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Assessing Human Exposure to Chemicals in Materials, Products and Articles:

A Modular Mechanistic Framework

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ABSTRACT

1. INTRODUCTION

Rapid prioritization of large numbers of chemicals in numerous building materials, consumer products and other indoor articles (here collectively referred to as sources) has become an increasing focus of chemical management strategies to protect humans from potentially harmful exposures.¹⁻³ Although these strategies emphasize the need for high-quality exposure data and validated, mechanistic (i.e., process-based) exposure models, approaches for implementation are highly fragmented among countries, national agencies and research institutions, as shown by Eichler et al.⁴ Despite the progress that has been made in understanding the fundamental mechanisms governing indoor exposure to chemicals released from sources, especially for semi-volatile organic compounds (SVOCs), we need to consider the “bigger picture” within which this chemical risk management problem exists.^{2, 5-8} This is especially important because the number of chemicals and sources is increasing steadily, challenging the ability of traditional approaches to keep pace because key emission and exposure parameters have only been measured for very few chemical/source combinations.^{7, 9, 10} Potential approaches to facilitate the transition from hazard-driven, single-chemical assessments toward rapid, risk-based prioritization are already being developed and include procedures to estimate exposure, toxicity and toxicokinetics.^{3, 11-16} For example, high-throughput (HT) screening methods allow testing of large numbers of samples with highly automated instruments in combination with advanced data processing software.^{12, 17} Substantial efforts have been made in advancing HT hazard information and HT toxicokinetics,¹⁸ but essential information to predict human exposure to chemicals in indoor sources is often missing.¹⁹ To fully realize the potential of new chemical

55 risk assessment approaches in the most useful and efficient way, reliable chemical exposure models have
56 to be employed in combination with quickly accessible toxicity data.^{2, 20}

57 The objective of this paper is to describe a generic modular mechanistic framework for predicting chemical
58 emission from an indoor source, partitioning among indoor compartments and exposure to humans
59 present in the indoor environment within a risk assessment context and focusing on SVOCs. This will be
60 achieved by defining mechanistically-consistent source emission categories and describing exposure
61 pathways that are congruent with these source categories and the subsequent chemical distribution
62 among indoor compartments. The modular structure of the framework should make it possible to
63 subsequently include other classes of chemicals released indoors. Its purpose is to serve as a tool for rapid
64 risk ranking and screening for the general population, but excluding worker exposure.

65 Many of the specific elements and models forming the framework have been described elsewhere²¹⁻²³, but
66 to advance chemical risk assessment, it is necessary to combine and connect them in an agreed-upon way
67 that can be easily implemented. As the proposed framework evolves in an iterative fashion, the
68 combination of exposure estimates with toxicity and toxicokinetic information will allow rapid estimation
69 and ranking of risk for a wide range of chemical/source combinations, therefore providing consistent
70 evaluations for policy decision-making and new insights for manufacturers.

72 **2. INITIAL FOCUS ON SVOCs**

73 There are several definitions of SVOCs. The World Health Organization (WHO) defines SVOCs as a group of
74 chemicals with boiling points in the range of (240-260°C) to (380-400°C).²⁴ According to International
75 Standard ISO 16000-6:2011, SVOCs are eluting after n-hexadecane on a non-polar gas chromatography
76 capillary column.²⁵ Another definition refers to a vapor pressure range of 10^{-9} to 10 Pa.²⁶ SVOCs are present
77 in many different consumer products, building materials and other indoor articles where they are used,

for example, as plasticizers, flame retardants and pesticides. A large number of SVOCs have been associated with adverse health impacts, making them of particular concern to scientists, chemical managers and policy makers.²⁷⁻³⁰ Due to their physicochemical properties, quantifying SVOCs in indoor environments is challenging because they tend to partition among indoor compartments (gas phase, airborne particles, settled dust and surfaces) at different rates.³¹

SVOC emissions can occur during active source use (e.g., spraying of pesticides or application of varnish) or passively (e.g., migration from plastic products such as PVC shower curtains). Exposure to SVOCs is possible via inhalation, dermal uptake (i.e., transfer from a source to the skin surface) and ingestion.³² In 2006, Xu and Little³³ were the first to extend a model originally developed for volatile organic compounds (VOCs) to predict emission rates of SVOCs from polymeric materials. They showed that SVOC emission and transport are subject to external control, i.e. partitioning, convective mass transfer and adsorption to surfaces and airborne particles.³³ In 2008, Weschler et al.³⁴ investigated the distribution of phthalates among the gas phase, airborne particles and settled dust, and provided a model for the particle-gas partition coefficient K_p , which allows an estimation of the SVOC concentration in airborne particles if the gas-phase concentration is known. Weschler and Nazaroff (2008)²⁶ then presented the first framework for characterizing the equilibrium partitioning among indoor compartments for SVOCs. One key finding was that SVOCs might persist in indoor environments for years, depending on their vapor pressure, even after the original source has been removed.²⁶ Several studies followed, presenting both measurements and models describing SVOC emission, transport and subsequent exposure, often with a focus on phthalates such as DEHP.³⁵⁻³⁸

In 2012, Little et al.³¹ proposed a framework for rapid exposure estimates based on the source type in which the respective SVOC is present. Accounting for source composition and use as well as emission characteristics, a simple method to estimate exposure for additives in sources used indoors and for sources sprayed or applied to interior surfaces was developed.³¹ The key parameters needed for these models

have since been investigated and reliable measurement methods are increasingly available, with different levels of complexity.³⁹⁻⁴⁷ Other aspects, such as the influence of clothing on dermal SVOC exposure,^{48, 49} the previously underestimated dermal uptake of SVOCs from air,^{21, 50, 51} or the impact of organic films on indoor surfaces on SVOC dynamics^{52, 53}, have been studied in increasing detail.

With this paper, and during the further development of the framework, we hope to create consensus among researchers and stakeholders regarding SVOC exposure models, parameter estimation procedures, assumptions, limitations and conditions of use. We do not intend to review SVOC exposure models in detail, as several recent reviews exist.^{21-23, 54} The initial consensus points that underlie the framework and the equations that comprise the initial version of the framework are provided in the Supplementary Information (SI). The SI also provides a decision tree for identifying appropriate exposure scenarios based on the framework.

3. FRAMEWORK FOR PREDICTING EXPOSURE TO INDOOR SVOCs

Figure 1 shows the mechanistic modeling framework to be used for estimating exposure to SVOCs emitted from sources present or used in the indoor environment. The central elements of the framework are 1) modeling of emission based on mechanistically consistent source categories, 2) modeling of transport, chemical transformations (where applicable) and resulting concentrations in the respective indoor environmental compartments, and 3) estimating exposure via different pathways based on the concentrations in the compartments for different exposure scenarios. In the following sections, we describe the scientific background and underlying assumptions of the mechanistic models for emission, transport, chemistry and exposure, as well as their main parameter needs, uncertainties, and limitations and conditions of use. Availability and quality of input parameters impact the modeling outcome significantly and thus represent starting points for further research and the integration of existing data

sets, relationships and expert opinions intended to decrease uncertainties and improve the suite of models.

Dietary exposure to SVOCs present in food and beverages is an important aspect of overall exposure to certain SVOCs, for example for diethyl phthalate (DEP) and di-2-ethylhexyl phthalate (DEHP).⁵⁵⁻⁵⁷ To assess this particular exposure pathway, a framework equivalent to that discussed here is necessary, but this is considered beyond the scope of the current work.

Figure 1: A modular framework for modeling indoor SVOC emission, transport, chemistry and exposure.

In this framework, the focus is on mechanistic modeling as it resolves many of the key challenges posed when predicting exposure.⁵⁸ Mechanistic models, also referred to as process-based models¹⁹, rely on well-established physicochemical processes such as diffusion or sorption. They are generalizable and can be varied in complexity based on the needs of the assessment, in contrast to empirical models.⁵⁴ However, if

suitable mechanistic models are not available, other approaches such as machine-learning, expert opinions, statistics, or empirical models may serve in a preliminary role.⁵⁹

3.1 Assumptions

The following general assumptions are often made for SVOC emission, transport and exposure models. They are valid in many cases, but there are exceptions that increase the uncertainty of the derived exposure estimates.

The indoor compartments considered in this framework are the gas phase, airborne particles, dust and surfaces. We included clothing as an additional compartment because its role in exposure scenarios is rather complex.^{48, 60} Clean clothing has been shown to protect against dermal uptake of SVOCs from air, while clothing that had been exposed to contaminated air increases dermal uptake.^{48, 61} These characteristics together with other properties discussed below distinguish clothing from other environmental compartments.

The assumption of equilibrium between gas phase, airborne particles, dust and surfaces is assumed for most SVOC models because it eliminates some kinetic complexity.^{42, 62} However, the greater the capacity an environmental compartment has for SVOCs, the longer it will take to reach equilibrium with other compartments, in which case the use of models that include kinetics should be considered.

