A Modeling Framework for Estimating Children’s Residential Exposure and Dose to Chlorpyrifos Via Dermal Residue Contact and Nondietary Ingestion

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To help address the Food Quality Protection Act of 1996, a physically based probabilistic model has been developed to quantify and analyze dermal and nondietary ingestion exposure and dose to pesticides. The Residential Stochastic Human Exposure and Dose Simulation Model for Pesticides (Residential-SHEDS) simulates the exposures and doses of children contacting residues on surfaces in treated residences and on turf in treated residential yards. The simulations combine sequential time-location-activity information from children’s diaries with microlevel videotaped activity data, probability distributions of measured surface residues and exposure factors, and pharmacokinetic rate constants. Model outputs include individual profiles and population statistics for daily dermal loading, mass in the blood compartment, ingested residue via nondietary objects, and mass of eliminated metabolite, as well as contributions from various routes, pathways, and media. To illustrate the capabilities of the model framework, we applied Residential-SHEDS to estimate children’s residential exposure and dose to chlorpyrifos for 12 exposure scenarios: 2 age groups (0–4 and 5–9 years); 2 indoor pesticide application methods (broadcast and crack and crevice); and 3 postinsecticide application time periods (1–1, 1–7, and 8–30 days). Independent residential turf applications (liquid or granular) were included in each of these scenarios. Despite the current data limitations and model assumptions, the case study predicts exposure and dose estimates that compare well to measurements in the published literature, and provides insights to the relative importance of exposure scenarios and pathways. Key words: aggregate exposure, children, chlorpyrifos, exposure model, dermal, Food Quality Protection Act, nondietary ingestion, pesticides. Environ Health Perspect 108:505–514 (2000). [Online 13 April 2000] http://ehpnet1.niehs.nih.gov/docs/2000/108p505-514zartarian/abstract.html

The Food Quality Protection Act of 1996 (FQPA) mandates the Environmental Protection Agency (EPA) to consider aggregate human exposure, particularly for infants and children, when making pesticide regulatory decisions (1). Implementation of the FQPA necessitates developing new methodologies to assess aggregate nondietary exposures that can occur in a residential setting. As the first step in a tiered approach to assess these exposures, the EPA has developed single-pathway screening-level standard operating procedures (SOPs) for residential exposure assessment (2). The SOPs take a deterministic approach and are intended to result in conservatively high bounding estimates of exposure. If the screening-level estimates are unacceptable, more refined estimates are needed. Thus, the focus of the EPA now is to move toward probabilistic models to determine whether there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to the pesticide’s chemical residues… [1].

Probabilistic methods for assessing human exposure have been recommended by the National Research Council (3) and the EPA (4,5) because they can quantify exposure and dose at different percentiles of a population of interest, as well as the uncertainty associated with those percentile estimates.

A new probabilistic model [the Residential Stochastic Human Exposure and Dose Simulation Model for Pesticides (Residential-SHEDS)] has been developed to improve estimates of children’s aggregate exposure and dose to pesticides in the residential environment and to provide a framework for identifying and prioritizing measurement needs. This model currently focuses on the dermal and nondietary ingestion exposure routes because they are arguably the most difficult to quantify and because studies suggest that they may contribute more significantly to children’s exposure and dose than inhalation and dietary ingestion shortly after a residential pesticide application (6–9). Children have frequent contact with surfaces that may bear pesticide residues and their subsequent hand-to-mouth and object-to-mouth activities may lead to further pesticide exposure. Quantifying the dermal and nondietary ingestion exposure routes is challenging because the processes for dermal loading, removal, uptake, and distribution within the body are complex and vary in space and time, and because limited data are presently available for inputs required to model these processes.

This paper describes the Residential-SHEDS model and the results of applying it to an example exposure assessment for children to the insecticide chlorpyrifos.

Although the results should be viewed with caution because of critical limitations in the current model input database, the chlorpyrifos case study illustrates the utility of this new modeling framework and allows for relative comparison of various pathways and pesticide application scenarios.

**Methods**

**Model description.** Residential-SHEDS simulates dermal and nondietary ingestion exposure and dose to individuals who contact various types of surfaces in the home that may bear pesticide residues as well as turf in the residential yard that may also have been treated. Residential-SHEDS is a physically based probabilistic model coded in SAS (version 8; SAS Institute, Inc, Cary, NC); mechanistic equations are used to calculate exposure and dose, and Monte Carlo sampling is applied to select both individuals from the population and equation inputs from user-specified probability distributions. For a given exposure scenario (i.e., a specified age group, postapplication time period, and indoor residential pesticide application method), Residential-SHEDS generates daily exposure and dose time profiles for simulated individuals using the microactivity approach, then constructs population histograms of the desired exposure and dose metrics from the individual results. The algorithm for constructing a dermal exposure profile in Residential-SHEDS is based on Stanford University’s Dermal Exposure Reduction Model (DERM) (10–12). Whereas DERM was designed to...
estimate dermal exposure for individually videotaped children. Residential-SHEDS is designed to estimate both exposure and dose via the dermal and nondietary ingestion routes for age-specific cohorts of children in the general population.

Five types of model inputs are required. The first is macrolevel activity data (i.e., sequential time-location-activity information for individuals in the population of interest and probabilities of an individual's proximity to indoor and outdoor pesticide applications). The second and third inputs are microlevel activity data (i.e., skin-to-surface, hand-to-mouth, and object-to-mouth contact frequencies and durations) and probability distributions for residue surface loadings contacted. The fourth type of model input needed is probability distributions for exposure factors (i.e., surface area contacted, surface-to-skin residue transfer efficiency, and residue removal efficiency via liquid contact), and fifth, pharmacokinetic rate constants for the chemical of interest. Model outputs include individual profiles and population histograms for daily dermal loading, mass in the blood compartment, ingested residue via nondietary objects, and mass of eliminated metabolite, as well as relative contributions to exposure and dose from different media, routes, and pathways.

