Journal of Exposure Science and Environmental Epidemiology (2012) 22, 522 – 532

www.nature.com/jes

ORIGINAL ARTICLE

Comparison of four probabilistic models (CARES®, Calendex™, ConsExpo, and SHEDS) to estimate aggregate residential exposures to pesticides

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Two deterministic models (US EPA's Office of Pesticide Programs Residential Standard Operating Procedures (OPP Residential SOPs) and *Draft Protocol for Measuring Children's Non-Occupational Exposure to Pesticides by all Relevant Pathways* (*Draft Protocol*)) and four probabilistic models (CARES®, Calendex™, ConsExpo, and SHEDS) were used to estimate aggregate residential exposures to pesticides. The route-specific exposure estimates for young children (2–5 years) generated by each model were compared to evaluate data inputs, algorithms, and underlying assumptions. Three indoor exposure scenarios were considered: crack and crevice, fogger, and flying insect killer. Dermal exposure estimates from the OPP Residential SOPs and the *Draft Protocol* were 4.75 and 2.37 mg/kg/day (crack and crevice scenario) and 0.73 and 0.36 mg/kg/day (fogger), respectively. The dermal exposure estimates (99th percentile) for the crack and crevice scenario were 16.52, 12.82, 3.57, and 3.30 mg/kg/day for CARES, Calendex, SHEDS, and ConsExpo, respectively. Dermal exposure estimates for the fogger scenario from CARES and Calendex (1.50 and 1.47 mg/kg/day, respectively) were slightly higher than those from SHEDS and ConsExpo (0.74 and 0.55 mg/kg/day, respectively). The ConsExpo derived non-dietary ingestion estimates (99th percentile) under these two scenarios were higher than those from SHEDS, CARES, and Calendex. All models produced extremely low exposure estimates for the flying insect killer scenario. Using similar data inputs, the model estimates by route for these scenarios were consistent and comparable. Most of the models predicted exposures within a factor of 5 at the 50th and 99th percentiles. The differences identified are explained by activity assumptions, input distributions, and exposure algorithms.

Journal of Exposure Science and Environmental Epidemiology (2012) **22,** 522 – 532; doi:10.1038/jes.2012.54; published online 11 July 2012

Keywords: model; probabilistic; SHEDS; CARES; ConsExpo; Calendex

INTRODUCTION

The Food Quality Protection Act (FQPA, 1996) requires the United States Environmental Protection Agency (US EPA) to consider aggregate exposures and cumulative effects from pesticide residues that have a common mechanism of toxicity. Deterministic approaches for simplistic, screening-level evaluations of individual exposure routes have been used for many years. Probabilistic models have been developed, evaluated, and refined by industry, government, and academic experts to better characterize and understand the range of potential aggregate and cumulative exposures and health risks.[1]

Before FQPA, residential exposure assessments were conducted for various pesticides only when certain toxicity and exposure criteria were met.[2] FQPA expanded US EPA risk assessment requirements under the Federal Insecticide Fungicide and Rodenticide Act (FIFRA) and the Federal Food, Drugs, and Cosmetics Act by emphasizing protection of infants and children, including combining exposures from all potential pathways. Since 1996, the Office of Pesticide Programs (OPP) of the US EPA has attempted to quantify all major residential exposure scenarios for pesticides having food uses to enable aggregate and cumulative risk assessments. The methodologies for assessing residential exposure and risk were first presented to the FIFRA Scientific Advisory Panel (SAP) in 1997 and are known as the Standard Operating Procedures (SOPs) for Residential Exposure Assessments.[3] Based generally on standard US EPA exposure and risk assessment guidelines,[4] the document outlines various potential pesticide exposure scenarios, such as children playing on lawns or homeowners spraying gardens. The US EPA's Office of Research and Development's (ORD) National Exposure Research Laboratory (NERL) published the *Draft Protocol for Measuring Children's Non-Occupational Exposure to Pesticides by all Relevant Pathways* (*Draft Protocol*),[5] which is a deterministic approach to evaluate exposure to pesticides using a series of algorithms similar to the OPP Residential SOPs. These deterministic approaches to estimate exposure to pesticides (i.e., point estimates) laid the foundation for the development of probabilistic modeling approaches to estimate pesticide exposures (i.e., distribution estimates). Key features

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Received 1 July 2011; accepted 19 April 2012; published online 11 July 2012

of probabilistic approaches include stochastic selection of model input values based on distributions derived from empirical data, population-based assessments, and calendar-based (365 days) exposure determinations. Population-based assessments use statistical methods to simulate a virtual population of individuals. Calendar-based exposure determinations estimate exposures for every day of the simulation period as exposures to pesticides may be different from day to day.

Currently, there are numerous models being evaluated and refined[1,6] that can predict pesticide exposures using limited data inputs, including, but not limited to, the Stochastic Human Exposure and Dose Simulation Model (SHEDS), the Cumulative and Aggregate Risk Evaluation System (CARES®), Calendex™, and ConsExpo. However, there has been limited effort to systematically compare the various models being evaluated and refined in academia, government, and industry. As selected models become more routinely used for regulatory decision making in both the United States and European Union, a systematic understanding of how these models work and handle data inputs and outputs for various scenarios is critical. This comparison provides an evaluation of selected probabilistic models to compare the range of exposure estimates for the inhalation, dermal, and non-dietary ingestion exposure routes predicted at various percentiles, to understand the underlying assumptions each model uses, and to compare with standard deterministic exposure estimates. This work was originally presented as part of an invited model comparison workshop (Residential Exposure Model Algorithms: Comparisons by Exposure Pathways across Four Models) at the American Chemical Society 2008 annual meeting in Philadelphia, PA, USA.

This paper presents the results of this residential exposure pathway comparison using the OPP Residential SOPs (1997 version), the *Draft Protocol*, CARES, Calendex, ConsExpo, and SHEDS. We compared the route-specific (i.e., inhalation, non-dietary ingestion, dermal) residential exposure estimates generated by each model with regard to data inputs, algorithms, and underlying assumptions. Food and water were not included in this model comparison because dietary probabilistic models have shown consistent results because of similar consumption databases and dietary exposure equations.[7]

METHODS

In this model comparison, the authors examined indoor exposure estimates from the inhalation, dermal, and non-dietary (hand-to-mouth activity) ingestion pathways for selected scenarios: total release fogger (dermal and non-dietary), crack and crevice aerosol (dermal and non-dietary), and flying insect killer aerosol (inhalation). These scenarios represent typical use patterns for pesticide products containing a pyrethroid active ingredient and the pathways represent the most likely routes of exposure. Brief descriptions of the OPP Residential SOPs, *Draft Protocol*, CARES, Calendex, ConsExpo, and SHEDS are provided. For ease of comparison, model algorithms are listed in Table 1 and data inputs for the route-specific exposure estimates are provided in Tables 2–4. Data for a hypothetical pesticide were created based on the physical chemical properties of the class of pyrethroid pesticides and used for this model comparison (Table 5). Probabilistic models require use pattern data (e.g., monthly and daily probabilities) to create a temporal event profile (Table 6), which was based on an analysis of the Residential Exposure Joint Venture product use survey.[8] Route-specific exposures for each scenario were determined based on the potential exposures of young children (2–5 years), as FQPA emphasizes protection of infants and children, including aggregate exposures.

