Guidance Document for Conducting Class - based Exposure Assessments for Organohalogen Flame Retardants

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1. Introduction

An exposure assessment estimates or measures the magnitude, frequency, and duration of exposure to an agent and describes the population exposed (U.S. EPA, 2019b). Exposure assessments typically focus on single-pathway and single-chemical evaluations, wherein the results can be combined to determine aggregate (i.e., exposure to a single chemical from multiple sources and pathways) or cumulative (i.e., exposure to multiple chemicals from multiple sources and pathways) exposures. When multiple chemicals need to be evaluated, conducting assessments for each individual chemical can be time consuming. In addition, characterization of exposure requires information on the exposure scenario or chemical measurements from environmental media or biological matrices; however, there are often no data available to allow for exposure estimation.

This guide describes a process for conducting exposure assessments using a class-based approach for organohalogen flame retardants (OFRs) as an example. A class-based approach assesses multiple chemicals at one time, using the data available for data-rich members of the class and extrapolating to data-poor members in the class. Depending on the data available, class-based exposure estimates can be qualitative or semi-quantitative (e.g., providing exposure estimates for one chemical relative to another).

The focus of this guide is on OFRs, which are used in consumer and commercial products. In 2015, the Consumer Product Safety Commission (CPSC) was petitioned to ban the use of additive OFRs, as a class, from certain consumer products. In the 2019 report *A Class Approach to Hazard Assessment of Organohalogen Flame Retardants*, the National Academies of Sciences, Engineering, and Medicine (NASEM) subcommittee concluded that OFRs cannot be treated as a single class but rather 14 different subclasses of OFRs based on chemical structure, physicochemical properties, and predicted biological activity (NASEM, 2019). In this guide, the illustrative examples are based on a subset of OFRs from the polyhalogenated organophosphate (PHOP) subclass.

This guide, *Guidance Document for Conducting Class-based Exposure Assessments for Organohalogen Flame Retardants*, is a companion report to *Class-based Exposure Assessment of Polyhalogenated Organophosphate (PHOP) Flame Retardants*. The guide is written to cover many possible approaches for class-based exposure assessment. As the guide is applied to specific subclasses, approaches outlined herein may need to be adapted or refined based on available data and unique considerations specific to individual subclasses. CPSC staff can revisit the approaches described in the guide based on periodic review.

2. Overview of Class -based Exposure Assessment Approach

The overall class-based exposure assessment approach described here does not include the initial steps performed during the scoping phase (identifying potential sources of exposure and depicting these through a conceptual exposure model). This guide assumes there are sufficient data to proceed with exposure assessment using one or more of the exposure assessment methods described below for a subclass.

Several methods can be used to estimate exposure, with the choice dependent on data availability, the specific exposure scenario, and the purpose of the assessment, among other factors. In this guide, the following four methods are used:

1. Mechanistic models: use of mechanistic models based on first principles to estimate indoor environmental concentrations and/or doses associated with consumer products used in indoor or quasi-indoor environments.

2. Empirical measurements: includes (a) use of chemical migration measurements from products to people to estimate direct consumer exposure or (b) use of chemical emissions measurements from products to indoor environments to estimate indirect consumer exposure.

3. Indoor dust monitoring data: use of measured concentrations of indoor dust to estimate dose from all consumer products in an indoor environment.

4. Reverse dosimetry: use of occurrence data in biological matrices and chemical-specific toxicokinetic data to estimate the dose that would be consistent with the measured biomonitoring level.

For the purposes of this guide, the four methods listed above are referred to as Approach 1, Approach 2, Approach 3, and Approach 4, respectively. All chemicals in a subclass are first evaluated using mechanistic models (Approach 1). In this approach, consumer exposure scenarios, which describe how exposure takes place, are first identified and are each defined as a combination of the consumer product (i.e., source), the pathway, and the receptor. Using available use information, each chemical is then mapped to one or more exposure scenarios.

From a class-based perspective, potential uses for chemicals without product use information can be determined by extrapolating from chemicals with data (e.g., based on similar physicochemical properties, similar structures, or known material type-product relationships). The one exposure scenario that (i) covers all pathways and (ii) has the greatest number of chemicals with known or extrapolated uses is selected as the scenario to be modeled for all chemicals. With the exception of the physicochemical

properties, all other model inputs (e.g., product properties, environmental inputs, population inputs) remain the same across chemicals. The estimated exposures can then be used to identify trends or to rank chemicals relative to one another by pathway, with the resulting differences due solely to differences in the chemicals and not any other factor.

Chemicals are then evaluated using the three approaches below if data are available:

- Empirical measurements (Approach 2), which include migration data into saliva or the skin and emissions from products;
- Indoor dust monitoring data (Approach 3), which refer to settled dust measurements together with models for the corresponding chemical concentrations in vapor and airborne dust; and
- Occurrence data in biological matrices (Approach 4), which includes back-calculating the exposure needed to produce those biomarker levels.

Approach 2 will provide an estimated dose for a scenario, Approach 3 will provide an estimated total dose for all sources related to indoor dust for each chemical, and Approach 4 will provide an estimated total dose for all sources and pathways that a person is exposed to for each chemical. Exposure to chemicals without chemical-specific measured input data can be estimated relative to a chemical with data using the trends and relative rankings identified in Approach 1. For example, if a group of three chemicals have no indoor dust data available, but the mechanistic modeling results of Approach 1 show that all three chemicals have estimated doses that are an order of magnitude lower than the other chemicals in the subclass, this trend can be used to extrapolate that the doses calculated from indoor dust data for these three chemicals would be lower than the doses calculated from the other chemicals (see Table 1).

In the illustrative example below, it is assumed that modeled doses fall into three bins: approximately equal to, greater than, or less than a value; however, the actual data may show different trends (e.g., one chemical with a significantly higher dose and the remaining chemicals grouped into two ranges). The example also assumes that when data are available for Approaches 2, 3, and 4, the trends obtained from those modeled doses are consistent with the trends observed in Approach 1. However, different approaches may show different trends. These issues will need to be addressed using professional judgment.

Table 1. Illustrative Example for a Subset of Polyhalogenated Organophosphates Showing Extrapolation of Doses for Approaches 2, 3, and 4 Based on Trends Identified in Approach 1.

Chemical CASRN	Approach 1 (Mechanistic)	Approach 2 (Empirical)	Approach 3 (Indoor Dust)	Approach 4 (Reverse Dosimetry)
115-96-8	Modeled dose ~ b	Extrapolated dose ~ c	Modeled dose ~ d	Modeled dose ~ f
126-72-7	Modeled dose ~ b	Modeled dose ~ c	Modeled dose ~ d	Modeled dose ~ f
13674-84-5	Modeled dose ~ b	Extrapolated dose ~ c	Modeled dose ~ d	Modeled dose ~ f
13674-87-8	Modeled dose << b	Extrapolated dose < c	Extrapolated dose < d	Extrapolated dose < f
19186-97-1	Modeled dose << b	Extrapolated dose < c	Extrapolated dose < d	Extrapolated dose < f
38051-10-4	Modeled dose << b	Extrapolated dose < c	Extrapolated dose < d	Extrapolated dose < f
76025-08-6	Modeled dose ~ b	Extrapolated dose ~ c	Modeled dose ~ d	Extrapolated dose ~ f

b, c, d, f represent modeled dose values for Approaches 1, 2, 3, and 4, respectively.
Green cells = exposures modeled and results used to determine trends and relative rankings across chemicals.
Yellow cells = exposures modeled using available data.
Blue cells = no data available for modeling; exposures extrapolated using modeled results for data-rich chemicals and the trends identified in Approach 1.

Multiple approaches should be used to corroborate the calculated and extrapolated doses. For example, doses calculated using human biomonitoring and toxicokinetic data should be compared to results from the indoor dust approach as both methods consider exposure from multiple sources (no source attribution) but one is direct and the other is indirect. Biomonitoring results reflect both indoor dust and sources that do not result in indoor dust exposure; thus, the doses calculated using Approach 4 would be expected to be somewhat higher than those calculated using Approach 3. As another example, aggregates dose-calculated using Approach 1 (i.e., combining doses from background exposures and multiple exposure scenarios [see Section 3]) can be compared to doses calculated using Approach 4. If the doses calculated from the two approaches do not overlap (i.e., they are greater than 1–2 orders of magnitude apart from each other), this can indicate that some potential sources were not considered in Approach 1 (or too many sources were considered) or can reflect potential uncertainty in the reverse dosimetry.

When using trends from Approach 1 to extrapolate for the other approaches, the trends from these other approaches should also be evaluated. In the example above, if any of the three chemicals have human biomonitoring and toxicokinetic data, the calculated dose should be compared to doses of the other chemicals to determine whether the observed trend is consistent with that in Approach 1. In addition, as discussed here and in Section 6, the trends from Approach 1 can be used to qualitatively or semi-quantitatively inform the trends for Approach 4.

The following sections describe in more detail each of the four approaches.

3. Approach 1: Mechanistic Models

Approach 1 uses mechanistic models to estimate exposure to OFRs from consumer products in indoor or quasi-indoor (e.g., garage) environments. Exposure scenarios, wherein the source, pathway, and receptor are specified, are first developed to describe how exposure occurs. Model equations are based on well-established mechanistic processes informed by physicochemical properties, with the models requiring source inputs (physicochemical properties and material/product properties), environmental inputs (room volume, air exchange rate), and population inputs (exposure factors, activity patterns). For each exposure scenario, an estimated dose can be determined and is specific to that scenario. The assessor then considers which scenarios always, sometimes, or never co-occur to identify those that should be considered for aggregation. These estimated exposures are combined with background exposures to estimate aggregate exposure.

3.1. Consumer Exposure Scenarios

3.1.1. Sources

Exposure models for households often categorize sources into two types: products and articles. Models assume that products episodically release chemicals each time they are used and that products do not release chemicals when not being used. Exposure assessment for products requires information on who is using them and how often. Articles are sources that are continuously present and releasing chemicals into the home. Examples include furniture, carpets, appliances, drapes, etc. No "user" is required, although some articles may be contacted directly. The sources to be considered in the OFR assessments are nearly all articles. However, the generic term "product" is frequently used below to apply to both products and articles.

For each subclass, commercial and consumer products in which OFRs are, have been, or may potentially be used are first identified using five data sources: (i) Interstate Chemicals Clearinghouse's High Priority Chemicals Data System (HPCDS); (ii) EPA's Chemical Data Reporting (CDR) database; (iii) literature sources; (iv) patent data from PubChem; and (v) UL's Prospector database. Data from sources (i) through (iv) have already been downloaded and made available in CPSC's Market Use Report: Characterizing OFR Chemistries, Sources, and Uses in the U.S. and International Markets, Volumes 1 (Main Report) and 2 (Appendices) (IEc, 2022a; IEc, 2022b). These data sources provide the following information:

- HPCDS[1], CDR, and literature sources provide the commercial/consumer product, the specific OFR(s) present in the product, and, in some cases, the concentration(s) or concentration range(s) of the OFR(s).
- Patent data provides potential future uses of OFRs in commercial and consumer products. A keyword search can be used to identify a prioritized list of patent application abstracts for review.
- The UL's Prospector database provides information on the product, the OFR present, and the material. This information can be used to understand how different OFRs are used in different materials in consumer products.