**Model approach.** There are two general approaches to modeling dermal and nondietary ingestion exposure, referred to as the microactivity and macroactivity approaches (13). In the microactivity approach, exposure is modeled as a series of transfers or removals resulting from each discrete contact event (e.g., right hand contacting toy for 10 sec, fingers contacting mouth for 3 sec). In the macroactivity approach, dermal exposure is modeled using empirically derived transfer coefficients to lump the mass transfer associated with a series of contact events (13). The Residential-SHEDS model currently uses the microactivity approach.

Sequential dermal and nondietary ingestion exposure and dose time profiles are simulated by combining measured surface residues and residue transfer efficiencies with actual microlevel activity data quantified from videotapes. Because the sequence of dermal loading and removal processes is preserved, such exposure profiles can improve estimates of time-dependent dermal absorption, which have traditionally assumed a fixed concentration at the skin surface. With information on frequency and duration of hand-to-mouth activities, these profiles can also improve estimates of ingested residues that are otherwise difficult to quantify. Exposure and dose profiles also provide various metrics of toxicologic interest (e.g., peaks, averages, and instantaneous values) and information about the relative contribution of exposure pathways. When combined with activity data, profiles can provide information on how exposures and doses occur and how they can be mitigated.

The Residential-SHEDS algorithm is illustrated in Figure 1. For each specified exposure scenario, the model randomly selects an individual from the National Human Activity Pattern Survey (NHAPS) (14,15) and simulates a sequence of object contact events (with object categories for smooth surface, textured surface, nothing, food, water, grass, and mouth) during each sequential location-activity combination reported in the individual's daily diary. Each object contacted is associated with an exposure pathway (i.e., skin-to-surface residue contact, skin-to-water contact, hand-to-mouth contact, or object-to-mouth contact) that allows the model to select the appropriate exposure and dose equation for each contact event.

The model then steps through every 5 sec in the simulated individual's day, combining proximity-specific surface residues with randomly sampled exposure factors for the appropriate pathway equation. Initial and final values are calculated for each sequential contact event in the person's database, and time profiles are generated for dermal exposure, nondietary ingestion, mass of metabolite in the blood compartment, and mass of metabolite eliminated (Figure 2) using pathway-specific equations (Appendix A). Exposure and dose metrics of interest are extracted from the time profiles, and the entire process is repeated 1,500 times to yield histograms for the specified exposure scenario.

**Model assumptions.** Residential-SHEDS currently assumes first-order linear absorption from the skin and gastrointestinal tract into the body and first-order urinary elimination of the pesticide metabolite from the body. This is an extremely simplified model of the absorption, metabolism, and elimination processes. Nonetheless, the half-life of 3,5,6-trichloro-2-pyridinol (TCP), a urinary metabolite of chlorpyrifos, in the body predicted by this set of equations is consistent with the limited published human data (16). Future research will include developing more complex and physiologically based pharmacokinetic models and incorporating them into Residential-SHEDS.

The model construct contains a number of other assumptions that can be refined with more research. For example, removal and loading of chemicals at the skin surface is assumed to be instantaneous and independent of number of skin-to-surface contacts, and the model does not track which portion of the skin contacts reside from one contact event to the next. For a given application method and postapplication time, deposited concentrations on targeted surfaces are assumed to be the same throughout a residence; nontargeted surfaces in the same residence are also assumed to be uniform, but may be different from targeted surfaces. Surface residue loadings are resampled for each simulated residence. The model time step is on the order of seconds (based on available skin-to-surface contact duration data), except during sleeping activities, when 30 min is used (the optimal time step for minimizing error in approximating the exact analytical solution to the differential exposure and dose equations with numerical difference equations). Because little information is available on the physical and chemical fate of pesticide residues indoors, nonparticle-bound residues are assumed for up to 30 days postapplication, and aerosol deposition and evaporation at the skin surface are not currently included. The individuals sampled are assumed to live in residences with independent indoor and lawn pesticide applications. The initial daily exposure and dose is assumed to be zero for a given individual. During a sleeping event the child's skin is assumed to contact nontargeted surface residues. Legs, arms, torso, and feet are treated as a single skin surface because body-part-specific microactivity data are currently lacking, except for hands and mouth. Because of the lack of data concerning the penetration of pesticide residues through clothing and the percent of skin surface that is clothed, the role of clothing is currently neglected in the model.

Residential-SHEDS is a useful tool for identifying data needs to encourage research so that the model can be developed and used reliably to make predictions when measurements are not feasible. In particular, the model can be used now as a research tool to identify critical data needs and relative contributions of pathways and model inputs, and can be used for regulatory purposes after it has been evaluated.

**Model inputs for chlorpyrifos exposure assessment.** We selected chlorpyrifos to demonstrate the model capabilities because it is one of the top five insecticides used in U.S. homes (17), because a relatively large exposure database exists, and because it is currently undergoing reregistration by the EPA Office of Pesticide Programs (Washington, DC). In conducting the example exposure assessment, we considered two age groups (0–4 and 5–9 years of age), two indoor application methods (broadcast and crack and crevice), three postindoor application time periods (<1, 1–7, and 8–30 days), and two body part groupings (hands and mouth; rest of body below neck). Only two age groups were selected because of limitations in age-specific sample sizes for available
time–location–activity diaries. Ideally, more activity data would be required to refine the strata selection because both macro- and microlevel activities may vary greatly as a function of age. Although residential broadcast applications of chlorpyrifos were phased out in 1997–1998 (18), we considered them as well as crack-and-crevice applications so that modeled estimates could be compared against measured data from studies conducted when broadcast applications were still in use [e.g., the National Human Exposure Assessment Survey (NHEXAS); (19)]. We based the three time periods on the scenario descriptors (duration of exposure) currently used by the EPA; these descriptors correspond to acute, short-term, and intermediate-term exposures (20).