SVOC emissions from source materials are considered externally controlled, meaning that internal mass transfer is much faster than external mass transfer.^{26, 33} Furthermore, the material-phase SVOC concentration C_0 can be considered constant as depletion happens at a much slower rate, as shown by Xu et al.⁶³, Xu and Little³³ and Pei et al.⁶⁴. However, these assumptions are only valid for sufficiently small external mass transfer coefficients and SVOCs with relatively low vapor pressures. Internal diffusion may become important when considering transfer into clothing.

It is generally assumed that the air in the indoor environment is well-mixed, but this may not be the case for indoor air in confined spaces, for example within cabinets and closets.

In some cases it may be reasonable to assume that background outdoor concentrations of SVOCs are small and thus negligible for exposure assessments of chemicals released by indoor sources. This assumption depends on the type of SVOC considered, as some are present both indoors and outdoors, e.g., pesticides and certain phthalates.⁶⁵⁻⁶⁷ If an SVOC has an outdoor source, the SVOC concentration in the infiltrating air including particle-phase SVOCs should be taken into account.

3.2 Model Formulation

3.2.1 Emission

The framework is structured to distinguish between Direct and Indirect Exposure (Figure 1). Direct Exposure can occur immediately via direct dermal uptake or ingestion of the source. Alternatively, emission from the source to environmental compartments occurs first, followed by partitioning and chemical transformations, resulting in accumulation in one or more compartments from which exposure occurs (Indirect Exposure). Chemical emission from a source depends largely on chemical characteristics, on the source type and on the environmental compartment into which the chemical is emitted.³¹ However, all indoor environmental compartments can serve as both sources and sinks, even simultaneously, depending on the chemical and the direction of the chemical fugacity gradient. The general direction for the context of this framework is the transport from sources with high fugacity to sinks (including humans) with lower fugacity, thus the arrows in Figure 1 point from the left (sources) to the right (human exposure). However, except for ingestion, the direction of the chemical fugacity gradient is reversible.

Classic emission sources are furniture, building materials including flooring and carpet, personal care products, as well as combustion processes (e.g., burning a scented candle) and meal preparation (e.g.,

heating oil in a pan). For our modeling framework, we derived emission source categories from a continuum of possible sources (Figure 2). We recognize that there is some overlap between the source categories and that some sources may not fit perfectly into one category. In such a case, multiple scenarios could be considered.

For SVOCs, Little et al.³¹ differentiated between two main source categories. One included solid sources in which SVOCs are present as additives and the other included sources containing SVOCs that are either sprayed or applied, with mechanistic emission models presented for both categories. Here, we propose to modify and extend the list to include the following emission source categories: solid sources, soft sources, sources that humans frequently contact, liquid applied sources, liquid sprayed sources, and high temperature sources, resulting in a total of six mechanistically consistent source emission categories (Figure 2), which cover most sources containing SVOCs.^{9, 68} The saturation vapor pressure p_s (Eq. I in the SI) and the octanol/air partition coefficient K_{oa} (Eq. II in the SI) are fundamental parameters needed for modeling SVOC emission and partitioning.

Figure 2: Classification of emission source categories from a continuum of possible sources, which range from solid to soft, from stationary to mobile, and including certain specific uses such as applied, sprayed, and heated/combusted.

Solid Sources

Solid sources containing SVOCs include, for example, PVC flooring, electronic devices such as TVs, plywood furniture and painted walls. They have larger emitting surface areas relative to the volume of most indoor environments or to the area that might come in contact with an exposed person. Exposure to SVOCs present in these solid sources mainly occurs by Indirect Exposure. Direct Exposure contributes much less to overall exposure.⁶⁹

As discussed above, depletion of the SVOC in the source can often be assumed to be negligible.⁷⁰ Including the variability of source strength over time in the model increases its complexity, but the mechanisms

governing emission from solid sources remain the same. A prerequisite for calculating the depletion rate is that C_0 is known.

From a solid source, emission may occur either into the gas phase or by migration onto dust in direct contact with the solid source material.^{31, 71} Governing parameters for emission into the gas phase are the SVOC gas-phase concentration immediately adjacent to the source material y_0 and the mass transfer coefficient h_m (Eq. 1a in the SI).^{22, 31} C_0 also impacts the SVOC gas-phase concentration immediately adjacent to the source material y_0 (Eq. III in the SI).⁴³ If it is assumed that a linear equilibrium relationship exists between the settled dust and the gas layer directly adjacent to the source material (Eq. 3 in the SI), the critical parameters for modeling emission onto dust are y_0 , h_m (Eq. IV in the SI), the dust/air partition coefficient, K_{dust} (Eq. VI in the SI), the particle deposition velocity v_d (literature values) and the concentration of airborne particles, which is usually given as Total Suspended Particles, *TSP* (measured).^{22, 35, 72}

Soft Sources

Exposure to soft sources can occur both via Direct Exposure due to frequent close contact of a person with these sources and via Indirect Exposure due to their often large emitting surface areas. Soft sources include cushions, mattresses, foams, carpets and clothing. New clothing may contain SVOCs introduced during manufacture, transport, storage, or from contact with packaging materials, or because they have been added deliberately for product enhancement, for example water-resistant coatings.⁶⁰ These SVOCs may be emitted into the indoor environment after the clothing has been brought home and even after laundering.⁶⁰ Stored clothing may accumulate SVOCs from the air and thus serve as an additional environmental compartment.⁴⁸ Emission from soft sources into the gas phase or onto settled dust can be modeled using Equations 1a and 3 in the SI, respectively.

Frequent Contact Sources

Exposure to certain SVOCs in sources that are frequently handled (e.g., smartphones, smartwatches, toys) or mouthed by children (e.g., teethingers) is more likely to occur via Direct Exposure. These sources are not stationary, usually irregularly shaped and their emitting surface area is comparatively small and thus contributes less to the SVOC concentrations in the environmental compartments, but emission may be modeled as for solid sources.⁶⁰

Applied sources

A liquid source that is directly applied to the body (e.g., body lotion, shampoo, sun screen) is mainly linked to Direct Exposure. With a liquid source applied to the body, emission into the gas phase and further partitioning occurs, which may contribute to total exposure to some extent, depending on the SVOC and individual behavior.^{73, 74}

If the liquid source is applied to a surface or remains open to the indoor air, Indirect Exposure dominates for more volatile SVOCs.⁸ Examples are floor care products, other cleaning products, detergents, or wet paint. Emission from an applied source is usually confined to a relatively short period of time during and shortly after application. For this type of pulse emission, dynamic models are needed (Eq. 1b in the SI). For certain cases, for example the application of paint, it might be necessary to look at the applied exposure scenario first, and then to consider exposure from the solid source after the paint has dried.

After initial release, SVOCs partition onto sink surfaces (including exposed skin, hair and clothing), airborne particles and dust, from where long-term exposure may occur even if the initial short-term source has evaporated or been depleted. In the case of dried paint or similar dried sources, emission into the gas phase can be modeled using the same approach as for emission into the gas phase from a solid source (Eq. 1a in the SI).³³

Sprayed Sources

A liquid source that is sprayed towards the body can participate in both Direct and Indirect Exposure. Dermal uptake by direct contact with the source occurs together with exposure by dermal uptake from air and inhalation of both gas and particle phases. Examples are deodorants, perfumes, or spray sun screen. If the source is sprayed away from a person, e.g., air freshener or window cleaner, Indirect Exposure contributes more.

Sprayed sources are pulse emission sources with constant or variable time patterns. The emission mechanism of sprayed sources differs from that of liquid sources because of the force with which the product is released within a relatively small volume of air, resulting in high concentrations for a short period of time. The formation of aerosol droplets which interact with airborne particles, dust and sink surfaces enhances the potential for exposure which may occur long after the initial release. Additionally, powdery sources may fall into this category, as their application can also emit high concentrations in a short period of time and releases particles into the indoor air. Equations 1c and 2a in the SI describe emission from sprayed sources into the gas phase and into the particle phase, respectively.

High Temperature Sources

High-temperature events like candle burning, cooking, or having a fire in the fireplace are pulse emission sources that can release gas-phase SVOCs (Eq. 1d in the SI) as well as airborne particles (Eq. 2b in the SI) over a longer period of time compared to sprayed sources.⁸ In addition, chemical reactions (oxidation) possibly happening during emission have to be taken into account. Exposure to these types of sources is primarily indirect. Although all sources may undergo temperature variations that influence their chemical activity and thus emission behavior, this particular category targets sources that participate in intentional events and experience high temperatures for a certain period of time.

3.2.2 Transport and Chemistry

Transport and chemistry of SVOCs indoors are highly complex and not yet completely understood.⁷⁵ Individual indoor environments are almost impossible to depict completely with models. However, for the sake of rapid risk assessment, a breakdown of basic transport mechanisms is possible and will yield useful average results that allow risk ranking and prioritization. Our understanding of reactions and chemical transformations that involve SVOCs is still limited. Thus, we will discuss indoor chemistry here only briefly and qualitatively.