For chemicals without any use information, the assessor can extrapolate potential product uses informed by multiple criteria, such as:

- A chemical in the same subclass with similar (i.e., ± a factor of 3) key physicochemical properties. These may include the octanol-air partition coefficient (log K_{OA}), octanol-water partition coefficient (log K_{OW}), vapor pressure, molecular weight, and others.
- A chemical in the same subclass with a similar structure. Chemical structures can be evaluated for similarity using the Tanimoto coefficient (T), wherein $T > 0.85$ is considered structurally similar.
- Known material type-product relationships derived from other chemicals in the subclass. For example, if two OFRs are known to be used in styrene polymer or copolymer but only one OFR has known applications of plastics, textiles, adhesives and coatings, and expanded and extruded polystyrene foams, it can be extrapolated that the second OFR could be used in the same applications.

Following review of these data sources and extrapolation from data-rich to data-poor chemicals, the assessor will have a list of products for each chemical in the subclass.

3.1.2. Exposure Pathways

Four mediated and two contact exposure pathways are considered and illustrated in Figure 1. In the mediated pathways, OFRs are emitted from products and partition between settled dust, airborne dust (particulates), and gas; exposure occurs through interaction with one of these media. In the contact pathways, the receptor interacts directly with the product.

1. Ingestion of indoor dust: this mediated pathway models incidental ingestion of settled dust (floor dust, surface dust).

[1] For HPCDS product descriptions, the HPCDS glossary directs the user to consult the GS1 Global Product Classification (GPC) standard.

2. Gas-phase air transfer to skin: this mediated pathway models the chemical deposition directly onto the skin from the gas phase, followed by dermal absorption.

3. Inhalation of particle dust: this mediated pathway models inhalation of airborne particulates, followed by absorption in the gastrointestinal tract.

4. Inhalation of gas: this mediated pathway models inhalation of gas, followed by lung absorption.

5. Dermal: this contact pathway models direct contact of the product with the skin, with chemical migration into the skin over time.

6. Mouthing/oral: this contact pathway models direct product-to-mouth contact, where the chemical migrates into saliva.

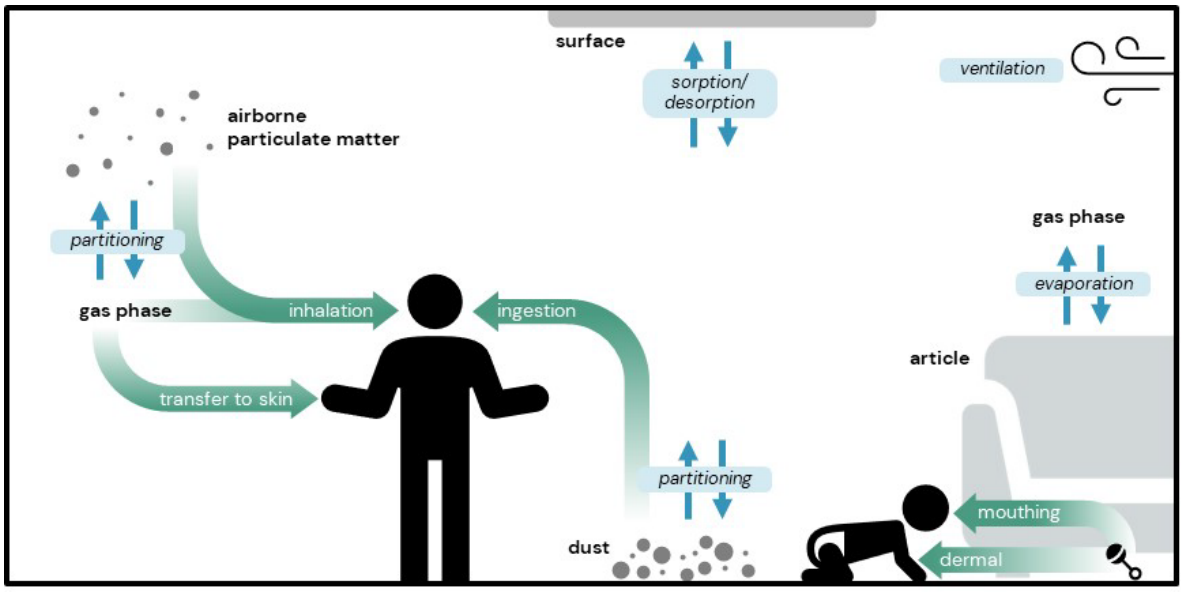

Figure 1. Schematic of the Chemical Movement from Source to Receptor through Various Media in an Indoor Environment .

3.1.3. Receptors

Human populations of all age groups are included.

3.1.4. List of Exposure Scenarios

To avoid having an overwhelming number of exposure scenarios across the 14 subclasses, a master list of exposure scenarios was first developed by combining the source information for all subclasses with the pathways and receptors considered . For a subclass , the list of relevant exposure scenarios is then a subset of this master list (i.e., a subclass will never have more scenarios than the master list).

Table 2 shows the master list of 18 exposure scenarios. Each of the specific consumer products identified is mapped to an exposure scenario. For example, televisions are mapped to "Non-handheld electronics and appliances where mediated exposure is likely for children and adults," whereas clothing is mapped to "Textiles where contact and mediated exposure is likely for children and adults." Each scenario is crosswalked to the six exposure pathways; relevant pathways for each scenario are indicated with an "x" in Table 2. A 19th scenario was also identified: "Handheld hard and soft plastic food contact materials (including rubber) where contact and mediated exposure is likely for children and adults"; however, most exposure via this scenario is considered under the U.S. Food and Drug Administration's jurisdiction (e.g., migration into food, mouthing as intended), rather than CPSC jurisdiction, and is therefore not modeled here.

The exposure scenarios and the exposure pathways considered here are consistent with the SVOCs consensus framework, a modular mechanistic framework for predicting human exposure that was developed by Eichler et al. (2020). The consensus framework classifies products into one of six source emission categories (solid, soft, frequent contact, applied, sprayed, and high temperature), and the 18 exposure scenarios in Table 2 can all be mapped to one of the emission source categories of the consensus framework. The first three of Eichler et al.'s (2020) six source emission categories contain nearly all of the 18 scenarios.

Table 2. Crosswalk of List of Consumer Exposure Scenarios Relevant to All OFR Subclasses , Example Products, and Pathways [a]

#	Exposure Scenario Description	Example Products	1	2	3	4	5	6
1	Handheld electronic casings (or appliances) where contact and mediated exposure is likely for children and adults	Cell phones, gaming devices, hairdryers	x	x	x	x	x	x
2	Non-handheld electronics and appliances where mediated exposure is likely for children and adults	Large televisions, computers, remote-controlled toy cars	x	x	x	x		
3	Small hand-held hard and soft plastic items (including foam) where contact and mediated exposure is likely for children and adults	Dolls, foam blocks, hard plastic bricks, artist and craft supplies, toys	x	x	x	x	x	x
4	Small hand-held hard and soft plastic items (including foam) where incidental ingestion/swallowing exposure is likely for children and adults	Play-based food/food serving products						x
5	Small hand-held rubber items where contact and mediated exposure is likely for children and adults	Bouncy/kick balls, dress up/Halloween masks, artist and craft supplies, toys	x	x	x	x	x	x
6	Large stationary hard and soft plastic items (including foam and rubber) where mediated exposure is likely for children and adults	Doll houses, playhouses, block-based castles, foam play forts/sofas, outdoor play structures	x	x	x	x		
7	Wearable plastic, rubber, or foam clothing and clothing accessories where contact and mediated exposure is likely for children and adults	Costume jewelry, rain gear (coats, boots, etc.), costumes	x	x	x	x	x	x
8	Textiles where contact and mediated exposure is likely for children and adults	Clothing, bedding, costumes, baby carriers and swings, car/booster seats, play pens	x	x	x	x	x	x
9	Textiles where mediated exposure is likely for children and adults	Wallpaper, tents, play tunnels, outdoor play structures	x	x	x	x		
10	Portable and stationary furnishings where contact and mediated exposure is likely for children and adults	Sofas, chairs, ottomans, car seats (foam)	x	x	x	x	x	x
11	Mattresses and mattress toppers where contact and mediated exposure is likely for children and adults	Innerspring mattresses, foam mattresses, mattress pads/toppers, waterproof mattress covers	x	x	x	x	x	x
12	Infant nap pads where contact and mediated exposure is likely for children	Nap pads	x	x	x	x	x	x

#	Exposure Scenario Description	Example Products	1	2	3	4	5	6
13	Foam carpet backing where contact and mediated exposure is likely for children and adults	Foam carpet backing, rubberized carpet backing (in carpet tiles), rubber flooring, foam or rubber floor mats	x	x	x	x	x	x
14	Prefabricated building insulation where mediated exposure is likely for children and adults	Prefabricated insulation (EPS, XPS panels)	x	x	x	x		
15	Custom site-applied building insulation where mediated exposure is likely for children and adults	Site-applied insulation (SPF)	x	x	x	x		
16	Coatings, adhesives, sealants, and elastomers for building materials where mediated exposure is likely for children and adults	Insulation (liquid applied), paint, stains, resins, floor wax	x	x	x	x		
17	Other task-based renovation, repair, or refurbishment of an existing exposure scenario	Products and Pathways determined on a case-by case basis	-	-	-	-		
18	Large stationary wooden (and other materials not covered elsewhere) structures where mediated exposure is likely for children and adults	Wood, wood-engineered products	X	x	x	x		
19	Handheld hard and soft plastic food contact materials (including rubber) where contact and mediated exposure is likely for children and adults	Products and Pathways determined on a case-by-case basis. Some of these are outside of CPSC's jurisdiction.					-	-

EPS = expanded polystyrene; XPS = extruded polystyrene; SPF = spray polyurethane foam.

[a]Pathway numbers refer to: 1= ingestion of indoor dust; 2 = gas-phase air transfer to skin; 3 = inhalation of particle dust; 4 = inhalation of gas; 5 = dermal contact; 6 = mouthing.

3.2. Available Tools

Several exposure modeling tools are readily available for use to estimate exposure from specific consumer products. The five tools considered have well-established documentation and/or were peer reviewed. The relevant processes and associated mathematical equations of each tool are described in their corresponding user's guide or web documentation, with a brief summary of the tool provided below.

- EPA's Consumer Exposure Model (CEM): CEM contains 21 individual models to estimate exposure to chemicals in consumer products—6 emission models, 3 inhalation models, 5 ingestion models, and 7 dermal models—and can distinguish between user and bystander exposure. Notably, CEM has a mass balance model for estimating emissions, indoor fate and transport, and exposure to SVOCs originating in consumer articles. The tool comes with 73 predefined product and article use scenarios and parameter estimators that can be used in the absence of published data. Users can also create new scenarios or modify existing scenarios as needed. Only one chemical and one product/article can be handled in each run. Both acute and chronic exposures are reported for persons of various ages, by exposure pathway.
- EPA's Stochastic Human Exposure and Dose Simulation-High Throughput (SHEDS-HT) model: SHEDS-HT belongs to the SHEDS series of models, which are probabilistic models that estimate the population distribution of total chemical exposure from four pathways: inhalation, skin contact, dietary ingestion, and non-dietary ingestion. In SHEDS-HT, the simulated individuals form a representative sample of the target population, and the model simulates one day for each individual, although the simulated day is not necessarily the day a product is used (this is not a relevant concern for articles since they are always present). Doses are reported by pathway and in total as distributions of daily exposure across the population (i.e., acute and chronic exposures are not reported separately). SHEDS-HT can handle many products and chemicals in one run. Predefined scenarios are not available, but example input files exist and can be modified.
- EPA's Indoor Environmental Concentrations in Buildings with Conditioned and Unconditioned Zones (IECCU): IECCU is a higher-tier tool originally designed for complex consumer product spray polyurethane foam. IECCU estimates gas phase, airborne particulate, and settled dust concentrations in buildings with multiple zones (including unconditioned attics, wall cavities, and crawl spaces) and multiple sources and sinks. Acute and chronic exposures for adults can be estimated from the modeled concentrations.
- RIVM's ConsExpo: ConsExpo is a web-based application that models exposures to chemicals found in a wide range of consumer products. ConsExpo provides a

number of generally applicable exposure models, with defaults available via a built-in database, or users can create their own assessments. Six inhalation models, five dermal models, and five ingestion (called "oral") models are available. Each ConsExpo run is for one chemical, one product, and one target person. For most inputs, the user can enter point values or distributions, with the latter used for probabilistic assessments. For inhalation exposures, ConsExpo does not distinguish between vapor and particulate phases in air. Both acute and chronic exposures are output in one run; adult and children must be run separately.

