air	1,82E+01	6,22E+01	1,27E+02	2,46E+02	5,88E+02	58
	DDderm-gas	4,05E+02	8,80E+02	1,52E+03	2,62E+03	5,46E+03	27
	ADD	4,46E+02	9,67E+02	1,67E+03	2,87E+03	5,96E+03	22
DiNP	DDing-dust	0	0	0	0	0	-
	DDinh-air	8,72E-01	3,29E+00	6,61E+00	1,18E+01	2,61E+01	58
	DDderm-gas	4,05E-01	2,03E+00	4,05E+00	6,26E+00	1,03E+01	91
	ADD	2,24E+00	6,48E+00	1,13E+01	1,78E+01	3,29E+01	68
BDE 28	DDing-dust	0	0	0	0	0	-
	DDinh-air	3,30E-02	1,31E-01	2,77E-01	5,31E-01	1,19E+00	37
	DDderm-gas	4,55E-03	2,40E-02	5,67E-02	1,16E-01	2,74E-01	50
	ADD	5,79E-02	1,80E-01	3,53E-01	6,45E-01	1,38E+00	29
BDE 47	DDing-dust	0	0	0	0	0	-
	DDinh-air	9,78E-02	5,13E-01	1,17E+00	2,23E+00	4,54E+00	35
	DDderm-gas	1,33E-01	5,71E-01	1,09E+00	1,75E+00	2,81E+00	47
	ADD	2,97E-01	1,22E+00	2,36E+00	3,94E+00	6,92E+00	31
BDE 85	DDing-dust	0	0	0	0	0	-
	DDinh-air	4,66E-04	1,82E-03	3,90E-03	8,29E-03	2,43E-02	36
	DDderm-gas	2,61E-04	1,46E-03	3,80E-03	8,91E-03	2,58E-02	59
	ADD	1,19E-03	3,72E-03	8,01E-03	1,73E-02	4,88E-02	27
BDE 99	DDing-dust	0	0	0	0	0	-
	DDinh-air	7,58E-02	2,30E-01	3,72E-01	5,47E-01	9,15E-01	35
	DDderm-gas	2,97E-01	3,77E-01	4,37E-01	5,08E-01	7,38E-01	63
	ADD	4,74E-01	6,53E-01	8,13E-01	1,02E+00	1,53E+00	39
BDE 100	DDing-dust	0	0	0	0	0	-
	DDinh-air	1,24E-01	5,15E-01	1,19E+00	2,53E+00	6,93E+00	34
	DDderm-gas	9,58E-02	1,34E-01	1,86E-01	2,95E-01	6,84E-01	37
	ADD	3,08E-01	7,58E-01	1,46E+00	2,82E+00	7,20E+00	29
BDE 153	DDing-dust	0	0	0	0	0	-
	DDinh-air	1,20E-03	4,07E-03	8,74E-03	1,95E-02	6,33E-02	35
	DDderm-gas	4,73E-03	1,22E-02	2,63E-02	5,90E-02	1,83E-01	44
	ADD	7,28E-03	1,74E-02	3,61E-02	7,91E-02	2,43E-01	25
BDE 154	DDing-dust	0	0	0	0	0	-
	DDinh-air	8,71E-04	3,05E-03	6,39E-03	1,34E-02	3,79E-02	36
	DDderm-gas	3,75E-03	1,11E-02	2,35E-02	4,96E-02	1,32E-01	38
	ADD	5,76E-03	1,51E-02	3,08E-02	6,34E-02	1,67E-01	24

[1]For the younger age group [0-1 month], the dust ingestion rate was considered equal to 0 mg, leading to a DDing-dust equal to zero and an ADD estimated from inhalation and dermal contact.

Table S9: Daily doses (DD) from each route of exposure (ingestion of dust, inhalation and dermal contact with the gas phase) and aggregated daily doses (ADD) estimated (ng/kg-bw/d) for 32 SVOCs for the age group of [1-3 months]

SVOCs	Estimated daily doses[1]	p5	p25	p50	p75	p95	Uncertainty on the mean (%)
Aldrin	DDing-dust	5,23E-05	2,67E-04	6,18E-04	1,29E-03	4,17E-03	74
	DDinh-air	5,46E-03	2,90E-02	6,35E-02	1,12E-01	2,20E-01	59
	DDderm-gas	1,02E-03	5,08E-03	1,02E-02	1,57E-02	2,67E-02	122
	ADD	8,51E-03	3,72E-02	7,68E-02	1,31E-01	2,59E-01	51
Dieldrin	DDing-dust	1,46E-04	9,15E-04	2,68E-03	7,22E-03	2,78E-02	71
	DDinh-air	8,20E-02	3,04E-01	7,22E-01	1,58E+00	4,31E+00	56
	DDderm-gas	1,21E-03	6,06E-03	1,21E-02	1,88E-02	9,84E-02	166
	ADD	9,76E-02	3,24E-01	7,49E-01	1,62E+00	4,35E+00	55
Lindane	DDing-dust	9,17E-03	2,11E-02	3,95E-02	8,15E-02	4,06E-01	62
	DDinh-air	1,92E-01	6,58E-01	1,56E+00	3,67E+00	1,28E+01	59
	DDderm-gas	1,18E-02	5,25E-02	8,97E-02	2,45E-01	1,62E+00	126
	ADD	2,87E-01	8,17E-01	1,84E+00	4,23E+00	1,48E+01	68
Chlorpyrifos	DDing-dust	3,80E-04	2,06E-03	6,22E-03	1,85E-02	8,65E-02	44
	DDinh-air	9,27E-03	3,42E-02	6,96E-02	1,20E-01	2,29E-01	58
	DDderm-gas	8,68E-03	4,32E-02	8,64E-02	1,33E-01	2,11E-01	104
	ADD	3,16E-02	1,01E-01	1,81E-01	2,73E-01	4,72E-01	49
Tributylphosphate	DDing-dust	4,82E-02	1,13E-01	2,11E-01	3,98E-01	1,04E+00	82
	DDinh-air	1,83E-02	8,50E-02	2,09E-01	4,54E-01	1,07E+00	56
	DDderm-gas	6,17E-02	3,12E-01	7,34E-01	1,58E+00	3,49E+00	55
	ADD	2,65E-01	6,92E-01	1,32E+00	2,41E+00	5,01E+00	37
Galaxolide	DDing-dust	7,64E-02	3,00E-01	7,09E-01	1,61E+00	5,06E+00	92
	DDinh-air	7,18E+00	2,17E+01	4,51E+01	9,34E+01	2,89E+02	56
	DDderm-gas	3,75E+00	9,59E+00	1,84E+01	3,50E+01	8,55E+01	140
	ADD	1,61E+01	3,90E+01	7,23E+01	1,35E+02	3,44E+02	64
Tonalide	DDing-dust	5,49E-02	1,48E-01	2,95E-01	5,92E-01	1,62E+00	96
	DDinh-air	2,11E+00	5,98E+00	1,25E+01	2,74E+01	9,64E+01	56
	DDderm-gas	1,52E+00	2,69E+00	4,35E+00	7,38E+00	1,67E+01	65
	ADD	5,16E+00	1,08E+01	1,93E+01	3,63E+01	1,05E+02	46
Anthracene	DDing-dust	9,97E-04	5,67E-03	1,55E-02	3,89E-02	1,34E-01	56
	DDinh-air	1,45E-02	6,67E-02	1,52E-01	3,11E-01	9,18E-01	9
	DDderm-gas	2,12E-02	1,07E-01	2,25E-01	4,27E-01	1,22E+00	40
	ADD	5,47E-02	2,11E-01	4,24E-01	7,83E-01	2,18E+00	21
Benzo[a]pyrene	DDing-dust	5,82E-04	3,25E-03	9,19E-03	2,45E-02	9,63E-02	50
	DDinh-air	6,24E-03	3,35E-02	9,68E-02	2,57E-01	9,06E-01	10
	DDderm-gas	2,88E-02	3,63E-02	4,16E-02	4,71E-02	5,55E-02	21
	ADD	5,94E-02	9,97E-02	1,69E-01	3,29E-01	9,69E-01	11
Fluorene	DDing-dust	2,20E-03	5,25E-03	9,65E-03	1,77E-02	4,24E-02	68
	DDinh-air	2,29E-02	1,01E-01	5,13E-01	1,19E+00	3,92E+00	10
	DDderm-gas	1,39E-02	6,94E-02	4,91E-01	8,09E-01	2,63E+00	38
	ADD	5,44E-02	1,89E-01	1,11E+00	2,00E+00	6,65E+00	16

Phenanthrene	DDing-dust	1,42E-02	4,94E-02	1,15E-01	2,63E-01	8,66E-01	53
	DDinh-air	6,70E-01	1,48E+00	2,63E+00	5,74E+00	1,53E+01	10
	DDderm-gas	1,99E+00	2,91E+00	4,97E+00	1,10E+01	2,62E+01	23
	ADD	3,13E+00	4,68E+00	7,93E+00	1,73E+01	4,09E+01	14
PCB 28	DDing-dust	4,42E-04	1,93E-03	4,85E-03	1,18E-02	4,04E-02	36
	DDinh-air	2,21E-03	1,17E-02	2,54E-02	4,42E-02	7,88E-02	56
	DDderm-gas	1,02E-03	5,14E-03	1,03E-02	1,57E-02	2,27E-02	21
	ADD	1,10E-02	2,81E-02	4,69E-02	7,02E-02	1,13E-01	37
PCB 31	DDing-dust	1,83E-04	1,15E-03	3,37E-03	9,00E-03	3,28E-02	64
	DDinh-air	1,17E-01	2,42E-01	3,50E-01	4,85E-01	7,67E-01	118
	DDderm-gas	6,68E-02	8,41E-02	9,65E-02	1,09E-01	1,29E-01	120
	ADD	2,17E-01	3,45E-01	4,55E-01	5,93E-01	8,79E-01	112
PCB 52	DDing-dust	3,84E-04	3,03E-03	1,15E-02	4,31E-02	2,86E-01	55
	DDinh-air	2,82E-02	9,36E-02	2,15E-01	5,04E-01	1,75E+00	56
	DDderm-gas	1,25E-03	6,26E-03	1,25E-02	1,95E-02	4,15E-02	112
	ADD	4,99E-02	1,35E-01	2,83E-01	6,17E-01	1,96E+00	48
PCB 101	DDing-dust	3,60E-03	2,53E-02	8,24E-02	2,52E-01	1,18E+00	52
	DDinh-air	2,88E-03	1,32E-02	2,80E-02	4,92E-02	1,12E-01	60
	DDderm-gas	1,16E-03	5,85E-03	1,17E-02	1,80E-02	3,61E-02	43
	ADD	2,48E-02	6,98E-02	1,39E-01	3,36E-01	1,32E+00	36
PCB 105	DDing-dust	2,88E-05	2,32E-04	8,93E-04	3,37E-03	2,24E-02	72
	DDinh-air	2,45E-02	9,41E-02	2,67E-01	7,63E-01	3,40E+00	61
	DDderm-gas	6,09E-03	7,67E-03	8,80E-03	9,97E-03	1,17E-02	370
	ADD	3,53E-02	1,07E-01	2,81E-01	7,79E-01	3,42E+00	55
PCB 118	DDing-dust	2,68E-03	6,57E-03	1,34E-02	3,32E-02	2,05E-01	51
	DDinh-air	2,10E-02	4,30E-02	6,12E-02	8,27E-02	1,21E-01	288
	DDderm-gas	2,20E-02	2,77E-02	3,18E-02	3,60E-02	4,24E-02	272
	ADD	6,29E-02	9,02E-02	1,15E-01	1,51E-01	3,14E-01	230
PCB 138	DDing-dust	1,11E-03	8,22E-03	2,88E-02	9,74E-02	5,31E-01	37
	DDinh-air	1,23E-02	2,54E-02	3,63E-02	4,92E-02	7,35E-02	227
	DDderm-gas	1,17E-02	1,48E-02	1,69E-02	1,92E-02	2,26E-02	284
	ADD	4,01E-02	6,20E-02	8,93E-02	1,58E-01	5,90E-01	132
PCB 153	DDing-dust	7,49E-04	5,65E-03	2,05E-02	7,17E-02	4,11E-01	49
	DDinh-air	1,29E-02	2,67E-02	3,81E-02	5,14E-02	7,61E-02	228
	DDderm-gas	1,34E-02	1,69E-02	1,94E-02	2,19E-02	2,58E-02	250
	ADD	4,14E-02	6,21E-02	8,56E-02	1,38E-01	4,77E-01	173
BBP	DDing-dust	1,76E+01	9,12E+01	2,07E+02	4,13E+02	1,01E+03	42
	DDinh-air	5,31E-01	1,12E+00	1,74E+00	2,85E+00	8,14E+00	57
	DDderm-gas	9,67E-02	4,86E-01	9,77E-01	1,58E+00	4,48E+00	75
	ADD	2,15E+01	9,53E+01	2,11E+02	4,18E+02	1,01E+03	41
DBP	DDing-dust	1,54E+00	7,92E+00	1,79E+01	3,58E+01	8,77E+01	45
	DDinh-air	4,21E+01	1,19E+02	2,83E+02	7,57E+02	3,35E+03	56
	DDderm-gas	5,47E+01	1,14E+02	1,71E+02	2,46E+02	3,84E+02	47
	ADD	1,65E+02	3,19E+02	5,23E+02	1,00E+03	3,60E+03	39

DEHP	DDing-dust	5,32E+01	2,73E+02	6,19E+02	1,24E+03	3,02E+03	50
	DDinh-air	2,19E+00	6,12E+00	1,29E+01	2,89E+01	9,69E+01	57
	DDderm-gas	9,15E-01	4,57E+00	9,12E+00	1,40E+01	2,19E+01	84
	ADD	8,40E+01	3,09E+02	6,57E+02	1,28E+03	3,07E+03	51
DEP	DDing-dust	7,03E-01	1,60E+00	2,95E+00	5,95E+00	2,60E+01	37
	DDinh-air	3,51E+01	1,08E+02	2,47E+02	6,19E+02	2,58E+03	60
	DDderm-gas	6,40E+00	1,22E+01	1,95E+01	3,13E+01	5,95E+01	88
	ADD	5,37E+01	1,35E+02	2,80E+02	6,56E+02	2,63E+03	47
DiBP	DDing-dust	1,94E+01	9,98E+01	2,26E+02	4,52E+02	1,11E+03	36
	DDinh-air	1,94E+01	5,25E+01	9,94E+01	1,84E+02	4,18E+02	58
	DDderm-gas	3,70E+02	8,07E+02	1,39E+03	2,40E+03	5,00E+03	27
	ADD	5,06E+02	1,10E+03	1,85E+03	3,06E+03	5,99E+03	22
DiNP	DDing-dust	6,21E+01	3,15E+02	7,13E+02	1,43E+03	3,50E+03	71
	DDinh-air	9,43E-01	2,84E+00	5,17E+00	8,75E+00	1,84E+01	58
	DDderm-gas	3,70E-01	1,86E+00	3,71E+00	5,74E+00	9,43E+00	91
	ADD	7,20E+01	3,25E+02	7,24E+02	1,44E+03	3,51E+03	68
BDE 28	DDing-dust	7,61E-05	1,78E-04	3,33E-04	6,58E-04	1,91E-03	33
	DDinh-air	3,53E-02	1,12E-01	2,19E-01	3,96E-01	8,43E-01	37
	DDderm-gas	4,17E-03	2,20E-02	5,20E-02	1,06E-01	2,51E-01	50
	ADD	5,43E-02	1,54E-01	2,87E-01	5,02E-01	1,03E+00	29
BDE 47	DDing-dust	3,85E-03	1,05E-02	2,31E-02	5,54E-02	2,19E-01	39
	DDinh-air	1,01E-01	4,48E-01	9,34E-01	1,66E+00	3,15E+00	35
	DDderm-gas	1,22E-01	5,24E-01	9,98E-01	1,60E+00	2,58E+00	47
	ADD	3,01E-01	1,10E+00	2,06E+00	3,32E+00	5,53E+00	31
BDE 85	DDing-dust	2,36E-04	1,22E-03	2,82E-03	5,89E-03	1,60E-02	42
	DDinh-air	4,92E-04	1,53E-03	3,05E-03	6,27E-03	1,76E-02	36
	DDderm-gas	2,39E-04	1,34E-03	3,50E-03	8,16E-03	2,38E-02	59
	ADD	2,90E-03	6,59E-03	1,17E-02	2,09E-02	4,77E-02	27
BDE 99	DDing-dust	7,19E-03	1,66E-02	3,09E-02	6,20E-02	2,32E-01	43
	DDinh-air	9,57E-02	1,98E-01	2,84E-01	3,90E-01	6,21E-01	35
	DDderm-gas	2,71E-01	3,45E-01	4,01E-01	4,67E-01	6,77E-01	63
	ADD	4,79E-01	6,20E-01	7,41E-01	9,01E-01	1,39E+00	39
BDE 100	DDing-dust	5,70E-04	2,97E-03	7,97E-03	2,03E-02	7,35E-02	38
	DDinh-air	1,28E-01	4,39E-01	9,40E-01	1,90E+00	4,98E+00	34
	DDderm-gas	8,75E-02	1,23E-01	1,71E-01	2,71E-01	6,28E-01	37
	ADD	3,04E-01	6,75E-01	1,21E+00	2,19E+00	5,27E+00	29
BDE 153	DDing-dust	1,25E-03	6,52E-03	1,54E-02	3,41E-02	1,17E-01	34
	DDinh-air	1,28E-03	3,38E-03	6,83E-03	1,47E-02	4,61E-02	35
	DDderm-gas	4,35E-03	1,12E-02	2,41E-02	5,41E-02	1,68E-01	44
	ADD	1,53E-02	3,36E-02	6,01E-02	1,11E-01	2,93E-01	25
BDE 154	DDing-dust	1,19E-03	6,17E-03	1,46E-02	3,22E-02	1,07E-01	34
	DDinh-air	9,33E-04	2,56E-03	4,99E-03	1,01E-02	2,74E-02	36
	DDderm-gas	3,44E-03	1,01E-02	2,16E-02	4,54E-02	1,22E-01	38
	ADD	1,29E-02	2,94E-02	5,21E-02	9,32E-02	2,13E-01	24

Table S10: Daily doses (DD) from each route of exposure (ingestion of dust, inhalation and dermal contact with the gas phase) and aggregated daily doses (ADD) estimated (ng/kg-bw/d) for 32 SVOCs for the age group of [3-6 months]

SVOCs	Estimated daily doses[1]	p5	p25	p50	p75	p95	Uncertainty on the mean (%)
Aldrin	DDing-dust	4,20E-05	2,14E-04	4,96E-04	1,03E-03	3,32E-03	74
	DDinh-air	6,07E-03	2,99E-02	6,20E-02	1,04E-01	1,95E-01	59
	DDderm-gas	9,45E-04	4,74E-03	9,48E-03	1,46E-02	2,49E-02	122
	ADD	8,43E-03	3,71E-02	7,42E-02	1,21E-01	2,31E-01	51
Dieldrin	DDing-dust	1,16E-04	7,36E-04	2,16E-03	5,78E-03	2,22E-02	71
	DDinh-air	9,00E-02	3,05E-01	7,00E-01	1,48E+00	3,91E+00	56
	DDderm-gas	1,12E-03	5,63E-03	1,13E-02	1,75E-02	9,13E-02	166
	ADD	1,04E-01	3,23E-01	7,23E-01	1,52E+00	3,95E+00	55
Lindane	DDing-dust	7,36E-03	1,69E-02	3,15E-02	6,52E-02	3,25E-01	62
	DDinh-air	2,12E-01	6,54E-01	1,52E+00	3,45E+00	1,18E+01	59
	DDderm-gas	1,09E-02	4,88E-02	8,33E-02	2,27E-01	1,52E+00	126
	ADD	2,91E-01	7,89E-01	1,76E+00	3,94E+00	1,37E+01	68
Chlorpyrifos	DDing-dust	3,05E-04	1,65E-03	4,99E-03	1,48E-02	6,93E-02	44
	DDinh-air	1,03E-02	3,51E-02	6,78E-02	1,11E-01	2,02E-01	58
	DDderm-gas	8,08E-03	4,02E-02	8,03E-02	1,23E-01	1,95E-01	104
	ADD	2,91E-02	9,37E-02	1,69E-01	2,51E-01	4,21E-01	49
Tributylphosphate	DDing-dust	3,88E-02	9,10E-02	1,69E-01	3,19E-01	8,33E-01	82
	DDinh-air	1,99E-02	8,59E-02	2,04E-01	4,28E-01	9,65E-01	56
	DDderm-gas	5,76E-02	2,90E-01	6,80E-01	1,46E+00	3,25E+00	55
	ADD	2,30E-01	6,15E-01	1,18E+00	2,19E+00	4,61E+00	37
Galaxolide	DDing-dust	6,17E-02	2,42E-01	5,69E-01	1,29E+00	4,06E+00	92
	DDinh-air	7,99E+00	2,18E+01	4,31E+01	8,70E+01	2,63E+02	56
	DDderm-gas	3,48E+00	8,92E+00	1,71E+01	3,25E+01	7,96E+01	140
	ADD	1,57E+01	3,75E+01	6,82E+01	1,26E+02	3,15E+02	64
Tonalide	DDing-dust	4,42E-02	1,18E-01	2,36E-01	4,73E-01	1,29E+00	96
	DDinh-air	2,33E+00	5,97E+00	1,20E+01	2,57E+01	8,87E+01	56
	DDderm-gas	1,41E+00	2,50E+00	4,04E+00	6,85E+00	1,55E+01	65
	ADD	5,04E+00	1,04E+01	1,82E+01	3,39E+01	9,67E+01	46
Anthracene	DDing-dust	7,93E-04	4,56E-03	1,24E-02	3,11E-02	1,07E-01	56
	DDinh-air	1,59E-02	6,75E-02	1,46E-01	2,89E-01	8,37E-01	9
	DDderm-gas	1,96E-02	9,94E-02	2,08E-01	3,96E-01	1,14E+00	40
	ADD	5,01E-02	1,95E-01	3,91E-01	7,18E-01	2,00E+00	21
Benzo[a]pyrene	DDing-dust	4,65E-04	2,63E-03	7,40E-03	1,96E-02	7,67E-02	50
	DDinh-air	6,65E-03	3,36E-02	9,39E-02	2,43E-01	8,34E-01	10
	DDderm-gas	2,68E-02	3,38E-02	3,87E-02	4,37E-02	5,13E-02	21
	ADD	5,58E-02	9,30E-02	1,57E-01	3,05E-01	8,89E-01	11
Fluorene	DDing-dust	1,76E-03	4,21E-03	7,73E-03	1,41E-02	3,38E-02	68
	DDinh-air	2,48E-02	9,76E-02	5,39E-01	1,10E+00	3,64E+00	10
	DDderm-gas	1,29E-02	6,47E-02	4,57E-01	7,53E-01	2,44E+00	38
	ADD	5,08E-02	1,77E-01	1,08E+00	1,84E+00	6,07E+00	16

Phenanthrene	DDing-dust	1,14E-02	3,97E-02	9,23E-02	2,12E-01	6,93E-01	53
	DDinh-air	7,77E-01	1,44E+00	2,49E+00	5,42E+00	1,39E+01	10
	DDderm-gas	1,85E+00	2,70E+00	4,61E+00	1,02E+01	2,43E+01	23
	ADD	2,98E+00	4,33E+00	7,36E+00	1,61E+01	3,79E+01	14
PCB 28	DDing-dust	3,58E-04	1,55E-03	3,89E-03	9,42E-03	3,23E-02	36
	DDinh-air	2,45E-03	1,21E-02	2,49E-02	4,10E-02	6,88E-02	56
	DDderm-gas	9,48E-04	4,78E-03	9,55E-03	1,46E-02	2,11E-02	21
	ADD	1,00E-02	2,61E-02	4,36E-02	6,38E-02	9,85E-02	37
PCB 31	DDing-dust	1,47E-04	9,26E-04	2,70E-03	7,17E-03	2,61E-02	64
	DDinh-air	1,47E-01	2,44E-01	3,28E-01	4,35E-01	6,63E-01	118
	DDderm-gas	6,22E-02	7,83E-02	8,96E-02	1,01E-01	1,19E-01	120
	ADD	2,38E-01	3,38E-01	4,24E-01	5,35E-01	7,66E-01	112
PCB 52	DDing-dust	3,07E-04	2,42E-03	9,19E-03	3,47E-02	2,28E-01	55
	DDinh-air	3,11E-02	9,31E-02	2,08E-01	4,74E-01	1,61E+00	56
	DDderm-gas	1,16E-03	5,81E-03	1,16E-02	1,81E-02	3,86E-02	112
	ADD	5,00E-02	1,29E-01	2,65E-01	5,68E-01	1,77E+00	48
PCB 101	DDing-dust	2,87E-03	2,02E-02	6,59E-02	2,01E-01	9,45E-01	52
	DDinh-air	3,18E-03	1,35E-02	2,72E-02	4,54E-02	9,80E-02	60
	DDderm-gas	1,07E-03	5,42E-03	1,09E-02	1,67E-02	3,36E-02	43
	ADD	2,20E-02	6,15E-02	1,18E-01	2,76E-01	1,08E+00	36
PCB 105	DDing-dust	2,30E-05	1,86E-04	7,15E-04	2,70E-03	1,78E-02	72
	DDinh-air	2,59E-02	9,38E-02	2,60E-01	7,24E-01	3,15E+00	61
	DDderm-gas	5,68E-03	7,14E-03	8,17E-03	9,24E-03	1,09E-02	370
	ADD	3,57E-02	1,05E-01	2,72E-01	7,38E-01	3,17E+00	55
PCB 118	DDing-dust	2,16E-03	5,30E-03	1,08E-02	2,67E-02	1,65E-01	51
	DDinh-air	2,68E-02	4,37E-02	5,77E-02	7,40E-02	1,03E-01	288
	DDderm-gas	2,05E-02	2,58E-02	2,96E-02	3,34E-02	3,92E-02	272
	ADD	6,35E-02	8,52E-02	1,05E-01	1,33E-01	2,63E-01	230
PCB 138	DDing-dust	8,81E-04	6,57E-03	2,31E-02	7,79E-02	4,24E-01	37
	DDinh-air	1,57E-02	2,58E-02	3,41E-02	4,40E-02	6,30E-02	227
	DDderm-gas	1,09E-02	1,38E-02	1,58E-02	1,78E-02	2,09E-02	284
	ADD	3,95E-02	5,68E-02	7,85E-02	1,34E-01	4,81E-01	132
PCB 153	DDing-dust	5,97E-04	4,54E-03	1,64E-02	5,74E-02	3,28E-01	49
	DDinh-air	1,65E-02	2,70E-02	3,58E-02	4,60E-02	6,49E-02	228
	DDderm-gas	1,25E-02	1,57E-02	1,80E-02	2,03E-02	2,39E-02	250
	ADD	4,10E-02	5,75E-02	7,60E-02	1,18E-01	3,89E-01	173
BBP	DDing-dust	1,42E+01	7,30E+01	1,65E+02	3,30E+02	8,04E+02	42
	DDinh-air	6,44E-01	1,12E+00	1,63E+00	2,61E+00	7,49E+00	57
	DDderm-gas	9,02E-02	4,53E-01	9,07E-01	1,46E+00	4,16E+00	75
	ADD	1,78E+01	7,68E+01	1,69E+02	3,34E+02	8,08E+02	41
DBP	DDing-dust	1,24E+00	6,37E+00	1,44E+01	2,87E+01	7,02E+01	45
	DDinh-air	4,57E+01	1,17E+02	2,73E+02	7,16E+02	3,08E+03	56
	DDderm-gas	5,07E+01	1,06E+02	1,59E+02	2,29E+02	3,57E+02	47
	ADD	1,57E+02	3,00E+02	4,92E+02	9,38E+02	3,30E+03	39

DEHP	DDing-dust	4,28E+01	2,20E+02	4,98E+02	9,90E+02	2,42E+03	50
	DDinh-air	2,42E+00	6,07E+00	1,24E+01	2,71E+01	8,83E+01	57
	DDderm-gas	8,48E-01	4,25E+00	8,48E+00	1,30E+01	2,03E+01	84
	ADD	7,11E+01	2,53E+02	5,33E+02	1,03E+03	2,46E+03	51
DEP	DDing-dust	5,64E-01	1,28E+00	2,37E+00	4,76E+00	2,09E+01	37
	DDinh-air	3,87E+01	1,07E+02	2,37E+02	5,82E+02	2,37E+03	60
	DDderm-gas	5,97E+00	1,14E+01	1,81E+01	2,91E+01	5,53E+01	88
	ADD	5,51E+01	1,32E+02	2,68E+02	6,16E+02	2,41E+03	47
DiBP	DDing-dust	1,57E+01	7,99E+01	1,81E+02	3,61E+02	8,81E+02	36
	DDinh-air	2,19E+01	5,26E+01	9,54E+01	1,71E+02	3,77E+02	58
	DDderm-gas	3,45E+02	7,49E+02	1,30E+03	2,23E+03	4,62E+03	27
	ADD	4,61E+02	9,97E+02	1,68E+03	2,78E+03	5,47E+03	22
DiNP	DDing-dust	4,97E+01	2,53E+02	5,74E+02	1,15E+03	2,80E+03	71
	DDinh-air	1,08E+00	2,88E+00	4,96E+00	8,05E+00	1,65E+01	58
	DDderm-gas	3,42E-01	1,72E+00	3,45E+00	5,33E+00	8,76E+00	91
	ADD	5,88E+01	2,63E+02	5,84E+02	1,16E+03	2,81E+03	68
BDE 28	DDing-dust	6,11E-05	1,43E-04	2,67E-04	5,25E-04	1,53E-03	33
	DDinh-air	3,99E-02	1,13E-01	2,11E-01	3,68E-01	7,52E-01	37
	DDderm-gas	3,90E-03	2,05E-02	4,83E-02	9,89E-02	2,33E-01	50
	ADD	5,56E-02	1,50E-01	2,73E-01	4,68E-01	9,26E-01	29
BDE 47	DDing-dust	3,09E-03	8,42E-03	1,86E-02	4,43E-02	1,74E-01	39
	DDinh-air	1,13E-01	4,59E-01	9,09E-01	1,54E+00	2,78E+00	35
	DDderm-gas	1,14E-01	4,86E-01	9,26E-01	1,49E+00	2,39E+00	47
	ADD	2,81E-01	1,04E+00	1,94E+00	3,10E+00	5,02E+00	31
BDE 85	DDing-dust	1,91E-04	9,74E-04	2,26E-03	4,71E-03	1,27E-02	42
	DDinh-air	5,61E-04	1,53E-03	2,92E-03	5,86E-03	1,59E-02	36
	DDderm-gas	2,22E-04	1,24E-03	3,25E-03	7,59E-03	2,20E-02	59
	ADD	2,59E-03	5,83E-03	1,03E-02	1,85E-02	4,29E-02	27
BDE 99	DDing-dust	5,78E-03	1,33E-02	2,48E-02	4,98E-02	1,85E-01	43
	DDinh-air	1,21E-01	2,00E-01	2,67E-01	3,49E-01	5,39E-01	35
	DDderm-gas	2,53E-01	3,21E-01	3,72E-01	4,33E-01	6,30E-01	63
	ADD	4,66E-01	5,83E-01	6,83E-01	8,15E-01	1,25E+00	39
BDE 100	DDing-dust	4,60E-04	2,39E-03	6,38E-03	1,61E-02	5,86E-02	38
	DDinh-air	1,42E-01	4,42E-01	9,05E-01	1,78E+00	4,51E+00	34
	DDderm-gas	8,14E-02	1,14E-01	1,58E-01	2,52E-01	5,82E-01	37
	ADD	3,04E-01	6,58E-01	1,16E+00	2,04E+00	4,78E+00	29
BDE 153	DDing-dust	1,01E-03	5,21E-03	1,24E-02	2,73E-02	9,32E-02	34
	DDinh-air	1,43E-03	3,35E-03	6,54E-03	1,38E-02	4,23E-02	35
	DDderm-gas	4,03E-03	1,04E-02	2,24E-02	5,03E-02	1,56E-01	44
	ADD	1,35E-02	2,96E-02	5,28E-02	9,83E-02	2,61E-01	25
BDE 154	DDing-dust	9,67E-04	4,95E-03	1,17E-02	2,59E-02	8,56E-02	34
	DDinh-air	1,05E-03	2,54E-03	4,78E-03	9,41E-03	2,48E-02	36
	DDderm-gas	3,21E-03	9,40E-03	2,00E-02	4,22E-02	1,13E-01	38
	ADD	1,14E-02	2,59E-02	4,58E-02	8,21E-02	1,88E-01	24

Table S11: Daily doses (DD) from each route of exposure (ingestion of dust, inhalation and dermal contact with the gas phase) and aggregated daily doses (ADD) estimated (ng/kg-bw/d) 32 SVOCs for the age group of [6-12 months]

SVOCs	Estimated daily doses[1]	p5	p25	p50	p75	p95	Uncertainty on the mean (%)
Aldrin	DDing-dust	3,34E-05	1,71E-04	3,94E-04	8,26E-04	2,66E-03	74
	DDinh-air	6,38E-03	3,15E-02	6,51E-02	1,09E-01	2,04E-01	59
	DDderm-gas	8,85E-04	4,42E-03	8,87E-03	1,36E-02	2,31E-02	122
	ADD	8,45E-03	3,82E-02	7,66E-02	1,25E-01	2,37E-01	51
Dieldrin	DDing-dust	9,32E-05	5,86E-04	1,72E-03	4,63E-03	1,78E-02	71
	DDinh-air	9,47E-02	3,21E-01	7,37E-01	1,56E+00	4,11E+00	56
	DDderm-gas	1,05E-03	5,26E-03	1,06E-02	1,63E-02	8,52E-02	166
	ADD	1,07E-01	3,37E-01	7,59E-01	1,59E+00	4,15E+00	55
Lindane	DDing-dust	5,87E-03	1,35E-02	2,51E-02	5,21E-02	2,60E-01	62
	DDinh-air	2,24E-01	6,87E-01	1,60E+00	3,63E+00	1,25E+01	59
	DDderm-gas	1,02E-02	4,57E-02	7,77E-02	2,11E-01	1,41E+00	126
	ADD	2,94E-01	8,07E-01	1,81E+00	4,07E+00	1,42E+01	68
Chlorpyrifos	DDing-dust	2,42E-04	1,32E-03	4,00E-03	1,18E-02	5,51E-02	44
	DDinh-air	1,08E-02	3,70E-02	7,14E-02	1,17E-01	2,12E-01	58
	DDderm-gas	7,55E-03	3,75E-02	7,51E-02	1,15E-01	1,81E-01	104
	ADD	2,77E-02	9,05E-02	1,64E-01	2,44E-01	4,08E-01	49
Tributylphosphate	DDing-dust	3,08E-02	7,26E-02	1,35E-01	2,55E-01	6,69E-01	82
	DDinh-air	2,10E-02	9,06E-02	2,14E-01	4,52E-01	1,02E+00	56
	DDderm-gas	5,37E-02	2,71E-01	6,35E-01	1,37E+00	3,04E+00	55
	ADD	2,03E-01	5,58E-01	1,09E+00	2,06E+00	4,36E+00	37
Galaxolide	DDing-dust	4,89E-02	1,92E-01	4,52E-01	1,03E+00	3,24E+00	92
	DDinh-air	8,38E+00	2,28E+01	4,54E+01	9,15E+01	2,77E+02	56
	DDderm-gas	3,27E+00	8,33E+00	1,60E+01	3,03E+01	7,40E+01	140
	ADD	1,57E+01	3,75E+01	6,87E+01	1,27E+02	3,23E+02	64
Tonalide	DDing-dust	3,52E-02	9,41E-02	1,88E-01	3,78E-01	1,03E+00	96
	DDinh-air	2,46E+00	6,27E+00	1,26E+01	2,69E+01	9,32E+01	56
	DDderm-gas	1,32E+00	2,34E+00	3,77E+00	6,40E+00	1,44E+01	65
	ADD	4,98E+00	1,04E+01	1,84E+01	3,46E+01	1,00E+02	46
Anthracene	DDing-dust	6,31E-04	3,62E-03	9,92E-03	2,48E-02	8,56E-02	56
	DDinh-air	1,67E-02	7,12E-02	1,54E-01	3,04E-01	8,79E-01	9
	DDderm-gas	1,83E-02	9,30E-02	1,95E-01	3,70E-01	1,06E+00	40
	ADD	4,76E-02	1,88E-01	3,79E-01	7,01E-01	1,96E+00	21
Benzo[a]pyrene	DDing-dust	3,71E-04	2,09E-03	5,89E-03	1,57E-02	6,14E-02	50
	DDinh-air	7,00E-03	3,53E-02	9,89E-02	2,55E-01	8,76E-01	10
	DDderm-gas	2,51E-02	3,16E-02	3,61E-02	4,08E-02	4,76E-02	21
	ADD	5,25E-02	8,91E-02	1,55E-01	3,09E-01	9,23E-01	11
Fluorene	DDing-dust	1,41E-03	3,36E-03	6,17E-03	1,13E-02	2,70E-02	68
	DDinh-air	2,60E-02	1,03E-01	5,67E-01	1,15E+00	3,82E+00	10
	DDderm-gas	1,21E-02	6,04E-02	4,27E-01	7,02E-01	2,29E+00	38
	ADD	4,93E-02	1,75E-01	1,07E+00	1,85E+00	6,11E+00	16

