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Comparison of Four Probabilistic Models (CARES®, Calendex™, ConsExpo, SHEDS) to Estimate Aggregate Residential Exposures to Pesticides

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ABSTRACT

Two deterministic models (U.S. 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, 1.47 mg/kg/day, respectively) were slightly higher than those from SHEDS and ConsExpo (0.74, 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.

INTRODUCTION

Legislative mandate (Food Quality Protection Act [FQPA], 1996) requires the United States Environmental Protection Agency (U.S. EPA) to consider aggregate exposures to pesticides, to consider cumulative effects of pesticide residues that have a common mechanism of toxicity, and to develop new approaches to the study of complex mixtures. 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 (NAS, 2007).

Prior to FQPA, residential exposure assessments were conducted for various pesticides only when certain toxicity and exposure criteria were met. FQPA expanded U.S. 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 U.S. EPA's Office of Pesticide Programs (OPP) has attempted to quantify all major residential exposure scenarios for pesticides having food uses to enable aggregate and cumulative risk assessments. 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 (U.S. EPA, 1997). Based generally on standard U.S. EPA exposure and risk assessment guidelines (U.S. EPA, 1992), the document presented to the SAP outlined various potential pesticide exposure scenarios, such as children playing on lawns or homeowners spraying gardens. Methods for estimating dermal, inhalation, and non-dietary ingestion exposure specifically tailored for each scenario were presented,

including descriptions and sources for exposure factors needed in the algorithms. Since 1997, the Residential SOPs have been used to assess exposure for pesticide registration and re-registration decisions within OPP, as required under FQPA. Recently, OPP presented revised Residential SOPs to the SAP (U.S. EPA, 2009a). The U.S. 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* (U.S. EPA, 2001), which is a deterministic approach to evaluate exposure by each route 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 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 since exposures to pesticides may be different from day to day.

Currently, there are numerous models being refined and evaluated (NAS, 2007; Williams et al., 2010) 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 little effort to systematically compare the various models being developed in academia, government, and industry. This comparison provides an evaluation of selected probabilistic models to indicate model reliability, to understand the underlying

assumptions each model uses, to compare the range of exposure estimates for the inhalation, dermal, and non-dietary ingestion exposure routes predicted at various percentiles, and to compare to standard deterministic exposure estimates.

This paper presents the results of a residential exposure pathway comparison using the OPP Residential SOPs (1997 version), the *Draft Protocol*, CARES, Calendex, ConsExpo, and SHEDS. For this residential model comparison, we compared the route-specific (e.g., inhalation, non-dietary ingestion, dermal) residential exposure estimates generated by each model in 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 due to similar consumption databases and dietary exposure equations (FIFRA SAP, 2004a).

METHODS

In this model comparison, the authors examined indoor exposure estimates from the inhalation, dermal, and non-dietary 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. A hypothetical pesticide was 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 (Jacobs et al., 2003). Route-specific exposures for each scenario were determined based on the potential exposures of young children (2-5 years) since FQPA emphasizes protection of infants and children, including aggregate exposures. For this comparison, non-dietary ingestion includes hand-to-mouth activity only.

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 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

Office of Pesticide Programs' Residential Standard Operating Procedures (hereafter "OPP Residential SOPs")

The U.S. EPA's Office of Pesticide Programs (OPP) uses a set of standard operating procedures (SOPs) to estimate exposures for adults and children in and around residences that have been treated with pesticides (U.S. EPA, 1997). These SOPs are used to evaluate exposures immediately following an application and may be used with registrant supplied data or default screening values found in the SOPs.

Draft Protocol for Measuring Children's Non-Occupational Exposure to Pesticides by All Relevant Pathways (hereafter "Draft Protocol")

The U.S. EPA's *Draft Protocol*, 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 (Tulve et al., 2010; U.S. EPA, 2001) and for this comparison, was used deterministically.

Probabilistic Models

Cumulative and Aggregate Risk Evaluation System (CARES®)

The Cumulative and Aggregate Risk Evaluation System (CARES, 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 FIFRA SAP model review process in 2002 and 2004 (FIFRA SAP, 2002, 2004b). The model uses demographic data from the U.S. Census Public Use Micro Data Sample which is statistically representative of the 1990 U.S. Census. CARES estimates exposure for each individual in the selected population for one year (i.e., 365 days) creating a temporal profile of daily exposures for a user-specified subset.

The residential module in CARES simulates route-specific aggregate and cumulative exposures (e.g., dermal, non-dietary, and inhalation) 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

166 "Reference Population" are only estimated for those persons who have been assigned applicator
167 or post-application exposure scenarios. Each individual's exposure is estimated based on route-
168 specific algorithms and parameters from user-specified probability distributions. Route-specific
169 exposure algorithms for dermal and inhalation exposure are based on the OPP Residential SOPs.
170 The non-dietary ingestion exposure algorithm is based on the OPP Residential SOP (i.e., CARES
171 [EPA method]), as well as a newly developed exposure algorithm (i.e., CARES [mass balance])
172 (Table 1).

173 ***Calendex™***

174 Calendex™ is a software platform that enables probabilistic calendar-based aggregate and
175 cumulative exposure assessment calculations using Monte Carlo techniques. Calendex was
176 originally developed by Durango Software and Novigen Sciences (now Exponent, Inc.) and
177 externally peer-reviewed by the FIFRA SAP model review process in 2000.