The models used for this comparison provide a tiered approach from deterministic equations to complex probabilistic methods. The OPP Residential SOPs and *Draft Protocol* estimate exposures using single-point deterministic equations based on a combination of central tendency and high-end statistics for the input variables. These methods are intended to provide a conservative approach for regulatory applications. The *Draft Protocol* allows for refinement of exposure estimates by using field data (multimedia measurements). Probabilistic models incorporate parameter distributions based on real-world data to estimate daily exposures for each individual in a population.

Deterministic Models

OPP Residential SOPs. The OPP of the US EPA uses a set of SOPs to estimate exposures for adults and children in and around residences that have been treated with pesticides.[3] These SOPs are used to evaluate exposures immediately following an application and may be used with registrant-supplied data or default values found in the SOPs.

Draft Protocol. The *Draft Protocol* of the US EPA, developed by ORD, details a systematic measurement-based approach to evaluate exposure by each route using a series of algorithms. Each algorithm mathematically expresses exposure for a specific route as a function of chemical concentration and selected exposure factors, explicitly identifying the data requirements. The *Draft Protocol* primarily relies on field data for multimedia concentrations[5,9] and, for this comparison, was used deterministically.

Probabilistic Models

CARES®. The CARES[10] (Version 3.0, developed by CropLife America and currently managed by the International Life Sciences Institutes' Risk Science Institute) is a population- and calendar-based probabilistic exposure and risk model designed to simulate dietary (including drinking water) and residential exposures for representative individuals. CARES was externally peer-reviewed by the US EPA's peer review process for models in 2002 and 2004.[11] The model uses demographic data from the US Census Public Use Micro Data Sample that is statistically representative of the 1990 US Census. CARES estimates exposure for each individual in the selected population for 1 year (i.e., 365 days) creating a temporal profile of daily exposures.

The residential module in CARES simulates route-specific aggregate and cumulative exposures for an individual who may come in contact with a pesticide in a given scenario and day. An "Event Allocation" module estimates the temporal profile of exposure event occurrence throughout the calendar year based on label and product use information. Daily residential exposures to individuals represented in the CARES "Reference Population" are only estimated for those persons who have been assigned applicator or postapplication exposure scenarios. Each individual's exposure is estimated based on route-specific algorithms and parameters from user-specified probability distributions. Route-specific exposure algorithms for dermal and inhalation exposure are based on the OPP Residential SOPs. The non-dietary ingestion exposure algorithm is based on the OPP Residential SOP (i.e., CARES (EPA method)), as well as a newly developed exposure algorithm (i.e., CARES (mass balance)[12–14]; Table 1).

Calendex™. Calendex is a software platform that enables probabilistic calendar-based aggregate and cumulative exposure assessment calculations using Monte Carlo techniques. Calendex was originally developed by Durango Software and Novigen Sciences (now Exponent) and externally peer-reviewed by the US EPA's peer review process for models in 2000.

Calendex is a "shell" that can be used to estimate any type of exposure scenario using whatever parameters and inputs the modeler desires. For the purposes of this comparison, exposure calculations were performed using algorithms from the OPP Residential SOPs and input parameters listed in Tables 2–4. Demographic data are "hard-wired" in the model, whereas all other data (e.g., contact parameters, residue data, and exposure algorithms) must be specified by the modeler. The user specifies the parameters to calculate both contact and residue functions over time, and exposure is calculated as the product of these functions. Calendex tracks residue functions over a 1-year period, and contact is estimated for each day using the specified parameters. For day of application exposures, applications were specified to occur on day 1, and exposures were calculated for that day only. For other exposure durations, timing of the

Table 1. Model algorithms used in the comparison.

Exposure route	*Model*	*Algorithm*
Inhalation (E_i)	OPP Residential SOP	$E_i = \frac{(AC)(IR)}{BW}$
	Draft Protocol, CARES, Calendex	$E_i = \frac{(AC)(IR)(ED)}{BW}$
	SHEDS	$E_i = \frac{(AC)(IR)(ET)(METS)}{BW}$
	ConsExpo	$E_i = \left(\frac{IR}{BW}\right)\left(\frac{AC}{(V)\left(q+\frac{v_s(d)}{h}\right)}\right)\left(1-e^{-\left(q+\frac{v_s(d)}{h}\right)(ED)}\right)$ where $AC=(RR)(SD)(WF)$
Dermal (E_d)	OPP Residential SOP, *Draft Protocol*, CARES, Calendex, ConsExpo	$E_d = \frac{(SR)(TC)(ED)}{BW}$
	SHEDS	$E_d = \frac{(SR)\left(TC_{hand/body}\right)(ET)(Adj)}{BW}$
Non-dietary ingestion (E_{nd})	OPP Residential SOP, CARES (SOP method), Calendex	$E_{nd} = \frac{(AR)(FD)(SA)(TE)(F)(ED)}{BW}$
	Draft Protocol	$E_{nd} = \frac{(HR)(SA)(TE)(F)(T)}{BW}$
	CARES (mass balance method)	$E_{nd} = \frac{(HR)\left(\frac{SA_{H2M}}{SA_{hand}}\right)\left((TE)(\sum(F)(ED))(1-TE)^{n-1}\right)}{BW}$ where $HR=(SR)(TC)(ED)(F_{hand})$
	SHEDS	$E_{nd} = \frac{\left(\frac{HR}{2}\right)(HF)\left(1-(1-TE)^{((F)(ET))}\right)}{BW}$ where $HR=(SR)(TC_{hand})(T)$
	ConsExpo	$E_{nd} = (\text{fraction hands})\,(\text{fraction transferred})\,(E_d)$

Abbreviations: AC, air concentration (mg/m^3); Adj, adjustment factor for clothing (unitless); AR, application rate (mg/cm^2); BW, body weight (kg); d, aerosol diameter (μm); ED, exposure duration (h/day); ET, diary event duration (h); F, frequency of hand-to-mouth events (events/h); FD, fraction dislodgeable (unitless); F_{hand}, fraction dermal exposure on hand (unitless); h, room height (m); HF, fraction of one hand that enters the mouth (unitless); HR, pesticide residue on the hands (mg/cm^2); HR, hand residue (mg); IR, inhalation rate (m^3/h); METS, metabolic equivalents (energy expenditure during an activity relative to basal expenditure) (unitless); q, room ventilation rate (times/h); RR, spray release rate (g/s); SA, surface area of hand that contacts and transfers residue to the mouth (cm^2/event); SA_{H2M}, surface area of hand that is mouthed (cm^2); SA_{hand}, surface area of the hand (cm^2); SD, spray duration (s); SR, surface residue (mg/cm^2); T, time available for mouthing (h/day); TC, transfer coefficient (cm^2/h); TE, transfer efficiency (unitless); V, room volume (m^3); v_s (d), aerosol size dependent Stokes settling velocity (m/h); WF, weight fraction airborne (%).

applications was specified by month and day, exposures were calculated over an entire year, and the resulting distributions reflected the full range of exposures on all days (which may or may not include a day when an application was made).