Phenanthrene	DDing-dust	9,04E-03	3,18E-02	7,35E-02	1,69E-01	5,49E-01	53
	DDinh-air	8,20E-01	1,51E+00	2,62E+00	5,70E+00	1,45E+01	10
	DDderm-gas	1,74E+00	2,52E+00	4,31E+00	9,53E+00	2,27E+01	23
	ADD	2,88E+00	4,20E+00	7,13E+00	1,56E+01	3,69E+01	14
PCB 28	DDing-dust	2,83E-04	1,23E-03	3,10E-03	7,50E-03	2,59E-02	36
	DDinh-air	2,57E-03	1,27E-02	2,61E-02	4,31E-02	7,26E-02	56
	DDderm-gas	8,92E-04	4,46E-03	8,92E-03	1,36E-02	1,96E-02	21
	ADD	9,27E-03	2,50E-02	4,26E-02	6,31E-02	9,79E-02	37
PCB 31	DDing-dust	1,17E-04	7,36E-04	2,15E-03	5,73E-03	2,10E-02	64
	DDinh-air	1,55E-01	2,56E-01	3,45E-01	4,59E-01	6,96E-01	118
	DDderm-gas	5,83E-02	7,33E-02	8,38E-02	9,46E-02	1,10E-01	120
	ADD	2,39E-01	3,43E-01	4,35E-01	5,50E-01	7,90E-01	112
PCB 52	DDing-dust	2,43E-04	1,94E-03	7,34E-03	2,75E-02	1,83E-01	55
	DDinh-air	3,30E-02	9,80E-02	2,18E-01	4,98E-01	1,70E+00	56
	DDderm-gas	1,09E-03	5,43E-03	1,09E-02	1,69E-02	3,60E-02	112
	ADD	5,00E-02	1,30E-01	2,68E-01	5,78E-01	1,82E+00	48
PCB 101	DDing-dust	2,31E-03	1,61E-02	5,27E-02	1,61E-01	7,53E-01	52
	DDinh-air	3,34E-03	1,43E-02	2,86E-02	4,77E-02	1,04E-01	60
	DDderm-gas	1,01E-03	5,07E-03	1,01E-02	1,56E-02	3,13E-02	43
	ADD	2,04E-02	5,67E-02	1,06E-01	2,33E-01	9,27E-01	36
PCB 105	DDing-dust	1,84E-05	1,48E-04	5,68E-04	2,15E-03	1,42E-02	72
	DDinh-air	2,73E-02	9,88E-02	2,72E-01	7,61E-01	3,31E+00	61
	DDderm-gas	5,31E-03	6,68E-03	7,64E-03	8,62E-03	1,01E-02	370
	ADD	3,64E-02	1,09E-01	2,83E-01	7,72E-01	3,33E+00	55
PCB 118	DDing-dust	1,72E-03	4,21E-03	8,59E-03	2,12E-02	1,30E-01	51
	DDinh-air	2,82E-02	4,59E-02	6,06E-02	7,78E-02	1,09E-01	288
	DDderm-gas	1,92E-02	2,42E-02	2,76E-02	3,12E-02	3,64E-02	272
	ADD	6,19E-02	8,37E-02	1,03E-01	1,30E-01	2,33E-01	230
PCB 138	DDing-dust	7,04E-04	5,24E-03	1,85E-02	6,21E-02	3,37E-01	37
	DDinh-air	1,66E-02	2,71E-02	3,59E-02	4,63E-02	6,61E-02	227
	DDderm-gas	1,02E-02	1,29E-02	1,47E-02	1,66E-02	1,94E-02	284
	ADD	3,87E-02	5,56E-02	7,51E-02	1,20E-01	3,94E-01	132
PCB 153	DDing-dust	4,78E-04	3,62E-03	1,31E-02	4,56E-02	2,62E-01	49
	DDinh-air	1,74E-02	2,84E-02	3,77E-02	4,85E-02	6,83E-02	228
	DDderm-gas	1,17E-02	1,47E-02	1,68E-02	1,90E-02	2,22E-02	250
	ADD	4,01E-02	5,64E-02	7,37E-02	1,08E-01	3,23E-01	173
BBP	DDing-dust	1,13E+01	5,83E+01	1,32E+02	2,63E+02	6,44E+02	42
	DDinh-air	6,79E-01	1,18E+00	1,72E+00	2,75E+00	7,88E+00	57
	DDderm-gas	8,40E-02	4,23E-01	8,47E-01	1,37E+00	3,90E+00	75
	ADD	1,49E+01	6,21E+01	1,36E+02	2,67E+02	6,49E+02	41
DBP	DDing-dust	9,77E-01	5,06E+00	1,15E+01	2,29E+01	5,59E+01	45
	DDinh-air	4,83E+01	1,23E+02	2,87E+02	7,52E+02	3,25E+03	56
	DDderm-gas	4,75E+01	9,89E+01	1,49E+02	2,13E+02	3,33E+02	47
	ADD	1,53E+02	2,94E+02	4,87E+02	9,54E+02	3,46E+03	39

DEHP	DDing-dust	3,44E+01	1,76E+02	3,97E+02	7,91E+02	1,94E+03	50
	DDinh-air	2,55E+00	6,39E+00	1,31E+01	2,85E+01	9,28E+01	57
	DDderm-gas	7,93E-01	3,97E+00	7,92E+00	1,21E+01	1,89E+01	84
	ADD	6,17E+01	2,09E+02	4,34E+02	8,29E+02	1,98E+03	51
DEP	DDing-dust	4,48E-01	1,02E+00	1,89E+00	3,78E+00	1,66E+01	37
	DDinh-air	4,07E+01	1,12E+02	2,49E+02	6,15E+02	2,51E+03	60
	DDderm-gas	5,58E+00	1,06E+01	1,69E+01	2,71E+01	5,16E+01	88
	ADD	5,56E+01	1,36E+02	2,77E+02	6,45E+02	2,54E+03	47
DiBP	DDing-dust	1,25E+01	6,37E+01	1,44E+02	2,88E+02	7,04E+02	36
	DDinh-air	2,32E+01	5,53E+01	1,00E+02	1,80E+02	3,95E+02	58
	DDderm-gas	3,22E+02	7,00E+02	1,21E+03	2,08E+03	4,32E+03	27
	ADD	4,25E+02	9,16E+02	1,54E+03	2,56E+03	5,07E+03	22
DiNP	DDing-dust	3,95E+01	2,01E+02	4,56E+02	9,14E+02	2,24E+03	71
	DDinh-air	1,14E+00	3,03E+00	5,22E+00	8,46E+00	1,73E+01	58
	DDderm-gas	3,22E-01	1,61E+00	3,23E+00	4,98E+00	8,16E+00	91
	ADD	4,87E+01	2,10E+02	4,67E+02	9,25E+02	2,25E+03	68
BDE 28	DDing-dust	4,86E-05	1,14E-04	2,13E-04	4,18E-04	1,22E-03	33
	DDinh-air	4,22E-02	1,19E-01	2,21E-01	3,87E-01	7,90E-01	37
	DDderm-gas	3,64E-03	1,91E-02	4,51E-02	9,23E-02	2,17E-01	50
	ADD	5,67E-02	1,54E-01	2,79E-01	4,80E-01	9,54E-01	29
BDE 47	DDing-dust	2,46E-03	6,74E-03	1,48E-02	3,54E-02	1,40E-01	39
	DDinh-air	1,19E-01	4,84E-01	9,55E-01	1,62E+00	2,93E+00	35
	DDderm-gas	1,06E-01	4,55E-01	8,66E-01	1,39E+00	2,23E+00	47
	ADD	2,73E-01	1,02E+00	1,91E+00	3,06E+00	5,00E+00	31
BDE 85	DDing-dust	1,50E-04	7,78E-04	1,80E-03	3,76E-03	1,01E-02	42
	DDinh-air	5,92E-04	1,61E-03	3,07E-03	6,15E-03	1,68E-02	36
	DDderm-gas	2,06E-04	1,16E-03	3,03E-03	7,08E-03	2,05E-02	59
	ADD	2,39E-03	5,35E-03	9,51E-03	1,72E-02	4,09E-02	27
BDE 99	DDing-dust	4,60E-03	1,06E-02	1,98E-02	3,96E-02	1,48E-01	43
	DDinh-air	1,28E-01	2,10E-01	2,80E-01	3,67E-01	5,64E-01	35
	DDderm-gas	2,37E-01	3,00E-01	3,48E-01	4,03E-01	5,84E-01	63
	ADD	4,50E-01	5,66E-01	6,64E-01	7,93E-01	1,20E+00	39
BDE 100	DDing-dust	3,66E-04	1,90E-03	5,09E-03	1,29E-02	4,67E-02	38
	DDinh-air	1,49E-01	4,66E-01	9,50E-01	1,87E+00	4,73E+00	34
	DDderm-gas	7,62E-02	1,07E-01	1,48E-01	2,35E-01	5,44E-01	37
	ADD	3,00E-01	6,68E-01	1,18E+00	2,11E+00	4,97E+00	29
BDE 153	DDing-dust	8,06E-04	4,16E-03	9,89E-03	2,17E-02	7,47E-02	34
	DDinh-air	1,52E-03	3,53E-03	6,87E-03	1,45E-02	4,47E-02	35
	DDderm-gas	3,76E-03	9,72E-03	2,09E-02	4,69E-02	1,46E-01	44
	ADD	1,23E-02	2,65E-02	4,75E-02	8,92E-02	2,39E-01	25
BDE 154	DDing-dust	7,69E-04	3,94E-03	9,37E-03	2,06E-02	6,76E-02	34
	DDinh-air	1,11E-03	2,67E-03	5,03E-03	9,88E-03	2,61E-02	36
	DDderm-gas	2,99E-03	8,80E-03	1,87E-02	3,94E-02	1,06E-01	38
	ADD	1,03E-02	2,32E-02	4,10E-02	7,38E-02	1,70E-01	24

Table S12: Daily doses (DD) from each route of exposure (ingestion of dust, inhalation and dermal contact with the gas phase) and aggregated daily doses (ADD) estimated (ng/kg-bw/d) for 32 SVOCs for the age group of [1-2 years]

SVOCs	Estimated daily doses[1]	p5	p25	p50	p75	p95	Uncertainty on the mean (%)
Aldrin	DDing-dust	6,36E-05	3,19E-04	6,50E-04	1,10E-03	2,54E-03	74
	DDinh-air	3,94E-03	2,15E-02	4,80E-02	8,65E-02	1,73E-01	59
	DDderm-gas	7,92E-04	3,99E-03	8,02E-03	1,25E-02	2,14E-02	122
	ADD	6,47E-03	2,82E-02	5,87E-02	1,01E-01	2,06E-01	51
Dieldrin	DDing-dust	1,76E-04	1,02E-03	2,72E-03	6,51E-03	2,10E-02	71
	DDinh-air	5,93E-02	2,27E-01	5,48E-01	1,21E+00	3,36E+00	56
	DDderm-gas	9,46E-04	4,74E-03	9,55E-03	1,50E-02	7,80E-02	166
	ADD	7,18E-02	2,43E-01	5,70E-01	1,24E+00	3,39E+00	55
Lindane	DDing-dust	1,52E-02	2,47E-02	3,60E-02	6,20E-02	3,34E-01	62
	DDinh-air	1,39E-01	4,93E-01	1,19E+00	2,82E+00	9,85E+00	59
	DDderm-gas	9,17E-03	4,11E-02	7,17E-02	1,96E-01	1,30E+00	126
	ADD	2,17E-01	6,21E-01	1,41E+00	3,27E+00	1,15E+01	68
Chlorpyrifos	DDing-dust	4,70E-04	2,25E-03	6,20E-03	1,66E-02	6,83E-02	44
	DDinh-air	6,64E-03	2,55E-02	5,30E-02	9,30E-02	1,81E-01	58
	DDderm-gas	6,82E-03	3,38E-02	6,79E-02	1,06E-01	1,71E-01	104
	ADD	2,54E-02	7,96E-02	1,43E-01	2,15E-01	3,71E-01	49
Tributylphosphate	DDing-dust	7,68E-02	1,33E-01	2,04E-01	3,26E-01	6,98E-01	82
	DDinh-air	1,33E-02	6,37E-02	1,59E-01	3,49E-01	8,37E-01	56
	DDderm-gas	4,86E-02	2,45E-01	5,81E-01	1,25E+00	2,74E+00	55
	ADD	2,42E-01	5,67E-01	1,04E+00	1,90E+00	3,90E+00	37
Galaxolide	DDing-dust	1,01E-01	3,44E-01	7,12E-01	1,41E+00	3,63E+00	92
	DDinh-air	5,13E+00	1,62E+01	3,42E+01	7,17E+01	2,24E+02	56
	DDderm-gas	2,93E+00	7,55E+00	1,45E+01	2,78E+01	6,83E+01	140
	ADD	1,23E+01	3,00E+01	5,58E+01	1,05E+02	2,68E+02	64
Tonalide	DDing-dust	7,98E-02	1,70E-01	2,91E-01	5,00E-01	1,09E+00	96
	DDinh-air	1,52E+00	4,48E+00	9,54E+00	2,11E+01	7,47E+01	56
	DDderm-gas	1,18E+00	2,12E+00	3,44E+00	5,88E+00	1,33E+01	65
	ADD	3,98E+00	8,34E+00	1,49E+01	2,81E+01	8,19E+01	46
Anthracene	DDing-dust	1,21E-03	6,39E-03	1,58E-02	3,49E-02	9,90E-02	56
	DDinh-air	1,06E-02	4,95E-02	1,15E-01	2,39E-01	7,07E-01	9
	DDderm-gas	1,65E-02	8,39E-02	1,78E-01	3,40E-01	9,79E-01	40
	ADD	4,40E-02	1,65E-01	3,31E-01	6,14E-01	1,72E+00	21
Benzo[a]pyrene	DDing-dust	7,16E-04	3,64E-03	9,26E-03	2,20E-02	7,31E-02	50
	DDinh-air	4,58E-03	2,50E-02	7,35E-02	1,96E-01	7,03E-01	10
	DDderm-gas	2,13E-02	2,83E-02	3,31E-02	3,81E-02	4,56E-02	21
	ADD	4,81E-02	7,96E-02	1,32E-01	2,53E-01	7,51E-01	11
Fluorene	DDing-dust	3,43E-03	6,28E-03	9,54E-03	1,45E-02	2,65E-02	68
	DDinh-air	1,68E-02	7,65E-02	3,76E-01	9,19E-01	3,02E+00	10
	DDderm-gas	1,09E-02	5,47E-02	3,81E-01	6,47E-01	2,13E+00	38
	ADD	4,26E-02	1,46E-01	8,51E-01	1,57E+00	5,21E+00	16

Phenanthrene	DDing-dust	1,88E-02	5,59E-02	1,15E-01	2,31E-01	6,27E-01	53
	DDinh-air	4,73E-01	1,11E+00	2,02E+00	4,39E+00	1,20E+01	10
	DDderm-gas	1,53E+00	2,31E+00	3,94E+00	8,70E+00	2,09E+01	23
	ADD	2,43E+00	3,68E+00	6,23E+00	1,36E+01	3,23E+01	14
PCB 28	DDing-dust	5,65E-04	2,18E-03	4,86E-03	1,04E-02	2,98E-02	36
	DDinh-air	1,61E-03	8,65E-03	1,92E-02	3,40E-02	6,23E-02	56
	DDderm-gas	8,01E-04	4,03E-03	8,07E-03	1,25E-02	1,84E-02	21
	ADD	9,68E-03	2,26E-02	3,69E-02	5,49E-02	8,80E-02	37
PCB 31	DDing-dust	2,21E-04	1,28E-03	3,40E-03	8,14E-03	2,48E-02	64
	DDinh-air	8,01E-02	1,80E-01	2,68E-01	3,79E-01	6,08E-01	118
	DDderm-gas	4,94E-02	6,55E-02	7,68E-02	8,83E-02	1,06E-01	120
	ADD	1,60E-01	2,61E-01	3,51E-01	4,65E-01	6,98E-01	112
PCB 52	DDing-dust	4,49E-04	3,25E-03	1,14E-02	3,96E-02	2,38E-01	55
	DDinh-air	2,03E-02	7,01E-02	1,63E-01	3,87E-01	1,37E+00	56
	DDderm-gas	9,81E-04	4,90E-03	9,85E-03	1,56E-02	3,35E-02	112
	ADD	3,84E-02	1,05E-01	2,20E-01	4,81E-01	1,52E+00	48
PCB 101	DDing-dust	4,27E-03	2,77E-02	8,25E-02	2,29E-01	9,38E-01	52
	DDinh-air	2,08E-03	9,80E-03	2,12E-02	3,81E-02	8,84E-02	60
	DDderm-gas	9,10E-04	4,58E-03	9,18E-03	1,43E-02	2,88E-02	43
	ADD	2,22E-02	6,22E-02	1,26E-01	2,95E-01	1,04E+00	36
PCB 105	DDing-dust	3,38E-05	2,49E-04	8,87E-04	3,09E-03	1,84E-02	72
	DDinh-air	1,80E-02	7,07E-02	2,03E-01	5,85E-01	2,64E+00	61
	DDderm-gas	4,51E-03	5,97E-03	7,00E-03	8,06E-03	9,64E-03	370
	ADD	2,66E-02	8,11E-02	2,14E-01	5,97E-01	2,66E+00	55
PCB 118	DDing-dust	4,26E-03	7,33E-03	1,20E-02	2,76E-02	1,72E-01	51
	DDinh-air	1,43E-02	3,18E-02	4,68E-02	6,46E-02	9,66E-02	288
	DDderm-gas	1,63E-02	2,16E-02	2,53E-02	2,91E-02	3,48E-02	272
	ADD	4,89E-02	7,09E-02	9,17E-02	1,21E-01	2,57E-01	230
PCB 138	DDing-dust	1,30E-03	8,90E-03	2,88E-02	8,90E-02	4,30E-01	37
	DDinh-air	8,52E-03	1,89E-02	2,78E-02	3,85E-02	5,88E-02	227
	DDderm-gas	8,68E-03	1,15E-02	1,35E-02	1,55E-02	1,86E-02	284
	ADD	3,16E-02	5,09E-02	7,55E-02	1,36E-01	4,77E-01	132
PCB 153	DDing-dust	8,87E-04	6,09E-03	2,04E-02	6,56E-02	3,38E-01	49
	DDinh-air	8,88E-03	1,98E-02	2,91E-02	4,01E-02	6,06E-02	228
	DDderm-gas	9,92E-03	1,31E-02	1,54E-02	1,77E-02	2,12E-02	250
	ADD	3,23E-02	5,00E-02	7,07E-02	1,17E-01	3,91E-01	173
BBP	DDing-dust	2,16E+01	1,09E+02	2,21E+02	3,62E+02	6,25E+02	42
	DDinh-air	3,69E-01	8,42E-01	1,34E+00	2,22E+00	6,33E+00	57
	DDderm-gas	7,57E-02	3,82E-01	7,69E-01	1,26E+00	3,56E+00	75
	ADD	2,47E+01	1,12E+02	2,24E+02	3,65E+02	6,29E+02	41
DBP	DDing-dust	1,89E+00	9,49E+00	1,92E+01	3,15E+01	5,41E+01	45
	DDinh-air	3,04E+01	8,94E+01	2,15E+02	5,78E+02	2,58E+03	56
	DDderm-gas	4,22E+01	8,91E+01	1,35E+02	1,96E+02	3,11E+02	47
	ADD	1,27E+02	2,48E+02	4,07E+02	7,72E+02	2,78E+03	39

DEHP	DDing-dust	6,56E+01	3,28E+02	6,64E+02	1,09E+03	1,88E+03	50
	DDinh-air	1,58E+00	4,62E+00	9,86E+00	2,22E+01	7,48E+01	57
	DDderm-gas	7,15E-01	3,58E+00	7,17E+00	1,11E+01	1,78E+01	84
	ADD	9,06E+01	3,55E+02	6,92E+02	1,12E+03	1,92E+03	51
DEP	DDing-dust	1,17E+00	1,89E+00	2,73E+00	4,49E+00	2,09E+01	37
	DDinh-air	2,52E+01	8,10E+01	1,88E+02	4,76E+02	1,99E+03	60
	DDderm-gas	4,97E+00	9,59E+00	1,54E+01	2,49E+01	4,78E+01	88
	ADD	4,03E+01	1,03E+02	2,15E+02	5,05E+02	2,03E+03	47
DiBP	DDing-dust	2,38E+01	1,19E+02	2,42E+02	3,96E+02	6,81E+02	36
	DDinh-air	1,38E+01	3,92E+01	7,58E+01	1,42E+02	3,28E+02	58
	DDderm-gas	2,88E+02	6,34E+02	1,10E+03	1,91E+03	4,00E+03	27
	ADD	4,10E+02	8,89E+02	1,47E+03	2,42E+03	4,73E+03	22
DiNP	DDing-dust	7,57E+01	3,78E+02	7,65E+02	1,26E+03	2,17E+03	71
	DDinh-air	6,66E-01	2,11E+00	3,93E+00	6,76E+00	1,44E+01	58
	DDderm-gas	2,90E-01	1,45E+00	2,92E+00	4,57E+00	7,56E+00	91
	ADD	8,34E+01	3,85E+02	7,73E+02	1,26E+03	2,18E+03	68
BDE 28	DDing-dust	1,24E-04	2,07E-04	3,13E-04	5,33E-04	1,40E-03	33
	DDinh-air	2,52E-02	8,38E-02	1,66E-01	3,05E-01	6,60E-01	37
	DDderm-gas	3,27E-03	1,73E-02	4,10E-02	8,43E-02	2,01E-01	50
	ADD	4,08E-02	1,17E-01	2,20E-01	3,89E-01	8,04E-01	29
BDE 47	DDing-dust	5,61E-03	1,15E-02	2,20E-02	4,82E-02	1,67E-01	39
	DDinh-air	7,27E-02	3,33E-01	7,08E-01	1,28E+00	2,50E+00	35
	DDderm-gas	9,52E-02	4,09E-01	7,87E-01	1,27E+00	2,08E+00	47
	ADD	2,36E-01	8,59E-01	1,61E+00	2,61E+00	4,37E+00	31
BDE 85	DDing-dust	2,89E-04	1,45E-03	2,97E-03	5,07E-03	1,07E-02	42
	DDinh-air	3,55E-04	1,14E-03	2,32E-03	4,81E-03	1,36E-02	36
	DDderm-gas	1,88E-04	1,06E-03	2,76E-03	6,48E-03	1,89E-02	59
	ADD	2,66E-03	5,71E-03	9,48E-03	1,62E-02	3,63E-02	27
BDE 99	DDing-dust	1,19E-02	1,94E-02	2,87E-02	4,84E-02	1,79E-01	43
	DDinh-air	6,58E-02	1,47E-01	2,17E-01	3,05E-01	4,96E-01	35
	DDderm-gas	2,02E-01	2,70E-01	3,20E-01	3,78E-01	5,48E-01	63
	ADD	3,68E-01	4,85E-01	5,84E-01	7,16E-01	1,11E+00	39
BDE 100	DDing-dust	7,06E-04	3,34E-03	8,01E-03	1,80E-02	5,49E-02	38
	DDinh-air	9,17E-02	3,29E-01	7,15E-01	1,47E+00	3,87E+00	34
	DDderm-gas	6,68E-02	9,71E-02	1,36E-01	2,16E-01	5,01E-01	37
	ADD	2,31E-01	5,16E-01	9,31E-01	1,70E+00	4,10E+00	29
BDE 153	DDing-dust	1,54E-03	7,69E-03	1,59E-02	2,90E-02	7,81E-02	34
	DDinh-air	9,17E-04	2,55E-03	5,21E-03	1,13E-02	3,60E-02	35
	DDderm-gas	3,39E-03	8,82E-03	1,90E-02	4,29E-02	1,34E-01	44
	ADD	1,39E-02	2,94E-02	4,95E-02	8,72E-02	2,37E-01	25
BDE 154	DDing-dust	1,46E-03	7,26E-03	1,50E-02	2,74E-02	7,36E-02	34
	DDinh-air	6,68E-04	1,91E-03	3,80E-03	7,73E-03	2,13E-02	36
	DDderm-gas	2,70E-03	7,96E-03	1,70E-02	3,61E-02	9,73E-02	38
	ADD	1,18E-02	2,58E-02	4,32E-02	7,39E-02	1,68E-01	24

Table S13: Daily doses (DD) from each route of exposure (ingestion of dust, inhalation and dermal contact with the gas phase) and aggregated daily doses (ADD) estimated (ng/kg-bw/d) for 32 SVOCs for the age group of [2-3 years]

SVOCs	Estimated daily doses[1]	p5	p25	p50	p75	p95	Uncertainty on the mean (%)
Aldrin	DDing-dust	4,9E-05	2,4E-04	4,9E-04	8,3E-04	1,9E-03	74
	DDinh-air	5,8E-03	2,9E-02	6,2E-02	1,1E-01	2,0E-01	59
	DDderm-gas	7,0E-04	3,5E-03	7,0E-03	1,1E-02	1,9E-02	122
	ADD	7,8E-03	3,5E-02	7,1E-02	1,2E-01	2,4E-01	51
Dieldrin	DDing-dust	1,3E-04	7,8E-04	2,1E-03	4,9E-03	1,6E-02	71
	DDinh-air	8,7E-02	3,0E-01	7,0E-01	1,5E+00	4,1E+00	56
	DDderm-gas	8,3E-04	4,2E-03	8,4E-03	1,3E-02	6,8E-02	166
	ADD	9,7E-02	3,2E-01	7,2E-01	1,5E+00	4,1E+00	55
Lindane	DDing-dust	1,2E-02	1,9E-02	2,7E-02	4,7E-02	2,5E-01	62
	DDinh-air	2,0E-01	6,5E-01	1,5E+00	3,5E+00	1,2E+01	59
	DDderm-gas	8,1E-03	3,6E-02	6,3E-02	1,7E-01	1,1E+00	126
	ADD	2,7E-01	7,6E-01	1,7E+00	3,9E+00	1,4E+01	68
Chlorpyrifos	DDing-dust	3,6E-04	1,7E-03	4,7E-03	1,3E-02	5,1E-02	44
	DDinh-air	9,9E-03	3,5E-02	6,8E-02	1,1E-01	2,1E-01	58
	DDderm-gas	6,0E-03	3,0E-02	6,0E-02	9,2E-02	1,5E-01	104
	ADD	2,5E-02	8,0E-02	1,4E-01	2,2E-01	3,7E-01	49
Tributylphosphate	DDing-dust	5,8E-02	1,0E-01	1,5E-01	2,5E-01	5,3E-01	82
	DDinh-air	1,9E-02	8,5E-02	2,0E-01	4,3E-01	1,0E+00	56
	DDderm-gas	4,3E-02	2,2E-01	5,1E-01	1,1E+00	2,4E+00	55
	ADD	2,0E-01	5,0E-01	9,4E-01	1,8E+00	3,6E+00	37
Galaxolide	DDing-dust	7,6E-02	2,6E-01	5,4E-01	1,1E+00	2,8E+00	92
	DDinh-air	7,6E+00	2,2E+01	4,4E+01	8,9E+01	2,7E+02	56
	DDderm-gas	2,6E+00	6,6E+00	1,3E+01	2,4E+01	5,9E+01	140
	ADD	1,4E+01	3,4E+01	6,3E+01	1,2E+02	3,1E+02	64
Tonalide	DDing-dust	6,1E-02	1,3E-01	2,2E-01	3,8E-01	8,3E-01	96
	DDinh-air	2,2E+00	5,9E+00	1,2E+01	2,6E+01	9,1E+01	56
	DDderm-gas	1,0E+00	1,9E+00	3,0E+00	5,1E+00	1,2E+01	65
	ADD	4,3E+00	9,3E+00	1,7E+01	3,2E+01	9,7E+01	46
Anthracene	DDing-dust	9,2E-04	4,8E-03	1,2E-02	2,6E-02	7,5E-02	56
	DDinh-air	1,5E-02	6,7E-02	1,5E-01	3,0E-01	8,7E-01	9
	DDderm-gas	1,5E-02	7,4E-02	1,6E-01	3,0E-01	8,5E-01	40
	ADD	4,3E-02	1,6E-01	3,3E-01	6,2E-01	1,7E+00	21
Benzo[a]pyrene	DDing-dust	5,4E-04	2,8E-03	7,0E-03	1,7E-02	5,5E-02	50
	DDinh-air	6,5E-03	3,3E-02	9,5E-02	2,5E-01	8,6E-01	10
	DDderm-gas	1,9E-02	2,5E-02	2,9E-02	3,3E-02	3,9E-02	21
	ADD	4,6E-02	8,1E-02	1,4E-01	2,9E-01	9,0E-01	11
Fluorene	DDing-dust	2,6E-03	4,8E-03	7,2E-03	1,1E-02	2,0E-02	68
	DDinh-air	2,4E-02	9,9E-02	5,2E-01	1,1E+00	3,7E+00	10
	DDderm-gas	9,6E-03	4,8E-02	3,4E-01	5,6E-01	1,8E+00	38
	ADD	4,5E-02	1,6E-01	9,3E-01	1,7E+00	5,6E+00	16

Phenanthrene	DDing-dust	1,4E-02	4,2E-02	8,7E-02	1,8E-01	4,7E-01	53
	DDinh-air	7,3E-01	1,4E+00	2,5E+00	5,5E+00	1,4E+01	10
	DDderm-gas	1,4E+00	2,0E+00	3,4E+00	7,6E+00	1,8E+01	23
	ADD	2,4E+00	3,6E+00	6,2E+00	1,3E+01	3,2E+01	14
PCB 28	DDing-dust	4,3E-04	1,6E-03	3,7E-03	7,9E-03	2,2E-02	36
	DDinh-air	2,4E-03	1,2E-02	2,5E-02	4,2E-02	7,3E-02	56
	DDderm-gas	7,0E-04	3,5E-03	7,1E-03	1,1E-02	1,6E-02	21
	ADD	9,4E-03	2,3E-02	3,9E-02	5,9E-02	9,3E-02	37
PCB 31	DDing-dust	1,7E-04	9,7E-04	2,6E-03	6,2E-03	1,9E-02	64
	DDinh-air	1,3E-01	2,4E-01	3,3E-01	4,5E-01	7,1E-01	118
	DDderm-gas	4,5E-02	5,8E-02	6,7E-02	7,6E-02	9,1E-02	120
	ADD	2,0E-01	3,1E-01	4,1E-01	5,3E-01	7,8E-01	112
PCB 52	DDing-dust	3,4E-04	2,5E-03	8,6E-03	3,0E-02	1,8E-01	55
	DDinh-air	3,0E-02	9,3E-02	2,1E-01	4,8E-01	1,7E+00	56
	DDderm-gas	8,6E-04	4,3E-03	8,6E-03	1,4E-02	2,9E-02	112
	ADD	4,6E-02	1,2E-01	2,6E-01	5,6E-01	1,8E+00	48
PCB 101	DDing-dust	3,3E-03	2,1E-02	6,3E-02	1,7E-01	7,1E-01	52
	DDinh-air	3,1E-03	1,3E-02	2,7E-02	4,7E-02	1,0E-01	60
	DDderm-gas	8,0E-04	4,0E-03	8,0E-03	1,2E-02	2,5E-02	43
	ADD	2,1E-02	5,9E-02	1,1E-01	2,4E-01	8,7E-01	36
PCB 105	DDing-dust	2,6E-05	1,9E-04	6,7E-04	2,3E-03	1,4E-02	72
	DDinh-air	2,5E-02	9,4E-02	2,6E-01	7,3E-01	3,3E+00	61
	DDderm-gas	4,1E-03	5,3E-03	6,1E-03	7,0E-03	8,3E-03	370
	ADD	3,3E-02	1,0E-01	2,7E-01	7,4E-01	3,3E+00	55
PCB 118	DDing-dust	3,3E-03	5,6E-03	9,1E-03	2,1E-02	1,3E-01	51
	DDinh-air	2,4E-02	4,3E-02	5,9E-02	7,7E-02	1,1E-01	288
	DDderm-gas	1,5E-02	1,9E-02	2,2E-02	2,5E-02	3,0E-02	272
	ADD	5,3E-02	7,6E-02	9,7E-02	1,2E-01	2,3E-01	230
PCB 138	DDing-dust	9,9E-04	6,8E-03	2,2E-02	6,7E-02	3,3E-01	37
	DDinh-air	1,4E-02	2,5E-02	3,5E-02	4,6E-02	6,7E-02	227
	DDderm-gas	7,8E-03	1,0E-02	1,2E-02	1,3E-02	1,6E-02	284
	ADD	3,4E-02	5,3E-02	7,4E-02	1,2E-01	3,8E-01	132
PCB 153	DDing-dust	6,7E-04	4,6E-03	1,5E-02	4,9E-02	2,5E-01	49
	DDinh-air	1,5E-02	2,7E-02	3,6E-02	4,8E-02	6,9E-02	228
	DDderm-gas	8,9E-03	1,2E-02	1,3E-02	1,5E-02	1,8E-02	250
	ADD	3,5E-02	5,3E-02	7,1E-02	1,1E-01	3,1E-01	173
BBP	DDing-dust	1,6E+01	8,3E+01	1,7E+02	2,8E+02	4,7E+02	42
	DDinh-air	5,9E-01	1,1E+00	1,7E+00	2,7E+00	7,7E+00	57
	DDderm-gas	6,6E-02	3,3E-01	6,7E-01	1,1E+00	3,1E+00	75
	ADD	2,0E+01	8,6E+01	1,7E+02	2,8E+02	4,8E+02	41
DBP	DDing-dust	1,4E+00	7,2E+00	1,5E+01	2,4E+01	4,1E+01	45
	DDinh-air	4,4E+01	1,2E+02	2,8E+02	7,3E+02	3,2E+03	56
	DDderm-gas	3,7E+01	7,8E+01	1,2E+02	1,7E+02	2,7E+02	47
	ADD	1,3E+02	2,6E+02	4,4E+02	8,9E+02	3,4E+03	39

DEHP	DDing-dust	5,0E+01	2,5E+02	5,0E+02	8,2E+02	1,4E+03	50
	DDinh-air	2,3E+00	6,1E+00	1,3E+01	2,8E+01	9,1E+01	57
	DDderm-gas	6,3E-01	3,1E+00	6,3E+00	9,7E+00	1,5E+01	84
	ADD	7,6E+01	2,8E+02	5,4E+02	8,6E+02	1,5E+03	51
DEP	DDing-dust	8,9E-01	1,4E+00	2,1E+00	3,4E+00	1,6E+01	37
	DDinh-air	3,7E+01	1,1E+02	2,4E+02	6,0E+02	2,5E+03	60
	DDderm-gas	4,4E+00	8,4E+00	1,3E+01	2,2E+01	4,2E+01	88
	ADD	5,0E+01	1,3E+02	2,6E+02	6,2E+02	2,5E+03	47
DiBP	DDing-dust	1,8E+01	9,0E+01	1,8E+02	3,0E+02	5,2E+02	36
	DDinh-air	2,1E+01	5,2E+01	9,6E+01	1,8E+02	3,9E+02	58
	DDderm-gas	2,5E+02	5,6E+02	9,6E+02	1,7E+03	3,5E+03	27
	ADD	3,6E+02	7,7E+02	1,3E+03	2,1E+03	4,2E+03	22
DiNP	DDing-dust	5,7E+01	2,9E+02	5,8E+02	9,5E+02	1,6E+03	71
	DDinh-air	1,0E+00	2,8E+00	5,0E+00	8,3E+00	1,7E+01	58
	DDderm-gas	2,5E-01	1,3E+00	2,6E+00	4,0E+00	6,6E+00	91
	ADD	6,6E+01	2,9E+02	5,9E+02	9,6E+02	1,6E+03	68
BDE 28	DDing-dust	9,4E-05	1,6E-04	2,4E-04	4,0E-04	1,1E-03	33
	DDinh-air	3,8E-02	1,1E-01	2,1E-01	3,8E-01	7,9E-01	37
	DDderm-gas	2,9E-03	1,5E-02	3,6E-02	7,4E-02	1,7E-01	50
	ADD	5,1E-02	1,4E-01	2,6E-01	4,5E-01	9,1E-01	29
BDE 47	DDing-dust	4,3E-03	8,7E-03	1,7E-02	3,6E-02	1,3E-01	39
	DDinh-air	1,1E-01	4,5E-01	9,1E-01	1,6E+00	2,9E+00	35
	DDderm-gas	8,4E-02	3,6E-01	6,9E-01	1,1E+00	1,8E+00	47
	ADD	2,4E-01	9,0E-01	1,7E+00	2,7E+00	4,6E+00	31
BDE 85	DDing-dust	2,2E-04	1,1E-03	2,2E-03	3,8E-03	8,1E-03	42
	DDinh-air	5,3E-04	1,5E-03	2,9E-03	6,0E-03	1,7E-02	36
	DDderm-gas	1,6E-04	9,2E-04	2,4E-03	5,7E-03	1,6E-02	59
	ADD	2,5E-03	5,2E-03	8,7E-03	1,5E-02	3,6E-02	27
BDE 99	DDing-dust	9,1E-03	1,5E-02	2,2E-02	3,7E-02	1,4E-01	43
	DDinh-air	1,1E-01	2,0E-01	2,7E-01	3,6E-01	5,8E-01	35
	DDderm-gas	1,8E-01	2,4E-01	2,8E-01	3,3E-01	4,8E-01	63
	ADD	3,7E-01	4,9E-01	5,9E-01	7,2E-01	1,1E+00	39
BDE 100	DDing-dust	5,4E-04	2,5E-03	6,1E-03	1,4E-02	4,2E-02	38
	DDinh-air	1,4E-01	4,4E-01	9,1E-01	1,8E+00	4,7E+00	34
	DDderm-gas	5,9E-02	8,5E-02	1,2E-01	1,9E-01	4,4E-01	37
	ADD	2,6E-01	6,0E-01	1,1E+00	2,0E+00	4,9E+00	29
BDE 153	DDing-dust	1,2E-03	5,8E-03	1,2E-02	2,2E-02	5,9E-02	34
	DDinh-air	1,4E-03	3,3E-03	6,6E-03	1,4E-02	4,4E-02	35
	DDderm-gas	3,0E-03	7,7E-03	1,7E-02	3,7E-02	1,2E-01	44
	ADD	1,2E-02	2,5E-02	4,3E-02	7,7E-02	2,1E-01	25
BDE 154	DDing-dust	1,1E-03	5,5E-03	1,1E-02	2,1E-02	5,6E-02	34
	DDinh-air	1,0E-03	2,5E-03	4,8E-03	9,6E-03	2,6E-02	36
	DDderm-gas	2,4E-03	7,0E-03	1,5E-02	3,1E-02	8,5E-02	38
	ADD	1,0E-02	2,2E-02	3,7E-02	6,4E-02	1,5E-01	24

Table S14: Daily doses (DD) from each route of exposure (ingestion of dust, inhalation and dermal contact with the gas phase) and aggregated daily doses (ADD) estimated (ng/kg-bw/d) for 32 SVOCs for the age group of [3-6 years]

SVOCs	Estimated daily doses[1]	p5	p25	p50	p75	p95	Uncertainty on the mean (%)
Aldrin	DDing-dust	3,39E-05	1,69E-04	3,52E-04	6,15E-04	1,47E-03	74
	DDinh-air	5,14E-03	2,52E-02	5,21E-02	8,88E-02	1,70E-01	59
	DDderm-gas	6,12E-04	3,06E-03	6,21E-03	9,90E-03	1,73E-02	122
	ADD	6,60E-03	3,00E-02	6,05E-02	1,01E-01	1,97E-01	51
Dieldrin	DDing-dust	9,26E-05	5,48E-04	1,48E-03	3,60E-03	1,18E-02	71
	DDinh-air	7,57E-02	2,57E-01	5,94E-01	1,26E+00	3,39E+00	56
	DDderm-gas	7,23E-04	3,63E-03	7,39E-03	1,20E-02	6,09E-02	166
	ADD	8,42E-02	2,68E-01	6,09E-01	1,28E+00	3,41E+00	55
Lindane	DDing-dust	7,49E-03	1,33E-02	2,02E-02	3,52E-02	1,87E-01	62
	DDinh-air	1,78E-01	5,53E-01	1,29E+00	2,95E+00	1,01E+01	59
	DDderm-gas	7,02E-03	3,15E-02	5,74E-02	1,58E-01	1,02E+00	126
	ADD	2,27E-01	6,38E-01	1,44E+00	3,27E+00	1,14E+01	68
Chlorpyrifos	DDing-dust	2,46E-04	1,21E-03	3,38E-03	9,18E-03	3,82E-02	44
	DDinh-air	8,66E-03	2,94E-02	5,72E-02	9,50E-02	1,78E-01	58
	DDderm-gas	5,22E-03	2,60E-02	5,26E-02	8,37E-02	1,41E-01	104
	ADD	2,09E-02	6,76E-02	1,23E-01	1,88E-01	3,24E-01	49
Tributylphosphate	DDing-dust	3,83E-02	7,15E-02	1,12E-01	1,83E-01	4,00E-01	82
	DDinh-air	1,68E-02	7,26E-02	1,73E-01	3,65E-01	8,38E-01	56
	DDderm-gas	3,71E-02	1,90E-01	4,54E-01	9,75E-01	2,14E+00	55
	ADD	1,57E-01	4,10E-01	7,98E-01	1,52E+00	3,18E+00	37
Galaxolide	DDing-dust	5,22E-02	1,84E-01	3,89E-01	7,85E-01	2,07E+00	92
	DDinh-air	6,66E+00	1,83E+01	3,67E+01	7,47E+01	2,28E+02	56
	DDderm-gas	2,21E+00	5,84E+00	1,14E+01	2,19E+01	5,46E+01	140
	ADD	1,18E+01	2,88E+01	5,36E+01	1,01E+02	2,61E+02	64
Tonalide	DDing-dust	4,08E-02	9,12E-02	1,60E-01	2,80E-01	6,31E-01	96
	DDinh-air	1,96E+00	5,04E+00	1,02E+01	2,20E+01	7,60E+01	56
	DDderm-gas	8,80E-01	1,64E+00	2,70E+00	4,66E+00	1,07E+01	65
	ADD	3,73E+00	7,98E+00	1,44E+01	2,76E+01	8,15E+01	46
Anthracene	DDing-dust	6,32E-04	3,42E-03	8,56E-03	1,93E-02	5,66E-02	56
	DDinh-air	1,34E-02	5,68E-02	1,24E-01	2,47E-01	7,26E-01	9
	DDderm-gas	1,26E-02	6,46E-02	1,39E-01	2,70E-01	7,77E-01	40
	ADD	3,56E-02	1,40E-01	2,86E-01	5,37E-01	1,52E+00	21
Benzo[a]pyrene	DDing-dust	3,74E-04	1,95E-03	5,04E-03	1,22E-02	4,13E-02	50
	DDinh-air	5,64E-03	2,85E-02	7,98E-02	2,07E-01	7,19E-01	10
	DDderm-gas	1,49E-02	2,14E-02	2,61E-02	3,10E-02	3,85E-02	21
	ADD	3,83E-02	6,79E-02	1,20E-01	2,45E-01	7,53E-01	11
Fluorene	DDing-dust	1,72E-03	3,34E-03	5,24E-03	8,17E-03	1,53E-02	68
	DDinh-air	2,09E-02	8,28E-02	4,46E-01	9,41E-01	3,13E+00	10
	DDderm-gas	8,38E-03	4,25E-02	2,87E-01	5,19E-01	1,73E+00	38
	ADD	3,72E-02	1,34E-01	7,98E-01	1,45E+00	4,85E+00	16