178 Calendex is a "shell" that can be used to estimate any type of exposure scenario using
179 whatever parameters and inputs the modeler desires. "Hard-wired" data are limited to
180 demographic and food consumption data from the United States Department of Agriculture's
181 *Continuing Survey of Food Intakes by Individuals* (CSFII). All other data (e.g., contact
182 parameters, residue data, exposure algorithms) must be specified by the modeler. The user
183 specifies the distributions of parameters to calculate both contact and residue functions over
184 time. Calendex assigns and tracks the residue functions over a one-year period, and contact is
185 estimated for each day employing user specified parameters. Calendex can incorporate timing of
186 applications, seasonal variability, residue degradation over time, and other factors. Calendex can
187 run several types of analyses, including single day (general, day-specific, series range), weekly,
188 annual, and rolling averages of specified duration. For the purposes of this comparison,

illustrative exposure calculations were performed using algorithms from the OPP Residential SOPs and specified input parameters.

ConsExpo

ConsExpo is a general estimation tool for predicting human exposures to chemicals found in consumer products (Delmaar et al., 2005). 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. Year averaged exposures follow from assumptions on the frequency at which these exposure events take place. 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.

Stochastic Human Exposure and Dose Simulation Model (SHEDS-Multimedia Version 3) (hereafter "SHEDS")

SHEDS is the U.S. EPA/ORD/NERL's physically-based probabilistic model that can simulate aggregate (single chemical) residential exposures over time via multiple routes of exposure for different types of chemicals and scenarios. To date, SHEDS has been used in the U.S. EPA and other government agencies, academia, and industry for a variety of regulatory and research purposes (e.g., Stout and Mason, 2003; Hore et al., 2006; California EPA, 2007;

212 Syngenta Crop Protection, personal communication). SHEDS was externally peer-reviewed by
213 the U.S. EPA's OPP FIFRA SAP (FIFRA SAP, 2007). Version 3 uses a macro-activity
214 approach for dermal exposure that incorporates both loading and removal (e.g., from mouthing,
215 hand washing, bathing) processes, includes state-of-the-science hand-to-mouth ingestion
216 exposure and other algorithms, reflects variability of activity patterns within a day, and
217 incorporates 2-stage Monte Carlo sampling to assess uncertainty as well as variability (Zartarian
218 et al., 2008).

219 SHEDS estimates the chemical exposure and/or dose for a user-specified population
220 cohort via three primary exposure routes: inhalation, non-dietary ingestion (i.e., via soil/dust
221 ingestion, hand or object mouthing pathways), and dermal contact in a residential setting. To do
222 this, it simulates the daily activities and locations of individuals using sequential
223 time/location/activity diaries from the U.S. EPA's Consolidated Human Activity Database
224 (CHAD; McCurdy et al., 2000). SHEDS utilizes the Glen et al. (2008) approach for longitudinal
225 diary assembly. SHEDS individuals are stochastically-created synthetic individuals whose
226 collective properties reflect the simulated population and scenarios of interest. A simulated
227 individual's contacts with chemical concentrations in various media are probabilistically
228 determined, thus generating the individual's exposure (or dose) time profile for multiple routes
229 using physically-based exposure (or dose) algorithms for each route. Repeating this process over
230 a large number of simulated individuals using Monte Carlo sampling produces the population
231 exposure distributions (Zartarian et al., 2008).

232 SHEDS inputs include chemical usage information, environmental concentration and
233 residue data in various media, exposure factors (human activity- and chemical transfer-related),
234 and dose factors. Outputs from SHEDS include population and individual outputs for various

exposure or dose metrics. A simulated individual's raw data, exposure calculations, and exposure time profiles can be saved and examined for code verification, examination of extremes, and inputs to dose estimation models. SHEDS population outputs can include summary statistics tables, box plots, and cumulative distribution functions that reflect variability and uncertainty. From these, key exposure routes, pathways, and factors can be identified (Xue et al., 2006).

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 deterministic and probabilistic 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 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/d 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/d 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 (approximately 90% dermal, 10% non-dietary ingestion), which is due to 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 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, while for the fogger scenario a contact probability of 100% 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 due to 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 to 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 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 to the other models which 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.

A methodology similar to SHEDS has been incorporated into OPP's revised Residential SOPs to more accurately account for treated and untreated surfaces after a pesticide application, and also mouthing algorithms (U.S. EPA, 2009a). 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, i.e., grams of formulation per second per square foot of target surface. Alternatively, the U.S. 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 $\mu g/cm^2$ for a 0.5% spray (U.S. EPA, 2009a). An alternative source of experimental deposition data can be found in Keenan et al. (2010). All of these estimates for treated surfaces incorporate the SHEDS approach of treated and untreated surfaces after an application. Comparisons to real world data would suggest that pesticide residues are heterogeneously distributed on surfaces after an application (e.g., Stout et al., 2009; Tulve et al., 2006), 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 U.S. EPA (2009a).

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 U.S. EPA's newly proposed algorithm would result in estimates of "effective" surface residues for perimeter and spot treatment that would be approximately 1/3 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 U.S. EPA, which has summarized them in the recently revised Residential SOPs (U.S. EPA, 2009a).

While 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. In certain instances, the values were modified and Tables 2-4 show the final data inputs used. 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 since 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 to 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 to 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 to the fixed algorithms of the others) to prioritize data needs; exploring the impact of underlying time activity and location assumptions; exploring modelrefinements; 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, since the U.S. EPA and other agencies currently regulate at the 99^{th} percentile for acute effects.

CONCLUSIONS

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 50^{th} and 99^{th} 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.