- RIVM's DustEx: DustEx is an online tool for modeling dust-mediated exposure to sources in homes. Four pathways are considered: inhalation of gas phase, inhalation of airborne particulates, dermal absorption from gas phase, and oral ingestion. The model effectively consists of a single room containing the source, sorption surfaces, floor and airborne dust, and a person, with cleaning and ventilation rates for the room. Both deterministic and probabilistic evaluations are possible, with default values available for several of the inputs.

The five tools can be divided into Tier 1 (simple or screening-level) or Tier 2 (complex) tools based on (i) the number of inputs required and the ability to generate those inputs and (ii) the type of output (i.e., deterministic versus probabilistic). Using a Tier 1 tool repeatedly while varying inputs to establish ranges of output can also be considered a Tier 2 exercise. For the purposes of this class-based exposure assessment, the Tier 1 tools were considered to be CEM, SHEDS-HT, and ConsExpo, and the Tier 2 tools were IECCU and DustEx, recognizing that some tools may have both simple and complex parts. Tier 2 tools are used if the results from Tier 1 modeling are of interest (e.g., high exposure). For example, for prefabricated building insulation by which mediated exposure is likely for children and adults (scenario # 14), the predefined scenario "Plastic articles: Foam Insulation" in CEM can be used to model Tier 1 exposure. If Tier 2 modeling is needed, IECCU can be used.

3.2.1. Tool Selection

To help select the appropriate Tier 1 tool, Table 3 provides a brief comparison of CEM, SHEDS-HT, and ConsExpo with respect to the exposure pathways modeled and the output types. More detail is available in Appendix A.

Table 3. Comparison of CEM, SHEDS-HT, and ConsExpo.

	CEM	SHEDS-HT	ConsExpo
Exposure Pathways			
Ingestion of indoor dust	Yes	Yes	No
Gas-phase air transfer to dermal	Yes	No	No
Inhalation of particle dust	Yes	Yes	No
Inhalation of gas	Yes	Yes	Yes
Dermal contact	Yes	Yes	Yes
Mouthing/oral	Yes	Yes	Yes
Model Outputs			
Acute exposure or chronic exposure	Both	No[a]	Both
Adult or child population	Both	Both	Both[b]
Point estimates or population distribution	Point Estimates	Population Distribution	Both

[a]Doses are reported as a distribution across the population, which includes both acute and chronic cases.
[b]One simulation does not provide results for both adults and children; separate simulations are required.

To limit the number of modeling runs needed, CEM is the suggested tool to use because it models all six exposure pathways. CEM provides a summary report of each run listing input settings and exposure results. Note that while CEM is the preferred choice of the three shown here, it has its limitations. In particular, it requires a separate run for each chemical or product/article of interest.

Table 4 shows the mapping of the 18 exposure scenarios to CEM's predefined scenarios. Within CEM, the term "exposure model" is used to describe an exposure pathway. Table 4 also lists the CEM exposure models that may be selected for each of the 18 exposure scenarios.

Table 4. Crosswalk of Exposure Scenarios to CEM's Predefined Scenarios and Relevant CEM Exposure Models.

#	Exposure Scenario Description	CEM Scenario (s)	CEM Exposure Model (s)
1	Handheld electronic casings (or appliances) where contact and mediated exposure is likely for children and adults	Electronic appliances	A_INH1, A_ING1, A_ING2, A_ING3, A_DER1, A_DER2, A_DER3
2	Non-handheld electronics and appliances where mediated exposure is likely for children and adults	Electronic appliances	A_INH1, A_ING1, A_ING3, A_DER1, A_DER3
3	Small hand-held hard and soft plastic items (including foam) where contact and mediated exposure is likely for children and adults	Plastic articles: Other objects with potential for routine contact (toys, foam blocks, tents)	A_INH1, A_ING1, A_ING2, A_ING3, A_DER1, A_DER2, A_DER3
4	Small hand-held hard and soft plastic items (including foam) where incidental ingestion/swallowing exposure is likely for children and adults	Plastic articles: Objects intended to be mouthed (pacifiers, teethers, toy food)	A_ING2
5	Small hand-held rubber items where contact and mediated exposure is likely for children and adults	Rubber articles: with potential for routine contact (baby bottle nipples, pacifiers, toys)	A_INH1, A_ING1, A_ING2, A_ING3, A_DER1, A_DER2, A_DER3
6	Large stationary hard and soft plastic items (including foam and rubber) where mediated exposure is likely for children and adults	Plastic articles: Foam insulation	A_INH1, A_ING1, A_ING3, A_DER1, A_DER3
7	Wearable plastic, rubber, or foam clothing and clothing accessories where contact and mediated exposure is likely for children and adults	Plastic articles: Other objects with potential for routine contact (toys, foam blocks, tents) Rubber articles: with potential for routine contact (baby bottle nipples, pacifiers, toys)	A_INH1, A_ING1, A_ING2, A_ING3, A_DER1, A_DER2, A_DER3
8	Textiles where contact and mediated exposure is likely for children and adults	Fabrics: Blanket, comfort object, fabric doll, stuffed animal Fabrics: Clothing Fabrics: Furniture covers, car seat covers, tablecloths	A_INH1, A_ING1, A_ING2, A_ING3, A_DER1, A_DER2, A_DER3
9	Textiles where mediated exposure is likely for children and adults	Fabrics: Curtains, rugs, wall coverings	A_INH1, A_ING1, A_ING3, A_DER1, A_DER3

#	Exposure Scenario Description	CEM Scenario (s)	CEM Exposure Model (s)
10	Portable and stationary furnishings where contact and mediated exposure is likely for children and adults	Fabrics: Furniture covers, car seat covers, tablecloths	A_INH1, A_ING1, A_ING2, A_ING3, A_DER1, A_DER2, A_DER3
11	Mattresses and mattress toppers where contact and mediated exposure is likely for children and adults	Plastic articles: Mattresses	A_INH1, A_ING1, A_ING2, A_ING3, A_DER1, A_DER2, A_DER3
12	Infant nap pads where contact and mediated exposure is likely for children	Plastic articles: Other objects with potential for routine contact (toys, foam blocks, tents) Rubber articles: with potential for routine contact (baby bottle nipples, pacifiers, toys)	A_INH1, A_ING1, A_ING2, A_ING3, A_DER1, A_DER2, A_DER3
13	Foam carpet backing where contact and mediated exposure is likely for children and adults	Rubber articles: Flooring, rubber mats	A_INH1, A_ING1, A_ING2, A_ING3, A_DER1, A_DER2, A_DER3
14	Prefabricated building insulation where mediated exposure is likely for children and adults	Plastic articles: Foam insulation	A_INH1, A_ING1, A_ING3, A_DER1, A_DER3
15	Custom site-applied building insulation where mediated exposure is likely for children and adults	Plastic articles: Foam insulation	A_INH1, A_ING1, A_ING3, A_DER1, A_DER3
16	Coatings, adhesives, sealants, and elastomers for building materials where mediated exposure is likely for children and adults	Generic article	A_INH1, A_ING1, A_ING3, A_DER1, A_DER3
17	Other task-based renovation, repair, or refurbishment of an existing exposure scenario	Generic article	Depends on details of scenario
18	Large stationary wooden (and other materials not covered elsewhere) structures where mediated exposure is likely for children and adults	Wood articles: hardwood floors, furniture	A_INH1, A_ING1, A_ING3, A_DER1, A_DER3

3.2.2. Input Data

The equations used in CEM to model exposure are available in the CEM User's Guide (U.S. EPA, 2019a). For the relevant CEM exposure models (A_INH1, A_ING1, A_ING2, A_ING3, A_DER1, A_DER2, and A_DER3), CEM has built-in estimators or default values for many of the required input variables. Table 5 lists the inputs that must be provided by the assessor (i.e., estimators are not available in CEM).

Table 5. CEM Inputs Required from the User.

Variable	Units	Source
Chemical Inputs		
Vapor pressure	torr	Possible sources for measured or estimated values: • PubChem • CompTox Chemicals Dashboard • EPI Suite • OPERA
Molecular weight	g/mol	See above
Octanol-water partition coefficient	-	See above
Octanol-air partition coefficient	-	See above
Water solubility	mg/mL	See above
Henry's law constant	atm-m^3/mol	See above
Product Inputs		
Density of product/article	g/cm^3	Defaults are provided, but the assessor should update the values for the specific article.
Surface area of article	m^2	See above
Thickness of article surface layer	cm	See above
Duration of article contact	min/day	See above
Area of article mouthed	cm^2	See above
Chemical migration rate	mg/cm^2/hr	See above
Frequency of article contact	events/day	See above

3.3. Modeling Runs

The model runs required are listed below, with an illustrative example provided in Table 6.

1. Model one scenario across all chemicals, as described in Section 2, wherein all modeling inputs remain the same across chemicals except the physicochemical properties. These results are used to determine trends or relative rankings of

chemicals, and the trends are applied to extrapolate doses for other approaches (as described in Section 2) and for other chemical-scenario combinations.

   a. As indicated in Section 2, the scenario selected has the greatest number of chemicals with known or extrapolated uses and must include all six exposure pathways so the relative contribution of each pathway can be determined. It is possible that some chemicals do not have known or extrapolated uses for the selected scenario—these chemicals will still be modeled.

2. Model one chemical across all scenarios—these results are used to determine the relative contribution of each scenario.
   a. The chemical selected is the one with the most known or extrapolated use scenarios.

3. Use results from the steps above to extrapolate exposures for remaining chemical-use scenarios. Extrapolation consists of using ratios to adjust for (i) difference in chemical properties, (ii) difference in scenario, and (iii) difference in chemical concentration in the product.

4. Model a subset of chemical-use scenarios to validate the extrapolated results.

Table 6. Illustrative Example for a Subset of Polyhalogenated Organophosphates Showing Chemical-use Scenarios Modeled, Extrapolated, and Validated.

Chemical CASRN	Electronic appliances	Plastic articles: Other objects with potential for routine contact (toys, foam blocks, tents)	Plastic articles: Foam insulation	Plastic articles: mattresses	Fabrics: Curtains, rugs, wall coverings	Fabrics: Blanket, comfort object, fabric doll, stuffed animal
115-96-8		x			x	
126-72-7		x				
13674-84-5	x	x	x	x	x	x
13674-87-8		x		x	x	x
19186-97-1						
38051-10-4						
76025-08-6				x		

x = known or extrapolated use.
Green cells = exposures modeled and results used to determine trends and relative rankings or contributions.
Blue cells = exposures extrapolated from modeled runs.
Yellow cells = exposures extrapolated from modeled runs and validated directly by running CEM.