Phenanthrene	DDing-dust	9,79E-03	3,00E-02	6,27E-02	1,28E-01	3,57E-01	53
	DDinh-air	6,41E-01	1,21E+00	2,13E+00	4,63E+00	1,20E+01	10
	DDderm-gas	1,12E+00	1,82E+00	3,10E+00	6,84E+00	1,68E+01	23
	ADD	2,04E+00	3,17E+00	5,39E+00	1,18E+01	2,84E+01	14
PCB 28	DDing-dust	2,95E-04	1,17E-03	2,66E-03	5,77E-03	1,69E-02	36
	DDinh-air	2,08E-03	1,02E-02	2,09E-02	3,50E-02	6,06E-02	56
	DDderm-gas	6,12E-04	3,08E-03	6,25E-03	9,85E-03	1,51E-02	21
	ADD	7,33E-03	1,91E-02	3,27E-02	4,95E-02	7,85E-02	37
PCB 31	DDing-dust	1,16E-04	6,87E-04	1,85E-03	4,49E-03	1,40E-02	64
	DDinh-air	1,20E-01	2,02E-01	2,78E-01	3,77E-01	5,91E-01	118
	DDderm-gas	3,46E-02	4,97E-02	6,06E-02	7,19E-02	8,93E-02	120
	ADD	1,76E-01	2,64E-01	3,43E-01	4,46E-01	6,64E-01	112
PCB 52	DDing-dust	2,37E-04	1,76E-03	6,21E-03	2,18E-02	1,33E-01	55
	DDinh-air	2,63E-02	7,87E-02	1,76E-01	4,06E-01	1,39E+00	56
	DDderm-gas	7,49E-04	3,76E-03	7,62E-03	1,24E-02	2,72E-02	112
	ADD	3,86E-02	1,02E-01	2,13E-01	4,64E-01	1,47E+00	48
PCB 101	DDing-dust	2,27E-03	1,48E-02	4,49E-02	1,26E-01	5,26E-01	52
	DDinh-air	2,69E-03	1,14E-02	2,29E-02	3,88E-02	8,76E-02	60
	DDderm-gas	6,99E-04	3,51E-03	7,11E-03	1,14E-02	2,32E-02	43
	ADD	1,64E-02	4,56E-02	8,60E-02	1,83E-01	6,78E-01	36
PCB 105	DDing-dust	1,80E-05	1,34E-04	4,83E-04	1,71E-03	1,04E-02	72
	DDinh-air	2,18E-02	7,96E-02	2,20E-01	6,18E-01	2,73E+00	61
	DDderm-gas	3,15E-03	4,53E-03	5,53E-03	6,56E-03	8,14E-03	370
	ADD	2,82E-02	8,70E-02	2,28E-01	6,26E-01	2,74E+00	55
PCB 118	DDing-dust	2,13E-03	3,97E-03	6,69E-03	1,53E-02	9,56E-02	51
	DDinh-air	2,18E-02	3,61E-02	4,87E-02	6,40E-02	9,25E-02	288
	DDderm-gas	1,14E-02	1,64E-02	2,00E-02	2,37E-02	2,94E-02	272
	ADD	4,41E-02	6,36E-02	8,09E-02	1,04E-01	1,85E-01	230
PCB 138	DDing-dust	6,88E-04	4,79E-03	1,57E-02	4,91E-02	2,42E-01	37
	DDinh-air	1,28E-02	2,13E-02	2,88E-02	3,81E-02	5,64E-02	227
	DDderm-gas	6,07E-03	8,72E-03	1,06E-02	1,26E-02	1,57E-02	284
	ADD	2,81E-02	4,31E-02	6,02E-02	9,61E-02	2,89E-01	132
PCB 153	DDing-dust	4,67E-04	3,29E-03	1,11E-02	3,60E-02	1,88E-01	49
	DDinh-air	1,35E-02	2,24E-02	3,02E-02	3,98E-02	5,81E-02	228
	DDderm-gas	6,93E-03	9,97E-03	1,22E-02	1,44E-02	1,79E-02	250
	ADD	2,90E-02	4,34E-02	5,85E-02	8,71E-02	2,40E-01	173
BBP	DDing-dust	1,13E+01	5,73E+01	1,19E+02	2,02E+02	3,65E+02	42
	DDinh-air	5,25E-01	9,33E-01	1,39E+00	2,26E+00	6,45E+00	57
	DDderm-gas	5,82E-02	2,93E-01	5,98E-01	1,01E+00	2,82E+00	75
	ADD	1,40E+01	6,02E+01	1,22E+02	2,05E+02	3,69E+02	41
DBP	DDing-dust	9,93E-01	5,01E+00	1,04E+01	1,76E+01	3,18E+01	45
	DDinh-air	3,84E+01	9,91E+01	2,32E+02	6,11E+02	2,65E+03	56
	DDderm-gas	3,13E+01	6,82E+01	1,06E+02	1,56E+02	2,53E+02	47
	ADD	1,11E+02	2,21E+02	3,77E+02	7,58E+02	2,80E+03	39

DEHP	DDing-dust	3,42E+01	1,73E+02	3,58E+02	6,07E+02	1,10E+03	50
	DDinh-air	2,03E+00	5,13E+00	1,06E+01	2,33E+01	7,63E+01	57
	DDderm-gas	5,49E-01	2,75E+00	5,54E+00	8,80E+00	1,47E+01	84
	ADD	5,54E+01	1,98E+02	3,85E+02	6,38E+02	1,13E+03	51
DEP	DDing-dust	5,74E-01	1,01E+00	1,52E+00	2,56E+00	1,17E+01	37
	DDinh-air	3,23E+01	9,05E+01	2,02E+02	5,00E+02	2,04E+03	60
	DDderm-gas	3,72E+00	7,41E+00	1,21E+01	1,98E+01	3,84E+01	88
	ADD	4,28E+01	1,07E+02	2,22E+02	5,22E+02	2,06E+03	47
DiBP	DDing-dust	1,25E+01	6,29E+01	1,30E+02	2,21E+02	3,98E+02	36
	DDinh-air	1,83E+01	4,42E+01	8,09E+01	1,46E+02	3,27E+02	58
	DDderm-gas	2,16E+02	4,90E+02	8,63E+02	1,51E+03	3,21E+03	27
	ADD	3,00E+02	6,57E+02	1,11E+03	1,86E+03	3,76E+03	22
DiNP	DDing-dust	3,96E+01	2,00E+02	4,12E+02	6,99E+02	1,26E+03	71
	DDinh-air	9,10E-01	2,42E+00	4,19E+00	6,90E+00	1,44E+01	58
	DDderm-gas	2,21E-01	1,12E+00	2,26E+00	3,62E+00	6,12E+00	91
	ADD	4,64E+01	2,07E+02	4,20E+02	7,08E+02	1,27E+03	68
BDE 28	DDing-dust	6,13E-05	1,11E-04	1,74E-04	3,00E-04	7,90E-04	33
	DDinh-air	3,37E-02	9,54E-02	1,79E-01	3,14E-01	6,53E-01	37
	DDderm-gas	2,50E-03	1,34E-02	3,19E-02	6,66E-02	1,60E-01	50
	ADD	4,40E-02	1,20E-01	2,21E-01	3,83E-01	7,72E-01	29
BDE 47	DDing-dust	2,85E-03	6,21E-03	1,21E-02	2,68E-02	9,47E-02	39
	DDinh-air	9,53E-02	3,85E-01	7,66E-01	1,32E+00	2,43E+00	35
	DDderm-gas	7,26E-02	3,14E-01	6,11E-01	1,01E+00	1,69E+00	47
	ADD	2,04E-01	7,67E-01	1,45E+00	2,36E+00	3,98E+00	31
BDE 85	DDing-dust	1,51E-04	7,66E-04	1,61E-03	2,83E-03	6,15E-03	42
	DDinh-air	4,68E-04	1,28E-03	2,48E-03	5,01E-03	1,38E-02	36
	DDderm-gas	1,43E-04	8,16E-04	2,15E-03	5,11E-03	1,51E-02	59
	ADD	1,92E-03	4,14E-03	7,14E-03	1,28E-02	3,10E-02	27
BDE 99	DDing-dust	5,83E-03	1,04E-02	1,60E-02	2,74E-02	1,00E-01	43
	DDinh-air	9,91E-02	1,66E-01	2,26E-01	3,03E-01	4,82E-01	35
	DDderm-gas	1,42E-01	2,05E-01	2,53E-01	3,08E-01	4,53E-01	63
	ADD	3,06E-01	4,17E-01	5,08E-01	6,24E-01	9,59E-01	39
BDE 100	DDing-dust	3,69E-04	1,78E-03	4,37E-03	9,99E-03	3,11E-02	38
	DDinh-air	1,19E-01	3,72E-01	7,67E-01	1,52E+00	3,90E+00	34
	DDderm-gas	4,86E-02	7,55E-02	1,07E-01	1,72E-01	4,01E-01	37
	ADD	2,27E-01	5,17E-01	9,36E-01	1,70E+00	4,08E+00	29
BDE 153	DDing-dust	8,06E-04	4,06E-03	8,63E-03	1,62E-02	4,51E-02	34
	DDinh-air	1,19E-03	2,83E-03	5,55E-03	1,18E-02	3,66E-02	35
	DDderm-gas	2,58E-03	6,85E-03	1,49E-02	3,38E-02	1,06E-01	44
	ADD	9,58E-03	2,03E-02	3,52E-02	6,47E-02	1,79E-01	25
BDE 154	DDing-dust	7,75E-04	3,86E-03	8,18E-03	1,53E-02	4,24E-02	34
	DDinh-air	8,83E-04	2,14E-03	4,06E-03	8,06E-03	2,14E-02	36
	DDderm-gas	2,05E-03	6,18E-03	1,33E-02	2,84E-02	7,75E-02	38
	ADD	8,10E-03	1,77E-02	3,04E-02	5,37E-02	1,26E-01	24

Table S15: Daily doses (DD) from each route of exposure (ingestion of dust, inhalation and dermal contact with the gas phase) and aggregated daily doses (ADD) estimated (ng/kg-bw/d) for 32 SVOCs for the age group of [6-11 years]

SVOCs	Estimated daily doses[1]	p5	p25	p50	p75	p95	Uncertainty on the mean (%)
Aldrin	DDing-dust	1,84E-05	9,26E-05	1,95E-04	3,53E-04	8,78E-04	74
	DDinh-air	3,32E-03	1,63E-02	3,42E-02	6,03E-02	1,21E-01	59
	DDderm-gas	4,82E-04	2,43E-03	4,93E-03	7,92E-03	1,41E-02	122
	ADD	4,35E-03	1,99E-02	4,06E-02	6,96E-02	1,40E-01	51
Dieldrin	DDing-dust	5,07E-05	3,04E-04	8,29E-04	2,04E-03	6,88E-03	71
	DDinh-air	4,85E-02	1,69E-01	3,94E-01	8,52E-01	2,35E+00	56
	DDderm-gas	5,71E-04	2,88E-03	5,88E-03	9,61E-03	4,83E-02	166
	ADD	5,46E-02	1,77E-01	4,05E-01	8,69E-01	2,37E+00	55
Lindane	DDing-dust	3,91E-03	7,27E-03	1,15E-02	2,05E-02	1,07E-01	62
	DDinh-air	1,14E-01	3,64E-01	8,58E-01	1,99E+00	6,94E+00	59
	DDderm-gas	5,55E-03	2,49E-02	4,60E-02	1,27E-01	8,15E-01	126
	ADD	1,48E-01	4,26E-01	9,74E-01	2,23E+00	7,89E+00	68
Chlorpyrifos	DDing-dust	1,35E-04	6,75E-04	1,91E-03	5,23E-03	2,22E-02	44
	DDinh-air	5,54E-03	1,91E-02	3,76E-02	6,46E-02	1,27E-01	58
	DDderm-gas	4,12E-03	2,05E-02	4,18E-02	6,69E-02	1,14E-01	104
	ADD	1,43E-02	4,76E-02	8,81E-02	1,37E-01	2,41E-01	49
Tributylphosphate	DDing-dust	2,01E-02	3,93E-02	6,33E-02	1,05E-01	2,35E-01	82
	DDinh-air	1,08E-02	4,75E-02	1,14E-01	2,44E-01	5,85E-01	56
	DDderm-gas	2,93E-02	1,51E-01	3,62E-01	7,77E-01	1,71E+00	55
	ADD	1,02E-01	2,86E-01	5,80E-01	1,12E+00	2,39E+00	37
Galaxolide	DDing-dust	2,82E-02	1,01E-01	2,18E-01	4,48E-01	1,21E+00	92
	DDinh-air	4,25E+00	1,20E+01	2,44E+01	5,08E+01	1,57E+02	56
	DDderm-gas	1,75E+00	4,65E+00	9,06E+00	1,76E+01	4,39E+01	140
	ADD	8,19E+00	2,01E+01	3,77E+01	7,15E+01	1,86E+02	64
Tonalide	DDing-dust	2,17E-02	5,01E-02	8,95E-02	1,60E-01	3,69E-01	96
	DDinh-air	1,24E+00	3,29E+00	6,83E+00	1,49E+01	5,24E+01	56
	DDderm-gas	6,93E-01	1,31E+00	2,16E+00	3,73E+00	8,61E+00	65
	ADD	2,58E+00	5,56E+00	1,01E+01	1,93E+01	5,70E+01	46
Anthracene	DDing-dust	3,48E-04	1,89E-03	4,80E-03	1,10E-02	3,27E-02	56
	DDinh-air	8,70E-03	3,70E-02	8,22E-02	1,68E-01	4,98E-01	9
	DDderm-gas	1,01E-02	5,12E-02	1,11E-01	2,16E-01	6,25E-01	40
	ADD	2,47E-02	1,00E-01	2,08E-01	3,96E-01	1,13E+00	21
Benzo[a]pyrene	DDing-dust	2,07E-04	1,08E-03	2,83E-03	6,94E-03	2,39E-02	50
	DDinh-air	3,63E-03	1,87E-02	5,30E-02	1,40E-01	4,94E-01	10
	DDderm-gas	1,16E-02	1,69E-02	2,08E-02	2,50E-02	3,17E-02	21
	ADD	2,71E-02	4,72E-02	8,22E-02	1,68E-01	5,21E-01	11
Fluorene	DDing-dust	9,07E-04	1,83E-03	2,94E-03	4,70E-03	9,16E-03	68
	DDinh-air	1,34E-02	5,49E-02	2,83E-01	6,41E-01	2,16E+00	10
	DDderm-gas	6,62E-03	3,38E-02	2,26E-01	4,16E-01	1,39E+00	38
	ADD	2,53E-02	9,42E-02	5,58E-01	1,05E+00	3,58E+00	16

Phenanthrene	DDing-dust	5,28E-03	1,65E-02	3,52E-02	7,35E-02	2,09E-01	53
	DDinh-air	3,97E-01	7,98E-01	1,44E+00	3,12E+00	8,32E+00	10
	DDderm-gas	8,80E-01	1,45E+00	2,48E+00	5,47E+00	1,34E+01	23
	ADD	1,47E+00	2,36E+00	4,03E+00	8,81E+00	2,14E+01	14
PCB 28	DDing-dust	1,60E-04	6,44E-04	1,49E-03	3,28E-03	9,81E-03	36
	DDinh-air	1,33E-03	6,57E-03	1,37E-02	2,37E-02	4,33E-02	56
	DDderm-gas	4,86E-04	2,45E-03	4,96E-03	7,87E-03	1,23E-02	21
	ADD	4,58E-03	1,25E-02	2,20E-02	3,41E-02	5,69E-02	37
PCB 31	DDing-dust	6,34E-05	3,81E-04	1,04E-03	2,55E-03	8,09E-03	64
	DDinh-air	7,30E-02	1,29E-01	1,86E-01	2,62E-01	4,29E-01	118
	DDderm-gas	2,68E-02	3,92E-02	4,83E-02	5,80E-02	7,35E-02	120
	ADD	1,16E-01	1,77E-01	2,37E-01	3,17E-01	4,89E-01	112
PCB 52	DDing-dust	1,31E-04	9,77E-04	3,49E-03	1,24E-02	7,59E-02	55
	DDinh-air	1,67E-02	5,18E-02	1,17E-01	2,75E-01	9,58E-01	56
	DDderm-gas	5,96E-04	2,98E-03	6,07E-03	9,95E-03	2,20E-02	112
	ADD	2,48E-02	6,72E-02	1,41E-01	3,11E-01	1,00E+00	48
PCB 101	DDing-dust	1,24E-03	8,24E-03	2,52E-02	7,18E-02	3,04E-01	52
	DDinh-air	1,73E-03	7,40E-03	1,51E-02	2,65E-02	6,31E-02	60
	DDderm-gas	5,49E-04	2,78E-03	5,66E-03	9,12E-03	1,87E-02	43
	ADD	1,02E-02	2,87E-02	5,40E-02	1,11E-01	4,21E-01	36
PCB 105	DDing-dust	9,87E-06	7,47E-05	2,71E-04	9,66E-04	5,91E-03	72
	DDinh-air	1,40E-02	5,24E-02	1,46E-01	4,17E-01	1,87E+00	61
	DDderm-gas	2,45E-03	3,57E-03	4,40E-03	5,28E-03	6,70E-03	370
	ADD	1,89E-02	5,78E-02	1,52E-01	4,23E-01	1,87E+00	55
PCB 118	DDing-dust	1,12E-03	2,20E-03	3,83E-03	8,81E-03	5,55E-02	51
	DDinh-air	1,33E-02	2,29E-02	3,24E-02	4,45E-02	6,84E-02	288
	DDderm-gas	8,87E-03	1,29E-02	1,59E-02	1,91E-02	2,43E-02	272
	ADD	2,93E-02	4,27E-02	5,58E-02	7,39E-02	1,26E-01	230
PCB 138	DDing-dust	3,79E-04	2,66E-03	8,81E-03	2,79E-02	1,39E-01	37
	DDinh-air	7,82E-03	1,35E-02	1,92E-02	2,65E-02	4,15E-02	227
	DDderm-gas	4,72E-03	6,87E-03	8,47E-03	1,02E-02	1,29E-02	284
	ADD	1,85E-02	2,87E-02	4,05E-02	6,29E-02	1,75E-01	132
PCB 153	DDing-dust	2,58E-04	1,83E-03	6,23E-03	2,05E-02	1,08E-01	49
	DDinh-air	8,20E-03	1,42E-02	2,01E-02	2,77E-02	4,30E-02	228
	DDderm-gas	5,39E-03	7,85E-03	9,68E-03	1,16E-02	1,48E-02	250
	ADD	1,92E-02	2,91E-02	3,99E-02	5,85E-02	1,47E-01	173
BBP	DDing-dust	6,24E+00	3,16E+01	6,61E+01	1,15E+02	2,18E+02	42
	DDinh-air	3,23E-01	6,05E-01	9,40E-01	1,56E+00	4,44E+00	57
	DDderm-gas	4,58E-02	2,32E-01	4,76E-01	8,11E-01	2,26E+00	75
	ADD	8,09E+00	3,36E+01	6,83E+01	1,17E+02	2,21E+02	41
DBP	DDing-dust	5,45E-01	2,75E+00	5,75E+00	1,00E+01	1,90E+01	45
	DDinh-air	2,43E+01	6,54E+01	1,55E+02	4,13E+02	1,81E+03	56
	DDderm-gas	2,48E+01	5,42E+01	8,45E+01	1,25E+02	2,05E+02	47
	ADD	7,90E+01	1,58E+02	2,69E+02	5,31E+02	1,94E+03	39

DEHP	DDing-dust	1,90E+01	9,55E+01	1,99E+02	3,46E+02	6,58E+02	50
	DDinh-air	1,29E+00	3,38E+00	7,06E+00	1,57E+01	5,29E+01	57
	DDderm-gas	4,33E-01	2,18E+00	4,41E+00	7,03E+00	1,19E+01	84
	ADD	3,31E+01	1,13E+02	2,17E+02	3,68E+02	6,87E+02	51
DEP	DDing-dust	3,01E-01	5,54E-01	8,65E-01	1,49E+00	6,73E+00	37
	DDinh-air	2,06E+01	5,94E+01	1,35E+02	3,38E+02	1,40E+03	60
	DDderm-gas	2,92E+00	5,89E+00	9,65E+00	1,58E+01	3,11E+01	88
	ADD	2,85E+01	7,20E+01	1,50E+02	3,55E+02	1,42E+03	47
DiBP	DDing-dust	6,83E+00	3,45E+01	7,21E+01	1,26E+02	2,39E+02	36
	DDinh-air	1,16E+01	2,88E+01	5,37E+01	9,94E+01	2,28E+02	58
	DDderm-gas	1,71E+02	3,89E+02	6,88E+02	1,21E+03	2,58E+03	27
	ADD	2,22E+02	4,89E+02	8,37E+02	1,43E+03	2,94E+03	22
DiNP	DDing-dust	2,17E+01	1,09E+02	2,28E+02	3,98E+02	7,53E+02	71
	DDinh-air	5,78E-01	1,56E+00	2,78E+00	4,71E+00	1,01E+01	58
	DDderm-gas	1,76E-01	8,83E-01	1,80E+00	2,90E+00	4,94E+00	91
	ADD	2,65E+01	1,14E+02	2,34E+02	4,04E+02	7,61E+02	68
BDE 28	DDing-dust	3,22E-05	6,12E-05	9,85E-05	1,73E-04	4,61E-04	33
	DDinh-air	2,14E-02	6,20E-02	1,18E-01	2,14E-01	4,62E-01	37
	DDderm-gas	1,99E-03	1,06E-02	2,55E-02	5,33E-02	1,29E-01	50
	ADD	2,94E-02	8,17E-02	1,52E-01	2,68E-01	5,57E-01	29
BDE 47	DDing-dust	1,52E-03	3,45E-03	6,86E-03	1,53E-02	5,48E-02	39
	DDinh-air	6,20E-02	2,50E-01	5,05E-01	8,91E-01	1,73E+00	35
	DDderm-gas	5,80E-02	2,49E-01	4,86E-01	8,04E-01	1,37E+00	47
	ADD	1,44E-01	5,49E-01	1,04E+00	1,72E+00	2,97E+00	31
BDE 85	DDing-dust	8,27E-05	4,20E-04	8,93E-04	1,62E-03	3,62E-03	42
	DDinh-air	2,99E-04	8,41E-04	1,66E-03	3,40E-03	9,47E-03	36
	DDderm-gas	1,13E-04	6,50E-04	1,71E-03	4,08E-03	1,21E-02	59
	ADD	1,21E-03	2,71E-03	4,84E-03	9,02E-03	2,27E-02	27
BDE 99	DDing-dust	3,06E-03	5,72E-03	9,07E-03	1,59E-02	5,80E-02	43
	DDinh-air	6,03E-02	1,05E-01	1,50E-01	2,11E-01	3,50E-01	35
	DDderm-gas	1,10E-01	1,62E-01	2,02E-01	2,49E-01	3,69E-01	63
	ADD	2,15E-01	2,97E-01	3,71E-01	4,66E-01	7,19E-01	39
BDE 100	DDing-dust	2,02E-04	9,86E-04	2,45E-03	5,69E-03	1,80E-02	38
	DDinh-air	7,63E-02	2,44E-01	5,10E-01	1,03E+00	2,71E+00	34
	DDderm-gas	3,80E-02	6,00E-02	8,61E-02	1,38E-01	3,22E-01	37
	ADD	1,58E-01	3,55E-01	6,42E-01	1,17E+00	2,86E+00	29
BDE 153	DDing-dust	4,43E-04	2,24E-03	4,83E-03	9,30E-03	2,66E-02	34
	DDinh-air	7,54E-04	1,86E-03	3,72E-03	8,00E-03	2,51E-02	35
	DDderm-gas	2,03E-03	5,44E-03	1,19E-02	2,71E-02	8,57E-02	44
	ADD	6,38E-03	1,37E-02	2,44E-02	4,65E-02	1,29E-01	25
BDE 154	DDing-dust	4,22E-04	2,12E-03	4,57E-03	8,79E-03	2,49E-02	34
	DDinh-air	5,57E-04	1,40E-03	2,72E-03	5,48E-03	1,49E-02	36
	DDderm-gas	1,62E-03	4,90E-03	1,06E-02	2,27E-02	6,21E-02	38
	ADD	5,37E-03	1,19E-02	2,11E-02	3,83E-02	9,14E-02	24

Table S16: Daily doses (DD) from each route of exposure (ingestion of dust, inhalation and dermal contact with the gas phase) and aggregated daily doses (ADD) estimated (ng/kg-bw/d) for 32 SVOCs for the age group of [11-16 years]

SVOCs	Estimated daily doses[1]	p5	p25	p50	p75	p95	Uncertainty on the mean (%)
Aldrin	DDing-dust	1,01E-05	5,12E-05	1,08E-04	1,97E-04	5,09E-04	74
	DDinh-air	2,24E-03	1,12E-02	2,39E-02	4,26E-02	8,84E-02	59
	DDderm-gas	3,77E-04	1,92E-03	3,97E-03	6,48E-03	1,17E-02	122
	ADD	3,01E-03	1,41E-02	2,89E-02	4,99E-02	1,02E-01	51
Dieldrin	DDing-dust	2,81E-05	1,68E-04	4,62E-04	1,15E-03	3,88E-03	71
	DDinh-air	3,27E-02	1,17E-01	2,75E-01	6,02E-01	1,69E+00	56
	DDderm-gas	4,54E-04	2,29E-03	4,73E-03	7,88E-03	3,91E-02	166
	ADD	3,74E-02	1,23E-01	2,85E-01	6,16E-01	1,70E+00	55
Lindane	DDing-dust	2,16E-03	4,03E-03	6,37E-03	1,16E-02	6,06E-02	62
	DDinh-air	7,67E-02	2,52E-01	6,00E-01	1,41E+00	4,96E+00	59
	DDderm-gas	4,36E-03	1,99E-02	3,77E-02	1,04E-01	6,63E-01	126
	ADD	1,02E-01	2,98E-01	6,87E-01	1,59E+00	5,72E+00	68
Chlorpyrifos	DDing-dust	7,43E-05	3,75E-04	1,06E-03	2,93E-03	1,24E-02	44
	DDinh-air	3,76E-03	1,32E-02	2,62E-02	4,56E-02	9,24E-02	58
	DDderm-gas	3,25E-03	1,64E-02	3,36E-02	5,47E-02	9,57E-02	104
	ADD	1,01E-02	3,51E-02	6,58E-02	1,03E-01	1,85E-01	49
Tributylphosphate	DDing-dust	1,11E-02	2,18E-02	3,52E-02	5,91E-02	1,34E-01	82
	DDinh-air	7,38E-03	3,28E-02	7,99E-02	1,73E-01	4,24E-01	56
	DDderm-gas	2,32E-02	1,21E-01	2,93E-01	6,31E-01	1,40E+00	55
	ADD	6,74E-02	2,06E-01	4,34E-01	8,63E-01	1,87E+00	37
Galaxolide	DDing-dust	1,56E-02	5,62E-02	1,21E-01	2,51E-01	6,83E-01	92
	DDinh-air	2,87E+00	8,26E+00	1,71E+01	3,59E+01	1,13E+02	56
	DDderm-gas	1,37E+00	3,71E+00	7,34E+00	1,43E+01	3,61E+01	140
	ADD	5,99E+00	1,48E+01	2,77E+01	5,25E+01	1,37E+02	64
Tonalide	DDing-dust	1,20E-02	2,79E-02	5,00E-02	8,98E-02	2,09E-01	96
	DDinh-air	8,35E-01	2,28E+00	4,79E+00	1,06E+01	3,76E+01	56
	DDderm-gas	5,37E-01	1,05E+00	1,75E+00	3,05E+00	7,10E+00	65
	ADD	1,89E+00	4,07E+00	7,39E+00	1,41E+01	4,13E+01	46
Anthracene	DDing-dust	1,93E-04	1,05E-03	2,67E-03	6,13E-03	1,85E-02	56
	DDinh-air	5,91E-03	2,55E-02	5,72E-02	1,19E-01	3,57E-01	9
	DDderm-gas	7,91E-03	4,08E-02	8,95E-02	1,77E-01	5,12E-01	40
	ADD	1,79E-02	7,50E-02	1,57E-01	3,02E-01	8,71E-01	21
Benzo[a]pyrene	DDing-dust	1,14E-04	6,00E-04	1,58E-03	3,89E-03	1,35E-02	50
	DDinh-air	2,48E-03	1,29E-02	3,71E-02	9,88E-02	3,52E-01	10
	DDderm-gas	8,62E-03	1,34E-02	1,69E-02	2,07E-02	2,70E-02	21
	ADD	2,01E-02	3,44E-02	5,90E-02	1,20E-01	3,73E-01	11
Fluorene	DDing-dust	5,00E-04	1,02E-03	1,64E-03	2,63E-03	5,21E-03	68
	DDinh-air	9,14E-03	3,84E-02	1,94E-01	4,52E-01	1,54E+00	10
	DDderm-gas	5,23E-03	2,73E-02	1,78E-01	3,41E-01	1,14E+00	38
	ADD	1,81E-02	6,97E-02	4,13E-01	7,89E-01	2,70E+00	16

Phenanthrene	DDing-dust	2,93E-03	9,19E-03	1,96E-02	4,11E-02	1,18E-01	53
	DDinh-air	2,65E-01	5,53E-01	1,02E+00	2,21E+00	5,95E+00	10
	DDderm-gas	6,77E-01	1,17E+00	2,02E+00	4,43E+00	1,11E+01	23
	ADD	1,11E+00	1,81E+00	3,12E+00	6,80E+00	1,67E+01	14
PCB 28	DDing-dust	8,83E-05	3,57E-04	8,29E-04	1,84E-03	5,56E-03	36
	DDinh-air	9,06E-04	4,51E-03	9,54E-03	1,67E-02	3,17E-02	56
	DDderm-gas	3,82E-04	1,94E-03	3,98E-03	6,42E-03	1,03E-02	21
	ADD	3,00E-03	8,65E-03	1,56E-02	2,45E-02	4,19E-02	37
PCB 31	DDing-dust	3,51E-05	2,11E-04	5,78E-04	1,43E-03	4,57E-03	64
	DDinh-air	4,80E-02	8,87E-02	1,30E-01	1,86E-01	3,19E-01	118
	DDderm-gas	1,99E-02	3,10E-02	3,93E-02	4,81E-02	6,27E-02	120
	ADD	8,24E-02	1,27E-01	1,71E-01	2,30E-01	3,68E-01	112
PCB 52	DDing-dust	7,25E-05	5,42E-04	1,94E-03	6,91E-03	4,28E-02	55
	DDinh-air	1,12E-02	3,57E-02	8,22E-02	1,94E-01	6,84E-01	56
	DDderm-gas	4,69E-04	2,36E-03	4,88E-03	8,16E-03	1,83E-02	112
	ADD	1,71E-02	4,64E-02	9,80E-02	2,17E-01	7,13E-01	48
PCB 101	DDing-dust	6,88E-04	4,57E-03	1,41E-02	4,01E-02	1,71E-01	52
	DDinh-air	1,18E-03	5,06E-03	1,05E-02	1,87E-02	4,72E-02	60
	DDderm-gas	4,34E-04	2,21E-03	4,54E-03	7,44E-03	1,56E-02	43
	ADD	6,65E-03	1,89E-02	3,48E-02	6,88E-02	2,62E-01	36
PCB 105	DDing-dust	5,45E-06	4,15E-05	1,51E-04	5,40E-04	3,36E-03	72
	DDinh-air	9,59E-03	3,63E-02	1,02E-01	2,93E-01	1,33E+00	61
	DDderm-gas	1,82E-03	2,83E-03	3,58E-03	4,38E-03	5,71E-03	370
	ADD	1,34E-02	4,04E-02	1,07E-01	2,97E-01	1,33E+00	55
PCB 118	DDing-dust	6,17E-04	1,22E-03	2,13E-03	4,96E-03	3,07E-02	51
	DDinh-air	8,72E-03	1,58E-02	2,26E-02	3,16E-02	5,09E-02	288
	DDderm-gas	6,58E-03	1,02E-02	1,29E-02	1,58E-02	2,07E-02	272
	ADD	2,10E-02	3,07E-02	4,00E-02	5,29E-02	8,96E-02	230
PCB 138	DDing-dust	2,10E-04	1,47E-03	4,90E-03	1,56E-02	7,77E-02	37
	DDinh-air	5,13E-03	9,30E-03	1,34E-02	1,88E-02	3,09E-02	227
	DDderm-gas	3,51E-03	5,45E-03	6,89E-03	8,44E-03	1,10E-02	284
	ADD	1,31E-02	2,02E-02	2,80E-02	4,21E-02	1,06E-01	132
PCB 153	DDing-dust	1,42E-04	1,02E-03	3,46E-03	1,14E-02	6,10E-02	49
	DDinh-air	5,39E-03	9,78E-03	1,40E-02	1,97E-02	3,20E-02	228
	DDderm-gas	3,99E-03	6,23E-03	7,87E-03	9,64E-03	1,26E-02	250
	ADD	1,38E-02	2,07E-02	2,81E-02	4,03E-02	9,17E-02	173
BBP	DDing-dust	3,46E+00	1,75E+01	3,68E+01	6,42E+01	1,24E+02	42
	DDinh-air	2,15E-01	4,17E-01	6,59E-01	1,11E+00	3,22E+00	57
	DDderm-gas	3,62E-02	1,84E-01	3,83E-01	6,65E-01	1,86E+00	75
	ADD	4,81E+00	1,90E+01	3,84E+01	6,60E+01	1,26E+02	41
DBP	DDing-dust	3,00E-01	1,53E+00	3,20E+00	5,59E+00	1,08E+01	45
	DDinh-air	1,64E+01	4,53E+01	1,09E+02	2,92E+02	1,30E+03	56
	DDderm-gas	1,90E+01	4,31E+01	6,83E+01	1,02E+02	1,71E+02	47
	ADD	5,82E+01	1,18E+02	2,00E+02	3,87E+02	1,40E+03	39

DEHP	DDing-dust	1,04E+01	5,28E+01	1,11E+02	1,93E+02	3,71E+02	50
	DDinh-air	8,65E-01	2,33E+00	4,95E+00	1,11E+01	3,78E+01	57
	DDderm-gas	3,43E-01	1,73E+00	3,54E+00	5,76E+00	1,00E+01	84
	ADD	2,03E+01	6,50E+01	1,25E+02	2,09E+02	3,94E+02	51
DEP	DDing-dust	1,66E-01	3,07E-01	4,81E-01	8,43E-01	3,78E+00	37
	DDinh-air	1,40E+01	4,12E+01	9,45E+01	2,39E+02	1,01E+03	60
	DDderm-gas	2,26E+00	4,71E+00	7,82E+00	1,29E+01	2,57E+01	88
	ADD	2,02E+01	5,11E+01	1,07E+02	2,52E+02	1,02E+03	47
DiBP	DDing-dust	3,75E+00	1,92E+01	4,02E+01	7,01E+01	1,36E+02	36
	DDinh-air	7,79E+00	1,99E+01	3,76E+01	7,04E+01	1,65E+02	58
	DDderm-gas	1,33E+02	3,11E+02	5,57E+02	9,86E+02	2,13E+03	27
	ADD	1,67E+02	3,73E+02	6,50E+02	1,12E+03	2,36E+03	22
DiNP	DDing-dust	1,20E+01	6,07E+01	1,27E+02	2,22E+02	4,30E+02	71
	DDinh-air	3,87E-01	1,07E+00	1,94E+00	3,34E+00	7,39E+00	58
	DDderm-gas	1,38E-01	7,01E-01	1,44E+00	2,37E+00	4,11E+00	91
	ADD	1,56E+01	6,44E+01	1,31E+02	2,27E+02	4,36E+02	68
BDE 28	DDing-dust	1,78E-05	3,39E-05	5,48E-05	9,71E-05	2,59E-04	33
	DDinh-air	1,44E-02	4,28E-02	8,26E-02	1,51E-01	3,35E-01	37
	DDderm-gas	1,57E-03	8,46E-03	2,05E-02	4,33E-02	1,06E-01	50
	ADD	2,09E-02	5,87E-02	1,10E-01	1,95E-01	4,13E-01	29
BDE 47	DDing-dust	8,43E-04	1,92E-03	3,82E-03	8,53E-03	3,10E-02	39
	DDinh-air	4,17E-02	1,72E-01	3,52E-01	6,30E-01	1,26E+00	35
	DDderm-gas	4,55E-02	1,98E-01	3,92E-01	6,57E-01	1,14E+00	47
	ADD	1,05E-01	4,10E-01	7,86E-01	1,30E+00	2,28E+00	31
BDE 85	DDing-dust	4,57E-05	2,33E-04	4,96E-04	9,05E-04	2,05E-03	42
	DDinh-air	2,00E-04	5,80E-04	1,16E-03	2,40E-03	6,87E-03	36
	DDderm-gas	8,98E-05	5,18E-04	1,38E-03	3,31E-03	9,93E-03	59
	ADD	7,97E-04	1,84E-03	3,39E-03	6,57E-03	1,73E-02	27
BDE 99	DDing-dust	1,69E-03	3,17E-03	5,04E-03	8,96E-03	3,25E-02	43
	DDinh-air	3,97E-02	7,23E-02	1,05E-01	1,50E-01	2,63E-01	35
	DDderm-gas	8,25E-02	1,29E-01	1,65E-01	2,07E-01	3,12E-01	63
	ADD	1,59E-01	2,24E-01	2,81E-01	3,55E-01	5,63E-01	39
BDE 100	DDing-dust	1,11E-04	5,48E-04	1,36E-03	3,18E-03	1,02E-02	38
	DDinh-air	5,12E-02	1,68E-01	3,57E-01	7,29E-01	1,97E+00	34
	DDderm-gas	2,90E-02	4,82E-02	7,02E-02	1,13E-01	2,66E-01	37
	ADD	1,15E-01	2,56E-01	4,63E-01	8,47E-01	2,09E+00	29
BDE 153	DDing-dust	2,45E-04	1,24E-03	2,69E-03	5,21E-03	1,51E-02	34
	DDinh-air	5,06E-04	1,28E-03	2,61E-03	5,67E-03	1,81E-02	35
	DDderm-gas	1,60E-03	4,36E-03	9,62E-03	2,20E-02	7,03E-02	44
	ADD	4,42E-03	9,54E-03	1,74E-02	3,44E-02	9,70E-02	25
BDE 154	DDing-dust	2,33E-04	1,18E-03	2,55E-03	4,93E-03	1,41E-02	34
	DDinh-air	3,73E-04	9,71E-04	1,90E-03	3,87E-03	1,06E-02	36
	DDderm-gas	1,27E-03	3,93E-03	8,59E-03	1,85E-02	5,11E-02	38
	ADD	3,69E-03	8,33E-03	1,50E-02	2,83E-02	6,88E-02	24