ConsExpo. ConsExpo is a general estimation tool for predicting human exposures to chemicals found in consumer products.[15] ConsExpo comprises a number of mechanistic, source-to-dose models that simulate single exposure events from the inhalation, dermal, and oral pathways. ConsExpo uses a mechanistic/first-order model to simulate air concentrations and inhaled dose from product properties, consumer use patterns, and room characteristics. Model evaluations may be done either deterministically or probabilistically depending on the specification of the model input parameters. For probabilistic calculations, ConsExpo implements single-stage Monte Carlo analysis. At present, ConsExpo evaluates single-chemical, single-product exposures. In support of the models, the ConsExpo tool includes a database with a compilation of information on exposure factors for various categories of consumer products including pest control products, paints, cosmetics, cleaning products, do-it-yourself products, and disinfectants.

SHEDS-Multimedia Version 3. SHEDS[16] is the physically based probabilistic model of the US EPA/ORD/NERL that can simulate aggregate (single chemical) or cumulative (multiple chemicals) exposures over time via multiple routes of exposure for different types of chemicals and scenarios. Details on applications of the model to date, algorithms, and model inputs and outputs can be found in Zartarian et al.[17] To date, SHEDS has been used in the US EPA and other government agencies, academia, and industry for a variety of regulatory and research purposes (see, e.g., refs. 18–20; Syngenta Crop Protection, personal communication). SHEDS was externally peer reviewed by the peer review process of the US EPA for models in 2007 and 2010.[21,22]

Version 3, used for the analyses in this paper, is an aggregate residential exposure model focusing on inhalation, dermal contact, and non-dietary ingestion routes of exposure. It uses a macro-activity approach for dermal exposure that incorporates both loading and removal (e.g., from mouthing,

Table 2. Residential input parameters for the inhalation exposure estimates.

Code	*Parameter*	*OPP Residential SOP*	*Draft Protocol*	*CARES and Calendex*	*SHEDS*	*ConsExpo*
AC	Air concentration ($\mu g/m^3$)	8 h. TWA 0.105	8 h. TWA 0.105	Uniform (0.105, 0.246)	Initial = 3.3; decayed rapidly	NA
IR	Inhalation rate	8.7 m^3/day	0.7 m^3/h	CARES: modeled Calendex: uniform (0.47–0.93) m^3/h	Modeled	Uniform (0.47–0.93) m^3/h
ED	Exposure duration (h/day)	NA	8	Triangular (2, 4, 8)	Based on CHAD diaries	8 h
METS	Ventilation rate ratio	NA	NA	NA	Based on diary-specific activity	NA
BW	Body weight (kg)	15	15	CARES: CSFII[30] matched to US Census Calendex: CSFII[30] reference population	Based on US Census	Lognormal (18.9, 1.22) (GM, GSD)
RR	Spray release rate (g/s)	NA	NA	NA	NA	2
SD	Spray duration (s)	NA	NA	NA	NA	5–10
WF	Weight fraction airborne (%)	NA	NA	NA	NA	0.5
V	Room volume (m^3)	NA	NA	NA	NA	58
q	Room ventilation rate (times/h)	NA	NA	NA	NA	0.6
d	Aerosol diameter (μm)	NA	NA	NA	NA	Lognormal (28, 1.6) (median, CV)
h	Room height (m)	NA	NA	NA	NA	2.5
E_i	Inhalation exposure (mg/kg/day)	6.1×10^{-05}	3.91×10^{-05}	Distribution	Distribution	Distribution

Table 3. Residential input parameters for the dermal exposure estimates.

Code	*Parameter*		*OPP Residential SOP*	*Draft Protocol*	*CARES and Calendex*	*SHEDS*	*ConsExpo*
AR	Application rate ($\mu g/cm^2$)	Fogger	4.41	4.41	4.41	4.41	NA
		Crack and crevice	48.88	48.88	48.88	48.88	NA
FD	Fraction dislodgeable (unitless)	Fogger	0.05	0.05	Uniform (0.0439, 0.057)	Uniform (0.0439, 0.057)	NA
		Crack and crevice	0.0297	0.0297	Uniform (0.0024, 0.057)	Uniform (0.0024, 0.057)	NA
SR	Surface residue (mg/cm^2)	Fogger	0.22	0.22	Uniform (0.19, 0.25)	Uniform (0.19, 0.25)	Uniform (0.19, 0.25)
		Crack and crevice	1.45	1.45	Uniform (0.12, 2.8)	Uniform (0.12, 2.8)	Uniform (0.12, 2.8)
TC	Transfer coefficient (cm^2/h) (SHEDS splits the value 50% for body and hand)		6130	6130	Lognormal (6130, 1.68, 0, 20,000)	Lognormal (3065, 1.68, 0, 10,000) Lognormal (3065, 1.68, 0, 10,000)	Lognormal (6130, 1.68, 0)
ED	Exposure duration (h/day)		8	4	Triangular (2, 4, 8)	Based on CHAD diaries	Triangular (2, 4, 8)
Adj	Percent hand uncovered (unitless) Percent body uncovered (unitless)		NA	NA	NA	Hands = 100 Body: β (3, 6.7)	NA
DA	Dermal absorption (unitless)		NA	NA	Triangular (0.0048, 0.0195, 0.0322)	Triangular (0.0048, 0.0195, 0.0322)	Triangular (0.0048, 0.0195, 0.0322)
BW	Body weight (kg)		15	15	CARES: CSFII[30] matched to US Census Calendex: CSFII[30] reference population	Based on modeled US Census	Lognormal (18.9, 1.22)
E_d	Dermal Exposure (mg/kg/day)	Fogger	0.73	0.36			
		Crack and crevice	4.75	2.37			

hand washing, and bathing) processes, reflects variability of activity patterns within a day, and incorporates two-stage Monte Carlo sampling to assess uncertainty and variability.[23] Daily activities and locations of individuals in the population cohort of interest are simulated using sequential time/location/activity diaries from the Consolidated Human Activity Database (CHAD;[24]) of the US EPA. SHEDS utilizes the Glen et al.[25]

Table 4. Residential input parameters for the non-dietary ingestion exposure estimates.