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520 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	$E_d = \frac{(SR)(TC_{hand/body})(ET)(Adj)}{BW}$
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)	$E_{nd} = \frac{(HR)\left(\frac{SA_{H2M}}{SA_{hand}}\right)\left((TE)\left(\sum(F)(ED)\right)(1-TE)^{n-1}\right)}{BW}$ where $HR = (SR)(TC)(ED)(F_{hand})$

SHEDS	$E_{nd} = \frac{\left(\frac{HR}{2}\right)(HF)\left(1-(1-TE)^{((F)(ET))}\right)}{BW}$ $HR = (SR)(TC_{hand})(T)$
ConsExpo	$E_{nd} = (fraction\ hands)(fraction\ transferred)(E_d)$

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

AR = application rate (mg/cm^2)
FD = fraction dislodgeable (unitless)
HF = fraction of one hand that enters the mouth (unitless)

551 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 (μg/m^3)	8 hr. TWA 0.105	8 hr. 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/hr	CARES: Modeled Calendex: Uniform (0.47-0.93) m^3/hr	Modeled	Uniform (0.47-0.93) m^3/hr
ED	Exposure Duration (hr/d)	NA	8	Triangular (2,4,8)	Based on CHAD diaries	8 hr
METS	Ventilation Rate Ratio	NA	NA	NA	Based on diary specific activity	NA
BW	Body Weight (kg)	15	15	CARES: CSFII matched to U.S. Census Calendex: CSFII Reference Population	Based on U.S. 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/hr)	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/d)	6.1×10^{-05}	3.91×10^{-05}	Distribution	Distribution	Distribution

552

553 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 (μg/cm^2)	Fogger	4.41	4.41	4.41	4.41	NA
		Crack & 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 & 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 & 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/hr) (SHEDS splits the value 50% for body and hand)		6130	6130	Lognormal (6130, 1.68, 0, 20000)	Lognormal (3065, 1.68, 0, 10000) Lognormal (3065, 1.68, 0, 10000)	Lognormal (6130, 1.68, 0)
ED	Exposure Duration (hr/d)		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: Beta (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 matched to U.S. Census Calendex: CSFII Reference Population	Based on modeled U.S. Census	Lognormal (18.9, 1.22)

E_d	Dermal Exposure (mg/kg/d)	Fogger	0.73	0.36
		Crack & Crevice	4.75	2.37

554

555 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 ½ TC)
	Mean # of Hand Washes (unitless)		NA	NA	NA	Lognormal (3.74, 2.63, 1, 12)
	Maximum Dermal Loading (mg/d)		NA	NA	NA	Triangular (0.1, 0.6, 2.1)
	Hand Residue (mg/d)	Fogger	0.22	0.22	SR x TC x ED x FT	SR x TC x ED/2 Assuming one hand
		Crack & 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/hr)		8.5	8.5	Triangular (0.4, 8.5, 25.7)	Weibull (0.76, 11.04) (0.75, 12.59)
ED T	Exposure Duration Time available for mouthing (hr/d)		8	4	Triangular (2, 4, 8)	Based on CHAD diaries
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 matched to U.S. Census Calendex: CSFII Reference Population	Based on U.S. Census
E_{nd}	Non-dietary Ingestion Exposure (mg/kg/d)	Fogger	0.01	0.0008		
		Crack & Crevice	0.066	0.0053		

556

557

558 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

559 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[a] 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 & 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