Particles either infiltrate from outdoors or are emitted by occupants and occupant activities.⁷⁵ Gas/particle partitioning is described in Equation 4 in the SI. Equation 7 in the SI shows the mass balance for particle transport, taking into account particle infiltration and removal, deposition, dust resuspension, and particle generation. Particle residence time and air change rate correspond directly.⁶² The lower their vapor pressure, the more SVOCs tend to partition to particles or surfaces. For less volatile SVOCs, for which instantaneous equilibrium between gas and particle phase is not likely, dynamic models exist that account for particle residence times.⁶² For estimation of the gas/particle partition coefficient K_p , see Equation V in the SI.

Further partitioning may occur between the gas phase and dust settled on source surfaces (Eq. 5a in the SI) and on sink surfaces (Eq. 5b in the SI). A mass balance for dust settled on sink surfaces can be found in Equation 8 in the SI. See Equation VI in the SI for estimation of the dust/gas partition coefficient K_{dust} . Clausen et al.⁷⁶, Schripp et al.⁷⁷ and Liu et al.⁷¹ focus on the kinetic process of SVOC uptake by dust particles and explore the relationship between the source surface and layers of settled dust. Dust may furthermore contribute to SVOC losses due to a combination of abiotic and microbial degradation, if the relative humidity is elevated.⁷⁸ This possibility of enhanced SVOC removal should be kept in mind when considering unusual exposure scenarios.

From the gas phase, SVOCs also partition to sink surfaces. The surface/gas partition coefficient K_s depends on SVOC and material characteristics, and has been measured for some cases (Eq. VII in the SI).^{41, 46, 79, 80}

Equation 6a in the SI describes surface/gas partitioning for solid sink surfaces; Equation 6b in the SI describes surface/gas partitioning for soft sink surfaces with dust settled on those surfaces.

Further complexity to modeling the uptake of SVOCs by sink surfaces is added by including thin organic films that are likely present on all indoor surfaces (Eq. 6c in the SI). Their presence affects SVOC dynamics and is thus also relevant for modeling of partitioning onto surfaces, because the presence of organic material on surfaces changes partitioning parameters, especially K_s . Weschler and Nazaroff⁵² studied the growth of organic films on impermeable surfaces for SVOCs with different octanol/air partition coefficients K_{oa} and observed that SVOCs with a $\log(K_{oa})$ between 10 and 13 were predominantly present in the film. Furthermore, the growth rate of the film was initially high and decreased over time. Low molecular weight SVOCs reach their equilibrium surface concentration relatively quickly, compared to higher molecular weight SVOCs.^{21, 52} Eichler et al.⁵³ added a mass-transfer model that describes the initial formation of an organic film on clean impermeable surfaces, identifying a two-stage process that requires the film to reach a critical thickness before the growth model becomes applicable. This approach is supported by findings from Liang et al.⁸¹ Coarse particle deposition on upward-oriented surfaces is also likely to influence the growth of organic surface films, depending on the gas-phase concentration of SVOCs with higher $\log(K_{oa})$ values, the concentration of airborne particles and their fraction of organic matter.⁵²

Equation 9 in the SI shows the general mass balance for indoor SVOCs. The elements of the mass balance include infiltration of gas- and particle-phase SVOCs into the indoor environment, removal of gas- and particle-phase SVOCs, SVOC emission from source surfaces, mass transfer to sink surfaces, deposition of particles on source and sink surfaces, and resuspension of dust from source and sink surfaces.

Clothing has been identified in recent years as an important mediator of human exposure to chemicals and particles, potentially acting as a barrier to exposure or having a prolonging effect.^{49, 60} Newly purchased clothing as an emission source has been discussed above. Post-purchase, clothing contains a mix of SVOCs (among other chemicals) present at the time of purchase and those sorbed while stored or in use.⁶⁰ Several

studies have shown that SVOCs present in indoor air can accumulate in clothing.^{48, 49, 82-84} Partitioning between clothing and air can be modeled using Equation 10a in the SI. For very thin clothing, diffusion inside the clothing material can be ignored, and a simplified model can be applied (Eq. 10b in the SI). This can be described using the gas/clothing partition coefficient K_{ca} , which can be approximated for cotton based on K_{oa} .⁸³ Morrison et al.^{82, 83} and Cao et al.⁴⁷ reported values for K_{ca} for PCBs and phthalates in different types of clothing material (Eq. VIII in the SI). Additionally, clothing may take up SVOCs from personal care products applied to skin, from laundering detergents and dry-cleaning additives, and also from cross-contamination with other fabrics during laundering and storage.⁶⁰ Partitioning between clothing and particles has only been studied to a small extent, but clothing can serve as a source of biotic and abiotic particles that may contribute to the particle mass balance indoors and thus to human exposure. Potential strategies to determine emission rates of particles from clothing can be found in Licina et al.⁶⁰

Indoor chemistry involves thousands of species that undergo transformations, resulting in changes in gas phase composition, and countless different indoor materials serve as sinks, sources and reaction sites.^{21, 85, 86} Occupants change indoor chemistry as well, also serving as sinks and sources and providing surfaces for chemical transformations.⁸⁷ The formation of secondary organic aerosols (SOAs), i.e., the generation of particles as a result of the oxidation of some reactive organic species in the gas phase by ozone, is an important additional aspect to consider when evaluating gas/particle partitioning of SVOCs.⁸⁸⁻⁹⁰ However, because of their reactivity and composition, SOA emission rates and their partitioning can only be assessed using complex and detailed chemical models which are currently beyond the scope of the proposed framework.⁹¹ Nevertheless, the possibility of the formation of SVOCs should be addressed at least qualitatively as part of any exposure assessment.

Finally, ozone and other oxidants react with organic species sorbed to surfaces, including human skin.^{86-88, 92, 93} The reactivity of SVOCs with oxidizing agents varies greatly and thus indoor chemistry may not be relevant for all applications.⁹⁴ For chemical reactions in the gas phase to affect indoor environments, their

reaction rate has to be shorter than or close to the air exchange rate.⁷⁵ This time constraint does not apply to reactions on indoor surfaces, making them particularly important.⁷⁵ Indoor chemistry modeling approaches are available but still limited regarding their parametrization, especially for SVOCs, and represent a focus of ongoing research.^{75, 88, 90}

3.2.3 Exposure

Based on the equations discussed in the previous sections, SVOC concentrations in specific indoor compartments can be predicted, and then used to estimate exposure. The following general exposure pathways are considered: Dermal exposure, inhalation exposure and non-dietary ingestion. Dermal exposure can be regarded as a two-step process: Skin-surface lipid uptake refers to the transfer of a chemical to the skin surface, while transdermal uptake describes transfer through the skin into body tissues and blood. For transdermal uptake, the permeability of the skin becomes important.^{89, 95} For this framework, we focus on skin-surface lipid uptake.

Direct Exposure can occur via dermal uptake by direct contact with the source, by ingestion of a source and mouthing of the source (source-to-mouth behavior). Indirect Exposure pathways are dermal uptake from the gas phase, airborne particles and via contact with dust, sink surfaces, or clothing, inhalation of air (gas phase and airborne particles), ingestion of dust, mouthing of objects that are not the source, including clothing and hand-to-mouth behavior.

Dermal Uptake by Direct Contact with the Source

When the skin is in direct contact with a source (solid or liquid), partitioning of SVOCs between the source and the skin-surface lipids takes place (Eq. 12a in the SI). A simple approach to describe the flux from a solid source surface to the skin surface has been used by the U.S. Consumer Product Safety Commission (U.S. CPSC). It incorporates a migration rate and the skin surface area in contact with the source.⁹⁶ Other

approaches assume that the transferred amount of SVOC depends on the SVOC concentration in the source and relate this property to either a thin layer of SVOC present on the source surface or to the diffusive flux of SVOC from within the source to its exterior.^{97, 98} A summary of these equations can be found in Huang et al.²³ However, none of the mentioned approaches appears to be fully developed and further research has to be conducted for a mechanistically consistent model. For the transfer from liquid sources applied to the skin, a simplified form of the approaches used by Wormuth et al.⁵⁶ and Giovanoulis et al.⁹⁹ can be used.