3.4. Background and Aggregate Exposures

Background exposures from non-consumer products can be estimated using monitoring data. Relevant pathways include dietary ingestion, drinking water ingestion, soil ingestion, and inhalation of outdoor air. Monitoring data can be obtained from (i) the Multimedia Monitoring Database (MMDB), a database compiled from existing reputable monitoring databases, (ii) the Comparative Toxicogenomics Database (CTD), and (iii) literature screening efforts. Background exposures are added to the scenario-based exposures to estimate aggregate exposure.

4. Approach 2 : Empirical Measurements

Approach 2 uses empirical measurements (e.g., product testing emissions data, migration data) to estimate exposure to OFRs from consumer products. Similar to Approach 1 (mechanistic models), exposure scenarios are first developed and the estimated exposures are combined with background exposures to obtain an aggregate exposure. Typically, only one or two equations are needed to estimate exposure, and the primary input is an experimentally measured value. The distinction between Approach 1 and Approach 2 is not always clear because Approach 1 may use empirical measurements in its modeling. For the purposes of this guide, the two approaches are differentiated as follows:

Approach 1:

- Model equations are based on first principles with inputs from chemical, product, and environmental properties.
- Empirical measurements may be used as modeling inputs.

Approach 2:

- Uses empirical measurements to calculate dose in one step or
- First extrapolates empirical measurements to a different set of conditions (e.g., different temperature or indoor environment) using regressions, then uses extrapolated value to calculate dose.
- Equations are not based on first principles.

The following sections briefly describe four types of empirical measurements used. Note that some of the parameters for which empirical measurements can be obtained can also be derived mechanistically; an example is provided in the first section below.

4.1. Migration Rates into Saliva

Chemical migration rates from product to saliva can be used to estimate direct product-to-mouth contact, also referred to as mouthing. Testing is conducted using artificial saliva, which are commercially available or can be prepared on site in the laboratory. Using the measured migration rate, the dose can be estimated as (Aurisano et al., 2022):

$$Dose = \frac{R_{mgr} \times A_{contact} \times t_m}{BW} \quad \text{(Eq. 1)}$$

Where:

$Dose$ = (µg/kg/day)
R_{mgr} = migration rate of chemical to saliva (µg/10 cm^2/min)
$A_{contact}$ = mouthing contact area (cm^2)
t_m = mouthing duration per day (min/day)
BW = body weight (kg)

The migration rate can be determined experimentally, or it can be estimated from a regression model fit to the measured values.

In addition to experimentally measuring migration rates, they can be predicted mechanistically, and in that instance, the derived dose would be considered an example of Approach 1. An example of both approaches from Aurisano et al. (2022) is shown below.

- Approach 1 (referred to as mechanistic material-saliva model): Aurisano et al. (2022) adapted a previously developed mechanistic model for chemicals in food packaging to predict the migration from children's products into saliva. The adapted model consists of a short-term diffusion-dominated model and a longer-term two exponentials saturation model. The model is applicable for organic chemicals and does not require specific experimental data. The final set of equations is given by:

$$R_{mgr} = \frac{f_{mgr} \times m_0}{A_{contact} \times t} \quad \text{(Eq. 2)}$$

$$f_{mgr} = \begin{cases} f_{ts}, if\ t \le t_{dev} \\ f_{tdev} + \left(\frac{\alpha}{1+\alpha} - f_{tdev}\right) \cdot \left(A \cdot \left(1 - e^{-B \cdot \beta \cdot (t - t_{dev})}\right) + (1 - A) \cdot \left(1 - e^{-C \cdot \beta \cdot (t - t_{dev})}\right)\right), if\ t > t_{dev} \end{cases} \quad \text{(Eq. 3)}$$

$$t_{dev} = \begin{cases} \frac{d_p^2}{D_p} \cdot \left(\frac{0.3552}{1 + 85.88 \cdot e^{-3.506 \cdot \log(\alpha)}}\right), if\ \alpha > 0.2; \\ \frac{d_p^2}{D_p} \cdot 0.0085 \cdot e^{4.458 \cdot \log(\alpha)}, if\ \alpha \le 0.2 \end{cases} \quad \text{(Eq. 4)}$$

$$f_{ts} = \frac{2}{d_p} \cdot \left(\frac{D_p \cdot t}{\pi}\right)^{1/2} \quad \text{(Eq. 5)}$$

$$f_{tdev} = \frac{2}{d_p} \cdot \left(\frac{D_p \cdot t_{dev}}{\pi}\right)^{1/2} \quad \text{(Eq. 6)}$$

$$\alpha = \frac{1}{K_{pf}} \cdot \frac{V_f}{V_p} \quad \text{(Eq. 7)}$$

$$\beta = \frac{1}{d_p} \cdot \sqrt{\frac{D_p}{\pi \cdot t_{dev}} \cdot \left(\frac{\alpha}{1+\alpha} - f_{tdev}\right)} \quad \text{(Eq. 8)}$$

$$A = 0.7\ for\ x_1 = 10^{0.12 \cdot \log(\alpha) + \log(0.8)} < 0.7; 1\ for\ x_1 > 1;\ x_1\ elsewhere \quad \text{(Eq. 9)}$$

$$B = 0.3\ for\ x_2 = 10^{0.22 \cdot \log(\alpha) + \log(0.5)} < 0.3; 0.9\ for\ x_2 > 0.9;\ x_2\ elsewhere \quad \text{(Eq. 10)}$$

$$C = 0.004\ for\ x_3 = 10^{0.7 \cdot \log(\alpha) + \log(0.08)} < 0.3; 1\ for\ x_3 > 1;\ x_3\ elsewhere \quad \text{(Eq. 11)}$$

Where:

R_{mig} = migration rate of chemical to saliva (µg/10 cm^2/min)
f_{mgr} = fraction of the product of the chemical originally in that product that is migrated to the saliva after a certain duration (-)
m_0 = initial chemical mass in the product (µg)
$A_{contact}$ = mouthing contact area (cm^2)
t = mouthing duration (min in R_{mgr} Eq. 2; s in f_{mgr} in Eq. 3)
t_{dev} = time of deviation from the simple diffusion model (s)
d_p = thickness of the product (cm)
D_p = chemical's diffusion coefficient inside the product (cm^2/s)
K_{pf} = chemical's product-food (here product-saliva) partition coefficient (-)
V_f = volume of food (here saliva) (cm^3)
V_p = volume of product (cm^3)

- Approach 2 (referred to as regression-based model): Aurisano et al. (2022) performed a systematic literature review and collected data on 437 chemical

migration rates into saliva from 66 unique chemical-material combinations. These data originate from 60 chemicals, including polybrominated diphenyl ethers, and from five materials, spanning seven orders of magnitude. The authors performed a multiple linear regression using forward parameter selection. The final regression model is given by:

$$\log_{10}R_{mgr} = 3.23 + 0.73log_{10}D_p + 0.92log_{10}C_0 - 0.06log_{10}K_{ow} \quad \text{(Eq. 12)}$$

Where:

R_{mgr}= migration rate of chemical to saliva (µg/10 cm^2/min)
D_p = chemical's diffusion coefficient inside the product (cm^2/s)
C_0 = initial chemical concentration in the product (µg/g)
K_{ow} = octanol-water partition coefficient (-)

4.2. Handwipe Data

Handwipe data can be used to measure a chemical on skin surface directly. Using these data, direct dermal exposure can be estimated as (Tay et al., 2018):

$$Dose = \frac{C_{hw} \times SA \times AF \times ED \times EF}{BW \times 24} \quad \text{(Eq. 13)}$$

Where:

$Dose$ = (pg/kg/day)
C_{hw} = surface area normalized chemical mass of chemical in handwipes (pg/cm^2)
SA = hand skin surface area exposed per event (cm^2/event)
AF = absorption fraction (-)
ED = exposure duration in one day (t/24, where in t is assumed to be 24 hr or 1 day)
EF = exposure frequency (event/day, assumed to be 1)
BW = body weight (kg)
24 = (hr/day)

4.3. Product Emissions

Emission of chemicals from articles can be characterized by a parameter "y_0" that measures the equilibrium chemical concentration in air in the boundary layer near the object. The parameter y_0 depends on the type of material in the article and the content of the chemical of interest and is defined as:

$$y_0 = \frac{C_0}{K_{ma}} \quad \text{(Eq. 14)}$$

Where:

y_0 = equilibrium chemical concentration in air close to the solid material (µg/m^3)
C_0 = content of the chemical in the solid material (µg/m^3)
K_{ma} = material-air partition coefficient (-)

y_0 is simple to measure in laboratory experiments on a variety of articles without destructive analysis. Approximately 10 methods have been developed for experimental determination of y_0. They fall into two groups: dynamic chamber methods and static chamber methods.

The steady state gas-phase concentration is related to y_0 by:

$$y = \frac{y_0}{1+\frac{Q_{star}}{h\_y_0 \times f\_area \times a\_floor}} \quad \text{(Eq. 15)}$$

Where:

y = steady state vapor phase concentration in house (µg/m^3)
y_0 = vapor phase concentration near article surface (µg/m^3)
Q_{star} = modified air exchange rate with outdoors (m^3/hr)
h_y_0 = gas-phase mass transfer coefficient (m/hr)
f_area = ratio of article surface area to floor area (-)
a_floor = floor area of the house (m^2)

Inhalation exposure due to the gas phase can be estimated as:

$$AD_{inh} = \frac{(C_g \times 10^{-3}) \times Inh \times f_{home} \times f_{abs\_inh}}{BW} \quad \text{(Eq. 16)}$$

Where:

AD_{inh} = inhalation absorbed dose (mg/kg/day)
C_g = concentration of chemical in gas-phase (µg/m^3)
Inh = inhalation rate (m^3/day)
f_{home} = fraction of time spent at home (-)
f_{abs_inh} = absorption fraction for inhalation (-)
BW = body weight (kg)
10^{-3} = (mg/µg)

Note that to account for particle-bound concentrations, additional equations are needed (see Section 5.1).

The y_0 approach described above assumes the OFR emissions from indoor sources do not change over time. For non-steady state emissions, there are over 30 mass transfer

models available for predicting semi-volatile organic compound emission rates as a function of time, with all requiring three key parameters: the initial content of the chemical in the solid material (C_0 in µg/m^3), the material/air partition coefficient (K_{ma}, dimensionless), and the solid-phase diffusion coefficient (D_m in m^2/h).

4.4. Personal Air Monitoring

Personal inhalation exposure can be estimated using personal air monitoring devices. These are small badge-like instruments that attach to one's lapel, and they measure the air concentration in the personal bubble near the nose and mouth. Because these are co-located with the exposed person, there is no need to characterize sources or the time/location data for the person. This is both an advantage and a disadvantage; these devices are easy to use, but when an exposure occurs, the source of the chemical is not always apparent. The concentrations measured reflect time spent indoors, outdoors, and commuting; for only indoor exposures, the data would need to come from studies in which the participants were only indoors.