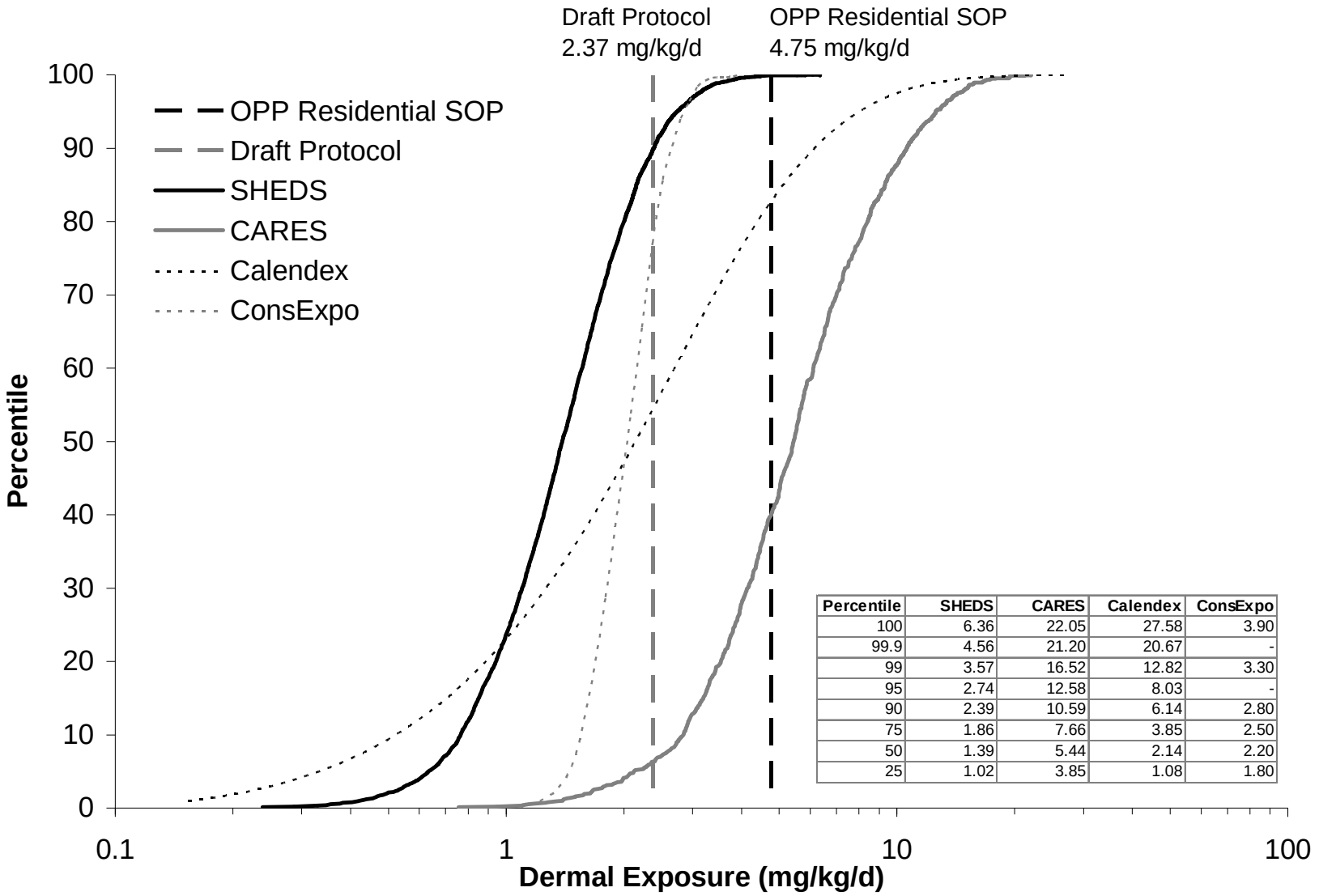
560

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[a] Aerosol	0.14286	0.14286	0.14286	0.14286	0.14286	0.14286	0.14286	5	7
Crack & Crevice	0.14286	0.14286	0.14286	0.14286	0.14286	0.14286	0.14286	5	14

561 [a]Flying Insect Killer.

562

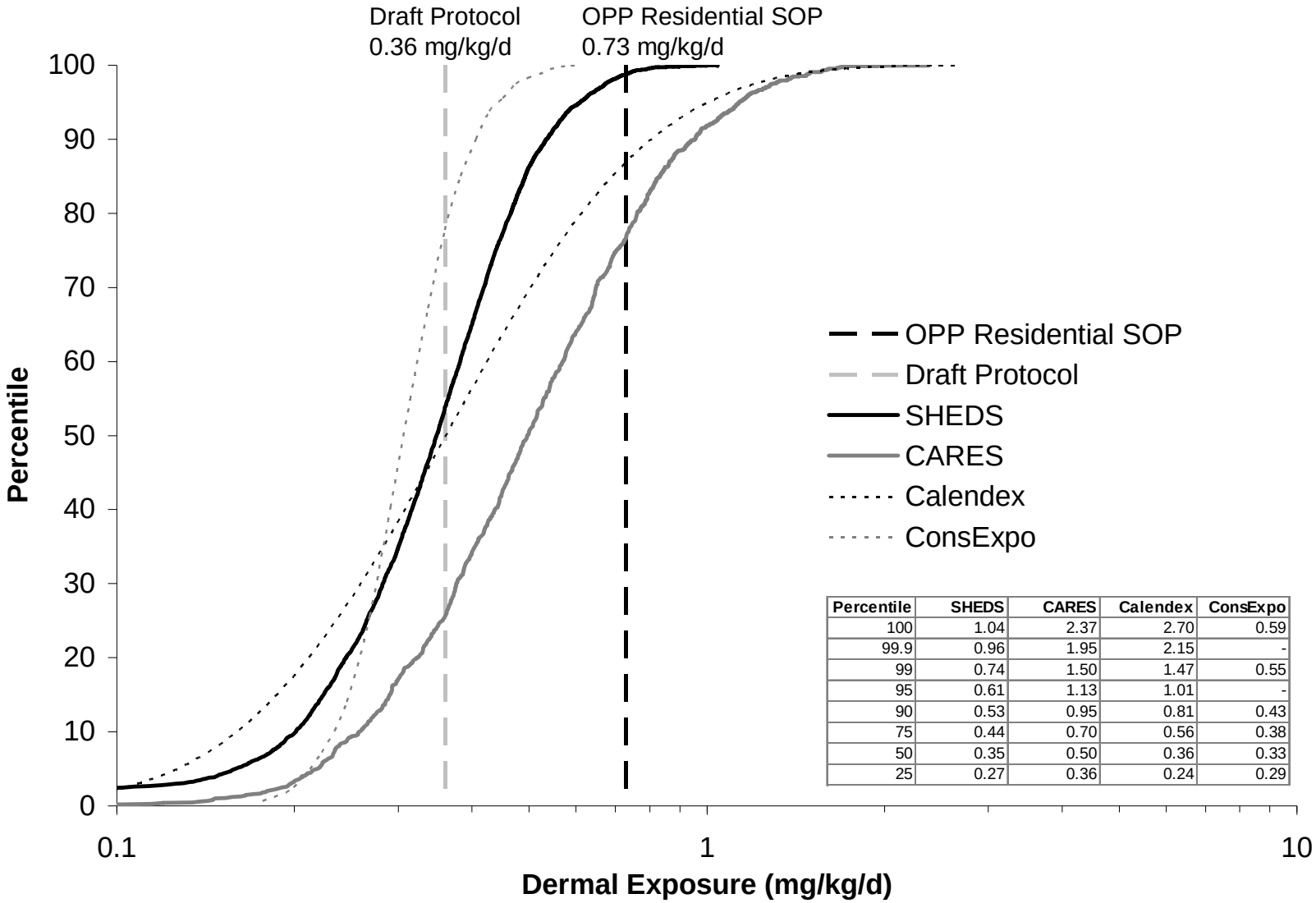
571 Figure 1.



