ASSESSMENT OF CHILDREN'S EXPOSURE TO SURFACE METHAMPHETAMINE RESIDUES IN FORMER CLANDESTINE METHAMPHETAMINE LABS, AND IDENTIFICATION OF A RISK-BASED CLEANUP STANDARD FOR SURFACE METHAMPHETAMINE CONTAMINATION

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Assessment of Children's Exposure to Surface Methamphetamine Residues in Former Clandestine Methamphetamine Labs, and Identification of a Risk-Based Cleanup Standard for Surface Methamphetamine Contamination

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Executive Summary

Clandestine synthesis of methamphetamine in California is a significant public health and environmental concern. Although the magnitude of the problem has declined in recent years, well over 100 clandestine methamphetamine laboratories were discovered in California in 2007, and nearly 10 percent of these were so-called "super labs" engaged in the production of more than 10 pounds of the drug. The chemicals required to produce the drug are hazardous and the wastes generated are often disposed of improperly, resulting in contamination of air, soil and water. The structures where these activities were conducted become contaminated as well, and cleaning them up has been a challenge to local health officials for more than a decade.

In October 2005, Governor Schwarzenegger signed Senate Bill 536 (Bowen, Chapter 587, Statutes of 2005) that required development of cleanup standards for properties contaminated by the clandestine manufacture of methamphetamine. This legislation required that the Department of Toxic Substances Control (DTSC), working in collaboration with the Office of Environmental Health Hazard Assessment (OEHHA), develop a health-based cleanup standard for methamphetamine on residential indoor surfaces. This exposure assessment document, together with a concurrently released document characterizing the toxicity of methamphetamine[1], provides the scientific justification for the cleanup standard.

The framework for establishing a risk-based methamphetamine cleanup standard requires (1) identification of the adverse effects of the drug and the doses that are required to elicit these effects and (2) estimation of the exposure that individuals living in a former clandestine methamphetamine lab would receive. The ultimate goal of this two-phase effort is to ensure that the estimated exposure to methamphetamine is below the amount required to produce *any* manifestations of toxicity.

The cleanup standard is based on a post-remediation exposure scenario and presumes that all interior surfaces have been cleaned to a target remediation standard. It also assumes that no "reservoirs" of methamphetamine contamination (such as contaminated air ducts) exist, and the concentration of methamphetamine is assumed to be constant throughout a 90-day exposure period. By virtue of age-specific behaviors and their frequent contact with the floor, children 6-24 months of age were identified as the primary concern because they are a "most exposed" population. Given the approximate six-month interval between initial discovery of a clandestine lab and its re-occupancy, and the fact that interior surfaces have been cleaned prior to re-occupancy, the exposure scenario also incorporates the assumption that inhalation of airborne methamphetamine does not constitute a significant exposure pathway.

Two models, originally developed by U.S. EPA to assess indoor exposure to pesticide residues, were evaluated to estimate exposure to methamphetamine on indoor surfaces. The Standard Operating Procedures for Residential Exposure Assessments (SOPs; U.S. EPA, 1997 and 2001) is a deterministic model comprised of three simple algebraic expressions for calculating point estimates of exposure via dermal contact with residues on carpet and hard surfaces, as well as incidental ingestion resulting from hand-to-mouth transfer. The Stochastic Human Exposure and

[1] *Development of a Reference Dose (RfD) for Methamphetamine* (Revised Draft, OEHHA, 2008)

Dose Simulation Model for multimedia, multipathway chemicals (SHEDS-Multimedia; U.S. EPA, 2007) utilizes distributions rather than point estimates for input variables and Monte Carlo sampling to generate a distribution of exposure estimates for a population. SHEDS-Multimedia provides estimates of exposure via hand contact with surfaces, body contact with surfaces, and incidental ingestion via hand-to-mouth and object-to-mouth transfer. With both models, exposure via transdermal absorption was based on the results of studies conducted at UC San Francisco showing that the efficiency of dermal absorption of methamphetamine is 57 percent.

Results from the two models were evaluated and compared, and justification for using SHEDS-Multimedia as a basis deriving a risk-based target cleanup standard for methamphetamine was provided. The model was run iteratively at increasing surface residue levels until the 95th percentile estimate of total exposure was less than or equal to the proposed reference dose (RfD, an estimate of the threshold for toxicity) for methamphetamine. It was determined that a surface concentration of 1.5 µg/100 cm^2 produced a 95th percentile estimate of exposure (0.0278 µg/kg-day) that was just below the RfD (0.03 µg/kg-day). Exposure via dermal absorption of methamphetamine residue on the body accounted for 80 percent of total exposure. Dermal absorption of methamphetamine on the hands and incidental ingestion each accounted for about 10 percent of total exposure. A sensitivity analysis indicated that alteration of the efficiency of surface-to-skin transfer had a direct, nearly 1:1 impact on the total exposure estimate, reflecting the predominance of the dermal exposure pathways.

Introduction

The Natural History of a Clandestine Methamphetamine Lab

From its initial establishment through its ultimate re-occupancy, a clandestine methamphetamine lab goes through four phases that vary with the nature of activities. The four phases may generally be described as

- *Operational*: clandestine methamphetamine synthesis takes place
- *Discovery & Removal*: the lab is "busted" (discovered by law enforcement) and bulk chemicals and equipment are removed
- *Remediation & Verification*: samples are collected to characterize the distribution of contaminants within the residence, the contaminants are remediated, and samples are collected to verify that residual contaminant levels are below target cleanup standards
- *Re-Occupancy*: a new group of residents occupies the residence which housed the former clandestine lab

Each phase represents a distinct exposure scenario with different primary contaminants, contaminant sources, exposure pathways and potentially exposed populations. Contaminant classes, sources and potentially exposed populations are summarized in Table 1. During the first two phases, inhalation of airborne contaminants (such as methamphetamine, acidic and corrosive gases, and phosphine) probably represents the greatest hazard. Once the primary sources[2] of airborne contaminants have been physically removed, secondary sources may still remain in the residence. Secondary sources include solvent spills and "soft" media (such as upholstered furniture, drapes, carpet and wallboard) that have absorbed solvent vapors and volatile contaminants[3] during the operational phase of the clandestine laboratory. Re-release (or "off-gassing") of volatile chemicals that have been absorbed into soft media appears to represent the primary inhalation hazard during cleanup and verification activities. By the time a clandestine laboratory has been completely remediated and is ready for re-occupancy, several months after its initial discovery, inhalation exposure is minimal because the process of off-gassing has largely gone to completion. Thus, as the laboratory progresses through these four phases, the significance of inhalation as a pathway of exposure declines markedly.

Non-volatile compounds, such as the hydrochloride salt of methamphetamine, represent another general class of contaminants encountered at clandestine labs. Methamphetamine has been detected on interior surfaces at former labs and appears to be persistent (Martyny et al., 2007). Pathways of exposure to non-volatile compounds include dermal absorption following skin contact with contaminated surfaces, and ingestion following skin contact and subsequent hand-to-mouth activities. With few exceptions, remediation efforts at former clandestine labs focus exclusively on methamphetamine levels. Therefore, the magnitude of exposure to surface methamphetamine residues – and the consequent health risk – is controlled by the target remediation goal for methamphetamine.

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[2] Primary sources include reaction vessels, solvents stored in their original containers, solvents transferred to other containers, and tanks of compressed gases such as ammonia and hydrogen chloride.

[3] As discussed in the section on the fate and transport of methamphetamine in indoor environments, the free base form of methamphetamine is also volatile.

The purpose of this report is to describe the processes for assessing the exposure to surface methamphetamine residues, so that potential health hazards may be controlled by establishing a clean-up standard that ensures that total exposure via all relevant pathway does not exceed the reference dose (RfD) for methamphetamine. The exposure estimates are based on a re-occupancy scenario, with very young children (approximately 6 months to 2 years of age) as the sub-population of greatest concern.

The two sections that follow summarize the anticipated timeline for remediation of a clandestine methamphetamine lab, and the results of several recent studies that characterize the fate and transport of methamphetamine in indoor residential environments during and up to 18 hours after synthesis. The data from these studies provide methamphetamine-specific information that was used to justify several of the assumptions in the post-remediation, re-occupancy exposure scenario. Subsequent sections provide detailed description of exposure scenario and modeling assumptions, a comparison of the two U.S.EPA models that were used to calculate exposure estimates, justification for the decision to utilize the results of one of the models as a basis for deriving a health-based cleanup standard for methamphetamine, and a sensitivity analysis of the impact that the values for several individual exposure parameters had on the total exposure estimate.

Table 1. Summary of the exposure scenarios (contaminants, exposure pathways, and potentially exposed populations) associated with different phases in the life of a clandestine methamphetamine lab.

Scenario	Potentially Exposed Populations	Contaminants & Exposure Pathways
Operational Clandestine Lab	Operators Visitors Innocent by-standers Neighbors	Primary: Inhalation of volatile contaminants Intentional dosing (all routes) Secondary: Dermal contact with non-volatile residues on surfaces Non-dietary ingestion via hand-to-mouth activities
Discovery and Removal	Law enforcement Removal personnel Industrial hygienists	Inhalation of volatile contaminants stored in original containers Inhalation of re-suspended, particle-adsorbed contaminants Dermal contact with non-volatile residues on surfaces *Exposure minimized by personal protective equipment*
Cleanup and Verification	Cleanup personnel Industrial hygienists	Inhalation of volatile contaminants off-gassing from "soft" media[4] Inhalation of re-suspended, particle-adsorbed contaminants *Exposure minimized by personal protective equipment*
Re-occupancy	Residents (including sensitive sub-populations)	Dermal contact with methamphetamine residues on surfaces[5] Dermal contact with non-volatile chemicals on surfaces that lack cleanup standards Inhalation of volatile contaminants off-gassing from "soft" media (assumed to be minimal)[6]

[4] "Soft" media include upholstered furniture, drapes and carpet (assuming they have not been removed as part of cleanup operations), and wallboard. During this phase, the primary sources of volatile contaminants - storage containers - will have been removed. Secondary sources, such as solvents that were spilled or improperly disposed of, will still be present.

[5] For re-occupancy to occur in California, methamphetamine residues on surfaces *must* be cleaned up to the specified cleanup standard.

[6] Based on the 6-month cleanup timeline specified in Chapter 6.9.1 of the Health and Safety Code, off-gassing of volatile chemicals from soft media is assumed to be minimal. Limited data from a 24-hour study by Van Dyke et al. (2009, Table II) indicate that airborne methamphetamine dissipates rapidly after the drug is synthesized, although additional research on the long-term time course of airborne methamphetamine dissipation is warranted.

Timeline for Remediation of a Clandestine Methamphetamine Lab

The provisions of Chapter 6.9.1 of the Health and Safety Code specify a time frame for completing the investigation and remediation of a former clandestine methamphetamine lab. A summary of the mandated tasks and deadlines that must be achieved by the local health officer (LHO) or the property owner is shown in the table below.

Table 2. Action items and statutory timetable for remediation of a former clandestine methamphetamine laboratory, according to provisions of Chapter 6.9.1 of the Health and Safety Code.

Action Item	***Statutory Timetable***
Law enforcement agency notifies LHO*	Day 0
LHO records property lien and issues order prohibiting property use and occupancy	Day 15
Authorized contractor retained	Day 45
Site assessment work plan submitted to LHO	Day 75
Work plan found deficient or approved	Day 100
Remediation complete	Day 190
Site assessment report submitted to LHO	Not specified
LHO reviews site assessment report and determines if no further action (NFA) is required	Not specified
LHO releases property lien	10 Days after NFA determination

* LHO: Local Health Officer or the Designated Local Agency authorized to implement the responsibilities of the LHO.

It is noteworthy that the time required to complete all phases of the investigation and remediation exceeds six months. The process can take even longer if the property owner requests an extension and the request is approved by the LHO. In practice, it is difficult to complete the entire statutorily-mandated remediation and review process within the stipulated timeframe (C. Yep, Cal/EPA, Department of Toxic Substances Control, personal communication). Therefore, six months should probably be viewed as the minimum time required to complete the remediation process. This long duration would likely provide ample time for airborne methamphetamine residues to dissipate and supports the conclusion that inhalation does not represent a significant exposure pathway in a post-remediation re-occupancy exposure scenario. The inhalation pathway is also discussed on page 24 as the third exposure scenario assumption.

Investigation of the Fate and Transport of Methamphetamine in an Indoor Residential Environment

Martyny et al. (2007) conducted studies to determine residual methamphetamine levels on indoor surfaces resulting from the clandestine manufacture of methamphetamine. Two types of studies were conducted. In the first, surface wipe samples were collected during the initial investigation of fourteen separate clandestine methamphetamine laboratories by law enforcement. In the second, air and surface wipe samples were collected during and shortly after the controlled synthesis of methamphetamine in buildings that were slated for demolition. The latter investigations were referred to as "controlled cooks," and were intended to simulate exposures that might actually occur in a clandestine methamphetamine lab. In both types of studies, surface wipe samples were collected from 100 cm^2 areas, delineated by a 10 cm x 10 cm template, using 4-inch by 4-inch cotton gauze wetted with isopropanol or methanol.

Surface methamphetamine concentrations detected at fourteen former clandestine labs ranged from below the detection limit (0.6 µg/100 cm^2) to 16,000 µg/100 cm^2 (data shown below). The number of samples collected at each lab ranged from three to thirteen. In eleven of the fourteen labs, all the samples collected were positive for methamphetamine, even though some samples were collected from vertical surfaces or unusual locations (e.g., ceiling fans and air return grates). According to the authors, these data suggest that methamphetamine is released as an aerosol during the production process and transported by air to locations distant from the site of synthesis. They further hypothesized that the primary mechanism of aerosol release is "salting out" the free base form of methamphetamine (the initial product of methamphetamine synthesis) using hydrogen chloride gas.

The authors also noted, "Even labs that had been shut down several months prior to testing had high contamination levels of methamphetamine present on many surfaces within the building." These results indicate that methamphetamine residues may persist for at least several months on interior residential surfaces in the absence of any human activity or remediation efforts. These results are consistent with anecdotal information reported by individuals involved in the investigation and cleanup of former clandestine methamphetamine labs.

The authors also collected air samples at several of the former clandestine labs and analyzed them for hydrocarbons, phosphine, hydrogen chloride and iodine, all of which are volatile. Results for hydrocarbons were difficult to interpret due to the presence of significant indoor background levels of these compounds from commonly used commercial products. Air samples from three laboratories were analyzed for phosphine, but the results were suspect and thought to be false positives because the field blank also indicated very high levels of the compound. Hydrogen chloride was detected in two of the laboratories, but the concentrations were extremely low (0.005 and 0.13 ppm). In many of the laboratories, iodine stains were present on carpeting and walls and it was thought that airborne iodine might be high in these locations. Nevertheless, eight of the twelve air samples collected from these laboratories were non-detect for iodine (limit of detection: 0.0007 ppm), and the highest concentration detected was just 0.002 ppm.

Table 3. Results of methamphetamine wipe samples taken at suspected clandestine methamphetamine laboratories during Scenario 1

Lab Location Number	Number of Samples	Mean[a] (μg/Sample)	Median[a] (μg/Sample)	Range (μg/Sample)
1	5	134	120	6–370
2	5	202	28	9–920
3	6	150	26	1–150
4	6	3	2	ND–7
5	13	48	3	1–520
6	8	2788	925	71–16,000
7	5	3057	2400	25–10,000
8	7	42	37	13–64
9	9	96	17	1–430
10	7	312	250	64–790
11	9	46	1	ND–300
12	3	24	10	ND–63
13	3	438	650	4–660
14	3	33	14	8–78
Overall	89	511	28	ND–16,000

ND: none detected at levels above the limit of detection of 0.6 μg/sample.
[a] None detected samples were assigned a value of 0.01 μg/sample for the purpose of analysis.

Data from Martyny et al., 2007. Surface methamphetamine levels, expressed as μg methamphetamine per 100 square centimeters of surface area, were determined in fourteen former clandestine labs. Wipe samples were collected shortly after their discovery, during law enforcement operations. None of the labs were active when the samples were collected.

Controlled cook studies were conducted in eight residential structures – five houses, two duplexes and one hotel room. They evaluated three different methods that are often used to synthesize methamphetamine from ephedrine or pseudoephedrine: the red phosphorus plus iodine method, the hypophosphorous acid plus iodine method, and the Birch reduction method which requires anhydrous ammonia plus an alkali metal (lithium or sodium). While interference with the detection of airborne methamphetamine was noted in samples collected during the anhydrous ammonia cooks, airborne methamphetamine appeared to be much higher when the drug was synthesized using red phosphorus or hypophosphorous acid (data shown below). This difference may be explained by the fact that the phosphorus methods require boiling the reaction mixture, and any leakage of vapor from the reaction vessel, auxiliary glassware and/or exhaust hoses would result in release of methamphetamine to the air. This mechanism of methamphetamine release would not be expected to occur with the anhydrous ammonia method because the reaction mixture is cold, and it is unlikely that a methamphetamine aerosol would be produced under these conditions. Nevertheless, the phosphorus methods and the anhydrous ammonia method both require salting out methamphetamine base, and this represents another mechanism of methamphetamine release to the air. The results of these studies also demonstrate that airborne methamphetamine levels in locations distant from the synthesis area often approach those detected in the immediate vicinity of the cook.

Table 8. Airborne methamphetamine levels

Manufacturing Method	Manufacturing Area (ug/m^3)	Remote Area (ug/m^3)
Red phos. #2	5500	4200
Red phos. #3	520	99
Red phos. #4	760	510
Anhydrous #1[a]	>680	>12
Anhydrous #2[a]	>79	>2.6
Anhydrous #3[a]	>170	>158
Hypophos. #1	3800	4000
Hypophos. #2	680	NA
Mean	1524 (2252)	1283 (2202)
Median	680 (760)	158 (2255)

NA: not available; ( ): calculation of mean and median results excluding the values for cooks using the anhydrous ammonia method of manufacture.
[a] Interference noted by analytical laboratory.

Data from Martyny et al., 2007. Airborne methamphetamine levels detected during the "controlled cook" of methamphetamine by three different synthesis methods: *Red phos.* (red phosphorus + iodine), *Anhydrous* (anhydrous ammonia + alkali metal, also know as Birch reduction), and *Hypophos.* (hypophosphorous acid + iodine). All three methods utilize ephedrine or (more commonly) pseudoephedrine as the immediate precursor.

Data from surface wipe samples collected during the controlled cook studies also indicate that the phosphorus methods of synthesis produce higher levels of methamphetamine contamination than the anhydrous ammonia method (data shown below). As expected, methamphetamine levels or surfaces nearest the location of synthesis were higher than those detected at more distant locations.

Table 9. Methamphetamine wipe sample results obtained during controlled cooks to determine potential exposures during the clandestine manufacture of methamphetamine (Scenario 2)

Distance from Cook (m)	Number of Samples	Mean (ug/100 cm^2)	Median (ug/100 cm^2)	Range (ug/100 cm^2)
Phosphorous cooks ($n = 5$)				
<2	14	100.9	21.5	0.1–860.0
2–4	11	40.7	19.0	0.8–45.0
>4	4	21.7	22.1	11.6–31.0
Anhydrous ammonia cooks ($n = 3$)				
<2	8	25.2	3.7	0.1–160
2–4	8	1.0	0.9	0.2–2.3
>4	8	0.4	0.2	0.1–1.2

Data from Martyny et al., 2007. Surface methamphetamine levels detected at varying distances from red phosphorus and anhydrous ammonia (Birch reduction) cooks.

In a recently published report, Martyny et al (2008) described the results of studies that simulated the smoking of different amounts of methamphetamine. Based on the results of published

research reports, the authors estimated that 67 to 90 percent of the methamphetamine volatilized by smoking the drug is absorbed by the user, and that 7-15 percent of the methamphetamine loaded into a smoking pipe is released into the immediate environment from a combination of side-stream vapor and exhaled, unabsorbed methamphetamine.

The studies were conducted in a 253 square foot room of a hotel that was slated for demolition. A simple wall-mounted heat ventilator was operated over the course of the investigation. Four separate "smoking" sessions were conducted. In the first two, 100 mg of methamphetamine was heated in a glass pipe using a propane torch. In the third, 250 mg of methamphetamine was heated in the same manner. In the fourth, 2,000 mg of methamphetamine was placed in an aluminum pan and heated with an electric hot plate. Methamphetamine purity was 91 percent. Airborne concentrations were measured during the course of each simulated smoke. The authors stated that the 100 mg sessions were intended to represent an amount of methamphetamine commonly used by an individual, while the 250 and 2,000 mg sessions were designed to simulate multiple smoking sessions of a multiple user smoking session.

Airborne levels detected after the 100 mg sessions ranged from 300 to 520 mg/m^3 (data shown below), and higher concentrations were generally observed in samples collected nearest the "smoking" area. Nevertheless, the levels did not necessarily reflect the mass of the drug that was heated. In part, this result reflects the fact that the methamphetamine heated on a hot plate in smoke #4 caught fire at one point, probably causing pyrolysis of the drug rather than vaporization. It is also possible that the smoke did not disperse in the room uniformly, and that the air sample collected after smoke #4 was relatively more dilute than samples collected after the previous three sessions. The table below also provides an estimate of the airborne concentration that would have been achieved if 67 percent or 90 percent of the methamphetamine vapor had been absorbed by the lungs of the person smoking the drug.

Table 3. Results of Airborne Methamphetamine Sampling During the Simulated Smoking of Methamphetamine

Location	Sample Area	Smoke #	Measured Airborne Level (μg/m^3)	Predicted Low Airborne Level[a] (μg/m^3)	Predicted High Airborne Level[b] (μg/m^3)
A	Smoke area	1	520	52	172
A	Smoke area	2	300	30	99
A	Smoke area	3	1,600	160	528
A	Smoke area	4	1,200	120	396
D	East wall	1	340	34	112
D	East wall	2–4	1,400	140	462
E	Bathroom sink	1	330	33	109
E	Bathroom sink	2–4	1,500	150	495
G	Heater area	1–4	1,400	140	462

[a] Predicted airborne level assuming 90% uptake by user.[11]
[b] Predicted airborne level assuming 67% uptake by user.[10]

Data from Martyny et al. (2008). The amounts of methamphetamine heated during each "smoking" session were 100 mg (smoke # 1 and #2), 250 mg (smoke #3) and 2,000 mg (smoke #4).

Wipe samples were collected after each successive smoking session. Thus, the first sample represented methamphetamine deposited by smoke from the first session, the second an accumulation of methamphetamine deposited by smoke from sessions 1 and 2, and so on. Pre-smoking samples revealed the presence of low levels of methamphetamine on five of the seven sampling sites, indicating that the drug had been used in this room or a nearby room some time

before the experiments were conducted (data shown below). Accounting for background and the mass of drug deposited by smoke from the previous sessions, the mean surface concentrations detected after each smoking session were 0.18, 0.45, 1.31 and 13.45 µg/100 cm^2, representing deposition from vaporizing 100, 100, 250 and 2,000 mg of methamphetamine, respectively.