We included independent residential turf applications for each indoor application scenario. That is, for a selected individual in a given indoor application scenario (e.g., children 0–4 years of age in a broadcast-treated home < 1 day postapplication), we assumed that if the individual's diary included time spent on his or her residential lawn, the lawn had been treated with a liquid or granular application either < 1, 1–7, 8–30, or 31–365 days before the individual's contact. We assumed that the probabilities of these four categories of lawn treatment were independent of indoor residential treatments.

Macroactivity data. We grouped sequential time–location–activity diaries of children 0–9 years of age from NHAPS (14,15) into 575 children 0–4 years of age and 521 children 5–9 years of age for macroactivity data used in the exposure assessment. We used four location categories: in the treated residence at the targeted application site; in the treated residence at nontargeted application sites; outdoors on the treated residential lawn; and far from the residence (e.g., school, other home, or mall).

No data were available on children's activities related to proximity to pesticide applications. Thus, for indoor crack-and-crevice treatments, we assumed that 10% of the time a child in the residence contacted surfaces at the targeted application site, and 90% of the time the child contacted surfaces near the targeted site. For indoor broadcast treatments, we assumed that 50% of the time a child in the residence contacted the most contaminated surfaces (e.g., floors), and 50% of the time the child contacted less-contaminated surfaces (e.g., furniture). These scenarios seem reasonable for demonstrating Residential-SHEDS capabilities. An advantage of this modeling framework is that sensitivity of modeled estimates to different model inputs, e.g., inputs for which data are limited or unavailable, can later be determined.

We estimated probabilities for children spending time on lawns treated with granular or liquid chlorpyrifos applications using information for frequency of home lawn applications from the National Home and Garden Pesticide Use Survey (21). We constructed a probability density function for the number of annual lawn applications (ranging from 1 to 12). We assumed equal probability of granular and liquid applications and no more than one application per month.

Microactivity data. Because microlevel activity data are difficult, labor-intensive, and costly to gather from direct observation methods such as scorecards or videotaping, limited information is available. Residential-SHEDS currently assumes a 5-sec time interval for every contact event, based on data from four children 2–4 years of age (22). However, if the same surface type is sampled several times in a row when the model

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**Figure 1.** Flow chart for Residential-SHEDS. NHAPS, National Human Activity Pattern Survey.

**Figure 2.** Example daily exposure and dose profiles for a child. TCP, 3,5,6-trichloro-2-pyridinol. (A) Dermal chlorpyrifos exposure. (B) Daily TCP body burden profile. (C) Daily urinary TCP profile.
simulates contact events, those events are aggregated by contact duration and treated as one contact event with one instance of surface-to-skin residue transfer. This results in a distribution of contact durations that seems to be consistent with preliminary analyses of new videotaped activity data (23). Ideally, probability distributions of contact durations for each type of object contacted by each body part would be used.

Based on published videotape data from 34 children in two studies (22,24,25), we assumed hand-to-object contact frequencies as given in Table 1. Hand-to-object and hand-to-mouth contact frequencies were assumed to be the same for children 0-4 and 5-9 years of age; object-to-mouth contact frequencies were assumed to be different. For children 0-4 years of age, we assumed that 3% of hand-to-object contacts result in an object-to-mouth contact, and we assumed the percentage was 0.1% for those 5-9 years of age (29). No published microlevel activity data for body parts other than hands and mouth of children (i.e., trunk, arms, legs, and feet) were identified; assumptions made for these are also presented in Table 1. Several research groups are in the process of gathering additional microactivity data for hands and other body parts.

Chlorpyrifos surface residue loading data. We fitted probability distributions to literature values (26-37) for residential indoor and turf surface chlorpyrifos loadings using Crystal Ball software (version 4.0; Decisioneering, Denver, CO) (Figure 3, Table 2). Sample collection methods varied both between and within studies, and included the use of α cellulose coupons, cotton fabric coupons, gauze pads, and aluminum foil. Where available, we used individual measurements from the literature in generating the surface-loading probability distributions; otherwise, we used the average values reported. For time periods >30 days postapplication, we assumed that the residues were zero both indoors and on the lawn. Because pesticide residue data are unavailable for nonresidential locations such as schools, day-care centers, and parks, we assumed that chlorpyrifos residues outside of an individual's residence or home lawn were negligible in this case study.

Two types of surface residue loading data were available in the literature for broadcast applications of chlorpyrifos: a) measurements from targeted surfaces (e.g., carpets and hard floors where the pesticide was directly applied) and b) measurements from nontargeted surfaces (e.g., furniture in a room where pesticide was applied to the carpet or hard floor). We chose lognormal distributions as the best fitting distributions for all of these broadcast application data (Table 2 and Figure 3).

No measurements of deposited chlorpyrifos surface loadings were available in the literature for >2 days after broadcast application. For the 1- to 7-day time period, we fitted a residue loading distribution from data 1-2 days postapplication at target sites and from data 1 day postapplication at nontarget sites. We back-calculated the distribution for deposited surface residue loadings at the target site 8-30 days postapplication from a distribution of the dislodgable measurements for carpets from 15 to 93 days postapplication (29) and from the distribution for transfer efficiency from carpets. We used this calculation because deposited residues estimated from dislodgable measurements for the 1- to 7-day postapplication time period were of the same order of magnitude as the actual deposited measurements for this time period (estimated median = 1,500 ng/cm²; actual median = 4,800 ng/cm²). Because measurements of deposited chlorpyrifos surface residue loadings on nontarget surfaces 8-30 days postbroadcast application were not available in the literature, we used the 1- to 7-day deposited surface loading distribution.