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

572

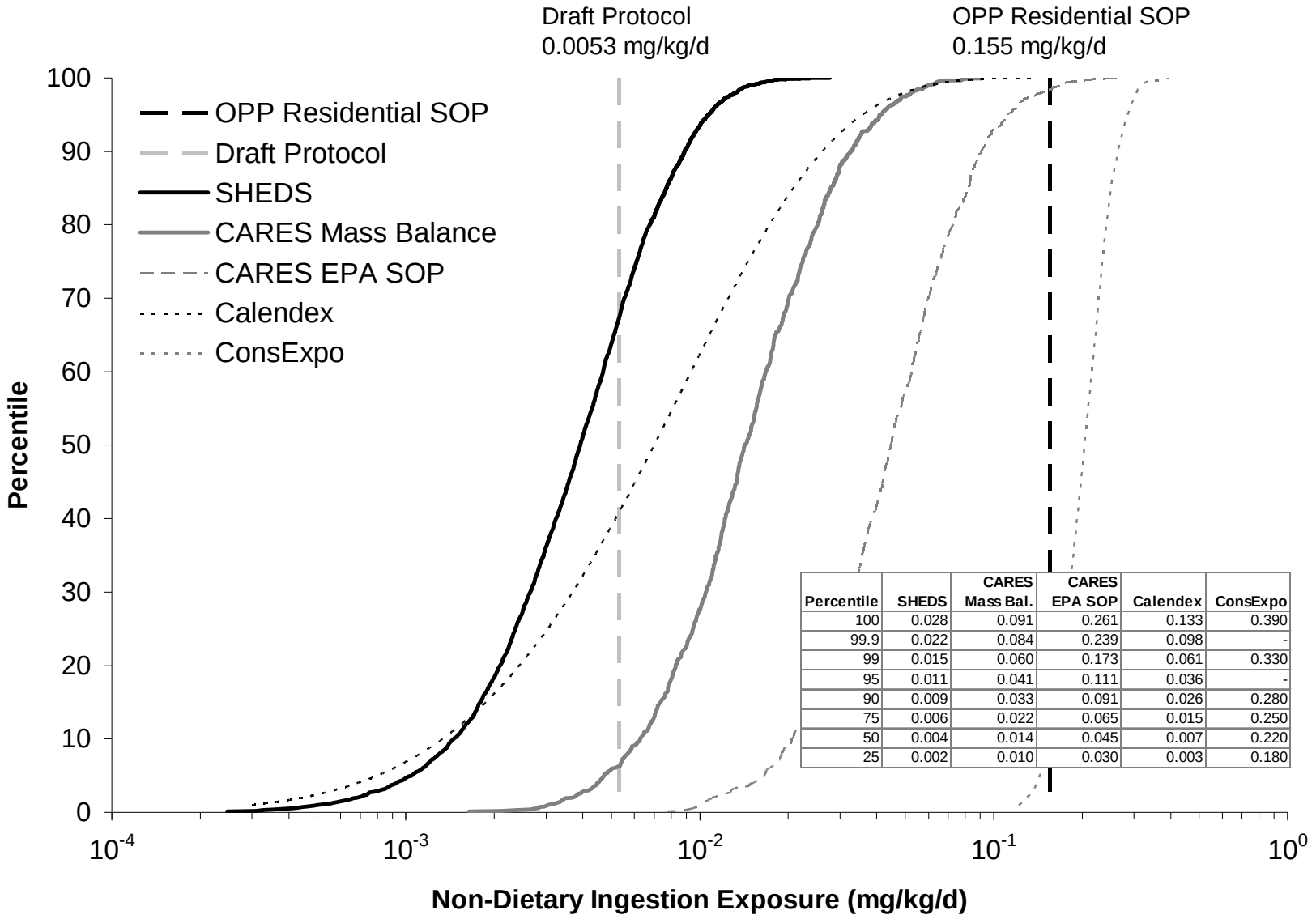
573 Figure 2.



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

574

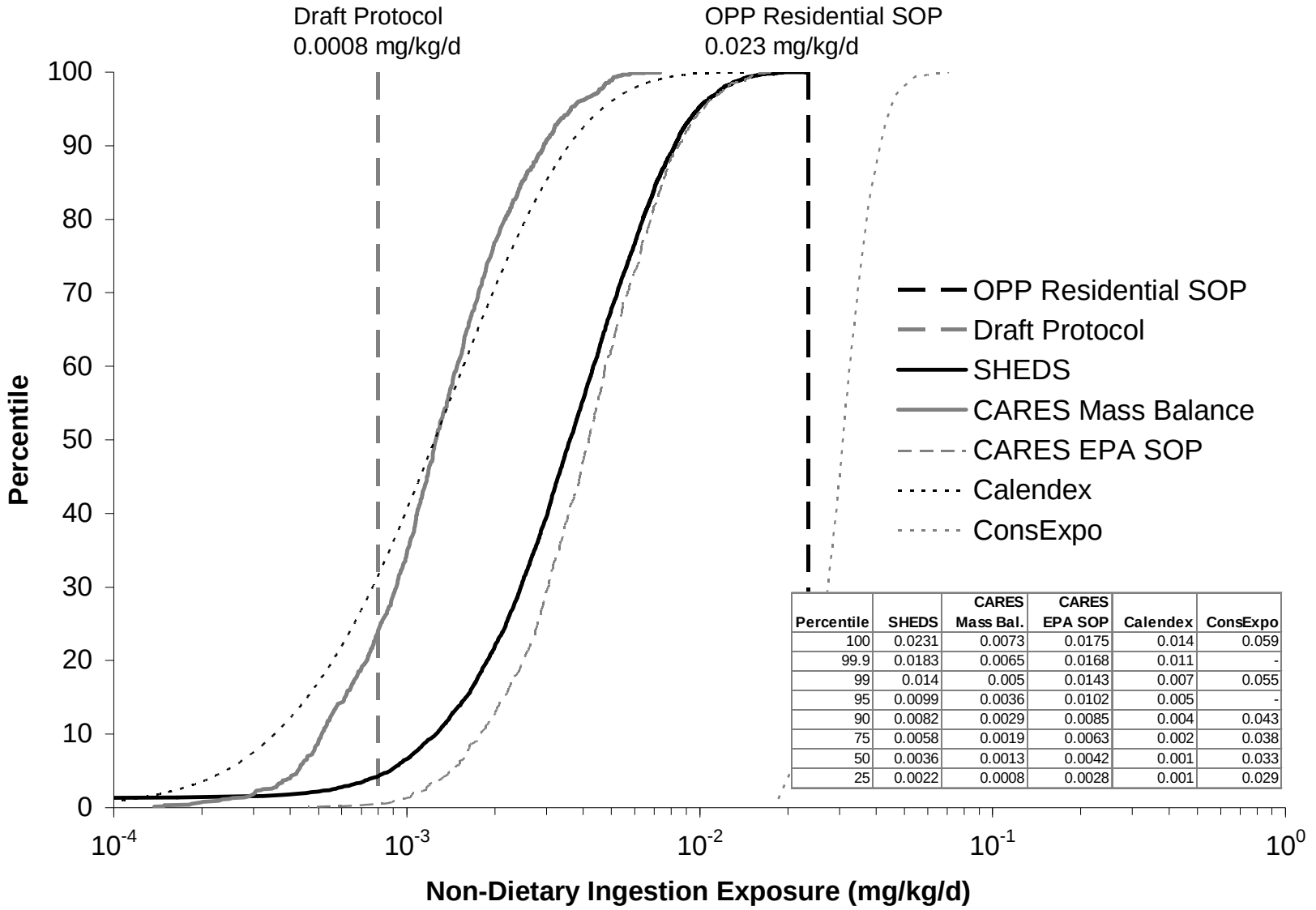
575 Figure 3.