Following the transfer from the source to the skin-surface lipids, the subsequent transdermal uptake from the skin-surface lipids to the dermal capillaries can be described by multiplying the concentration of SVOCs on the skin surface C_{ssl} with the dermal permeability coefficient k_{p_ssl} .^{21, 89}

Dermal Uptake

The transdermal exposure rate Ex_{trans} from SVOCs present in the gas phase to dermal capillaries depends on the SVOC gas phase concentration C_g , the overall transdermal permeability coefficient k_{p_g} and the exposed body surface area A_{exp} (Eq. 13a in the SI).⁹⁵ k_{p_g} can be calculated based on a resistor-in-series model that takes into account the mass transfer coefficient from the bulk gas phase through the boundary layer of the skin as well as the compound-specific permeability coefficient through the stratum corneum/viable epidermis composite.^{21, 89, 95} The model has been extended under dynamic conditions by Gong et al.¹⁰⁰ and further by Morrison et al.⁵⁰

Dermal absorption of SVOCs associated with airborne particles is expected to be much smaller than dermal absorption from the gas phase because particles diffuse much more slowly than gases.⁹⁵ A specific model for dermal uptake of SVOCs associated with airborne particles or dust is given in Equation 13b in the SI. From the skin-surface lipids, transdermal uptake could be modeled as for direct dermal contact with a source. Equation 13c in the SI describes the dermal uptake of SVOCs from sink surfaces. The equation employs a contact rate and an availability factor, because it can be assumed that not all the SVOC

deposited on the sink surface is transferred when touched.¹⁰¹ Both parameters however are not well-established for SVOCs and further research is necessary.²³ Dermal uptake from contact with clothing materials can be modeled using Equation 13d in the SI. Critical parameters are the SVOC concentration in skin-surface lipids, which depends on the partitioning between clothing and skin-surface lipids and the SVOC concentration in the clothing material, the transdermal permeability coefficient from the skin-surface lipids into dermal capillaries and the exposed skin surface area. The model can be varied in complexity as described in Morrison et al.⁴⁹ and Cao et al.⁸⁴ However, because Equation 13d assumes equilibrium between the skin-surface lipids and the clothing, it describes a worst-case scenario. In many cases, the duration of contact between clothing and skin is shorter than the time needed to reach equilibrium.²⁶

Inhalation

For inhalation exposure, the inhalation rate IR_{inh} and the total SVOC concentration in the air are critical parameters (Eq. 14 in the SI).²¹ IR_{inh} is well documented by the U.S. EPA Exposure Factors Handbook for different age ranges, activity levels and genders.¹⁰² However, larger particles may be deposited along the way and some fraction may be exhaled again or swallowed.^{21, 23, 103} Thus intake and bioavailability fractions should be taken into account.

Ingestion and Mouthing of a Source

Non-dietary ingestion of a source (e.g., shampoo, lotion) and mouthing of a source is particularly relevant for young children (Eqs. 12b and 12c in the SI). Studies have also been conducted to explore the solubility and leachability of chemicals in saliva from various children's products.^{96, 104}

Ingestion of Dust, Hand-to-mouth and Object-to-mouth Exposure

Ingestion of dust can occur via hand-to-mouth and object-to-mouth contact, especially for young children.¹⁰⁵ Exposure via dust ingestion can be estimated using the dust intake rate IR_{dust} and the weight

fraction of SVOCs associated with the dust (Eq. 15a in the SI).^{21, 23} As with IR_{inh} , the U.S. EPA Exposure Factors Handbook provides values for IR_{dust} .²¹ SVOC bioaccessibility in dust has to be taken into account as well, as discussed in Raffy et al. 2018¹⁰⁶.

For calculation of exposure to SVOCs present on the skin (but not adhered to dust) via hand-to-mouth and object-to-mouth (e.g. clothing) contact, the frequency of contact events per hour and the amount transferred to the mouth at each contact have to be taken into account.^{21, 23} Also, the amount present on the hand or object must be known along with the fraction of the surface area in contact with the mouth.^{21, 23} Huang et al.²³ propose a removal efficiency relationship that has also been used in similar form by Isaacs et al.¹⁰¹, who obtained their relationship by using SHEDS-MM to fit available data.

3.3 Uncertainty

Uncertainty is introduced in the equations at any point where a parameter is being estimated. Additionally, measured parameters are restricted to the test conditions with inherent errors. Here, we plan to include uncertainty as probability distributions if available. The material-phase concentration C_0 , the octanol/air partition coefficient K_{oa} and the saturation vapor pressure p_s are critical parameters for modeling SVOC emission, transport and subsequent exposure, because they are commonly used to estimate partition coefficients.^{26, 34, 43, 107} Dust and particle properties such as the settled dust density ρ_{dust} , the particle density ρ_{part} and the organic content of dust (f_{om_dust}) and particles (f_{om_part}) are also necessary to describe SVOC distribution between different phases indoors.^{107, 108} Dust and particle properties vary greatly among different indoor environments (e.g., due to smoking, pets, or occupant habits) thus modeling cannot account for individual settings but has to rely on averages based on measurements. Salthammer and Schripp¹⁰⁸ reviewed the results of several dust sampling campaigns, with some of the data listed in the SI for reference. Other frequently used values can be found in Weschler and Nazaroff³⁵. The uncertainty

associated with any of these parameters propagates further when using them to obtain other modeling parameters.

C_0 can be measured relatively easily with chemical extraction methods and GC-MS analysis.^{109, 110} Suspect-screening analysis and non-targeted analysis of chemicals in products can further expand our knowledge of product composition.¹¹¹ Databases such as the U.S. EPA's Chemical and Products Database (CPDat), which is part of the CompTox Chemistry Dashboard, provide additional information on product composition and reference values that can be used for modeling.^{112, 113}

p_s and K_{oa} , on the other hand, are often insufficiently known for SVOCs, particularly at room temperature and for less volatile compounds, which makes calculating partition coefficients challenging.¹⁰⁸ Salthammer and Schripp¹⁰⁸ reviewed the available literature and reported that values of p_s for one SVOC can span several orders of magnitude based on different measurement techniques. They estimated that the uncertainty for a given p_s is given as $p_s \pm 0.95 \cdot p_s$, following a normal distribution.¹⁰⁸

Determining K_{oa} experimentally requires substantial effort, thus most K_{oa} values found in the literature have been derived from the air/water partition coefficient K_{aw} , the octanol/water partition coefficient K_{ow} and/or Henry's law constant H .^{108, 114, 115} The uncertainty of K_{oa} can be calculated as the combined uncertainty of the parameters used to obtain K_{oa} . For example, if $K_{oa} = K_{ow}RT/H$ is used, the uncertainty of K_{oa} is the combined uncertainty of K_{ow} and H .¹⁰⁸ Alternatively, K_{oa} can be determined from linear free energy relationships as described by Schwarzenbach et al. (2017).¹¹⁶ Numerous algorithms and quantitative-structure-property relationship (QSPR) approaches have been developed for the prediction of chemical properties.¹¹⁷ These are available via software tools like SPARC, EPI Suite and LSER to estimate K_{oa} and p_s .^{108, 118} However, the results might differ depending on the selected algorithm and, in case of QSPR approaches, on the quality of the input data. Moreover, associated uncertainties are difficult to quantify.¹¹⁴

K_p calculated using K_{oa} can be quite different from K_p calculated using p_s .¹¹⁴ Additional uncertainty might arise from the sigmoidal shape of the equation predicting the particle fraction, especially for compounds of medium volatility (10^{-6} Pa < p_s < 10^{-2} Pa). Small changes in p_s , K_{ow} and H (and thus K_{oa}) result in large differences in the concentration ratio between gas and particle phase.^{108, 114} In those cases, it is not possible to tell if an SVOC is predominantly in the gas or in the particle phase. Generally, the range of error of both experimentally derived and calculated values for K_p is within one order of magnitude.¹¹⁸

y_0 is a critical parameter to describe emission, and can be measured directly.^{39, 44} Furthermore, y_0 can also be derived from correlations with C_0 for certain SVOCs^{43, 46}. Similarly, regressions for different classes of SVOCs partitioning to certain types of sink materials have been established to estimate K_s .^{33, 81, 119} However, these correlations also depend on p_s and have similar challenges as discussed above.

When calculating distributions, Monte-Carlo simulations are helpful to quantify how uncertainties propagate to derived parameters. Wei et al.¹⁰⁷ reviewed published data for K_p and K_{dust} and described the distributions of $\log_{10}K_p$ and $\log_{10}K_{dust}$ for 72 SVOCs that can be used as references for Monte-Carlo simulations. They also developed an empirical linear relationship between $\log_{10}K_p$ and $\log_{10}K_{dust}$, which may serve to estimate K_{dust} based on K_p or vice versa, if no other sources are available.¹⁰⁷ Additionally, modeling parameters, especially partition coefficients, are influenced by indoor environmental factors, e.g., temperature, humidity, ventilation, size fractions of airborne particles and potential biodegradation of SVOCs.^{22, 42, 78, 79, 120} These relationships still require further research, but utilizing parameter distributions as model inputs provide some sense of the uncertainty associated with their estimation.