Table 4. Wipe Sample Results by "Smoke" Collected During the Simulated "Smoking" of Methamphetamine

Location	Pre-Smoke (µg/100 cm^2)	1st Smoke (µg/100 cm^2)	2nd Smoke (µg/100 cm^2)	3rd Smoke (µg/100 cm^2)	4th Smoke (µg/100 cm^2)
A	0.07	0.31	1.36	3.80	16.00
B	0.10	0.22	1.50	3.00	12.00
C	ND	0.17	0.39	0.94	47.00
D	ND	0.25	0.50	2.60	17.00
E	0.03	0.17	0.22	0.70	2.80
F	0.04	0.20	0.32	0.98	4.80
G	0.04	0.26	0.50	1.90	8.50
Mean	0.05	0.23	0.68	1.99	15.44
Reduced mean A	NA	0.07	0.23	0.66	5.10
Reduced mean B	NA	0.02	0.07	0.20	1.54

ND = <0.05 µg/wipe; NA = not applicable; reduced mean A = assumed absorption of 65% (mean − (mean × 0.65); reduced mean B = assumed absorption of 90% (mean − (mean × 0.90).

Data from Martyny et al. (2008). The amounts of methamphetamine heated during each "smoking" session were 100 mg (smoke # 1 and #2), 250 mg (smoke #3) and 2,000 mg (smoke #4).

Wipe samples were also collected from tiles that had been placed on the floor of the room. After all four smoking sessions had been completed, the concentrations of methamphetamine on the surfaces of these tiles ranged from 22 to 35 µg/100 cm^2.

Van Dyke *et al.* (2009) evaluated the persistence and fate of contaminants in a residential setting during the first 24 hours after methamphetamine had been synthesized twice using the red phosphorus + iodine method. The studies were conducted to evaluate the initial extent of methamphetamine contamination in a small 5-room house, the persistence of methamphetamine contamination within the structure for the 24-hour period after the cook, and the effects of daily human activities on the re-suspension of methamphetamine residues from contaminated surfaces to air.

The studies were conducted in a one-story 500 ft^2 home that had been donated to the local fire department for a training exercise. The home was divided into four living spaces of approximately equal size: the kitchen, the living room, a bedroom, and a den with an adjacent bathroom. Methamphetamine was synthesized in the kitchen.

The study was divided into two days. Day one was devoted to controlled synthesis of two three-gram batches of methamphetamine. Both "cooks" were conducted by chemists from the U.S. Drug Enforcement Agency and required approximately four hours each to complete. Surface wipe samples were collected in six separate locations prior to commencement of the studies and after each of the two cooks. Air samples were collected after each cook in the kitchen (in the immediate vicinity of the synthesis area) and the den (approximately fifteen feet away). Three different air sampling methods were used to determine total airborne methamphetamine, the fraction of airborne methamphetamine that was respirable, and the aerosol size distribution of airborne methamphetamine.

One day two, samples were collected to assess the effect of different levels of activity on airborne and surface methamphetamine levels. Initial "no activity" samples were collected approximately 13 hours after the second cook. Three hours later (16 hours after the second cook), samples representing the effects of "medium" activities were collected. Examples of this level of activity included walking through the home, sitting on the couch, and opening and closing cabinet doors. Two hours later, the effects of "heavy" activities were assessed. Examples of heavy activity included vacuuming, fluffing pillows and walking or crawling thought the house. Day two air samples were only collected in the kitchen, approximately 4 feet from the location where the drug was synthesized. Surface samples were collected from the same six locations as the day one samples.

Airborne methamphetamine levels detected over the course of the two-day study are presented below. First day samples collected in the kitchen, where the drug was synthesized, were 520 and 760 $\mu g/m^3$. Further away in the den, the levels detected were 99 $\mu g/m^3$ after the first cook and 510 $\mu g/m^3$ after the second. Total and respirable concentrations were comparable. Aerosol size selective sampling results indicated that the majority of particles were less than 1 µm. According to the authors of the study, the mass median aerodynamic diameter of the methamphetamine aerosol was less than 0.1 µm.

Airborne methamphetamine was still detected on the second day, approximately 13 hours after the second cook, even though very little activity had occurred in the residence. The concentrations of total and respirable methamphetamine detected at the beginning of day two were approximately 10 percent of the concentrations that had been detected at the end of the previous day. Moderate and heavy activity in the residence caused a two- to three-fold increase in total and respirable methamphetamine, indicating that re-suspension of surface methamphetamine occurs in proportion the level of activity in the residence. Furthermore, vast majority of re-suspended methamphetamine was respirable (<0.1 µm).

	Day 1				Day 2		
	Cook #1		Cook #2		No Activity	Moderate Activity	Heavy Activity
	Kitchen	Den	Kitchen	Den			
Airborne Methamphetamine (µg/m^3)							
Total Airborne Methamphetamine	520	99	760	510	70	170	210
Respirable Methamphetamine	720	97	780	460	76	150	180
Aerosol Size-Specific Meth (µg/m^3)							
2.5 to 10 µm	48	7.2	19	85	0.66	1.1	1.9
1.0 to 2.5 µm	56	6.5	26	18	0.77	1.3	1.4
< 1.0 µm	230	99	370	250	79	110	99

Data from Van Dyke et al. (2009).

Results obtained from surface wipe samples indicated methamphetamine concentrations ranging from 1.5 to 230 µg/100 cm^2. The highest concentration was detected on a toy truck that had been placed approximately two feet above the cook area. Samples collected before these studies were initiated also indicated the presence of methamphetamine, indicating that the drug had been used in this residence in the past. On day one, methamphetamine levels on surfaces generally increased after each cook, with walls throughout the residence having comparable levels (29 to 45 µg/100 cm^2). In contrast, the concentration of methamphetamine detected on the kitchen floor was significantly lower. The latter observation may reflect the small aerosol particle size generated during synthesis of the drug and consequent slow rate of vertical deposition. Data from samples collected on day two indicated that activity in the home caused at most a moderate increase in the concentration of methamphetamine on interior surfaces.

	Day 1			Day 2, Activity Level		
Surface Concentration (µg/100 cm^2)	Pre-Cook	After Cook #1	After Cook #2	None/Light (13 hr later)	Moderate (16 hr later)	Heavy (18 hr later)
Area 1 (kitchen wall)	13	31	45	46	68	46
Area 2 (kitchen wall)	23	39	45	41	59	44
Area 3 (den wall)	18	45	29	31	33	42
Area 4 (bedroom wall)	14	29	19	32	36	35
Area 5 (kitchen floor)	1.5	6.9	8.6	6.1	6.7	10
Area 6 (living room wall)	5.7	29	30	36	23	37
Toy truck above cook area						230

Data from Van Dyke et al. (2009).

In their discussion of the data from this study, Van Dyke et al. suggest that the size distribution of airborne methamphetamine particles is consistent with a condensation aerosol and propose that methamphetamine is initially released as a vapor during the “salting out” process. (This occurs when methamphetamine base is precipitated out of solution by bubbling hydrogen chloride gas through it to produce methamphetamine hydrochloride.) Once released, the vapor

condenses into very small particles that stay suspended in air and are able to migrate to all portions of a residence. From the perspective of potential hazard to human health, once these small particles are inhaled, they will penetrate into the deep pulmonary portion of the lung and be absorbed quickly into the bloodstream.

The studies conducted by Van Dyke et al. also characterized the effect of typical human activities on re-suspension of methamphetamine residue from indoor surfaces. The ease of resuspension was assessed less than one day after the drug was synthesized. These conditions differ significantly from the exposure scenario modeled in this document, insofar as the exposure assessment upon which the proposed cleanup standard is based presumes that the residence has been remediated before it is re-occupied. Once all surfaces have been remediated to the proposed target cleanup level, the mass of methamphetamine available for re-suspension will be reduced substantially. Furthermore, the ease of re-suspension will be reduced significantly because the residue that is easily dislodged from the surface will have been removed by the cleaning process.

Martyny (2008) recently completed studies to evaluate the efficacy of decontaminating different types of building materials using the cleaning and degreasing agent Simple Green®[7]. The building materials tested were painted drywall, painted plywood, galvanized metal used for air ducts, and glass. The wallboard and plywood samples were painted with two coats of latex enamel paint two days prior to commencement of the studies. Four panels of each material were placed in an exposure chamber containing approximately 200 mg of "street grade" drug consisting of 77 percent methamphetamine and small amounts of amphetamine, ephedrine and pseudoephedrine. The drug was placed in a glass beaker and aerosolized by heating. A fan was placed in the chamber to disperse the aerosol.

The methamphetamine-exposed panels were subjected to the following treatments to evaluate the efficacy of decontamination:

- One panel was never washed and sampled.
- One panel was washed one time with Simple Green® and then sampled.
- One panel was washed two times with Simple Green® and then sampled.
- One panel was washed three times with Simple Green® and then sampled.

The wallboard and plywood panels were divided into a 6 x 6 grid consisting of 10 cm x 10 cm quadrants (100 cm^2 squares). Seven quadrants on each panel were selected randomly using a random number table and sampled. Seven samples were collected prior to treatment (not washed, or washed once, twice or three times) and seven randomly selected samples were collected after treatment. Since the glass and galvanized metal panels were smaller, just five pre- and post-treatment samples were collected from these materials. Surface wipe samples were collected using 3" x 3" cotton gauze wetted with 3 ml of methanol.

To wash the panels, Simple Green® was applied full strength from a spray bottle in accordance with label directions for maximum degreasing. After approximately 1.5 minutes of contact time, the cleaner was washed off using a cloth and clean water. The surface of the panel was not

[7] The Material Safety Data Sheet for Simple Green indicates that it is a water-based cleaner with a pH of 9.5. It contains < 4 percent 2-butoxyethanol. No other ingredients were listed.

scrubbed hard. The panels were allowed to dry completely prior to subsequent cleanings or post-treatment sampling.

Data from the decontamination of painted drywall are shown in the table below. While the first wash removed 77 percent of the methamphetamine residue, the second and third washes were only marginally effective at removing additional residue.

	Surface Concentration of Methamphetamine ($\mu g/100\ cm^2$)				
	Before Cleaning		**After Cleaning**		**Mean Reduction**
	Mean	**Median**	**Mean**	**Median**	
No Cleaning	13	13	14	14	-10%
First Wash	37	30	8.5	8.5	77%
Second Wash	23	24	5.2	4.5	77%
Third Wash	17	16	3.2	3	81%

Data from Martyny (2008). Results of decontamination of painted drywall using Simple Green®. Each treatment (not washed, or washed once, twice or three times) was evaluated using a separate panel, accounting for the differences in the "before cleaning" surface concentrations of methamphetamine.

Similar results were obtained with painted plywood (data shown below) insofar as the second and third washes were not as effective as the first wash. According to the author of the report, "…after the initial wash, the remaining methamphetamine was not easily removed."

	Surface Concentration of Methamphetamine ($\mu g/100\ cm^2$)				
	Before Cleaning		**After Cleaning**		**Mean Reduction**
	Mean	**Median**	**Mean**	**Median**	
No Cleaning	11	12	13	12	-11%
First Wash	12	12	5.7	6	53%
Second Wash	11	11	4.2	4.5	63%
Third Wash	18	18	3.6	3.6	80%

Data from Martyny (2008). Results of decontamination of painted plywood using Simple Green®.

In contrast to the results obtained with painted drywall and plywood, sheet metal and glass were easily decontaminated (data shown below). In both cases, all of the methamphetamine residue was removed by a single washing with Simple Green®[8]. The amount of methamphetamine that condensed on these materials in the exposure chamber was generally quite a bit less than the amount that adhered to wallboard and plywood. Nevertheless, the surface concentration of methamphetamine on the "one wash" sheet metal panel was comparable to some of the loadings obtained with wallboard and plywood, and the removal efficiency for a single wash was still 100 percent.

[8] The detection limit for methamphetamine was 0.05 $\mu g/100\ cm^2$.

	Surface Concentration of Methamphetamine ($\mu g/100\ cm^2$)				
	Before Cleaning		**After Cleaning**		**Mean Reduction**
	Mean	**Median**	**Mean**	**Median**	
No Cleaning	3.6	3.7	3.2	2.8	12%
First Wash	11.4	12	0	0	100%
Second Wash	1	.9	0	0	100%

Data from Martyny (2008). Results of decontamination of sheet metal using Simple Green®.

	Surface Concentration of Methamphetamine ($\mu g/100\ cm^2$)				
	Before Cleaning		**After Cleaning**		**Mean Reduction**
	Mean	**Median**	**Mean**	**Median**	
No Cleaning	0.1	0.1	0.2	0.2	-50%
First Wash	0.2	0.2	0	0	100%
Second Wash	12.5	12	0	0	100%

Data from Martyny (2008). Results of decontamination of glass using Simple Green®.

In the discussion of the results obtained with painted drywall and plywood, the author of this study noted,

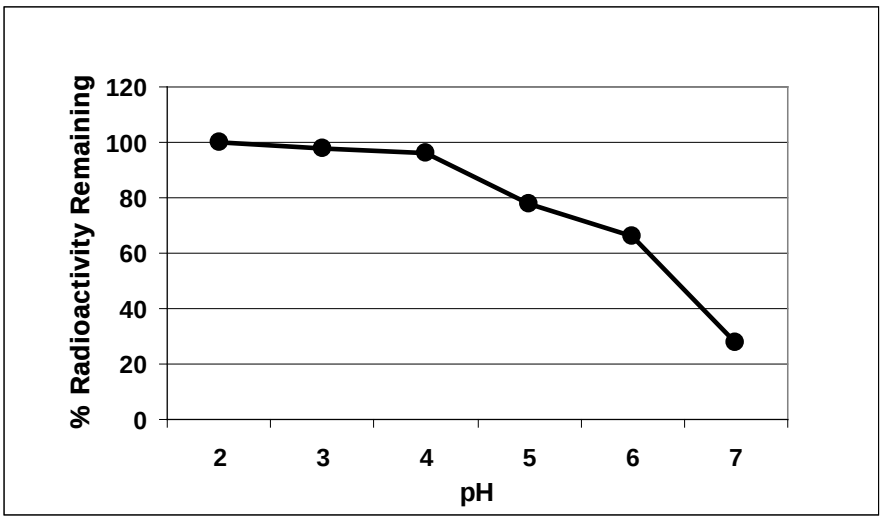
> *It is possible that after the first 50 percent [of methamphetamine residue] is removed…the remaining methamphetamine may not easily leave the surface of the porous materials simply due to touch or simple cleaning. Exposures therefore, may be significantly reduced after the initial cleaning.*

The results of this study are highly relevant to estimating exposures that may occur in a remediated clandestine methamphetamine lab, as they demonstrate that surface residues of the drug in an environment where surfaces have been remediated just one time are not readily dislodgeable. Therefore the ability of a cleaning and degreasing agent like Simple Green to remove the remaining residue is diminished considerably. If moderately aggressive cleaning removes just a small increment of methamphetamine from surface that has been cleaned once, then it is reasonable to conclude that skin contact would not be an effective means of removing the drug either. The possibility that these difficult-to-remove residues could be re-suspended into the air by routine human activities such as walking across a remediated surface seems remote as well. The results of these decontamination studies indicate that a relatively simple cleaning process appears to remove most (in the case of drywall and plywood) or all (in the case of glass and sheet metal) of the surface methamphetamine residue from that is potentially available for exposure.

In the course of conducting an investigation of the *in vitro* absorption of carbon-14 labeled *d*-methamphetamine hydrochloride (^{14}C-*d*-meth HCl) across human skin, Hui and Maibach (2007) observed that a significant portion of the radioactivity applied to the skin was lost over the course of the 24-hour incubation period. Suspecting that the hydrochloride salt may be unstable at

neutral to alkaline pH, the investigators set up a simple study to evaluate the pH-dependence of ^{14}C-meth HCl stability. Ten microliters of the aqueous dose solution containing 0.5 µCi of radioactivity was added to each of six glass scintillation vials containing 1 ml of water adjusted to pH values of 2, 3, 4, 5, 6, or 7. The vials were left open in a ventilation hood for 20 hours until completely dried, and radioactivity remaining in the vials was counted.

The results of this study demonstrate that the stability of the hydrochloride salt of methamphetamine is pH-dependent (graph shown below). When the environmental pH exceeds 4 or 5, the salt becomes unstable and methamphetamine free base – which is volatile – is produced. At neutral pH, well over half the radioactivity was lost due to evaporation.



Data from Hui and Maibach (2007). Data show the pH-dependence of the conversion of methamphetamine hydrochloride to methamphetamine free base, which is volatile. Conversion to the free base occurs at pH values above 4, and the free base form of the drug is lost via evaporation.

In *in vitro* dermal absorption studies, the pH of skin can be modified by changing the pH of the receptor fluid. Standard protocols for analysis of dermal uptake utilize a receptor fluid with a pH of 7.4 even though normal skin pH varies between 4.5 and 5. When the initial dermal absorption studies were conducted at pH 7.4, most of the compound was lost due to evaporation. In subsequent studies, the pH of the receptor fluid was changed to 5.0, and evaporative loss was significantly reduced while dermal absorption was correspondingly enhanced. The results of these studies demonstrate that skin pH can be a critical factor affecting the rate and magnitude of dermal absorption.

The results of this study also have implications for understanding the fate and transport of methamphetamine in an indoor environment. The initial product of methamphetamine synthesis is the free base form of the drug, which is volatile. To prevent evaporative loss and facilitate storage and transport of the drug, methamphetamine base is converted to methamphetamine hydrochloride (a salt) using hydrogen chloride gas. Van Dyke et al. (2009) have suggested that "salting out" is a major mechanism for release of methamphetamine to the indoor environment. It is possible that both forms of methamphetamine – the hydrochloride salt and the free base – are released at this stage of synthesis. If this were the case, the base would not be expected to

persist due to its volatility, but the salt would likely persist under most environmental conditions. However, if the hydrochloride salt comes into contact with moisture and the pH is greater than 4, the free base would be regenerated and the drug would once again have a tendency to volatilize. pH-dependent regeneration of the free base may be particularly important in understanding the success (or lack thereof) of using detergents to clean methamphetamine-contaminated surfaces, or using water-based latex paint to encapsulate the contamination, since cleaning detergents and latex paints are both alkaline. Nevertheless, the recent decontamination studies conducted by Martyny (2008) indicate that Simple Green®, a cleaning agent with a pH of 9.5, is very effective in removing methamphetamine hydrochloride from a variety of contaminated surfaces. This suggests that our understanding of the fate of methamphetamine under various environmental conditions is still incompletely understood, and additional studies in this area are warranted.

Exposure Scenario Assumptions

1. The primary population of concern is children in the age range of 6 months to 2 years. These children, by virtue of age-specific behaviors and frequent contact with the floor, constitute a "most exposed" population in an indoor residential exposure scenario.

   Age-specific behaviors that greatly increase the exposure of young children to surface residues were recently summarized in a report by Firestone et al. (2007). Beginning at 6 months of age, children's "floor mobility" increases, leading to more frequent contact with surfaces. Also, children in this age bracket are increasingly likely to place non-food items in their mouth. Between 1 and 2 years of age, participation in play activities increase, and extreme curiosity and poor judgment (based in part on lack of knowledge of potential consequences) motivate exploratory and/or "risky" behaviors. The frequency of mouthing of hands and objects in children in this age range is high. Between ages 2 and 3, the frequency begins to moderate and the amount of time spent outdoors increases.

   In justifying specific values for individual exposure parameters, age-specific exposure and behavioral data for children in the 6 months to 2 years age range are frequently limited. Nevertheless, a number of published reports have investigated the exposure of children in this approximate age range to surface contaminants (e.g., Cohen-Hubal et al., 2006), and additional studies are currently underway. In conducting the exposure assessment presented in this report, an attempt was made to utilize parameter values specific for the 6 months to 2 years age range when age-specific supporting data were available.

2. A sub-chronic duration of exposure (3-4 months) is assumed.

   In the quantitative analysis presented below, two methods are used to estimate daily exposure to surface methamphetamine residues in units of mg methamphetamine per kilogram body weight (mg/kg-day). Both estimates are based on the assumptions that the source concentration is constant (non-depleting) and that the exposed child spends 100 percent of his/her time in the remediated environment. For this reason, the duration of exposure does not affect the estimates of daily exposure to methamphetamine.[9]

   Nevertheless, we recognize that the activities of the individuals living in the residence *will* reduce surface methamphetamine concentrations over time. Mechanisms of contaminant depletion include routine cleaning and contact with uncontaminated skin, clothing and other objects. In reality, these removal processes will cause the daily exposure to decline over time. Also, as noted above, children 6 months to 2 years of age are more likely to spend time indoors, have more frequent contact with the floor, and are much more likely to place their hands, toys and other objects in their mouths. Therefore,

[9] While the output from the SHEDS-multimedia model was based on a 90-day exposure duration, the surface concentration of methamphetamine was assumed to be constant. Therefore, the 90-day exposure estimates simply reflect variation in the behavior (surface contact rates, mouthing frequencies, etc.) of children in the age range of 6 months-2 years.

the "critical window" for exposure to residues on indoor surfaces appears to last about one and a half years. This is approximately equivalent to a sub-chronic duration of exposure.

3. Inhalation of airborne methamphetamine residues does *not* represent a significant exposure pathway.

While inhalation of airborne methamphetamine is likely to occur during the operational, discovery and removal, and cleanup and verification phases in the life of a clandestine methamphetamine lab, it is unlikely to be a significant exposure route during the post-cleanup re-occupancy phase. During this phase, surface methamphetamine residues have been remediated to the designated cleanup standard, so the mass of contaminant available for re-suspension is exceedingly small. Furthermore, the results of decontamination studies conducted by Martyny (2008) indicate that methamphetamine residues are resistant to removal once surfaces have been cleaned with a moderately aggressive cleaning agent (Simple Green®).[10] Additionally, methamphetamine base has a relatively low octanol:water partition coefficient (log P = 2.07), suggesting that it does not readily adsorb to soil and dust particles. Together, these considerations suggest that routine activities such as walking and vacuuming are unlikely to generate significant levels of airborne methamphetamine.

Van Dyke et al. (2009) measured airborne methamphetamine concentrations in a small single story residence during two methamphetamine "cooks" and 13-18 hours thereafter. Concentrations detected at the later time points were approximately 10-30 percent of the concentrations detected during synthesis, suggesting that airborne methamphetamine dissipates quickly once the source of indoor emissions has been eliminated. Results of an investigation by Hui and Maibach (2007) indicate that the free base of methamphetamine is readily volatile, and therefore it would not be expected to be present in a post-cleanup exposure scenario.