Code	Parameter		OPP Residential SOP	Draft Protocol	CARES and Calendex	SHEDS
FT	Fraction transferred to hand (unitless)		1.0	1.0	Triangular (0.06, 0.14, 0.22)	0.5 (based on 1/2 TC)
	Mean no. of hand washes (unitless)		NA	NA	NA	Lognormal (3.74, 2.63, 1, 12)
	Maximum dermal loading (mg/day)		NA	NA	NA	Triangular (0.1, 0.6, 2.1)
	Hand residue (mg/day)	Fogger	0.22	0.22	SR × TC × ED × FT	SR × TC × ED/2 Assuming one hand
		Crack and crevice	1.45	1.45		
SA	Surface area mouthed (cm^2)		20	20	Triangular (1, 7, 20)	Fraction of mouthed Triangular (0.007, 0.05, 0.14)
	Surface area hand (cm^2)				Single (452)	
F	Contact frequency (events/h)		8.5	8.5	Triangular (0.4, 8.5, 25.7)	Weibull (0.76, 11.04) (0.75, 12.59)
ED	Exposure duration		8	4	Triangular (2, 4, 8)	Based on CHAD diaries
T	Time available for mouthing (h/day)					
TE	Saliva extraction transfer efficiency (unitless)		0.5	0.08	Triangular (0.0024, 0.0815, 0.13)	Triangular (0.0024, 0.0815, 0.13)
BW	Body weight (kg)		15	15	CARES: CSFII[30] matched to US Census Calendex: CSFII[30] reference population	Based on US Census
E_{nd}	Non-dietary ingestion exposure (mg/kg/day)	Fogger	0.01	0.0008		
		Crack and crevice	0.066	0.0053		

Table 5. Hypothetical pesticide physical chemical properties.

Parameter	Value
Molecular weight	390
Boiling point	200 °C at 0.1 mm Hg
Water solubility	0.21 mg/l at 20 °C
Vapor pressure	0.07 mPa at 20 °C (approx. 2.07E–8 mg Hg) 2.18E–8 mm Hg at 25 °C
Octanol/water partition coefficient	log $P_{ow} = 4.19$ at 20 °C
Dissipation rate or half-life	10% or 6.58 days

approach for longitudinal diary assembly. SHEDS individuals are stochastically created synthetic individuals whose collective properties reflect the simulated population and scenarios of interest.

RESULTS

To focus on high-end exposures, we used the 99th percentile of the maximum day of each individual's route-specific exposure as a common point of comparison across the probabilistic models. We then compared these values to the values estimated by the deterministic models. Additional statistics are included in the figures. Potential dermal exposure from the crack and crevice scenario was estimated as 4.75 and 2.37 mg/kg/day using the OPP Residential SOP and *Draft Protocol* algorithms, respectively. The 99th percentile dermal exposure estimates from the crack and crevice scenario were 3.57, 16.52, 12.82, and 3.30 mg/kg/day for SHEDS, CARES, Calendex, and ConsExpo, respectively (Figure 1).

Under the fogger scenario, potential dermal exposure was estimated as 0.73 and 0.36 mg/kg/day using the OPP Residential SOP and *Draft Protocol* methods, respectively. The 99th percentile for the dermal exposure estimates from the fogger scenario was 0.74, 1.50, 1.47, and 0.55 mg/kg/day for SHEDS, CARES, Calendex, and ConsExpo, respectively (Figure 2).

Non-dietary ingestion from the crack and crevice scenario resulted in potential exposures of 0.155 and 0.0053 mg/kg/day from the OPP Residential SOP and *Draft Protocol* algorithms, respectively. The 99th percentile for the non-dietary ingestion exposure estimates from the crack and crevice scenario was 0.015, 0.060, 0.173, 0.061, and 0.330 mg/kg/day for SHEDS, CARES (mass balance), CARES (EPA method), Calendex, and ConsExpo, respectively (Figure 3).

Non-dietary ingestion from the fogger scenario resulted in a potential exposure of 0.023 and 0.0008 mg/kg/day from the OPP Residential SOP and *Draft Protocol* algorithms, respectively. The 99th percentile for the non-dietary ingestion exposure estimates from the crack and crevice scenario was 0.014, 0.005, 0.0143, 0.007, and 0.055 mg/kg/day for SHEDS, CARES (mass balance), CARES (EPA method), Calendex, and ConsExpo, respectively (Figure 4).

The flying insect killer aerosol scenario resulted in a potential inhalation exposure of 6.05E–05 and 3.92E–05 mg/kg/day using the OPP Residential SOP and *Draft Protocol* algorithms, respectively. The 99th percentile for the potential inhalation exposure using the aerosol scenario was 4.37E–05, 3.32E–05, 8.70E–05, and 9.90E–04 mg/kg/day for SHEDS, CARES, Calendex, and ConsExpo, respectively (Figure 5).

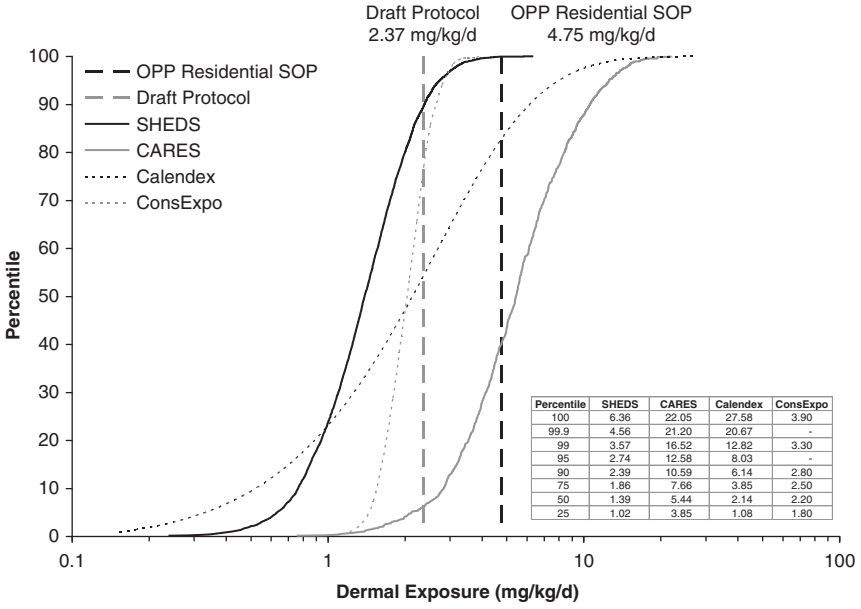
The results of the comparison of model estimates by route for these scenarios were within a factor of 5 at the 50th and 99th percentiles among all probabilistic models with the exception of ConsExpo, which was often much higher. For the fogger scenario, the dermal exposure estimates predicted by each probabilistic model were within a factor of 1.5 at the 50th percentile and 2.2 at the 99th percentile. In the case of the non-dietary exposure estimates, four of the five models were within a factor of 3.2 at the 50th percentile, and within a factor of 2.8 at the 99th percentile. For the crack and crevice scenario, the dermal exposure estimates

Table 6. Indoor exposure scenario use patterns.