3.4 Limitations and Conditions of Use

As discussed above, the greatest limitation of this framework is the model parametrization. It is often not possible or feasible to measure parameters directly, thus they have to be estimated or obtained from

databases. The implementation of the proposed framework has to include ways to access databases like the U.S. EPA CompTox Chemistry Dashboard and other platforms that contain data derived from HT screening approaches or quantitative-structure-activity relationships (QSARs) which can serve as input for mechanistic models.^{113, 121, 122} Parameter estimation approaches vary greatly in their accuracy, from 50-year old literature values to data derived from chemistry software, and thus different forms of uncertainty are introduced, which have to be addressed appropriately. The SI supplies information on approaches to estimate important parameters together with ranges of applicability and uncertainty, if available.

The modular structure of the framework allows aspects of exposure modeling to chemicals released indoors to be included or excluded. The framework could, for example, be adjusted to include volatile organic compounds (VOCs), or other groups of chemicals, such as per- and polyfluoroalkyl substances (PFAS). Some modules are better understood than others, making it tempting to ignore those that might introduce complexity. However, even if some parts of the framework are not addressed quantitatively, they should be part of the broader discussion of the resulting exposure estimates so that they can be placed in the right context.

In addition to chemical-related model parameters, those describing specific exposure scenarios may also be unknown or highly uncertain. Whenever possible, variability has to be taken into account with respect to exposed populations and occupant characteristics,¹²³ occupant behaviors,^{8, 124} and indoor environmental settings^{125, 126}. Applying Monte Carlo-based approaches to include parameter distributions and addressing certain “special case” scenarios to identify particularly sensitive populations should be part of the application of the framework. It has been shown, for example, that cooking and cleaning activities greatly enhance the levels of SVOCs in indoor environments compared to background levels.⁸ The possibility of stacked exposures due to certain occupant behaviors and potential consequences for exposed individuals should thus be incorporated in the exposure assessment.

Concepts of bioaccessibility and bioavailability, as discussed for example in Wei et al. 2018¹⁰³ for inhalation exposure and in Raffy et al. 2018¹⁰⁶ for dust ingestion, should be considered. SVOC bioaccessibility can span a wide range, depending on the pathway, the specific substance, and many other factors.^{103, 106} Thus, when calculating intake rates based on the models presented in the SI, adjusting factors should be taken into account where available. If they are not available, the resulting intake rates might overestimate actual exposure. For higher complexity modeling purposes, exposure estimates derived with this framework may be combined with mechanistic model describing, for example, the fate of gas and particle phase in the human respiratory tract, possibly followed by the application of physiologically-based pharmacokinetic (PBPK) models to quantitatively predict concentrations in plasma or target tissue.^{2, 103}

Additional uncertainty may be introduced when evaluating SVOC sources that are not in direct contact with the indoor environment, such as those present in the building envelope (e.g. rim joists, vapor barriers). Strongly varying temperatures and infiltration paths into the indoor environment may significantly affect the infiltration rate of SVOCs into the indoor environment.

4. CONCLUSION

Mechanistic models have been identified as most suitable to address key challenges in exposure modeling. Mechanistically consistent source emission categories are the basis of the proposed framework and allow modelers and users to identify relevant exposure pathways. For modeling these pathways, mechanistic models with different levels of complexity are available and can be applied to derive exposure estimates. Factors influencing the complexity of modeling SVOC emission, transport and exposure in indoor environments include the following:

1. Assumption of equilibrium or dynamic conditions;

2. Consideration of the influence of indoor environmental factors on modeling parameters, especially on partition coefficients (e.g., temperature, humidity, ventilation, size fractions of airborne particles, source loading factor), and respective uncertainties;
3. Consideration of indoor chemistry and SVOC transformation products resulting from oxidation, hydrolysis and other reactions;
4. Consideration of more than one SVOC and the effect of chemical mixtures on partitioning behavior, reactivity and subsequent exposure; and
5. Influence of occupancy (e.g., in terms of surface soiling, dust re-suspension, cleaning habits and other occupant behavior) and occupant characteristics (e.g., age, gender, variability of exposure factors).

Modeling complex scenarios such as indoor environments is a challenging task. We will always have to make concessions, accept uncertainty and even unpredictability, and adapt to new developments. However, this should not stop our progress, but instead, if handled with awareness and transparency, can guide us in our attempts to reasonably reflect the real world in our models.

5. OUTLOOK

We envision this mechanistic exposure modeling framework to be developed as a community model and to be situated within larger chemical risk assessment frameworks to better understand interdependencies with existing and ongoing research and policies. To achieve this, toxicity data for different endpoints together with toxicokinetic mechanisms have to be combined with exposure estimates, ensuring that the overall goal of rapid and efficient risk ranking and chemical prioritization is being achieved, as generated for example by the U.S. EPA's Toxicity Forecaster (ToxCast), which uses HT screening methods and computational approaches.¹²⁷⁻¹²⁹ For example, Shin et al. 2015¹³⁰ proposed a strategy to combine exposure estimates based on intake rates with toxicity data derived from ToxCast in vitro bioactivity assays, deriving

bioactivity quotients (BQ) for HT risk ranking and prioritization. The approach relies on comprehensive near-field exposure models, as they are presented in our framework. The concept of Intake Fraction (IF) can be used to provide further insight into exposure estimates for screening purposes.¹³¹

The proposed framework can be employed in other contexts. Gwinn et al. 2017¹³² proposed a conceptual model for a public health perspective for chemical risk assessment, emphasizing public-health focused risk assessment rather than traditional risk assessment.¹³² Our framework complements this approach, because it incorporates robust mechanistic data and can furthermore inform novel exposure science and biomonitoring approaches that are being used in epidemiology. Additionally, our framework can be integrated with the work of Jolliet et al. 2015¹³³ and Fantke et al. 2016¹³⁴ who developed an approach to integrate near- and far-field exposure assessments with life cycle impact assessment (LCIA), and also for chemical alternatives assessment and risk-based HT purposes.

Further validation of the proposed framework, including models and parameters, is needed in an ongoing process. As emphasized before, the modular structure of the framework and the vision to establish it as the basis for an indoor exposure community model are intended to allow rapid and simple optimization of different components, depending on the user's needs and the knowledge available. The iterative implementation process will initially focus on SVOCs, but as work progresses, the source categories can be adjusted, VOC and aerosol emissions can be added, and indoor chemistry can be included. The Community Multiscale Air Quality (CMAQ) model¹³⁵ could serve as an example of how the framework can be developed, with open-source contributions from researchers worldwide and participation of all interested stakeholders. Although the structure of the framework is clear, much remains to be done to fill in the details.

Exposure science plays a crucial role in a fully integrated system of chemical risk assessment to inform and prioritize toxicity testing, describe and rank risks, and develop and validate models.⁶ As recognized by the U.S. National Research Council (NRC) in their 2007 report, *Toxicity Testing in the 21st Century: A Vision and*

*a Strategy*¹³⁶, exposure science must be considered at every step of any testing and risk assessment strategy⁶. This is reinforced in the NRC report from 2012 *Exposure Science in the 21st Century: A Vision and a Strategy*¹³⁷. In 2017, *Using 21st Century Science to Improve Risk-Related Evaluations*¹³⁸ picks up where the previous NRC reports left off and provides strategies for integrating new scientific methods, new ways of data validation, approaches to integrate divergent data streams, approaches to address uncertainties and ways to communicate new approaches to stakeholders.

Understanding the health effects of exposures to chemicals has real implications for public health. Currently, chemicals management authorities focus on evaluating risks from exposures to individual or groups of chemicals based on the properties of those chemicals. This approach rarely enables policy makers to link increased risk of public health outcomes to chemical management actions. As a result, chemical managers are challenged to anticipate impacts of chemical use and focus resources on addressing the most pressing concerns. A public health perspective starts with the disease of concern and incorporates multiple data streams to inform preventative policy decisions. The goal is to extend the scope of considerations that support chemical management decisions and advance the tools for integrating this more complex information.

Epidemiological studies increasingly report observations of adverse health effects at chemical exposure levels predicted from animal toxicology studies to be safe for humans. Understanding public health risk from environmental chemical exposures is complicated by factors that include population variability and susceptibility, latencies between critical exposures and disease outcomes, and background environmental exposures. To protect public health more effectively, future risk assessments will need to take a more holistic perspective, consider the full range of available data, draw on innovative methods to integrate diverse data streams, and consider health endpoints that better reflect impacts observed in human populations. In concert with current advances in exposure science (e.g., as describe in Thomas et al.

607 2019¹²⁹), the proposed framework will further enable the goal of combining chemical risk and population
608 health perspectives.

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610 **APPENDIX: Signatories**

611 List of signatories who support the proposed framework

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613 **Disclaimer**

614 The views expressed in this article are those of the authors and do not necessarily represent the views or
615 policies of any agency.