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

576

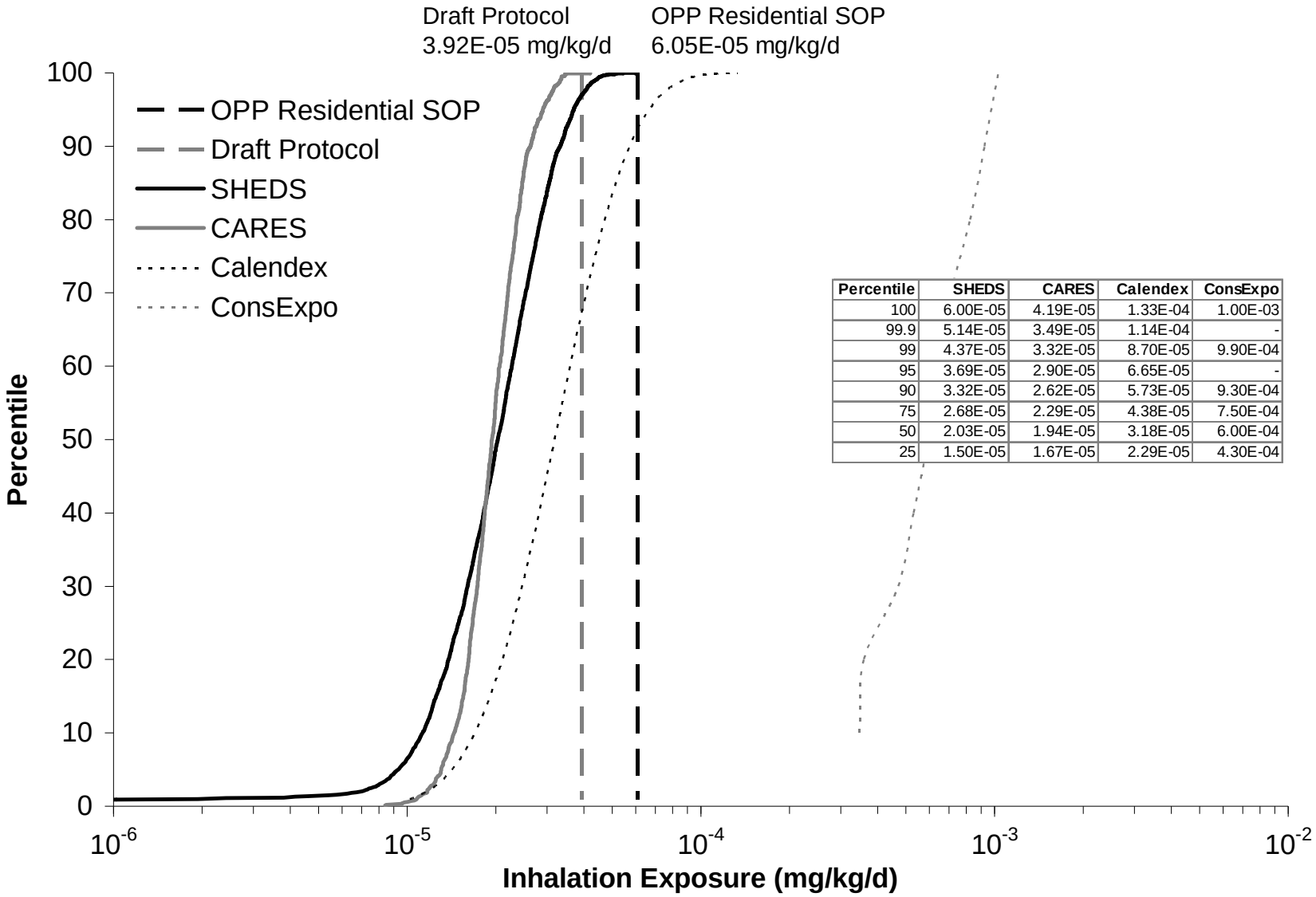
577 Figure 4.