Scenario description	*Monthly probabilities*											
	Jan	*Feb*	*Mar*	*Apr*	*May*	*Jun*	*Jul*	*Aug*	*Sep*	*Oct*	*Nov*	*Dec*
Fogger	0.0110	0.0055	0.0440	0.0165	0.2527	0.1703	0.1264	0.1429	0.0549	0.0989	0.0495	0.0275
FIK Aerosol	0.0157	0.0231	0.0257	0.0581	0.1937	0.1534	0.1613	0.1401	0.1007	0.0631	0.0398	0.02573
Crack and crevice	0.0157	0.0231	0.0257	0.0581	0.1937	0.1534	0.1613	0.1401	0.1007	0.0631	0.0398	0.02573

Scenario description	*Daily probabilities*							*Number of applications*	*Days between applications*
	Sun	*Mon*	*Tue*	*Wed*	*Thu*	*Fri*	*Sat*		
Fogger	0.25	0.1	0.1	0.1	0.1	0.1	0.25	2	30
FIK Aerosol	0.14286	0.14286	0.14286	0.14286	0.14286	0.14286	0.14286	5	7
Crack and crevice	0.14286	0.14286	0.14286	0.14286	0.14286	0.14286	0.14286	5	14

Abbreviation: FIK, flying insect killer.



Percentile	SHEDS	CARES	Calendex	ConsExpo
100	6.36	22.05	27.58	3.90
99.9	4.56	21.20	20.67	-
99	3.57	16.52	12.82	3.30
95	2.74	12.58	8.03	-
90	2.39	10.59	6.14	2.80
75	1.86	7.66	3.85	2.50
50	1.39	5.44	2.14	2.20
25	1.02	3.85	1.08	1.80

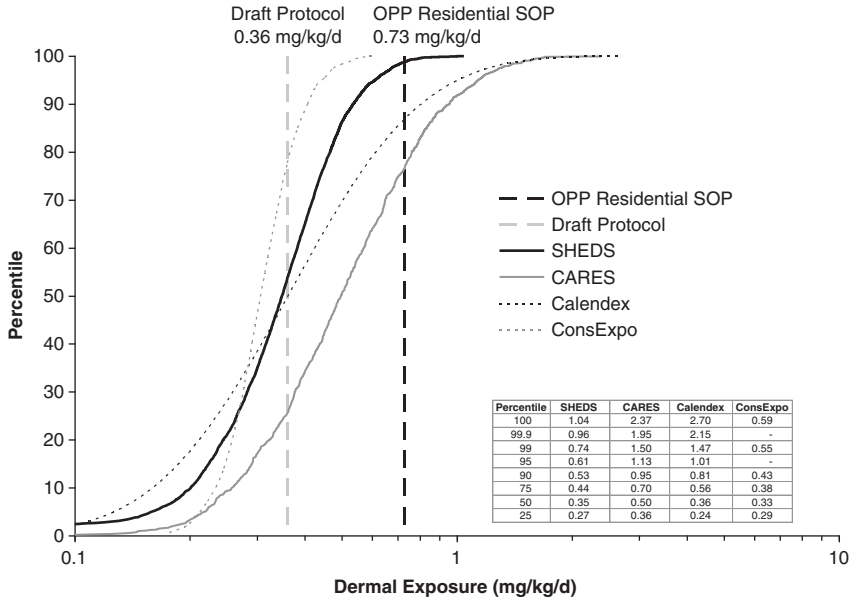
Figure 1. Percentile distribution of dermal exposure from the crack and crevice scenario.

predicted by each model were within a factor of 3.9 at the 50th percentile and 5.0 at the 99th percentile. For the non-dietary exposure estimate, four of the five models were within a factor of 3.5 at the 50th percentile and within a factor of 4.5 at the 99th percentile. For the flying insect killer scenario, inhalation exposure estimates for three of the four models were within a factor of 1.6 at the 50th percentile, and within a factor of 4.5 at the 99th percentile. Inhalation exposure estimates from ConsExpo were at least an order of magnitude higher than all other models.

Results from the total absorbed dose estimates showed more variability among the probabilistic models. At the upper percentiles ($>$80th), the results from the fogger scenario were consistent for Calendex, CARES, and SHEDS (Figure 6), whereas the results from the crack and crevice scenario were consistent for Calendex and CARES (Figure 7). The 99th percentile absorbed dose estimates for the fogger scenario were 0.003, 0.01, 0.01, and 0.052 mg/kg/day for SHEDS, CARES, Calendex, and ConsExpo, respectively (Figure 6). The 99th percentile absorbed dose estimates for the crack and crevice scenario were 0.004, 0.108, 0.124, and 0.336 mg/kg/day for SHEDS, CARES, Calendex, and ConsExpo, respectively (Figure 7). Contribution analysis by exposure pathway at the upper tail of the distribution was completed for each scenario for CARES, SHEDS, and Calendex (Figure 8). CARES and Calendex predicted similar route contributions for both scenarios ($\sim$90% dermal, 10% non-dietary ingestion), which is because of the similarity of the algorithms programmed into CARES and, for the purposes of this comparison, into Calendex. SHEDS predicted different route contributions (fogger: 31% dermal, 69% non-dietary ingestion; crack and crevice: 48% dermal, 52% non-dietary ingestion).

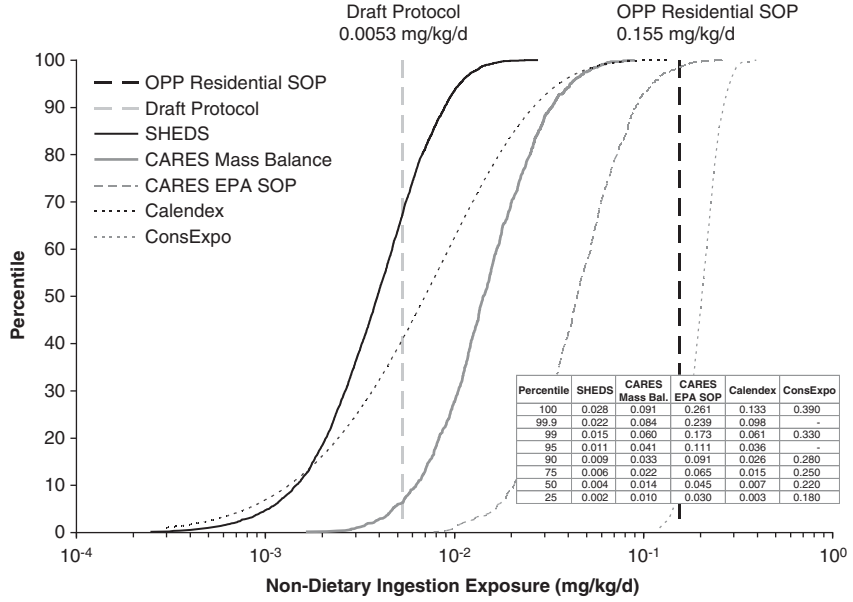
DISCUSSION

Model algorithms for estimating dermal exposure were similar for the deterministic and probabilistic models (Table 1). Comparison of dermal exposure estimates was more consistent for the fogger scenario than the crack and crevice scenario. The differences were due, in large part, to the assumed importance of contact with