Whereas mean surface loadings for crack-and-crevice treatments at the target site were ~30 times lower after 1 day postapplication, the loadings at the nontarget sites did not vary significantly with respect to postapplication time (Table 2). In fact, there appears to be a slight increase in surface loadings over time for nontarget sites, possibly due to sampling and/or analysis issues or physical migration in the residence. We assumed the same distributions for target and nontarget sites for the 1- to 7-day and 8- to 30-day periods because residue

| Table 1. Microactivity data assumptions. |
|----------------------------------------|
| Body part | Activity | Location | Surface | Probability of contacting surface for a given contact event |
|-----------|----------|----------|---------|-----------------------------------------------------------|
| Hands     | All except bathing and sleeping/napping | Indoors | Smooth | 0.3⁹ |
|           |          |          | Textured | 0.3⁹ |
|           |          |          | Mouth | 0.015⁹ |
|           |          |          | Nothing (air or zero-residue object) | 0.35⁹ |
|           |          |          | Food | 0.03⁹ |
|           |          |          | Water | 0.005⁹ |
| Hands     | All      | Lawn     | Grass | 0.3⁹ |
|           |          |          | Mouth | 0.015⁹ |
|           |          |          | Nothing (air or zero-residue object) | 0.055⁹ |
| Hands and body | Bathing | All | Water | 1.0⁹ |
| Hands and body | Sleeping/napping | All | Textured | 1.0⁹ |
| Body      | Most     | Indoors  | Smooth | 0.1⁹ |
|           |          |          | Textured | 0.1⁹ |
|           |          |          | Nothing | 0.0⁹ |
| Body      | All      | Lawn     | Grass | 0.5⁹ |
|           |          |          | Nothing (air or zero-residue object) | 0.5⁹ |

*Based on data from Zartarian et al. (22,24) and Reed (29); children 18 months to 5 years of age. *No published data available; estimates assumed.

Figure 3. Summary of input surface chlorpyrifos residue loading data.
*Units for broadcast target surface residues are micrograms per square centimeter; units for all other residues are nanograms per square centimeter.
data measured at different locations were similar within the respective time intervals.

Because deposited chlorpyrifos residues were reported by only one study (38) and because residue transfer efficiencies from turf are not available, we based dislodgeable turf residue loading distributions on the data reported by Vaccaro et al. (36,37). Data for broadcast liquid applications 1–2 days postapplication were similar to the < 1-day postapplication data and may not be representative of the 1- to 7-day time period because of outdoor degradation processes; thus, we assumed that the mean turf residue loadings for 1–7 days were approximately an order of magnitude lower than the < 1-day residues, with the same coefficient of variation, based on the results of Sears et al. (39). Because no data were available for turf chlorpyrifos measurements 8–30 days after broadcast liquid and granular applications, we assumed that the distribution was the same as for the 1- to 7-day time period.

**Exposure factor data.** Probability distributions for exposure factors required by Residential-SHEDS were also fitted to literature values using Crystal Ball software. Distributions were developed for surface-to-skin residue transfer efficiency, liquid removal efficiency, and skin surface area contacted.

Numerous studies (26–29,31,40,41) have reported surface-to-skin residue transfer efficiency (i.e., ratio of dislodgeable to deposited surface residue loading) for chlorpyrifos based on measurements with a drag sled, polyurethane foam (PUF) roller, cloth roller, human hand press, wipe sample, or cloth dosimeter extraction. We developed probability distributions for transfer efficiencies from textured and smooth surfaces based on measured data from carpets and smooth surfaces (vinyl flooring and furniture), respectively (Table 3). Because the PUF roller may more accurately simulate the human hand than the drag sled or cloth roller do (29), we did not include results from the drag sled and cloth roller in the case study. We used a transfer efficiency of 1% for turf because we used dislodgeable rather than deposited residue values.

Based on the raw data from several studies, we used a uniform distribution ranging from 10 to 50% for saliva removal efficiency. One study reported that chlorpyrifos on freshly spiked human hands was removed at approximately 50% efficiency by human saliva (42). It is estimated that 50% represents the maximum mouthing removal efficiency for fresh or dried pesticide residues (43). Another study presented results of a laboratory-based examination of hand-to-mouth transfer of soil from thumb sucking and finger mouthing, and found 10.1 and 15.9% removal for the two activities, respectively (44).

Because we did not find any studies that reported the percentage of chemical residue which is removed from the skin from bathing, we assumed a uniform distribution ranging from 50 to 100%. Possible biases in the NHAPS diaries due to underreporting of bathing/washing events would lead to conservatively higher estimates of exposure if washing does in fact remove a significant fraction of residue from skin before it is absorbed. Such underreporting is suggested by discrepancies in reported hand-washing events between the NHAPS daily activity diaries and a water-use questionnaire also administered as part of NHAPS (15).

We computed normal probability distribution parameters for surface area of hands and the rest of the body (legs, arms, torso, and feet) for boys and girls 0–9 years of age from Tables 6-6 to 6-8 in the EPA Exposure Factors Handbook (45). Because we found no data for the fraction of skin surface area contacted by children during normal activities, we assumed uniform distributions, as shown in Table 4.

**Pharmacokinetic rate constants.** The dermal absorption, gastrointestinal absorption, and elimination rate constants used in Residential-SHEDS were 8.56 x 10^-6, 4.167 x 10^-4, and 7.167 x 10^-6/ sec, respectively, based on a clinical trial involving six human subjects (16). Chlorpyrifos was converted to TCP inside the body by multiplying by the