Table S17: Daily doses (DD) from each route of exposure (ingestion of dust, inhalation and dermal contact with the gas phase) and aggregated daily doses (ADD) estimated (ng/kg-bw/d) for 32 SVOCs for the age group of [16-21 years]

SVOCs	Estimated daily doses[1]	p5	p25	p50	p75	p95	Uncertainty on the mean (%)
Aldrin	DDing-dust	6,55E-06	3,36E-05	7,23E-05	1,32E-04	3,35E-04	74
	DDinh-air	1,49E-03	7,65E-03	1,67E-02	3,06E-02	6,40E-02	59
	DDderm-gas	2,82E-04	1,45E-03	3,05E-03	5,10E-03	9,34E-03	122
	ADD	2,12E-03	9,93E-03	2,06E-02	3,63E-02	7,42E-02	51
Dieldrin	DDing-dust	1,82E-05	1,11E-04	3,06E-04	7,61E-04	2,58E-03	71
	DDinh-air	2,16E-02	8,03E-02	1,93E-01	4,30E-01	1,23E+00	56
	DDderm-gas	3,34E-04	1,73E-03	3,64E-03	6,23E-03	3,00E-02	166
	ADD	2,51E-02	8,53E-02	2,00E-01	4,41E-01	1,24E+00	55
Lindane	DDing-dust	1,37E-03	2,68E-03	4,27E-03	7,67E-03	3,99E-02	62
	DDinh-air	5,05E-02	1,75E-01	4,19E-01	1,00E+00	3,54E+00	59
	DDderm-gas	3,24E-03	1,51E-02	2,94E-02	8,11E-02	5,20E-01	126
	ADD	6,99E-02	2,11E-01	4,86E-01	1,14E+00	4,10E+00	68
Chlorpyrifos	DDing-dust	4,79E-05	2,47E-04	7,04E-04	1,95E-03	8,26E-03	44
	DDinh-air	2,47E-03	9,01E-03	1,84E-02	3,28E-02	6,70E-02	58
	DDderm-gas	2,40E-03	1,23E-02	2,58E-02	4,30E-02	7,66E-02	104
	ADD	7,35E-03	2,58E-02	4,89E-02	7,75E-02	1,39E-01	49
Tributylphosphate	DDing-dust	7,09E-03	1,44E-02	2,36E-02	3,96E-02	8,93E-02	82
	DDinh-air	4,88E-03	2,26E-02	5,60E-02	1,23E-01	3,07E-01	56
	DDderm-gas	1,72E-02	9,19E-02	2,26E-01	4,89E-01	1,11E+00	55
	ADD	4,84E-02	1,52E-01	3,25E-01	6,56E-01	1,43E+00	37
Galaxolide	DDing-dust	9,98E-03	3,70E-02	8,06E-02	1,67E-01	4,56E-01	92
	DDinh-air	1,88E+00	5,72E+00	1,21E+01	2,56E+01	8,13E+01	56
	DDderm-gas	1,00E+00	2,83E+00	5,68E+00	1,12E+01	2,85E+01	140
	ADD	4,31E+00	1,08E+01	2,03E+01	3,85E+01	9,99E+01	64
Tonalide	DDing-dust	7,71E-03	1,84E-02	3,33E-02	5,99E-02	1,40E-01	96
	DDinh-air	5,48E-01	1,58E+00	3,37E+00	7,51E+00	2,70E+01	56
	DDderm-gas	3,90E-01	8,03E-01	1,36E+00	2,39E+00	5,64E+00	65
	ADD	1,36E+00	2,97E+00	5,38E+00	1,03E+01	3,01E+01	46
Anthracene	DDing-dust	1,25E-04	6,90E-04	1,77E-03	4,09E-03	1,23E-02	56
	DDinh-air	3,88E-03	1,75E-02	4,04E-02	8,48E-02	2,56E-01	9
	DDderm-gas	5,82E-03	3,10E-02	6,91E-02	1,39E-01	4,04E-01	40
	ADD	1,31E-02	5,57E-02	1,18E-01	2,28E-01	6,57E-01	21
Benzo[a]pyrene	DDing-dust	7,35E-05	3,94E-04	1,05E-03	2,58E-03	8,97E-03	50
	DDinh-air	1,68E-03	8,89E-03	2,59E-02	6,98E-02	2,52E-01	10
	DDderm-gas	5,92E-03	1,02E-02	1,32E-02	1,66E-02	2,19E-02	21
	ADD	1,47E-02	2,54E-02	4,27E-02	8,62E-02	2,68E-01	11
Fluorene	DDing-dust	3,17E-04	6,74E-04	1,10E-03	1,77E-03	3,47E-03	68
	DDinh-air	6,08E-03	2,70E-02	1,31E-01	3,24E-01	1,10E+00	10
	DDderm-gas	3,89E-03	2,10E-02	1,33E-01	2,69E-01	8,98E-01	38
	ADD	1,31E-02	5,13E-02	3,03E-01	5,90E-01	1,99E+00	16

Phenanthrene	DDing-dust	1,88E-03	6,06E-03	1,30E-02	2,73E-02	7,80E-02	53
	DDinh-air	1,71E-01	3,86E-01	7,18E-01	1,56E+00	4,31E+00	10
	DDderm-gas	4,90E-01	9,09E-01	1,57E+00	3,45E+00	8,80E+00	23
	ADD	8,10E-01	1,37E+00	2,35E+00	5,14E+00	1,27E+01	14
PCB 28	DDing-dust	5,71E-05	2,35E-04	5,51E-04	1,23E-03	3,68E-03	36
	DDinh-air	6,01E-04	3,06E-03	6,68E-03	1,20E-02	2,31E-02	56
	DDderm-gas	2,82E-04	1,46E-03	3,06E-03	5,04E-03	8,26E-03	21
	ADD	2,10E-03	6,15E-03	1,12E-02	1,79E-02	3,07E-02	37
PCB 31	DDing-dust	2,27E-05	1,39E-04	3,83E-04	9,52E-04	3,05E-03	64
	DDinh-air	2,98E-02	6,12E-02	9,25E-02	1,35E-01	2,31E-01	118
	DDderm-gas	1,37E-02	2,35E-02	3,07E-02	3,83E-02	5,08E-02	120
	ADD	5,67E-02	9,11E-02	1,24E-01	1,69E-01	2,69E-01	112
PCB 52	DDing-dust	4,76E-05	3,57E-04	1,29E-03	4,60E-03	2,85E-02	55
	DDinh-air	7,40E-03	2,47E-02	5,76E-02	1,38E-01	4,94E-01	56
	DDderm-gas	3,45E-04	1,78E-03	3,75E-03	6,42E-03	1,46E-02	112
	ADD	1,17E-02	3,26E-02	6,91E-02	1,54E-01	5,14E-01	48
PCB 101	DDing-dust	4,43E-04	3,00E-03	9,30E-03	2,67E-02	1,14E-01	52
	DDinh-air	7,70E-04	3,47E-03	7,39E-03	1,35E-02	3,36E-02	60
	DDderm-gas	3,19E-04	1,67E-03	3,50E-03	5,86E-03	1,24E-02	43
	ADD	4,60E-03	1,33E-02	2,45E-02	4,76E-02	1,81E-01	36
PCB 105	DDing-dust	3,57E-06	2,74E-05	1,00E-04	3,60E-04	2,22E-03	72
	DDinh-air	6,46E-03	2,52E-02	7,21E-02	2,09E-01	9,45E-01	61
	DDderm-gas	1,26E-03	2,15E-03	2,81E-03	3,50E-03	4,64E-03	370
	ADD	9,39E-03	2,83E-02	7,55E-02	2,12E-01	9,49E-01	55
PCB 118	DDing-dust	3,95E-04	8,12E-04	1,43E-03	3,30E-03	2,06E-02	51
	DDinh-air	5,37E-03	1,09E-02	1,62E-02	2,30E-02	3,70E-02	288
	DDderm-gas	4,55E-03	7,76E-03	1,01E-02	1,27E-02	1,67E-02	272
	ADD	1,48E-02	2,24E-02	2,95E-02	3,90E-02	6,35E-02	230
PCB 138	DDing-dust	1,36E-04	9,76E-04	3,25E-03	1,04E-02	5,17E-02	37
	DDinh-air	3,17E-03	6,43E-03	9,58E-03	1,37E-02	2,25E-02	227
	DDderm-gas	2,42E-03	4,14E-03	5,40E-03	6,74E-03	8,92E-03	284
	ADD	9,22E-03	1,46E-02	2,04E-02	3,02E-02	7,22E-02	132
PCB 153	DDing-dust	9,25E-05	6,70E-04	2,30E-03	7,63E-03	4,04E-02	49
	DDinh-air	3,34E-03	6,74E-03	1,00E-02	1,43E-02	2,33E-02	228
	DDderm-gas	2,77E-03	4,72E-03	6,17E-03	7,70E-03	1,02E-02	250
	ADD	9,69E-03	1,51E-02	2,05E-02	2,92E-02	6,32E-02	173
BBP	DDing-dust	2,21E+00	1,15E+01	2,44E+01	4,31E+01	8,27E+01	42
	DDinh-air	1,35E-01	2,89E-01	4,71E-01	8,00E-01	2,30E+00	57
	DDderm-gas	2,68E-02	1,40E-01	2,96E-01	5,25E-01	1,45E+00	75
	ADD	3,18E+00	1,26E+01	2,56E+01	4,44E+01	8,44E+01	41
DBP	DDing-dust	1,94E-01	9,99E-01	2,13E+00	3,74E+00	7,18E+00	45
	DDinh-air	1,09E+01	3,16E+01	7,65E+01	2,07E+02	9,29E+02	56
	DDderm-gas	1,37E+01	3,27E+01	5,29E+01	8,07E+01	1,37E+02	47
	ADD	4,23E+01	8,73E+01	1,48E+02	2,81E+02	1,00E+03	39

DEHP	DDing-dust	6,70E+00	3,46E+01	7,37E+01	1,30E+02	2,48E+02	50
	DDinh-air	5,68E-01	1,62E+00	3,49E+00	7,91E+00	2,72E+01	57
	DDderm-gas	2,51E-01	1,30E+00	2,72E+00	4,51E+00	8,01E+00	84
	ADD	1,38E+01	4,36E+01	8,39E+01	1,42E+02	2,65E+02	51
DEP	DDing-dust	1,05E-01	2,04E-01	3,23E-01	5,59E-01	2,52E+00	37
	DDinh-air	9,22E+00	2,85E+01	6,67E+01	1,70E+02	7,20E+02	60
	DDderm-gas	1,65E+00	3,59E+00	6,07E+00	1,02E+01	2,04E+01	88
	ADD	1,41E+01	3,62E+01	7,60E+01	1,79E+02	7,30E+02	47
DiBP	DDing-dust	2,41E+00	1,26E+01	2,68E+01	4,71E+01	9,02E+01	36
	DDinh-air	5,04E+00	1,37E+01	2,66E+01	5,04E+01	1,20E+02	58
	DDderm-gas	9,72E+01	2,37E+02	4,32E+02	7,74E+02	1,69E+03	27
	ADD	1,22E+02	2,81E+02	4,96E+02	8,67E+02	1,85E+03	22
DiNP	DDing-dust	7,76E+00	3,97E+01	8,45E+01	1,49E+02	2,86E+02	71
	DDinh-air	2,47E-01	7,36E-01	1,37E+00	2,41E+00	5,35E+00	58
	DDderm-gas	1,02E-01	5,28E-01	1,11E+00	1,86E+00	3,28E+00	91
	ADD	1,05E+01	4,24E+01	8,75E+01	1,53E+02	2,91E+02	68
BDE 28	DDing-dust	1,13E-05	2,25E-05	3,67E-05	6,47E-05	1,73E-04	33
	DDinh-air	9,34E-03	2,94E-02	5,83E-02	1,08E-01	2,43E-01	37
	DDderm-gas	1,17E-03	6,44E-03	1,58E-02	3,38E-02	8,41E-02	50
	ADD	1,46E-02	4,21E-02	7,96E-02	1,43E-01	3,04E-01	29
BDE 47	DDing-dust	5,42E-04	1,27E-03	2,55E-03	5,70E-03	2,06E-02	39
	DDinh-air	2,71E-02	1,17E-01	2,47E-01	4,52E-01	9,16E-01	35
	DDderm-gas	3,34E-02	1,50E-01	3,02E-01	5,14E-01	9,12E-01	47
	ADD	7,63E-02	3,02E-01	5,85E-01	9,74E-01	1,72E+00	31
BDE 85	DDing-dust	2,96E-05	1,53E-04	3,30E-04	6,05E-04	1,37E-03	42
	DDinh-air	1,30E-04	4,00E-04	8,21E-04	1,71E-03	4,93E-03	36
	DDderm-gas	6,71E-05	3,95E-04	1,07E-03	2,58E-03	7,80E-03	59
	ADD	5,58E-04	1,32E-03	2,48E-03	4,87E-03	1,30E-02	27
BDE 99	DDing-dust	1,08E-03	2,11E-03	3,38E-03	5,97E-03	2,18E-02	43
	DDinh-air	2,46E-02	5,02E-02	7,53E-02	1,09E-01	1,89E-01	35
	DDderm-gas	5,72E-02	9,81E-02	1,29E-01	1,65E-01	2,50E-01	63
	ADD	1,13E-01	1,67E-01	2,13E-01	2,71E-01	4,22E-01	39
BDE 100	DDing-dust	7,17E-05	3,60E-04	9,06E-04	2,12E-03	6,77E-03	38
	DDinh-air	3,37E-02	1,16E-01	2,51E-01	5,21E-01	1,41E+00	34
	DDderm-gas	2,06E-02	3,70E-02	5,50E-02	8,90E-02	2,10E-01	37
	ADD	8,28E-02	1,84E-01	3,35E-01	6,13E-01	1,50E+00	29
BDE 153	DDing-dust	1,56E-04	8,16E-04	1,79E-03	3,48E-03	1,01E-02	34
	DDinh-air	3,33E-04	8,92E-04	1,84E-03	4,03E-03	1,30E-02	35
	DDderm-gas	1,19E-03	3,35E-03	7,45E-03	1,71E-02	5,53E-02	44
	ADD	3,18E-03	6,96E-03	1,28E-02	2,58E-02	7,34E-02	25
BDE 154	DDing-dust	1,49E-04	7,74E-04	1,69E-03	3,29E-03	9,39E-03	34
	DDinh-air	2,43E-04	6,70E-04	1,34E-03	2,75E-03	7,66E-03	36
	DDderm-gas	9,41E-04	3,00E-03	6,64E-03	1,44E-02	4,03E-02	38
	ADD	2,66E-03	6,08E-03	1,11E-02	2,11E-02	5,21E-02	24

Table S18: Daily doses (DD) from each route of exposure (ingestion of dust, inhalation and dermal contact with the gas phase) and aggregated daily doses (ADD) estimated (ng/kg-bw/d) for 32 SVOCs for the age group of [21-30 years]

SVOCs	Estimated daily doses[1]	p5	p25	p50	p75	p95	Uncertainty on the mean (%)
Aldrin	DDing-dust	3,09E-06	1,64E-05	3,95E-05	8,66E-05	2,96E-04	74
	DDinh-air	1,83E-03	9,07E-03	1,92E-02	3,36E-02	6,75E-02	59
	DDderm-gas	3,48E-04	1,77E-03	3,66E-03	6,04E-03	1,09E-02	122
	ADD	2,45E-03	1,16E-02	2,37E-02	4,00E-02	7,83E-02	51
Dieldrin	DDing-dust	8,68E-06	5,68E-05	1,72E-04	4,78E-04	1,91E-03	71
	DDinh-air	2,68E-02	9,37E-02	2,19E-01	4,73E-01	1,31E+00	56
	DDderm-gas	4,12E-04	2,10E-03	4,38E-03	7,37E-03	3,62E-02	166
	ADD	3,08E-02	9,93E-02	2,27E-01	4,85E-01	1,32E+00	55
Lindane	DDing-dust	5,12E-04	1,30E-03	2,57E-03	5,53E-03	2,76E-02	62
	DDinh-air	6,29E-02	2,02E-01	4,77E-01	1,11E+00	3,88E+00	59
	DDderm-gas	4,00E-03	1,83E-02	3,50E-02	9,65E-02	6,21E-01	126
	ADD	8,35E-02	2,41E-01	5,49E-01	1,27E+00	4,54E+00	68
Chlorpyrifos	DDing-dust	2,27E-05	1,29E-04	4,03E-04	1,22E-03	5,91E-03	44
	DDinh-air	3,06E-03	1,07E-02	2,11E-02	3,59E-02	7,03E-02	58
	DDderm-gas	2,96E-03	1,50E-02	3,10E-02	5,10E-02	8,93E-02	104
	ADD	7,97E-03	2,93E-02	5,61E-02	8,82E-02	1,54E-01	49
Tributylphosphate	DDing-dust	2,69E-03	7,00E-03	1,36E-02	2,69E-02	7,43E-02	82
	DDinh-air	6,00E-03	2,63E-02	6,38E-02	1,36E-01	3,24E-01	56
	DDderm-gas	2,10E-02	1,11E-01	2,71E-01	5,86E-01	1,30E+00	55
	ADD	4,57E-02	1,66E-01	3,67E-01	7,55E-01	1,65E+00	37
Galaxolide	DDing-dust	4,47E-03	1,87E-02	4,57E-02	1,08E-01	3,55E-01	92
	DDinh-air	2,35E+00	6,66E+00	1,36E+01	2,82E+01	8,76E+01	56
	DDderm-gas	1,25E+00	3,43E+00	6,80E+00	1,33E+01	3,37E+01	140
	ADD	5,09E+00	1,25E+01	2,33E+01	4,36E+01	1,10E+02	64
Tonalide	DDing-dust	3,12E-03	9,09E-03	1,90E-02	3,96E-02	1,14E-01	96
	DDinh-air	6,84E-01	1,84E+00	3,80E+00	8,30E+00	2,91E+01	56
	DDderm-gas	4,88E-01	9,68E-01	1,62E+00	2,84E+00	6,66E+00	65
	ADD	1,63E+00	3,45E+00	6,16E+00	1,16E+01	3,27E+01	46
Anthracene	DDing-dust	5,83E-05	3,51E-04	9,96E-04	2,59E-03	9,37E-03	56
	DDinh-air	4,77E-03	2,06E-02	4,58E-02	9,37E-02	2,79E-01	9
	DDderm-gas	7,25E-03	3,76E-02	8,30E-02	1,65E-01	4,79E-01	40
	ADD	1,45E-02	6,40E-02	1,36E-01	2,61E-01	7,55E-01	21
Benzo[a]pyrene	DDing-dust	3,44E-05	2,02E-04	5,90E-04	1,62E-03	6,69E-03	50
	DDinh-air	2,02E-03	1,04E-02	2,95E-02	7,77E-02	2,74E-01	10
	DDderm-gas	7,64E-03	1,23E-02	1,58E-02	1,95E-02	2,54E-02	21
	ADD	1,68E-02	2,86E-02	4,80E-02	9,59E-02	2,92E-01	11
Fluorene	DDing-dust	1,23E-04	3,24E-04	6,25E-04	1,20E-03	3,03E-03	68
	DDinh-air	7,41E-03	3,06E-02	1,58E-01	3,56E-01	1,20E+00	10
	DDderm-gas	4,78E-03	2,53E-02	1,63E-01	3,19E-01	1,06E+00	38
	ADD	1,48E-02	5,88E-02	3,58E-01	6,69E-01	2,25E+00	16

Phenanthrene	DDing-dust	8,19E-04	3,07E-03	7,41E-03	1,76E-02	6,08E-02	53
	DDinh-air	2,20E-01	4,43E-01	7,99E-01	1,73E+00	4,62E+00	10
	DDderm-gas	6,12E-01	1,09E+00	1,87E+00	4,12E+00	1,04E+01	23
	ADD	9,65E-01	1,59E+00	2,72E+00	5,97E+00	1,47E+01	14
PCB 28	DDing-dust	2,60E-05	1,19E-04	3,11E-04	7,81E-04	2,81E-03	36
	DDinh-air	7,38E-04	3,66E-03	7,66E-03	1,32E-02	2,41E-02	56
	DDderm-gas	3,48E-04	1,78E-03	3,68E-03	5,99E-03	9,64E-03	21
	ADD	1,98E-03	6,69E-03	1,26E-02	1,98E-02	3,28E-02	37
PCB 31	DDing-dust	1,09E-05	7,13E-05	2,16E-04	5,93E-04	2,26E-03	64
	DDinh-air	4,04E-02	7,23E-02	1,03E-01	1,45E-01	2,39E-01	118
	DDderm-gas	1,77E-02	2,86E-02	3,66E-02	4,51E-02	5,87E-02	120
	ADD	7,15E-02	1,07E-01	1,41E-01	1,85E-01	2,84E-01	112
PCB 52	DDing-dust	2,31E-05	1,89E-04	7,37E-04	2,83E-03	1,94E-02	55
	DDinh-air	9,23E-03	2,87E-02	6,55E-02	1,53E-01	5,33E-01	56
	DDderm-gas	4,25E-04	2,17E-03	4,52E-03	7,62E-03	1,71E-02	112
	ADD	1,35E-02	3,64E-02	7,61E-02	1,68E-01	5,51E-01	48
PCB 101	DDing-dust	2,15E-04	1,57E-03	5,28E-03	1,66E-02	8,11E-02	52
	DDinh-air	9,52E-04	4,11E-03	8,42E-03	1,47E-02	3,53E-02	60
	DDderm-gas	3,95E-04	2,03E-03	4,20E-03	6,96E-03	1,46E-02	43
	ADD	4,06E-03	1,23E-02	2,21E-02	3,97E-02	1,63E-01	36
PCB 105	DDing-dust	1,74E-06	1,45E-05	5,76E-05	2,22E-04	1,50E-03	72
	DDinh-air	7,79E-03	2,91E-02	8,15E-02	2,32E-01	1,04E+00	61
	DDderm-gas	1,61E-03	2,61E-03	3,34E-03	4,11E-03	5,36E-03	370
	ADD	1,12E-02	3,27E-02	8,52E-02	2,36E-01	1,04E+00	55
PCB 118	DDing-dust	1,51E-04	4,11E-04	8,82E-04	2,23E-03	1,38E-02	51
	DDinh-air	7,35E-03	1,29E-02	1,81E-02	2,46E-02	3,79E-02	288
	DDderm-gas	5,83E-03	9,45E-03	1,21E-02	1,49E-02	1,94E-02	272
	ADD	1,77E-02	2,55E-02	3,25E-02	4,14E-02	6,24E-02	230
PCB 138	DDing-dust	6,55E-05	5,13E-04	1,85E-03	6,42E-03	3,63E-02	37
	DDinh-air	4,31E-03	7,62E-03	1,07E-02	1,47E-02	2,31E-02	227
	DDderm-gas	3,10E-03	5,02E-03	6,43E-03	7,92E-03	1,03E-02	284
	ADD	1,07E-02	1,58E-02	2,09E-02	2,87E-02	5,94E-02	132
PCB 153	DDing-dust	4,50E-05	3,53E-04	1,31E-03	4,70E-03	2,80E-02	49
	DDinh-air	4,54E-03	8,00E-03	1,12E-02	1,53E-02	2,39E-02	228
	DDderm-gas	3,56E-03	5,73E-03	7,34E-03	9,05E-03	1,18E-02	250
	ADD	1,14E-02	1,66E-02	2,16E-02	2,88E-02	5,39E-02	173
BBP	DDing-dust	1,05E+00	5,55E+00	1,32E+01	2,76E+01	7,23E+01	42
	DDinh-air	1,79E-01	3,38E-01	5,22E-01	8,68E-01	2,48E+00	57
	DDderm-gas	3,29E-02	1,69E-01	3,55E-01	6,21E-01	1,73E+00	75
	ADD	2,05E+00	6,81E+00	1,46E+01	2,91E+01	7,41E+01	41
DBP	DDing-dust	9,04E-02	4,82E-01	1,15E+00	2,40E+00	6,22E+00	45
	DDinh-air	1,35E+01	3,63E+01	8,60E+01	2,30E+02	1,01E+03	56
	DDderm-gas	1,72E+01	3,97E+01	6,33E+01	9,56E+01	1,60E+02	47
	ADD	5,00E+01	1,01E+02	1,70E+02	3,18E+02	1,10E+03	39

DEHP	DDing-dust	3,16E+00	1,67E+01	3,96E+01	8,32E+01	2,17E+02	50
	DDinh-air	7,10E-01	1,87E+00	3,93E+00	8,77E+00	2,94E+01	57
	DDderm-gas	3,11E-01	1,59E+00	3,28E+00	5,37E+00	9,38E+00	84
	ADD	1,02E+01	2,67E+01	5,17E+01	9,75E+01	2,35E+02	51
DEP	DDing-dust	3,92E-02	9,91E-02	1,93E-01	4,04E-01	1,78E+00	37
	DDinh-air	1,14E+01	3,30E+01	7,50E+01	1,88E+02	7,79E+02	60
	DDderm-gas	2,06E+00	4,34E+00	7,25E+00	1,21E+01	2,40E+01	88
	ADD	1,69E+01	4,20E+01	8,60E+01	1,99E+02	7,90E+02	47
DiBP	DDing-dust	1,14E+00	6,05E+00	1,44E+01	3,01E+01	7,89E+01	36
	DDinh-air	6,41E+00	1,61E+01	3,00E+01	5,53E+01	1,27E+02	58
	DDderm-gas	1,21E+02	2,87E+02	5,17E+02	9,20E+02	1,99E+03	27
	ADD	1,42E+02	3,25E+02	5,74E+02	1,01E+03	2,14E+03	22
DiNP	DDing-dust	3,61E+00	1,93E+01	4,57E+01	9,56E+01	2,50E+02	71
	DDinh-air	3,17E-01	8,72E-01	1,55E+00	2,62E+00	5,65E+00	58
	DDderm-gas	1,26E-01	6,47E-01	1,34E+00	2,21E+00	3,85E+00	91
	ADD	6,65E+00	2,26E+01	4,93E+01	9,96E+01	2,54E+02	68
BDE 28	DDing-dust	4,28E-06	1,10E-05	2,17E-05	4,44E-05	1,35E-04	33
	DDinh-air	1,17E-02	3,46E-02	6,60E-02	1,19E-01	2,56E-01	37
	DDderm-gas	1,43E-03	7,79E-03	1,90E-02	4,03E-02	9,91E-02	50
	ADD	1,76E-02	4,91E-02	9,09E-02	1,60E-01	3,31E-01	29
BDE 47	DDing-dust	2,19E-04	6,56E-04	1,50E-03	3,70E-03	1,50E-02	39
	DDinh-air	3,38E-02	1,39E-01	2,82E-01	4,97E-01	9,61E-01	35
	DDderm-gas	4,13E-02	1,82E-01	3,62E-01	6,12E-01	1,07E+00	47
	ADD	8,76E-02	3,52E-01	6,76E-01	1,12E+00	1,92E+00	31
BDE 85	DDing-dust	1,39E-05	7,44E-05	1,80E-04	3,93E-04	1,12E-03	42
	DDinh-air	1,65E-04	4,67E-04	9,21E-04	1,89E-03	5,31E-03	36
	DDderm-gas	8,21E-05	4,77E-04	1,28E-03	3,08E-03	9,25E-03	59
	ADD	5,25E-04	1,33E-03	2,63E-03	5,39E-03	1,47E-02	27
BDE 99	DDing-dust	4,04E-04	1,03E-03	2,01E-03	4,20E-03	1,59E-02	43
	DDinh-air	3,34E-02	5,92E-02	8,38E-02	1,17E-01	1,96E-01	35
	DDderm-gas	7,32E-02	1,19E-01	1,54E-01	1,94E-01	2,92E-01	63
	ADD	1,36E-01	1,95E-01	2,44E-01	3,04E-01	4,69E-01	39
BDE 100	DDing-dust	3,38E-05	1,84E-04	5,11E-04	1,33E-03	5,08E-03	38
	DDinh-air	4,19E-02	1,35E-01	2,84E-01	5,74E-01	1,51E+00	34
	DDderm-gas	2,61E-02	4,46E-02	6,52E-02	1,05E-01	2,48E-01	37
	ADD	9,95E-02	2,16E-01	3,82E-01	6,83E-01	1,62E+00	29
BDE 153	DDing-dust	7,42E-05	3,99E-04	9,91E-04	2,28E-03	8,21E-03	34
	DDinh-air	4,17E-04	1,03E-03	2,07E-03	4,46E-03	1,40E-02	35
	DDderm-gas	1,46E-03	4,03E-03	8,92E-03	2,04E-02	6,52E-02	44
	ADD	3,10E-03	7,04E-03	1,36E-02	2,82E-02	8,24E-02	25
BDE 154	DDing-dust	7,10E-05	3,78E-04	9,38E-04	2,16E-03	7,47E-03	34
	DDinh-air	3,08E-04	7,80E-04	1,51E-03	3,04E-03	8,27E-03	36
	DDderm-gas	1,16E-03	3,63E-03	7,95E-03	1,72E-02	4,78E-02	38
	ADD	2,55E-03	6,15E-03	1,17E-02	2,30E-02	5,88E-02	24

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Dear Dr. GLORENNEC,

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Chapitre 4 : Évaluation des risques sanitaires liés aux expositions cumulées aux COSV présents dans les logements français

La conduite d'une ERS comporte, une fois le problème formulé, quatre étapes avec : 1) l'identification des dangers, 2) la définition de relations dose-réponse, 3) l'évaluation de l'exposition et 4) la caractérisation des risques.[27] Les deux premières étapes visent à caractériser les dangers et à établir des valeurs toxicologiques de références (VTR) pour les contaminants étudiés. Dans le cadre de ce travail de thèse, les VTR utilisées ont été majoritairement recherchées dans la littérature et sont issues d'instances internationales ou de structures nationales. La troisième étape consistait à évaluer les expositions et a fait l'objet du chapitre 3.3 précédent. Pour la quatrième et dernière étape, traitée dans ce chapitre 4, les expositions agrégées estimées pour les 32 COSV ont été confrontées aux VTR afin de caractériser les risques sanitaires posés lors de l'exposition de l'Homme à ces composés. Ce travail a été conduit pour trois populations différentes : le fœtus (en considérant l'exposition d'une femme enceinte âgée de 21-30 ans), le jeune enfant (en considérant un enfant âgé de 0-2 ans) et l'adulte (en considérant un adulte âgé de 21-30 ans).

Une ERS a d'abord été conduite pour les composé pris individuellement, pour des effets à seuil par l'estimation de quotient de danger (QD) et pour des effets sans seuil par l'estimation « d'excès de risque individuel » (ERI). Ensuite, une ERSC a été réalisée pour des mélanges de composés selon les étapes d'une approche par paliers (Meek et al., 2011). La première étape visait à évaluer les risques, par l'estimation de HI ou d'ERI cumulés, pour des mélanges de composés ayant des effets toxiques communs. Pour l'estimation des HI, sur la base des travaux menés par Fournier et al. (2016, 2017), deux groupes ont été distingués pour les effets

[27] Démarche d'évaluation quantitative des risques sanitaires proposée pour la première fois en 1983 par le National Research Council des Etats-Unis d'Amérique et qui fait toujours référence

neurotoxiques et les effets reprotoxiques. L'estimation d'ERI cumulés n'a pu être conduite, notamment en raison de sites d'action différents pour les composés cancérigènes étudiés. La deuxième étape visait à évaluer les risques à une échelle biologique plus fine, pour des mélanges de composés ayant des mécanismes d'action ou des effets cellulaire en commun. Des approches employant des RPF ou des « Toxic equivalency factor » (TEF) ont été utilisées pour différents mélanges allant de 2 à 9 composés. Pour la famille des PCB, l'emploi d'une VTR cumulée, établie directement à partir d'une exposition aux composés en mélange, a permis d'évaluer leurs effets immunotoxiques.

Les résultats obtenus par l'ERS révèlent un risque inacceptable (QD>1) pour 50 % des enfants exposés au BDE 47 et pour 5 % des enfants exposés au lindane et au DBP. Les effets sanitaires en cause étant des effets immunotoxiques pour le lindane et des effets reprotoxiques pour le BDE 47 et le DBP.

Les résultats de l'approche cumulée pour des effets toxiques communs ont fourni des informations complémentaires. Pour 95 % des enfants et 5 % des femmes enceintes, exposés à des mélanges de composés reprotoxiques, les effets sont susceptibles de survenir (HI>1). Les PCB 101 et 118, le BDE 47 et le DBP étant les contributeurs majoritaires à ce risque.

Les résultats obtenus par l'ERSC pour des mécanismes d'action ou des effets cellulaires communs, ont révélé un risque inacceptable pour 95 % des enfants exposés à 9 composés neurotoxiques induisant une mort neuronale, pour 5 % des enfants exposés aux PCB 105 et 118 dont les effets toxiques sont médiés par une liaison au récepteur aux hydrocarbures aromatiques (AhR) et pour 25 % des enfants et 5% des adultes exposés à 4 composés reprotoxiques (induisant une diminution du

taux de testostérone). Le DEHP, le PCB 105 et le DEP étant les contributeurs majoritaires à ces risques respectivement.

Des effets immunotoxiques sont également susceptibles de survenir pour 5 % des enfants exposés à 8 PCB.

Concernant les effets cancérigènes des composés génotoxiques, les résultats des ERS conduites pour le lindane et le benzo[a]pyrène ont révélés des risques acceptables pour un adulte exposé pendant 30 ans. Les résultats obtenus par l'ERSC pour la survenue de cancers gastro-intestinaux ont révélés un risque acceptable pour un adulte exposé de sa naissance à ses 30 ans à un mélange de 4 HAP.

Les méthodologies mises en place ainsi que les résultats obtenus ont fait l'objet d'une publication soumise dans *Environmental Health Perspectives* et sont présentés sous forme d'article soumis dans la suite de ce chapitre 4.

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

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Running Title: Health risk of indoor SVOCs in France

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KEY WORDS

Environment, health, impact assessment, mixture.

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) method, was supplemented by a cumulative risk assessment (CRA) using a hazard index (HI) method, as well as higher tier approaches using relative potency factor (RPF) or toxic equivalency factor (TEF). 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 refined toxicological data for some compounds.

INTRODUCTION

People are exposed to an increasing number of chemicals, present in all media such as food, water, air, soil, clothes, etc. 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 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). SVOCs 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 2010; Inserm 2013). Many SVOCs thus have common toxic effects, justifying cumulative risk assessment (CRA). Fournier et al. (2014b) proposed an exposure-based framework for grouping indoor SVOCs based on similar health effects. On the basis of French indoor contamination data (Mandin et al., 2014, 2016), they proposed 2 groups of SVOCs based on neurotoxic and reprotoxic effects, respectively.

CRA refers to 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 than the previous one (Meek et al., 2011). Among current literature referring to CRAs on SVOCs, most focus on hazard index (HI) and relative potency factor (RPF) methods (Pelletier et al., 2017b). HI entails the addition of each chemical's risk indicator, and is considered a Tier 1 approach for CRA. Because they rely on both the existence of a common mode of action and high quality dose-response data, RPFs may be considered a higher tier method for CRA. Similarly, the toxic equivalency factor (TEF) approach relies on the existence of a clearly identified principal mechanism of action common to all chemicals included in the mixture. Both the RPF and TEF approaches convert the dose of each compound into an index chemical-equivalent dose by scaling its toxicity relative to the index chemical.

96 The objective of this study was, within the framework of the ECOS project (Glorennec et al.,
97 2011), to assess the public health risk posed by the 32 SVOCs for which indoor aggregated
98 exposures in dwellings have been assessed in France (Pelletier et al., 2017b). A chemical-by-
99 chemical risk assessment was completed using lower to higher tier CRA, as recommended by
100 Meek et al. (2011).

101 **METHODS**

102 **Chemical-by-chemical risk assessment**

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

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

104 With

105 ADD: Aggregate Daily Dose (mg/kg-bw/d)

106 RfD: Reference dose (mg/kg-bw/d)

107 f_{oral}: Oral bioavailability

108 ADDs were retrieved from a previous exposure study encompassing air inhalation, dust
109 ingestion, and dermal contact and are expressed as internal doses (Pelletier et al. 2017b). RfD
110 is an estimate of a daily oral exposure that is likely to be without an appreciable risk of
111 deleterious effects during a lifetime (US EPA 2002). RfDs based on oral exposure were
112 preferred because they concern most SVOCs. RfDs, or their equivalents (minimal risk levels
113 or acceptable daily intakes), were retrieved from the following online databases: the
114 Integrated Risk Information System (IRIS) from US EPA (https://www.epa.gov/iris), the
115 toxicological profiles from Agency for Toxic Substances and Disease Registry (ATSDR)
116 (https://www.atsdr.cdc.gov/), the Joint Meeting on Pesticide Residues (JMPR) from the WHO

117 (http://apps.who.int/pesticide-residues-jmpr-database/Home/Range/A-C), the Joint
118 FAO/WHO Expert Committee on Food Additives (JECFA) (http://apps.who.int/food-
119 additives-contaminants-jecfa-database/search.aspx), the Office of Environmental Health
120 Hazard Assessment (OEHHA) (http://oehha.ca.gov/chemicals), Health Canada
121 (https://www.canada.ca/en/health-canada.html), the French agency for food, environment and
122 occupational safety (ANSES) (https://www.anses.fr/fr), and the EU pesticide database from
123 European Commission (http://www.efsa.europa.eu/). RfDs were selected according to the
124 following criteria: i) status = final (non-provisional), ii) methods = derived from classical
125 dose-response data, and iii) update = not the oldest value. Finally, where previous criteria
126 were met for several RfDs, the most conservative was chosen (see Table S1). Where no RfDs
127 were available for individual PCBs or PBDEs compounds, we made the assumption of similar
128 toxic potency between congeners having the same molecular formula (same number of
129 halogenated atoms) and used the RfD of the known congener. Because ADDs are internal
130 doses, RfDs were converted into internal doses using oral bioavailability coefficients (f_{oral}).
131 These are the fraction of a contaminant reaching the digestive system and absorbed into the
132 systemic circulation (Rostami and Juhasz 2011). See Table S2 for corresponding f_{oral}
133 coefficient for each compound. Where RfDs were based on studies using adult mammals, the
134 risk was assessed for the exposure of both an adult (aged 21 to 30 years, as an example) and a
135 child (from birth to the age of 2 years, as an example). Given that early-life (pre- and
136 postnatal periods) is considered as a very vulnerable period, where RfDs were based on
137 prenatal studies, the risk was assessed only for the exposure of a pregnant woman (aged 21-30
138 years, as an example). And where RfDs were based on postnatal studies, the risk was assessed
139 only for the exposure of a child (from birth to the age of 2 years, as an example). Lastly, HQs
140 were calculated for median and high uptake estimates (ADD 50th and 95th percentiles,
141 respectively).