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

578

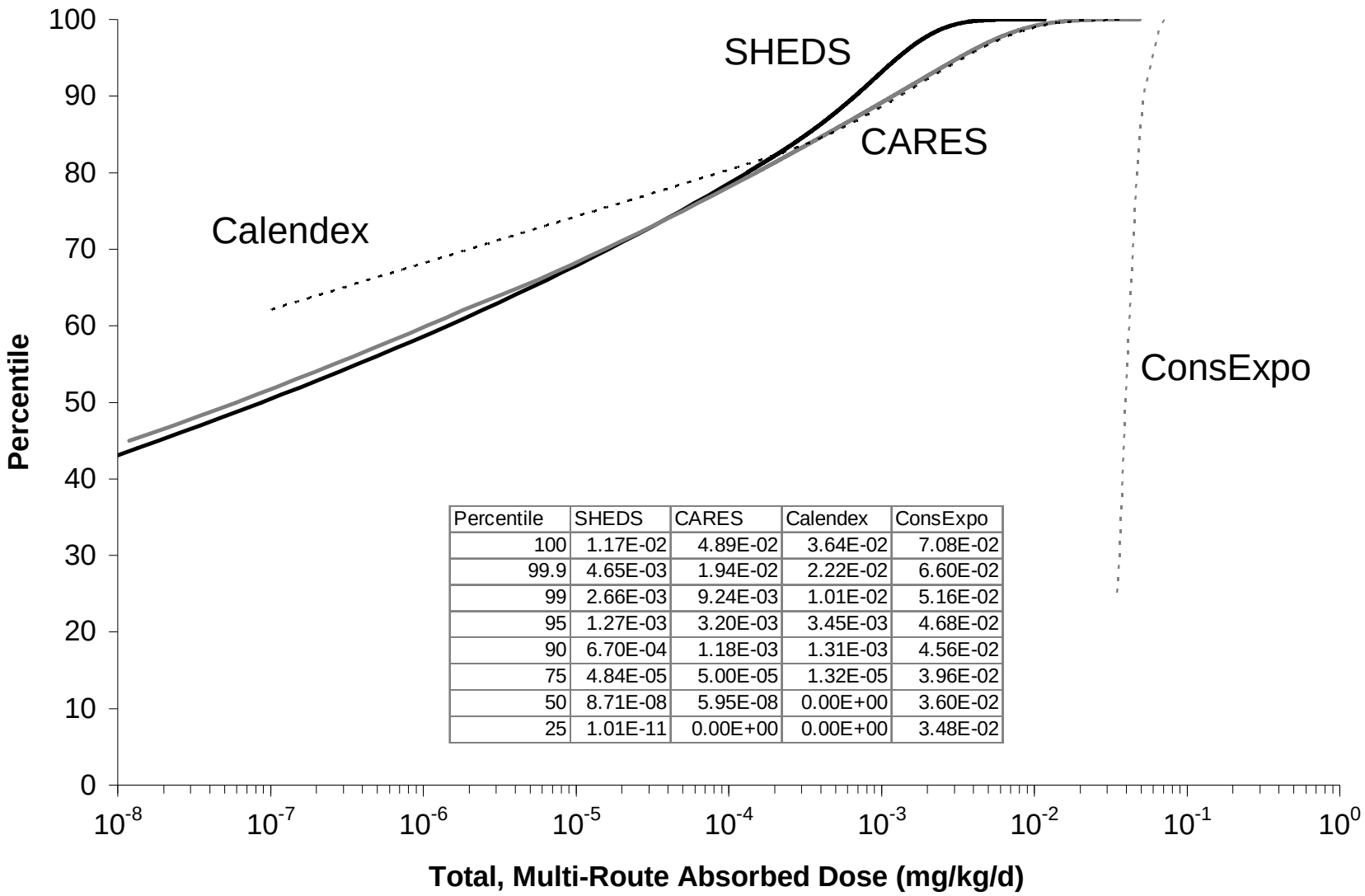
579 Figure 5.



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

580

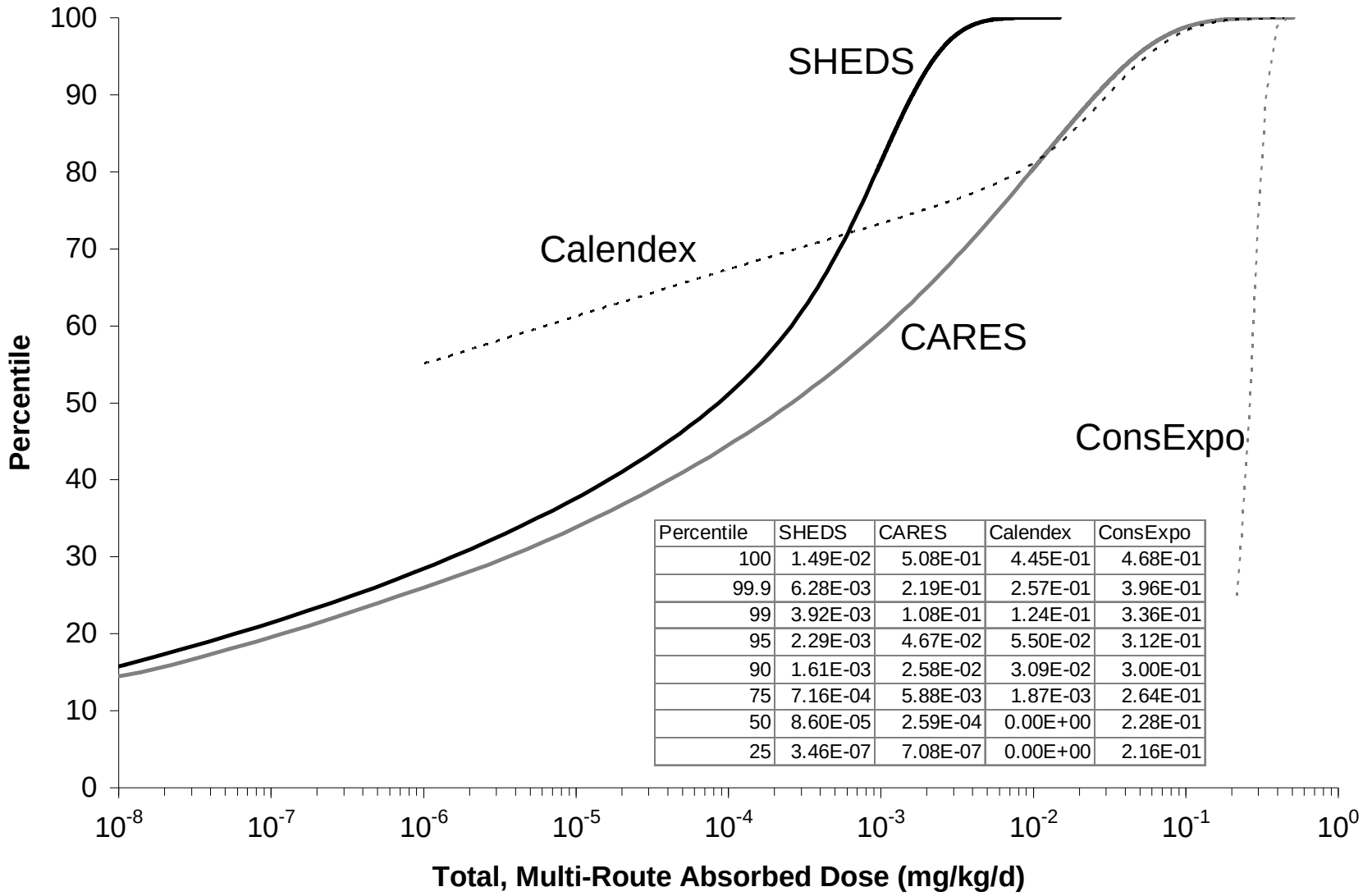
581 Figure 6.