### Table 2. Summary of input surface chlorpyrifos-loading distributions.

| Application type | Time period | Distribution type | Mean or min, max (ng/cm²) | GM (ng/cm²) | GSD | Range (ng/cm²) | Data points (n) | Notes |
|------------------|-------------|-------------------|---------------------------|-------------|-----|----------------|----------------|-------|
| **Deposited chlorpyrifos surface residue loadings** | | | | | | | | |
| Broadcast (target) | < 1 day | Lognormal | 8,989 | 7,907 | 6,749 | 2.13 | 1,371–38,400 | 110 | 1–2 days post-application |
| | 1–7 days | Lognormal | 5,754 | 6,065 | 3,960 | 2.37 | 1,521–13,170 | 20 | See text |
| Broadcast (nontarget) | 8–30 days | Lognormal | 491 | 1,832 | 127 | 5.18 | 0.2–4 | 11 | See text |
| Crack and crevice | < 1 day (target) | Normal | 1.55 | 1.68 | 1.05 | 2.41 | 98–100 | 3 | See text |
| | < 1 day (nontarget) | Lognormal | 0.94 | 1.1 | 0.61 | 2.54 | 0.2–4 | 12 | See text |
| | 1–7 days (target and nontarget) | Lognormal | 1.55 | 1.68 | 1.05 | 2.41 | 98–100 | 3 | See text |
| | 8–30 days (target and nontarget) | Lognormal | 4.77 | 5.87 | 3.01 | 2.61 | 0.39–13 | 22 | See text |
| **Dislodgeable chlorpyrifos surface residue loadings** | | | | | | | | |
| Turf | Liquid broadcast | Normal | 23.7 | 5.9 | 16–30 | 6 | Dow sled | See text |
| | 1–7 days | Normal | 3 | 0.75 | | | | | |
| | 8–30 days | Normal | 7 | 0.75 | | | | | |
| | Granular broadcast | < 1 day | Lognormal | 3.1 | 1.56 | 2.62 | 1.8 | 1.0–6.0 | 8 | See text |
| | 1–7 days | Uniform | 0.01 | 1.22 | | | | | |
| | 8–30 days | Uniform | 0.01 | 1.22 | | | | | |

**Abbreviations:** GM, geometric mean; GSD, geometric standard deviation; max, maximum; min, minimum.
TCP: chlorpyrifos molecular weight ratio of 0.566. In the Residential-SHEDS assessment, we assumed that 70% of ingested chlorpyrifos was available for absorption from the gastrointestinal tract (the remainder was excreted in feces) (16). We also assumed that all chlorpyrifos mass on the skin was available for dermal absorption. Because the existing published data on dermal absorption studies do not provide detailed information on subject-specific dermal exposure patterns accounting for loading and removal processes (e.g., residue contact, washing, and mouthing), it is difficult to assess the significance of this assumption regarding our results.

These rate constants, in particular the two absorption rate constants, may be specific to the vehicle of administration and the exposure scenario for which they were derived. In a controlled experiment with five volunteers, chlorpyrifos was applied to the skin as a dilute aqueous emulsion to mimic an exposure that might occur during residential application (46). The calculated dermal absorption rate of 3.61 x 10^(-4) nmol chlorpyrifos/cm^2/sec, based on a dermal application of 1.046 nmol/cm^2, resulted in a rate constant of 3.46 x 10^{-7}/sec, an order of magnitude lower than the rate constant used in Residential-SHEDS. Because the exposure conditions (e.g., dosing vehicle, dermal loading, and dermal occlusion) were different in the Nolan et al. (16) study and the Griffin et al. (46) study, different values of their absorption rate constants are expected. Because of the uncertainty regarding the appropriate constant for the exposure conditions in Residential-SHEDS, we chose the more conservative (higher absorption rate) constant from Nolan et al. (16) for the case study.

Maximum dermal loading. Because Residential-SHEDS currently does not account for decreasing residue-to-skin transfer efficiency with repeated contacts, as suggested by Brouwer et al. (47), we set a maximum dermal loading so that the thickness of residue on the skin did not reach an unrealistic value before a removal process occurred. We assumed a uniform distribution ranging from 0.4 to 2.3 µg/cm^2 for maximum dermal loading. This distribution was based on equilibrium values reached for glove and sock dosimeter chlorpyrifos residues measured in an adult Jazzercise (Jazzercise, Carlsbad, CA) study (48) after a pesticide application and on surface area estimates from the EPA Exposure Factors Handbook (45).

This assumed maximum dermal loading may be conservatively high for the < 1-day postapplication scenarios because Jazzercise reflects unusually frequent skin-to-surface contacts and because cotton dosimeters may absorb more pesticide than skin does (49). However, the estimates may be low for the 1- to 7- and 8- to 30-day postapplication times if the residues are dried or dust-bound rather than in liquid phase as assumed. The maximum dermal loading was reached only in the modeled broadcast application exposure scenarios in which surface residues were higher than crack-and-crevice scenario residues.

The maximum loading parameter also helps to account for the loss of residues from the skin surface to a less-contaminated surface. For each contact event the maximum allowable mass loading on the skin surface is sampled randomly. If residue added to the skin during a contact event leads to a dermal loading exceeding the sampled maximum loading, and if the maximum loading is smaller than the final dermal loading from the previous time step, the model effectively removes mass from the skin surface for that contact event. More research and data are needed to properly account for mass transfer of pesticide residues from skin to surfaces.

**Results**

Our results from the chlorpyrifos exposure assessment with the Residential-SHEDS model emphasize relative comparisons across exposure scenarios and pathways rather than absolute numbers because we used numerous assumptions in the assessment. The primary purpose of presenting these results is to demonstrate the capabilities of the model framework.

Box plots for mean daily dermal chlorpyrifos loading, final daily mass of TCP in the blood compartment, daily eliminated mass of TCP, and daily ingested chlorpyrifos via nondietary objects for the 12 exposure scenarios modeled are presented in Figure 4. In generating the results, we randomly sampled 1,500 children with replacement from the NHAPS diaries for each exposure scenario (i.e., 1,500 from diaries of 575 children 0-4 years of age and 521 children 5-9 years of age). Modeled estimates of eliminated TCP use daily urinary output volumes of 500 and 800 ml for the children 0-4 and 5-9 years of age, respectively, based on Lentner (50). An analysis of the sensitivity of exposure and dose statistics to the number of iterations revealed that 1,500 iterations yielded acceptable stability in the results. In almost all cases the difference in mean, median, and 90th percentile between different model runs using 1,500 iterations was < 10%; the difference was between 10 and 20% in only a few cases.