4. All interior surfaces are uniformly contaminated, and the surface concentration of methamphetamine[11] is equivalent to the specified cleanup standard.

The exposure scenario modeled in this report presumes a post-cleanup, residential exposure scenario. The maximum concentration of methamphetamine on all interior surfaces is assumed to equal the cleanup standard. This might appear to be a health protective assumption since the synthesis of methamphetamine in a clandestine lab usually occurs in a specific location within the residence (typically the kitchen), and portions of the residence distant from the source of contamination (such as the bedrooms) may be uncontaminated or only lightly contaminated. Nevertheless, studies conducted by Van Dyke et al. (2009) suggest that methamphetamine residues are transported throughout the residence to locations distant from the site of synthesis. Therefore, in a

[10] The results of the decontamination studies are reviewed in the section, "Investigation of the Fate and Transport of Methamphetamine in an Indoor Residential Environment."
[11] The surface concentration is expressed in units of mass per area, e.g., µg of methamphetamine/100 cm^2.

post-cleanup scenario, a uniform maximum residue level throughout the residence is in fact reasonable assumption based on the results of recent research.

5. <u>There are no additional sources or reservoirs of methamphetamine (e.g., contaminated air ducts) that would have the potential to elevate the concentration of methamphetamine on surfaces above the target cleanup standard.</u>

   It is assumed that the cleanup standard will be applied to all surfaces in the residence, even those that are unlikely to be contacted directly by residents. Assuming the presence of an unremediated source within in the residence would also add a significant layer of complexity to the exposure model, since it would require assumptions about the mass of contaminant present at the source, the efficacy of the release mechanism (e.g., air blowing through an air duct) and the rate of release, and contaminant dispersion and deposition within the residence.

6. <u>The source concentration does not decline over time, i.e., there is no depletion of the surface methamphetamine concentration.</u>

   Data from environmental studies of former clandestine methamphetamine labs (Martyny et al., 2007) suggest that methamphetamine levels may persist long after lab activities have ceased.[12] Anecdotal information provided by individuals engaged in the remediation of former clandestine methamphetamine labs also suggests that methamphetamine residues may persist long after drug synthesis activities have ceased.[13]

   While these results are limited, they appear to support the assumption that methamphetamine residues on indoor surfaces may persist for long periods of time *when the residence is unoccupied*. However, as a practical reality, there are several mechanisms that will cause surface contaminant concentrations to decline over time. For example, cleaning with common household cleaning agents will reduce contaminant concentrations on surfaces. In addition, contact by the skin, clothing and shoes of persons living in the residence will result in transfer of methamphetamine residues away from contaminated surfaces. Slowly, these residues will be removed from the environment when the residents bathe, wash their clothing or leave the residence, the latter resulting in the transfer from the source area (the interior of the residence) to uncontaminated areas (outside the residence). Over the very long term, re-painting and replacement of carpets and hard surface floor coverings (e.g., vinyl and linoleum) will also reduce surface contaminant levels. Therefore, the assumption that methamphetamine concentrations are constant over time should be regarded as health protective insofar as it will lead to over-estimation of the time-weighted average daily exposure.

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[12] Martyny et al. (2007) state, "Even labs that had been busted several months prior to testing still had high contamination levels of methamphetamine present on many surfaces within the building." Nevertheless, data supporting this statement were not provided.

[13] Carolyn Comeau, Washington Department of Health, personal communication.

7. <u>The exposed individual spends 100 percent of his/her time in the remediated former methamphetamine lab environment.</u>

   In a residential exposure scenario, it is appropriate to account for the time spent away from the residence. For an adult with a job away from the home, it would be reasonable to assume that this individual spends 9-10 hours/day, 5 days/week at his/her job, with 2 weeks of vacation each year. However, it is not unreasonable to assume that a 6 month to 2 year old child will spend most if not all of his/her time indoors, particularly if the period of residence coincides with the cold winter months or the hot summer months.

Exposure Estimation Models

During methamphetamine synthesis, the fate and transport processes that lead to deposition of methamphetamine on interior surfaces have yet to be completely characterized. Clearly, additional studies in this area are warranted. Based on current knowledge, it appears that one or more steps in the methamphetamine synthesis process generate an aerosol or vapor of airborne methamphetamine which is transported widely throughout the interior of a residence (Van Dyke et al., 2009). When the vapor contacts a surface, it condenses and forms a film, similar to film that deposits on surfaces when pesticides are applied using broadcast spraying or an indoor fogger. Since the film of methamphetamine generated during clandestine methamphetamine synthesis is physically similar to the chemical film produced by indoor application of pesticides, models that have been developed to estimate indoor exposure to pesticide residues can also be used to estimate indoor exposure to methamphetamine residues. A central assumption in this report is that the pathways and mechanisms of exposure to pesticide residues on surfaces are the same as the pathways and mechanisms of exposure to surface methamphetamine residues.

Two models were used to calculate estimates of exposure. The first is based on the U.S. EPA's draft guidance document, *Standard Operating Procedures (SOPs) for Residential Exposure Assessments* (U.S.EPA, 1997; revised 2001). The SOPs provide standard default methods for exposure assessments in a residential scenario when chemical- and/or site-specific information are limited. They provide algorithms for calculating *screening level* exposure estimates for each complete pathway. The algorithms are deterministic; that is, they specify point values for each exposure parameter and generate a single point estimate of exposure. The document also provides different default parameter values to calculate individual exposure estimates for children and adults. The SOPs account for exposure via the following three pathways:

- Dermal exposure following contact with contaminants on carpet
- Dermal exposure following contact with contaminants on hard surfaces (e.g., linoleum floors, plastic laminate counter tops) in the kitchen or bathroom
- Incidental non-dietary ingestion following hand-to-mouth transfer

In a document prepared for the FIFRA Scientific Advisory Panel in 1999, the U.S. EPA stated "These SOPs are the backbone of the Agency's current approach for completing residential exposure assessments." The SOPs were intended to be used both as a screening tool, and for more refined risk assessments when chemical-specific data and information are available.

Alternative exposure estimates were derived using the Stochastic Human Exposure and Dose Simulation for multimedia, multi-route/pathway chemicals (SHEDS-Multimedia) model (Version 3). This model has been in development by the U.S. EPA Office of Research and Development (ORD), National Exposure Research Laboratory (NERL) since 1998. According to its developers, SHEDS-Multimedia "…is a state-of-science computer model for improving estimates of aggregate (single-chemical, multi-route/pathway) and cumulative (multi-chemical, multi-route/pathway) human exposure and dose." It is designed to simulate aggregate exposures and doses for user-specified population cohorts and multi-media chemicals, and relies on data from time-location-activity diaries compiled in U. S. EPA's Consolidated Human Activity Database (CHAD). The history of development of SHEDS-Multimedia is reviewed in the technical manual for the current version (U.S. EPA, 2007). From 2002-2004, a scenario-specific version of the model, SHEDS-Wood, was developed to estimate the exposure and dose of children to chromated copper arsenate (CCA) wood preservatives that had been applied to play structures and decks. In 2005 and 2006, NERL and its contractor Alion Science and Technology developed a graphic user interface (GUI) for SHEDS-Multimedia version 3, along with user and technical manuals for the model. The most recent revisions to SHEDS-Multimedia, made in March, 2007, consisted primarily of correcting several minor "bugs" in the model and modifying the GUI. The model was again reviewed by FIFRA Scientific Advisory Panel (SAP) in August 2007.

SHEDS-Multimedia is a probabilistic model that estimates exposures via inhalation of contaminated air, dermal absorption following contact with contaminated surfaces, and ingestion from hand-to-mouth or object-to-mouth activities. The model generates time series exposure for user-specified population cohorts. Monte Carlo simulation is used to produce distributions of exposure that reflect the variability and/or uncertainty in the input variables.

According to the developers of the model, "SHEDS-Multimedia is the EPA/ORD's principal model for simulating human exposures to a variety of multimedia, multipathway environmental chemicals such as pesticides, metals and persistent bioaccumulative toxins."

The following sections summarize the exposure estimates provided by the two models (i.e., the residential SOPs and SHEDS-Multimedia), and provide analysis and interpretation of their results.

Exposure Estimates based on Algorithms Presented in *Standard Operating Procedures for Residential Exposure Assessments* (U.S.EPA, 1997; revised 2001)

Introduction

Standard Operating Procedures (SOPs) for Residential Exposure Assessment is a draft guidance document prepared in 1997 by the Residential Exposure Assessment Work Group. The work group was composed of staff from the Health Effects Division of the USEPA's Office of Pesticide Programs and Versar, Inc. The SOPs provide standard default methods for exposure assessments in a residential scenario when chemical- and/or site-specific information are limited. They were developed in response to passage of the Food Quality Protection Act (FQPA) in 1996, which mandated the U.S. EPA to immediately begin considering aggregate exposure to pesticides. Non-dietary and non-occupational pesticide exposures for the general population were a primary focus of this effort. Examples of these exposure pathways include inhalation of vapors following pesticide application inside a home and dermal contact with pesticide residues by children playing on a treated lawn. The SOPs provide a means of calculating single pathway, screening level exposure estimates. In a document prepared for the FIFRA Scientific Advisory Panel in 1999, the U.S. EPA stated, "These SOPs are the backbone of the Agency's current approach for completing residential exposure assessments." The SOPs were intended to be used both as a screening tool, and for more refined risk assessments when chemical-specific data and information are available. They address two different exposure scenarios:

- Homeowner, handler exposures that result when an individual applies a pesticide, when such activity is not a condition of his employment
- Residential, post-application exposure that results from activity in an environment previously treated with a pesticide. These exposures, which may result from occupational or homeowner applications, may occur in any number of settings such as homes, schools, and day care centers.

In an indoor residential environment, certain types of pesticide application produce the same widespread surface contamination that results when methamphetamine is synthesized. For example, an indoor fogger is an effective means of applying a pesticide indoors because it disperses a film of pesticide on interior surfaces. Similarly, emissions from methamphetamine synthesis deposit a film of chemical residue throughout an entire house or apartment. For this reason, SOPs that were developed to estimate residential exposure to pesticides applied using an indoor fogger may be adopted to estimate residential exposure to post-cleanup methamphetamine residues on interior surfaces. The following calculations are based on SOP algorithms to estimate

- Dermal exposure following contact with contaminants on carpet
- Dermal exposure following contact with contaminants on hard surfaces (floors and counter tops) in the kitchen or bathroom
- Incidental non-dietary ingestion following hand-to-mouth transfer

Post-Application Dermal Dose from Pesticide Residues on Carpets[14]

Exposure scenario: Pesticide residues are transferred to the skin of adults, toddlers and infants who come in contact with pesticide residues on carpets for recreation, housework and other occupant activities.

Assumptions[15]:

1. **5 percent** of the application rate is available on the carpet as dislodgable residue.
2. Homeowners can contact the treated carpet immediately after pesticide application.
3. Dissipation of pesticide residues should be based on chemical-specific data.
4. Dermal transfer coefficients[16] are assumed to be
    1. Adults: **16,700 cm^2/hr**
    2. Children (1 to 6 years of age): **6,000 cm^2/hr**
5. Body weights are assumed to be
    1. Adults: 71.8 kg
    2. Adult females (for reproductive or developmental toxicity): 60 kg
    3. Children[17]: 15 kg
6. Duration of exposure: 8 hours/day [Note: This is the assumed duration of exposure for contact with carpet. An additional 4 hours/day of contact with hard surfaces (e.g., vinyl) is also assumed, and is calculated in the next section.]

Calculation: potential dermal dose rate on day "t" [PDR_t (mg/day)]

$$PDR_t = ISR_t * CF1 * Tc * ET$$

where:

ISR_t	=	indoor surface residue on day "t" (mg/cm^2)
CF1	=	conversion factor (0.001 mg/µg)
Tc	=	transfer coefficient (cm^2/hr)
ET	=	exposure time (hr/day)

and

$$ISR_t = AR * F * (1-D)^t * CF2 * CF3$$

where:

AR	=	application rate (pounds active ingredient/ft^2)
F	=	fraction of active ingredient retained on carpet (unitless)
D	=	fraction of residue dissipating daily (unitless)
t	=	post-application day on which exposure is assessed
CF2	=	conversion factor (4.54×10^8 µg/pound)

[14] See U.S. EPA (1997), Section 8.2.1; and U.S. EPA (2001), p. 6. Parameter values in **BOLD** were revised per Policy 12 of the Science Advisory Council for Exposure (2001).

[15] The methodology is based on assumptions when adequate chemical- specific field data are unavailable.

[16] The revised value for adults is based on Jazzercise data published by Ross et al. (1990 and 1991). The value for children is based on data from an adult crawling across treated carpet (U.S. EPA, 1996).

[17] The 1997 SOP document provided separate transfer coefficients and associated body weights for toddlers (3 years of age) and infants (6 months to 1 ½ years of age). The 2001 revisions only specified a transfer coefficient for children 1-6 years of age and did not specify a body weight, so 15 kg was assumed.

CF3 = conversion factor (1.08×10^{-3} ft^2/cm^2)

For former meth labs, the post-cleanup concentration of methamphetamine residues on surfaces (i.e., the indoor surface residue) is the target cleanup level, which in most states is 0.1 µg/100 cm^2, or 0.001 µg/cm^2 (U.S. EPA, 2008). Since dissipation data for methamphetamine are not available, it is conservatively assumed that dissipation does not occur. Therefore, using the above equations, it is not necessary to calculate ISR_t; the value for this parameter is simply the target cleanup level. *In the absence of chemical-specific data, it is conservatively assumed that 100 percent of the methamphetamine residue present on carpet is dislodgeable*[18].

Therefore, the dermal dose rate for an child contacting carpet is

$$0.001\ \mu g/cm^2 * 0.001\ mg/\mu g * 6{,}000\ cm^2/hr * 8\ hr/day = 0.048\ mg/day$$

Normalized to the average body weight of a 2-3 year-old child (15 kg), the estimated exposure resulting from contact with methamphetamine residue on carpets would be 0.0032 mg/kg-day. The SOP does <u>not</u> include any assumptions about dermal absorption, indicating that the calculated daily dose rate "…be used in conjunction with toxicity data to assess risk." This implies that it is appropriate to assume 100 percent dermal absorption. Given that the experimentally determined average dermal absorption of methamphetamine was 57 percent (Hui and Maibach, 2007), this assumption produces approximately a 50 percent over-estimation of the dermally absorbed dose.

Post-Application Dermal Dose from Pesticide Residues on Hard Surfaces[19]

The <u>exposure scenario</u> and <u>assumptions</u> are similar to those specified for calculating the dermal dose from residues on carpets. For hard surfaces, however, 10 percent of the applied pesticide is assumed to be dislodgeable residue (U.S. EPA, 2001) and the duration of exposure is assumed to be just 4 hours/day. The latter value is justified on the basis that it represents the mean of the 90th percentile values for time spent on the kitchen and bathroom for all age groups (adults and children).

<u>Calculation</u>: The equations and parameters that are used to calculate the dermal dose from residues on hard surfaces are identical to those used for calculating the dermal dose from carpets. Therefore, using the same equation described above for calculating potential dermal dose rate on day "t" (PDR_t), the dermal dose rate for a child contacting hard surfaces is

$$0.001\ \mu g/cm^2 * 0.001\ mg/\mu g * 6{,}000\ cm^2/hr * 4\ hr/day = 0.024\ mg/day$$

Normalized to a child's body weight (15 kg), the estimated exposure resulting from contact with methamphetamine residues on carpets would be 0.0016 mg/kg-day. The SOP does <u>not</u> include any assumptions about dermal absorption, indicating that the calculated daily dose rate "…be used in conjunction with toxicity data to assess risk." This implies that it is appropriate to assume 100 percent dermal absorption. Given that the experimentally determined dermal absorption of

[18] The assumption is consistent with the procedure used to assess compliance with a cleanup standard, since the amount detected on a wipe sample is by definition dislodgeable.
[19] See U.S. EPA (1997), Section 8.2.1; and U.S. EPA (2001), p. 6.

methamphetamine is 57 percent (Hui and Maibach, 2007), this assumption produces approximately a 50 percent over-estimation of the dermally absorbed dose.

Post-Application Dose Estimate for Toddlers from Incidental Non-Dietary Ingestion of Pesticide Residues on Indoor Surfaces from Hand-to-Mouth Transfer[20]

[Note: Parameter values for this pathway were not revised in Policy 12 of the Science Advisory Council for Exposure (2001).]

Exposure scenario: Pesticide residues are transferred to the skin of toddlers during post-application contact with treated indoor areas and are subsequently ingested as a result of hand-to-mouth transfer. The 3 year old age group was selected for his scenario because, at the time the SOP was written, this was the youngest age group for which data on hand-to-mouth activity were available.

Assumptions:

1. 5 percent of the application rate from broadcast or crack and crevice treatments) is available as dislodgable residue.
2. Homeowners can contact the treated carpet immediately after pesticide application.
3. Dissipation of pesticide residues should be based on chemical-specific data.
4. The average surface area of both hands is 350 cm^2 for a toddler (3 years of age).[21]
5. Replenishment of the hands with pesticide residues is an implicit factor in this assessment, suggesting that there is no maximum dermal loading value.
6. *The surface-to-skin transfer efficiency of dislodgable residues is 100 percent.*[22]
7. The average rate of hand-to-mouth activity is 0.026 events/minute (1.56 events/hour) for toddlers (3-5 year olds).
8. The duration of exposure to indoor surfaces is 4 hours/day. (See justification in Section II above.)
9. The average weight of a toddler (age 3 years) is 15 kg.

Calculation: potential dose rates from ingestion [PDR (mg/day)]

$$PDR = ISR * SA * FQ * ET$$

where:

ISR	=	indoor surface residue (mg/cm^2)
SA	=	surface area of the hands that contact indoor surfaces and subsequently transfer residues to the mouth during a given event (cm^2/event)
FQ	=	frequency of hand-to-mouth events (events/hour)
ET	=	exposure time (hours/day)

[20] See U.S. EPA (1997), Section 8.4.
[21] Based on the 1996 U.S. EPA exposure Factors Handbook
[22] The guidance document is explicit in this regard: "…if the dislodgable residue on the indoor surface is 1 mg/cm^2, the residue on skin is also 1 mg/cm^2 after contacting the surface."

As discussed above, the post-cleanup concentration of methamphetamine residues on surfaces at former meth labs (i.e., the indoor surface residue) is the target cleanup level, which in most states is 0.1 µg/100 cm^2 (0.001 µg/cm^2, or 0.001 x 10^{-3} mg/cm^2). Since dissipation data for methamphetamine residues on surfaces are not available, it is conservatively assumed that dissipation does not occur.

Therefore, the incidental ingestion dose among toddlers following contact with contaminated surfaces and subsequent hand-to-mouth activity is

0.001×10^{-3} mg/cm^2 ∗ 350 cm^2/event ∗1.56 events/hour ∗ 4 hours/day = 0.0022 mg/day

Normalized to a toddler's body weight (15 kg), the estimated exposure would be 0.00015 mg/kg-day.

Total Estimated Exposure via All Three Pathways

Dermal Dose from Pesticide Residues on Carpets:	0.0032 mg/kg-day
Dermal Dose from Pesticide Residues on Hard Surfaces:	0.0016 mg/kg-day
Incidental Ingestion Dose from Hand-to-Mouth Activity:	0.00015 mg/kg-day
TOTAL:	**0.00495 mg/kg-day**

Analysis and Interpretation

Based on the SOP algorithms and using default values for input parameters, 97 percent of total exposure for a child resulted from dermal contact with "soft" surfaces such as carpet and hard surfaces such as linoleum. Ingestion, which occurs secondarily to dermal contact with contaminated surfaces and subsequent hand-to-mouth activity, accounted for just 3 percent of total exposure. However, the default value for hand-to-mouth frequency (1.56 contacts/hour) prescribed in the original SOP guidelines was based on a draft report that had not yet been peer reviewed. More recent analysis of data from several published and unpublished research reports (Xue et al., 2007) indicates that this value is low by approximately one order of magnitude. Based on data from four studies of children 6 to ≤ 12 months of age, the mean indoor hand-to-mouth frequency was 18.9 contacts/hour. Data from three studies of children 1 to ≤ 2 years provided a mean of 19.6 contacts/hour. 95th Percentile estimates for both age groups were 52 and 63 contacts/hour, respectively. When exposure via incidental ingestion was re-calculated using an average hand-to-mouth contact frequency of 19 contact/s hour and an average body weight of 12 kg (U.S.EPA, 1997; Table 7-3), the exposure estimate for this pathway increased to 0.0266 mg/day, or 0.0022 mg/kg-day. Using this value, total exposure is estimated to be 0.007 mg/kg-day, and incidental ingestion accounts for approximately one-third of total exposure.

The experimentally determined mean dermal absorption efficiency for methamphetamine was determined to be 57 percent (Hui and Maibach, 2007). Had this value been used in the SOP equations, the dose estimates for the two dermal absorption pathways would have been reduced by approximately one-third.

Even using the higher estimated hand-to mouth contact frequency from Xue et al. (2007), the results obtained using the SOP algorithms are largely driven by the default value for the dermal transfer coefficient for a child 1 to 6 years of age (6,000 cm^2/hour). The guidance document does not provide justification for this value. However, the results of a recent study conducted by Cohen Hubal et al. (2006) suggest that this default value appears to be very health protective. In this study, children's exposure to surface pesticide residues was evaluated in a child care center where the pesticide esfenvalerate had been applied the previous day. Transfer coefficients were based on surface sampling data and pesticide loadings on cotton body suits that the children wore to monitor their dermal exposure. Transfer coefficients were calculated using the equation

Dermal transfer coefficient = dermal exposure / surface loading

where the dermal exposure was the mass of pesticide on the body suit divided by the monitoring duration (nanograms/hour) and the surface loading was based on the results of surface wipe sampling (micrograms/square centimeter). Transfer coefficients were calculated for infants (6-12 months of age) and pre-schoolers (2-3 years of age).

Dermal transfer coefficients calculated using the data obtained from this study ranged from 10 to 6,000 cm^2/hour. Therefore, the SOPs specify a default value for the transfer coefficient for a child that is equivalent to the maximum value obtained by Cohen Hubal et al. The authors of this study concluded, "…results of this work suggest that the default assumption used by the U.S. EPA OPP [i.e., the SOPs] is reasonable." In addition, it appears that dermal transfer coefficients for children have a wide range of variability, and dermal exposure may be more appropriately estimated using a stochastic model that accounts for the wide range of children's behaviors and activities.

With one exception, the algorithms and default parameter values prescribed by the SOPs appear to be appropriate for obtaining very health protective, screening level estimates of exposure. However, based on data that has been collected since the SOP guidelines were first made available, the default hand-to-mouth contact frequency for children is clearly too low. Using the default value may likely result in under-estimation of exposure via the incidental ingestion pathway. On the other hand, the algorithm for non-dietary ingestion also incorporates a default value for contact surface area (350 cm^2/event), which is equivalent to the average surface area of both hands. Assuming that an area equivalent to the surface of both hands is contacted by the mouth an average of 19.6 times per hour would appear to be excessive, even for a 1-2 year old.