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

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

144

145 With

146 CSF: Cancer slope factor $(\text{mg/kg-bw/d})^{-1}$

147 ED: Exposure duration (30 years)

148 LD: Life duration (70 years)

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

153 **Cumulative risk assessment**

154 The Tier 1 consists of the estimation of HIs for non-carcinogenic compounds. Of the 32
155 compounds studied, only benzo[a]pyrene and lindane are carcinogenic and genotoxic, and
156 these were not assessed within the Tier 1 because they do not induce the same type of tumor
157 (i.e. gastrointestinal and liver respectively). The Tier 2 uses RPF and TEF approaches to
158 estimate cumulative hazard quotients (CumHQ) or cumulative excess risks (CumER).

159 <u>Tier 1:</u>

160 Of the 32 SVOCs, 17 were grouped for their neurotoxic properties and 15 for their reprotoxic
161 properties (update from Fournier et al., 2016, 2017).

162 HI (unitless) is the sum of n HQs for n SVOCs, using equation (3):

$$HI = \sum_{x=1}^{n} \frac{ADD_x}{RfD_x \times f_{oral_x}} \quad (3)$$

163 Oral RfDs for neurotoxic and reprotoxic effects were retrieved from the same databases as for
164 the chemical-by-chemical assessment (see Tables S4 and S6). Where no RfD based on
165 reprotoxic or neurotoxic endpoint was available, a literature survey was conducted in order to
166 retrieve neurotoxic or reprotoxic points of departure (POD). Using the Web Of Knowledge™
167 website (Thomson Reuters, www.webofknowledge.com) publications were selected primarily
168 by searching in the 'topic' field (title, abstract, and key words): ("*SVOC name*" AND
169 (neurotoxicity OR (reproductive OR reprotoxic OR endocrine disruptor)). Secondly, abstract
170 reading was used as a means of filtering out irrelevant publications. Next, study selection
171 criteria included: i) *in vivo* oral exposure of mammals (by diet or gavage) and where possible
172 ii) testing several (or at least one) dose(s) in comparison with a control group. Lastly, if
173 previous criteria were met, PODs were chosen preferentially if benchmark doses (BMD) > no
174 observed adverse effect level (NOAEL) > low observed adverse effect level (LOAEL). RfDs
175 were calculated by dividing the available POD by uncertainty factors (UF). UF were applied
176 for intraspecies variability (UF_H), interspecies variability (UF_A), extrapolation from a LOAEL
177 to a NOAEL (UF_L), database deficiency (UF_D), and extrapolation from acute/subchronic (<
178 28 days/28 to 90 days) to chronic exposure (> 90 days) (UF_S) (US EPA 2008). f_{oral}
179 coefficients were used to convert RfDs into internal doses (see Table S2). Finally, HIs were
180 calculated for median and high uptake estimates (ADD 50th and 95th percentiles, respectively).

181 <u>Tier 2:</u>

182 Specific RPFs and TEFs were retrieved from previous work from Fournier et al. (2014a,
183 2016). This concerned 2 PCBs for toxic effects mediated by the aryl hydrocarbon receptor

184 (AhR) (Van den Berg 1998, 2006), 4 PAHs for carcinogenic effects (Ineris 2003), 3 or 5
185 phthalates respectively (Benson et al., 2009; Hannas et al., 2011) for reprotoxic effects, and 4
186 SVOCs belonging to different chemical classes: HAPs and phthalates, for reprotoxic effects
187 (Fournier et al., 2016). We also estimated RPFs from comparable BMDs based on neuronal
188 death and published by Fournier et al. (2017) for 9 SVOCs: benzo[a]pyrene, diethylhexyl
189 phthalate (DEHP), PCB 52, PCB 153, dieldrin, chlorpyrifos, lindane, BDE 47, and BDE 99
190 (see Table S9). Chlorpyrifos was chosen as the index compound according to the following
191 criteria: i) well-known neurotoxic effect and ii) available RfDs from databases of good quality
192 and covering as many age groups as possible. RPFs (unitless) express the potency of a
193 compound "x" according to the index compound "i" and were estimated as follows:

$$RPF_x = \frac{BMD_i}{BMD_x} \quad (4)$$

194 For non-carcinogenic SVOCs, CumHQs (unitless) were then calculated as follows for n
195 compounds:

$$CumHQ = \frac{\sum_{x=1}^{n}(ADD_x \times RPF_x)}{RfD_i \times f_{oral_i}} \quad (5)$$

196 Where RfD_i is the RfD of the index compound. The same equation is used for the TEF
197 approach, replacing the RPFs with TEFs.

198 For genotoxic carcinogen SVOCs, CumERs (unitless) were then calculated as follows for n
199 compounds:

$$CumER = \sum_{x=1}^{n}(ADD_x \times RPF_x) \times (CSF_i \times f_{oral_i}) \times \frac{ED}{LD} \quad (6)$$

200 Where CSF_i is the CSF of the index compound.

201 <u>Special case of PCBs:</u>

202 RfDs were available for industrial mixtures of PCBs (Aroclor). The RfD of 20 ng/kg-bw/d for
203 immunotoxic effect of Aroclor 1254 was chosen, because this mixture contains our 8 PCBs.
204 This RfD was proposed by the US EPA in 1996 (US EPA 1996), and extended to the 209
205 PCBs congeners by the ATSDR (ATSDR 2000), RIVM (Baars et al. 2001) and Afssa (Afssa
206 2003). Because the 8 congeners included in this study (PCB 28, 31, 52, 101, 105, 118, 138,
207 and 153) represent 34% of the total composition of Aroclor 1254 (ATSDR 2000), we consider
208 an RfD of 7 ng/kg-bw/d (20*34/100) (see Table S10).

209 In this case HI (unitless) is estimated using equation (7):

$$HI = \frac{\sum (ADD_x \times \frac{1}{f_{oral_x}})}{RfD_{Aroclor\ 1254} \times 0{,}34} \quad (7)$$

210

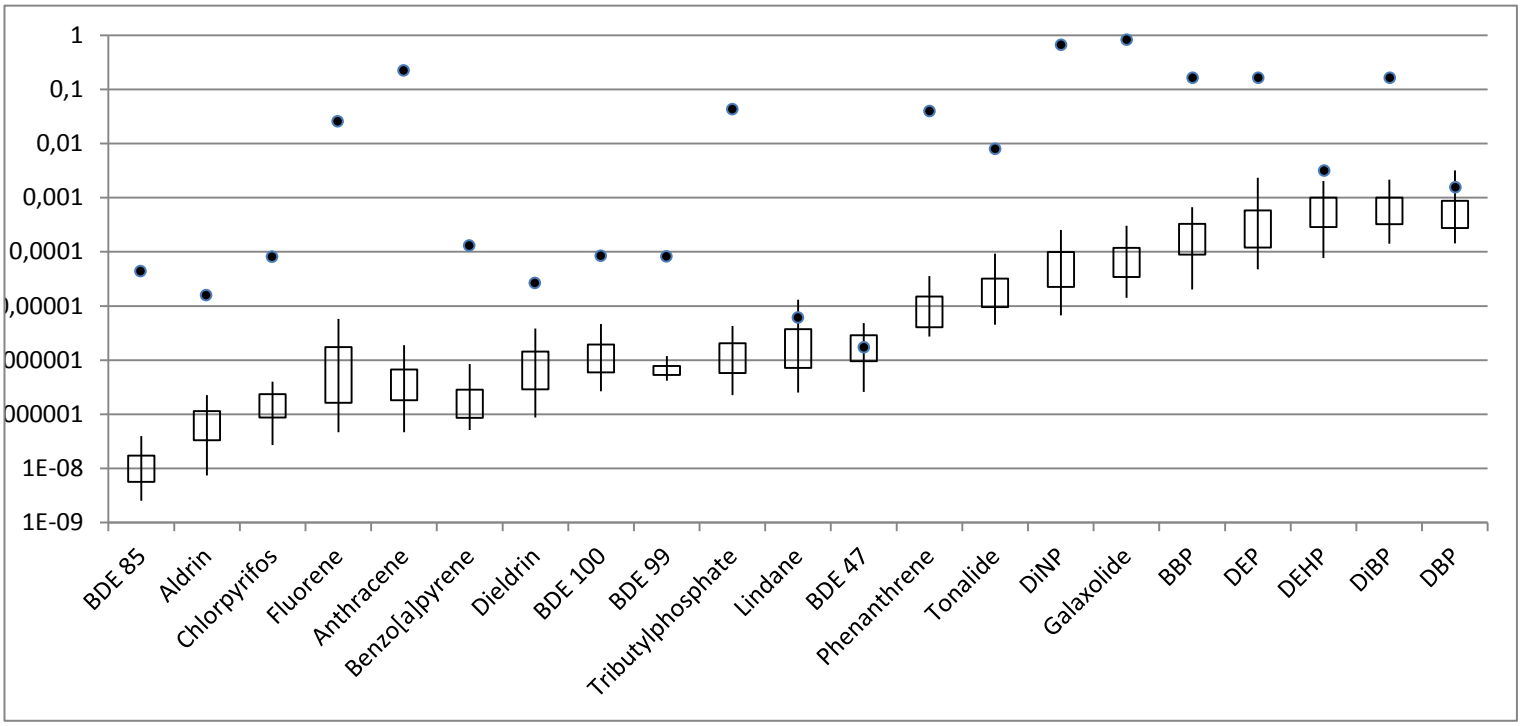
211 **RESULTS**

212 **Chemical-by-chemical risk assessment**

213 Risk assessment could be carried out for 21 SVOCs of the 32 initially considered: 19, 16, and
214 9 for the exposures of children, adults, and pregnant women respectively. Indeed, no RfDs
215 were available in the databases for PCBs (28, 31, 52, 101, 105, 118, 138, and 153) and BDEs
216 (28, 153, and 154) or for their congeners having the same molecular formula.

217 ADD compared to oral RfD*f_{oral} are presented in Figure 1 for the population having the
218 highest HQ for each compound. HQs are >1 for part of the population if ADD box plot
219 intersects the RfD. For di-isononyl phthalate (DiNP) and di-isobutyl phthalate (DiBP), RfDs
220 were available only following in utero exposure (see Table S1), which enable risk
221 assessments only for pregnant women exposure. Detailed HQs are presented in Table S3.

222 **Figure 1:** Comparison between residential indoor aggregate daily doses (5th, 25th, 75th, and
223 95th percentiles) with internal reference doses (RfD*f_{oral}) represented by dots. Unit is mg/kg-
224 bw/d. France 2003-2011.

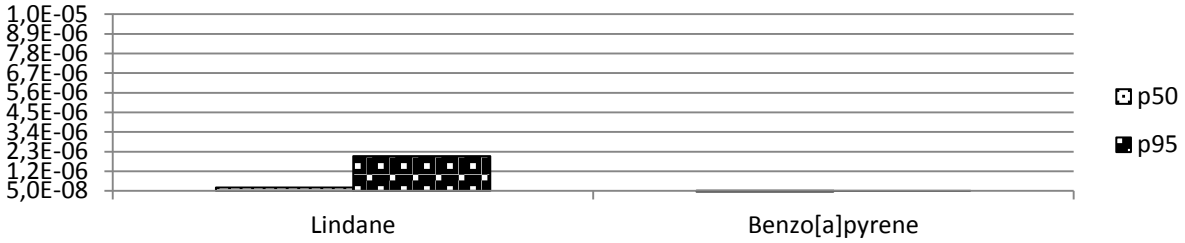


225

226 Health effects may occur for 3 SVOCs considered separately. HQs were above 1 for 50% of
227 children for BDE 47 for reprotoxic effect, and for 5% of children for lindane for immunotoxic
228 effect and dibutyl phthalate (DBP) for reprotoxic effect. For the other compounds, the risk
229 associated with residential SVOC exposure may be considered as acceptable with HQs much
230 lower than 1.

231 ERs of the genotoxic carcinogens: benzo[a]pyrene and lindane are shown in Figure 2. They
232 are lower than 10^{-5} (Y axis) and may therefore be considered as acceptable (WHO 2008).

233 **Figure 2:** Excess risk for residential indoor exposure to benzo[a]pyrene and lindane (50th and
234 95th percentiles) for an adult continuously exposed from birth to the age of 30 years. France
235 2003-2011.



236

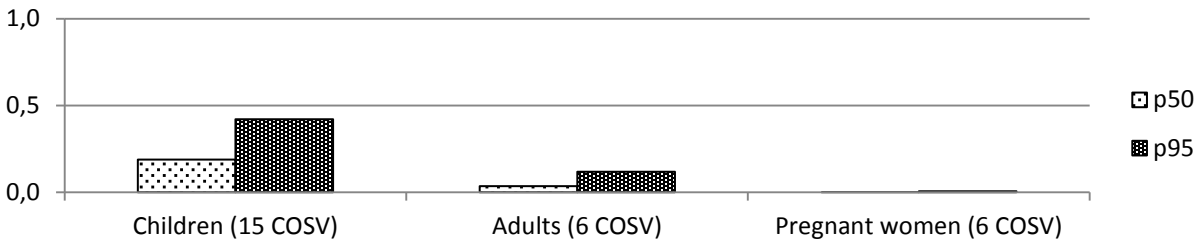
237 **Cumulative risk assessment**

238 Tier 1 assessment for the neurotoxic SVOCs:

239 Tier 1 CRA for neurotoxic effects could be carried out for 17 SVOCs of the 32 initially
240 considered: 15, 6, and 6 were considered for the exposures of children, adults, and pregnant
241 women, respectively. Seven RfDs were retrieved from literature and 10 were constructed (see
242 Table S4).

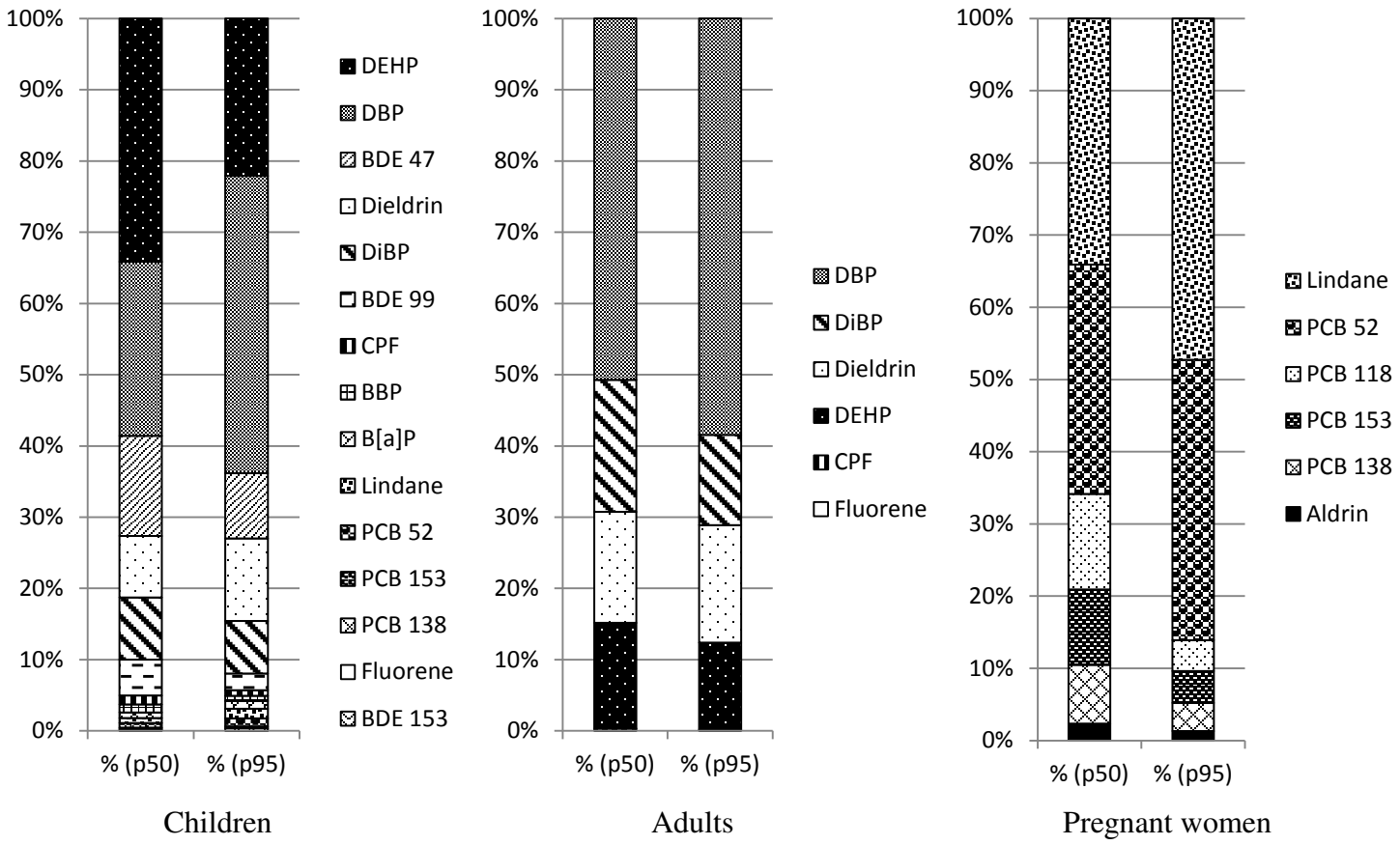
243 HIs were always below 1 (Figure 3 and Table S5 for detailed results). Neurotoxic risks for
244 each age group may therefore be considered acceptable.

245 **Figure 3:** Hazard index for neurotoxic effects due to residential exposure to indoor SVOCs
246 (50th and 95th percentiles). France 2003-2011.



247

248 **Figure 4:** Relative contribution of chemicals to the neurotoxic hazard index.



249

250 B[a]P: benzo[a]pyrene; CPF: chlorpyrifos.

251

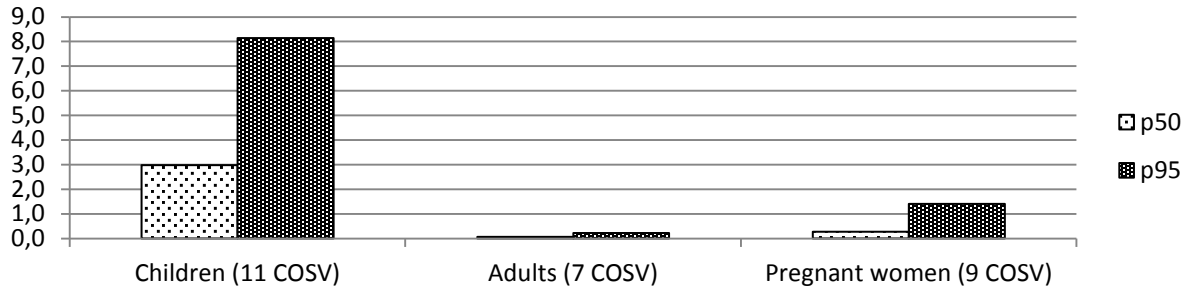
252 Figure 4 shows the relative contribution of each chemical to neurotoxic HIs for the exposures
253 of children, adults and pregnant women. For the children's exposure, DEHP and DBP each
254 contributed 22% and 42% to the 95th percentile of HI respectively, followed by dieldrin
255 (12%). Other SVOCs contributed less than 10% each. For the adults' exposure, DBP
256 contributed 59% to the 95th percentile of HI, followed by dieldrin (17%), DiBP (13%) and
257 DEHP (12%). Other SVOCs contributed less than 10% each. For the pregnant women's
258 exposure, lindane contributed to 47% of the neurotoxic risk for offspring, followed by PCB
259 52 (39%) for the highest exposure. Other SVOCs contributed less than 5% each. Similar
260 results were found for the median exposure for all populations.

261 Tier 1 assessment for the reprotoxic SVOCs:

262 Tier 1 CRA for reprotoxic effects could be carried out for 15 SVOCs of the 32 initially
263 considered: 11, 7, and 9 were considered for the exposures of children, adults, and pregnant
264 women, respectively. Eleven RfDs were retrieved from literature and 5 were constructed (see
265 Table S6).

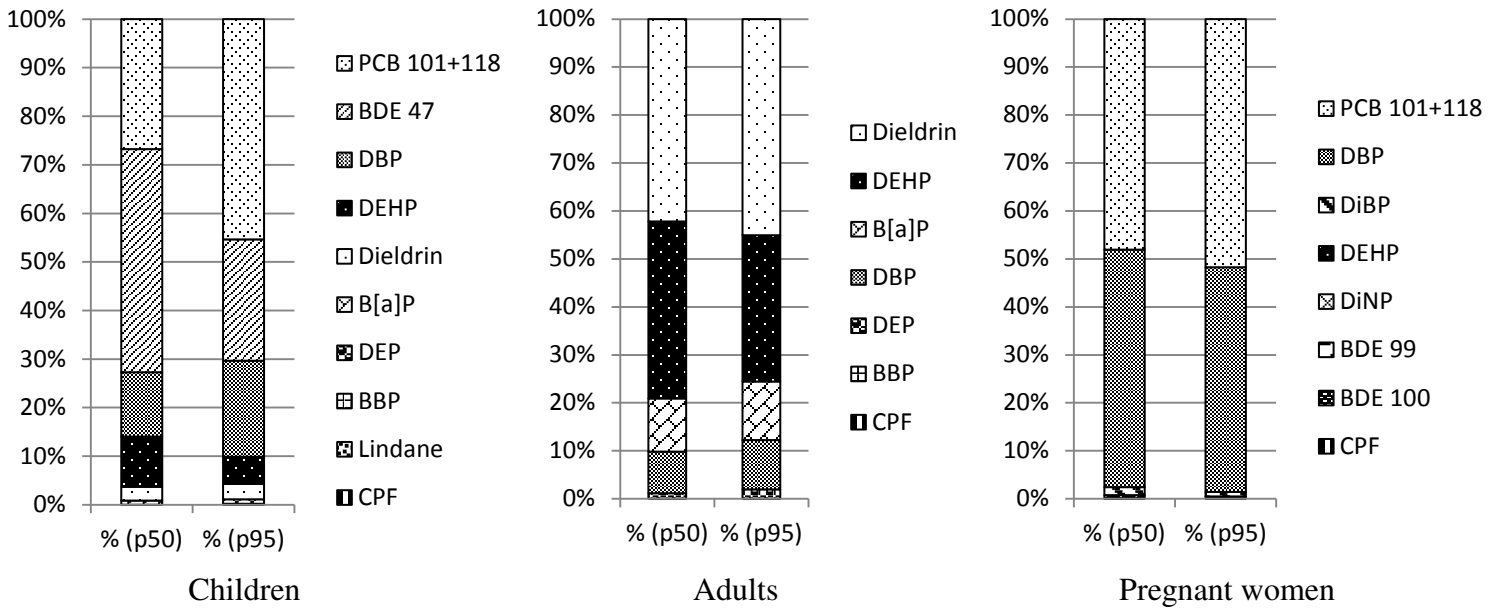
266 Reprotoxic effects may occur for some mixtures. HIs were above 1 for 95% of children (5th
267 percentiles, data not shown), and close to 9 for 5% of them, for the mixture of 11 reprotoxic
268 SVOCs. For the pregnant women's exposure, HIs were above 1 for 5% of them, for the
269 mixture of 9 reprotoxic SVOCs (Figure 5). For adults, HIs were lower than 1 for the mixture
270 of 7 SVOCs (see Table S7 for detailed results).

271 **Figure 5:** Hazard index for reprotoxic effects due to residential exposure to indoor SVOCs
272 (50th and 95th percentiles). France 2003-2011.



273

274 **Figure 6:** Relative contribution of chemicals to the reprotoxic hazard index.



275

276 B[a]P: benzo[a]pyrene; CPF: chlorpyrifos.

277

278 Figure 6 shows the relative contribution of each chemical to reprotoxic HIs for the exposures
279 of children, adults and pregnant women. For the children's exposure, PCBs 101/118
280 contributed 45% to the 95th percentile of HI, followed by BDE 47 (25%) and DBP (20%).
281 Other SVOCs contributed less than 10% each. For the adults' exposure, dieldrin contributed
282 45% to the 95th percentile of HI, followed by DEHP (31%), benzo[a]pyrene (12%) and DBP
283 (10%). Other SVOCs contributed less than 10% each. For the pregnant women's exposure,
284 the sum of PCBs 101/118 contributed to 52% of the reprotoxic risk for offspring, followed by
285 DBP (47%) for the highest exposure. Other SVOCs contributed less than 1% each. Similar
286 results were found for the median exposure for all populations (Figure 6).

287 Tier 2 assessment:

288 **Table 1:** Cumulative hazard quotient (CumHQ) and cumulative excess risk (CumER) using
289 toxic equivalency factors (TEF) and relative potency factors (RPF).

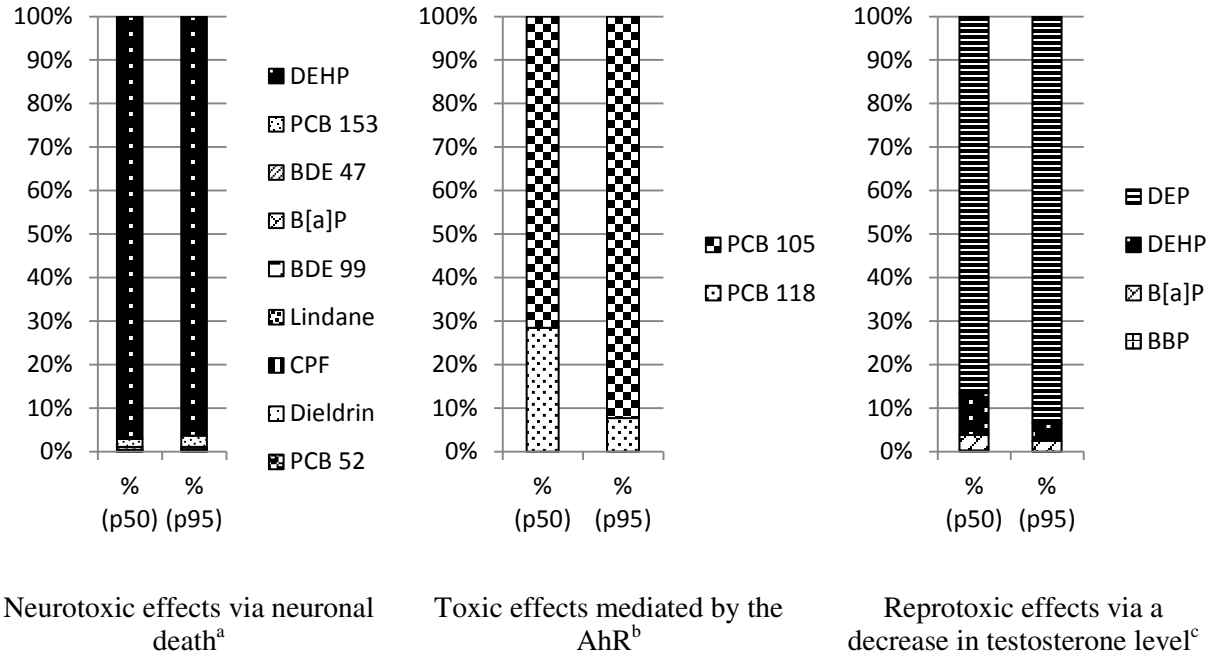
SVOCs (effect considered)	Relative toxicity indicator	Risk indicator	Children		Adults		Pregnant women	
			p50	p95	p50	p95	p50	p95
Benzo[a]pyrene, anthracene, fluorene, phenanthrene (gastrointestinal cancer)	TEF (Ineris 2003) [a]	CumER[b]			1.1E-08	5.6E-08		
PCB 105, PCB 118 (toxic effects mediated by the AhR[c])	TEF (Van den Berg 1998, 2006) [d]	CumHQ	0.2	**1.8**	0.07	0.6		
DEHP, BBP, DBP, DiBP, DiNP (anti-androgenic)	RPF (Benson 2009) [e]	CumHQ					0.01	0.04
DEHP, DiBP, DiNP (anti-androgenic)	RPF (Hannas et al., 2011) [f]	CumHQ					0.0007	0.002
Benzo[a]pyrene, DEHP, DEP, BBP (decrease in testosterone level)	RPF (Fournier et al., 2016) [g]	CumHQ	0.5	**4**	0.2	**1.4**		
Chlorpyrifos, benzo[a]pyrene, DEHP, PCB 52, PCB 153, dieldrin, lindane, BDE 47, BDE 99 (neuronal death)	RPF (this study based on Fournier et al., 2017) [h]	CumHQ	**17**	**40**	0.1	0.6		

290 [a] Ineris selected benzo[a]pyrene as reference chemical; [b] For an adult continuously exposed from birth to the age
291 of 30 years; [c] The aryl hydrocarbon receptor (AhR) is a ligand-activated transcription factor that controls the
292 expression of a diverse set of genes; [d] Van den Berg (1998, 2006) selected 2,3,7,8-TCDD as reference chemical;
293 [e] Benson (2009) selected DEHP as reference chemical; [f] Hannas et al. (2001) selected DPP as reference
294 chemical; [g] Fournier et al. (2016) selected cypermethrin as reference chemical; [h] We selected chlorpyrifos as
295 reference chemical for our RPFs construction.
296 CumHQ of concern are in bold font.
297

298 Tier 2 CRA could be carried out for 19 SVOCs of the 32 initially considered but for relatively
299 simple mixtures containing 2 to 9 compounds, as reported in Table 1. For children, neurotoxic
300 effects via neuronal death due to a mixture of 9 SVOCs from different chemical classes were
301 likely to occur for 95% of them (5th percentiles, data not shown). Toxic effects mediated by
302 the AhR due to a mixture of 2 PCBs were likely to occur for 5% of children. Reprotoxic
303 effects via a decrease in testosterone level due to a mixture of benzo[a]pyrene and 3
304 phthalates were likely to occur for 25% of children and 5% of adults. For pregnant women's

305 exposure, CumHQs were below 1 for exposure to mixtures of 5 and 3 phthalates with anti-
306 androgenic effects.

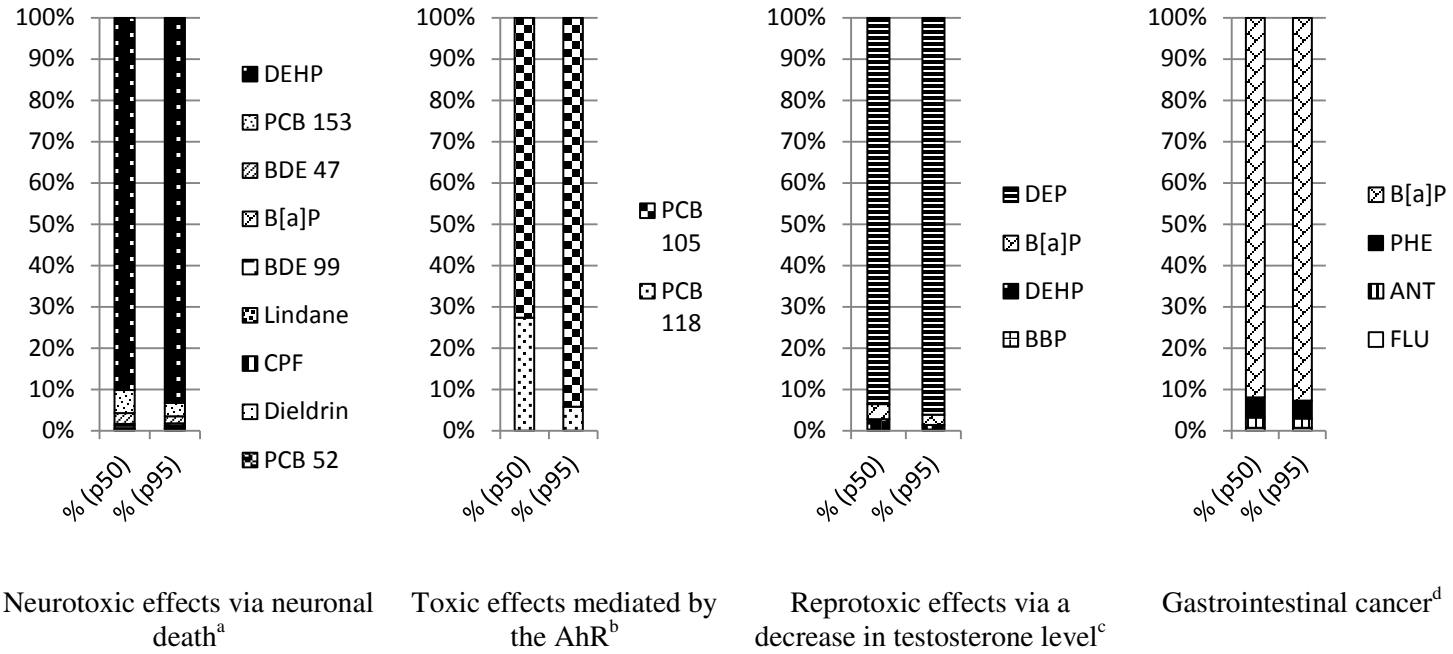
307 **Figure 7**: Relative contribution of chemicals to cumulative hazard quotients for children's
308 exposure.



309
310 [a] RPF (this study from Fournier et al., 2017); [b] TEF (Van den Berg 1998, 2006); [c] RPF (Fournier et al., 2016;
311 B[a]P: benzo[a]pyrene; CPF: chlorpyrifos.
312

313 **Figure 8**: Relative contribution of chemicals to cumulative hazard quotients and cumulative

314 excess risks for adults' exposure.



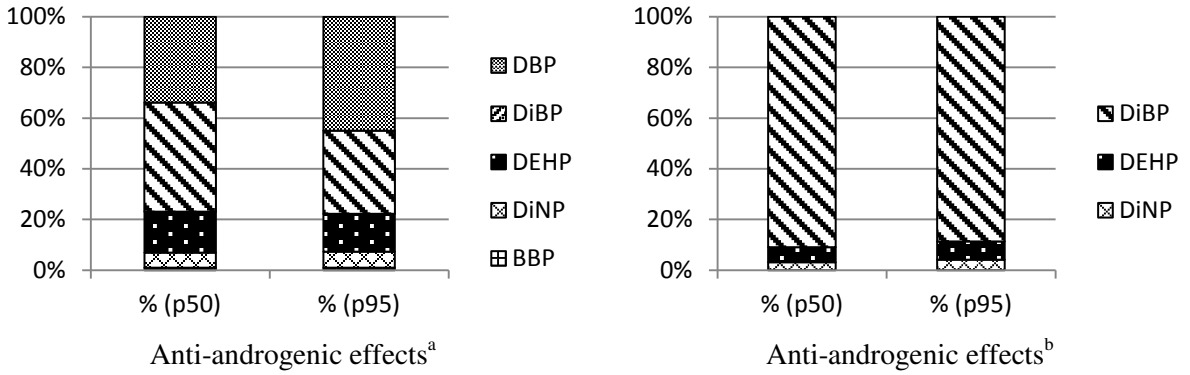
315

316 [a] RPF (this study from Fournier et al., 2017); [b] TEF (Van den Berg 1998, 2006); [c] RPF (Fournier et al., 2016); [d]
317 TEF (Ineris 2003); ANT: anthracene; B[a]P: benzo[a]pyrene; CPF: chlorpyrifos; FLU: fluorene; PHE:
318 phenanthrene.

319

320 **Figure 9**: Relative contribution of chemicals to cumulative hazard quotients for pregnant

321 women's exposure.



322

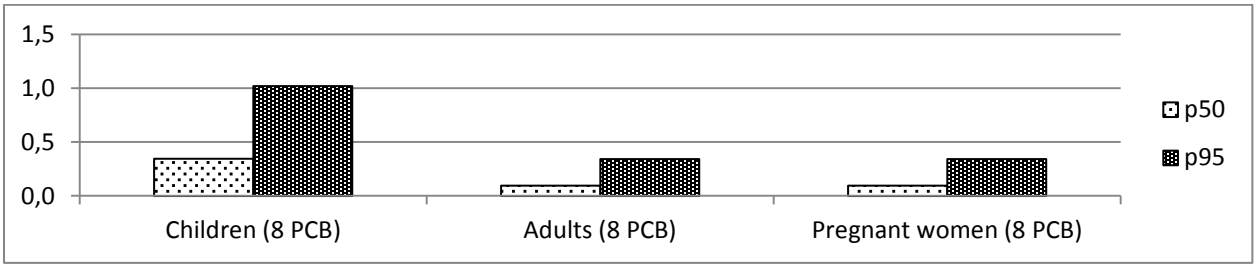
323 [a] RPF (Benson 2009); [b] RPF (Hannas et al., 2011).

Figures 7, 8 and 9 show the relative contribution of each chemical to CumERs and CumHQs for each age group. PCB 105 for toxic effects mediated by the AhR, diethyl phthalate (DEP) for reprotoxic effects via a decrease in testosterone level, and DEHP for neurotoxic effects via neuronal death contributed largely to the 50th and the 95th percentiles of CumHQs for both children's and adults' exposure (Figures 7 and 8). For the gastrointestinal cancer risk associated with PAH exposure of adults, benzo[a]pyrene contributed largely to the 50th and the 95th percentiles of CumER (Figure 8). For pregnant women's exposure, DBP and DiBP contributed most to the 50th and the 95th percentiles of CumHQs (Figure 9).