Because of differences in surface residue loadings via the two application methods, median exposure and dose results for broadcast applications were 1-2 orders of magnitude higher than those corresponding to crack-and-crevice exposure scenarios for the same time period postapplication. Although the broadcast use pattern has been phased out, it was modeled to help evaluate the Residential-SHEDS predictions against available biomonitoring results. Broadcast results for < 1-day postapplication were not significantly different than those for the 1- to 7-day postapplication time period. This is because residue data for 1-2 days postapplication, which were very close to the < 1-day residue values, were the only data available to represent the entire 1- to 7-day postapplication period. Results for the 8- to 30-day post-broadcast application were lower than for the 1- to 7-day time period, reflecting surface residue loadings an order of magnitude lower than for the other two time periods at the targeted application site. The crack-and-crevice exposure and dose results were higher for the < 1-day post-application period than for the other two time periods, which also directly reflects the higher input surface residue loadings soon after the application at the target site. Median modeled estimates for the 8- to 30-day crack-and-crevice scenarios were higher than for the 1- to 7-day crack-and-crevice scenarios, reflecting the higher input surface residue loadings due to

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### Table 3. Surface-to-skin residue transfer efficiency (%).

| Surface type          | DT        | Mean or min, max | SD | GM | GSD | Range    | Reference | Data points (n) |
|-----------------------|-----------|------------------|----|----|-----|----------|-----------|----------------|
| Carpet (textured)     | Lognormal | 0.88             | 2.23 | 0.32 | 4.12 | 0.03-7  | (28-29,31,40) | 25             |
| Smooth                | Uniform   | 0.7, 10          |     |     | 2.6-8.2 | (29,41)  |               | 4              |

**Table 4. Assumed fraction of skin surface area contacted.**

| Age group | Body part | Surfaces        | Fraction of skin surface area contacting surface for a given contact event |
|-----------|-----------|-----------------|---------------------------------------------------------------|
| 0-9       | Hands     | Smooth, textured, grass, food | 0.05-0.5                                                   |
|           | Mouth     | Smooth, textured, grass (assuming 1–3 fingers inserted in mouth) | 0.05-0.3                                                   |
| 0-4       | Body³    | Smooth, textured, grass | 0.05-0.5                                                   |
| 5-9       | Body³    | Smooth, textured, grass | 0.05-0.25                                                  |
| 0-9       | Hands and body³ | Water | 0.9-1.0                                                   |

³In years. *Trunk, arms, legs, and feet.

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migration or mixing that may have occurred several days after application.

For all 12 scenarios, the younger children had higher exposures and doses than the older children. These results suggest that the frequency of object-to-mouth contacts and the fraction of skin surface area contacting surfaces may be important contributors to exposure and dose because these model inputs were assumed to be greater for the younger children.

Nondietary ingestion contributed more than dermal uptake to dose in the scenarios where deposited surface residues were the highest, i.e., < 1 day and 1-7 day post-broadcast application. The input children's hand-to-mouth and object-to-mouth contact frequencies were lower than input dermal contact frequencies. However, because the ingestion absorption rate constant is 2 orders of magnitude higher than the dermal absorption rate constant, the nondietary ingestion contribution will be greater if the surface residue loadings contacted are very high, as they were in the two broadcast scenarios. Although the nondietary ingestion to dermal absorption ratios were > 1 for the four high-residue-loading broadcast scenarios, the ratios were smaller (but still > 1) for the older children than for the younger ones. The reason for this difference is that the assumed object-to-mouth contact frequency was an order of magnitude lower for the older children.

For the children 0-4 years of age, object-to-mouth contacts contributed more to dose than hand-to-mouth contacts only for the broadcast scenarios < 1 day and 1-7 days postapplication. Although hand-to-mouth contacts were assumed to be more frequent than object-to-mouth contacts, object mouthing involves the ingestion of 10-50% of the surface residue loading on the mouthed object, whereas finger mouthing involves 10-50% removal of residue loading on the hand at the instant the fingers are mouthed. Thus, if deposited surface residues are significantly higher than hand loadings (e.g., in the two broadcast scenarios with the highest assumed surface residue loadings), the ingested residue from mouthed objects is expected to be higher than from mouthed fingers. Conversely, for the children 5-9 years of age, nondietary ingested mass from hand-to-mouth contacts was consistently greater than nondietary ingested mass from object-to-mouth contacts because it was assumed that only 0.1% of hand-to-object contacts result in object-to-mouth contacts (vs. 3% for the younger children).

For all scenarios, smooth surfaces contributed more to dermal loading than did textured surfaces because of the higher input transfer efficiency. Turf contact on residential lawns contributed less than either indoor smooth or textured surfaces for the broadcast scenarios because the time children spent on the residential lawn was relatively small as compared to time they spent indoors, and the indoor residue loadings were higher than the turf residue loadings. For the crack-and-crevice scenarios, turf contributed more (but still less than smooth and textured surfaces) because the indoor residue loadings were more comparable to the turf loadings.

**Discussion**

Direct comparison of these Residential-SHEDS results to available biomonitoring data is difficult because the exposure scenarios are not identical. Nevertheless, in spite of input and model uncertainties, the modeled eliminated urinary TCP estimates from the dermal and nondietary ingestion routes
compare well with available measurement data from published biomonitoring studies. Studies designed to collect activity data, environmental surface residues, and biomonitoring results simultaneously will be helpful in further developing and evaluating the Residential-SHEDS model.

The Residential-SHEDS simulations for children exposed < 1 day after crack-and-crevice application yielded 9–10 μg daily urinary eliminated TCP above background levels. Byrne et al. (33) reported ~ 1.4 μg as the 11-day average daily excretion (not including background levels) of TCP for adults performing normal routines for at least 12 hr/day in crack-and-crevice-treated homes. They concluded that crack-and-crevice applications do not contribute significantly to exposure because background levels in volunteers ranged from 8 to 61 μg. It is difficult to compare the two studies directly because TCP results on day 1 in Byrne et al. (33) may have been significantly higher than the 11-day average. Also, in that study chlorpyrifos was applied only in the bathroom and kitchen, and the adults did not perform hand-to-mouth and object-to-mouth ingestion activities.