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

582

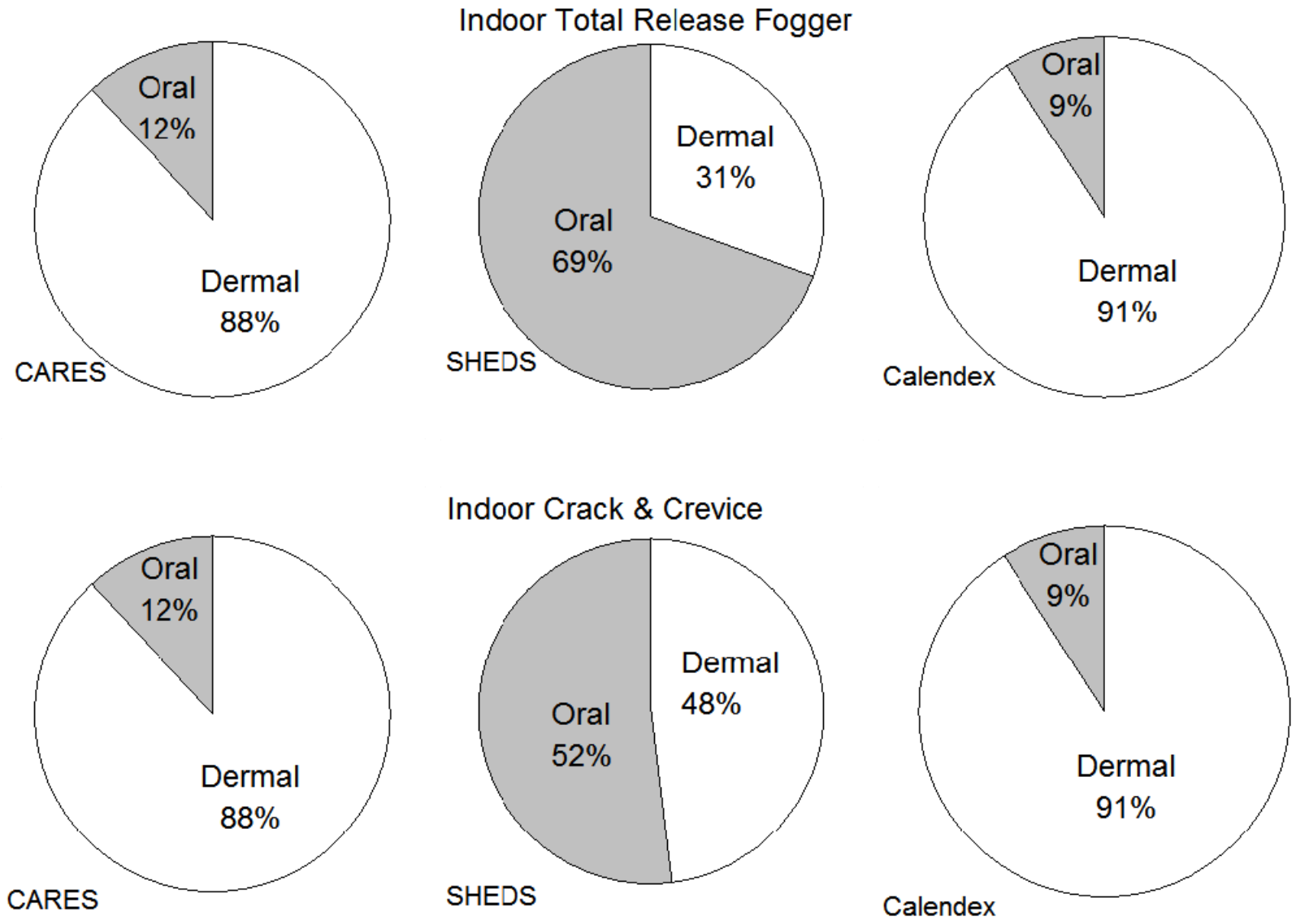
583 Figure 7.



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

584

585 Figure 8.



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