Exposure Estimates based on the Stochastic Exposure and Dose Simulation Model for Multimedia, Multipathway Chemicals (SHEDS-Multimedia), Version 3

Introduction: Overview of SHEDS-Multimedia

The Stochastic Human Exposure and Dose Simulation for multimedia, multi-route/pathway chemicals (SHEDS-Multimedia) model (Version 3) has been in development by the U.S. EPA Office of Research and Development (ORD), National Exposure Research Laboratory (NERL) since 1998. According to its developers, SHEDS-Multimedia "…is a state-of-science computer model for improving estimates of aggregate (single-chemical, multi-route/pathway) and cumulative (multi-chemical, multi-route/pathway) human exposure and dose." It simulates aggregate exposures and doses for user-specified population cohorts and multi-media chemicals, and relies on data from time-location-activity diaries compiled in U. S. EPA's Consolidated Human Activity Database (CHAD).

As defined in the Technical Manual for the model, *exposure* is the contact between the chemical agent and the human "target" at the skin, lung and gastrointestinal tract exposure surfaces. *Dose* is defined as the amount of chemical that enters the target after crossing the exposure surfaces.

SHEDS-Multimedia estimates absorbed doses that are the result of exposure via inhalation, ingestion (from mouthing the hands or objects) and dermal contact in a residential setting. The model uses Monte Carlo simulation to simulate a population of stochastically created "virtual" persons whose collective characteristics reflect the simulated population and input distributions for exposure-related variables. For each individual, SHEDS-Multimedia generates a series of activities, media concentrations, and resulting exposures over the selected simulation period. These individual exposure time series are then aggregated over time to produce time-integrated or time-averaged exposures, as shown in the hypothetical individual exposure profile in Figure 1.

Exposure estimates presented in this report were generated by a "standard" SHEDS-Multimedia run, also called a "variability run," which generates exposures for a random sample of individuals in the target population using Monte Carol sampling. The fundamental modeling unit in SHEDS-Multimedia is the individual, and each individual is generated as a representative random sample. These individual exposure estimates provide the basis for the exposure distribution for the population.

SHEDS-Multimedia can also be run as a two-stage Monte Carlo model (also called an "uncertainty run"), which consists of a series of variability runs with the input variables modified between each variability run to represent uncertainty in the input parameters of the variability runs. However, two stage Monte Carlo simulations were *not* completed for this report.

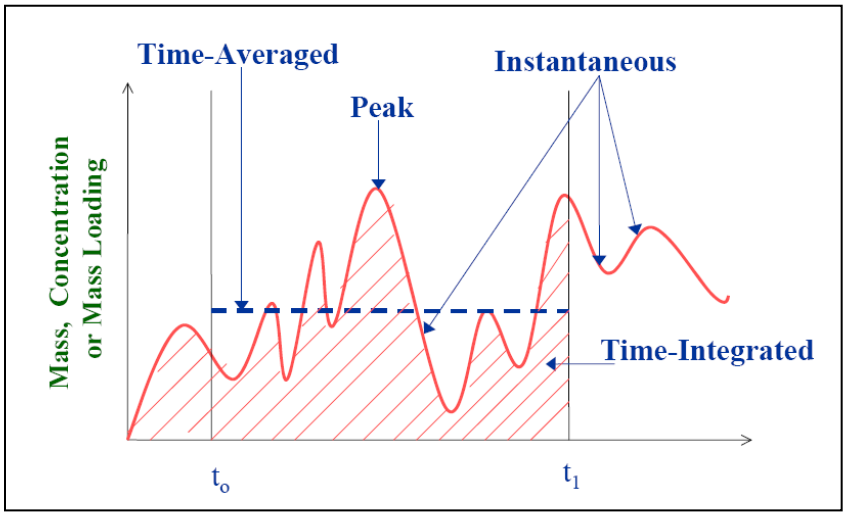


Figure 1. Hypothetical exposure profile for an individual over time. (Reproduced from USEPA, 2007)

As outlined in the Technical Manual for SHEDS-Multimedia version 3 (U.S. EPA, 2007), the following general steps are applied for each individual in a SHEDS run:

1. Given the distribution of the target population, randomly select the age, gender and other demographic properties of interest.
2. Using the CHAD diaries that are built into the model, generate a longitudinal activity diary that indicates the sequence and duration of activities and locations for the individual.
3. Generate concentration-time series for each potential contact medium (e.g., indoor air, indoor smooth surfaces, indoor textured surfaces, indoor dust).[23]
4. Simulate the contacts between the individual and the affected media. These depend on the diary activity and location information and user-specified contact probabilities.[24]
5. Calculate exposure-time series for the individual using the results from steps 3 and 4 and user-specified distributions for exposure factors.
6. Generate an approximation for the dose time series, if desired, using the simple physiologically-based pharmacokinetic (PBPK) model in SHEDS.
7. Export exposure time series for use in a PBPK model, or extract desired metrics or summary statistics from the exposure or dose time series.

SHEDS-Multimedia repeats this process for an individual many times (the number of iterations is specified by the user) using Monte Carlo simulation to obtain population estimates. A diagram

[23] As discussed in the following section, concentrations on smooth and textured surfaces are assumed to equal the target cleanup level for methamphetamine. Concentrations on both types of surfaces are assumed to be constant (non-depleting) for the entire 90-day exposure duration. The indoor air concentration is assumed to be zero, and the concentration in indoor dust is assumed to be zero. These assumptions are consistent with the goal of identifying a risk-based cleanup standard for methamphetamine on surfaces.

[24] Contact probabilities and exposure parameters are age-specific, to the extent that age-specific data are available for them.

of the steps involved in generating exposure and dose estimates using the SHEDS model is shown in Figure 2.

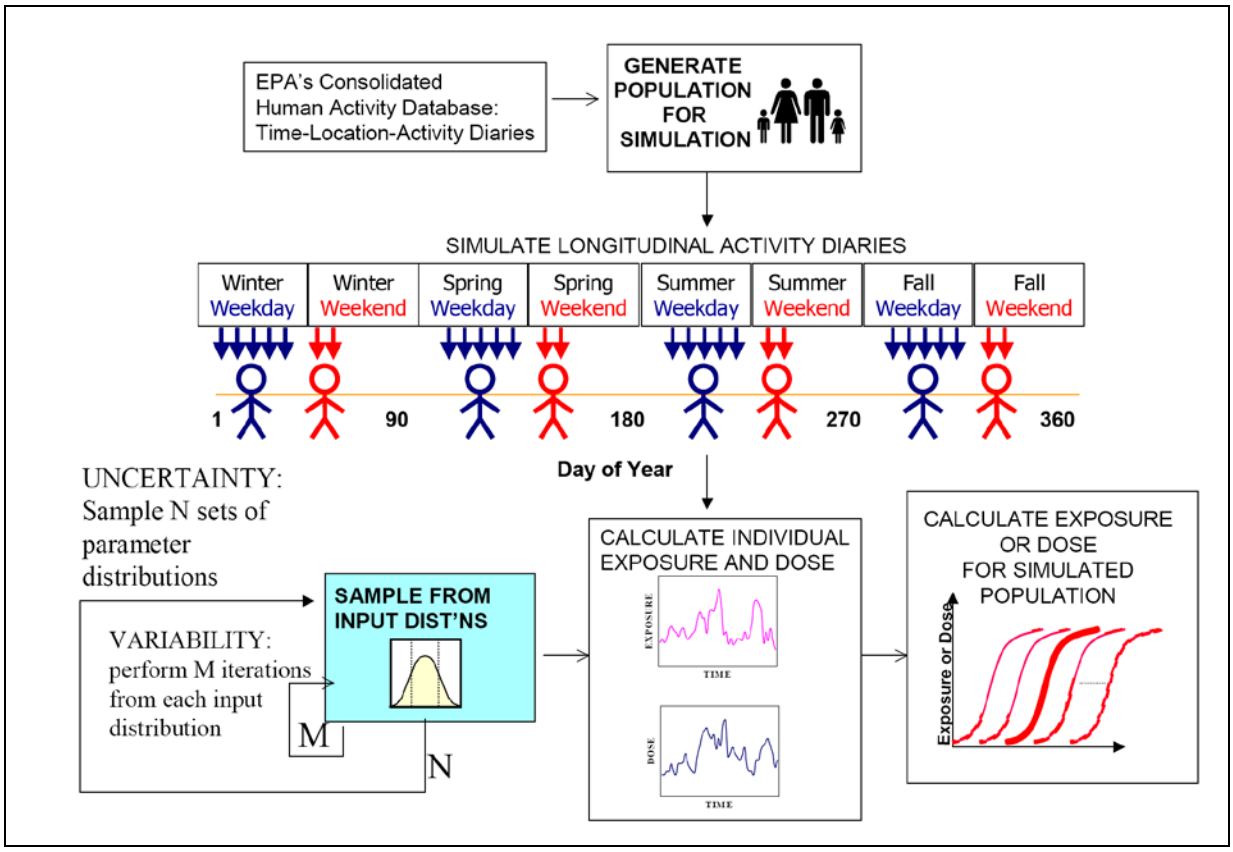


Figure 2. Diagrammatic overview of the SHEDS methodology. (Reproduced from Zartarian et al., 2006)

Additional Exposure Assumptions for SHEDS-Multimedia

In addition to the exposure assumptions discussed on pages 9-12, the following additional assumptions are required to run SHEDS-Multimedia.

1. <u>The oral bioavailability of ingested methamphetamine residues following hand-to-mouth or object-to-mouth movements was assumed to be 100 percent.</u>

   While some chemicals may be incompletely absorbed following ingestion, an oral bioavailability of 100 percent for methamphetamine was assumed in this analysis. The drug is known to be well absorbed by all routes of exposure, including ingestion. In addition, its rapid rate of dermal absorption suggests the drug passes readily through biological membranes.

   Since the post-remediation surface concentration of methamphetamine is anticipated to be extremely low (the prevailing default cleanup standard is 1 ng/cm^2), the mass of the drug transferred to the mouth via hand-to-mouth activities is anticipated to be

correspondingly small. Given the extremely low rate of ingestion of the drug, assuming 100 percent oral bioavailability appears reasonable.

2. Based on experimental data, the mean dermal absorption efficiency of methamphetamine was estimated to be 57 ± 7.6 percent (mean ± SD).

   In vitro studies of the dermal absorption of methamphetamine were recently completed by Drs. Xiaoying Hui and Howard Maibach at the University of California San Francisco (UCSF).[25] These studies, which were based on a standard protocol utilizing Franz diffusion cells and human skin samples, indicate that methamphetamine is well absorbed across the skin. Experimental details are provided in a draft report of the UCSF studies, included as an appendix to this report.

   Interpreting data from these studies requires an understanding of the basic cellular structure of skin. Simply described, skin is composed of three distinct layers: the outermost epidermis, the intermediate dermis, and an underlying layer of subcutaneous fat. The stratum corneum consists only of dead cells, called corneocytes, which lack any contact with the circulation in living skin. As noted in a recent review by Van de Sandt et al. (2007), the outermost layer of the epidermis, the stratum corneum, is the rate-limiting barrier of skin. These authors also made the following recommendations for interpretation of data from dermal absorption studies:

   > *For risk assessment purposes, the chemical adsorbed to the stratum corneum at the end of the experiment is considered as non-bio-available. The amount of penetrated substance found in the receptor fluid (in vitro)…at the end of the experiment is considered systemically available. In addition, amounts present in the epidermis (minus the stratum corneum) and dermis at that time are often considered to be systemically available as a conservative assumption.*

   The UCSF data were interpreted in a manner consistent with these recommendations. The overall estimate of dermal absorption efficiency is based on cumulative data collected over a 24-hour incubation period.

3. The maximum dermal loading of methamphetamine residues on the skin (body and hands) was assumed to be ten times greater than the target cleanup concentration for methamphetamine on surfaces.

   SHEDS-Multimedia incorporates separate variables for maximum dermal loading on the hands and body, although the values for the two variables are usually identical. They are included in the model to prevent multiple contacts from adding to the dermal load indefinitely. Therefore, when the maximum dermal loading is obtained, no additional contaminant can be transferred to the skin.

[25] These studies were conducted under contract with funding provided by the California Environmental Protection Agency, Department of Toxic Substances Control.

The target cleanup standard first proposed by the state of Washington and subsequently adopted by several other states is 0.1 µg/100 cm^2, or 1 ng/cm^2. Since the surface cleanup standard is so low, we have assumed that the skin can accumulate up to ten times the state of Washington's cleanup standard. This assumption combined with methamphetamine's high rate of dermal uptake suggests that dermal loading is the primary factor that limits the mass of methamphetamine taken up via the dermal pathway.

4. <u>The mean surface residue-to-skin transfer efficiency for methamphetamine was estimated to be 7 percent for all types of surfaces.</u>

   Residue-to-skin transfer efficiency is likely dependent on the chemical properties of the contaminating substance and (if applicable) the carrier in which the chemical is present. Nevertheless, the transfer efficiencies reported by Camann et al. (2000) for chlorpyrifos, pyrethrin I and piperonyl butoxide – three chemically distinct substances – typically varied over a range of 2-fold or less.[26] Based on an evaluation of data from several studies, Beamer et al. (2008) developed lognormal distributions for the transfer efficiency distributions of these same three chemicals, and found that the geometric mean values for transfer from carpet and vinyl ranged from 0.01 to 0.04, while the mode values were all between 0.01 and 0.02.

   The default distributions for the transfer efficiency parameter (beta distribution; shape 1: 0.6; shape 2: 8.4; mean 0.07) that were supplied with the SHEDS model is based on two references, one conducted by Nishioka (2003) under contract to U.S. EPA and the other published by Cohen Hubal et al. (2005). Both studies were based on analysis of transfer of fluorescent tracers that were used as surrogates for pesticides.

   Data from the *in vitro* surface-to-skin transfer studies conducted at UC San Francisco were *not* used to estimate a value for residue-to-skin transfer efficiency in SHEDS-Multimedia. This decision was based primarily on the fact that the experimental techniques developed by UCSF should at present be regarded as experimental. The methodology has not been validated by comparing its results with data from *in vivo* hand press transfer studies of other chemicals [e.g., chlorpyrifos, pyrethrin I and piperonyl butoxide (Camann et al., 2000)].

   Furthermore, in the UCSF studies, the contact durations required for significant transfer to occur were significantly longer than those employed in standard "hand press" studies. For example, the transfer of methamphetamine from vinyl tile to skin after contact durations of 15 seconds and 5 minutes was just 0.15 percent and 5.41 percent, respectively. In contrast, in an evaluation of a cotton glove press test for assessing transfer of pesticides from plush carpet, Roberts and Camann (1989) utilized a contact duration of two seconds. In two more recent studies, Camann et al. (2000) and Clothier (2000) utilized contact durations of just one second.

[26] Typically, a two-fold difference in transfer efficiency for the three chemicals was observed. The nature of the surface had a much greater effect on transfer efficiency: according to the authors, transfers from vinyl flooring were 2- to 10-fold greater than from plush carpets.

The UCSF studies indicated that residue to skin transfer *in vitro* was highly dependent on contact duration, a result that contrasts markedly with the results obtained *in vivo* by Cohen Hubal et al. (2005), where transfer was found *not* to depend on contact duration. The duration-dependence of transfer efficiency found in the UCSF studies is also problematic because the SHEDS model does not incorporate a parameter for contact duration.

In summary, the results of the UCSF studies are not easily reconciled with the published literature. In part, this may the result of the physical and mechanical differences between the hand press technique and the in vitro methods developed by UCSF. Nevertheless, validation studies of the UCSF methodology have not been completed. For this reason, we decided to incorporate the default SHEDS distribution into our analysis of methamphetamine exposure.

5. Contact with uncontaminated surfaces or objects was assumed *not* to deplete methamphetamine residues from the skin.

   SHEDS allows the user to specify a value for contaminant depletion from the skin as result of contact with uncontaminated surfaces (parameter 3 (d), "removal efficiency during events without water"). The exposure scenario that this exposure analysis is based on assumes that all surfaces are uniformly contaminated with methamphetamine, so contact with uncontaminated surfaces would be unlikely to occur. We have conservatively assumed that contact with uncontaminated surfaces is not a mechanism of contaminant depletion from the skin; all the residue that adheres to the skin as a result of contact with contaminated surfaces is assumed to remain on the skin until removed (albeit partially) by washing.[27]

6. Methamphetamine is assumed to be present on surfaces as a chemical film or residue; soil and dust inside the home were assumed *not* to be contaminated with methamphetamine.

   SHEDS-Multimedia has separate inputs for contaminant concentration as a "residue" on surfaces and as a constituent of soil and dust in the home. We have assumed that methamphetamine is only present as a surface residue; the concentration in soil and dust inside the residence is assumed to be zero. This assumption is based in part on the relatively low octanol:water partition coefficient of methamphetamine (log P = 2.07). In the outdoor environment, chemicals with partition coefficients this low do not adsorb readily to soil and translocate readily from the surface to groundwater if spilled onto soil. There are no data available on the physical form of methamphetamine as a contaminant inside a residence. A portion of the chemical may indeed be adsorbed to soil or dust particles, but there is no basis for estimating the percentage that is adsorbed to particles and the percentage that is not. Since a single distribution was used to characterize the surface-to-skin transfer of methamphetamine residues, this assumption should not have a material effect on the exposure estimates generated by the model.

[27] See section VI ("Other Sources of Uncertainty") for discussion of the effectiveness of washing with soap and water as a means of removing methamphetamine residue from the skin.

Justification for Parameter Values used in SHEDS-Multimedia

SHEDS-Wood and SHEDS-Multimedia have been reviewed on several occasions by the FIFRA Scientific Advisory Panel. A report from a December 2003 meeting on the use of SHEDS-Wood to assess children's exposure to residues from wood treated with chromated copper arsenic (CCA) stated,

> *It was the consensus of the Panel that, by and large, the best information on input variables at this time has been used…Even though on can question specific choices of distributional assumptions, overall the work seemed a reasonable effort and a sound basis for risk assessment within the limitations of available information…Even though one can question specific choices of distributional assumptions, overall the work seemed a reasonable effort and a sound basis for risk assessment within the limitations of available information.*

To estimate exposure to surface methamphetamine residues, data supporting methamphetamine-specific parameter values and distributions are not available, and it is unlikely that they will become available in the foreseeable future. For this reason, several of the parameter values and distributions utilized for analysis of methamphetamine exposure were the values and distributions that were provided with the model, which are based on experimental data for other chemicals. In some cases, support for selecting a particular value or distribution could be gained by comparing the similarity, or dissimilarity, of chemical and physical properties of methamphetamine with the chemical and physical properties of chemicals for which relevant data are available.

Values for several parameters were adopted because they were judged to be health protective and not entirely unreasonable, or because their effect on the total exposure estimate was found to be minimal. For example, assuming 100 percent oral bioavailability of ingested methamphetamine residues may indeed be conservative, but the effect of this assumption on the SHEDS-Multimedia estimate of exposure was small because the ingestion pathway only accounted for about 10 percent of total exposure. Therefore, even if the bioavailability of ingested methamphetamine had been assumed to be 50 percent, the net effect would be just a 5 percent decrease in the total exposure estimate. Similar results were found for several other parameters. These are discussed in the section, "Sensitivity Analysis: Evaluation of Changes in the Values of Individual Parameter on Estimates of Exposure" below.

Values and distributions for a number of exposure parameters were developed in consultation with Drs. Luther Smith and Graham Glen of Alion Science and Technology, U.S. EPA's primary contractor for development of the SHEDS-Multimedia model. The far right column of parameter values table (Table 3) notes several references to this correspondence.

Table 3. SHEDS Multimedia Model Version 3, General exposure and dose factors: Data & information supporting selected parameter values and distributions

Variability Groups and Variable Descriptions	Variable	Units	Default[28] Distribution	Default[28] Parameters	Comments	USEPA (2005; Table 10) or Hore et al. (2006; Table 3)
1. Activity-related						
a) Probability of having a vegetable garden	[has_garden_p]	[-]	point	1	not applicable; **assume 0**	
b) Probability of having a lawn	[has_lawn_p]	[-]	point	1	not applicable; **assume 0**	
c) Probability of having a dog or cat	[has_pet_p]	[-]	point	1	**assume 0**	
2. Transfer-related						
a) Soil-skin adherence factor	[adherence]	mg/cm^2	point	0	not applicable; **assume 0**[29] (soil pathway incomplete)	
b) Body-surface fractional contact rate	[contactb]	hr^{-1}	triangle	min: 0 mode: 0.36 max: 1.08	**use default**	p. 61 ($F_{contact,\ res,\ body}$) & pp. 70-71 values >1 account for multiple contacts
c) Hand-surface fractional contact rate	[contacth]	hr^{-1}	triangle	min: 0.6 mode: 1.2 max: 1.5	**use default**	p. 61 ($F_{contact,\ res,\ hand}$) & p. 70 values >1 account for multiple contacts see 12/15 & 12/19 notes from Dr. Glen
d) Fraction of body unclothed (non-hand)	[f_uncloth]	[-]	beta	shape1: 3 shape2: 6.7	same as SHEDS-Wood **use default**	p. 61 ($F_{uncl,body}$); p. 70
e) Fraction of surface of one hand that enters mouth	[hm_fraction]	[-]	beta	shape 1: 3.7 shape 2: 25 (mean = 0.13)	same as SHEDS-Wood **use default**	p. 62 ($F_{hand\text{-}mouth}$); p. 73 0.085 ("default SHEDS"); $Frac_{HM}$
f) Hand mouthing events per hour[30]	[hm_freq]	events/hr	triangle	min: 0.4 mode: 8.5 max: 25.7	**use** age-specific (1 to <2 yrs) indoor data from Xue: (**Weibull**; **18.79, 0.91**) 19.6 ± 19.6 (mean ± SD)	Weibull: scale 6.93, shape 0.73 p. 62 (N_{hm}); p.74 10 ± 7 (range: 1-18); $Freq_{HM}$

[28] These distributions and parameter values were included with the SHEDS model as received.
[29] The log K_{OW} for methamphetamine is 2.07, suggesting that methamphetamine does not readily adhere to soil particles.
[30] Values for this parameter could also be based on "mouth-hand" data for children ≤ 24 months published by Tulve et al. (2002; Table 2; children ≤ 24 months): mean 18, median 12, 95 percent CI 9-16 events/hour

Table 3. Continued

Variability Groups and Variable Descriptions		Variable	Units	Default[31] Distribution	Default[31] Parameters	Comments	USEPA (2005; Table 10) or Hore et al. (2006; Table 3)
g)	Dust ingestion rate (indoor, direct only)	[ingestion_indoor]	mg/hour	point	1	no dust data; **assume 0**	
h)	Soil ingestion rate (outdoor, direct only)	[ingestion_outdoor]	mg/hr	point	1	not applicable; **assume 0**	p. 62 (IR_{soil}); pp. 71-2
i)	Object-surface concentration ratio[32]	[object_ratio]	[-]	point	0	**use uniform: 0 (min), 0.2 (max)** per information from Drs. Glen & Smith	not evaluated in SHEDS-Wood 0.5 ("default SHEDS"); $Ratio_{OBJ-SURF}$ see 12/19/06 and 1/16/07 notes from Dr. Glen
j)	Object-mouth contact area	[om_area]	cm^2	uniform	min: 0; max: 20	**use exponential: 1 (min), 10 (mean), 50 (max)**	see 1/16/07 note from Glen/Smith 35 ("default SHEDS"); SA_{OBJ}
k)	Object-mouth contact rate[33]	[om_freq]	events/hr	point	0	**use Hore et al. distribution**[34]	**5 ± 4 (range: 1.4 – 15)**; $Freq_{OM}$
l)	Object-mouth transfer efficiency	[om _transfer]	[-]	uniform	min: 0.1; max: 0.5	**use default**	0.3 ("default SHEDS"); $Eff_{SAL-REM}$
m)	Residue-skin transfer efficiency	[transfer_dermal]	[-]	beta	shape1: 0.6 shape2: 8.4	**use default**	references from Glen/Smith (12/15/06)

[31] These distributions and parameter values were included with the SHEDS model as received.