Special case of PCBs:

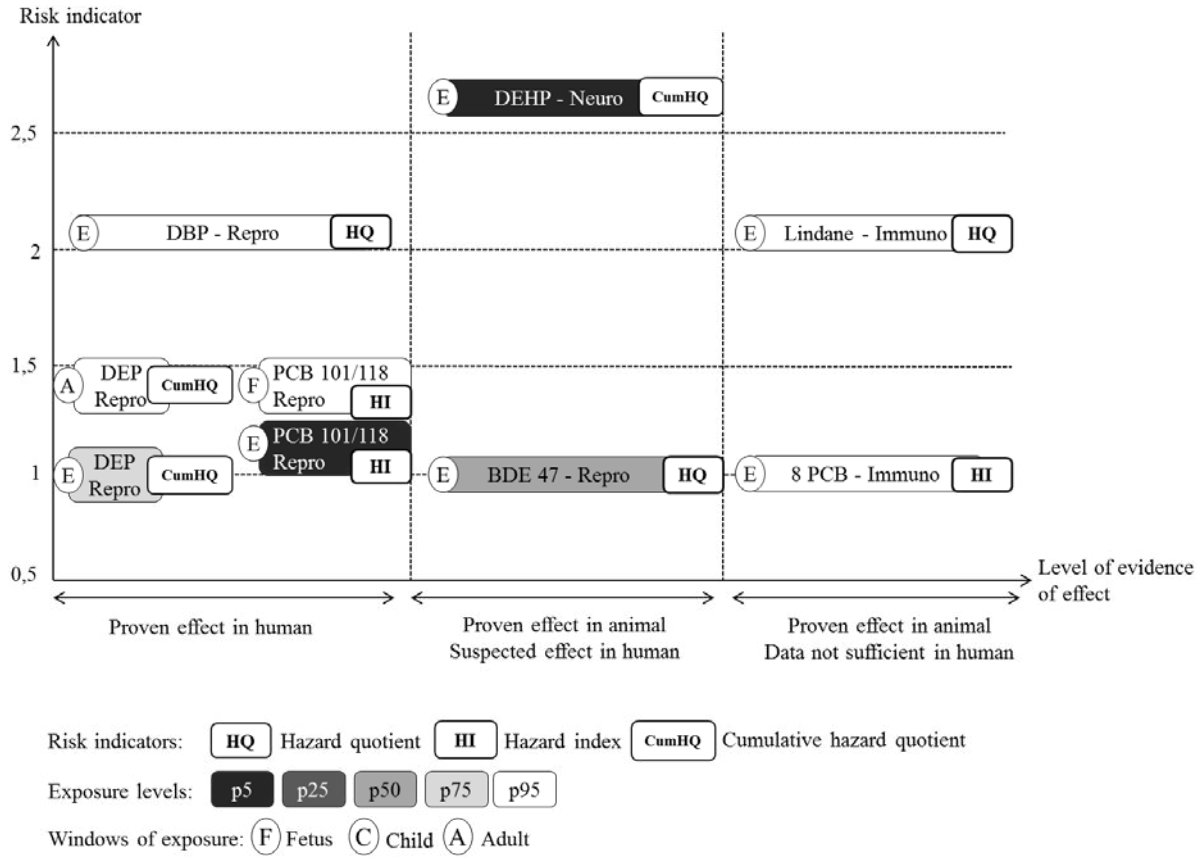
Immunotoxic risks may occur for 5% of children because of exposure to the 8 PCBs. For adults and pregnant women's exposure, HIs were lower than 1 (Figure 10).

Figure 10: Hazard index for immunotoxic effects due to residential exposure to indoor PCBs (50th and 95th percentiles). France 2003-2011.



338 A summary of the main findings for both chemical-by-chemical and cumulative risk
339 assessments is presented in Figure 11.

340 **Figure 11:** Summary of the main results of the chemical-by-chemical and cumulative risk
341 assessment.



342

343 **DISCUSSION**

344 Health risks posed by residential indoor exposure to SVOCs in France were assessed. The
345 chemical-by-chemical assessment revealed unacceptable risk for children because of their
346 exposures to BDE 47 (reprotoxic effect), DBP (reprotoxic effect), and lindane (immunotoxic
347 effect) (Figure 1).

348 The CRA approach provided additional information. The Tier 1 of CRA revealed
349 unacceptable reprotoxic risks (HI>1) for children and for pregnant women's exposure. The

350 following SVOCs were contributing most to the risk: PCB 101 and 118, BDE 47, and DBP
351 (Figure 6).

352 The higher tier CRA approach showed that neurotoxic effects via neuronal death could be
353 hazardous for children, due to a mixture of chlorpyrifos, benzo[a]pyrene, DEHP, PCB 52,
354 PCB 153, dieldrin, lindane, BDE 47, and BDE 99 (Table 1). The most contributive pollutant
355 was DEHP (Figures 7 and 8), mainly because exposure to this compound was much higher
356 than for the others (2 µg/kg-bw/d, p95 values for a children's exposure estimated from
357 Pelletier et al. (2017b), data not shown). According to our RPF estimation, DEHP is twice as
358 potent as the index compound: chlorpyrifos. Much higher CumHQs were observed for
359 children than for adults, because chlorpyrifos' RfD for a sensitive effect was employed for
360 children (see Table S8). Also for reprotoxic effects, associated with a decrease in testosterone
361 level, the exposure to benzo[a]pyrene, DEHP, DEP, and benzyl butyl phthalate (BBP) might
362 be hazardous for highly exposed children and adults (Table 1). The most contributive
363 pollutant was DEP (Figures 7 and 8), mainly because exposure to this compound was much
364 higher than for the others (2.3 µg/kg-bw/d, 95th percentile values for a children's exposure,
365 estimated from Pelletier et al. (2017b)). According to the RPF estimation by Fournier et al.
366 (2016), DEP is 23 times more potent than the index compound: cypermethrin. For toxic
367 effects mediated by the AhR, exposure to PCB 105 and PCB 118 might be hazardous for
368 highly exposed children (Table 1). Equal TEFs were estimated by the WHO (Van den Berg et
369 al., 1998, 2006) for both compounds and we found PCB 105 to be the most contributive
370 pollutant (Figures 7 and 8) only because its exposure was higher than PCB 118 (3 ng/kg-
371 bw/d, p95 values for a children's exposure estimated from Pelletier et al. (2017b), data not
372 shown).

373 Lastly, the special case of PCBs CRA revealed unacceptable immunotoxic risk for children's
374 exposure to 8 indoor PCBs (Figure 10).

375 Study strengths include: i) CRA of numerous SVOCs from different chemical families for
376 different populations, ii) use of nationwide representative exposure estimates, and iii) use of
377 refined, tiered CRA approaches with HI, RPF and TEF being used successively.

378 Study limitations include the existence of uncertainties, mainly due to: i) transposition of
379 effects from animal to human, ii) number of compounds included in the mixtures, iii)
380 exposure data, and iv) RfD and RPF/TEF construction.

381 The assessment requires a certain level of caution for accurate interpretation, due mainly to
382 the transposition of effects from animal to human.

383 In terms of reprotoxic effects, no RfD for reprotoxic endpoint were available in literature for
384 PCBs. The RfD_{rep} value we constructed for PCB 101 and 118 was based on decreased relative
385 testes and ovary weight in offspring (F1 and F2) after subchronic exposure of pregnant mice
386 from GD 0 to PND 21 (see Table S6). Human studies supported the endocrine-disrupting
387 capacity of PCBs (Dallinga et al., 2002; Den Hond et al., 2002). Dallinga et al. (2002)
388 observed a significantly decreased sperm count in relation to an elevated PCBs (included PCB
389 118) metabolites level in the blood of men with normal semen quality and Den Hond et al.
390 (2002) showed a significant delay in puberty in boys (reduction in the genitals and lower
391 testicular volume). These results confirmed the relevance of this endpoint for humans. For
392 BDE 47 the RfD was based on a specific female endpoint: decreased uterus weight in 2
393 month-old female rats after a single exposure on postnatal day (PND) 10 (see Table S1). This
394 endpoint appears relevant to humans. For phthalates (DBP, DEP, and DEHP) toxicity
395 indicators were based on their anti-androgenic properties, which have been extensively
396 studied (Gray et al., 2006; Kay et al., 2014). Furthermore, epidemiological and experimental
397 studies have also confirmed their effects as endocrine disruptors as well as their reprotoxic

398 effects on human health (Swan et al. 2005; Habert et al., 2009). This endpoint therefore
399 appears relevant to humans.

400 In terms of neurotoxic effects, phthalates were the most contributive compounds. While
401 contrasting results are observed in epidemiological studies, for neurobehavioral
402 developmental effects (psychomotor development, intelligence quotient, primitive reflexes
403 etc.), supporting animal data provide potential evidence of their neurotoxicity (Miodovnik et
404 al., 2014).

405 In terms of immunotoxic effects, the RfD for lindane was based on biphasic changes in cell-
406 and humoral-mediated immunity to red blood cells in adult female mice after chronic
407 exposure (24 weeks) (see Table S1). Although the immunotoxic effects of lindane have been
408 confirmed by other oral studies (Dorsey 2005), it is difficult to relate human health effects to
409 specific immunotoxic parameters in laboratory animals due to the complexities of the immune
410 system (Abadin et al., 2007) and there is no evidence for this endpoint in humans. For PCBs
411 (sum of 8 congeners), the RfD of the Tier 2 assessment was based on immunological effects
412 in adult monkeys (see Table S10). Monkeys appeared more sensitive than other species (rats,
413 mice, guinea pigs and rabbits) for effects on antibody responses after oral exposure and
414 provided a better animal model due to phylogenetic and biological similarities to humans
415 (Tryphonas 1994, 1995). However, due to limited information on the immunological effect of
416 PCBs in humans, and insufficient information on exposure-response relationships, the
417 evidence of PCB immunotoxicity in humans is limited.

418 To summarize, given the present state of knowledge, reprotoxic critical effects appear
419 transferable to humans for PCB 101 and PCB 118, DEP and DBP indoor exposure, and in a
420 lesser extent for BDE 47. For phthalates, extrapolation of neurotoxicity data from animal
421 models to humans has led to a lower level of confidence. The same conclusion could be

422 reached for lindane and PCB immunotoxicity, though their effects in humans have been
423 studied less extensively.

424 The refinement of this risk assessment strongly depends on data availability and is linked to
425 the number of compounds included in the mixtures, e.g. the RPF and TEF approaches were
426 conducted for mixtures of only 2 PCBs for toxic effects mediated by the AhR, 4 SVOCs and 5
427 or 3 phthalates for reprotoxic effects and 9 SVOCs for neurotoxic effects (Table 1). We also
428 made a distinction between pre- and postnatal periods and adulthood, and this resulted in
429 studying different mixtures containing different SVOCs for each age group, e.g. neurotoxic
430 CRA was conducted for 15 compounds for the children's exposure, for 9 compounds for the
431 adults' exposure, and for 6 compounds for the pregnant women's exposure (Figure 3). In
432 terms of effects, age-related differences in susceptibility to contaminants are due to the fact
433 that critical periods of structural and functional development are happening during pre- and
434 postnatal life. The nervous, immune, respiratory, reproductive and endocrine systems are in a
435 particularly sensitive stage of development at these early periods of life (Selevan et al., 2000).
436 Increasing evidence of sensitive populations, in terms of exposure and toxic effects, demands
437 better distinction between the different windows of exposure (US EPA 2002), in particular to
438 avoid overestimation of the risk for adults. Thorough studies may allow the inclusion of new
439 compounds in the different mixtures, which could raise the risk – for example, HI for
440 children's exposure to 15 neurotoxic SVOCs was found to be 0.6, but could reach (or even
441 exceed) 1 were other SVOCs to be included.

442 Uncertainty in results may also be due to the exposure data. However, ADDs were estimated
443 using a probabilistic approach and two-dimensional Monte Carlo simulations. Compared to a
444 more traditional deterministic approach, this has the main advantage of taking into account
445 both uncertainty (lack of knowledge about a parameter) and variability (heterogeneity of a
446 parameter in a population) of input parameters. The sensitivity analysis conducted by Pelletier

447 et al. (2017b) revealed that exposure estimate variance was mainly driven by indoor
448 contamination variability (C_{gas}, C_{part} and C_{dust}), and only secondarily by uncertainty in
449 physical and chemical parameters. Furthermore, because ADDs decrease with age (due to the
450 increased body weight), where risks related to a single effect could be estimated for several
451 age groups, they were always higher for those children exposed from birth to the age of 2
452 years. Regarding exposure, the main limitation seems to be that, despite the relatively high
453 number of SVOCs we studied, many could not be included in this study because they were
454 not taken into account in the study by Pelletier et al. (2017b) (e.g. pyrethroids, bisphenols,
455 etc.).

456 The uncertainty linked to RfD construction may also strongly influence the results. For
457 several chemicals of concern, the RfDs had a UF as high as 1,000 (i.e. BDE 47, DBP, and
458 lindane) or even 3,000 (i.e. PCB 101 and PCB 118) – this could be considered as low
459 confidence, reflecting major uncertainties in the databases and in particular because of using
460 LOAELs instead of NOAELs and BMDs. Furthermore, internal RfDs were estimated using
461 oral bioavailability coefficients. Averaged values for f_{oral} were used (see Table S2). For
462 chemical-by-chemical risk assessment, internal RfDs were also estimated using the minimum
463 and maximum values (data not shown) of f_{oral} distributions from Pelletier et al. (2017b). HQ
464 results could be up to 10 times higher when using minimum f_{oral} values and up to 2 times
465 lower when using maximum f_{oral} values for some SVOCs having broad distribution for this
466 parameter (e.g. lindane and dieldrin). The most contrasted example is lindane, with an HQ of
467 22 when using the minimum value and of 1 when using the maximum value (for the p95 of
468 children's exposure). However, although results may vary depending on the f_{oral} value,
469 identification of the compounds that are at risk remains unchanged. Uncertainties could also
470 be related to the read-across extrapolations, required where some of the congeners lacked
471 toxicological data, i.e. RfDs for BDE and PCB congeners. Finally, for RPF and TEF

472 construction, the uncertainties mainly depend on data comparability: for example concerning
473 different exposure routes (intratracheal, breast implants, and cutaneous contact) (Ineris 2003),
474 endpoints (decrease in fetal testosterone level for all phthalates versus smallness - or absence
475 of - male reproductive organs for DEHP) (Benson 2009), windows of exposure (prenatal,
476 postnatal, and adult), and types of experimental systems (cell lines versus primary cultures),
477 strains (mice, rats, and humans) and types of cells (e.g. pheochromocytoma versus
478 neuroblastoma cells) (Fournier et al., 2017).

479 **CONCLUSIONS**

480 This risk assessment, notably its cumulative aspect, allowed the identification of residential
481 aggregated indoor exposures that lead to unacceptable risk for a certain portion of the French
482 population. Furthermore, it allowed the identification of the most contributive compounds for
483 different health effects namely DBP, DEP, DEHP, BDE 47, lindane, and PCBs. According to
484 evidence for effects in humans, it is thus possible to prioritize chemicals for prevention (DBP,
485 DEP, and some PCBs) and for supplemental scientific studies to clarify their impact in terms
486 of risk to human health (BDE 47, DEHP, lindane, and PCBs). More generally, to enable a
487 broader cumulative risk assessment, it seems important to ensure that contamination data
488 encompass new chemicals and that toxicological studies are comparable and publicly
489 available. Finally, it is interesting to note that in certain cases, i.e. exposure to neurotoxic
490 compounds, Tier 1 assessments were less conservative than Tier 2 assessments. This finding
491 reveals that, in cumulative risk assessment, lower tier may not be sufficient in every case.

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SUPPLEMENTAL MATERIAL

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

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Table S10: Reference doses (RfD) constructed for the 8 PCBs included in this study from the RfD retrieved from literature for the Aroclor 1254 for immunotoxic effect

References

Table S1: Reference doses (RfD) and cancer slope factors (CSF) retrieved from literature for most critical effect for SVOCs and used for chemical by chemical risk assessment by estimation of hazard quotients and excess risks

SVOC	RfD[a] (µg/kg-bw/d)	CSF (mg/kg /d)$^{-1}$	Reference	Critical effect (following oral exposure)	Point of departure (mg/kg-bw/d)	Uncertainty factor
Aldrin	0.03		ANSES[b] (2015) ATSDR[c] (2002) US EPA[d] (1988)	Liver lesions and increased relative liver weight in adult male and female rats after chronic exposure (2 years)	LOAEL=0.025	UFH=10 UFA= 10 UFL=10
Aldrin	2 (gest)		ATSDR[c] (2016)	Decreased body weight and electroconvulsive shock threshold in offspring male and female after acute exposure (7 days) of pregnant mice	LOAEL=2	UFH= 10 UFA = 10 UFL=10
Anthracene	300		US EPA[d] (1991)	No observed effects in adult male and female mice after subchronic exposure (90 days)	NOAEL=1000	UFH= 10 UFA= 10 UFS= 30
BBP	200		US EPA[d] (2000)	Increased relative liver and brain weights in adult male rats after chronic exposure (6 months)	NOAEL=159	UFH= 10 UFA= 10 UFS= 10
BDE 47	0.002 (child)		Li et al. (2014)	Decreased relative uterus weight in 2 months female rats after single dose exposure at PND 10	BMDL=0.002	UFA=10 UFH=10 UFS=10 MF=1
BDE 99[e]	0.1 (child)		US EPA[d] (2008)	Neurobehavioral developmental effects in adult male and female mice after exposure to single dose at PND 10	$BMDL_{1SD}$=0.29	UFH= 10 UFA= 10 UFS= 3 UFD= 10
BDE 99[e]	10 (gest)		Kortenkamp and Faust (2010)	Suppression of testosterone levels, reductions of anogenital distance in offspring male after acute exposure (10 days) of pregnant rats	NOAEL=1	UFH= 10 UFA= 10
Benzo[a]pyrene	0.3 (child)		US EPA[d] (2017)	Neurobehavioral impairment in adult male and female rats after postnatal exposure from PND 5 to PND 11	$BMDL_s$=0.092	UFH= 10 UFA= 10 UFD= 3
Benzo[a]pyrene		1	US EPA[d] (2017)	Tumor response in the alimentary tract (forestomach, esophagus, tongue, and larynx) of female mice after oral chronic exposure (2 years).	$BMDL_{10}$[f]	
Chlorpyrifos	0.1 (child)		OEHHA[g] (2010)	Reduced plasma and red blood cells cholinesterase activity in adult Beagle dogs after chronic exposure (2 years)	NOAEL=0.03	UFH=10 UFA=3 UF[h]=10
Chlorpyrifos	1		ATSDR[c] (2016) ANSES[b] (2015)	Reduced red blood cells cholinesterase activity in adult male and female rats after chronic exposure (2 years)	NOAEL=0.1	UFH= 10 UFA= 10
DBP	2 (gest/ child)		ANSES[b] (2008)	Reduction of spermatocyte development and mammary glands dysplasia in offspring male after subchronic exposure of pregnant rats and offspring from GD 15 to PND 21	LOAEL=2	UFH= 10 UFA= 10 UFL= 10

DBP	52		RIVM (2001)	Decreased number and body weight of offspring rats (without maternal toxicity) after a two-generation reproductive toxicity study	LOAEL=52	UFH= 10 UFA= 10 UFL= 10
DEHP	44 (gest)		Health Canada (1994)	Decreased fetus number after acute exposure (17 days) of pregnant mice	NOAEL=44	1000
DEHP	3.7		RIVM (2001)	Sertoli cells vacuolation in adult male rats after subchronic exposure (13 weeks)	NOAEL=3.7	UFH= 10 UFA= 10 UFS= 10
DEP	200		RIVM (2001)	Degenaration and atrophy of testes and spermatogenesis impairment in adult male rats after chronic exposure (16 weeks)	NOAEL=100	UFH= 10 UFA= 10 UFD= 5
DiBP	200 (gest)		Kortenkamp and Faust (2010)	Suppression of fetal testosterone synthesis after acute exposure (10 days) of pregnant rats	BMDL=40	200
Dieldrin	0.05		ATSDR[c] (2016) ANSES[b] (2009) US EPA[d] (1998)	Increased relative liver weight and hepatic lesions in adult female rats after chronic expsoure (2 years)	NOAEL=0.005	UFH= 10 UFA= 10
DiNP	800 (gest)		Benson (2009)	Decreased fetal testosterone and retained areolas/nipples in offspring male after acute exposure (14 days) of pregnant rats	LOAEL=750	UFH= 10 UFA= 10 UFL=10
Fluorene	40		US EPA[d] (1990)	Decreased red blood cells, packed cell volume and hemoglobin in adult male mice after subchronic exposure (13 weeks)	LOAEL=125	UFH= 10 UFA= 10 UFS=10 UFL= 3
Galaxolide	1500		Bonvallot et al. (2010)	Increased body weight and relative liver weight in adult male and female rats after subchronic exposure (90 days)	NOAEL=150	UFH= 10 UFA= 10
Lindane	0.01		ATSDR[c] (2016)	Biphasic changes in cell- and humoral-mediated immunity to red blood cells in adult female mice after chronic exposure (24 weeks)	LOAEL=0.012	UFH= 10 UFA= 10 UFL= 10
Lindane		1.1	OEHHA[g] (2011)	Increased in liver tumor of male mice after oral chronic exposure (2 years)	q_{animal}[i]	
Phenanthrene	40		RIVM (2001)	Decreased body weight, increased relative liver and kidney weight (unknown species and duration of exposure)	na	UFH= 10 UFA= 10
Tributyl phosphate	1100 (gest)		ATSDR[c] (2016)	Decreased maternal body weight gain after acute exposure (10 days) of pregnant rats	$BMDL_{1SD}$=110	UFH= 10 UFA= 10
Tributyl phosphate	80		ATSDR[c] (2016)	Urinary bladder hyperplasia in adult male rats after chronic exposure (2 years)	$BMDL_{10}$=8.03	UFH= 10 UFA= 10
Tonalide	15		Bonvallot et al. (2010)	Increased relative liver weight in adult rats after subchronic exposure (90 days)	NOAEL=1.5	UFH= 10 UFA= 10

BMDL: benchmark dose modelling; GD: gestational days; LOAEL: low observed adverse effect level; na: not available; MF: modifying factor; NOAEL: no observed adverse effect level; PND: postnatal day; UF_A: interspecies uncertainty factor; UF_D: database deficiency uncertainty factor; UF_H: intraspecies uncertainty factor; UF_L: LOAEL uncertainty factor; UF_S: acute/subchronic uncertainty factor.

[a] "Gest"correspond to RfD specific to gestational exposure and "child"to RfD specific to postnatal exposure.
[b] Retrieved from: *https://www.anses.fr/fr/content/les-valeurs-de-r%C3%A9f%C3%A9rence*
[c] Retrieved from: *https://www.atsdr.cdc.gov/mrls/mrllist.asp*
[d] Retrieved from: *https://cfpub.epa.gov/ncea/iris/search/index.cfm?*
[e] Assumption of similar toxic potency between congeners having the same molecular formula (same number of halogenated atoms) led to use the RfD of BDE 99 also for BDE 85 and BDE 100.
[f] $BMDL_{10}$: the animal cancer potency was estimated from a linear extrapolation from the 90% confidence bound on the BMD_{10} (estimated using multistage-Weibull model).
[g] Retrieved from: *https://oehha.ca.gov/chemicals*
[h] Additional factor for children extrapolation.
[i] q_{animal}: correspond to the animal cancer potency estimated from the upper 95% confidence bound on the linear extrapolation using the Crump linearized multistage polynomial model.

Table S2: SVOC oral bioavailabilities (f_{oral}) used for the estimation of internal reference doses (average values) retrieved from Pelletier et al. (2017) and online databases

SVOC	f_{oral} (-)[1]	SVOC	f_{oral} (-)[1]
Aldrin	0.53	**Dieldrin**	0.53
Anthracene	0.68	**Fluorene**	0.60
BBP	0.75	**Lindane**	0.62
BDE 47	0.85	**Galaxolide**	0.50
BDE 85	0.44	**PCB101**	0.70
BDE 99	0.82	**PCB105**	0.80
BDE 100	0.84	**PCB118**	0.64
BDE 153	0.85	**PCB138**	0.89
Benzo[a]pyrene	0.43	**PCB153**	0.72
Chlorpyrifos	0.83	**PCB28**	0.78
DBP	0.75	**PCB31**	0.79
DEHP	0.75	**PCB52**	0.83
DEP	0.75	**Phenanthrene**	0.93
DiBP	0.75	**Tonalide**	0.50
DiNP	0.75	**Tributyl phosphate**	0.50
DPP	0.75	**2,3,7,8-TCDD**	0.76
Cypermethrin	0.36		

[1] Arithmetic mean estimate from retrieved values from online databases (Agency for toxic substances and disease registry (ATSDR); Hazardous substances data bank (HSBD)).

Table S3: Hazard quotients estimated for indoor SVOCs in France (median and high uptakes with percentiles 50th and 95th respectively)

SVOC	Highest hazard quotient		Children		Adults		Pregnant women	
	p50	p95	p50	p95	p50	p95	p50	p95
Aldrin	0.004	0.01	0.004	0.01	0.001	0.005	0.00002	0.00007
Dieldrin	0.03	0.1	0.03	0.1	0.009	0.05		
Lindane	0.3	2.1	0.3	2.1	0.09	0.7		
Chlorpyrifos	0.002	0.005	0.002	0.005	0.00007	0.0002		
Tributylphosphate	0.00003	0.0001	0.00003	0.0001	0.000009	0.00004	0.0000007	0.000003
Galaxolide	0.00008	0.0004	0.00008	0.0004	0.00003	0.0001		
Tonalide	0.002	0.01	0.002	0.01	0.0008	0.004		
Anthracene	0.000002	0.000009	0.000002	0.000009	0.0000007	0.000004		
Benzo[a]pyrene	0.001	0.007	0.001	0.007				
Fluorene	0.00004	0.0002	0.00004	0.0002	0.00001	0.00009		
Phenanthrene	0.0002	0.001	0.0002	0.001	0.00007	0.0004		
BBP	0.001	0.004	0.001	0.004	0.0001	0.0005		
DBP	0.3	2.1	0.3	2.1	0.004	0.03	0.1	0.7
DEHP	0.2	0.7	0.2	0.7	0.02	0.08	0.002	0.007
DEP	0.002	0.02	0.002	0.02	0.0006	0.005		
DiBP	0.004	0.01					0.004	0.01
DiNP	0.00008	0.0004					0.00008	0.0004
BDE 47	1	2.7	1	2.7				
BDE 85	0.0002	0.0009	0.0002	0.0009	0.00006	0.0003	0.0000006	0.000003
BDE 99	0.008	0.01	0.008	0.01			0.00003	0.00006
BDE 100	0.01	0.06	0.01	0.06	0.005	0.02	0.00005	0.0002

Table S4: Neurotoxic reference doses (RfD) retrieved from literature or established by the authors for neurotoxic cumulative assessment group

SVOC	RfD[a] (µg/kg-bw/d)	Reference	Critical effect (following oral exposure, excepted if specified)	Point of departure (mg/kg-bw/d)	Uncertainty factor
Aldrin	2 (gest)	ATSDR[b] (2016)	Decreased body weight and electroconvulsive shock threshold in offspring male and female after acute exposure (7 days) of pregnant mice	LOAEL=2	UFH= 10 UFA = 10 UFL=10
BBP	170 (child)	This study (from Min et al., 2014)	Learning and memory impairment, decreased locomotor activity and induce depression in 1 month-old male rats after acute exposure (2 weeks)	NOAEL=50	UFA=10 UFH=10 UFS=3
BDE 47	0.1 (child)	US EPA[c] (2008)	Spontaneous motor behavior impairment and decreased habituation capability in adult male mice after single dose exposure at PND 10	$BMDL_{1SD}$=0.35	UFH= 10 UFA= 10 UFD= 10 UFS= 3
BDE 99	0.1 (child)	US EPA[c] (2008)	Neurobehavioral developmental effects in adult male and female mice after single dose exposure at PND 10	$BMDL_{1SD}$ =0.29	UFH= 10 UFA= 10 UFD= 10 UFS= 3
BDE 153	3 (child)	This study (from Zhang et al., 2013)	Decreased spontaneous behavior in 1 and 2 months-old male rats after intraperitoneal[d] single dose exposure at PND 10	NOAEL=1	UFA=10 UFH=10 UFS=3
Benzo[a]pyrene	0.3 (child)	US EPA[c] (2017)	Neurobehavioral impairment in adult male and female rats after postnatal exposure from PND 5 to PND 11	$BMDL_s$=0.092	UFH= 10 UFA= 10 UFD= 3
Chlorpyrifos	1	ATSDR[b] (2016) ANSES[e] (2015)	Reduced red blood cells cholinesterase activity in adult male and female rats after chronic exposure (2 years)	NOAEL=0.1	UFH= 10 UFA= 10
Chlorpyrifos	0.1 (child)	OEHHA[f] (2010)	Reduced plasma and red blood cells cholinesterase activity in adult Beagle dogs after chronic exposure (2 years)	NOAEL=0.03	UFH=10 UFA=3 UF[g]=10
DBP	17	This study (from Yan et al., 2016)	Anxiety and oxidative stress in brain tissue in 10 weeks male rats after 1 month exposure	NOAEL=5	UFA=10 UFH=10 UFS=3
DEHP	17	This study (from Tang et al., 2015)	Spatial learning impairment and memory dysfunction in 2 months-old male mice after acute exposure (10 days)	NOAEL=5	UFA=10 UFH=10 UFS=3
DiBP	170	This study (from Ma et al., 2013)	Learning impairment and increased apoptosis rate of hippocampal cells in adult male and female mice after subchronic exposure (8 weeks)	NOAEL=500	UFA=10 UFH=10 UFD=10 UFS=3

Dieldrin	0.1	ATSDR[b] (2016)	Learning impairment in young adult male monkeys after subchronic exposure (55 days)	NOAEL=0.01	UFH= 10 UFA= 10
Fluorene	33	This study (from Peiffer et al., 2016)	Spatial learning ability impairment in adult male rats after acute exposure (4 weeks)	NOAEL=10	UFA=10 UFH=10 UFS=3
PCB 52	0.3 (gest/ child)	This study (from Boix et al., 2010, 2011)	Motor coordination impairment in 4 months-old male and female rats after subchronic exposure of pregnant rats from GD 7 to PND 21	LOAEL=1	UFA=10 UFH=10 UFL=10 UFS=3
PCB 118	0.4 (gest)	This study (from Kuriyama and Chahoud 2004)	Spontaneous reflexes impairment and increased motor activity in offspring male and female after single dose exposure of pregnant rats	LOAEL=0.375	UFA=10 UFH=10 UFL=10
PCB 138[h]	0.3 (gest/ child)	This study (from Boix et al., 2010, 2011)	Spontaneous motor activity and learning impairment in 4 months-old male and female rats after subchronic exposure of pregnant rats from GD 7 to PND 21	LOAEL=1	UFA=10 UFH=10 UFL=10 UFS=3
Lindane	2.7 (gest/ child)	This study (from Myers 1999)	Increased motor activity and decreased motor reflex in offspring rats after subchronic exposure of pregnant rats from GD 6 to PND 10	NOAEL=0.8	UFA=10 UFH=10 UFS=3

BMDL: benchmark dose modelling; GD: gestational days; LOAEL: low observed adverse effect level; NOAEL: no observed adverse effect level; PND: postnatal day; UF_A: interspecies uncertainty factor; UF_D: database deficiency uncertainty factor; UF_H: intraspecies uncertainty factor; UF_L: LOAEL uncertainty factor; UF_S: acute/subchronic uncertainty factor.

[a] "Gest"correspond to RfD specific to gestational exposure and "child"to RfD specific to postnatal exposure.

[b] Retrieved from: *https://www.atsdr.cdc.gov/mrls/mrllist.asp*

[c] Retrieved from: *https://cfpub.epa.gov/ncea/iris/search/index.cfm?*

[d] For BDE 153, no studies performing *in vivo* oral exposures of mammalian species were found and the one of Zhang et al. (2013) performing *in vivo* intraperitoneal exposure of rats was selected.

[e] Retrieved from: *https://www.anses.fr/fr/content/les-valeurs-de-r%C3%A9f%C3%A9rence*

[f] Retrieved from: *https://oehha.ca.gov/chemicals*

[g] Additional factor for children extrapolation.

[h] Assumption of similar toxic potency between congeners having the same molecular formula (same number of halogenated atoms) led to use the RfD of PCB 138 also for PCB 153.

Table S5: Hazard indexes for neurotoxic indoor SVOCs in France (median and high uptakes with percentiles 50th and 95th respectively)

SVOC	Children		Adults		Pregnant women	
	p50	p95	p50	p95	p50	p95
Aldrin					0.00002	0.00007
Dieldrin	0.01	0.07	0.004	0.02		
Lindane	0.001	0.008			0.0003	0.003
Chlorpyrifos	0.002	0.005	0.00007	0.0002		
Benzo[a]pyrene	0.001	0.007				
Fluorene	0.00005	0.0003	0.00002	0.0001		
PCB 52	0.001	0.007			0.0003	0.002
PCB 118					0.0001	0.0002
PCB 138	0.0003	0.002			0.00008	0.0002
PCB 153	0.0003	0.002			0.0001	0.0003
BBP	0.002	0.004				
DBP	0.04	0.2	0.01	0.09		
DEHP	0.05	0.1	0.004	0.02		
DiBP	0.01	0.04	0.005	0.02		
BDE 47	0.02	0.05				
BDE 99	0.008	0.01				
BDE 153	0.00002	0.0001				
Hazard index	**0.2**	**0.4**	**0.03**	**0.1**	**0.001**	**0.005**

Table S6: Reprotoxic reference doses (RfD) retrieved from literature or established by the authors for reprotoxic cumulative assessment group

SVOC	RfD[a] (µg/kg-bw/d)	Reference	Critical effect (following oral exposure)	Point of departure (mg/kg-bw/d)	Uncertainty factor
BBP	1200	OEHHA[b] (2013)	Reduced birth weight in F1 male and female rats after a two-generation reproductive toxicity study	NOAEL=20	1000
BDE 47	0.002 (child)	Li et al. (2014)	Decreased relative uterus weight in 2 months female rats after single dose exposure at PND 10	BMDL=0.002	UFA=10 UFH=10 UFS=10 MF=1
BDE 99[c]	10 (gest)	Kortenkamp and Faust (2010)	Suppression of testosterone levels, reductions of anogenital distance in offspring male after acute exposure (10 days) of pregnant rats	NOAEL=1	UFH= 10 UFA= 10
Benzo[a]pyrene	0.02	This study (from Fournier et al., 2016)	Decreased in testosterone synthesis in adult male rats after subchronic exposure (90 days)	$BMDL_{10}$=0.002	UFA=10 UFH=10
Chlorpyrifos	40 (gest)	This study (from Shin et al., 2015)	Sperm motility impairment in offspring male after acute exposure (10 days) of pregnant mice	NOAEL=4	UFA=10 UFH=10
Chlorpyrifos	27	This study (from Sai et al., 2014)	Reduced sperm counts, motility in caudal epididymidis, testosterone level and altered seminiferous tubules in adult male rats after subchronic exposure (90 days)	NOAEL=2.7	UFA=10 UFH=10
DBP	2 (gest/ Child)	ANSES[d] (2008)	Reduction of spermatocyte development and mammary glands dysplasia in offspring male after subchronic exposure of pregnant rats from GD 15 to PND 21	LOAEL=2	UFH= 10 UFA= 10 UFL= 10
DBP	52	RIVM (2001)	Decreased number and body weight of offspring rats (without maternal toxicity) after a two-generation reproductive toxicity study	LOAEL=52	UFH= 10 UFA= 10 UFL= 10
DEHP	44 (gest)	Health Canada (1994)	Decreased fetus number after acute exposure (17 days) of pregnant mice	NOAEL=44	1000
DEHP	3.7	RIVM (2001)	Sertoli cells vacuolation in adult male and female rats after subchronic exposure (13 weeks)	NOAEL=3.7	UFH= 10 UFA= 10 UFS= 10
DEP	200	RIVM (2001)	Degenaration and atrophy of testes and spermatogenesis impairment in adult male rats after chronic exposure (16 weeks)	NOAEL=100	UFH= 10 UFA= 10 UFD= 5

DiBP	200 (gest)	Kortenkamp and Faust (2010)	Suppression of fetal testosterone synthesis after acute exposure (10 days) of pregnant rats	BMDL=40	200
Dieldrin	0.02	This study (from Perobelli et al., 2010)	Increased immotile sperm in adult male rats after subchronic exposure (8 weeks)	LOAEL=0.05	UFA=10 UFH=10 UFL=10 UFS=3
DiNP	750 (gest)	Benson (2009)	Decreased fetal testosterone and retained areolas/nipples in offspring male after acute exposure (14 days) of pregnant rats	LOAEL=750	UFH= 10 UFA= 10 UFL=10
PCB 101 and 118[e]	0.0003 (gest/ child)	This study (from Pocar et al., 2011)	Decreased relative teste and ovary weight in offspring (F1 and F2) after subchronic exposure of pregnant mice from GD 0 to PND 21	LOAEL=0.001	UFA=10 UFH=10 UFL=10 UFS=3
Lindane	3 (child)	ATSDR[f] (2016)	Reduced relative testicular and epididymis weight, spermatid and sperm counts, and testosterone level in male offspring of rats after acute exposure (6 days) during lactation	LOAEL=1	UFH= 10 UFA= 10 UFL= 3

BMDL: benchmark dose modelling; GD: gestational days; LOAEL: low observed adverse effect level; MF: modifying factor; NOAEL: no observed adverse effect level; PND: postnatal day; UF_A: interspecies uncertainty factor; UF_D: database deficiency uncertainty factor; UF_H: intraspecies uncertainty factor; UF_L: LOAEL uncertainty factor; UF_S: acute/subchronic uncertainty factor.

[a] "Gest"correspond to RfD specific to gestational exposure and "child"to RfD specific to postnatal exposure.

[b] Retrieved from: *https://oehha.ca.gov/chemicals*

[c] Assumption of similar toxic potency between congeners having the same molecular formula (same number of halogenated atoms) led to use the RfD of BDE 99 also for BDE 100.

[d] Retrieved from: *https://www.anses.fr/fr/content/les-valeurs-de-r%C3%A9f%C3%A9rence*

[e] For PCB 101 and 118, only Pocar et al. (2011) studied combined exposure to both congener and their LOAEL for reprotoxic effects was employed to construct a common RfD_{rep}.

[f] Retrieved from: *https://www.atsdr.cdc.gov/mrls/mrllist.asp*

Table S7: Hazard indexes for reprotoxic indoor SVOCs in France (median and high uptakes with percentiles 50th and 95th respectively)

SVOC	Children		Adults		Pregnant women	
	p50	p95	p50	p95	p50	p95
Dieldrin	0.07	0.3	0.02	0.1		
Lindane	0.0009	0.01				
Chlorpyrifos	0.000007	0.00002	0.000003	0.000007	0.000002	0.000005
Benzo[a]pyrene	0.02	0.1	0.006	0.03		
∑PCB 101+118	1	5			0.1	1
BBP	0.0002	0.0006	0.00002	0.00008		
DBP	0.3	2.1	0.004	0.03	0.1	0.7
DEHP	0.2	0.6	0.02	0.08	0.002	0.007
DEP	0.002	0.02	0.0006	0.005		
DiBP					0.004	0.01
DiNP					0.00009	0.0004
BDE 47	1	2.7				
BDE 99					0.00004	0.00009
BDE 100					0.00005	0.0002
Hazard index	**3**	**8.1**	**0.07**	**0.2**	**0.3**	**1.4**

Table S8: Reference compounds's cacer slope factor (CSF) or reference dose (RfD) retrieved from literature or established by the authors for specific health effects and used for cumulative risk assessment by using toxicity equivalency factor and relative potency factor approaches

SVOC	CSF(mg/kg-bw/d)$^{-1}$/RfD[a] (mg/kg-bw/d)	Reference	Critical effect (following oral exposure)	Point of departure (mg/kg-bw/d)	Uncertainty factor
Benzo[a]pyrene	CSF=1	US EPA[b] (2017)	Based on the tumor response in the alimentary tract (forestomach, esophagus, tongue, and larynx) of female mice after oral chronic exposure of 2 years	na	na
Chlorpyrifos	RfD=0.0001 (child)	OEHHA[c] (2010)	Reduced plasma and red blood cells cholinesterase activity in adult Beagle dogs after chronic exposure (2 years)	NOAEL=0.03	UFH=10 UFA=3 UF[d]=10
Chlorpyrifos	RfD=0.001	ATSDR[e] (2016) ANSES[f] (2015)	Reduced red blood cells cholinesterase activity in adult male and female rats after chronic exposure (2 years)	NOAEL=0.1	UFH=10 UFA=10
Cypermethrin	RfD_{rep} = 0.04	This study (from Fournier et al., 2016)	Decreased testosterone level in adult male rats after acute exposure (15 days)	$BMDL_{10}$=3.7	UFA=10 UFH=10
DEHP	RfD=0.044 (gest)	Health Canada (1994)	Decreased fetus number after acute exposure (17 days) of pregnant mice	NOAEL=44	1000
DPP	RfD=0.2 (gest)	Benson (2009)	Decreased fetal testosterone production after acute exposure (10 days) of pregnant rats	$BMDL_{1SD}$=17	100
2,3,7,8-TCDD	RfD=7.10^{-10}	US EPA[b] (2012)	Decreased sperm count and motility in men exposed to TCDD as boys. Increased TSH in noenates.	LOAEL=2.10^{-8}	UFH=3 UFL=10

na: not available

[a] "Gest"correspond to RfD specific to gestational exposure and "child"to RfD specific to postnatal exposure.