For children exposed < 1 day after a broadcast application, Residential-SHEDS estimated 278–459 μg daily eliminated TCP. Although these estimates may seem high, Vaccaro et al. (36) reported an average of 199 μg eliminated TCP in adults (with no hand-to-mouth or object-to-mouth ingestion) who conducted active and passive exercises for 4 hr on turf immediately after treatment with broadcast chlorpyrifos applications.

Preliminary results for median and maximum urinary TCP concentrations for NHEXAS Minnesota urban children were 7.98 and 45.1 μg/L, respectively (50). These numbers are comparable to mid-to-upper tail results from Residential-SHEDS for all crack-and-crevice scenarios (Figure 4); however, the frequency of broadcast versus crack-and-crevice applications and the time since pesticide applications in the NHEXAS study are unknown.

Although most of the assumptions used in the Residential-SHEDS case study are likely to result in conservatively high modeled estimates of dermal and nondietary ingestion exposure and dose, they may be partially offset by the assumption that every child’s initial daily exposure and dose are zero. Because the mass in the blood compartment and eliminated TCP continue to increase after 1 day because of the slow dermal absorption and urinary elimination rates, 30-day continuous profiles were constructed in a separate analysis. Using 1-day averages for the 1- to 7-day and 8- to 30-day time periods with initial conditions of zero (as assumed in this paper) instead of continuous 30-day time profiles could lead to underestimates by a factor of 2–4, depending on the scenario. To obtain more realistic results over time, exposure and dose profiles could be constructed from weekly, monthly, or longer sequential time–location–activity diaries for each child if more complete temporal and spatial surface loading residue data also become available.

Shurdut et al. (52) described a probabilistic calendar-based aggregate chlorpyrifos exposure model accounting for inhalation, dermal, and dietary exposures to children and adults from termite, indoor crack and crevice, and outdoor lawn treatments. This model incorporated probabilities of pesticide use patterns to estimate aggregate absorbed doses of a sampled individual for each day of the year; Residential-SHEDS yields histograms of daily dermal and nondietary ingestion exposure and aggregated absorbed dose for different postapplication time periods that can be weighted with pesticide use pattern information. The Shurdut et al. model assumed a uniform distribution of 1–3% for dermal absorption and did not include a pharmacokinetic model; Residential-SHEDS includes a single compartment pharmacokinetic model to account for both dermal uptake and urinary elimination over time. Shurdut et al. (52) used a scenario-based macroactivity approach to quantify dermal exposure and did not include nondietary ingestion; Residential-SHEDS uses a sequential microactivity approach to obtain daily time profiles of dermal and nondietary ingestion exposure and dose. The results of the two models are difficult to compare directly because of these differences. However, despite these differences, the median modeled doses from the two models are very close. For example, children in the Shurdut et al. (52) model at the 50th percentile received 2.41 × 10^4 μg TCP/child (equivalent to 4.82 μg chlorpyrifos/day or 2.73 μg TCP/day for a 20-kg child), whereas the median mass of TCP eliminated by Residential-SHEDS children for the crack-and-crevice scenarios ranged from 1.08 to 10.85 μg/day. Future work on the Residential-SHEDS model will include incorporating the chronic case (> 30 days), the inhalation and dietary ingestion routes, and scenarios corresponding to indoor residential applications only and outdoor residential applications only. The exposure and dose histograms for each scenario and age cohort will then be weighted according to annual pesticide usage information and combined in a Monte Carlo simulation to produce aggregate population estimates that can be more readily compared to the Shurdut et al. (52) model results and to field study data such as the NHEXAS study results (50).

Conclusions

The model framework described in this paper was developed to improve estimates of human exposure and dose to pesticides and we presented a case study for chlorpyrifos and children to demonstrate the model capabilities. Although the chlorpyrifos example contains many assumptions because of current data limitations, it demonstrates that Residential-SHEDS can predict dermal and nondietary ingestion exposure and dose estimates that compare well to measurements in the published literature. However, to refine and evaluate the model for use as a regulatory decision-making tool, more robust data sets are needed for human activity patterns (particularly microlevel activities for infants and toddlers), surface residues for the most relevant surface types, and cohort-specific exposure factors. Specific research needs include the following: evaluating liquid removal efficiency as a function of contact duration; examining factors (e.g., number of contacts) affecting residue-to-skin transfer efficiency; examining transfer of residue on the skin to a less-contaminated surface; assessing clothing habits for different cohorts and the effect of clothing on pesticide exposure; measuring pesticide residues in schools, day-care centers, parks, and other nonresidential locations; examining pathways related to pet applications; examining when phase changes of pesticides occur over time and the relationship between residue composition and residue-to-skin transfer efficiency, maximum dermal loading, and dermal absorption; and refining inputs and methodologies for pharmacokinetic models.

Future work will include incorporating into Residential-SHEDS the inhalation and dietary ingestion routes, pesticide usage information, and two-stage Monte Carlo sampling to characterize uncertainty as well as variability in population estimates. Further comparisons will be conducted between the cross-sectional approach (using daily profiles assuming zero initial body burden) and a longitudinal approach (using a 365-day profile to account for accumulation in the body from day to day). Sensitivity and uncertainty analyses will be conducted to determine the most important model inputs to help prioritize future data collection efforts.

Residential-SHEDS was designed to estimate, for different postapplication time periods, daily exposures and doses incurred via multiple pathways that may occur concurrently or separately over time. The model could also be applied to simulate potential exposures from scenario-specific independent use patterns, as conducted historically for product registration purposes. Furthermore, whereas Residential-SHEDS currently uses
the microactivity approach, modeled estimates for specific exposure scenarios (e.g., children playing for several hours on turf) could be compared against estimates obtained with the microactivity approach as transfer coefficient data become available.