[32] "This variable refers to the ratio of the mass loading of chemical residue on an object sitting on a surface (e.g., a toy on the floor) to the mass loading of the surface that the object is sitting on." (Ref: November 2, 2006 Draft SHEDS-Multimedia Technical Manual, page 38). Drs. Glen & Smith stated, "We consider it [this variable] to be one of the most uncertain variables in our model" (see email note dated 1/16/07). Values for this parameter depend on the specific details of the poet-cleanup exposure scenario (e.g., whether or not toys and mouthable objects are disposed of or decontaminated to the same target remediation level as interior surfaces).

[33] Values for this parameter could also be based on "mouth-toy" data for children ≤ 24 months published by Tulve et al. (Table 2): mean 45 and median 39; 95 percent CI on the median: 31-48 events/hour

[34] Assume lognormal distribution with arithmetic mean of 5 and arithmetic standard deviation of 4. See distribution generated by Crystal Ball. Parameter values cited by Hore et al. (2006) were based on child-specific microlevel activity data obtained from the Children's Post-Pesticide Application Exposure Study (CPPAES). Original reference is Paromita Hore's PhD dissertation (2003). Drs. Glen & Smith noted "The [object-mouth] contact frequency rates cited by Paromita Hore seem reasonable to us" (12/19/06).

Table 3. Continued

Variability Groups and Variable Descriptions	Variable	Units	Default[35] Distribution	Default[35] Parameters	Comments	USEPA (2005; Table 10) or Hore et al. (2006; Table 3)
3. Removal-related						
a) Maximum dermal loading for body	[dermaxb]	ug/cm^2	uniform	min: 0.4; max: 2.0	**assume point value: 0.01** (10x "default" cleanup level)	see 12/15 & 12/19 notes from Dr. Glen
b) Maximum dermal loading for hands[36]	[dermaxh]	ug/cm^2	uniform	min: 0.4; max: 2.0	**assume point value: 0.01**[37] (10x "default" cleanup level)	see 12/15 & 12/19 notes from Dr. Glen
c) Removal efficiency during bath/shower	[remv_bath]	[-]	beta	shape1: 17.1 shape 2: 5.1 (mean = 0.77)	same as SHEDS-Wood **use default**	p. 62 (F_{bath}); p. 74 0.85 ("default SHEDS")
d) Removal efficiency during events w/o water	[remv_dry]	[-]	point	0	**assume 0**[38]	
e) Removal efficiency during mouthing (skin-to-mouth only)	[remv_mouth]	[-]	triangle	min: 0 mode: 0.16 max: 0.32	default apparently based on Kissel et al. (1998) **use uniform: 0.1 (min), 0.5 (max)**[39]	p. 63 ($F_{hm\text{-}remov}$) & p. 75 (mean = 0.78) 0.3 ("default SHEDS"); $Eff_{SAL\text{-}REM}$
f) Removal efficiency during hand washing	[remv_wash]	[-]	beta	shape1: 32 shape2: 22 (mean = 0.59)	same as SHEDS-Wood **use uniform: 0.3 (min), 0.45 (max)**[40]	p. 62 (F_{hw}); p. 74 0.15 ("default SHEDS")
g) Mean # hand washes/day per person	[washprob]	day^{-1}	lognormal	geo mean: 3.74 geo std dev: 2.63	same as SHEDS-Wood **use default**	p. 62; p. 74

[35] These distributions and parameter values were included with the SHEDS model as received.

[36] Both 5(c) and 5(d) are variables that limit dermal loading. These limits, which are usually given the same value, apply to the sum of the chemical across all phases (soil, dust and residue). They are included to prevent multiple contacts from adding to the dermal loading indefinitely, i.e., when the maximum loading is attained, no more contaminant can be transferred to skin. Dr. Glen's 12/15 recommendation: assume the ratio of dermal loading to surface concentration is one, meaning that skin loadings cannot exceed the surface concentration. However, since the surface cleanup standard is so low (1 ng/cm^2), we have assumed the skin can accumulate 10x the cleanup standard. Dr. Glen's note of 12/19 supports this logic: "…your suggestion of using 10 ng/cm^2 sounds reasonable." This value may need to be changed if the cleanup standard changes significantly.

[37] Assumed values for maximum dermal loading of hands and body are 10x the current target remediation goal for methamphetamine residues on surfaces (0.001 µg/cm^2). This assumption may need to be re-evaluated if it is apparent that the risk-based target cleanup goal is considerably higher than the current value

[38] This conservative assumption is based on the uneven texture of the skin, and takes into consideration the small mass of contaminant loading on the skin that is anticipated to occur under the post-cleanup exposure scenario.

[39] See Zartarian et al. (2000), using data generated by Camann et al. (1995) for saliva removal of chlorpyrifos on freshly spiked human hands. The mid-point of a 0.1 to 0.5 uniform distribution is 0.3, which is the default point value adopted for the SHEDS-Wood model. Zartarian et al. (2000) state, "It is estimated that 50 percent represents the maximum mouthing removal efficiency for fresh and dried pesticide residues" by human saliva and reference a personal communication from Robert Lewis (U.S.EPA, NERL). The SHEDS-Wood documentation also references a personal communication from R. Lewis.

[40] Based on Dr. Glen's note of January 16, 2007. Obtaining appropriate values for this parameter is problematic. The reference for SHEDS-Wood parameter values is Wester et al. (1993), in which two concentrations of arsenic-73 mixed in soil or water was applied to skin of rhesus monkeys. Whether these data are applicable to methamphetamine residues on the skin is uncertain. Also problematic is the "wash-in" phenomenon described by Moody and Maibach (2006), where dermal absorption of some contaminants is enhanced by washing with soap and water. The wash-in effect for DEET (an amide with a log K_{OW} nearly identical to that of methamphetamine) is very strong. If the wash-in effect applies to methamphetamine, the value for "remv_wash" and "remv_bath" may be considerably lower than the SHEDS defaults.

Table 3. Continued

Variability Groups and Variable Descriptions	Variable	Units	Default[41] Distribution	Default[41] Parameters	Comments	USEPA (2005;Table 10) or Hore et al. (2006; Table 3)
4. Dose-related						
a) Absorption fraction for lungs	[absf_lung]	[-]	point	1	not applicable **assume 0**[42]	
b) Dermal absorption rate/day for dust or soil	[absr_dm]	day^{-1}	uniform	min: 0.001 max: 0.3	not applicable **assume 0**	
c) Dermal absorption rate/day for surface residues	[absr_dr]	day^{-1}	point	0.03	**use uniform: 0.5 (min), 0.9 (max)** (preliminary UCSF data)	
d) GI tract absorption rate per day for dust or soil	[absr_gm]	day^{-1}	triangle	min: 0.01 mode: 0.1 max: 1.0	not applicable **assume 0**	
e) GI tract absorption rate/day for surface residue	[absr_gr]	day^{-1}	triangle	min: 0.01 mode: 0.1 max: 1.0	**assume 1**	
f) Bioavailability fraction for dust/soil	[bioavm]	[-]	point	1	not applicable[43] **assume 0**	
g) Bioavailability fraction of surface residues	[bioavr]	[-]	point	1	**assume 1**[44]	
h) Elimination rate from the blood	[elimr_blood]	day^{-1}	lognormal	geo mean: 0.6 geo st dev: 1.2	**use default**[45]	
i) Molecular weight mass ratio of the metabolite to the parent compound[46]	[metab_ratio]	[-]	point	1	**assume 1**	
5. Baths						
a) Maximum number of days between baths	[bathdays]	days	probability vector **1:** 0.75; **2:** 0.14; **3:** 0.07; **4:** 0.01; **5:** 0.01; **6:** 0.01; **7:** 0.01		same as SHEDS-Wood **use default**	p. 75, Table 11 see also EFH, Table 15-9

[41] These distributions and parameter values were included with the SHEDS model as received.
[42] In the post-remediation exposure scenario, airborne levels of methamphetamine will be extremely low because (1) meth-HCl is non-volatile, (2) while methamphetamine base is volatile, it will have evaporated from all contaminated surfaces by the time a residential structure is re-occupied, and (3) on account of the relatively low K_{OW} of methamphetamine base (2.07), adsorption of methamphetamine to soil and dust particles is not expected, and re-suspension of surface dust is unlikely to generate significant airborne levels of methamphetamine.
[43] Significant adsorption of soil or dust is not anticipated given the relatively low K_{OW} of methamphetamine (2.07)
[44] Assumption of 100 percent bioavailability based on (1) the high water solubility of meth-HCl, (2) the low molecular weight of methamphetamine, and (3) the small mass of dermal loading that is anticipated to occur under the post-cleanup exposure scenario
[45] The current version of SHEDS incorporates a simple pharmacokinetic module to estimate blood concentration. The values for the elimination rate and the parent compound:metabolite MW mass ration do not affect the estimate of absorbed dose (Luther Smith and Graham Glen, Alion Science and Technology, personal communication).
[46] The parameter is required for the SHEDS pharmacokinetic module to estimate blood concentration. The primary metabolite of methamphetamine (MW 149.2) is amphetamine (MW 135.2), so this ratio is 0.91. In humans, a significant traction of ingested methamphetamine is excreted unchanged in the urine. (See November 2, 2006 Draft SHEDS-Multimedia Technical Manual, page 39)

Pathway-Specific and Total Absorbed Dose Estimates Using SHEDS-Multimedia

Absorbed dose estimates based on SHEDS-Multimedia were initially calculated based on a "unit" surface residue concentration of 0.001 µg methamphetamine/cm^2 (equivalent to 0.1 µg/100 cm^2), which is the cleanup originally developed by the state of Washington and subsequently adopted by several states. The Washington standard was based on technical feasibility, that is, the lowest amount of methamphetamine that could be reliably detected in surface wipes using a standardized sampling protocol. It is *not* based on in-depth analysis of the toxicity of methamphetamine or quantitative evaluation of potential exposure to surface methamphetamine residues.

The model was run for a population of 100 children 1-2 years age. The exposure duration was assumed to be 90 days, but assuming longer or shorted durations would not alter the dose estimates because the residue concentration was assumed to be constant for the entire duration of exposure and doses were calculated on a mg/kg-day basis. However, assuming a 90-day exposure duration is advantageous because SHEDS-Multimedia generates graphical output of the day-to-day variation in absorbed dose estimates for an individual, and this visual representation facilitates appreciation for the variability of exposure even under "static" (constant source concentration) conditions.

Since SHEDS-Multimedia is a stochastic model, each run will generate slightly different results. However, in this application of the model, run-to-run variability is minimized because mean daily dose estimates are based on 100 children and the surface methamphetamine residue concentration is a fixed value for the entire 90-day exposure period. Therefore, the estimate of each child's absorbed dose is calculated as the average of 90 single-day dose estimates, leading to minimal variation between runs.

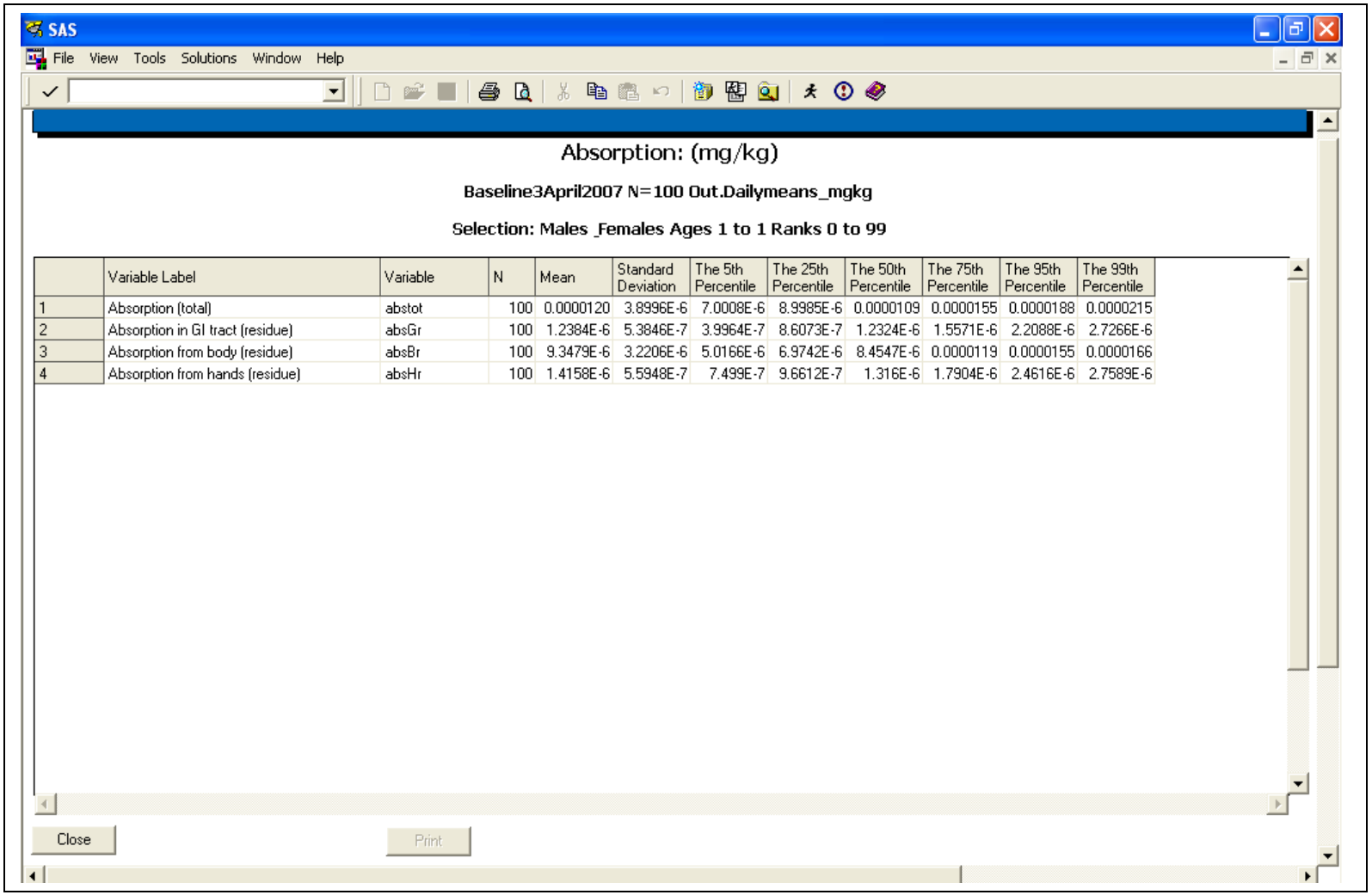
Total and pathway-specific estimates of absorbed dose are provided in Table 4, reproduced directly from the computer image of the model output. Average exposure via all three complete pathways (dermal absorption of methamphetamine residues on the body, dermal absorption of methamphetamine residues on the hands, and ingestion of methamphetamine following hand-to-mouth or body-to-mouth activity) was estimated to be 0.012 ± 0.004 µg/kg-day (mean ± SD). Percentile exposure estimates were 0.011, 0.016 and 0.021 mg/kg-day for the 50th, 75th and 95th percentiles, respectively. The relative contributions of each pathway to total exposure are shown in Figure 3, and it is clear that dermal absorption of methamphetamine residues on the body is by far the most significant exposure pathway, accounting for approximately 78 percent of the total absorbed dose. Dermal absorption of methamphetamine residues on the hands, and inadvertent ingestion resulting from hand-to-mouth activity, account for the remaining 12 and 10 percent of the total, respectively.

An example of the day-to-day variation in the absorbed dose estimates for a single individual is shown in Figure 4, with the black line representing total absorbed dose, the blue line representing dermal absorption of residues on the body, green representing inadvertent ingestion of residues on the hands and body, and red representing dermal absorption of residues on the hands. Note that all three pathways generally move in parallel with one another, so that days when exposure via transdermal absorption of residues on the body spike upward are days when exposure via the

other two pathways spike upward as well. In this example, daily absorbed dose estimates for a single individual range from approximately 0.002 to 0.024 µg/kg-day, or about 12-fold. Figure 5 provides a second example of the day-to-day variation in absorbed dose for an individual. In this case the variation on daily absorbed dose is only about 7-fold (0.005 to 0.035 µg/kg-day), while the significance of inadvertent ingestion and dermal absorption of methamphetamine residues on the hands is not as pronounced as it is in the first example. Comparing boys *vs.* girls, no dramatic differences were apparent: the estimate of absorbed dose was 0.0117 ± 0.0039 µg/kg-day for boys and 0.0125 ± 0.0039 µg/kg-day (mean ± SD) for girls.[47]

Note that exposure via all other potential pathways (e.g., inhalation airborne methamphetamine, dermal contact with soil and dust contaminated with methamphetamine and subsequent transdermal absorption and inadvertent ingestion) is zero because the concentration of methamphetamine in the source media (e.g., air, soil and dust) was assumed to be zero. Justification for these assumptions was provided in previous sections of this report.

[47] In this particular model run, absorbed dose estimates were made for 60 boys and 40 girls. This ratio will vary from run to run; the sex of each child is randomly selected by the model.



Absorption: (mg/kg)

Baseline3April2007 N=100 Out.Dailymeans_mgkg

Selection: Males _Females Ages 1 to 1 Ranks 0 to 99

	Variable Label	Variable	N	Mean	Standard Deviation	The 5th Percentile	The 25th Percentile	The 50th Percentile	The 75th Percentile	The 95th Percentile	The 99th Percentile
1	Absorption (total)	abstot	100	0.0000120	3.8996E-6	7.0008E-6	8.9985E-6	0.0000109	0.0000155	0.0000188	0.0000215
2	Absorption in GI tract (residue)	absGr	100	1.2384E-6	5.3846E-7	3.9964E-7	8.6073E-7	1.2324E-6	1.5571E-6	2.2088E-6	2.7266E-6
3	Absorption from body (residue)	absBr	100	9.3479E-6	3.2206E-6	5.0166E-6	6.9742E-6	8.4547E-6	0.0000119	0.0000155	0.0000166
4	Absorption from hands (residue)	absHr	100	1.4158E-6	5.5948E-7	7.499E-7	9.6612E-7	1.316E-6	1.7904E-6	2.4616E-6	2.7589E-6

Table 4. SHEDS output: total absorbed dose and pathway-specific doses of methamphetamine for a population of 100 children 1-2 years of age. Surface residue concentration assumed to be 0.001 µg/cm^2.

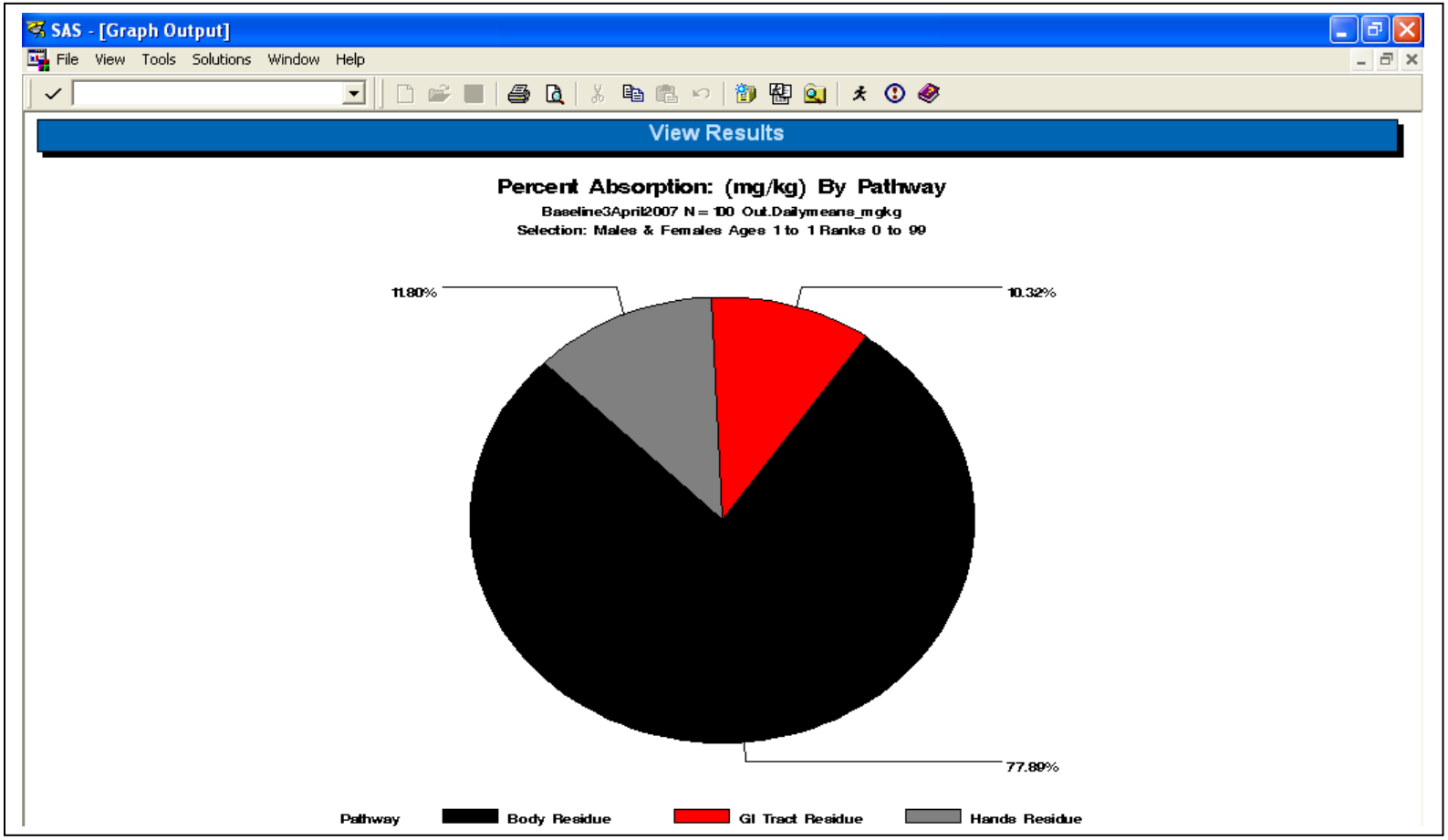


Figure 3. SHEDS output: pathway-specific doses of methamphetamine as a percentage of total dose for a population of 100 children 1-2 years of age.