Personal inhalation exposure can be estimated as:

$$AD_{inh} = \frac{(C \times 10^{-3}) \times Inh \times f_{abs\_inh}}{BW} \quad \text{(Eq. 17)}$$

Where:

AD_{inh} = inhalation absorbed dose (mg/kg/day)
C = concentration of chemical in air (µg/m^3)
Inh = inhalation rate (m^3/day)
f_{abs_inh} = absorption fraction for inhalation (-)
BW = body weight (kg)
10^{-3} = (mg/µg)

5. Approach 3: Indoor Dust Monitoring Data

Approach 3 estimates exposure to OFRs based on chemical measurements of settled dust and relevant chemical properties. The estimated exposure represents the aggregate exposure to all consumer products in an indoor environment. There are three phases to consider for the chemical—settled dust, airborne dust (particulates), and gas—and three exposure pathways are evaluated: (i) inhalation (gas + particulates), (ii) ingestion (settled dust), and (iii) dermal deposition from gas phase. The associated equations are based on those of Weschler and Nazaroff (2010) to determine chemical partitioning between the three phases at steady state and Mitro et al. (2016)/Pelletier et al. (2017) to estimate exposure via the three exposure pathways. See source publications for equation

derivations. A fourth pathway—dermal intake through dust adherence—is not included, with both Mitro et al. (2016) and Pelletier et al. (2017) noting that this pathway is expected to be minor, and the input parameters required are often not available.

5.1. Equations

The goal is to estimate chemical concentrations in gas (vapor) and airborne particulates from measurements of X_{dust}, the chemical concentration in the settled house dust. This may be achieved either by assuming chemical equilibrium or by solving for steady-state dynamic balance. Once all the concentrations are known, the three exposure pathways may be evaluated.

5.1.1. Settled Dust to Gas

From Weschler and Nazaroff (2010), gas-phase chemical concentration can be calculated as:

$$C_g = \frac{(\rho_{dust} \times 10^{12}) \times X_{dust}}{f_{om\_dust} \times K_{oa}} \quad \text{(Eq. 18)}$$

Where:

C_g = gas-phase chemical concentration (µg/m^3)
ρ_{dust} = density of settled dust particles (g/cm^3)
X_{dust} = chemical mass fraction in settled dust (-)
f_{om_dust} = organic matter fraction in settled dust (-)
K_{oa} = octanol-air partition coefficient (-)
10^{12} = (µg/g) × (cm^3/m^3)

The above equation represents the default method of estimating gas-phase concentration from settled dust (using chemical equilibrium), with studies in the literature building on this work to consider additional factors. For example, Li et al. (2022) considered the rate at which a chemical can move from gas phase to airborne particles and balanced that against the rate of loss of airborne particles by air exchange or deposition. Their assumption is that the replacement particles are free of the chemical, and hence, the airborne particles never achieve full chemical equilibrium with the gas phase (this matters primarily at high K_{oa} values).

Use of these alternative approaches and/or different input values for f_{om_dust}, ρ_{dust}, and K_{oa} would provide a range of estimates and could be used to estimate variability.

5.1.2. Gas to Air (Gas + Particulates)

From Weschler and Nazaroff (2010), particulate-phase chemical concentration can be calculated as:

$$C_p = \frac{C_g \times TSP \times f_{om\_part} \times K_{oa}}{(\rho_{part} \times 10^{12})} \quad \text{(Eq. 19)}$$

Where:

C_p = concentration of chemical attached to airborne particles (µg/m^3)
C_g = gas-phase chemical concentration (µg/m^3)
TSP = total suspended particulates (µg/m^3)
f_{om_part} = organic matter fraction in airborne particles (-)
K_{oa} = octanol-air partition coefficient (-)
ρ_{part} = density of airborne particles (g/cm^3)
10^{12} = (µg/g) × (cm^3/m^3)

Total air concentration is then estimated as:

$$C_a = C_g + C_p \quad \text{(Eq. 20)}$$

Where:

C_a = concentration of chemical in gas-phase and attached to airborne particles (µg/m^3)
C_p = concentration of chemical attached to airborne particles (µg/m^3)
C_g = gas-phase chemical concentration (µg/m^3)

5.1.3. Inhalation of Air (Gas + Particulates)

Based on the equations from Mitro et al. (2016) and Pelletier et al. (2017), the inhalation absorbed dose is given by:

$$AD_{inh} = \frac{(C_a \times 10^{-3}) \times Inh \times f_{home} \times f_{abs\_inh}}{BW} \quad \text{(Eq. 21)}$$

Where:

AD_{inh} = inhalation absorbed dose (mg/kg/day)
C_a = concentration of chemical in gas-phase and attached to airborne particles (µg/m^3)
Inh = inhalation rate (m^3/day)
f_{home} = fraction of time spent at home (-)
f_{abs_inh} = absorption fraction for inhalation (-)

BW = body weight (kg)
10^{-3} = (mg/µg)

Intake doses can be calculated by excluding the f_{abs_inh} term.

5.1.4. Ingestion of Settled Dust

Based on the equations from Mitro et al. (2016) and Pelletier et al. (2017), the ingestion absorbed dose is given by:

$$AD_{ing} = \frac{X_{dust} \times Ing \times f_{home} \times f_{abs\_ing}}{BW} \quad \text{(Eq. 22)}$$

Where:

AD_{ing} = ingestion absorbed dose (mg/kg/day)
X_{dust} = chemical mass fraction in settled dust (-)
Ing = dust ingestion rate (mg/day)
f_{home} = fraction of time spent at home (-)
f_{abs_ing} = absorption fraction for ingestion (-)
BW = body weight (kg)

Intake doses can be calculated by excluding the f_{abs_ing} term.

Ingestion of settled dust can occur via two ways: mouthing of dust objects, such as plush toys, or first getting dust on the hands and then transferring by hand-to-mouth contact. The Ing variable in the equation above is the sum of the two. An additional variable f_{ing_htm} may be added to distinguish the fraction of the ingestion amount coming from the hands. This is relevant to prevent double counting if a dermal absorption pathway for dust is included in the model. Thus, the dust mass ingested from the hands is:

$$Ing_{hands} = Ing \times f_{ing\_htm} \quad \text{(Eq. 23)}$$

Where:

Ing_{hands} = dust ingestion rate due to hand-to-mouth transfer (mg/day)
Ing = dust ingestion rate (mg/day)
f_{ing_htm} = fraction of ingested dust due to hand-to-mouth transfer (-)

5.1.5. Dermal Absorption of Dust

This pathway was not included in Mitro et al. (2016) or Pelletier er al. (2017), although they mentioned it. The reason for exclusion was primarily the difficulty of quantification and its large interpersonal variability. This is a two-step process in which the person first

contacts the settled dust, most often (but not exclusively) with their hands. Especially for children playing on the floor, the rest of their skin surface may pick up substantial dust.

Unlike dermal deposition and absorption from the gas phase (see Section 5.1.6), this process is rather slow because even after the dust adheres to the skin, the chemical is initially particle-bound. It needs to dissolve into the film on the skin surface before it is absorbed. On a daily basis, this delay is not significant, but if hand-to-mouth contact occurs, then some dust will be ingested, which means it is then unavailable for dermal absorption. Since hand-to-mouth contact is relatively frequent (several contacts per hour), it may be assumed that the hand-to-mouth removal occurs before any dermal absorption.

There are several ways to estimate the amount of dust adhering to the skin. Three are:

1. Dust-skin adherence, in which a given dust mass adheres to each unit area of skin per unit time interval (often one day). If this is used, then it applies to just the hands, or, if the body is included, then a smaller adherence value should be used for the non-hands skin because it is often clothed and has less contact with house surfaces.

2. Transfer coefficients, in which the mass transferred depends on the mass on the floor (or other contacted surface) and the contact time. Thus, dustier floors produce more dust on the skin, unlike the adherence approach.

3. Transfer efficiency, which requires estimation of three factors: skin area contacting surfaces per unit time, the amount of dust available on the contacted surface, and the efficiency of transferring the dust from the latter to the former.

The adherence method requires the least amount of model inputs, so it may be preferred in the absence of site-specific (and person-specific) data. The transfer efficiency method is the most data intensive and is used (for example) in the SHEDS_Multimedia model, which is a high-tier model; transfer efficiency is not suitable for a screening model.

$$Dust_{hands} = Adh \times SA_{hands} \times f_{home} \quad \text{(Eq. 24)}$$

Where:

$Dust_{hands}$ = mass of dust adhering to hands (mg/day)
Adh = dust-skin adherence factor (mg/cm^2/day)
SA_{hands} = surface area of hands (cm^2)
f_{home} = fraction of time at home

Once the amount of dust picked up on the hands has been determined, the amount ingested from the hands should be subtracted. The remainder is subject to dermal

absorption. The simplest method of estimating dermal absorption uses an absorption fraction. Note that this fraction is likely smaller for a chemical bound to dust than for a chemical in vapor or liquid form.

$$Dust_{hands,adj} = Dust_{hands} - Ing_{hands} \quad \text{(Eq. 25)}$$

$$AD_{dust} = \frac{Dust_{hands,adj} \times C_d \times f_{abs\_derm}}{BW} \quad \text{(Eq. 26)}$$

Where:

$Dust_{hands,adj}$ = mass of dust adhering to hands available for dermal absorption (mg/day)
$Dust_{hands}$ = mass of dust adhering to hands (mg/day)
Ing_{hands} = dust ingestion rate due to hand-to-mouth transfer (mg/day)

AD_{dust} = dermal absorbed dose from dust (mg/kg/day)
C_d = chemical concentration in settled dust (mg/g)
f_{abs_derm} = absorption fraction for dermal (-)
BW = body weight (kg)

5.1.6. Dermal Deposition from Gas Phase

Based on the equations from Mitro et al. (2016) and Pelletier et al. (2017), the dermal absorbed dose from gas-phase deposition is given by:

$$AD_{der} = \frac{(C_g \times 10^{-3}) \times (k_{p-g} \times 10^{-2} \times 24) \times BSA \times f_{home}}{BW} \quad \text{(Eq. 27)}$$

Where:

AD_{der} = dermally absorbed dose (mg/kg/day)
C_g = gas-phase chemical concentration (µg/m^3)
k_{p-g} = indoor air transdermal permeability coefficient (cm/h)
BSA = human body surface area (m^2)
f_{home} = fraction of time spent at home (-)
BW = body weight (kg)
10^{-3} = (mg/µg)
10^{-2} = (m/cm)
24 = (hr/day)

The transdermal permeability coefficient is calculated with the following equations (further details and original sources cited in Pelletier et al., 2017):

$$k_{p\_cw} = 10\text{^}(0.7 \times \log K_{ow} - 0.0722 \times MW^{\frac{2}{3}} - 5.252) \times 3600 \quad \text{(Eq. 28)}$$

$$B = \frac{k_{p\_cw} \times MW^{0.5}}{2.6} \quad \text{(Eq. 29)}$$

$$k_{p\_w} = \frac{k_{p\_cw}}{1+B} \quad \text{(Eq. 30)}$$

$$k_{p\_b} = \frac{k_{p\_w}}{K_{aw}} \quad \text{(Eq. 31)}$$

$$k_{p\_g} = \frac{1}{\frac{1}{V_d} + \frac{1}{k_{p\_b}}} \quad \text{(Eq. 32)}$$

Where:

k_{p_cw} = water phase permeability coefficient through stratum corneum (cm/h)
K_{ow} = octanol-water partition coefficient (-)
MW = molecular weight of chemical (g/mol)
B = ratio of stratum corneum to viable epidermis permeabilities (-)
k_{p_w} = water phase permeability through stratum corneum and viable epidermis (cm/h)
k_{p_b} = gas phase permeability coefficient through skin surface (cm/h)
K_{aw} = air-water partition coefficient (-)
k_{p_g} = transdermal permeability coefficient (cm/h)
V_d = air-to-skin deposition velocity (cm/h)

If K_{aw} is not known, it can be calculated using other input parameters:

$$K_{aw} = \frac{K_{ow}}{K_{oa}} = \frac{H}{R \times T} \quad \text{(Eq. 33)}$$

Where:

K_{aw} = air-water partition coefficient (-)
K_{ow} = octanol-water partition coefficient (-)
K_{oa} = octanol-air partition coefficient (-)
H = Henry's law constant (Pa m^3/mol)
R = universal gas constant =8.314 Pa m^3 / (mol K)
T = temperature (K)

5.2. Input Data

Table 7 lists the inputs that must be provided by the assessor. For some inputs for which specific values have been suggested in the literature, these values are provided below. For the remaining inputs, Table 7 provides possible sources to consult.