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623

624 **Supplementary Information**

625 Nomenclature, List of Consensus Points, Mechanistic Modeling Framework to Predict Exposure to SVOCs
626 (Figure S1), Emission and Transport Modeling Equations, Exposure Modeling Equations, Estimation
627 Approaches for Model Parameters, Comparison of K_{oa} values (Figure S2)

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Supplementary Information for

Assessing Human Exposure to Chemicals in Materials, Products and Articles:

A Modular Mechanistic Framework

Table of Contents:

- 1) Nomenclature
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1) Nomenclature

$A_{contact}$	Contact area between skin and sink surface (m^2)
A_{exp}	Exposed body surface area (m^2)
$A_{mouthing}$	Mouthed object surface area (m^2)
A_s	Surface area of sink (non-source) surfaces (m^2)
A_{ss}	Surface area of source surfaces (m^2)
ACH	Air change rate; $ACH = Q/V$ (1/h)
AR_{source}	Application rate of source ($\mu g/h$)
bw	Body weight (kg)
C_0	Material-phase SVOC concentration ($\mu g/m^3$)
$C_{a,sat}$	Saturation concentration in air ($\mu g/m^3$)
C_m	SVOC concentration in clothing material ($\mu g/m^3$)
$C_{o,sat}$	Saturation concentration in octanol ($\mu g/m^3$)
C_{pm}	Gas-phase SVOC concentration in porous material ($\mu g/m^3$)
C_s	Concentration of SVOCs on sink surfaces ($\mu g/m^2$)
C_{ssl}	Concentration of SVOCs associated with skin-surface lipids ($\mu g/m^3$)
C_t	Particle- and gas-phase SVOC concentration in the gas phase ($\mu g/m^3$)
CR_s	Rate of contact with sink surfaces (m^2/h)
d	Exposure duration (h)
D_a	Diffusion coefficient of the SVOC in air (m^2/h)
D_m	Diffusion coefficient of the SVOC in clothing material (m^2/h)
DI	Daily intake ($\mu g/kg$)
E	Emission rate of SVOCs from source materials ($\mu g/(m^2 \cdot h)$)
EF	Exposure frequency (1/h)
Ex_{cloth_d}	Dermal exposure rate to clothing ($\mu g/h$)
Ex_{dust_ing}	Dust ingestion exposure rate ($\mu g/h$)
Ex_{gas_d}	Transdermal exposure rate from the gas phase ($\mu g/h$)
Ex_{inh}	Inhalation exposure rate ($\mu g/h$)
$Ex_{mouthing}$	Mouthing exposure rate for mouthing of source ($\mu g/h$)
$Ex_{mouthing_other}$	Mouthing exposure rate for mouthing of objects with sink surfaces (μg)
Ex_{part_d}	Transdermal exposure rate for particles adhered to exposed skin ($\mu g/h$)
Ex_{source_d}	Exposure rate for direct contact of source with the skin ($\mu g/h$)
Ex_{source_ing}	Source ingestion exposure rate ($\mu g/h$)
Ex_{surf_d}	Transdermal exposure rate for dermal contact with sink surfaces ($\mu g/h$)
F	Particle-phase concentration of SVOCs in indoor environments ($\mu g/m^3$)
F_{out}	Outdoor particle-phase concentration of SVOCs ($\mu g/m^3$)
f_A	Fraction of chemical available for uptake (-)
f_{om_dust}	Fraction of organic matter in dust (-)
f_{om_part}	Fraction of organic matter associated with airborne particles (-)
f_{ret}	Retention fraction of a source (-)
H	Henry's law constant ($m^3 \cdot Pa/mol$)
$h_{m,s}$	Mass transfer coefficient for the sink (non-source) surface (m/h)
h_m	Mass transfer coefficient for the surface of a source (m/h)

IR_{dust}	Dust intake rate (g/h)
IR_{inh}	Inhalation intake rate (m^3/h)
IR_{source}	Source intake rate (g/h)
j	Represents a specific SVOC out of N SVOCs (-)
J_{source_ssl}	Flux from source to skin-surface lipids ($\mu g/(m^2 \cdot h)$)
J_{ssl_c}	Flux from skin-surface lipids to dermal capillaries ($\mu g/(m^2 \cdot h)$)
k_{p_g}	Transdermal permeability coefficient from the gas phase (m/h)
k_{p_ssl}	Transdermal permeability coefficient from the skin-surface lipids to dermal capillaries (m/h)
K_{dust}	Dust/gas partition coefficient (m^3/g)
K_{aw}	Air/water partition coefficient (-)
K_{ca}	Clothing/gas partition coefficient (-)
K_m	Dust/material partition coefficient (m^3/g)
K_{oa}	Octanol/air partition coefficient (-)
K_{ow}	Octanol/water partition coefficient (-)
K_p	Gas/particle partition coefficient of SVOCs ($m^2/\mu g$)
K_s	Sink surface/gas partition coefficient (m)
K_{ssl}	Partition coefficient between skin-surface lipids (SSL) and clothing (-)
L	Thickness of the porous material (m)
L_c	Characteristic length (m)
L_m	Thickness of clothing material (m)
M_s	Mass loading of settled dust on sink (non-source) surfaces ($\mu g/m^2$)
M_{ss}	Mass loading of settled dust on source surface ($\mu g/m^2$)
MR	Migration rate during mouthing ($g/(m^2 \cdot h)$)
m_x	Dust mass concentration at the depth of x ($\mu g/m^3$)
n	Freundlich constant (-)
N	Number of SVOCs considered (-)
$P_{dust,s}$	Concentration of SVOCs in the dust settled on the sink (non-source) surfaces ($\mu g/g$)
P_{dust}	Concentration of SVOCs in the dust settled on the source surface ($\mu g/g$)
P_p	Size-dependent particle penetration factor (-)
p_s	Saturation vapor pressure of pure SVOCs (Pa; mmHg)
Q	Ventilation rate (m^3/h)
q_{part_skin}	Transfer rate from particles adhered to skin (m/h)
R	Universal gas constant ($m^3 \cdot Pa/(K \cdot T)$)
R_p	Size-dependent particle resuspension rate (1/h)
Re	Reynolds number
r_{uptake}	Chemical uptake rate (1/h)
S	Generation rate of particles from indoor sources ($\mu g/h$)
Sc	Schmidt Number
Sh	Sherwood Number
t	Time (h)
T	Temperature (K)
TSP	Mass concentration of total suspended particles in the room ($\mu g/m^3$)
TSP_{out}	Mass concentration of total suspended particles outdoors ($\mu g/m^3$)
V	Volume of the room (m^3)

v_d	Size-dependent particle deposition velocity (m/h). Could be v_{dv} , v_{du} , or v_{dd} depending on the orientation of the surface.
v_{dv}	Size-dependent particle deposition velocity to a vertical wall (m/h)
v_{du}	Size-dependent particle deposition velocity to an upward-facing horizontal surface (m/h)
v_{dd}	Size-dependent particle deposition velocity to a downward-facing horizontal surface (m/h)
w_0	SVOC mass fraction in the source ($\mu\text{g/g}$)
w_{dust}	SVOC mass fraction in dust settled on source surfaces ($\mu\text{g/g}$)
$w_{dust,s}$	SVOC mass fraction in dust settled on sink (non-source) surfaces ($\mu\text{g/g}$)
x	Depth from the surface of the material (m)
y (or C_g)	Gas-phase concentration of SVOCs in indoor environments ($\mu\text{g/m}^3$)
y_0	Gas-phase concentration of SVOCs in the layer immediately adjacent to the source ($\mu\text{g/m}^3$)
Y_{out}	Outdoor gas-phase concentration of SVOCs ($\mu\text{g/m}^3$)
y_s	Gas-phase concentration of SVOCs in the layer immediately adjacent to the non-source surfaces ($\mu\text{g/m}^3$)
δ	Thickness of the organic film (m)
δ_0	Critical film thickness at which adsorption transforms to absorption (m)
ε	Porosity of material (-)
ρ_{dust}	Density of dust ($\mu\text{g/m}^3$)
ρ_{part}	Density of airborne particles ($\mu\text{g/m}^3$)
ρ_{source}	Density of source ($\mu\text{g/m}^3$)

2) List of Consensus Points

Consensus Point 1: To address challenges posed by exposure modeling, mechanistic models are preferred. Mechanistic models are based on physicochemical principles and are thus more generalizable in contrast to empirical models. They can be selected and varied in their level of complexity based on the application. Diverse data sets and the estimation of key input parameters using structure-based or other predictive relationships can be included in mechanistic modeling approaches. It is clear that mechanistic models have to be validated, and input parameter development and validation still require good data, which often does not exist.

Consensus Point 2: The environmental compartments relevant to modeling chemical exposure indoors are the gas phase, airborne particles, settled dust and exposed indoor surfaces, including those of the occupants. Additionally, clothing exposed to indoor air can serve as exposure mediator potentially increasing or decreasing dermal uptake.

Consensus Point 3: The assumption of equilibrium between gas phase, particle phase, dust and surfaces is a prerequisite for simpler SVOC models. However, this assumption has to be treated with caution. The greater the capacity of an environmental compartment, the longer it will take for that compartment to reach equilibrium with other compartments.