We believe that this model advances the science of assessing aggregate human exposure and dose to pesticides and offers several key advantages. The time-dependent nature of the model overcomes the limitations of summing exposures from individual pathways as all exposures and pharmacokinetic responses occur simultaneously. Although this historically used approach may be appropriate for obtaining conservatively high screening level estimates, the FQPA requires an understanding of more realistic upper-bound estimates for which uncertainties can be quantified. Because Residential-SHEDS is a probabilistic model, using distributions for model inputs rather than single point estimates, it can quantify exposure and dose at different percentiles of a population of interest, as well as the uncertainty associated with those percentiles. The advantages of the time-dependent and probabilistic methods incorporated in Residential-SHEDS will become increasingly important in exposure and risk assessments as upper percentiles become more of a focus in environmental regulatory decision-making.

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Appendix A. Equations Used in Residential-SHEDS

Initial dermal exposure
Skin-to-surface residue contact:
\[ M_s(t_{\text{r,initial}}) = M_s(t_{\text{r,final}}) + C_{\text{surf}} \times S_{\text{skin,r}} \times F_{\text{skin,r}} \times T_E \]  \[ \text{[A1]} \]

Skin-to-water or hand-to-mouth contact:
\[ M_s(t_{\text{r,initial}}) = M_s(t_{\text{r,final}}) \times F_{\text{skin,r}} \times T_E \]  \[ \text{[A2]} \]

Final dermal exposure
\[ M_s(t_{\text{r,final}}) = M_s(t_{\text{r,initial}}) - K_\alpha \times \Delta t_r \]  \[ \text{[A3]} \]

where
- \( t_r \) = time of contact event \( e \);
- \( t_{r-1} \) = time of previous contact event;
- \( \Delta t_r \) = duration of contact event \( e \);
- \( M_s(t_{\text{r,initial}}) \) = pesticide residue loading on the skin surface at the beginning of contact event \( e \) (in micrograms);
- \( M_s(t_{\text{r,final}}) \) = pesticide residue loading on the skin surface at the end of contact event \( e \) (in micrograms);
- \( C_{\text{surf}} \) = surface residue loading contacted by skin during contact event \( e \) (in micrograms per square centimeter);
- \( S_{\text{skin,r}} \) = total skin surface area for body part of interest (in square centimeters);
- \( F_{\text{skin,r}} \) = fraction of total skin surface area contacting a surface during contact event \( e \);
- \( T_E \) = surface-to-skin residue transfer efficiency or skin-to-medium removal efficiency during event \( e \) and
- \( K_\alpha \) = dermal absorption rate constant (per second).

Initial ingested mass pesticide in gastrointestinal tract
Hand-to-mouth contact:
\[ M_{\text{HM}}(t_{\text{r,initial}}) = M_{\text{HM}}(t_{\text{r,final}}) \times F_{\text{skin,r}} \times T_E \times f_{\text{absorbed}} \]  \[ \text{[A4]} \]

Object-to-mouth contact:
\[ M_{\text{OM}}(t_{\text{r,initial}}) = M_{\text{OM}}(t_{\text{r,final}}) + C_{\text{object},r} \times S_{\text{OM,r}} \times T_{E}\text{OM,r} \times f_{\text{absorbed}} \]  \[ \text{[A5]} \]

Final ingested mass pesticide in gastrointestinal tract
Hand-to-mouth contact:
\[ M_{\text{HM}}(t_{\text{r,final}}) = M_{\text{HM}}(t_{\text{r,initial}}) - K_{\text{g}} \times \Delta t_r \]  \[ \text{[A6]} \]

Object-to-mouth contact:
\[ M_{\text{OM}}(t_{\text{r,final}}) = M_{\text{OM}}(t_{\text{r,initial}}) - K_{\text{g}} \times \Delta t_r \]  \[ \text{[A7]} \]

Initial total nondietary ingested mass pesticide in gastrointestinal tract
\[ M(t_{\text{r,initial}}) = M_{\text{HM}}(t_{\text{r,initial}}) + M_{\text{OM}}(t_{\text{r,initial}}) + C_{\text{object},r} \times f_{\text{absorbed}} \times S_{\text{OM,r}} \times T_{E}\text{OM,r} \]  \[ \text{[A8]} \]

Final total nondietary ingested mass pesticide in gastrointestinal tract
\[ M(t_{\text{r,final}}) = M(t_{\text{r,initial}}) + C_{\text{object},r} \times f_{\text{absorbed}} \times S_{\text{OM,r}} \times T_{E}\text{OM,r} \]  \[ \text{[A9]} \]

Initial total mass metabolite in blood compartment
\[ M_B(t_{\text{r,initial}}) = M_B(t_{\text{r,final}}) \times K_{\text{e}} \times \Delta t_r \]  \[ \text{[A10]} \]

Final total mass metabolite in blood compartment
\[ M_B(t_{\text{r,final}}) = M_B(t_{\text{r,initial}}) + R_{MW} \times M_{\text{HM}}(t_{\text{r,final}}) \times K_{\text{e}} \times \Delta t_r + R_{MW} \times M_{\text{OM}}(t_{\text{r,initial}}) \times K_{\text{e}} \times \Delta t_r \]  \[ \text{[A11]} \]

Mass metabolite eliminated in urine
\[ M_{\text{U}}(t) = M_B(t_{\text{r,initial}}) \times K_{\text{e}} \times \Delta t_r \]  \[ \text{[A12]} \]

where
- \( M_B \) = mass of metabolite in the blood compartment (in micrograms);
- \( M_{\text{HM}} \) = mass pesticide ingested (in micrograms);
- \( M_{\text{OM}} \) = mass ingested via hand-to-mouth contact that is absorbed into the gastrointestinal tract (in micrograms);
- \( C_{\text{object},r} \) = fraction of ingested residue available for absorption from the gastrointestinal tract;
- \( f_{\text{absorbed}} \) = fraction of ingested residue loading on object inserted into mouth during contact event \( e \) (in micrograms per square meter);
- \( S_{\text{OM,r}} \) = surface area of object inserted into mouth during contact event \( e \) (in square centimeters);
- \( R_{MW} \) = ratio of molecular weight metabolite to molecular weight pesticide;
- \( K_{\text{e}} \) = gastrointestinal absorption rate constant (per second); and
- \( K_{\text{e}} \) = elimination rate constant (per second).
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