Table 7. Inputs Required from the User.

Symbol	Units	Variable	Value	Reference
Chemical Inputs				
X_{dust}	-	Chemical mass fraction in settled dust	variable	Dust monitoring studies
MW	g/mol	Molecular weight of chemical	variable	Measured or Estimated [A]
K_{ow}	-	Octanol-water partition coefficient	variable	Measured or Estimated [A]
K_{aw}	-	Air-water partition coefficient	variable	Measured or Estimated [A]
K_{oa}	-	Octanol-air partition coefficient	variable	Measured or Estimated [A]
H	Pa m^3/mol	Henry's law constant	variable	Measured or Estimated [A]
Dust Inputs				
TSP	µg/m^3	Total suspended particulates	20 µg/m^3	Weschler and Nazaroff (2010)
f_{om_dust}	-	Organic matter fraction in settled dust	0.2	Weschler and Nazaroff (2010)
ρ_{dust}	g/cm^3	Density of settled dust particles	2 g/cm^3	Weschler and Nazaroff (2010)
f_{om_part}	-	Organic matter fraction in airborne dust	0.4	Weschler and Nazaroff (2010)
ρ_{part}	g/cm^3	Density of airborne dust particles	1g/cm^3	Weschler and Nazaroff (2010)
Exposure Inputs				
BW	kg	Body weight	Varies by age	Exposure Factors Handbook
Inh	m^3/day	Inhalation rate	Varies by age	Exposure Factors Handbook
Ing	mg/day	Daily dust ingestion	Varies by age	Exposure Factors Handbook
BSA	m^2	Human body surface area	Varies by age	Exposure Factors Handbook
f_{home}	-	Fraction of time spent at home	Varies by age	Exposure Factors Handbook
f_{abs_inh}	-	Absorption fraction for inhalation	Varies by chemical	Chemical-specific; need to look up in literature
f_{abs_ing}	-	Absorption fraction for ingestion	Varies by chemical	Chemical-specific; need to look up in literature
V_d	cm/h	Air-to-skin deposition velocity	720 cm/h	Tamas et al. (2006) Pandrangi and Morrison (2008) Weschler and Nazaroff (2008)

Symbol	Units	Variable	Value	Reference
			660 cm/h	Rim et al. (2018)
			300 cm/h	
			800–1,000 cm/h	
[A]PubChem, CompTox Chemicals Dashboard, EPI Suite, OPERA. Only two of K_{ow}, K_{aw}, K_{oa} are needed				

5.3. Implementation

The above equations are coded into an R function, with a wrapper that calls the R function with a list of input settings, thus allowing for batch runs.

The DustEx model also estimates exposure from chemicals found in house dust; however, there are several differences between the (more complex) DustEx model and the calculations described above. First, DustEx is a mechanistic model that starts with products, their properties, and their usage frequency. DustEx considers product usage to release a bolus of chemical, which is assumed to become bound to settled dust. DustEx then models the dynamic transfer of this chemical to vapor and airborne particles and the resultant exposure.

By contrast, the above equations start with the chemical already in the settled dust without considering its origins. Next, the above equations assume steady state rather than time-varying chemical concentrations. This assumption is applicable to articles, such as furniture or carpets, that have a continual presence in the home and are continually emitting chemicals into the dust. Apart from a short transient period, the chemical levels in the house dust should be fairly constant over time.

6. Approach 4: Reverse Dosimetry

Approach 4 estimates exposure to OFRs based on reported chemical measurements in human biological matrices (i.e., biomonitoring data). Measurements may be available from

a variety of matrices, including urine, blood, breast milk, hair, nails, sweat, saliva,[2] and teeth. However, measurements in urine (for rapidly eliminated chemicals) and blood (for chemicals eliminated more slowly, with an elimination half-life of >8 hours) are most common and have the best-developed methods for reverse dosimetry and the best data for appropriately parameterizing the equations. Relevant biomonitoring data may be available from published studies (including exposure studies and studies of the effects of OFRs, wherein biomonitoring data were used as the dose metric) or from national biomonitoring databases such as the National Health and Nutrition Examination Study (NHANES). Studies that measured or modeled OFR exposures using another method in addition to biomonitoring (e.g., by measuring dust concentrations) are particularly useful for corroborating the results and for considering sources of exposure and/or indicating the presence of some previously unknown exposure source.

A recent report, *Guidance Document for Use of Human Biomonitoring Data for Exposure Assessment*, was prepared under Task Order No. 61320620F1013 of Contract No. CPSC-D-17-00001 (UC, 2021). Because that guidance provided extensive step-by-step directions for obtaining data and conducting the analysis, this guidance addresses the overall process only at a high level and focuses on issues specific to class-based assessments.

6.1. Evaluation of the Biomonitoring Study and Choice of Biomarker

The UC (2021) guidance includes an extensive discussion on biomonitoring study design, with an emphasis on study quality and appropriateness for the assessment of interest. In the context of a class-based assessment, the choice of biomarker is a key consideration, since chemically related OFRs may be metabolized to the same excreted metabolite. In that case, the level of the metabolite would reflect the cumulative exposure across multiple chemicals (see Aylward et al., 2018 for an example of a class of pesticides). Although such a cumulative metric could be useful for a class-based assessment, it could complicate the calculation of dose if different parent compounds have different values of the urinary excretion fraction, termed Fue (see Section 6.2). In that case, the preferred approach may be to choose a different biomarker that is unique to each chemical in the class, if appropriate biomonitoring data are available. Another alternative would be to use the Fue for a data-rich index chemical and consider exposures of the other related chemicals relative to this index chemical. Finally, bounding estimates of the Fue could be used, with or without estimates (e.g., from dust monitoring) of relative exposures of the

[2] Note that measurements of saliva in this context would need to be appropriately separated from any mouthing incidents, so the saliva reflects internal dose rather than recent exposure via mouthing.

potential parent chemicals, to estimate the possible ranges of exposures to the respective chemicals. Comparing the results of different approaches will also aid in understanding the potential exposure range and associated uncertainties.

6.2. Key Conversion Equations

UC (2021) provided the equations for conducting reverse dosimetry calculations based on biomarker measurements in a variety of biological matrices. The key equations are repeated here for context. All of these equations are based on a steady-state assumption. Equation 34 provides the conversion approach for biomarkers in urine, and equation 35 provides the calculation for biomarkers in blood or serum.

$$DI = \frac{C*V}{BW*F_{ue}} \quad \text{(Eq. 34)}$$

Where:

DI = daily intake of the parent compound (mg/kg-day)
C = biomarker concentration in urine (mg biomarker/L)
V = 24-hour urinary flow rate (L/day)
BW = body weight (kg)
Fue = fractional urinary excretion (mg biomarker excreted/mg parent compound intake) (If the Fue is based on molar percent, such as percent of a radioactive label, the DI needs to be further adjusted based on the ratio of the molecular weight of the parent to the molecular weight of the biomarker.)

$$D = C * CL \quad \text{(Eq. 35)}$$

Where:

D = dose (mg/kg-day)
C = concentration in blood, serum, plasma, etc. (mg/L)
CL = clearance (L/kg-day)

The National Toxicology Program's (NTP's) Integrated Chemical Environment (ICE) physiologically based pharmacokinetic tool (PBPK), available at https://ice.ntp.niehs.nih.gov/Tools?tool=pbpk, serves as an interface for the R package httk (high throughput toxicokinetics) and can also be used for reverse dosimetry. This is done by calculating the relationship between dose and blood level for several doses and then interpolating the results in the linear range to the blood level of interest. This model uses a combination of toxicokinetic parameters determined in vitro and parameters estimated using Quantitative Structure Activity Relationship (QSAR) modeling.

6.3. Identification of Chemical-specific Toxicokinetic Parameters

As described in UC (2021), the chemical-specific toxicokinetic parameters needed for reverse dosimetry calculations depend on the matrix in which the biomarker is evaluated. The key parameter for urinary biomarkers is the Fue (see equation 34), and the key parameter for blood or serum biomarkers is the clearance (see equation 35; alternatively, one can use the volume of distribution and first-order elimination rate). Potential sources of toxicokinetic data (in order of preference) are human data, animal data/in vitro data, and in silico or modelled data. UC (2021) described animal data as being preferred over in vitro data but also noted several caveats regarding animal data, including that some aspects of metabolism may not scale with size, that qualitative interspecies differences in metabolism are not accounted for, and that molecular weight cutoffs for glomerular filtration differ between rodents and humans. Based on an evaluation of 50 pharmaceuticals, Hosea et al. (2009) concluded that, for chemicals primarily cleared via P450 metabolism, the success in predicting human pharmacokinetic parameters by scaling from the intrinsic clearance (CL_{int}) of human liver microsomes was comparable to or slightly better than the success of scaling from in vivo data from a single experimental animal species. This suggests that the extrapolation approach is best determined based on the nature of metabolism, as well as the type of data available. For a class-based assessment, multiple types of data may be evaluated and used to fill data gaps and improve extrapolations.

When data are available on multiple chemicals in a class, it may be possible to extrapolate from chemicals with available toxicokinetic data to others without such data, based on physicochemical parameters such as molecular weight or K_{OW}. For example, preliminary work for the CPSC has found that the rodent Fue is negatively correlated with the molecular weight for phthalates and for chlorinated polyhalogenated organophosphates (PHOPs). Another possibility is to combine multiple data sources. For example, predictions based on a rat Fue could be combined with in vitro data comparing metabolism in rat and human liver microsome systems to refine the prediction from the in vivo data. Another approach was used by Geyer et al. (2004), who evaluated a diverse group of brominated flame retardants and found that, for chemicals for which the half-life in fat in rats was >10 days, there was a linear relationship to the predicted half-life in humans ($r^2 = 0.97$). Comparing the results from multiple approaches and/or multiple data sets can provide insights into the uncertainty of the extrapolation.

Another potential approach uses in silico predictions of parameters. Comparison of clearance predicted by the ICE PBPK tool for different members of a class can provide insight into trends or potential subgroups within a class (e.g., rapid vs. slow elimination).

Such analyses can also inform a determination of whether blood or urine are more appropriate for biomarker evaluation. In addition, such analyses provide insights into the uncertainties if only urine data are available, but clearance is longer than ideal for urine biomarkers. Dawson et al. (2021) developed open source QSAR models for prediction of toxicokinetic parameters that could be used in httk or other generic pharmacokinetic models. They noted that although their models are "currently unsuitable for setting regulatory limits, they are well-suited to help inform regulatory processes."