[b] Retrieved from: *https://cfpub.epa.gov/ncea/iris/search/index.cfm*?

[c] Retrieved from: *https://oehha.ca.gov/chemicals*

[d] Additional factor for children extrapolation

[e] Retrieved from: *https://www.atsdr.cdc.gov/mrls/mrllist.asp*

[f] Retrieved from: *https://www.anses.fr/fr/content/les-valeurs-de-r%C3%A9f%C3%A9rence*

Table S9: Relative potency factors (RPF) values established for 9 SVOCs, based on Fournier et al. (2017) benchmark doses (BMD_{10}) corresponding to a decrease of 10% in neuronal viability

SVOC	BMD_{10} (µM)	RPF
Chlorpyrifos	20.09	**1**
Benzo[a]pyrene	2.43	8.27
DEHP	10.64	1.89
PCB 52	39.89	0.5
PCB 153	0.072	279.03
Dieldrin	15.54	1.29
Lindane	38.93	0.52
BDE 47	4.83	4.16
BDE 99	6.8	2.95

Table S10: Reference doses (RfD) constructed for the 8 PCBs included in this study from the RfD retrieved from literature for the Aroclor 1254 for immunotoxic effect

SVOC	RfD (µg/kg-bw/d)	Reference	Critical effect (following oral exposure)	Point of departure (mg/kg-bw/d)	Uncertainty factor
∑ 8 PCB (28, 31, 52, 101, 105, 118, 138, 153)	0.007	This study (from Arnold et al., 1995 and Tryphonas et al., 1991)	Immunotoxicity in offspring after subchronic exposure to Aroclor 1254 of pregnant monkeys during gestation and lactation (46 weeks) and in adult after chronic exposure of 23 and 55 months	LOAEL=0.005* 0,34[a]	UFH= 10 UFA= 10 UFL= 3

[a] The LOAEL was multiplied by a factor of 0.34 which correspond to the proportion (34%) of the 8 congeners in the Aroclor 1254.

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Chapitre 5 : Discussion générale

5.1. Principaux résultats et apports de ce travail de thèse

Ce travail a en premier lieu permis d'estimer les expositions agrégées à 32 COSV fréquemment détectés dans les logements français.

- Trois voies d'exposition ont été prises en compte : l'ingestion des poussières déposées, l'inhalation d'air et le contact cutané avec les composés présents dans la phase gazeuse de l'air ;
- Une approche probabiliste a permis d'obtenir pour chaque composé et pour chaque tranche d'âge étudiée, allant de la naissance à 30 ans, une distribution représentative des expositions des individus des moins au plus exposés ;
- L'air a été identifié comme contributeur majoritaire dans les expositions agrégées pour 28 COSV sur 32 ;
- Enfin, les analyses de sensibilité ont révélé que les expositions étaient majoritairement influencées par la variabilité des données de contaminations puis par l'incertitude associée aux paramètres physico-chimiques.

Ensuite l'évaluation des risques réalisée pour 29 COSV a permis d'identifier les COSV les plus contributeurs au risque dans l'habitat selon différentes populations : le fœtus (en considérant l'exposition d'une femme enceinte âgée de 21-30 ans), le jeune enfant (en considérant un enfant âgé de 0-2 ans) et l'adulte (en considérant un adulte âgé de 21-30 ans).

- Les résultats de l'ERS composé par composé ont révélé que des effets immunotoxiques et reprotoxiques étaient susceptibles de survenir pour 5 %

des enfants exposés au lindane et au DBP respectivement, et des effets reprotoxiques étaient susceptibles de survenir pour 50 % des enfants exposés au BDE 47.

- Les résultats de l'ERSC pour des effets toxiques communs ont révélé que des effets reprotoxiques étaient susceptibles de survenir pour 95 % des enfants et pour 5 % des fœtus exposés pendant la grossesse à des mélanges de composés. Les PCB 101 et 118, le BDE 47 et le DBP ont été identifiés comme les contributeurs majoritaires dans la survenue de ce risque reprotoxique.

- Les résultats de l'ERSC pour des mécanismes d'action ou des effets cellulaires communs ont révélé un risque inacceptable pour 95 % des enfants exposés à 9 composés neurotoxiques induisant une mort neuronale, pour 5 % des enfants exposés aux PCB 105 et 118 dont les effets toxiques sont médiés par une liaison au récepteur AhR et pour 25 % des enfants et 5 % des adultes exposés à 4 composés reprotoxiques (induisant une diminution du taux de testostérone). Le DEHP, le PCB 105 et le DEP ont été identifiés comme les contributeurs majoritaires dans la survenue de ces risques respectivement.
- Les résultats de l'ERSC à 8 PCB étudiés en mélange pour leurs effets immunotoxiques ont révélé que des effets étaient susceptibles de survenir pour 5 % des enfants exposés.

Une synthèse de ces principaux résultats est présentée en Figure 7. Les résultats des ERSC conduites par une approche HI (pour des effets toxiques communs) sont indiqués par « ERSC I » et celles conduites par une approche RPF ou TEF (pour des mécanismes d'action ou des effets cellulaires communs) par « ERSC II ». Les résultats sont également classés, suivant l'abscisse, selon le niveau de preuve de

l'effet étudié chez l'Homme et, suivant l'ordonnée, selon les valeurs correspondantes des indicateurs de risque.

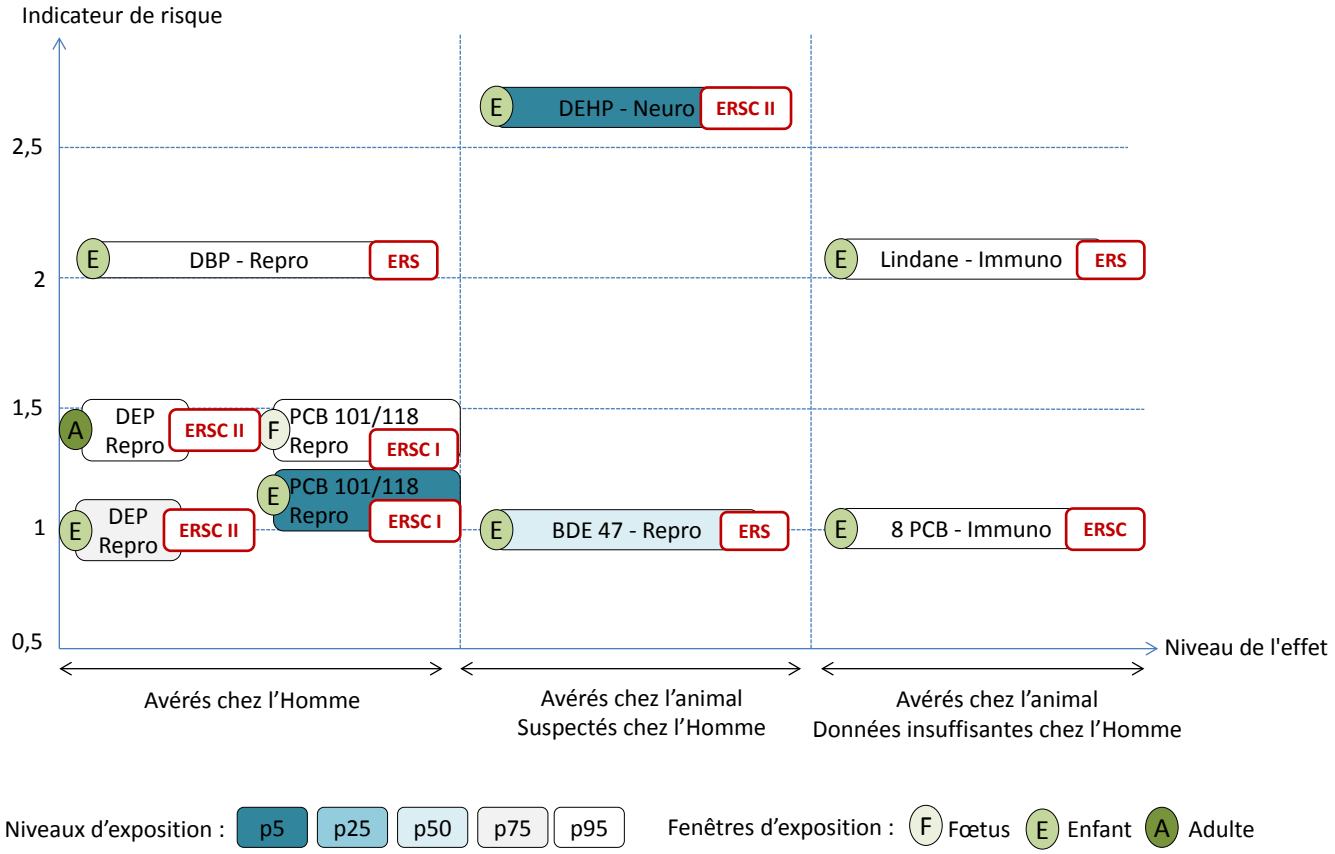

Figure 7 : Synthèse des principaux résultats de l'évaluation des risques.

5.1.1. Apports de la démarche probabiliste pour l'évaluation des expositions

L'estimation des expositions agrégées a été conduite selon une démarche probabiliste et à partir de données représentatives de la contamination des logements en France, afin de pouvoir quantifier l'incertitude des estimations et d'obtenir, pour chaque tranche d'âge étudiée, une distribution des expositions des individus. Cette approche a nécessité la modélisation de 14 paramètres, utilisés dans les équations de DJE, pour 32 COSV et pour 11 tranches d'âge allant de la naissance à 30 ans. La recherche de ces données dans la littérature peut, du fait de l'hétérogénéité des connaissances, conduire à des jeux de données non homogènes entre les composés, notamment pour les paramètres physico-chimiques, conduisant *in fine* à modéliser des distributions de formes différentes.

L'approche déterministe consiste à employer pour chaque paramètre une valeur numérique unique, qui peut être centrale (moyenne ou médiane) ou plus élevée (percentile 95, maximum), afin d'estimer des DJE moyennes ou maximales respectivement. Si les approches déterministes permettent de donner un premier aperçu de la variabilité des estimations, elles ne permettent pas de quantifier la proportion de la population au-delà d'un certain niveau d'exposition, et donc d'un certain niveau de risque, ni de prendre en compte les incertitudes associées aux paramètres d'entrée. Cependant, l'approche déterministe permet une estimation plus rapide et plus facile des expositions. Ainsi, pour un processus d'estimation des risques et dans une optique de gestion de ces risques, cette démarche permet de donner une première idée du niveau de risque moyen et maximal dans une population.

Afin de comparer les résultats obtenus par les deux approches, les DJE agrégées pour les 32 COSV ont donc également été estimées par une approche déterministe en deux temps :

- Dans un premier temps, pour une exposition moyenne considérant les valeurs moyennes des variables humaines d'exposition (le poids, la surface cutanée, la fréquence respiratoire, la quantité de poussières ingérée par jour et le temps passé dans le logement) et les valeurs moyennes (à défaut les médianes) des données de contamination. Pour les composés ayant des données de contamination majoritairement inferieures à la LD, la LD/2 a été utilisée.
- Dans un second temps, pour une forte exposition considérant les percentiles 95 des variables humaines d'exposition et les percentiles 95 (à défaut les maximums) des données de contamination.

Les résultats obtenus par l'approche déterministe pour la tranche d'âge des 2-3 ans sont comparés dans la Figure 8 aux DJE agrégées obtenues par l'approche probabiliste pour la même tranche d'âge, aux percentiles 50 et 95. Pour une exposition moyenne, les estimations sont comparables entre les deux approches. Pour une forte exposition, l'approche déterministe conduit à surestimer les DJE agrégées pour la majorité des composés. Ceci est lié, d'une part à l'utilisation des percentiles 95 pour les paramètres d'entrée et d'autre part à l'emploi des valeurs maximales des données de contamination, lorsque les percentiles 95 n'étaient pas disponibles pour certains composés.

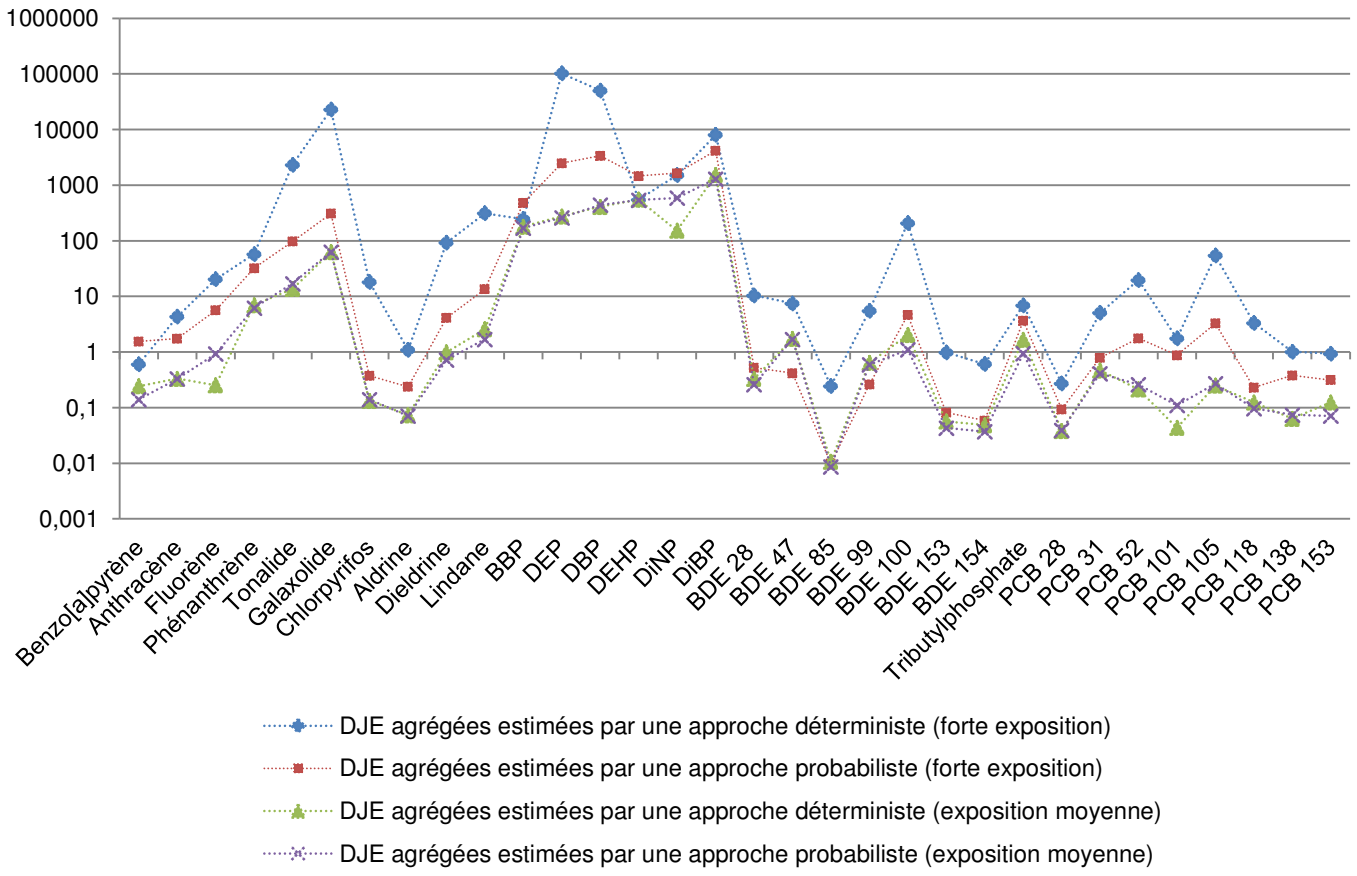

Figure 8 : Comparaison des résultats obtenus pour l'estimation des expositions agrégées pour 32 COSV chez l'enfant de 2-3 ans par une approche probabiliste et par une approche déterministe pour une exposition moyenne et une forte exposition.

Afin d'étudier l'impact de l'approche déterministe sur les résultats de la caractérisation des risques, une ERS a ensuite été conduite pour l'enfant âgé de 0-2 ans pour une exposition moyenne et pour une forte exposition. Les QD « déterministes » obtenus sont comparés dans le tableau 4 aux QD « probabilistes » pour des enfants moyennement exposés (percentile 50) et très exposés (percentile 95). Les mêmes VTR ont été utilisées pour les deux approches.

Tableau 4 : Comparaison des résultats obtenus pour l'évaluation des risques sanitaires pour l'enfant âgé de 0-2 ans, par estimation des quotients de danger (QD), par une approche déterministe et par une approche probabiliste réalisées pour une exposition moyenne et une forte exposition.

	Exposition moyenne			Forte exposition		
COSV	**QD Probabiliste**	**Comparaison →**	**QD Déterministe**	**QD Probabiliste**	**Comparaison →**	**QD Déterministe**
Aldrine	0,004	=	0,004	0,01	<	0,1
Dieldrine	0,03	=	0,03	0,1	<	**3,4**
Lindane	0,3	=	0,4	**2,1**	<	**49**
Chlorpyrifos	0,002	=	0,002	0,005	<	0,3
Tributylphosphate	0,00003	=	0,00005	0,0001	=	0,0002
Galaxolide	0,00008	=	0,00009	0,0004	<	0,03
Tonalide	0,002	=	0,002	0,01	<	0,3
Anthracène	0,000002	=	0,000002	0,000009	<	0,00002
Benzo[a]pyrène	0,001	=	0,002	0,007	=	0,005
Fluorène	0,00004	=	0,00001	0,0002	<	0,001
Phénanthrène	0,0002	=	0,0002	0,001	=	0,002
BBP	0,001	=	0,004	0,004	=	0,003
DBP	0,3	=	0,3	**2,1**	<	**32,7**
DEHP	0,2	=	0,3	0,7	=	0,3
DEP	0,002	=	0,002	0,02	<	0,7
BDE 47	**1**	=	**1**	**2,7**	=	**4,5**
BDE 85	0,0002	=	0,0003	0,0009	<	0,007
BDE 99	0,008	=	0,008	0,01	=	0,07
BDE 100	0,01	=	0,03	0,06	<	**2,4**

Les résultats de l'analyse de risque obtenus par l'approche déterministe, pour un enfant âgé de 0-2 ans moyennement exposé, sont identiques avec ceux obtenus par l'approche probabiliste au percentile 50. Dans le cas d'une forte exposition, l'ERS par une approche déterministe conduit à estimer des QD plus élevés que ceux obtenus par l'approche probabiliste et ainsi à identifier un risque inacceptable pour deux composés supplémentaires (BDE 100 et dieldrine).

Les résultats de cette comparaison étaient attendus. Ils confirment en effet que les approches déterministes peuvent être employées dans une démarche de gestion du

risque du fait qu'elles permettent de détecter les mêmes composés à risques que ceux révélés par une approche probabiliste. Dans le cadre d'une démarche d'ERS par paliers pour des expositions à des contaminants environnementaux, la conduite d'une première approche déterministe permet d'obtenir une première vue d'ensemble bien qu'elle ne permettent pas de quantifier l'incertitude des estimations et d'obtenir, pour chaque tranche d'âge étudiée, une distribution des expositions des individus des moins au plus exposés.

5.1.2. Apports de la démarche par paliers pour l'évaluation des risques

Dans un premier temps, l'évaluation des risques a été conduite pour l'effet le plus sensible pour chaque composé pris individuellement. Les risques ont ensuite été évalués pour des mélanges de composés, selon les étapes d'une démarche par paliers. La première étape visait à évaluer les risques pour des mélanges de composés ayant des effets neuro- ou reprotoxiques communs. La seconde étape visait à évaluer les risques à une échelle biologique plus fine pour des mélanges de composés ayant des mécanismes d'action ou des effets cellulaire en commun. Cette approche est en adéquation avec les recommandations formulées par Meek et al. (2011). Pour la suite de la discussion, l'exemple du DEHP sera étudié car l'ERSC a permis de mettre en évidence des effets neurotoxiques peu étudiés, qui n'avaient pas été révélés par une approche classique d'ERS de premier niveau.

Les phtalates ont des effets reprotoxiques connus chez l'Homme et le DEHP est classé reprotoxique présumé (catégorie 1b selon la classification CLP) pour ses effets sur la fertilité et sur le développement. Ce sont ces effets, considérés comme

les plus sensibles, qui ont été retenus pour l'ERS de premier niveau. Le QD était proche de 1 (égal à 0,7) pour des effets reprotoxiques chez les enfants les plus exposés (percentile 95).

L'ERSC de premier niveau pour un mélange de 11 COSV reprotoxiques a révélé un HI > 1 pour 95 % des enfants exposés (percentile 5). Après les PCB 101 et 118, le BDE 47 et le DBP, le DEHP contribue à la hauteur de 8 % de ce risque reprotoxique pour les enfants moyennement exposés et de 6 % pour les plus exposés. L'ERSC de second niveau a été conduite, par une approche RPF, pour un mélange de 4 COSV reprotoxiques engendrant une diminution du taux de testostérone. L'indicateur de risque était > 1 pour 25 % des enfants exposés (percentile 75). Après le DEP (95 %), le DEHP contribue à la hauteur de 10 % de ce risque reprotoxique pour les enfants moyennement exposés et de 4 % pour les plus exposés.

En complément, l'ERSC de premier niveau pour un mélange de 15 COSV neurotoxiques a révélé un HI proche de 1 (égal à 0,4) chez les enfants les plus exposés (percentile 95). Elle a identifié le DEHP et le DBP comme contributeurs majoritaires, à plus de 30 % chacun, de ce risque neurotoxique cumulé. Ce résultat a été confirmé par l'ERSC de second niveau (approche RPF) conduite pour un mélange de 9 COSV neurotoxiques via des mécanismes d'action engendrant une mort neuronale. Cette dernière a révélé un risque inacceptable pour 95 % des enfants exposés (percentile 5) et a permis d'identifier le DEHP comme contributeur majoritaire (96 %) dans la survenue de ce risque neurotoxique cumulé. Un résultat surtout expliqué par une DJE agrégée nettement plus élevée pour le DEHP (de l'ordre du µg/kg/j) que pour les autres COSV inclus dans le mélange (de l'ordre du ng/kg/j), mais aussi par le potentiel qu'a le DEHP d'engendrer la mort neuronale.

Bien qu'il n'y ait pas encore beaucoup de données concernant les effets neurotoxiques des phtalates, certaines études épidémiologiques indiquent que l'exposition des mères à ces composés pourrait engendrer l'apparition de troubles neurocomportementaux chez les enfants (développement psychomoteur, quotient intellectuel, réflexes primitifs, etc.). De plus, les études menées chez l'animal ont fourni des preuves de la neurotoxicité des phtalates (Miodovnik et al., 2014).

Ces résultats conduisent à envisager les effets neurotoxiques du DEHP comme plus sensibles que ses effets reprotoxiques. La conduite d'une ERSC a ainsi permis de mettre en évidence des effets moins étudiés, qui n'avaient pas été révélés par une approche classique.

Dans leur ensemble, les résultats de ce travail de thèse ont permis de répondre de manière affirmative à la question de recherche posée initialement par le projet ECOS-Habitat : « Les expositions cumulées aux multiples COSV présents dans les logements français posent-elles un problème de santé publique ? » et d'identifier les composés, médias et voies d'exposition les plus contributifs à ces risques. Cependant ces résultats doivent être accompagnés d'une analyse critique des limites associées aux méthodologies employées et aux données qui ont été utilisées. Ces limites ont fait l'objet de discussions spécifiques dans les précédents articles pour l'estimation des expositions agrégées (chapitre 3.3) et la caractérisation des risques (chapitre 4). La suite de ce chapitre 5 est consacrée à une discussion plus générale des limites associées à ce travail de thèse et permettra de formuler des recommandations concernant l'approche mise en œuvre.

5.2. Limites de ce travail de thèse

Ce travail a permis d'estimer l'exposition et d'évaluer les risques pour un grand nombre de COSV au regard de la littérature existante. En effet, la revue de la littérature a indiqué que la majorité des études ayant conduit une ERSC pour des COSV l'avait fait pour un nombre restreint de composés et pour la plupart issus de mêmes familles chimiques. Uniquement 5 études sur les 31 sélectionnées ont mené une ERSC pour des composés issus de familles chimiques différentes.

Cependant, depuis le début du projet ECOS-Habitat, plusieurs étapes ont conduit à restreindre le nombre de COSV finalement sélectionnés pour l'évaluation des risques : de 254 COSV potentiellement présents dans l'habitat, 40 disposaient de données de contamination dans les 3 médias étudiés, et 32 avaient des données de contamination suffisantes pour l'estimation des expositions (Figure 6). Finalement, l'évaluation des risques n'a pu être conduite que pour 29 d'entre eux (3 COSV disposaient de données toxicologiques insuffisantes en termes de relations dose-réponse).

Pour le travail de hiérarchisation (Bonvallot et al., 2010), seules les poussières avaient été considérées, ce qui a pu conduire à omettre les COSV les plus volatils. De plus, certains composés n'avaient pas été hiérarchisés du fait d'un manque de données de contamination ou de données toxicologiques. Cette hiérarchisation ayant été conduite sur la base de données publiées avant 2009, de nouveaux ou anciens COSV pourraient être à présent inclus du fait de leur utilisation ou de l'amélioration des techniques analytiques.

Ensuite, les composés qui étaient analysables par une approche multi résidus avec une séparation en chromatographie gazeuse (Mercier et al., 2012, 2014) ont été recherchés parmi les 66 hiérarchisés. Du fait de leur propriétés physico-chimiques particulières, certains composés n'ont pu être analysés par cette approche et ont *de facto* été exclus. Au final, 48 ont été mesurés dans les poussières (Mandin et al., 2014), 66 dans la phase particulaire (Mandin et al., 2016) et 57 dans la phase gazeuse de l'air (Blanchard et al., 2014).

L'étape d'évaluation des expositions agrégées nécessitait de disposer de données de contamination dans les trois médias étudiés pour chaque composé. Cette étape a conduit à la sélection des 40 composés remplissant cette condition. Afin d'éviter la surestimation de l'exposition, 8 autres COSV ont été exclus car ils ne disposaient pas de données suffisantes pour modéliser les concentrations par une approche probabiliste. Ce point de discussion concernant la disponibilité des données de contamination sera discuté au chapitre suivant (chapitre 5.2.1). L'estimation des expositions agrégées a finalement été conduite pour 32 COSV.

Pour finir, l'étape d'évaluation des risques nécessitait de disposer de données toxicologiques (relations dose-réponse) pour chaque composé. A l'exception des BDE 28, 153 et 154, vingt-neuf parmi les 32 composés remplissaient cette condition. Ce point de discussion concernant la disponibilité des données toxicologiques sera discuté dans un chapitre dédié (chapitre 5.2.2).

Ainsi, si la discussion traite des limites du travail réalisé, il faut garder à l'esprit les limites inhérentes au travail non réalisé. Ce point de discussion lié à la formulation du problème (composés considérés) sera discuté dans un chapitre dédié (chapitre 5.2.3).

5.2.1. Disponibilité des données de contamination

L'évaluation des expositions a été conduite suivant une approche probabiliste. Cependant, les données requises pour la modélisation des distributions des paramètres d'entrée des modèles ne sont pas disponibles de façon homogène selon les composés ce qui a conduit à modéliser des distributions de formes différentes (log normale, triangulaire, uniforme, etc.). Une analyse de sensibilité a identifié les données de contamination comme les paramètres les plus influents sur les résultats.

L'incertitude associée aux données de contamination pour un composé augmente quand sa détection dans les logements diminue, c'est-à-dire quand le nombre de logements ayant une concentration supérieure à la LD diminue. Les composés pour lesquels l'incertitude est la plus grande sont ceux pour lesquels 99% des données de contamination sont inférieures à la LD. Vingt et un COSV étaient concernés pour la phase gazeuse de l'air, dont 3 l'étaient également pour leurs données de contamination des poussières et de la phase particulaire de l'air. En effet, si l'emploi d'une analyse « multi résidus » pour la quantification dans les logements (Blanchard et al., 2014 ; Mandin et al., 2014, 2016) a permis d'étudier un large spectre de molécules de familles chimiques différentes elle a, en contrepartie, impliqué des LD et des limites de quantification (LQ) moins optimisées pour chaque famille chimique que pour des filières analytiques dédiées.

Afin de réduire ces incertitudes, ou du moins de ne pas les accroître, il a été décidé de rechercher dans la littérature d'autres études ayant quantifié ces 21 composés dans les médias concernés et de modéliser une distribution à partir de ces données publiées. Les études sélectionnées devaient employer des LD et/ou des LQ plus faibles que la technique « multi résidus ». Au final, 8 composés ont dû être exclus par

manque d'informations disponibles dans la littérature : le diazinon, l'endrine, l'alpha-endosulfan, la perméthrine, le BDE 119, le PCB 126, le PCB 77 et le bisphénol-A. Pour ces composés, faute de données plus précises, il a été testé de modéliser une distribution uniforme entre 0 et la LD et entre 0 et la LD/2. Du fait de l'emploi de LD élevées par rapport à la concentration réelle ce choix conduisait à surestimer les concentrations, notamment en phase gazeuse, et par conséquent à surestimer les voies d'exposition associées (par inhalation d'air et par contact cutané avec la phase gazeuse). La surestimation de la contamination en phase gazeuse engendrée pour le bisphénol-A par exemple, positionnait l'inhalation d'air comme la voie d'exposition majoritaire, bien que ce composé soit peu volatil et connu pour être peu présent en phase gazeuse. Cette option méthodologique avait en conséquence été abandonnée.

Plusieurs autres options ont été envisagées, notamment l'estimation de la contamination en phase gazeuse à partir des données de contamination quantifiées dans les autres compartiments, par l'emploi des modèles de prédiction à l'équilibre proposés par Weschler et Nazaroff (2010). Les travaux menés par Blanchard (2014) pour tester ces modèles sur les mêmes COSV que pour ce travail de thèse avaient abouti à la conclusion que leurs concentrations en phase gazeuse pouvaient être correctement estimées uniquement à partir de leurs concentrations dans l'air total (phases gazeuse et particulaire). Ces modèles présentaient certaines limites lorsque l'estimation de la fraction gazeuse était réalisée uniquement à partir de la concentration de la phase particulaire. Cependant, les données de contamination dans l'air total n'étaient pas disponibles pour l'ensemble des composés dans la littérature. Les travaux menés par Wei et al. (2017), pour estimer les concentrations

en phases gazeuse à partir des données de contamination en phase particulaire (Mandin et al., 2016) ont abouti au même constat que celui réalisé par Blanchard (2014). En effet, Wei et al. (2017) ont comparé les données estimées en phase gazeuse avec des données issues de la littérature et ont trouvé des résultats comparables uniquement pour les PBDE et des phtalates. Bien que ce dernier travail représente une avancée intéressante dans le domaine de l'estimation des expositions, notamment en termes de gain de temps et d'économie de moyens, les résultats n'étaient pas systématiquement comparables pour les autres familles, et notamment pour 7 des 8 COSV exclus (à l'exception du BDE 119). Cette option méthodologique n'a pas été retenue non plus.

Cependant, des avancées récentes concernant des modèles de prédiction dynamiques permettraient d'améliorer la prédiction des contaminations dans les différents compartiments des environnements intérieurs (Liu et al., 2013, 2015, 2016). Ces modèles sont plus représentatifs des conditions dynamiques des logements par la prise en compte des taux d'émissions des COSV à partir de leurs sources d'origines, des taux de renouvellement d'air des environnements intérieurs, mais aussi des coefficients de transfert massiques et de partages des COSV entre les différents compartiments. Leur développement et leurs applications en ERS doivent être étudiés avec intérêt.

Pour conclure, l'exclusion des composés pour lesquels les incertitudes de mesure et d'estimation étaient trop élevées permet d'aboutir à une estimation robuste. En contrepartie, elle conduit à une perte d'information pour la prise de décision. Cette vision partielle pourrait nécessiter de les réintégrer dans le cadre d'une démarche plus large d'aide à la décision.

5.2.2. Disponibilité des données toxicologiques

Pour les effets à seuil, des VTR étaient disponibles dans la littérature pour 29 des 32 COSV concernés par l'étape d'estimation des expositions (Figure 6), et des QD ont été estimés pour ces composés. Pour les effets sans seuil, des excès de risque unitaires (ERU) étaient disponibles dans la littérature pour les deux COSV génotoxiques : le lindane et le benzo[a]pyrène, ce qui a permis l'estimation d'ERI.

Par contre, l'ERS n'a pas été conduite pour toutes les tranches d'âge à chaque fois, et l'ERCS a été conduite pour des mélanges de composition variable, tant en nombre de COSV qu'en nature. En effet, l'absence de jeux de données toxicologiques comparables (mêmes systèmes étudiés, mêmes fenêtres d'exposition critiques, etc.) conduit à ne pas pouvoir considérer tous les COSV dans chaque groupe d'effet ni pour les différentes tranches d'âge. Ces limites sont décrites ci-après.

Pour ce travail de thèse, le choix a été fait d'analyser les risques selon trois fenêtres d'exposition distinctes couvrant les périodes prénatale, postnatale et l'âge adulte. En effet, des expositions pré- et postnatales à certains polluants, même à des très faibles doses, sont susceptibles d'engendrer l'apparition de troubles ou de maladies pendant l'enfance, l'adolescence et/ou l'âge adulte. Au cours de ces périodes à risque les différents organes et systèmes sont en développement et les mécanismes de défenses et de détoxification de l'organisme encore insuffisants ou même absents. Ainsi, les VTR basées sur des études réalisées chez l'animal adulte ont été utilisées pour évaluer les risques liés à l'exposition d'un adulte (en considérant un adulte âgé de 21-30 ans) mais aussi d'un enfant (en considérant un enfant âgé de 0-2 ans) en raison du facteur d'incertitude intra-espèce utilisé. Les VTR basées sur des études prénatales ont été utilisées pour évaluer les risques liés à l'exposition d'une

femme lors de la grossesse (en considérant un adulte âgé de 21-30 ans), et de ce fait de l'embryon et du fœtus. Enfin, les VTR basées sur des études postnatales ont été utilisées uniquement pour évaluer les risques liés à l'exposition d'un enfant (en considérant un enfant âgé de 0-2 ans), et non d'un adulte afin de ne pas surestimer l'exposition. Ce choix a permis d'utiliser des indicateurs toxicologiques adaptés et ainsi d'évaluer les risques de façon cohérente selon la fenêtre d'exposition étudiée. Cependant, les indicateurs toxicologiques ne sont pas systématiquement établis pour ces périodes à risque et ont conduit à devoir limiter le nombre de composés étudiés par tranche d'âge (individuellement et en mélange). C'est le cas notamment concernant l'évaluation des risques suite à l'exposition de la femme enceinte. En effet, les données toxicologiques pour une exposition prénatale sont les moins disponibles et peu de VTR sont développées afin d'étudier la survenue d'effets spécifiques (outre la tératogenèse) suite à une exposition prénatale. Par exemple, uniquement 9 COSV sur les 32 disposaient d'une VTR établie pour une exposition prénatale, contre 19 pour une exposition postnatale et 16 pour une exposition à l'âge adulte.

Il apparaît primordial de distinguer ces périodes d'exposition afin de conduire des évaluations des risques utilisables à terme pour la mise en place de mesures de protection des populations sensibles. Il est donc indispensable d'accroitre les données toxicologiques adaptées et il apparaît nécessaire de produire ces données en priorité pour des effets dont la survenue est liée, de manière établie ou présumée, à une exposition pendant les périodes fœtale, postnatale, ou de l'enfance.

Concernant l'ERSC de premier niveau, par l'estimation de HI, 17 et 15 COSV ont pu être étudiés en mélange pour des effets communs neuro- ou reprotoxiques

respectivement (Fournier et al., 2016, 2017). Les autres composés n'ont pas été inclus en raison de l'absence de données en terme d'études toxicologiques ou de relations dose-réponse. Cette absence de données peut être due à une toxicité encore non testée ou non mise en évidence, et ne signifie pas forcément une absence d'effet pour ces composés. Concernant l'ERSC à une échelle plus fine, par l'utilisation de RPF ou de TEF, des mélanges allant de 9 à 2 COSV uniquement ont pu être étudiés, en raison de l'insuffisance des données toxicologiques disponibles ou comparables (en termes d'espèces, de modèles étudiés, de fenêtres, de durée et de voies d'exposition, etc.).

La standardisation des protocoles expérimentaux notamment permettrait d'accroître le nombre de données comparables et de ce fait exploitables pour le calcul d'indicateurs de toxicité pour un plus grand nombre de composés. De plus, comme le recommande Fournier (2015), il apparaît essentiel de veiller à ce que les résultats et surtout les données brutes des études toxicologiques soient accessibles de façon à pouvoir être aisément utilisés par d'autres auteurs. Par ailleurs, disposer de davantage de données toxicologiques établies pour des expositions à des mélanges réels permettrait de s'affranchir de ces limites de comparabilité. Par exemple, Crépet et al. (2013) se sont intéressés à des profils d'expositions réels de la population française à des mélanges de pesticides par voie alimentaire. Ils ont ainsi ouvert la voie sur des estimations plus réalistes des risques cumulés.

5.2.3. Limites liée à la formulation du problème

Les composés perfluorés par exemple, n'ont pas été inclus lors de l'étape de développement analytique du fait de leurs propriétés physico-chimiques et n'ont pas été étudiés lors de ce travail de thèse. Ces composés sont cependant retrouvés dans les poussières des environnements intérieurs (Goosey et al., 2011) et ont des effets neurotoxiques (Johansson et al., 2008) et reprotoxiques (Mitro et al., 2016) identifiés chez l'animal. Mitro et al. (2016) ont estimé les expositions agrégées de plusieurs de ces composés à partir de leurs concentrations dans les poussières d'habitats Nord-Américains. Les auteurs ont également estimé les expositions à plusieurs retardateurs de flammes non étudiés dans le cadre de ce travail de thèse et de composés en commun dont certains phtalates, le galaxolide et le bisphénol-A. Pour ces derniers, les résultats obtenus sont comparables lorsque les données de contamination des poussières utilisées étaient du même ordre de grandeur. Concernant les retardateurs de flamme étudiés par Mitro et al. (2016), les expositions couvrent plusieurs ordres de grandeurs allant de quelques dizaines de pg/kg/j à plusieurs centaines de µg/kg/j. Les expositions estimées pour les perfluorés sont beaucoup plus faibles et n'excèdent pas les ng/kg/j. Les auteurs concluent que pour certains retardateurs de flamme, en raison d'expositions élevées, et pour les perfluorés, en raison de leurs effets toxiques, des mesures de réduction des expositions doivent être envisagées. Ces résultats et recommandations appellent à considérer également ces composés dans le cadre de mesures de prévention et de gestion des risques des COSV présents dans l'habitat français.