Consensus Point 4: SVOC emissions are assumed to be externally controlled, thus internal diffusion is neglected and the source is considered as non-depleting. Clothing is a special case due to differences in time scales, thus internal diffusion and source depletion may be relevant.

Consensus Point 5: It is assumed that the air in the indoor environment is well-mixed. An exception might be indoor air inside closed spaces such as closets and cabinets, which should be considered separately as needed.

Consensus Point 6: For some SVOCs emitted by indoor sources, outdoor air concentrations are low and can thus be neglected in exposure assessments. In other cases, indoor and outdoor concentrations may

be comparable, thus the question of the relevance of outdoor contributions has to be taken into account and concentrations of SVOCs in the infiltrating air may have to be considered.

Consensus Point 7: Exposure can occur immediately via dermal contact with or ingestion of the source (Direct Exposure). Alternatively, emission from the source to environmental compartments occurs first, followed by transport and chemical transformations, resulting in the SVOC's presence in one or more compartments from which exposure occurs (Indirect Exposure).

Consensus Point 8: Mechanistically consistent source emission categories, derived from a continuum of sources, serve as the starting point for modeling exposure to SVOCs emitted by sources in the indoor environment. These categories are: solid, soft, frequent contact, applied, sprayed and high temperature.

Consensus Point 9: Stationary non-porous sources that are not frequently handled or touched (e.g., furniture, TVs, or vinyl flooring) have large emitting surface areas relative to the volume of most indoor environments or to the area that might come in contact with an exposed person. Exposure to SVOCs present in these solid sources mainly occurs by Indirect Exposure.

Consensus Point 10: Soft sources include cushions, mattresses, foams, carpets and clothing. Exposure to soft sources can occur both via Direct Exposure due to frequent close contact of a person to these sources and via Indirect Exposure due to their often large emitting surface areas.

Consensus Point 11: Exposure to certain SVOCs in sources that are frequently handled (e.g., electronic devices, toys) or mouthed by children (e.g., teethingers) is more likely to occur via Direct Exposure. The emission category for this type of source is frequent contact.

Consensus Point 12: A liquid source that is directly applied to the body (e.g., body lotion, shampoo) is mainly linked to Direct Exposure. If the source is applied to a surface or is exposed to the indoor air (e.g., paint or detergent), Indirect Exposure dominates. Applied sources have to be considered pulse emission sources and thus require dynamic modeling approaches.

Consensus Point 13: A source that is sprayed towards the body can cause both Direct and Indirect Exposure (e.g., insect repellent). If the source is sprayed away from a person (e.g., air freshener), Indirect Exposure

contributes more. Both cases are pulse emissions and thus dynamic equations to model emission, transport and exposure are necessary.

Consensus Point 14: Combustion or heating processes such as burning a candle or cooking contribute mostly to Indirect Exposure. The relevant emission category is high temperature. This type of emission is a pulse emission that needs to include dynamic emission and chemical reactions.

Consensus Point 15: For modeling SVOC behavior in indoor environments, chemical transformations (e.g., oxidation, hydrolysis) should be discussed, even if they are not addressed quantitatively.

Consensus Point 16: Transport, partitioning and reactivity of SVOCs indoors are highly complex processes and not completely understood.

3) Mechanistic Modeling Framework to Predict Exposure to SVOCs

Figure S1: Dominant exposure pathways for SVOCs in indoor environments.

The red numbers refer to the equations listed below.

4) Emission and Transport Modeling Equations

1. Emission into the gas phase

- a. From solid sources, soft sources, and dried liquid sources:

$$E = h_m \cdot (y_0 - y)$$

Note: It is assumed that internal diffusion is negligible.

- b. From applied sources (pulse emission):

Dynamic model, research needed

- c. From sprayed sources (pulse emission):

Model development needed

- d. From high temperature sources (pulse emission):

Model development needed

2. Emission to airborne particles

- a. From sprayed sources (pulse emission):

Model development needed

- b. From high temperature sources (pulse emission):

Model development needed

3. Emission to settled dust

From both solid and soft sources and including emission into the gas phase:

$$E = h_m \cdot (y_0 - y) + v_d \cdot TSP \cdot P_{dust} - v_d \cdot F$$

4. Gas/particle partitioning

$$F = K_p \cdot TSP \cdot y$$

Note: Instant equilibrium is assumed.

5. Dust/gas partitioning

- a. For dust settled on source surfaces:

$$P_{dust} = K_{dust} \cdot y_0$$

Note: Alternatively, partitioning between dust and source material can be described using the dust/material partition coefficient K_m . See Liu et al. 2016¹ for details.

- b. For dust settled on sink surfaces:

$$P_{dust,s} = K_{dust} \cdot y_s$$

6. Surface/gas partitioning for sink surfaces

- a. For solid sink surfaces:

$$C_s = K_s \cdot y_s$$

- b. For soft sink surfaces:

$$[\varepsilon + (1 - \varepsilon) \cdot K_s + K_{dust} \cdot m_x] \frac{\partial C_{pm}}{\partial t} = \varepsilon \cdot D_a \frac{\partial^2 C_{pm}}{\partial x^2}$$

$$C_{pm} = 0 \text{ for } t = 0, 0 \leq x \leq L; \quad \frac{\partial C_{pm}}{\partial t} = 0 \text{ for } t > 0, x = L; \quad C_{pm} = y_s \text{ for } t > 0, x = 0$$

c. In the presence of an organic surface film:

$$\frac{dC_{s,j}}{dt} = h_{m,s,j} \left(y_j - \frac{C_{s,j}}{\delta \cdot K_{oa}} \right) + v_d \cdot F$$

$$\delta = \delta_0 + \sum_{j=1}^N \frac{C_{s,j}}{\rho_j}$$

Note: See Eichler et al. 2019² for further detail.

7. Mass balance for particle transport

$$V \frac{dTSP}{dt} = Q \cdot P_p \cdot TSP_{out} - Q \cdot TSP - v_d \cdot TSP \cdot (A_s + A_{ss}) + R_p \cdot M_s \cdot A_s + R_p \cdot M_{ss} \cdot A_{ss} + S$$

Change in particle mass concentration over time	Particles entering from outdoors with ventilation	Particles leaving with ventilation	Particles depositing on sink and source surfaces	Resuspension of dust from sink surfaces	Resuspension of dust from source surfaces	Particles being generated indoors
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$$\frac{dM_s}{dt} = v_d \cdot TSP - R_p \cdot M_{ss} \quad \text{or} \quad \frac{dM_s}{dt} = v_d \cdot TSP - R_p \cdot M_s$$

8. Mass balance for dust settled on sink surfaces

$$\frac{d(C_s + M_s \cdot P_{dust,s})}{dt} = h_{m,s} \cdot (y - y_s) + v_d \cdot F - R_p \cdot M_s \cdot P_{dust,s}$$

Change in SVOC concentration on sink surface and dust over time	Emission from the sink surface into the gas phase	SVOC concentration in dust deposited on sink surface	SVOC concentration in resuspended dust
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9. General mass balance for indoor SVOCs

$$V \frac{dy}{dt} + V \frac{dF}{dt} = Q \cdot (y_{out} + F_{out}) - Q \cdot (y + F) + h_m \cdot A_{ss} \cdot (y_0 - y) - h_{m,s} \cdot A_s \cdot (y - y_s) - v_d \cdot F \cdot (A_{ss} + A_s) + R_p \cdot M_{ss} \cdot P_{dust} \cdot A_{ss} + R_p \cdot M_s \cdot P_{dust,s} \cdot A_s$$

Note: If outdoor concentrations are assumed to be negligible, y_{out} and F_{out} equal 0, respectively.

Note: This mass balance does not include clothing-mediated effects.

10. Clothing/gas partitioning

a. General approach:

$$\frac{\partial C_m}{\partial t} = D_m \frac{\partial^2 C_m}{\partial x^2}$$

Boundary condition at clothing surface:

$$-D_m \frac{\partial C_m}{\partial x} \Big|_{x=L_m} = h_m \left(y - \frac{C_m}{K_{ca}} \right)$$

b. If diffusion in clothing can be ignored:

$$\frac{\partial C_m}{\partial t} = h_m \left(y - \frac{C_m}{L_m \cdot K_{ca}} \right)$$

Note: The diffusivity within the clothing material can be ignored, if the characteristic time required for clothing to reach equilibrium with the gas phase is much larger than the time required for diffusion to occur: $\frac{K_{ca} L_m}{h_m} \gg \frac{K_{ca} L_m^2}{D_m}$ (alternatively, if $\frac{h_m \cdot L_m}{D_m} \gg 1$).

Note: See Cao et al. 2016³ for further detail.