Regardless of the approach used, it is essential to match the toxicokinetic parameter to the type of biomarker data available. For example, a Fue for total urinary excretion would need to be applied to measurements of all excretion (including the parent chemical), whereas a Fue for a single metabolite should be applied only to the urinary concentration for that metabolite. Similarly, if reverse dosimetry is being applied to blood measurements using the volume of distribution (Vd), this Vd must be specific to the matrix in which the biomarker is measured (e.g., blood vs. serum) since protein binding can affect this parameter. Finally, as described by UC (2021), it is important to consider the relationship between sampling frequency and chemical half-life in the body and to use the intraclass correlation coefficient (ICC) to adjust for situations in which intraindividual variability is expected to be high relative to interindividual variability.

This text has assumed that a class-based approach can be used to address gaps in toxicokinetic parameters but not gaps in biomonitoring data; if biomonitoring data are not available, a quantitative exposure calculation is not possible. However, a qualitative prediction may be possible in some cases. For example, if a chemical is poorly absorbed, then the internal dose would be expected to be relatively low. In addition, environmental monitoring data or product content data could be used to estimate a range of potential internal doses, based on biomonitoring data and estimated internal dose for a well-studied chemical, as well as the ratio of the monitoring data between the data-rich chemical and the target chemical.

7. Summary

Class-based exposure assessments allow for multiple chemicals to be assessed at one time, using the data available for data-rich members of the class and extrapolating to data-poor members of the class. Four approaches to estimate exposure are considered: (i) mechanistic models (Approach 1), (ii) empirical measurements (Approach 2), (iii) indoor dust monitoring data (Approach 3), and (iv) reverse dosimetry (Approach 4). Mechanistic models are first applied to one exposure scenario, and the modeled doses are used to identify trends and rank chemicals based on physicochemical properties. These trends and relative rankings are then used to extrapolate doses for (i) other

exposure scenarios that can be modeled mechanistically (extrapolating doses helps reduce the number of model runs needed) and (ii) data-poor chemicals for the other three approaches. The extrapolated doses can be qualitative or semi-quantitative, for example, providing exposure estimates for one chemical relative to another. Multiple approaches should be used to corroborate the calculated and extrapolated doses, including comparing trends from the mechanistic models with trends from the other approaches.

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Appendix A. Summary of Exposure Modeling Tools by Pathway

A.1. Ingestion of Indoor Dust

	CEM	SHEDS-HT	ConsExpo	DustEx
Outputs				
Chemical concentration in dust (settled on floor) - steady state	Yes	Yes	n/a	Yes
Key Inputs				
Dust emitted from article (amount and chemical concentration)	Yes	No	n/a	No
C_0, y_0, K_{ma}, gas-particulate partitioning, settling velocity	Yes	Yes	n/a	Yes
Ambient suspended and settled dust (due to chemical evaporation and deposition)	Yes	Yes	n/a	Yes
Chemical concentration in product/material and surface area of product/material	Yes	Yes	n/a	Yes

CEM:

- In CEM, this is the A-ING3 model.
- Outputs: Apart from the gas-phase concentration (not required here), CEM produces 12 output timeseries (daily values), composed of "inventory" (amount of dust) and "concentration" (fraction of dust mass that is the chemical of interest) for both airborne and settled versions of three types of dust: TSP (large particles), dust (small particles), and abraded (dust shed by the item in question). The values do not vary much and follow a mild sawtooth pattern due to weekly cleaning.
- Inputs: CEM requires 17 chemical properties, 16 product properties, 4 house properties, 6 dust properties, 4 abraded dust properties, and 10 other dust-related properties (including cleaning frequency and efficiency). The CEM for fabric (furniture) computes A-ING3 (ingestion of dust) but also computes outputs for seven other pathways, so not all of these inputs would be required if only A-ING3 were run.

SHEDS-HT:

- Two relevant models: product.indirect and article.emission
- Output: For all SHEDS-HT exposure pathways, the outputs are descriptions of the population variability distribution, with summary statistics including percentiles based on the large number (thousands) of randomly sampled households.
- In product.indirect:
    - The pathway-specific inputs are:
        - Fraction of houses in which this source is used
        - Number of times per year this source is used
        - Mass in grams of product released per use

        - Likelihood this source type contains the chemical of interest
        - Fraction of product mass that is this chemical (if present)
    - Other inputs not specific to this pathway include house properties and personal exposure factors. A fugacity-based calculation is made of the dispersion and loss of chemical from the house compartments after the product is used. Multiple usage events are considered to replicate the first, apart from the time shift. While SHEDS-HT is cross sectional, meaning it evaluates just one exposure day per household, this day is selected at random and the residual chemical from all releases up to that day are considered. For example, a product might be used 12 times per year (every 30 days) and the day selected for exposure happens to be 10 days after the most recent usage. Then the exposure is from the residual chemical at 10 days plus 40 days plus 70 days etc. after product usage. In another house, both the frequency of usage and the days between last usage and exposure may be different.
- In article.emission:
    - The relevant inputs are:
        - Fraction of houses with this source
        - Ratio of article surface area to floor area
        - Likelihood this source contains the chemical of interest
        - Equilibrium clean air concentration near article surface
    - The last of these variables is called "y_0" and it effectively measures the chemical flux from the article. Other house variables include the amount of dust and the partition coefficient K_p for large and small dust particles. A modified loss rate "y" depends on "y_0" and on "Q_{star}" and other house and chemical variables. The released chemical is portioned between air and surfaces. Dermal contact with surfaces followed by hand-to-mouth contact results in ingestion of dust contaminated with chemical emitted by the article.

ConsExpo:

- Dust is not covered in ConsExpo.

DustEx:

- Web application of the tool (https://www.dustex.nl/); no user guide but equations available at https://www.rivm.nl/en/consexpo/related-tools/dustex-tool/help.
- DustEx is intended to be used only for SVOCs, with a $\log_{10}$Koa between 7 and 13.
- Output: DustEx produces average daily doses (averaged over the entire exposure duration) for each of the four pathways.
    - For deterministic evaluations, DustEx also produces five output time series (daily values) for gas phase air concentration, particle-bound air concentration, dust concentration, product concentration, and surface concentration. Time series of concentrations can be downloaded as a .csv file, but doses are available only on the screen.
    - For probabilistic evaluations, the median, 95th, and 99th percentiles for average daily dose are provided for each of the four pathways, as well as for total exposure. Doses as a function of quantiles can be downloaded as a .csv file.
- Input: DustEx requires two indoor environment (residence) properties, three product/emission properties, four dust properties, five chemical properties, three indoor surface/sink properties, four airborne particulate matter properties, four receptor properties, and six simulation parameters for exposure (duration, frequency, absorption), with default values supplied for many of these. The suggested default values lead to a conservative estimate of exposure. Most parameters can be input as a distribution; when at least one parameter is a distribution, the user is asked to specify the number of iterations drawn in the Monte Carlo simulation. When run, DustEx computes all pathways, so all inputs are required.

A.2. Gas-phase Air Transfer to Skin

	CEM	SHEDS-HT	ConsExpo	DustEx
Outputs				
Chemical concentration in gas-phase air	Yes	n/a	n/a	Yes
Chemical concentration on skin	Yes	n/a	n/a	No[a]
Key Inputs				
C_0, y_0 for chemical emissions	Yes	n/a	n/a	Yes
Dermal properties	Yes	n/a	n/a	Yes
Chemical deposition to skin	Yes	n/a	n/a	Yes[b]
Rate of penetration	Yes	n/a	n/a	Yes

[a] In DustEx, chemical concentration on skin is not reported, only chemical absorbed through skin.
[b] In DustEx, chemical deposition to skin and permeation through skin are both reflected in the transdermal permeability coefficient.

CEM:

- This is the P_DER1 or A_DER1 model in CEM. It requires the P_INH1 or A_ING1 model to estimate air concentration. The prefix "P" refers to products, and "A" refers to articles (items continuously present). Note that while the CEM manual discusses this exposure pathway in the context of both products, none of the default product scenarios use this model. It is common in CEM for articles to use the A_DER1 model.
- Output: CEM provides the gas and particulate steady-state air concentrations and the acute and chronic Vapor-to-Skin transfer. As with most CEM runs, the electronic appliances run produces other outputs since the A_DER1 model is not the only one considered.
- Input: House properties, dust parameters, chemical properties including K_{ow}, solubility, and Henry's law coefficient, along with article properties such as density, surface area, chemical mass fraction, and skin properties. Among skin properties, CEM uses both a skin permeability coefficient k_p and a transdermal permeability coefficient k_{p_g}. The latter applies to this exposure pathway, but it is not clear why it should be so much larger than the former (by more than 4 orders of magnitude).

SHEDS-HT:

- Gas-phase deposition on skin is not covered in SHEDS-HT. The model includes inhalation of air (both gas and particulate phase) chemical as well as dermal contact with surfaces after airborne chemical has deposited on them.

ConsExpo:

- Gas-phase deposition on skin is not covered in ConsExpo.

DustEx:

- See notes in Section A.1.
- For gas-phase air transfer to skin, DustEx assumes that wearing of clothing will not reduce dermal absorption from air.

A.3. Inhalation of Particle Dust

	CEM	SHEDS-HT	ConsExpo	DustEx
Outputs				
Chemical concentration in suspended dust in air by particle size	Yes	Yes	n/a	Yes[a]
Key Inputs				
C_o, y_o, K_{ma}, gas-particulate partitioning, settling velocity	Yes	Yes	n/a	Yes
Particle size distribution	Yes	Yes	n/a	No
General split of direct absorption to lung vs. absorption in GI tract based on particle size	Yes	No	n/a	No

[a]In DustEx, chemical concentration in suspended dust is for one particle size only.

CEM:

- This is the A_ING1 model in CEM. There are three particle types: RP (respirable particles), dust (larger particles), and Abr (particles abraded from the article).
- Output: Particulate steady-state air concentrations for the three particle types and the acute and chronic doses resulting from inhalation followed by transfer to the GI tract.
- Input: House properties, dust parameters, chemical properties including K_{ow}, solubility, and Henry's law coefficient, along with article properties such as density, surface area, and chemical mass fraction. The ingestion fractions IF are required for each of the three particle types. These appear to be all set to 0.1 by default, but larger particles should have higher ingestion fractions. CEM does not contain an estimator for IF.

SHEDS-HT:

- SHEDS-HT computes gas and particle-phase chemical concentrations in air resulting from emissions from articles, as well as in deposited particles on surfaces. The gas and particles both contribute to inhalation exposure and dose (based on breathing ventilation rate). However, SHEDS-HT does not subsequently partition the inhaled dose into fractions absorbed in the GI tract as opposed to the lungs.
- Output: Separate gas and particle phase air concentration, along with the inhaled dose of chemical for combined gas and particle phases.
- Input: House properties, chemical properties, dust properties, and article properties, as well as personal properties such as breathing rates and body mass. Inputs in SHEDS-HT are generally distributions, but point value inputs may be used.

ConsExpo:

- Dust is not covered in ConsExpo.

DustEx:

- See notes in Section A.1.

A.4. Inhalation of Gas

	CEM	SHEDS-HT	ConsExpo	DustEx
Outputs				
Chemical concentration in gas-phase air	Yes	Yes	Yes	Yes
Key Inputs				
C_0, y_0 for chemical emissions	Yes	Yes	Yes	Yes
Breathing ventilation rate	Yes	Yes	Yes	Yes

CEM:

- This is the A_INH1 model in CEM. It is calculated in conjunction with A_ING1 because both models use a partitioning of chemical between gas and particle phases in air.
- Output: Gas-phase air concentration for a one-zone house and the acute and chronic doses (ADR for acute and ADD for chronic). This is reported in conjunction with the particulate inhalation amounts and the total (gas plus particulate).
- Input: Same inputs as for Section A.3.