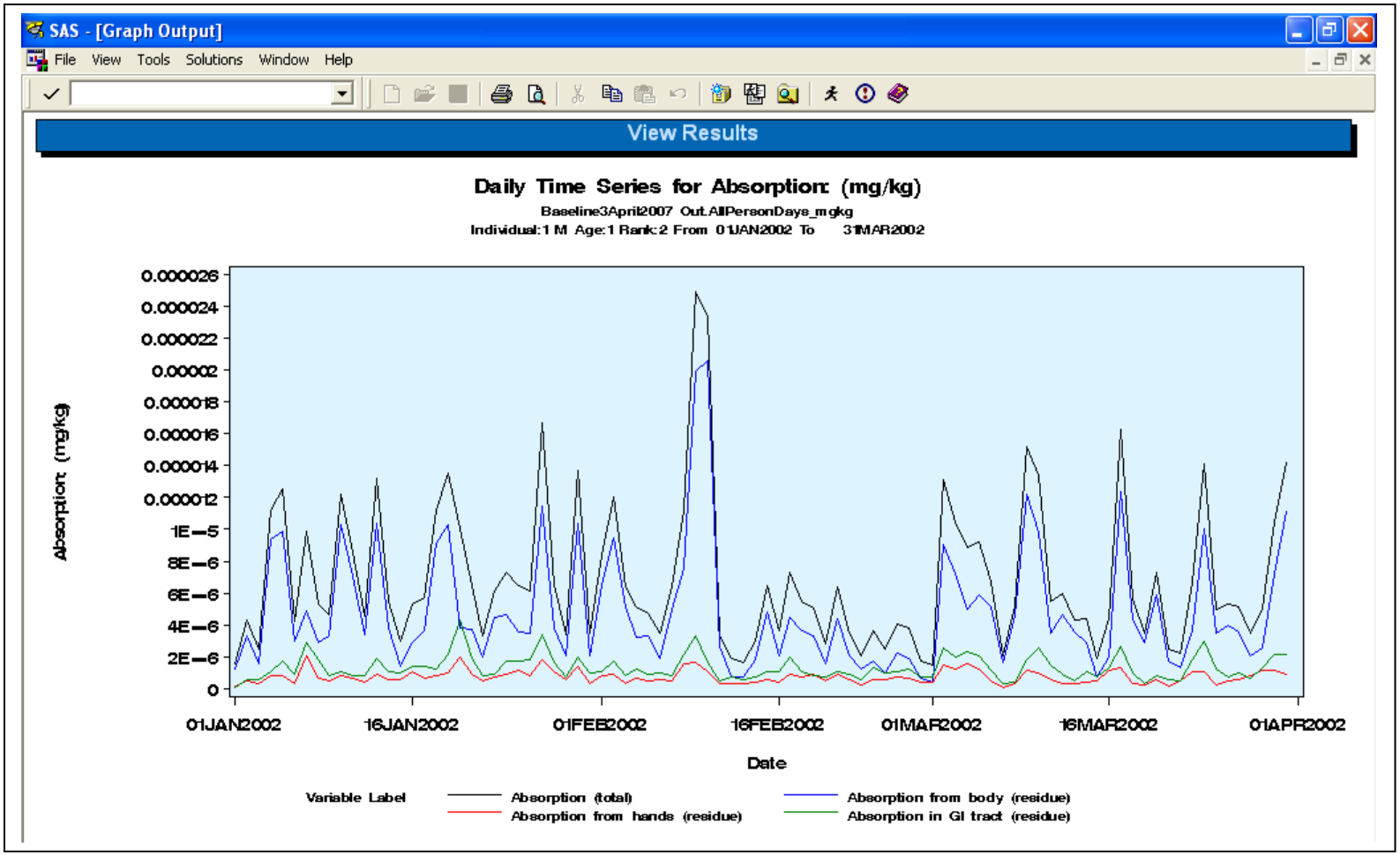


Figure 4. SHEDS output: example #1 of pathway-specific daily time series of absorbed methamphetamine dose for an individual (a one-year-old boy) over a 90-day exposure period.

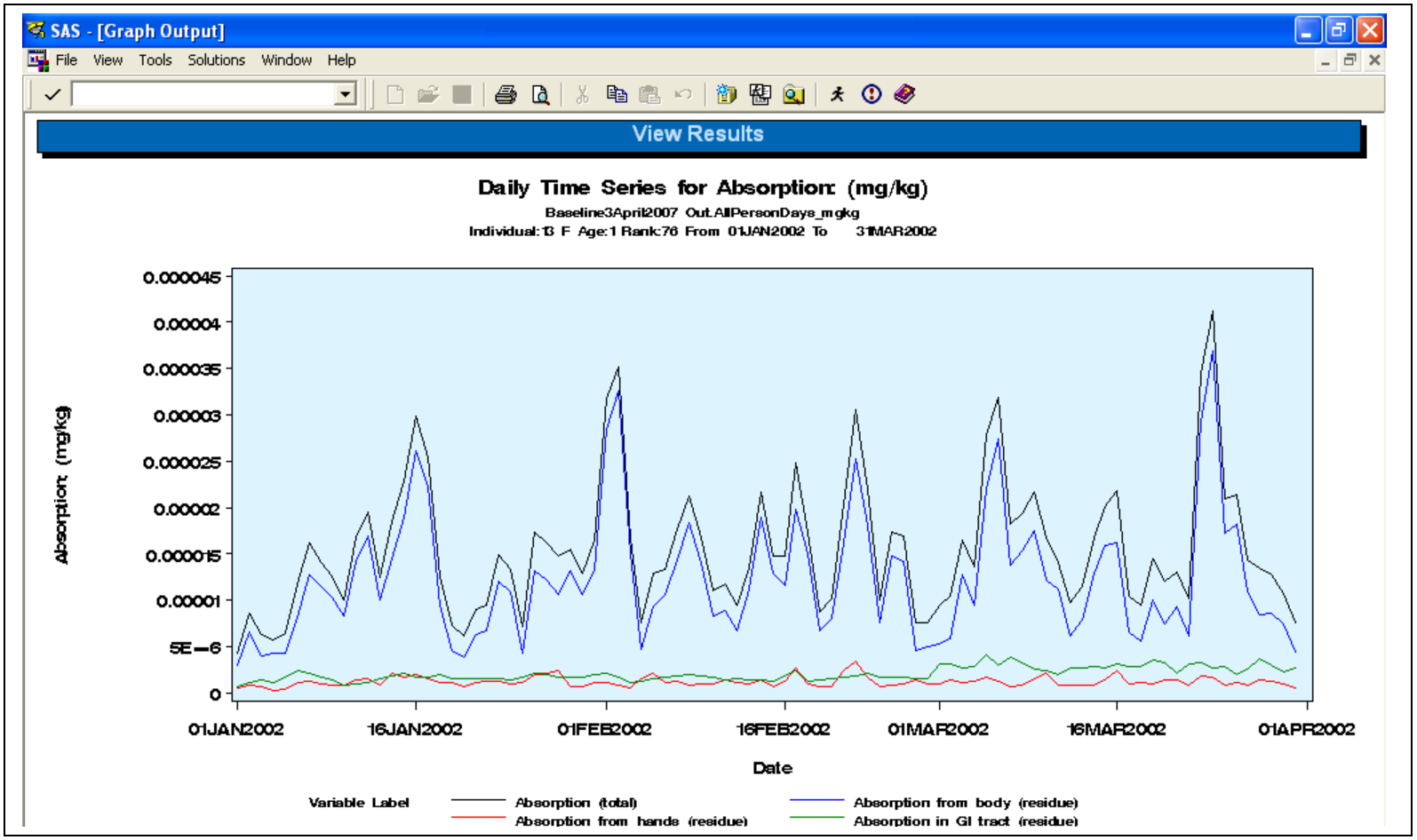


Figure 5. SHEDS output: example #2 of pathway-specific daily time series of absorbed methamphetamine dose for an individual (a one-year-old boy) over a 90-day exposure period.

Sensitivity Analysis: Evaluation of Changes in the Values of Individual Parameters on Estimates of Absorbed Dose

The effect of individual exposure parameters on the absorbed dose estimates calculated by SHEDS-Multimedia was analyzed by changing the value of different parameters one at a time. The parameters evaluated were

- Residue-skin transfer efficiency
- Maximum dermal loading for hands and body
- Removal efficiency during hand washing
- Object:surface concentration ratio
- Maximum diary event length

The results of this analysis are shown in Table 5. In this table, the 95th percentile estimate of absorbed dose differs from the value shown in Table 4 because a higher value was used for the dermal absorption of methamphetamine. Two- to three-fold increases or decreases in maximum dermal loading for hands and body, removal efficiency during hand washing, object:surface concentration ratio[48] and maximum diary event length had no appreciable effect on the 95th percentile absorbed dose estimate. However, a three-fold increase in the residue-skin transfer efficiency produced a corresponding 3-fold increase in the absorbed dose estimate. This latter result indicates that the transdermal absorption of methamphetamine is sufficiently high that any increase in methamphetamine loading on the skin leads to a proportional increase in absorbed dose.

[48] See footnote 26 for a definition of this parameter.

Table 5. SHEDS Sensitivity Analysis: Effect of Changing Values for Individual Exposure Parameters on the 95th Percentile Estimates of Absorbed Dose

Variable[49]	**Default**	**Changed to:**	**95th Percentile Estimate**[50]
No changes			0.000023
Residue-skin transfer efficiency [2m: transfer_dermal]	beta distribution, shape1: 0.6 shape 2: 8.4 (mean: 0.07)	point value: 0.20 (~3-fold increase)	0.000075 (~3-fold increase)
Maximum dermal loading for hands and body [3a & 3b: dermaxb & dermaxh]	point values 0.01 & 0.01	point values 0.003 & 0.003 (~3-fold decrease)	0.000023 (no change)
		point values 0.03 & 0.03 (~3-fold increase)	0.000024 (no change)
Removal efficiency during hand washing [3f: remv_wash]	uniform distribution, range: 0.3 – 0.45	point value: 0.15[51]	0.000024 (minor increase)
Object:surface concentration ratio 2i: object_ratio]	uniform distribution, 0.0 – 0.2	point value: 0.5	0.000024 (minor increase)
Maximum diary event length	60 minutes	20 minutes	0.000025 (minor increase)

[49] Parameter designations from SHEDS-Multimedia Technical Manual
[50] All exposure estimates are based on a uniform surface methamphetamine concentration of 0.001 µg/cm^2.
[51] This value was used in a 2006 report on the SHEDS model by Hore et al., Table 3

Effectiveness of Washing: Another Source of Uncertainty

As a means of removing methamphetamine residue from the skin, the effectiveness of washing with soap and water is uncertain, and experimental investigation of this and other decontamination procedures is warranted. Concern that routine washing is not particularly effective and may actually accelerate the transdermal uptake of methamphetamine was raised in a recent report by Moody and Maibach (2006), who cited studies that demonstrated dermal uptake of the insect repellant DEET (N,N-diethyl-*m*-toluamide). In *in vitro* tests of three commercial formulations of DEET, transdermal absorption across human skin was profoundly increased (up to 32-fold) by soap wash of the skin.

Experimental results obtained with DEET may be directly applicable to predicting the effectiveness of soap and water as a means of removing methamphetamine residues from the skin. Among other factors, the dermal absorption of chemicals is correlated with their molecular weight and octanol:water partition coefficient (also called the K_{ow}). Metham)phetamine and DEET both have molecular weights below 200 (149 and 191, respectively), and their octanol:water partition coefficients are essentially identical: the log K_{ow} values for methamphetamine and DEET are 2.07 and 2.18, respectively. Therefore, by extrapolation, it would be reasonable to predict that factors influencing the dermal uptake methamphetamine are similar to those that affect the dermal uptake of DEET, and that "wash in" is a likely mechanism for enhancing the uptake of methamphetamine. Nevertheless, experimental data supporting this hypothesis are lacking.

In the previous section, the effect of washing efficiency was evaluated by reducing the assumed efficiency of hand washing from a uniform distribution with a range of 0.3 to 0.45 (i.e., a removal efficiency of 30-45 percent) to a point value of 0.15. This two- to three-fold reduction in washing removal efficiency produced a very slight increase in the estimate of total absorbed dose. In large part, this lack of a significant effect probably reflects the fact that dermal absorption of methamphetamine residues on the hands only account for 12 percent of the total absorbed dose, so an increase in the post-washing residue concentration would be expected to have a small effect. Since bathing involves immersion of a significant portion of the body for a period of several minutes, the DEET *in vitro* data were regarded as being less relevant, and a corresponding evaluation of the effect of reducing removal efficiency during bathing (remv_bath; Table 3) was not conducted.

Knowing whether absorption of methamphetamine across the skin is enhanced by washing with soap and water is important for predicting the daily exposure of an individual residing in a former clandestine methamphetamine lab, the acute exposure of a first responder conducting a removal action, and the dose received by a child removed from an operational lab immediately after it is discovered. Clearly, additional research in the effectiveness of different decontamination procedures is warranted.

Comparison of Exposure Estimates based on SHEDS-Multimedia and the Standard Operating Procedures (SOPs) for Residential Exposure, and Rationale for Use of SHEDS-Multimedia to Derive a Risk-Based Cleanup Level for Methamphetamine

SHEDS-Multimedia (and its predecessor SHEDS-Wood) have been under development by the U.S. EPA since 1998. The model "…is a state-of-science computer model for improving estimates of aggregate (single-chemical, multi-route/pathway) and cumulative (multi-chemical, multi-route/pathway) human exposure and dose." It is designed to simulate exposures and doses for a variety of user-specified population cohorts and relies on data from time-location-activity diaries compiled in U. S. EPA's Consolidated Human Activity Database (CHAD). SHEDS-Multimedia has undergone extensive peer review, having been evaluated in depth by the FIFRA Scientific Advisory Panel (SAP) in August 2002, December 2003, and August 2007. The most recent version of SHEDS-Multimedia became available in March, 2007.

Because SHEDS-Multimedia permits the user to specify chemical- and scenario-specific parameter values and distributions as inputs, it provides less conservative and more realistic estimates of potential exposure. Critical exposure parameters such as surface-to-skin transfer efficiency and dermal absorption efficiency are based on experimental data, not conservatively estimated defaults. Furthermore, model estimates can be improved as scenario- and chemical-specific research data become available. The model also accounts for exposure via pathways (e.g., object-to-mouth) that are not considered using the Standard Operating Procedures methodology.

The *Standard Operating Procedures (SOPs) for Residential Exposure Assessment* was originally prepared in 1997. Minor modifications to the document were made in 2001. While still available on the U.S. EPA's web site, the document still includes "DRAFT - DO NOT CITE OR QUOTE" as a footer on each page. The SOPs provide algorithms for calculating *screening level* exposure estimates for via dermal contact with pesticide residues on smooth surfaces (e.g., linoleum), dermal contact with residues on carpet, and inadvertent ingestion resulting from hand contact with a contaminated surface followed by hand-to-mouth movements. As noted previously, this model is intended for use when chemical- and/or site-specific information are limited or unavailable, and the U.S. EPA's continues to accept exposure analyses that are based on this protocol (Jeffrey Dawson, U. S. EPA Office of Pesticide Programs; personal communication).

A critical parameter in the equations for estimating dermal contact with pesticide residues on hard surfaces and carpet is the dermal transfer coefficient, which has a default value of 6,000 cm^2/hour for a child 1 to 6 years of age. The degree of conservatism incorporated into the default value for this parameter was examined experimentally in a recent report by Cohen Hubal et al. (2006). In this study, dermal transfer coefficients were derived empirically by measuring surface pesticide concentrations in a daycare center dermal loading of pesticide residues on full-body cotton garments.[52] Based on data from nine children and two visits to the daycare center, dermal transfer coefficients ranged from 7.5 to 6,200 cm^2/hour, a range of over 800-fold. These values were obtained after the calculated transfer coefficients were increased 40 percent (somewhat arbitrarily)

[52] Dermal transfer coefficients (in units of cm^2/hour) were calculated as the mass of pesticide on the whole body garment divided by the monitoring duration (ng/hr) divided by the surface pesticide concentration (ng/cm^2).

to account for transfer to the hands and feet, which were not covered by the body suits during the study. Therefore, the default transfer coefficient prescribed using the SOP methodology is equivalent to the upper end of the range of transfer coefficients estimated by these researchers.

The authors of this study concluded that "…the results of this work suggest that the default assumption [i.e., the default transfer coefficient for children prescribed in the SOP methodology] used by the U. S. EPA OPP [Office of Pesticide Programs] is reasonable." An alternative interpretation would be that dermal transfer coefficients for children span a very wide range, and that dermal exposures would be more appropriately estimated using a stochastic model such as SHEDS-Multimedia, which accounts for the range of children's behaviors and activities. The algorithms and default parameter values prescribed by the SOPs appear to be appropriate for obtaining very conservative, screening level estimates of exposure and do not appear to be well supported by the available research data.

Identification of a Risk-Based Cleanup Level for Methamphetamine

The rationale and justification for the development of a reference dose (RfD) for methamphetamine are described in a separate report.[53] RfDs are concentrations or daily doses at or below which adverse health effects are not likely to occur. The RfD for methamphetamine was calculated to be 0.3 µg/kg-day, and the target remediation standard must be set at a level that ensures that the daily exposure to surface methamphetamine residues produces an absorbed dose that does not exceed the RfD. Using SHEDS-Multimedia iteratively to estimate the absorbed dose of methamphetamine at different residue concentrations, it was found that a residue concentration of 0.015 µg/cm^2 would result in an absorbed dose that is just below the RfD for methamphetamine.

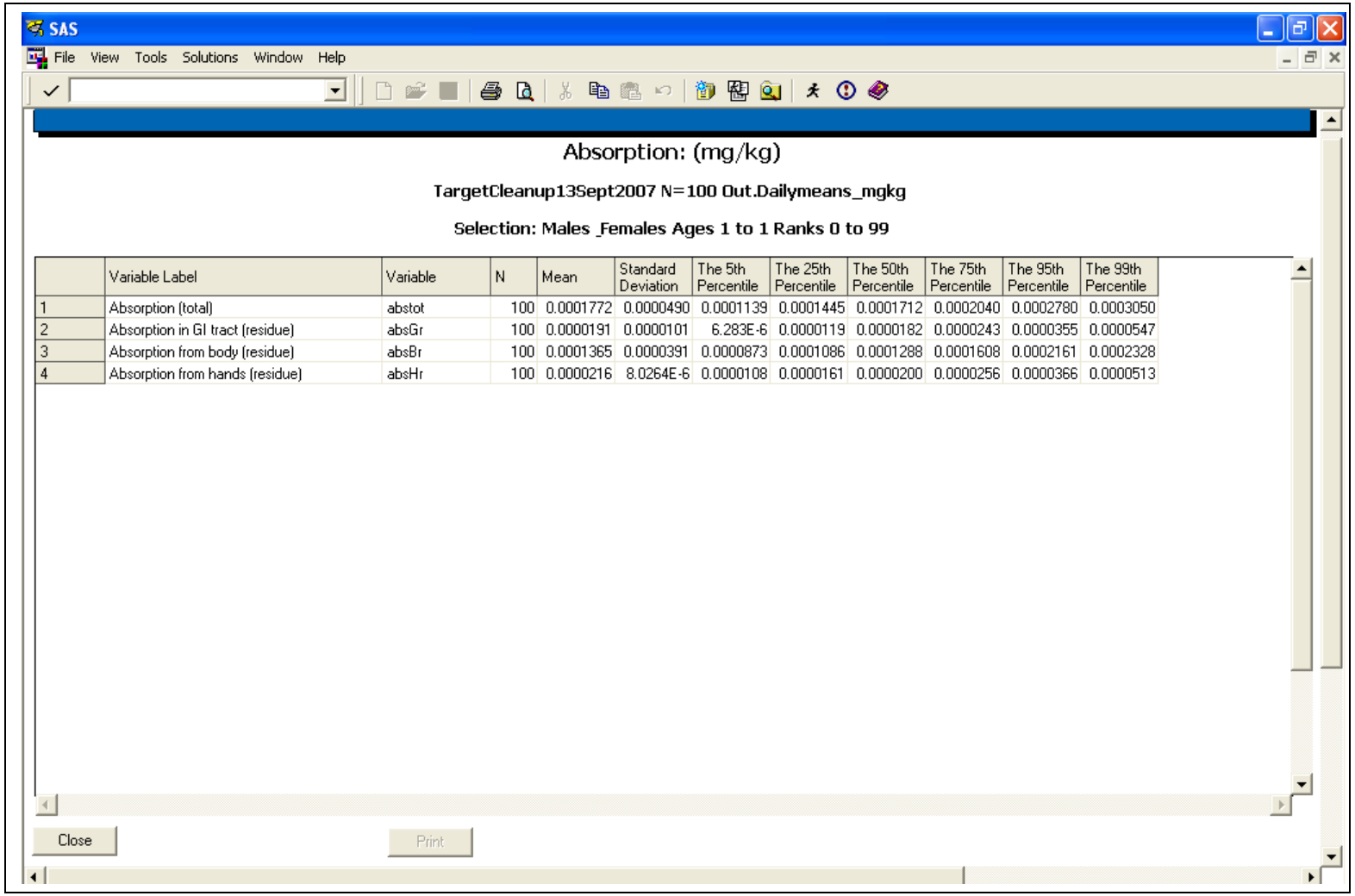
Total absorbed dose estimates calculated by SHEDS-Multimedia assuming a surface residue concentration of 0.015 µg methamphetamine/cm^2 (equivalent to 1.5 µg/100 cm^2) are shown in Table 6. The 95th and 99th percentile estimates of absorbed dose are 0.278 and 0.305 µg/kg-day, respectively, which are just below or equivalent to the RfD value of 0.3 µg/kg-day.[54] Therefore, based on the analysis presented in this report, the risk-based target remediation standard for methamphetamine on interior residential surfaces is 0.015 µg methamphetamine/cm^2, or 1.5 µg/100 cm^2.