Percentile	SHEDS	CARES	Calendex	ConsExpo
100	1.04	2.37	2.70	0.59
99.9	0.96	1.95	2.15	-
99	0.74	1.50	1.47	0.55
95	0.61	1.13	1.01	-
90	0.53	0.95	0.81	0.43
75	0.44	0.70	0.56	0.38
50	0.35	0.50	0.36	0.33
25	0.27	0.36	0.24	0.29

Figure 2. Percentile distribution of dermal exposure from the fogger scenario.

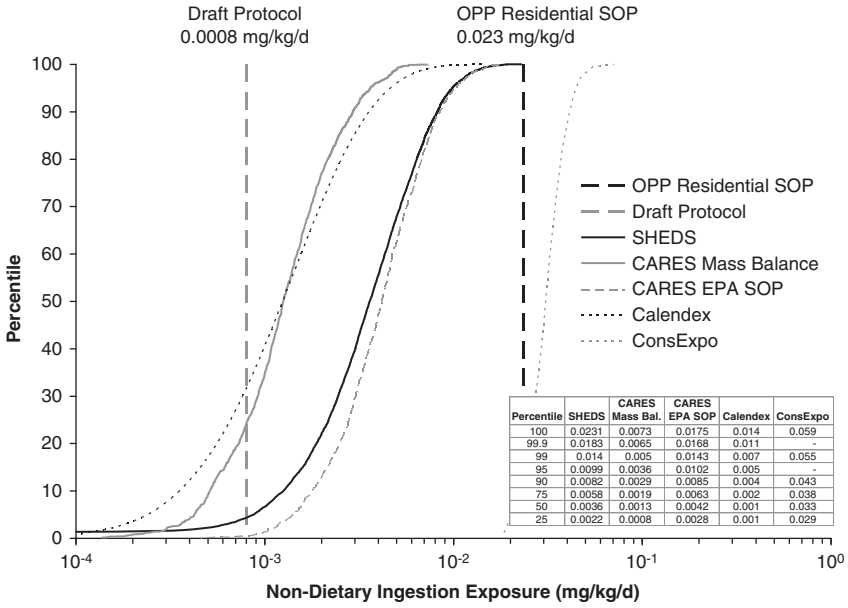


Percentile	SHEDS	CARES Mass Bal.	CARES EPA SOP	Calendex	ConsExpo
100	0.028	0.091	0.261	0.133	0.390
99.9	0.022	0.084	0.239	0.098	-
99	0.015	0.060	0.173	0.061	0.330
95	0.011	0.041	0.111	0.036	-
90	0.009	0.033	0.091	0.026	0.280
75	0.006	0.022	0.065	0.015	0.250
50	0.004	0.014	0.045	0.007	0.220
25	0.002	0.010	0.030	0.003	0.180

Figure 3. Percentile distribution of non-dietary (incidental or indirect) ingestion exposure from the crack and crevice scenario.

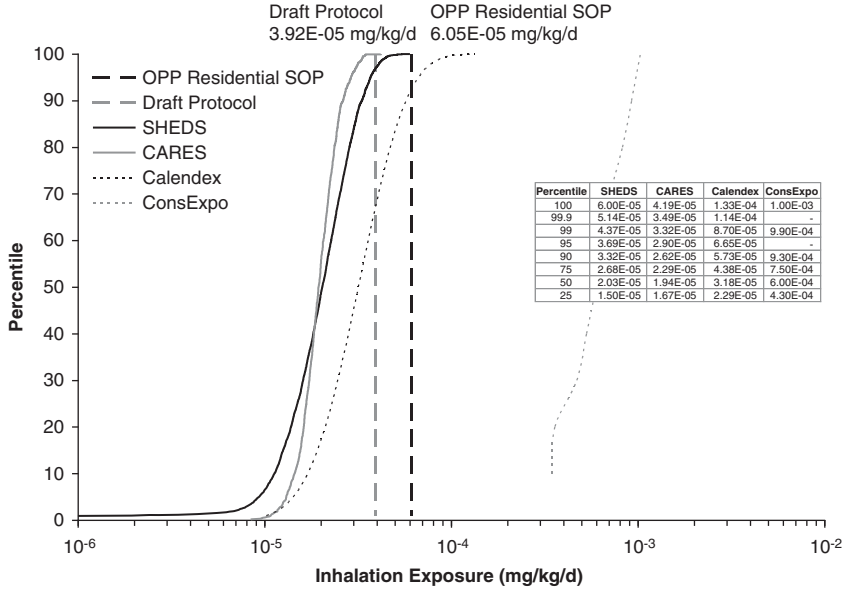
treated surfaces and body-part-specific contact rate assumptions. CARES, Calendex, and ConsExpo conservatively assumed that an individual spends all his/her time in the treated area, whereas SHEDS assumed an individual was in a treated area 50% of the time. SHEDS assumed for the crack and crevice scenario a contact probability in a treated room of 25% for treated surface and 75% for untreated surface, whereas for the fogger scenario a contact probability of 100% was assumed, with a 50% probability of being in the treated room. Also, SHEDS was the only model to incorporate sequential loading and removal processes on a diary event-level basis, thus more closely tying exposures to individual behavior.

The algorithms for estimating non-dietary exposure vary from simple assumptions to complex integrations of hand-to-mouth activities. CARES has two algorithms for non-dietary exposure: (1) one based on the OPP Residential SOP and (2) a mass balance equation similar to SHEDS. Although the equations in CARES are similar to the other models, the exposure distributions were dissimilar for both scenarios (Figures 3 and 4). These differences were attributed to the implementation of dermal exposure because of differences in assumptions about contact with treated surfaces and non-dietary ingestion exposure. ConsExpo currently assumes that non-dietary exposure is 10% of the dermal exposure, which is conservative compared with the methods used by the other models to estimate non-dietary exposure. However, this accounts for the comparatively higher non-dietary exposure estimates made by ConsExpo in the model comparisons. SHEDS splits the whole body transfer coefficient between the hands and



Percentile	SHEDS	CARES Mass Bal.	CARES EPA SOP	Calendex	ConsExpo
100	0.0231	0.0073	0.0175	0.014	0.059
99.9	0.0183	0.0065	0.0168	0.011	-
99	0.014	0.005	0.0143	0.007	0.055
95	0.0099	0.0036	0.0102	0.005	-
90	0.0082	0.0029	0.0085	0.004	0.043
75	0.0058	0.0019	0.0063	0.002	0.038
50	0.0036	0.0013	0.0042	0.001	0.033
25	0.0022	0.0008	0.0028	0.001	0.029

Figure 4. Percentile distribution of non-dietary (incidental or indirect) ingestion exposure from the fogger scenario.