SHEDS-HT:

- As described in Section A.3, SHEDS-HT computes both the gas and particulate phase air concentrations using chemical properties and dust properties. Two particle sizes are considered, generically called "large" and "small."
- Output: Separate gas and particle phase air concentration, along with the inhaled dose of chemical for combined gas and particle phases.
- Input: House properties (size and ventilation), chemical properties, dust properties for two sizes, and article properties (primarily y_0 and surface area), as well as personal properties such as time present, breathing rates, and body mass. Inputs in SHEDS-HT are generally distributions, but point value inputs may be used.

ConsExpo:

- Web application of the tool (https://www.consexpoweb.nl/) with user guide available (https://www.rivm.nl/bibliotheek/rapporten/2017-0197.pdf).
- Three models are available: "Exposure to Vapour," "Exposure to Spray," and "Emission from Solid Materials." In the first, three modes of release are available: Instantaneous Release, Constant Release, and Evaporation. In the second, two modes are available: Instantaneous Release and Spraying.
- Output: ConsExpo reports outputs on three time scales: during the exposure event, on the day of exposure, and year average exposure. Outputs are also differentiated by external (contact with the outer boundary of the body [i.e., skin, lung, or gut wall]) vs. internal exposures (amount absorbed over this boundary). Nine outputs are generated (the internal outputs are reported only if the "Absorption" box is checked): mean event concentration, peak concentration (15-minute time weighted average of the air concentration around its maximum; if exposure duration is <15 minutes, the mean event air concentration is given), mean concentration on day of exposure, year average exposure, external event dose, external dose on day of exposure, internal event dose, internal dose on day of exposure, and internal year average dose. Results are available on the screen but are not exportable to a file.

- Input:
    - In "Exposure to Vapour," the chemical evaporates from a liquid product into the air. The inputs include exposure duration, amount of product used, fraction of chemical in product, room volume, ventilation rate, and physical-chemical properties.
        - "Instantaneous Release" mode assumes all of the chemical is released at once into the room and subsequently removed by ventilation; this mode usually gives a relatively high exposure and can be used as a screening step. Concentration in air is limited to the saturated air concentration.
        - "Constant Rate" mode assumes the chemical is released at a constant rate over a period of time, with removal by ventilation. An additional input, emission duration, is needed.
        - "Evaporation" mode models chemical evaporation from the surface of the product. The rate of evaporation is dependent on the surface area of the product and the mass transfer coefficient; the latter can be estimated in ConsExpo using two approaches (as well as having a default value provided). Two additional inputs are needed: release area (total surface area on which the product is applied) and application/emission duration. Release area can be provided as a constant area or as an area that increases over time.
    - In "Exposure to Spray," consumer sprays release slowly evaporating or non-volatile substances in droplets or particles. For volatile substances released by a spray application, use the "Exposure to Vapour" model. The inputs include exposure duration, fraction of chemical in product, room volume, and ventilation rate.
        - "Instantaneous Release" mode assumes the sprayed materials are distributed homogeneously over the room air immediately upon release and subsequently removed by ventilation. Additional inputs include released mass of the spray.
        - "Spraying" mode takes into account the distribution of aerosol particles from spraying and subsequent removal by deposition and ventilation. Additional inputs include spray duration, room height, mass generation rate, aerosol diameter distribution, airborne fraction, density non-volatile (mass density of the total non-volatile substances), and inhalation cut-off diameter. An option is available to indicate that the scenario is one in which a person is inside the spray cloud; in this scenario, an input for cloud volume (volume of the cloud after 1 second) is required.
    - In "Emission from Solid Materials," the chemical diffuses to the surface of the material and transfers into air, with removal by ventilation only (no other indoor sinks considered). The inputs include product surface area, product thickness, product density, diffusion coefficient, fraction of chemical in product, product/air partition coefficient, mass transfer coefficient, ventilation rate, emission duration, and exposure duration.

DustEx:

- See notes in Section A.1.

A.5. Dermal Contact

	CEM	SHEDS-HT	ConsExpo	DustEx
Outputs				
1- per event transfer from surface to skin (mass per event)	Yes	Yes	Yes	n/a
2- sustained long-term contact with skin (mass per surface area per time)	Yes	Yes	Yes	n/a
Key Inputs				
1- transfer efficiency surface to skin | number of contacts | contact area of skin	Yes	Yes	Yes	n/a
2- migration rate to skin from surface contact | contact time | contact area of skin	Yes	Yes	Yes	n/a
1&2 - Dermal absorption parameters	Yes	Yes	Yes	n/a

CEM:

- CEM models this exposure pathway using several models: P_DER2a, P_DER2b, P_DER3, A_DER2, and A_DER3. The "P_" models are for intermittent-use products, and the "A_" models are for continuously present articles. A_DER2 considers direct contact with the article surface (e.g., a hand-held remote). The A_DER3 model considers hands picking up dust, which is also in contact with the article. This could be considered either direct or mediated (direct because the article must be contacted for the exposure to occur or else mediated because the chemical is first transferred to dust before being transferred to a human).
- Output: The dermal exposure outputs include skin contact (direct), vapor-to-skin transfer, and skin contact with dust. The direct contact term depends on the chemical migration rate. Surprisingly, the dermal exposure does not depend on the article contact duration, although this is an input.
- Input: The usual CEM inputs consisting of house, chemical, and article properties are required. If the chemical migration rate is zero, then so is the direct contact exposure, although the dermal contact with dust still occurs and is unchanged. This indicates that the dust is not obtaining chemical through chemical migration but (presumably) through surface ablation.

SHEDS-HT:

- There are two relevant exposure pathways in SHEDS-HT: "product.direct.dermal" and "article.emission." The first considers product usage events, with a portion of the mass used (released) contacting the skin. The second considers emissions characterized by the "y_0" parameter (air concentration near the article surface). These emissions exchange chemical with the air in the rest of the house, which then partitions into gas, suspended particles, and settled particles. Note that while articles seem to be the more appropriate scenario for this task, in SHEDS-HT the article.emission scenario amounts to mediated exposure. One can estimate direct contact exposure only with the product.direct.dermal model. For example, electronic devices such as remotes may be touched multiple times per day, and each contact can be considered a "product usage event." While chemicals may also be emitted from such devices when not in use, that falls under the mediated exposure pathways.
- Output: The population distribution of dermal exposure in µg/day and mg/kg/day, which reflects the amount of chemical that sticks to the skin after product use has ended.
- Input: This exposure pathway requires fraction of homes with this product, usage frequency, chemical mass released per use (or touch), likelihood of this product containing this chemical, fraction of product mass that is this chemical, fraction of product mass transferred to skin,

and the fraction of chemical loading on the skin remaining after product use (because sometimes one may wash hands or otherwise clean the skin after touching certain objects).

ConsExpo:

- This is the "Direct Contact with Product" model, with five modes available: Instant Application, Constant Rate, Rubbing Off, Migration, and Diffusion.
- Output: Six outputs are generated (the internal outputs are reported only if the "Absorption" box is checked): dermal load (amount of product per surface area of skin), external event dose, external dose on day of exposure, internal event dose, internal dose on day of exposure, and internal year average dose.
- Input:
    - In "Instant Application," the applied product comes into contact with the skin. The inputs include surface area of skin that is exposed, fraction of chemical in product, amount of total product applied to skin, and retention factor. Contact time is not an input. Absorption can be calculated using two methods: Fixed Fraction or Diffusion Through Skin, the latter of which also requires skin permeability, chemical concentration in product, and contact duration as inputs.
    - In "Constant Rate," the applied product comes into contact with the skin. The inputs include surface area of skin that is exposed, fraction of chemical in product, contact rate, and release duration.
    - In "Rubbing Off," the product is applied to a surface and the skin contacts the treated surface. The inputs include surface area of skin that is exposed, fraction of chemical in product, transfer coefficient (treated surface area in contact with the skin per unit of time), dislodgeable amount (amount of product applied to surface area that may be wiped off, per unit of surface area), contact time, and contacted surface (area of treated surface that is rubbed during exposure).
    - In "Migration," the chemical migrates from a material to the skin when dermal contact with the material occurs (e.g., exposure to dyes in clothing, whereby dyes leach to the skin). The inputs include surface area of skin that is exposed, amount of material in direct contact with the skin, leachable fraction (amount of chemical that migrates to the skin per unit amount of material), skin contact factor (fraction of material in contact with skin).
    - In "Diffusion," the applied product comes into contact with the skin. After application, the chemical diffuses through the product to the skin. The inputs include surface area of skin that is exposed, chemical concentration in product, diffusion coefficient, product layer thickness, and contact time. Absorption can be calculated using two methods: Fixed Fraction or Diffusion Through Skin, the latter of which also requires skin permeability as an input.

DustEx:

- Dermal contact with the product is not covered in DustEx. The model includes inhalation of gas, inhalation of particles, and dermal absorption from the gas phase.

A.6. Mouthing

	CEM	SHEDS-HT	ConsExpo	DustEx
Outputs				
Acute and chronic dose associated with direct mouthing	Yes	Yes	Yes	n/a
Key Inputs				
Chemical concentration in product – can be used as an estimator for migration rate to saliva	Yes	Yes	Yes	n/a
Time spent mouthing product | age dependency for mouthing times	Yes	Yes	Yes	n/a
Chemical migration rate to saliva – check mechanistic and empirical models from Aurisano et al. (2022)	Yes	Yes	Yes	n/a
Product surface area contacting mouth	Yes	Yes	Yes	n/a

CEM:

- This is the A_ING2 model in CEM. Like all CEM models, the default scenarios evaluate the result of several exposure pathways. Since the exposure from this pathway is proportional to the "contact area of mouthing, CA," one can turn this pathway on or off independently of other exposure pathways.
- Output: Both acute and chronic mouthing exposures are reported. These are called "potential doses" because they report the amount of chemical transferred to the saliva but do not include a GI tract absorption factor.
- Input: The main inputs for this pathway are chemical migration rate (from article to saliva), contact area of mouthing, and duration of mouthing. Note that the first of these variables should be proportional to the chemical concentration in the article, but CEM makes no such link and the user must ensure consistency.

SHEDS-HT:

- SHEDS-HT has three mouthing terms: one direct and two indirect. The direct is "product.direct.ingestion," which is meant to apply to products applied to the face or mouth, such as toothpaste, lip balm, etc. The other two are "product.indirect" and "article.emission," both of which relate oral exposure to dermal hand exposure on the assumption that the two should be proportional (although the ratio depends on age).
- Output: The ingested amount in units of µg/day and mg/kg/day.
- Input: The same variables that are needed to estimate dermal exposure, except for the addition of "om.ratio," which represents the ratio of mouthing exposure to dermal (hand) exposure. This variable is age dependent and (like nearly all variables) varies over the population of simulated individuals.

ConsExpo:

- This is the "Direct product contact" → "Product mouthing" model.
- Output: Five outputs are generated (the internal outputs are reported only if the "Absorption" box is checked): external event dose, external dose on day of exposure, internal event dose, internal dose on day of exposure, and internal year average dose.

- Input: The inputs are weight fraction of chemical in product, amount of product mouthed, duration of mouthing, contact area of mouthing, and initial chemical migration rate. Users can also specify fraction absorbed from the gut into the blood to calculate oral absorption.

DustEx:

- Mouthing the product is not covered in DustEx.