11. Clothing/particle partitioning

Model development needed

5) Exposure Modeling Equations

Note: The exposure modeling equations (Eq. 12-15) listed below do not account for different bioaccessibilities and have thus considered worst case scenarios. However, we recommend applying bioaccessibility factors if these are available.^{4, 5}

General conversion from exposure rate to daily intake:

$$DI = \frac{Ex \cdot d}{bw}$$

12. Direct Exposure

a. Dermal uptake via direct contact with a source:

Transfer from a solid source to skin surface: $Ex_{source_d} = J_{source_ssl} \cdot A_{contact}$

Transfer from liquid source to skin surface: $Ex_{source_d} = w_0 \cdot AR_{source} \cdot f_A \cdot f_{ret}$

Note: See Huang et al. 2017⁶, CHAP 2014⁷ and Wormuth et al. 2006⁸ for example approaches.

Transfer from skin surface to dermal capillaries: $J_{ssl_c} = C_{ssl} \cdot k_{p_ssl}$

b. Ingestion of a source:

$$Ex_{source_ing} = w_0 \cdot IR_{source}$$

c. Mouthing of a source:

$$Ex_{mouthing} = w_0 \cdot A_{mouthing} \cdot MR \cdot EF \cdot f_A \cdot d$$

13. Dermal uptake

a. From the gas phase to dermal capillaries:

$$Ex_{gas_d} = C_g \cdot k_{p_g} \cdot A_{exp}$$

Note: See Weschler and Nazaroff 2014⁹ for the calculation of k_{p_g} .

Note: See Gong et al. 2014¹⁰ and Morrison et al. 2016¹¹ for a dynamic modeling approach.

b. From airborne particles or dust particles:

$$Ex_{part_d} = F \cdot A_{exp} \cdot q_{part_skin} \cdot f_A$$

Note: See Wormuth et al. 2006⁸ and Giovanoulis et al. 2018¹² for values of f_A .

Note: F should be replaced by $P_{dust,s}$ for dust from sink surfaces and by $P_{dust,s}$ for dust from source surfaces.

c. From sink surfaces:

$$Ex_{surf_d} = C_s \cdot CR_s \cdot f_A$$

d. From clothing:

$$Ex_{cloth_d} = C_{ssl} \cdot k_{p_ssl} \cdot A_{exp}$$

$$C_{ssl} = K_{ssl} \cdot C_m$$

Note: See Morrison et al.¹³ and Cao et al. 2018¹⁴ for more detail. Eq. 13d is based on the assumption that the skin-surface lipids (SSL) are in equilibrium with the clothing. This is likely not the case for many

SVOCs because the timescale for reaching equilibrium¹⁵ is often longer than the duration of contact between clothing and the skin-surface lipids. Thus, this equation describes a worst case scenario.

14. Inhalation

Inhalation of gas phase and airborne particles:

$$Ex_{inh} = C_t \cdot IR_{inh}$$

$$\text{with } C_t = C_g + F$$

15. Ingestion

a. Ingestion of dust:

$$Ex_{dust_ing} = w_{dust} \cdot IR_{dust}$$

Note: For dust from sink surfaces, w_{dust} should be replaced by $w_{dust,s}$.

Note: w_{dust} can be approximated with f_{om_dust} .

b. Mouthing of objects/exposed clothing and hand-to-mouth:

See 13c. f_A might vary.

Note: Empirical equations available in Isaacs et al. 2014¹⁶ and Huang et al. 2017⁶.

6) Estimation Approaches for Model Parameters

I. Saturation vapor pressure (p_s)

Antoine equation (A, B, C are substance-specific coefficients)¹⁷:

$$\log(p_s) = A - \frac{B}{C + T}$$

Note: See Vyazovkin, Koga, and Schick 2018¹⁸ for an overview of experimental methods to determine the vapor pressure of chemicals with different volatilities. Wu et al. 2016¹⁹ developed a method to measure vapor pressure for SVOCs.

II. Octanol/air partition coefficient (K_{oa})

$$K_{oa} = \frac{K_{ow}}{K_{aw}} = \frac{K_{ow} \cdot R \cdot T}{H}$$

Relationship between p_s and K_{oa} :

$$K_{oa} = \frac{C_{o,sat}}{p_s/(RT)} = \frac{C_{o,sat}}{C_{a,sat}}$$

Figure S2: Comparison of K_{oa} values calculated by SPARC (ARChem) and the poly-parameter Linear-Free-Energy-Relationship (pp-LFER)²⁰ (LSER Database). The compounds in ascending order of K_{oa} (SPARC) values are DMP, DiBA, DnBA, DEP, DiBP, DnBP, TPP, DPP, DEHA, BBzP, TEHP, DINA, DEHTP, DINCH, DEHP, DINP, DPHP, and TOTM.

III. Gas-phase concentration immediately adjacent to the source (y_0)

General relationship between y_0 , p_s , and C_0 :

$$y_0 = \gamma \cdot w_0 \cdot p_s$$

$$\text{with } w_0 = \frac{C_0}{\rho_{product}}$$

For phthalates and phthalates alternatives (Eichler et al. 2018²¹):

$$y_0 = 3.70 \cdot w_0 \cdot p_s$$

For phthalates and organophosphate flame retardants (Liang et al. 2018²²):

$$y_0 = 3.405 \cdot w_0 \cdot p_s$$

IV. Mass-transfer coefficient (h_m)

$$h_m \text{ or } h_{m,s} = Sh \cdot \frac{D_a}{L_c}$$

$$Sh = 0.664 \cdot Re^{\frac{1}{2}} \cdot Sc^{1/3}$$

Note: This estimation of h_m and $h_{m,s}$ uses the correlations in Axley 1991²³. Typically, the average air velocity across interior surfaces is in the range of 0.01-0.16 m/s as reported by Huang et al. 2004²⁴. This value could be an underestimation, thus specific air velocity and characteristic lengths should be selected when estimating the mass transfer coefficient for particular indoor cases.

V. Gas/particle partition coefficient (K_p)

Definition (Pankow 1994²⁵):

$$K_p = \frac{F/TSP}{C_g}$$

Extended by Finizio et al. 1997²⁶:

$$K_p = \frac{f_{om_part} \times K_{oa}}{\rho_{part}}$$

$$\log(K_p) = \log(K_{oa}) + \log(f_{om_part}) - 11.91$$

Another method (Naumova et al. 2003²⁷, regression based on PAH data in atmosphere with PM_{2.5}):

$$\log(K_p) = -0.860 \log(p_s) - 4.67$$

See Salthammer and Schripp 2015²⁸ and Salthammer and Goss 2019²⁰ for more information on the determination of K_p .

VI. Dust/gas partition coefficient (K_{dust})

$$K_{dust} = \frac{P_{dust}}{C_g} = \frac{f_{om_dust} \times K_{oa}}{\rho_{dust}}$$

VII. Non-source surface/gas partition coefficient (K_s)

a. Wood floors, ceiling and walls, and furniture (Xu et al. 2009²⁹, regression for phthalates):

$$\log(K_s) = -0.779 \log(p_s) - 1.93$$

- b. Windows, mirrors, tile and ceramic fixtures:

Freundlich isotherm fitted by Xu and Little (2006)³⁰ for DEHP: $K_s = 3800$, $n = 1.5$

- c. Carpet (Xu et al. 2009²⁹, regression for phthalates):

$$\log(K_s) = -0.627 \log(p_s) - 1.08$$

- d. Stainless steel (Liang et al. 2018³¹):

Freundlich isotherm fitted for TCEP: $K_s = 31.6$, $n = 0.24$

Freundlich isotherm fitted for TCPP: $K_s = 67.1$, $n = 0.26$

- e. Polyurethane foam (Liang et al. 2019³²) depending on the temperature:

$$\text{For TCEP: } K_s = 2 \cdot 10^{-18} \cdot T^{0.5} \cdot e^{17335/T}$$

$$\text{For TCIPP: } K_s = 2 \cdot 10^{-16} \cdot T^{0.5} \cdot e^{15468/T}$$

- f. See also Liu et al. 2014³³ and Liu et al. 2016³⁴ for K_s values for polychlorinated biphenyls (PCBs) and organophosphorus flame retardants (OPFRs) for a variety of materials.

VIII. Gas/clothing partition coefficient (K_{ca})

- a. See Morrison et al. 2018³⁵ for gas/clothing partition coefficients for PCBs in cotton and polyester, and in blends of polyester, cotton, viscose/rayon, and/or elastane.
- b. See Cao et al. 2016³ for gas/clothing partition coefficients for diisobutyl phthalate (DiBP), di-n-butyl phthalate (DnBP), and bis(2-ethylhexyl) phthalate (DEHP) in cotton clothing.
- c. See Morrison et al. 2015³⁶ for gas/clothing partition coefficients for diethyl phthalate (DEP) and DnBP in cotton clothing.

7) Decision Tree

Figure S3: Decision tree for exposure mechanism selection based on source emission category.

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