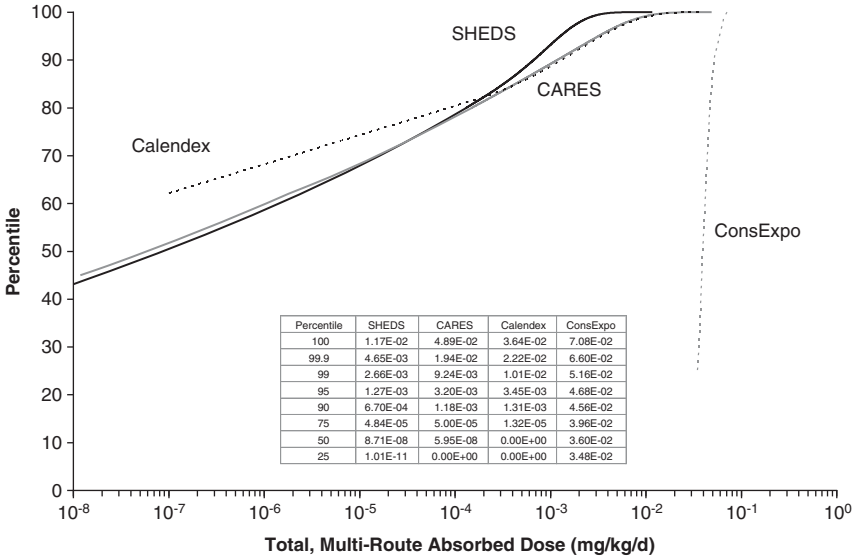


Percentile	SHEDS	CARES	Calendex	ConsExpo
100	6.00E-05	4.19E-05	1.33E-04	1.00E-03
99.9	5.14E-05	3.49E-05	1.14E-04	-
99	4.37E-05	3.32E-05	8.70E-05	9.90E-04
95	3.69E-05	2.90E-05	6.65E-05	-
90	3.32E-05	2.62E-05	5.73E-05	9.30E-04
75	2.68E-05	2.29E-05	4.38E-05	7.50E-04
50	2.03E-05	1.94E-05	3.18E-05	6.00E-04
25	1.50E-05	1.67E-05	2.29E-05	4.30E-04

Figure 5. Percentile distribution of inhalation exposure from the flying insect killer (FIK) scenario.

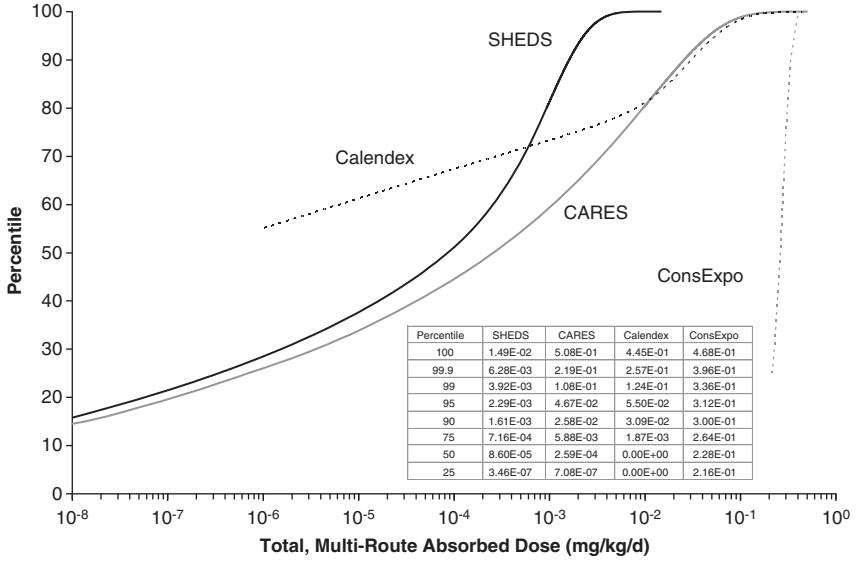
body. CARES (mass balance) maintains the whole body transfer coefficient to estimate whole body exposure, assigning a fraction to the residues on the hands. SHEDS incorporates both washing removal and a maximum dermal loading; the other models allow neither. This upper limit to dermal exposure has a significant influence on the ingestion exposures as compared with the other models that may generate overly conservative exposure estimates.

Inhalation exposure algorithms were similar between all models, with the exception of ConsExpo. Despite the similarities, activity data were treated differently. SHEDS varies time spent in each location based on the CHAD diaries and uses activity-specific inhalation rates. In addition, SHEDS exposes simulated people to different air concentrations in treated and untreated rooms. CARES and Calendex use daily average inhalation rates not associated with activity patterns and assume zero exposure in untreated rooms. CARES does not correlate between probabilistic variables for air concentrations (time-weighted averages) and exposure duration. Contrary to the other models, ConsExpo does not use the residential air concentrations measured after a spray event. Rather, ConsExpo simulates air concentrations after the use of an aerosol spray using product characteristics, such as mass generation rate and particle size distribution. Directly after mixing, the air concentration is assumed to be well-mixed. Removal is by ventilation and gravitational deposition. These differences in methodology are reflected in the observed inhalation exposure estimates (Table 1), resulting in a higher estimate for ConsExpo.



Percentile	SHEDS	CARES	Calendex	ConsExpo
100	1.17E-02	4.89E-02	3.64E-02	7.08E-02
99.9	4.65E-03	1.94E-02	2.22E-02	6.60E-02
99	2.66E-03	9.24E-03	1.01E-02	5.16E-02
95	1.27E-03	3.20E-03	3.45E-03	4.68E-02
90	6.70E-04	1.18E-03	1.31E-03	4.56E-02
75	4.84E-05	5.00E-05	1.32E-05	3.96E-02
50	8.71E-08	5.95E-08	0.00E+00	3.60E-02
25	1.01E-11	0.00E+00	0.00E+00	3.48E-02

Figure 6. Percentile distribution of total absorbed dose for the fogger scenario.