Based the exposure parameter values adopted for the analysis presented in this report, both the 95th and the 99th percentile estimates of absorbed dose support the adoption of 1.5 µg/100 cm^2 as a target remediation standard.

An alternative analysis based on different parameter values would generate different results that might require a decision regarding the appropriateness of the 95th or the 99th percentile estimate as a basis for determination of a cleanup standard. For example, using different parameter

[53] *Development of a Reference Dose (RfD) for Methamphetamine.* External Peer Review Draft, October 2007. California EPA, Office of Environmental Health Hazard Assessment, Integrated Risk Assessment Branch.
[54] Based on a surface residue concentration of 0.015 µg/cm^2, the relative contributions of the three complete exposure pathways (expressed as a percentage of the total absorbed dose) are essentially identical to those presented in Figure 3, which was based on a residue concentration of 0.001 µg/cm^2.

values, the 95th percentile estimate of exposure may generate an estimate of total absorbed dose that is below the methamphetamine RfD while the 99th percentile dose estimate exceeds the RfD. If this were the case, we would recommend use of the 95th percentile estimate because of the greater uncertainty associated with estimates at extreme right tail of the dose distribution.



Absorption: (mg/kg)

TargetCleanup13Sept2007 N=100 Out.Dailymeans_mgkg

Selection: Males _Females Ages 1 to 1 Ranks 0 to 99

	Variable Label	Variable	N	Mean	Standard Deviation	The 5th Percentile	The 25th Percentile	The 50th Percentile	The 75th Percentile	The 95th Percentile	The 99th Percentile
1	Absorption (total)	abstot	100	0.0001772	0.0000490	0.0001139	0.0001445	0.0001712	0.0002040	0.0002780	0.0003050
2	Absorption in GI tract (residue)	absGr	100	0.0000191	0.0000101	6.283E-6	0.0000119	0.0000182	0.0000243	0.0000355	0.0000547
3	Absorption from body (residue)	absBr	100	0.0001365	0.0000391	0.0000873	0.0001086	0.0001288	0.0001608	0.0002161	0.0002328
4	Absorption from hands (residue)	absHr	100	0.0000216	8.0264E-6	0.0000108	0.0000161	0.0000200	0.0000256	0.0000366	0.0000513

Table 6. SHEDS output: total absorbed dose and pathway-specific doses of methamphetamine for a population of 100 children 1-2 years of age. The surface residue concentration was assumed to be 0.015 µg/cm^2, and maximum dermal loading on the hands and body was assumed to be 0.15 µg/cm^2.

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Response to comments on the document, Assessment of Children's Exposure to Surface Methamphetamine Residues in Former Clandestine Methamphetamine Labs, and Identification of a Risk-Based Cleanup Standard for Surface Methamphetamine Contamination (OEHHA, December, 2007)

I. Comments from Dr. John Martyny, Associate Professor, Division of Environmental and Occupational Health Sciences, National Jewish Medical and Research Center, Denver, Colorado

1. (Referring to the bottom of page 8): *I am still concerned that meth levels in the environment will not dissipate as fast as you think. Maybe you could document this a little more.*

If a clandestine methamphetamine lab were simply vacated and not remediated, airborne methamphetamine would probably dissipate slowly and dislodgeable methamphetamine residue on surfaces would be easily resuspended. This was shown to be the case in the studies conducted by Van Dyke et al. (2009).

However, the analysis presented in this document provides an estimate of potential exposure that may occur in a *post-remediation* scenario. Therefore, we assume that the residual methamphetamine on all surfaces has been cleaned up to a specified target cleanup level.

As noted in the section of the report that addresses the fate and transport of methamphetamine in an indoor residential environment, the evaporation of the free base form of methamphetamine proceeds at a rapid rate (Hui and Maibach, 2007). We believe that the time interval between initial discovery of a clandestine lab and its re-occupancy should be more than sufficient for methamphetamine base – if present – to completely evaporate. As outlined in AB1078 (Keene, Chapter 570, Statutes of 2005), in order to remediate a former clandestine methamphetamine lab, the property owner is required to (1) assess the magnitude and extent of contamination, (2) develop a cleanup plan, (3) conduct cleanup operations, (4) collect post-remediation samples, and (5) prepare a post-cleanup report. Each step requires the oversight and approval of the local health officer, and the entire process will probably require several months to complete. We estimate that the time from initial discovery of a clandestine meth lab, to remediation and ultimately re-occupancy will probably be about six months, which should be ample time for complete evaporation of the free base.

Surfaces may also be contaminated with methamphetamine hydrochloride, which is not volatile. However, the recent decontamination studies of Martyny (2008) demonstrate that cleaning once with Simple Green® removes the majority of dislodgeable residue from a variety of surfaces. As a result, subsequent washes are not a particularly efficient means of removing additional residues. Therefore, if the interior surfaces in a residence have been cleaned at least once, the amount of

dislodgeable methamphetamine residue is substantially reduced, and routine activities of persons living in the structure are very unlikely to resuspend non-dislodgeable methamphetamine residue into the air.

2. (Referring to the second paragraph on page 9): *Same concern, what if you are wrong? Do you have any studies on which meth depletion is based? Will meth really behave like a pesticide?*

To the extent that information specific for methamphetamine is available, we attempted to incorporate it into our analysis. For example, based on data from UC San Francisco on the evaporation rate of methamphetamine base, we assumed that methamphetamine base has completely evaporated by the time a former clandestine methamphetamine lab is cleared for re-occupancy. Similarly, we assumed that the residual methamphetamine would not be dislodged and re-suspended in air by normal indoor activities because data from decontamination studies demonstrated that (1) methamphetamine is much more difficult to remove from semi-porous surfaces once it has been washed one time with a solvent-based cleaner (Simple Green®)[55] and (2) methamphetamine appears to be completely removed from non-porous materials like glass and sheet metal after just one washing.

Like a pesticide applied indoors, methamphetamine forms a film of contamination on interior surfaces. We made no additional assumptions about the physical nature of the film.

Our assumption regarding the surface-to-skin transfer efficiency of methamphetamine residues was indeed based on studies analyzing surface-to-skin transfer of pesticide residues. However, on page 24 of the draft report, we noted that surface-to-skin transfer appears depend more on the physical nature of the surface residue than the chemical structure of the chemical contaminant. Furthermore, studies on the surface-to-skin transfer of pesticide residues were conducted on *unremediated* surfaces, while our exposure scenario involves a completely remediated environment. In all likelihood, the dislodgeable residue on an unremediated surface exceeds that of a remediated surface by a significant margin, and the results of the decontamination studies (Martyny, 2008) support this conclusion. Therefore, while our assumption regarding surface-to-skin transfer of methamphetamine was based on studies of pesticides, we believe these data over-estimate the true transfer efficiency from a remediated surface. We regard this assumption as health protective because it results in a lower target remediation goal than would otherwise be estimated.

3. (Referring to the first paragraph on page 11): *Are we actually talking about meth base contamination in a home? I thought that it would be methamphetamine chloride. We found that simply walking in the home after a cook allowed for resuspension. We also found significant meth on the carpet dust vacuumed into a filter. The filter was such that it would allow a vapor to pass through, I believe.*

[55] Simple Green® contains 2-butoxyethanol, a glycol ether solvent.

The method we used is normally applied to allergens in the environment such as dog and cat dander, and other particulates.

This comment refers to the results of studies conducted by Van Dyke et al. (2009) examining the dispersion and surface deposition of methamphetamine during two methamphetamine "cooks" and up to 18 hours thereafter.

Again, Van Dyke et al. examined resuspension of methamphetamine in an unremediated environment with a high proportion of dislodgeable surface residue. This is very different from the remediated exposure scenario that we evaluated, where the great majority of dislodgeable residue has been removed by cleaning. The results of decontamination studies conducted by Martyny (2008) support this conclusion. Under the latter scenario, we believe it is very unlikely that routine human activities such as walking across a room will cause re-suspension of a surface residue that is not easily removed by aggressive cleaning.

Based on the UC San Francisco data, the evaporation of methamphetamine base should proceed to completion within a matter of several days.

4. (Referring to the final paragraph on page 25): *Same concern regarding soil and dust.*

Surfaces that have been remediated to meet a target remediation standard for methamphetamine residues are unlikely to have very much soil and dust on them. Furthermore, as discussed on page 11 of the draft report, we believe methamphetamine is unlikely to become strongly associated with soil and dust due to its relatively low octanol:water partition coefficient. While soil and dust will undoubtedly accumulate in a residence once it is re-occupied, we believe the tendency for methamphetamine to adsorb to it is low.

5. (Referring to the fourth paragraph on page 31): *I do agree that dermal may be the major contributor but inhalation may play a slightly higher role that you think. Again, I am sorry that we were unable to conduct the long-term study.*

The comment refers to a proposal to conduct a "long-term" investigation that would be similar to the study carried out by Van Dyke et al. (2009) but would last for a much longer duration, i.e., a period of weeks or months following a series of methamphetamine "cooks" instead of just 18 hours. This would allow for long-term evaluation of the fate and transport of methamphetamine in an indoor environment. It would include quantitative analysis of the dispersion, deposition, re-suspension, and degradation of methamphetamine residues. As yet, funds to conduct such a study have not been available.

Our conclusion that inhalation of airborne methamphetamine does not represent a significant exposure pathway *in a structure that has been completely remediated* is based on experimental results reported by Martyny (2008) demonstrating that the

methamphetamine residue remaining on a surface after it has been cleaned once is resistant to removal by additional washing. In these studies, initial and subsequent washes were conducted using Simple Green® and water, which is a relatively aggressive technique for decontaminating surfaces. For this reason, we believe it is unlikely that a significant amount of the methamphetamine remaining on a previously cleaned surface would be physically dislodged and re-suspended in air by the routine activities of the occupants of the residence.

II. Comments from Dr. Tim Wiegand, Assistant Adjunct Professor of Medicine, UC San Francisco and the California Poison Control Center – San Francisco Division

1. Exposure scenario assumptions

1. *Compared to volatile chemicals, the residue associated with methamphetamine persists in the environment, unless physically altered, over time.*

Under some conditions, methamphetamine is volatile. The physical properties of methamphetamine base and methamphetamine hydrochloride are described in a new the section of the report that addresses the fate and transport of methamphetamine in an indoor residential environment. Methamphetamine base, the initial product of synthesis, is significantly volatile and is expected to evaporate and dissipate quickly. Methamphetamine hydrochloride, produced by bubbling hydrogen chloride gas through a solution of methamphetamine base, is generally stable but is converted to the base if placed in a wet environment and the pH is greater than 4-5. Two circumstances where this may occur are: (1) when methamphetamine-contaminated surfaces are subjected to water-based detergent solutions, which invariably have a pH greater than 7, and (2) when the surface is covered with latex-based paint, which usually has a pH in the range of 7.5-9.5. Since methamphetamine base evaporates quickly, we do not believe it is present in the air of a former clandestine lab that has been remediated.

2. *Data regarding specific exposure assumptions involving clandestine methamphetamine laboratories from scientific study is limited. Additionally, exposure to methamphetamine residue is influenced by certain factors or variables. Thus, any calculations or formulas that attempt to provide a level of exposure must either provide ranges or be formulated so that a "worst case" scenario is the result.*

We agree. Limited data on the fate of methamphetamine in an indoor environment has recently been published, and the results of these studies have been summarized and reviewed in a new section of the report. In our analysis, uncertainty and lack of methamphetamine-specific data were generally addressed by making assumptions that would lead to a higher estimate of exposure than would have been made otherwise. For example, the exposure estimate was based in part on surface-to-skin transfer efficiencies that came from studies of unremediated surface contamination even though the dislodgeable residue on these surfaces is much greater than what would be found on a surface that had been cleaned. Although this undoubtedly over-

estimates the exposure that would occur in a remediated environment, we believe it is appropriate given the lack of data characterizing the transfer of methamphetamine from a remediated surface to skin.

3. *The use of a uniform standard, then, equivalent to the maximum concentration of methamphetamine present on all interior surfaces will thus over represent the amount of methamphetamine residue for potential to exposure, allowing for a level of safety… the use of a 'constant level of exposure' regarding REL post-remediation in part resolves the problems related to a lack of data regarding persistence of methamphetamine residue over time.*

[Note: The acronym "REL" refers to Reference Exposure Level, which is a medium-specific concentration (e.g., micrograms per cubic meter of air) or dose (micrograms per kilogram body weight) at or below which adverse health effects are not likely to occur. In OEHHA, chronic and acute RELs have been developed for dozens of toxic contaminants in air in conjunction with the Air Toxics "Hot Spots" program. The proposed target cleanup standard for methamphetamine on indoor residential surfaces has been referred to by Dr. Wiegand and others as a "surface REL."]

Data from studies published by Martyny et al. (2007) suggest that methamphetamine residues may persist on surfaces for long periods. The authors noted, "Even labs that had been shut down several months prior to testing had high contamination levels of methamphetamine present on many surfaces within the building." These results suggest that, in the absence of any human activity or remediation efforts, methamphetamine residues may persist on interior residential surfaces for at least several months.

We believe that assuming a constant level also provides a modest level of additional health protectiveness to the analysis because exposure cannot occur without the transfer of methamphetamine from surfaces to skin. Thus, by virtue of being exposed, the individuals living in a remediated former clandestine lab slowly deplete methamphetamine from the surfaces.

4. *Although methamphetamine levels have been shown to persist over time this has been based on studies of methamphetamine residue levels in "unoccupied residences".*

Data published by Martyny et al. (2007) provides the best information on the persistence of methamphetamine on indoor surfaces. As noted in the new section of the report on methamphetamine fate and transport, this study characterized surface concentrations of the drug in 14 suspected clandestine methamphetamine laboratories. In just one instance, the methamphetamine "cook" occurred on the same day of the investigation. The presence of residents would probably lead to more widespread dispersion of the contaminants, both inside and outside the structure.

5. *Although it is a health protective assumption [that is, assuming that an exposed individual spends 100 percent of his/her time indoors] this could be more precisely defined for age groups while still adding some degree of protection.*

Accounting for time spent away from the residence would in fact reduce the estimated daily exposure. According to the *Exposure Factors Handbook* (U. S. EPA, 1999; Table 5-131), children who are 1-4 years of age spend on average about 84 percent of their time indoors at home (1212 out of 1440 minutes/day). The relevant data [24-hour cumulative number of minutes spent indoors in a residence (all rooms)] are summarized in the table below.

					Percentiles			
N	**Mean**	**Std Dev**	**Min**	**Max**	**25**	**50**	**75**	**95**
498	1212	219	270	1440	1065	1260	1410	1440

The 95th percentile estimate for this parameter is 1440 minutes/day, or 100 percent of the time, and even the 75th percentile estimate is equivalent to 98 percent of the entire day. It is likely that these data underestimate the time that children in the population of greatest concern (6-18 months old) spend at home since children at the upper end of this range (3-4 years of age) are probably more likely to spend time away from home or outside the home than those who are 2-3 years younger. Therefore, this assumption should be regarded as reasonable for this age group, and the wording in the revised document has been changed accordingly.

6. *…the variables defined in this paper/review needed to calculate the exposure level incorporate overestimation of exposure and provide for estimates in a most vulnerable or 'most exposed' group.*

We agree with this statement, although the degree of overestimation is difficult to calculate because chemical-specific data for several exposure parameters are lacking. For example, there are no data on the efficiency of transfer of methamphetamine from a cleaned surface to skin, so we relied on estimates of chemical transfer efficiency from unremediated surfaces and assumed this would overestimate the true transfer efficiency.

In response to comments that we had received from Dr. Fenske, we have made changes to the descriptions of some exposure scenario assumptions and our assessment of whether or not they are health protective/conservative or are simply reasonable given the lack of chemical- or scenario-specific data.

7. *…the use of a 'constant level of exposure' regarding REL post-remediation in part resolves the problems related to a lack of data regarding persistence of methamphetamine residue over time… In order to avoid an underestimation of exposure the most reasonable option was to assume a constant, persistent, level of exposure.*

[Note our response to Dr. Wiegand's comment on page 5 regarding the acronym "REL."]

We agree. In fact, exposure via dermal contact requires that a portion of the surface residue be removed with each contact. (Conversely, if no residue is removed, there is no exposure.) This leads to the seemingly contradictory assumptions that contact results in the removal of a percentage of the surface residue, yet repeated contact does not lead to a decline in the concentration of residue on the surface.

2. Identification of 6-month to 2-year-old children as the "most exposed" population

This comment does not require a response.

3. Exposure estimation models

1. *The exposure estimation models are based on and used for pesticide exposure risk. Comparison of methamphetamine residue and pesticide residue suggest that this may be a valid model, however some specific data are lacking*

We agree; data that support exposure parameter values specifically for methamphetamine are not generally available. We have adopted two models that were developed to estimate exposure to pesticide residues on indoor surfaces and used them to assess potential exposure to methamphetamine residues.

As noted above, limited data on the fate of methamphetamine in an indoor environment are now available, and the results of several recently published and unpublished studies have been summarized and reviewed in a new section of the report. In our analysis, uncertainty and lack of methamphetamine-specific data were generally addressed by making assumptions that would lead to a higher estimate of exposure than would have been made otherwise. For example, the exposure estimate was based in part on surface-to-skin transfer efficiencies that came from studies of unremediated surface contamination even though the dislodgeable reside on these surfaces is much greater than what would be found on a recently cleaned surface. Although the transfer efficiency that we incorporated into our analysis over-estimates the exposure that would occur in a remediated environment, we believe it is appropriate given the lack of data characterizing the transfer of methamphetamine from a remediated surface to skin.

We made no assumptions about the physical and chemical properties of methamphetamine that were based on the physical and chemical properties of pesticides. Fortunately, the physical and chemical properties of methamphetamine are well characterized. Furthermore, we relied on the results of key studies conducted at UC San Francisco that describe the dermal absorption and pH-dependent evaporation of methamphetamine hydrochloride.

2. *The residue from methamphetamine is physically similar to the pesticide residue. If the methamphetamine residue is dispersed due to aerosolization during the 'cook' the physical properties which make it similar to the pesticide residue would likely influence dispersion in a similar way.*

We made no analogies between the physical and chemical properties of methamphetamine and the physical and chemical properties of pesticide formulations. We simply assumed that methamphetamine exists as a film of contamination on indoor surfaces.

Based on the results of their recently published studies, Van Dyke et al. (2009) have suggested that the size distribution of airborne methamphetamine particles is consistent with a condensation aerosol and propose that methamphetamine is initially released as a vapor during the "salting out" process. (This occurs when methamphetamine base is precipitated out of solution by bubbling hydrogen chloride gas through it to produce methamphetamine hydrochloride.) Once released, the vapor condenses into very small particles that stay suspended in air and are able to migrate to all portions of a residence. Once the particles have settled onto a surface, we believe the fate of methamphetamine may be further influenced by the nature of the surface (e.g., its composition and porosity) and the presence of other residues (e.g., paint, grease, dirt, and residue from cigarette smoke). However, we have no data on these potential fate processes.

3. *The alternative conclusion provided at the end of this section is appropriate in that dermal transfer coefficients for children have a wide range of variation and that the exposure would be more accurately modeled using the stochastic method the SHEDS-multimedia model employs, which accounts for the wide degree of variation of individual children's activities and behaviors.*

The dermal transfer coefficients estimated by Cohen Hubal et al. (2006) do indeed indicate a wide degree of inter-individual variation, a result not entirely unexpected given the wide variation in activity of children in the age range that was studied. In this study, children at a day care center were evaluated for exposure to surface residue of a pesticide that had been applied indoors the previous day. The authors utilized whole-body "garment samplers" (100 percent cotton body suits) to assess exposure, but this approach assumes that the material the clothing is made of captures and retains chemical residues in the same manner as skin. Furthermore, Fenske (1993) has noted that "…none of the garment samplers in common use has been systematically tested for retention efficiency." There is concern that garment samplers may overestimate exposure because the materials used are often selected for their absorbent properties.

Cohen Hubal et al. also incorporated a 40 percent (upward) correction factor to account for transfer of chemical residues to the hands and feet since the clothing they used did not cover these areas. The 40 percent value was derived from a study of adults engaged in Jazzercise® exercise conducted by Ross et al. (1990). Given the

very different nature of activities that toddlers and exercising adults engage in, the validity of applying this correction factor appears to be open to discussion.

4. *Apparently this [the SHEDS-multimedia model] can also be run as a "two-stage Monte Carlo model" which consists of a series of variability runs with input variables modified between the runs to represent uncertainty in the input variables. This was not represented in the report, however represents an intriguing exposure model for use in assessing methamphetamine residue exposure risk if the variables could be further defined…*

We had two reasons for not pursuing a two-stage Monte Carlo analysis. First, we felt that basing a proposed health-based cleanup standard on a more complicated analysis would reduce the transparency of the process we used to generate the standard. In workshops held in California in January and February 2008, just explaining a one-stage Monte Carlo analysis to health care providers, child protective services personnel, hazardous waste cleanup specialists, fire protection personnel and law enforcement officers was a challenge. Second, we did not believe we had sufficient chemical- and scenario-specific information to pursue a more intensive analysis. For example, we have no information on the surface-to-skin transfer of methamphetamine residues from remediated surfaces. We have relied on a conservative interpretation of the results of surface-to-skin transfer of fluorescent tracers and pesticides, and believe we have over-estimated the value for this parameter. Nevertheless, we have no way of knowing this for certain. Under these circumstances, a two-stage Monte Carlo analysis appears unwarranted.

4. Assumptions used to run SHEDS-multimedia

1. *The mean residue to skin transfer efficiency of 7 percent is based on in-vivo study of three distinct substances: chlorpyrifos, pyrethrin I and piperonyl butoxide. The transfer efficiencies were found not to vary significantly, despite different chemical characteristics, among these three examples. The average efficiency parameter was found to be 0.07.*

This represents a slight misinterpretation of the information presented in the exposure assessment report. The surface-to-skin transfer data for chlorpyrifos, pyrethrin I and piperonyl butoxide (Camann et al., 2000) were cited in support of the contention that the chemical structure of surface contaminants does not appear to have a major effect on transfer efficiency. However, these data were not used by the authors of the SHEDS model to identify a distribution for surface-to-skin transfer efficiency.

2. *The UCSF* [University of California, San Francisco] *studies* [of methamphetamine residue transfer from vinyl to skin] *employed time frames of 15 second and 5 minutes for transfer of methamphetamine from vinyl tile to skin. The results were 0.15 percent and 5.41 percent.*

This is correct. In the UCSF studies, transfer efficiency was clearly dependent on contact duration. However, for the purpose of identifying a transfer efficiency distribution, this finding is problematic because the SHEDS model does not incorporate "duration of contact" as an exposure parameter. More importantly, the experimental methodology used in the UCSF studies has not been validated by comparison with results obtained from *in vivo* studies.