De plus, outre son logement, l'Homme est exposé aux COSV dans d'autres environnements intérieurs (bureau, transports en commun, écoles, etc.) et par

d'autres médias avec entre autres : l'air extérieur (HAP), l'alimentation (PCB, pesticides) et les cosmétiques (phtalates, muscs de synthèse). Ces expositions sont parfois difficiles à maîtriser *a posteriori*, en raison notamment de la pérennité de certains COSV dans l'environnement et la chaîne alimentaire, du fait d'une longue demi-vie (pouvant aller jusqu'à plusieurs années) et/ou d'un réservoir d'émission important. Par ailleurs, de nouvelles molécules arrivent continuellement sur le marché et certains substituants ayant des effets potentiels sur la santé humaine (bisphénols, nouveaux retardateurs de flamme) ont été identifiés. C'est dans ce contexte global que la notion « d'exposome », introduite au début de ce manuscrit, prend tout son sens et que la recherche doit continuer de faire évoluer les connaissances relatives aux expositions environnementales et à leurs effets sur l'Homme, l'animal et l'environnement.

Chapitre 6 : Conclusion générale et perspectives

Dans une optique de santé publique il serait nécessaire de pouvoir agir en amont des expositions. La mise en place de restrictions pour limiter ou supprimer l'exposition des populations à de nombreux contaminants se fait malheureusement la plupart du temps *a posteriori*, notamment suite à la confirmation d'effets sanitaires toxiques par des données épidémiologiques. Ce décalage dans le temps rend les sources d'autant plus difficiles à identifier et à éliminer par la suite. Les règlementations récentes mises en place au niveau européen pour la production et l'utilisation des substances chimiques permettent de mieux encadrer leur mise sur le marché, bien qu'elles ne prennent pas encore suffisamment en compte l'ensemble des effets toxiques potentiels d'une substance. Par exemple, aujourd'hui, la classification des substances chimiques (en lien avec le règlement CLP) ne fait pas mention du potentiel neurotoxique d'une substance et de son caractère perturbateur endocrinien.

De plus, pour améliorer les connaissances relatives aux mélanges et à leurs effets, la première et principale question à résoudre est de mieux caractériser les mélanges auxquels la population est réellement exposée. Dans cette optique, de nombreux travaux de recherche conduisent à améliorer les méthodologies existantes et à générer des données de plus en plus réalistes. Par exemple, Kapraun et al. (2017) se sont intéressés à des profils d'expositions réels à des mixtures par l'emploi de données de biomonitoring aux États-Unis.

A l'issue de ce travail de thèse plusieurs perspectives de recherche concernant les risques liés aux COSV peuvent être débattues :

- Mieux caractériser les mélanges de contaminants pour conduire une ERSC représentative de l'exposition réelle dans les environnements intérieurs mais aussi dans les autres milieux ;
- Améliorer les connaissances relatives aux mécanismes d'action toxiques des contaminants afin de pouvoir les regrouper selon une échelle plus fine, notamment via des techniques de screening haut-débit ;
- Développer des protocoles d'études toxicologiques standardisés et homogènes (en termes d'espèces, de modèles étudiés, de fenêtres, de durée et de voies d'exposition, etc.) afin de disposer de données comparables (comme déjà recommandé par Fournier (2015)) ;
- Améliorer la communication des résultats des études afin de disposer de l'ensemble des informations nécessaires à l'estimation des expositions et des risques (données de contamination, relations dose-réponse, etc.) ;
- Développer des RPF et des TEF comparables pour un plus grand nombre de contaminants de familles chimiques différentes et en particulier pour les composés des mélanges courant.

L'expansion industrielle du 20ème siècle a généré un environnement chimique nouveau et son accélération continue de le complexifier chaque année. Si ces innovations procurent des bénéfices elles peuvent aussi générer des risques qui ne sont pas toujours détectables à court termes. C'est le cas notamment des progrès thérapeutiques chimiques qui ont permis d'éradiquer de nombreuses maladies mortelles ou encore d'améliorer la santé de la population générale, mais qui ont aussi leurs lots d'effets indésirables et même dans certains cas qui ont pu engendrer des scandales sanitaires par leurs effets toxiques, voir mortels, sur la santé humaine.

La mise sur le marché d'une substance chimique est déjà fortement encadrée et doit satisfaire, notamment pour les médicaments, le principe du bénéfice-risque. Dans le cas des additifs industriels ou même alimentaires, la réglementation se durcit également. Le principe de précaution devrait être davantage appliqué en l'attente de connaissances scientifiques formelles et notamment face à des résultats expérimentaux incertains. Mais il est parfois inévitable d'attendre de longues expositions pour déceler une toxicité. Cette attente se fait alors au détriment du progrès et du bénéfice attaché à telle ou telle nouvelle substance. On sait également qu'attendre se fait au détriment des intérêts financiers qui incitent parfois à quelques empressements. Ce n'est souvent que rétrospectivement que des mesures de restriction sont prises pour les substances qui s'avèrent dangereuses après plusieurs années de commercialisation et d'utilisation. Toute la difficulté réside dans cette question : quel niveau de preuves, même incomplet, serait suffisant pour décider de l'innocuité d'une substance chimique ? Car même si on ne doit pas arrêter le progrès, attendre la survenue de conséquences sanitaires ou environnementales néfastes conduit trop souvent à agir à retardement.

Pour cela, la recherche scientifique doit évidemment continuer d'enrichir les connaissances relatives aux composés chimiques et à leurs effets toxiques. La communauté européenne et les autres structures de régulation à travers le monde doivent également continuer d'encadrer la production et l'utilisation de ces produits. Les pouvoirs publics ont la responsabilité de rendre disponibles les informations relatives à l'utilisation de ces produits et sur les dangers potentiels, mêmes incertains, encourus. Enfin, pour que chacun devienne acteur de ce défi sanitaire, et faute de pouvoir contrôler le matraquage publicitaire que subissent nos sociétés de consommation, pour permettre à chaque personne désireuse de limiter son exposition de pouvoir adopter un mode de vie en adéquation avec ses principes, des conseils et des informations pratiques, clairs et efficaces doivent être émis et leurs mises en œuvre doivent être facilitées.

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Annexe 1 : Valorisation du travail de thèse

Articles scientifiques

- Pelletier, M., Bonvallot, N., Ramalho, O., Blanchard, O., Mercier, F., Mandin, C., Le Bot, B., & Glorennec, P. (2017). Dermal absorption of semivolatile organic compounds from the gas phase: Sensitivity of exposure assessment by steady state modeling to key parameters. *Environment International*, *102*, 106-113.

- Pelletier, M., Bonvallot, N., & Glorennec, P. (2017). Aggregating exposures & cumulating risk for semivolatile organic compounds: A review. *Environmental Research*, *158*, 649-659.

- Pelletier, M., Bonvallot, N., Ramalho, O., Mandin, C., Wei, W., Raffy, G., Mercier, F., Blanchard, O., Le Bot, B., & Glorennec, P. (2017). Indoor residential exposure to semivolatile organic compounds in France. *Environment International*, in press.

- Pelletier, M., Bonvallot, N., & Glorennec, P. (2017). Cumulative risk assessment of residential indoor exposure to semivolatile organic compounds in France. *Environmental Health Pespectives,* submitted.

- Wei, W., Mandin, C., Blanchard, O., Mercier, F., Pelletier, M., Le Bot, B., Glorennec, P., & Ramalho, O. (2017). Predicting the gas-phase concentration of semi-volatile organic compounds from airborne particles: Application to a French nationwide survey. *Science of the Total Environment*, *576*, 319-325.

Communications orales en congrès internationaux

- Aggregating exposures & cumulating risk to indoor semivolatile organic compounds in France. *ASPHER Deans' and Directors' Retreat.* Rennes, 31 mai-2 juin 2017.

Communications par affiches en congrès internationaux

- Aggregate exposures to indoor semivolatile organic compounds in France. *ISES* 2016. Utrecht, the Netherlands, 9-13 October 2016.

- Dermal absorption of semivolatile organic compounds from the gas-phase: Sensitivity of exposure assessment to key parameters. *Indoor Air* 2016. Gand, Belgium, 4-8 July 2016.

- Air to skin: An important exposure pathway for some semivolatile endocrine disruptors. *2nd Paris Workshop on Endocrine Disruptors Effects on Wildlife and Human Health*. Paris, 21-22 January 2016.

Communications orales en congrès nationaux

- Evaluation des expositions cumulées aux Composés Organiques Semi-Volatils dans l'habitat et risques sanitaires associés. *Rencontres scientifiques du Réseau doctoral EHESP*. Rennes, 15 mars 2017.

- Aggregating exposures & cumulating risk to indoor semivolatile organic compounds in France. *5th day of the young researchers of IRSET*. Rennes, 1st December 2016.

- Evaluation des expositions cumulées aux Composés Organiques Semi-Volatils dans l'habitat et risques sanitaires associés. *Journée des Doctorants Air de l'ADEME*. Paris, 1er juillet 2016.

- Evaluation des expositions cumulées aux Composés Organiques Semi-Volatils dans l'habitat et risques sanitaires associés. *Journées des Doctorants ADEME*. Angers, 1-3 février 2016.

Communications par affiches en congrès nationaux

- Evaluation de l'exposition cumulée aux Composés Organiques Semi-Volatils (COSV) de l'habitat et risques sanitaires associés. *Journées des Doctorants ADEME*. Angers, 2-4 février 2015.

Récompenses

- Evaluation de l'exposition cumulée aux Composés Organiques Semi-Volatils (COSV) de l'habitat et risques sanitaires associés. *Journées des Doctorants ADEME*. Angers, 2-4 février 2015. **1er prix**

- Concours « Projet innovant ». Doctoriales Bretagne 2016. Brest, 4-7 avril 2016. **1er prix**

Abstract Maud Pelletier

Title: Aggregating exposures & cumulating risk to indoor semivolatile organic compounds in France

Aim: Indoor semivolatile organic compounds (SVOCs): e.g. phthalates, PCBs, PBDEs, PAHs, bisphenols and pesticides partition between gas, suspended and settled dust. At home, humans are exposed through inhalation, dermal contact, and dust ingestion. Several SVOCs are suspected of reprotoxic and neurotoxic effects. The first objective of this work is to estimate global indoor exposure to SVOCs frequently detected in air and settled dust in French dwellings. The second is to assess cumulative risks assessments (CRA) for SVOCs having common toxic effects.

Methods: Firstly, exposures were estimated for 32 SVOCs of health interest, for 11 age groups from birth to 30 years, and for 3 pathways: dust ingestion, inhalation of air (gas and particulate phases) and dermal contact with gas phase using nationwide measurements and partitioning modeling with 2 dimensional Monte Carlo simulations to assess separately variability and uncertainty. Secondly, health risks were assessed by comparing exposures to published toxicity data i) for chemicals individually, ii) on the basis of a dose-addition assumption for groups of chemicals having similar mechanism/mode of neurotoxic or reprotoxic action.

Results: Exposures spanned from µg/kg.bw.d to pg/kg.bw.d. They were mainly driven by indoor SVOC concentrations. Air was the dominating media for most compounds, either by inhalation or dermal contact. Sensitivity analysis indicated that variance of exposure estimates was dominated by concentration variability, far ahead physical parameters uncertainty. The chemical by chemical approach led to inacceptable risks for 50% of the children for BDE 47, for 5% of the children for lindane, PCBs and DBP, and for 5% of the adults for lindane and BDE 47. Cumulative risks were close or exceeded (for exposure during pregnancy) acceptable risks for neurotoxic effects. Cumulative risks exceeded acceptable risks for 75% of the children and for 5% of the adults for neurotoxic effects.

Conclusion: SVOCs indoor exposure and risks need to be assessed simultaneously in order not to underestimate the health risks.

Tu-Po-37

Aggregate exposures to indoor semivolatile organic compounds in France

M. Pelletier[1,2]; N. Bonvallot[1,2]; O. Ramalho[3]; O. Blanchard[1,2]; F. Mercier[1,2,4]; C. Mandin[1,3,4]; Wenjuan Wei[3]; Jean Paul Lucas[5]; B. Le Bot[1,2,4]; P. Glorennec[1,2]

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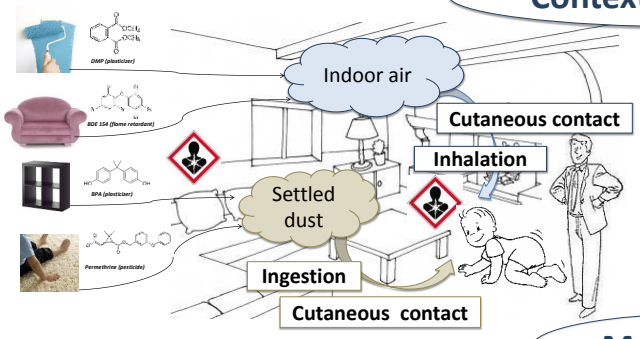
Context & Objectives

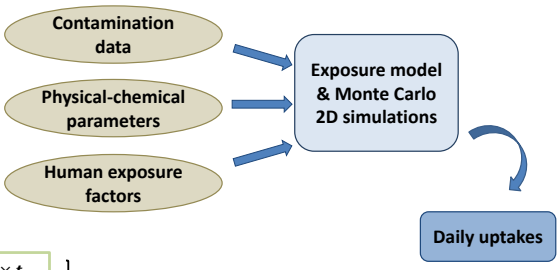


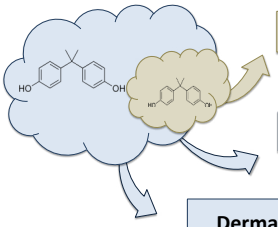
At home, humans are exposed to indoor semivolatile organic compounds (SVOCs): e.g. phthalates, PCBs, PBDEs, PAHs, bisphenols and pesticides through different routes. The objective of this exposure assessment is to estimate global indoor exposure to several SVOCs frequently detected in air and settled dust in French dwellings (Blanchard et al., *Environ.Sci.Technol*. 2014, 48; Mandin et al., *Atmospheric Environment*. 2016, 136). These aggregate exposures will enable in a cumulative risk assessment to indoor SVOCs with common toxic effects.

Methodology

Daily uptakes (DU) and aggregated daily uptakes (ADU) in ng/kg-bw/day are estimated:

- for **40 SVOCs** of health interest,
- for **11 age groups** from birth to 30 years,
- using partitioning modeling in **steady-state** conditions,
- for **3 pathways**: dust ingestion, inhalation of air (gas and particulate phases) and dermal contact with gas phase,
- with **2 dimensional Monte Carlo simulations** (Crystal Ball® software) to assess separately variability and parameters uncertainty.





Ingestion of settled dust

$$DU_{ing-dust} = \frac{C_{dust} \times DI \times f_1 \times f_2 \times t}{BW}$$

Inhalation of indoor air

$$DU_{inh-air} = \frac{(C_{part} + C_{gas}) \times IR \times f_3 \times t}{BW}$$

Dermal contact with gas phase

$$DU_{derm-gas} = \frac{\frac{C_{gas} \times k_{p-g} \times BSA \times t}{1000}}{BW}$$

$$\sum ADU = DU_{ing-dust} + DU_{inh-air} + DU_{derm-gas}$$

C_{dust}	ng/g	SVOC concentration in settled dust
C_{part}	ng/m³	SVOC concentration in the particulate phase
C_{gas}	ng/m³	SVOC concentration in the gaseous phase
DI	mg/d	Daily dust ingestion
BW	kg	Body weight
BSA	m²	Body surface area
IR	m³/d	Daily inhalation rate
t	h or (-)	Time spent in dwellings per day
f_1	(-)	Oral bioavailability
f_2	(-)	Dust bioaccessibility
f_3	(-)	Pulmonary bioavailability

For each SVOC human exposure factors were retrieved from US EPA Exposure factors handbook (2011), and absorption factors were retrieved from the literature.

$DU_{derm-gas}$ requires the calculation of indoor air transdermal permeability coefficient:

$$k_{p-g} = 1/\left(\frac{1}{\gamma_d} + \left(1/\frac{10^{(0.7\times\log(K_{ow}) - 0.0722\times MW^{2/3} - 5.252)} \times HRT}{1 + (10^{(0.7\times\log(K_{ow}) - 0.0722\times MW^{2/3} - 5.252)} \times MW^{0.5}/2.6)}\right)\right)$$

MW	g/mol	SVOC molecular weight
K_{ow}	(-)	Octanol/water partition coefficient
H	Pa.m³/mol	Henry's law constant
R	Pa.m³/mol.K	Ideal gas constant
T	K	Temperature
γ_d	m/h	External transport coefficient

For each SVOC physical-chemical parameters values were retrieved from the literature, online database, online calculators and EPI Suite software.

First results

As examples, Figure 1 presents daily uptakes (DU) and aggregated daily uptakes (ADU) of phenanthrene (ng/kg-bw/d) estimated for a children of 2-3 years old and an adult of 21-30 years old. Figure 2 shows relative contributions of each pathway for phenanthrene and permethrin.

Similar work is ongoing for 38 other SVOCs

Figure 1.

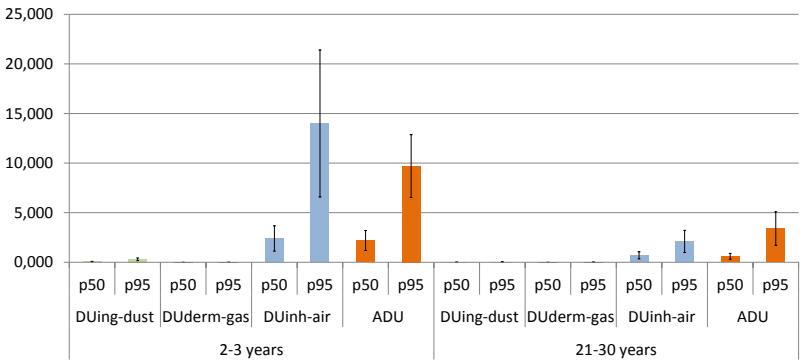
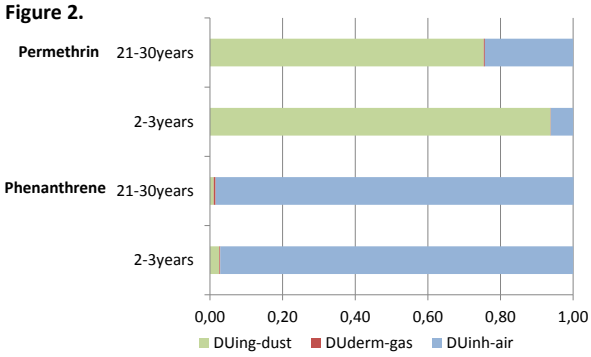


Figure 2.



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Dermal absorption of semivolatile organic compounds from the gas-phase: Sensitivity of exposure assessment to key parameters

M. Pelletier[1,2]; N. Bonvallot[1,2]; O. Ramalho[3]; O. Blanchard[1,2]; F. Mercier[1,2,4]; C. Mandin[1,3,4]; B. Le Bot[1,2,4]; P. Glorennec[1,2]

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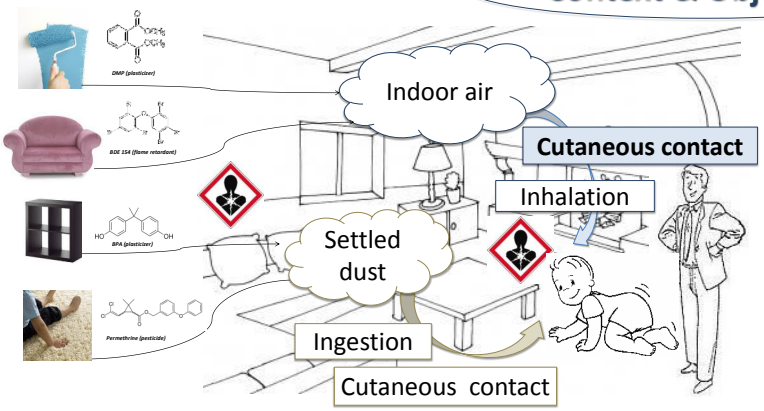
EHESP irset CSTB le futur en construction LERES ANALYSES - RECHERCHE

Context & Objectives



Humans are exposed to indoor semivolatile organic compounds (SVOCs): e.g. phthalates (DMP), PCBs, PBDEs, PAHs (phenanthrene), bisphenols (BPA) and pesticides (diazinon) through different routes. The dermal pathway, often considered up to now as negligible compared to ingestion and inhalation, has recently received great concern. Recent works suggest that dermal contact with the gas phase could be a significant contribution to exposure (Weschler and Nazaroff, *Indoor Air* 2012, 22; Morrison et al., *J. Expos. Sci. Environ. Epidemiol.* 2016, 26) and models to estimate this pathway have been developed. However their use is subject to criticism due to possible large uncertainties in input parameters.

The objective of this sensitivity analysis is to evaluate for 8 SVOCs the dermal intake variation that is caused by the uncertainty and variability of input parameters and to identify key parameters when using the model described by Weschler and Nazaroff (2012) for dermal absorption of gas phase SVOCs.

Methodology

Dermal intake model

Chronic daily intakes (DI) in µg/kg-bw/day of gas phase SVOC via the dermal pathway were estimated in steady-state conditions using the following equation adapted by Bekö et al (*Plos One* 2013, 8):

$$DI_{dermal-gas} = \frac{\frac{C_g \times k_{p-g} \times A \times t}{1000}}{W}$$

When not measured C_g can be estimated from C_a using the partitioning model proposed by Weschler and Nazaroff (*Atmos. Environ.* 2010, 44):

$$C_g = \frac{C_a}{1 + ([TSP] \times \frac{f_{om-part} \times K_{ow} \times R \times T}{\rho_{part} \times 10^6 \times H})}$$

Daily dermal intake requires the calculation of indoor air transdermal permeability coefficients (k_{p-g}) which can be estimated from recombining equations from steady-state model adapted by Weschler and Nazaroff (2012; *Environ. Sci. Technol.* 2014, 48):

$$k_{p-g} = 1/(\frac{1}{\gamma_d} + (H/\frac{10^{(0.7\times\log(K_{ow})-0.0722\times MW^{2/3}-5.252)} \times RT}{1 + (10^{(0.7\times\log(K_{ow})-0.0722\times MW^{2/3}-5.252)} \times MW^{0.5}/2.6)}))$$

Parameters distributions

C_g	ng/m³	SVOC concentration in the gas phase	Log normal or Uniform [0 - LOQ]
C_a	ng/m³	SVOC total concentration in indoor air	Log normal or Uniform [0 - LOQ]
K_{ow}	-	Octanol/water partition coefficient	Log normal or Triangular
H	Pa.m³/mol	Henry's law constant	Triangular
γ_d	m/h	External transport coefficient	Triangular
$f_{om-part}$	-	Volume fraction of organic matter associated with airborne particles	Normal
ρ_{part}	g/m³	Density of airborne particles	Normal
$[TSP]$	µg/m³	Total suspended particle concentration	Log normal
W	kg	Body weight	Log normal
A	m²	Body surface area	Log normal
t	h/day	Time spent in dwellings	Normal
MW	g/mol	SVOC molecular weight	One value
R	Pa.m³/mol.K	Ideal gas constant	= 8,314 Pa.m³/mol.K
T	K	Temperature	= 298 K

For each SVOC parameters values were retrieved from the literature, online database, online calculators and EPI Suite software.

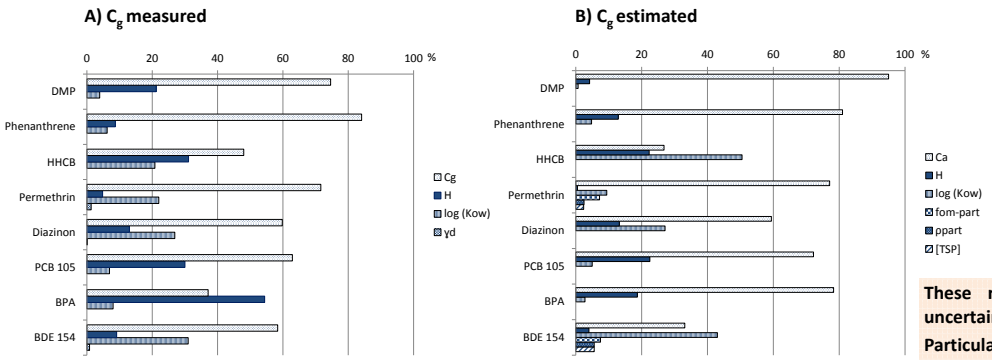
Sensitivity analysis

→ Dermal intake sensitivity analysis was then performed using Crystal Ball® software (Oracle©, version 11.1.1.3.00).

→ Monte Carlo simulations were carried out with 10^5 runs for each SVOC and for each of the two situations regarding C_g if it is measured (A) or estimated (B).

Results & Implications

Relative contribution (%) to total variation of gaseous SVOC daily dermal intakes (µg/kg-bw/d) according to key parameters: C_g, C_a, K_{ow}, H, ρ_{part}, [TSP], and γ_d for both situations: A) C_g is measured and B) C_g is estimated from C_a.



Parameters having a relative contribution that is always lower than 5% are not presented, that is, $f_{om-part}$ and each human parameter: W, A and t.

When assessing dermal absorption of gas phase SVOCs, variation of dermal intake estimation is driven firstly by variability and uncertainty in indoor air concentration (C_g or C_a), and secondly by uncertainty in SVOC physical-chemical parameters: K_{ow} and H. While exposure media properties such as transport coefficient (γ_d), particle density (ρ_{part}) and concentration ([TSP]) have a slight influence (less than 10%) for some compounds, volume fraction of organic matter in the particle phase ($f_{om-part}$) and human parameters such as body weight (W), body surface area (A) and daily exposure (t) have a marginal or null contribution (less than 5%) to the variance of dermal intake for a given age group.

These results support the importance of including an uncertainty analysis in exposure assessment.

Particular attention to C_g and C_a measurements associated to a reduction of log (K_{ow}) and H uncertainties could significantly reduce uncertainties in $DI_{dermal-gas}$ assessment.

Air to skin: An important exposure pathway for some semivolatile endocrine disruptors

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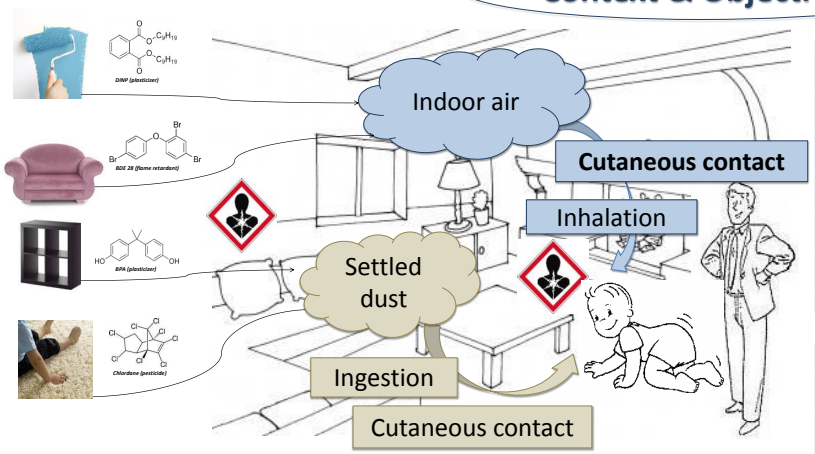
Context & Objectives



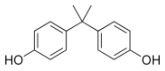
Some environmental endocrine disruptors are semivolatile organic compounds (SVOCs): e.g. phthalates (DEHP), PCBs, PBDEs, PAHs (benzo(a)pyrene), bisphenols (BPA) and pesticides (DDT, dieldrin, chlordane). They are found in many household sources and are able to migrate to and partition between different indoor compartments, including indoor air and settled dust. At home, people are permanently exposed to these molecules through different pathways: cutaneous contact with indoor air and settled dust, inhalation of indoor air and ingestion of settled dust.

Dermal exposure is rarely assessed in health risk assessments, because it is presumed to be negligible. Nevertheless, recent research has shown the importance of taking dermal exposure into account.

The aim of this work is to identify residential semivolatile endocrine disruptors for which the dermal pathway has a significant contribution in residential exposures from indoor air.

Methodology

Compounds selection



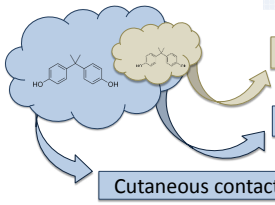
Compounds were selected from 57 SVOCs of health interest previously measured in 30 French dwellings (Blanchard et al., *Environ.Sci.Technol*. 2014, 48) separately in gas phase and in particulate phase.

Study population

Exposures were estimated for 6 age groups: [0-1 year], [1-6 years], [6-12 years], [12-16 years], [16-21 years] and > 21 years.

Exposures estimation

Daily intakes (DI) in µg/kg-bw/day were estimated for 3 pathways by using the following relationships developed by Weschler and Nazaroff (*Indoor Air* 2012, 22) and Bekö et al. (*Plos One* 2013, 8). Bekö et al (2013) found insignificant (< 1%) dermal exposure to settled dust regarding 5 phthalates. Similar results were found when assessing the same compounds with our values and this pathway was not assess for the other SVOCs.



Ingestion of settled dust

$$DI = \frac{C_d \times M_{ingestion-dust}}{BW}$$

Inhalation of indoor air

$$DI = \frac{\frac{(C_g + C_p) \times V_{inhalation}}{1000}}{BW}$$

Cutaneous contact with the gaseous phase

$$DI = \frac{\frac{C_g \times k_{p-g} \times BSA \times t}{1000}}{BW}$$

Daily dermal intake requires the calculation of indoor air transdermal permeability coefficients(K_{p-g}):

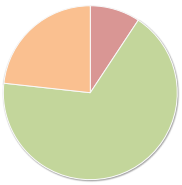
$$k_{p-g} = 1/\left(\frac{1}{\Upsilon_d} + \left(1/\frac{10^{(0.7\times\log(K_{ow}) - 0.0722\times MW^{2/3} - 5.252)} \times HRT}{1 + \left(10^{(0.7\times\log(K_{ow}) - 0.0722\times MW^{2/3} - 5.252)} \times MW^{0.5}/2.6\right)}\right)\right)$$

For each SVOC and each age group, parameters values were retrieved from the literature and EPI Suite software.

C_g	SVOC concentration in the gas phase (ng/m³)
C_p	SVOC concentration in the particulate phase (ng/m³)
C_d	Mass fraction of SVOC in settled dust (µg/g)
BSA	Body surface area (m²)
BW	Body weight (kg)
t	Time spent in dwellings (h/day)
$V_{inh.}$	Daily volume of air inhaled (m³/day)
$M_{ing.}$	Daily dust ingestion rate (g/day)
K_{ow}	Octanol/water partition coefficient
MW	SVOC molecular weight (g/mol)
H	Henry's law constant (atm.m³/mol)
R	Ideal gas constant (= 8.314 Pa.m³/mol.K)
T	Temperature (K)

Results & Perspectives

Contribution of the dermal pathway in the residential exposure are presented as a ratio (%) of the daily dermal intake compared to the summation of the daily intakes from the three involved pathways. One specific vulnerable age group of [0-1 year] is presented. Results found for the other age groups follow the same tendency.



Dermal pathway contribution for 41 semivolatile endocrine disruptors

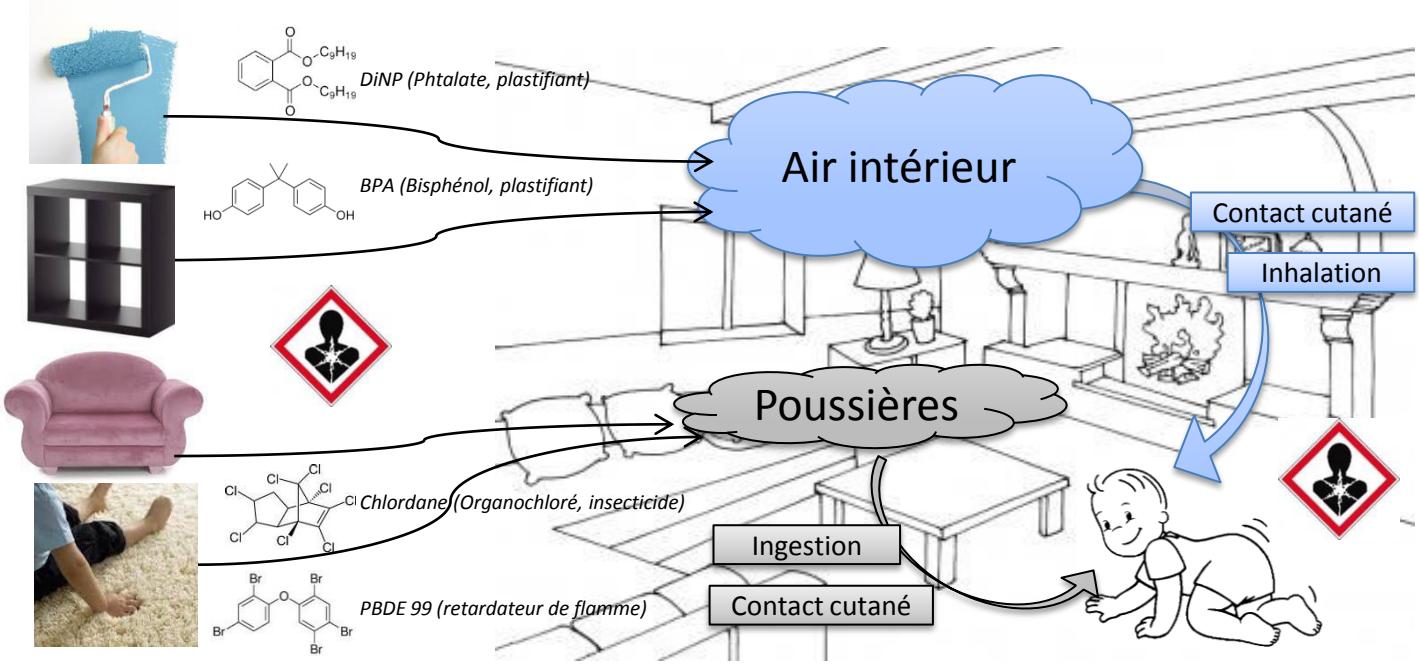
> 95 %	0	-
50-95 %	3	PCB 126, fluoranthene, diazinon.
5-50 %	28	DEP, DBP, BBP, DiBP, DiNP, BDE 28, 7 PCB (52-77-101-105-118-138-153), acenaphthene, benzo(a)pyrene, fluorene, phenanthrene, pyrene, galaxolide, tonalide, TBP, DDT, chlorpyrifos, permethrin, cis-chlordane, trans-chlordane, dieldrin, endrin.
< 5 %	10	DEHP, 6 BDE (47-99-100-153-154-209), PCB 180, BPA, aldrin.

Compounds concentrations in the studied medias were not available for 16 SVOCs because under the limit of quantification of the method.

These results support the importance to consider dermal absorption for assessing residential exposure to semivolatile endocrine disuptors and in general to SVOCs.

Evaluation de l'exposition cumulée aux Composés Organiques Semi-Volatils (COSV) de l'habitat et risques sanitaires associés

Les populations passent plus de **80%** de leur temps dans des espaces clos qui concentrent de **nombreuses sources** de substances chimiques (meubles, produits de décoration, de nettoyage, produits de combustion, sols…). Nombre d'entres elles sont semi-volatiles et persistent longtemps dans de **multiples compartiments** de l'habitat : poussières, phase particulaire et gazeuse de l'air (Blanchard et *al.,* 2014), en plus de l'alimentation et de l'air extérieur. Les expositions sont donc **multiples** et concernent **toutes les voies** (orale, respiratoire et cutanée) pour une grande **diversité** de molécules chimiques : bisphénols, PCB, phtalates, organochlorés, HAP… utilisées pour leur propriétés variées (plastifiants, retardateurs de flamme, insecticides…) et ayant des **effets toxiques** identifiés sur l'organisme humain (Fournier et *al.,* 2014).



Multiples COSV

Multiples voies d'exposition

Les expositions aux multiples COSV présents dans les logements posent-ils un problème de santé publique ?

Méthodes et outils

L'originalité du projet consiste à adopter une **approche agrégée** des expositions, selon les différentes voies d'absorption et pour différents polluants. Mais également la prise en compte de l'**additivité** des effets sanitaires pour les COSV ayant un mécanisme d'action toxiques commun.

Une démarche d'**évaluation des risques cumulés** sera mise en place pour répondre à la question de recherche.

Objectifs et résultats attendus

Ce travail de recherche permettra d'**identifier** les COSV les plus préoccupants et de **déterminer** les voies et les médias d'exposition les plus contributifs au risque.

Il sera donc utile à la **mise en place de mesures de santé publique préventives et de protection** de la population.

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Stage (IRSET - Inserm UMR1085) **:** Evaluation de l'exposition par la voie cutanée aux COSV présent dans l'habitat.
Stage (IRSTEA - UR TSAN) : Mise en place d'une évaluation des risques d'exposition aux produits phytopharmaceutiques des Entrepreneurs de Travaux Agricoles.

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Le président de jury,
(Nom et Prénom)

Maud PELLETIER, Expositions agrégées aux composés organiques semi-volatils dans l'habitat et risques sanitaires associés. Rennes, France, le 2 novembre 2017.

Résumé : Les populations sont exposées dans leur habitat à un nombre croissant de composés chimiques dont les composés organiques semi-volatils (COSV). Ils se distribuent sur les surfaces, les phases particulaire et gazeuse de l'air et les poussières, et participent ainsi à l'exposition des populations par ingestion, par inhalation et par contact cutané. Plusieurs de ces composés sont suspectés d'être toxiques pour l'Homme.

L'objectif de cette thèse est d'évaluer, par une démarche d'évaluation des risques sanitaires, l'impact sur la santé publique des expositions aux COSV fréquemment détectés dans les logements français.

Dans un premier temps, les expositions ont été estimées pour 32 composés à partir de données de contamination et de facteurs humains d'exposition comme le poids, le volume respiratoire, le temps passé dans l'habitat, etc. Les voies orale, pulmonaire et cutanée ont été agrégées pour les COSV les plus préoccupants présents dans l'habitat et pour plusieurs tranches d'âge de la naissance à 30 ans.

Dans un second temps, les risques pour la santé humaine ont été modélisés à partir de ces expositions et des données disponibles sur leur toxicité. Chaque composé a été pris en compte individuellement mais également en mélange sous l'hypothèse d'additivité des doses. Ce travail a permis l'obtention de distributions représentatives des expositions des populations dans l'habitat en France et d'identifier les voies et les médias dominants pour chaque composé ainsi que les COSV les plus à risque pour une certaine proportion de la population française.

Abstract: In housing, people are exposed to an increasing number of chemicals, including semivolatile organic compounds (SVOCs). SVOCs are present on surfaces, in the air gas phase, airborne particles and settled dust. Humans are exposed through ingestion, inhalation and dermal contact. Many of these compounds are suspected of toxic effects on human health.

The objective of this thesis is to assess, by a risk assessment approach, the public health risk due to the exposure to SVOCs frequently detected in French dwellings.

At first, indoor exposures were estimated for 32 compounds by using contamination data and human parameters such as body weight, inhalation rate, time spent in dwellings etc. Ingestion, inhalation and dermal contact exposure pathways were aggregated for the indoor SVOCs of greatest concern and for several age groups from birth to age 30.

In a second step, human health risks were modeled from these exposures and from available toxicity data. Each SVOC was considered separately and also in mixtures, based on the assumption of dose additivity. This work provided exposures distributions representative of the French population and identified the dominant media and exposure routes for each compound as well as the most at risk SVOCs for a certain portion of the French population.