Percentile	SHEDS	CARES	Calendex	ConsExpo
100	1.49E-02	5.08E-01	4.45E-01	4.68E-01
99.9	6.28E-03	2.19E-01	2.57E-01	3.96E-01
99	3.92E-03	1.08E-01	1.24E-01	3.36E-01
95	2.29E-03	4.67E-02	5.50E-02	3.12E-01
90	1.61E-03	2.58E-02	3.09E-02	3.00E-01
75	7.16E-04	5.88E-03	1.87E-03	2.64E-01
50	8.60E-05	2.59E-04	0.00E+00	2.28E-01
25	3.46E-07	7.08E-07	0.00E+00	2.16E-01

Figure 7. Percentile distribution of total absorbed dose for the crack and crevice scenario.

A methodology similar to SHEDS has been incorporated into the revised Residential SOPs of the OPP to more accurately account for treated and untreated surfaces after a pesticide application, and also mouthing algorithms.[26] To support the update to the Residential SOPs, OPP defined perimeter, spot, and crack and crevice applications and spatial deposition in indoor environments to estimate the amount of treated and untreated surface that may exist after these types of pesticide applications. Based on these definitions, the spatial deposition of residues in the indoor environment would include both treated and untreated surfaces. These definitions are based, in part, on the results of these model interpretations. The nominal application rate to treated surfaces (e.g., perimeter areas or spot treatments) can be conservatively derived based on the product's release rate and a conservative area treated, that is, grams of formulation per second per square foot of target surface. Alternatively, the US EPA has also recently provided a revised approach for estimating deposition rates of indoor sprays from a set of actual target surface deposition data. For indoor crack and crevice perimeter treatment, the best estimate of deposition is 9 μg/cm^2 for a 0.5% spray.[26] An alternative source of experimental deposition data can be found in Keenan et al.[27] All of these estimates for treated surfaces incorporate the SHEDS approach of treated and untreated surfaces after an application. Comparisons with real-world data would suggest that pesticide residues are heterogeneously distributed on surfaces after an application (see, e.g., refs 28 and 29), making this a reasonable approach.

Re-entry into a treated room after a perimeter, spot, or crack and crevice application is only expected to result in limited contact with treated areas based on the definitions and application rates. This is supported by spatial deposition studies and other data sources such as comparative biomonitoring studies of indoor crack and crevice *versus* broadcast treatment cited by the US EPA.[26]

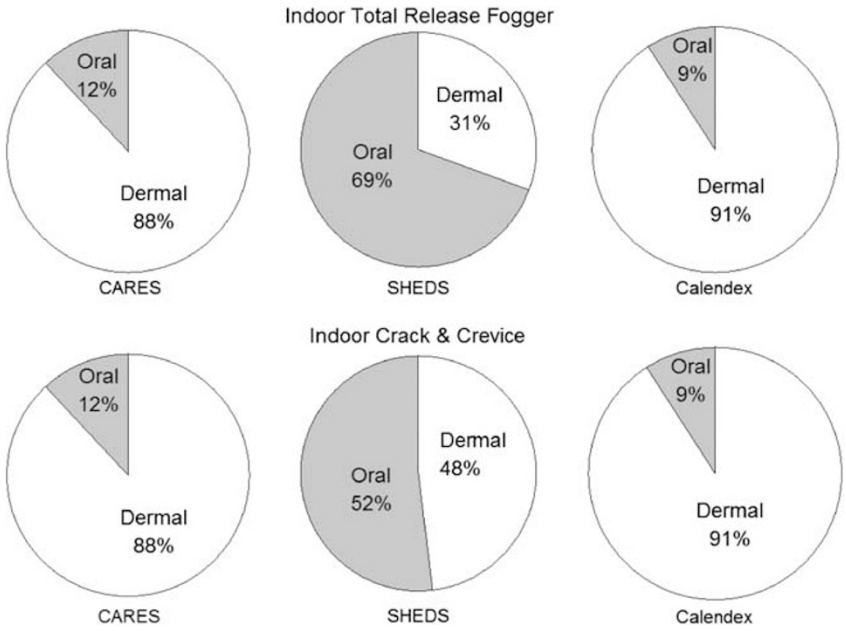


Figure 8. Contribution analysis at the 99th percentile for the fogger and crack and crevice scenarios.

Typically, floor surface residues in untreated, accessible areas have been shown to be at or near analytical limits of detection for the three types of applications relevant to this model comparison. The newly proposed algorithm of the US EPA would result in estimates of ''effective'' surface residues for perimeter and spot treatment that would be approximately one-third of the target deposition values derived above. McLaughlin Gormley King Company has conducted spatial deposition studies with esfenvalerate to verify residues on treated and non-treated surfaces and submitted these data to the US EPA, which has summarized them in the recently revised Residential SOPs.[26]

Although this model comparison is useful because it shows the similarities and differences in how SHEDS, CARES, Calendex, and ConsExpo estimate dermal, ingestion, and inhalation exposures, there are limitations that need to be acknowledged. For this comparison, each model was provided a common set of input values (Tables 2–4). All models handle time activity and location information differently. Research to understand the impact of time activity information is important. Alternatively, national time activity and location databases that are suitable for model data inputs should be available. Calendex has more flexibility than the other models as it requires both algorithm and data inputs to be specified, whereas CARES, ConsExpo, and SHEDS require only data inputs. The purpose of this model comparison was to compare the output for each exposure route with the others. However, model evaluation to real-world data is critical to verify if the models are providing reasonable information based on the data inputs.

Recommendations for future research include conducting model evaluations with real-world data and comparing with biological samples; conducting sensitivity and uncertainty analyses to identify key inputs, data gaps, and other uncertainties; exploring similarities/differences across models (e.g., flexibility of Calendex compared with the fixed algorithms of the others) to prioritize data needs; exploring the impact of underlying time activity and location assumptions; exploring model refinements; exploring refinements for key model inputs; explaining why the models predict higher exposures for crack and crevice than fogger applications; examining what is driving the differences at the upper tails of the model estimates, as the US EPA and other agencies currently regulate at the 99th percentile for acute effects.

CONCLUSION

Six models (two deterministic and four probabilistic) were compared for three scenarios and three pathways. For the scenarios and associated data inputs, the model-to-model pathway comparisons were consistent. The majority of the models predicted exposures that were within a factor of 5 at the 50th and 99th percentiles. We believe such differences are within reasonable expectations, given the activity assumptions, input distributions, and exposure algorithms. Dermal exposure was a key exposure route for the fogger and crack and crevice scenarios. Non-dietary ingestion exposure can also be a key route for the fogger and crack and crevice scenarios. Predicted inhalation exposures were relatively small and similar among the models, with differences chiefly influenced by activity data and inhalation rate assumptions. The results presented here show how exposure predictions vary between models and provide some indications of the reasons for these differences. This information is important to understand when choosing a model for research or regulatory purposes. Model comparisons are also important for future research needs.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGEMENTS

The US Environmental Protection Agency through its Office of Research and Development partially funded and managed the research described here. It has been subjected to Agency administrative review and approved for publication.

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