> *The UCSF findings are described as highly dependent on contact duration, when, in fact, contact duration has been found "not to influence" transfer in in-vivo work.*

While limited, the data published by Cohen-Hubal et al. (2006) do not indicate that transfer efficiency is dependent on duration of contact.

3. *Since a single distribution was used to characterize the surface-to-skin transfer of methamphetamine residue the assumption would not influence the effect of the exposure estimates generated by the model.*

Ideally, we would have preferred using a distribution for surface-to-skin transfer that was (1) methamphetamine-specific and (2) based on a protocol where the surfaces were cleaned before the efficiency transfer was determined. Given that these data are not available, our primary concern was to ensure that the true transfer efficiency would not be underestimated by the distribution that was incorporated in the SHEDS model. The decision to use the transfer efficiency distribution developed for the SHEDS model was based largely on the fact that was based on experimental data characterizing transfer efficiencies from surfaces that were *not* cleaned. Results of recent studies by Martyny (2008) indicate that the dislodgeable residue on a methamphetamine-loaded surface declines significantly after the surface has been cleaned just once. Therefore, by adopting the distribution developed for the SHEDS model, we are reasonably certain that we have not underestimated the surface-to-skin transfer of methamphetamine

5. Exposure parameter values adopted for SHEDS-multimedia

These comments do not require a response.

6. Use of exposure estimates from SHEDS-multimedia to calculate a surface REL

1. *Based on this review, use of the SHEDS-Multimedia model in conjunction with a proposed RfD for methamphetamine is a predictive model (which most reasonably represents risk while also being health protective) based on the best evidence available for determining a REL for methamphetamine.*

No response required.

[Note: Dr. Wiegand was also a peer reviewer of a separate draft report, Development of a Reference Dose (RfD) for Methamphetamine. This document and the exposure assessment document reviewed here provided the scientific basis for the proposed health risk-based target cleanup standard for methamphetamine. The acronym REL refers here to a Reference Exposure Level for methamphetamine on indoor residential surfaces. This is a surface concentration (in units of µg of methamphetamine/100 cm^2) which will result in a daily exposure (in units of µg of methamphetamine/kg body weight) at or below which adverse health effects are not likely to occur.]

2. *Taken as a whole this exposure analysis was a thorough and sound effort that established/proposed surface REL with limited scientific data and existing knowledge regarding exposure risks and particular data (as commented on above throughout) regarding clandestine methamphetamine manufacture. The models used are sound and based upon cogent principles regarding other exposure models (e.g. pesticide). The sample calculation demonstrated particularly illustrated the principals used and the rational for choosing a particular model (as use of either one may benefit given a particular question) as well as illustrating the effect of variables or degrees of uncertainty at various steps in a calculation/model.*

No response required.

7. Variation due to different synthetic methods

1. *If one relegates the dispersion of methamphetamine residue to a part of the synthetic process for methamphetamine production there should be variations in exposure patterns distinct to type of synthetic method… As heat is employed in one of these reactions while the reaction in the other is generated via addition of lithium to the anhydrous ammonia and precursor dissolved in solvent, one might expect distinct residue patterns as well as distinct patterns of waste, equipment use, type and set-up of apparatus. While it is possible that a wide dispersion of methamphetamine occurs during both these synthetic methods comparison between the two methods regarding methamphetamine residue may result in different exposure risks. I suspect, however, the effects would be most dramatic prior to remediation and thus not apply nor significantly affect the models and basis for use of REL in this report.*

We have added an additional section to the report on the fate and transport of methamphetamine in indoor environments, and one study in particular examined the differences between the two primary methods of synthesis. Studies conducted by Martyny et al. (2007 evaluated three different methods that are often used to synthesize methamphetamine from ephedrine or pseudoephedrine: the red phosphorus plus iodine method, the hypophosphorous acid plus iodine method, and the Birch reduction method which requires anhydrous ammonia plus an alkali metal (lithium or sodium). In general, airborne methamphetamine appeared to be much higher when the drug was synthesized using red phosphorus or hypophosphorous

acid. This difference is likely due to the fact that the phosphorus methods require boiling the reaction mixture, and any leakage of vapor from the reaction vessel, auxiliary glassware and/or exhaust hoses would result in release of methamphetamine to the air. This mechanism of methamphetamine release would not to occur with the anhydrous ammonia method because the reaction mixture is cold, and a methamphetamine aerosol would probably not be produced under these conditions. Nevertheless, both methods require salting out methamphetamine base, and this represents another mechanism of methamphetamine release to the air. Use of methamphetamine by smoking the drug represents another mechanism whereby surfaces can become contaminated (Martyny et al., 2008).

While different methods of methamphetamine synthesis are known to produce different by-products, these compounds are not analyzed in clandestine laboratory investigations. The primary focus in these investigations has always been methamphetamine, and it is generally assumed that remediation of methamphetamine to a health-based target cleanup goal will ensure that the concentrations of the by-products will also be below a level of concern. This may or may not be the case, however.

Results of a recent study by Van Dyke et al. (2009) suggest that, in a small 4-room residence, the distribution of methamphetamine on surfaces following one or two red phosphorus cooks was surprisingly uniform. These results are discussed in detail in the added section on indoor fate and transport of methamphetamine. Nevertheless, we agree with the statement that, insofar as methamphetamine levels on surfaces are concerned, remediation of the surfaces prior to re-occupancy should ensure that the differences in methamphetamine distribution throughout the residence, which may have been present initially, will be minimized.

8. Effect of a particular type of lab set-up or residence on REL

1. *With regard to specific data, evaluation of the concentrations of chemicals at various distances from the actual "cook" site demonstrate significant decrease in concentration as distance from the site increases… Focus of this report on the particular "post-remediation" phase of the clandestine lab limits this variability in theory and where variables exist "health-protective" assumptions are made. Focusing this report on one phase of the clandestine lab's life limits the variability of particular sites and even methods [of methamphetamine synthesis]…*

As noted above, Van Dyke et al. (2009) observed that the distribution of methamphetamine on indoor surfaces following one or two red phosphorus cooks varied by less than an order of magnitude. This result may reflect the relatively small size of the residence (500 square feet) and the manner in which methamphetamine was synthesized. Nevertheless, most of the airborne particles were < 1.0 µm and a significant fraction of these particles was still airborne 13 hours after the two "cooks,"

and these results suggest that the drug has the potential for very wide distribution throughout any residence.

III. Comments from James Morrison, PG, Technical Programs Manager, Tennessee Department of Environment and Conservation, Division of Remediation

1. *While I agree that children are at greatest risk from exposure to meth and all the other chemicals associated with the manufacture of methamphetamine as noted in #4 of the Exposure Scenario Assumptions. I also believe there is another group that may warrant consideration for similar reasons, that being women that have reached sexual maturity and that now find themselves pregnant stay-at-home moms. I did not note this as a scenario considered under the adult individual noted on Page 10/11. Unlike their working counterparts, a pregnant stay-at-home mom may be in these homes 24/7 along with their kids. This would not only potentially impact the mother to a greater degree over a working man or woman, but it could also have a greater affect on fetal development, and nursing infants, as compared to 2 year old children living in these circumstances.*

   We attempted to address concerns that *in utero* exposure may lead to neurodevelopmental toxicity in the draft document, *Development of a Reference Dose (RfD) for Methamphetamine*. The RfD includes an additional uncertainty factor of 3 to account for this potential adverse effect. In addition, the revised version of this document includes summaries and reviews of several recently published reports evaluating the infants of mothers who took methamphetamine recreationally while they were pregnant. The results of the studies that have been conducted thus far suggest that severe adverse may occur in the infants of mothers who are addicted to the drug. In contrast, an ongoing prospective study of a cohort of mothers who generally discontinued use of the drug once they realized they were pregnant has revealed much less dramatic effects, although the authors of this study caution that more significant adverse effects may be revealed as the children grow older. In all of these studies, the adverse effects of concurrent use of other psychoactive substances such as alcohol, tobacco, cocaine and marijuana, as well as the effects of poor prenatal medical care and low socioeconomic status, are difficult to separate from effects that may be attributable to use of methamphetamine.

   In utero exposure can only occur as a result of the activities of the mother, and based on age-related behavioral differences we suspected that the exposure of a woman of child-bearing age would be lower than that of a 6-18 month old child. Therefore, in response to this comment and other similar comments, we used the SOP algorithms to compare the daily exposure estimate for an adult with that of a toddler (3 years of age). Similarly, using the SHEDS model, the daily exposure estimate for women 20-30 years of age were calculated and compared to the estimates for 1-2 year old children.

   The results obtained with the SOP model were driven exclusively by the default values for dermal transfer coefficient and body weight, which are indicated in the

table below. The transfer coefficient:body weight ratio is 400 for a toddler but just 278 for an adult. Consequently, the SOP equations predict that the exposure of an adult, on a mg/kg body weight basis, would be approximately 70 percent of the exposure a toddler would receive.

	Transfer Coefficient (cm^2/hr)	Body Weight (kg)	Ratio
Adult ♀	16,700	60	278
Toddler	6,000	15	400

Preliminary results obtained using the SHEDS model[56] were similar, providing an exposure estimate for women 20-30 years of age that was approximately two-thirds of the exposure estimate for 1-2 year old children. The relative significance of each exposure pathway was similar to the results that were obtained for 1-2 year olds: 79 percent of total exposure was attributable to dermal absorption of residue on the body, 10.5 percent was attributable to dermal absorption of residue on the hands, and 10.5 percent was attributable to ingestion resulting from hand-to-mouth activity.

Both models predict that the daily exposure a woman would receive is approximately one-third lower than that of a young child. This provides an additional margin of safety where *in utero* exposure and potential neurodevelopmental toxicity are of concern.

2. *In a residential exposure scenario, it is appropriate to account for the time spent away from the residence. For an adult with a job away from the home, it would be reasonable to assume that this individual spends 9-10 hours/day, 5 days/week at his/her job, with 2 weeks of vacation each year. However, it is not unreasonable to assume that a 6 month to 2 year old child will spend most if not all of his/her time indoors, particularly if the period of residence coincides with the cold winter months or the hot summer months.*

We agree with this statement, and it is consistent with exposure scenario assumption #5 ("The exposed individual spends 100 percent of his/her time in the remediated former methamphetamine lab environment"). Data from the Exposure Factors Handbook (U.S. EPA, 1999; Table 15-131) suggest that women spend an average of around 6.5 hours a day outside the home (392 out of 1440 minutes/day). The relevant data [24-hour cumulative number of minutes spent indoors in a residence (all rooms)] are summarized in the table below. Nevertheless, we concur with Mr. Morrison that a pregnant stay-at-home mom spending 100 percent of her time in the residence is a reasonably likely exposure scenario.

[56] A rigorous evaluation of adult exposure parameter values for running the SHEDS model was not conducted. The model allows the user to specify the population of concern (in this case, 20-30 year old women). In addition, the object-to-mouth contact frequency was specified a 1 event per hour.

					Percentiles			
N	**Mean**	**Std Dev**	**Min**	**Max**	**25**	**50**	**75**	**95**
5070	1048	268	30	1440	840	1050	1280	1440

3. *The model of this study assumes no inhalation exposure. This does not seem to parallel the symptoms we get from complaints (breathing difficulties and nosebleed).*

Airborne methamphetamine should not produce breathing difficulties or nosebleeds. It is very likely that other chemicals present in the clandestine laboratory environment – such as anhydrous ammonia and hydrogen chloride gas – are responsible for these adverse health effects. We presume these complaints are from persons residing in a home where methamphetamine synthesis has occurred recently, or from individuals who moved in to a former clandestine laboratory that was not remediated. In these cases, it is probably some of the irritant chemicals that are needed to synthesize methamphetamine – particularly anhydrous ammonia and hydrogen chloride gas – that are responsible for the effects your describe.

Our analysis provides an estimate of potential exposure that may occur in a *post-remediation* scenario. It is based in part on the assumption that residual methamphetamine on all surfaces has been cleaned and the target cleanup level has been achieved. As noted in the newly added section on the indoor fate and transport of methamphetamine, the evaporation of the free base form of methamphetamine proceeds at a rapid rate (Hui and Maibach, 2007). We believe that the time interval between initial discovery of a clandestine lab and its re-occupancy should be more than sufficient for methamphetamine base – if present – to completely evaporate. In accordance with the provisions of AB1078 (Keene, Chapter 570, Statutes of 2005), we estimate that the time from initial discovery of a clandestine meth lab, to remediation and ultimately re-occupancy will probably be about six months, allowing ample time for evaporation of the free base.

Surfaces may also be contaminated with methamphetamine hydrochloride, which is not volatile. However, the recent decontamination studies of Martyny (2008) demonstrate that a single cleaning with Simple Green® removes the majority of dislodgeable residue from a variety of surfaces. Subsequent washes are not a particularly efficient means of removing additional residues. Therefore, if the interior surfaces in a residence have been cleaned at least once, the amount of dislodgeable methamphetamine residue is substantially reduced, and routine activities of persons living in the structure are very unlikely to resuspend non-dislodgeable methamphetamine residue into the air.

4. *The model does not consider newborns as a likely sensitive receptor. The complaints we have received would indicate otherwise.*

As noted in our response to your first comment, *in utero* exposure can only occur as a result of the activities of the mother. Newborns are less likely to contact indoor

surfaces than children 6-18 months of age because they have limited ability to move around and explore their environment on their own volition.

5. *Methamphetamine is the only chemical modeled in the paper…[but] methamphetamine labs frequently have many chemicals of concern (frequently there are significant unknowns). The scope of this proposed health-based standard should be kept in mind as it only applies to hazards from the drug itself and not the many other contaminants of drug manufacture.*

   We agree. Other chemicals are undoubtedly present in the clandestine laboratory environment, and they may or may not be remediated to non-hazardous levels by the actions taken to remediate methamphetamine. Nevertheless, the enabling legislation for this project requires OEHHA and DTSC to develop a risk-based target remediation standard for methamphetamine. The same legislation calls for subsequent development of target cleanup standards for phosphine, iodine and methyl iodide.

IV. *Comments from Dave McBride, Washington State Department of Health, Office of Environmental Health Assessments*

1. *Mr. McBride compared the exposure analysis developed by the Colorado Department of Health and Environment (CDHE) with OEHHA's exposure analysis, and used the respective reference doses (RfDs) developed the two agencies to estimate hazard quotients for methamphetamine at a surface residue level of 0.1 µg/100 cm2.*

   No response to Mr. McBride's summary is required.

V. *Comments from Dr. Richard Fenske, Professor and Associate Chair, Department of Environmental and Occupational Health Sciences, University of Washington*

1. General Comments

a) *This report presents a very thorough analysis of methods for the estimation of exposure and risk for young children in residences with surface methamphetamine contamination. The authors should be complimented for the systematic approach used in conducting the analysis, and the transparency with which they present their assumptions. Overall, I consider this report to be of high scientific quality. The questions and suggestions that I make in this review are intended to make a good report even better. Many of my comments can be considered 'food for thought' rather than as criticism.*

   No response required.

b) *The purpose of the report should be presented at the outset. The first part of the report should explain the basic structure of the report, and should indicate that the report is focused primarily on the comparison of two models for estimating*

residential exposures. An Executive Summary could address this concern, allowing the Introduction to be left more or less intact.

An Executive Summary has been added to the report. It briefly reviews the scope of the clandestine methamphetamine lab problem and describes the role of an exposure analysis in the development of a risk-based cleanup standard.

c) *The Introduction currently includes attempts to justify certain assumptions before the assumptions have been presented; e.g., assumption that inhalation is not an important exposure pathway. This should be avoided. This pattern recurs several times in the report; i.e., assumptions that have not yet been discussed are presented as part of the rationale for another assumption. This problem can be solved through careful review and editing.*

We agree with this comment, and the early discussion of exposure assumptions has been eliminated from the Introduction. The revised report has been edited in response to this comment and several others that Dr. Fenske suggested.

d) I suggest the authors consider reordering the seven Exposure Scenario assumptions as follows: 4 (population of concern), 7 (exposure duration), 6 (inhalation pathway), 1 (contamination), 3 (no additional sources), 2 (source concentration constant), 5 (full-time occupancy of residence). In particular, assumption #7 should be presented early on, since it defines the exposure duration of interest and the corresponding toxicologic benchmark to which exposure and dose estimates will be compared.

This is a good suggestion. We have re-ordered the sequence of exposure scenario assumptions accordingly.

e) The authors should determine whether fetal exposure in utero represents an exposure scenario that would or would not be protected by the proposed REL based on very young children.

Based on the available human toxicity data for methamphetamine and the level to which additional precaution was incorporated into our analysis, we do not believe that *in utero* exposure under the scenario described in this document would result in adverse effects on a developing fetus. This conclusion is based on the following:

- The proposed reference dose (RfD) for methamphetamine incorporates an additional 3-fold uncertainty factor to account for uncertainty in the toxicology database. The additional uncertainty factor was based on particular concern that methamphetamine may have the potential to produce adverse effects on neurological development *in utero* or post-natally.

- Ongoing studies of children born to mothers who took methamphetamine while they were pregnant have indicated some adverse effects that may be

related to methamphetamine exposure, but concurrent exposure of these women to high levels of other psychoactive compounds (e.g., nicotine and alcohol) precludes any conclusive findings.[57] The amount of methamphetamine these women were exposed to (~1 mg/kg or more) is more than three orders of magnitude higher than the exposure a pregnant woman would receive as a result of living in a former clandestine methamphetamine lab remediated in accordance with the proposed target cleanup level (< 1 µg/kg).

- *In utero* exposure can only occur as via the mother, and an adult's exposure is less than a child's. Based on results obtained with both the SOP algorithms and the SHEDS model, the exposure of an adult female is estimated to be about two- thirds the exposure of a 6-24 month old child on a mg/kg basis.

f) The exposure analyses in this report rely very heavily on residential pesticide exposure research. On page 12 it is stated that "a central assumption in this report is that the pathways and mechanisms of exposure to pesticide residues on surfaces are the same as the pathways and mechanisms of exposure to surface methamphetamine residues." I suggest that this assumption be moved into the Exposure Scenario section, given its importance for the report.

We agree that this assumption is an important aspect of the analysis presented in our report, but it is qualitatively different. Unlike the assumptions addressed in comment *(d)* (above), it does not characterize any aspect of the exposure scenario. Rather, it provides a foundational principle for the modeling approach that we took to estimate exposure: we adopted two models that were originally developed to estimate exposure to surface pesticide residues and applied them to estimate exposure to methamphetamine residues. For this reason, we decided to keep this statement where it was originally.

g) I am not convinced that the comparison of the results generated by the two models is a fair one. I came away with the impression that the Residential SOP model served as a 'straw man' for the SHEDS-Multimedia model. That is, the SOP model, which was published in 1997 and revised in 2001, was presented as is, with no new information added; whereas, the SHEDS model parameters were often based on the latest science available in this field. The report states (page 12), "the SOPs were intended to be used both as a screening tool, and for more refined risk assessments when chemical-specific data and information are available." If data and information from the more recent pesticide exposure studies were incorporated into the SOP model, I suspect that the gap between the models' estimates would narrow considerably.

[57] These studies are summarized and reviewed in a new section of the revised report, Development of a Reference Dose (RfD) for Methamphetamine (OEHHA; December, 2008)

We agree that the presentation of the results of the SOP model could be construed this way. Nevertheless, we believe we have incorporated the available methamphetamine-specific data into the analysis to the extent possible. Furthermore, the only variables in the SOP algorithms that can be modified using scenario- or chemical-specific data are the dermal transfer coefficient, the exposure duration and the mean body weight of the exposed population. Consistent with our general exposure scenario assumptions, the concentration of residue on the surface would remain a constant. Of course, exposure will vary directly with exposure duration and indirectly with body weight. Until data characterizing transfer coefficients of pesticides from remediated surfaces become available, it is unclear how results from recent pesticide exposure studies would significantly improve the analysis presented in the draft report. However, in response to this comment, the "Analysis and Interpretation" section of the original report was modified to include a more detailed evaluation of the effect of modifying the dermal transfer coefficient based on the data from Cohen Hubal et al. (2006).

h) *Conclusions regarding dermal absorption need to be revisited. This complicated subject is discussed in some detail in Section III of this review.*

Our response to this comment is presented in Section III (below).

i) *The authors have correctly identified 'residue-to-skin transfer' as the most critical variable in these modeling exercises. Unfortunately, the SHEDS model requires input of a transfer efficiency parameter (a unitless ratio) rather than a transfer coefficient (contact rate, expressed as square centimeters of surface contacted per hour). The use of transfer efficiencies in the SHEDS model was a major limitation identified by the August 2007 FIFRA Scientific Advisory Panel. The authors should review this issue carefully to determine how alteration of this parameter might affect their evaluation of the SHEDS versus SOP model results. This issue is discussed in more detail in Section III of this review.*

For clarification, we understand a transfer coefficient to be the ratio between dermal exposure, expressed in units of µg/hr, and surface loading, expressed in units of $\mu g/cm^2$ (Cohen Hubal et al., 2006). Therefore, a transfer coefficient has units of cm^2/hr, but it is not the same thing as a surface contact rate. It is our understanding that a transfer coefficient incorporates contact frequency, contact area, exposure duration and transfer efficiency under a single "umbrella" term.

The SHEDS model allows the user to utilize a transfer efficiency or a transfer coefficient to estimate dermal exposure to chemical residues on surfaces. We chose to base our exposure estimates on transfer efficiency because this parameter must be combined with age-specific distributions characterizing the contact behaviors of children in our target age range. Therefore, age-specific data describing the frequency of hand and body contact with surfaces (contact events/hr), contact area associated with each event (cm^2/contact event), and the fraction of body surface area that is unclothed could all be incorporated as separate variables into the analysis.

Certainly, each of these parameters has uncertainty associated with it, but each is subject to experimental investigation and the distributions describing them will be improved as new data become available. Taking the approach, the only "residual" uncertainty (i.e., the uncertainty that is unlikely to be addressed experimentally in the foreseeable future) is identifying a distribution to characterize the surface-to-skin transfer efficiency of methamphetamine from a remediated surface, which we believe we have over-estimated because the SHEDS model based the transfer distribution on studies of unremediated surfaces.

A transfer coefficient is an umbrella term. If its value changes under different exposure scenarios, we have no way of determining which of the component parameters changed or how much they changed. For example, one might hypothesize that differences in contact rate and contact area might be responsible for different transfer coefficients for 1-2 year olds vs. 10-12 year olds, but additional studies would need to be conducted in order to validate this hypothesis.

2. Key Issues: Scientific Basis of the Proposed Methodology

a) Exposure scenario assumptions

1) Assumption #1 *(uniform contamination) is reasonable, given the absence of data on the distribution of residues, but it is not necessarily health protective. The assumption requires its own assumption that the cleanup was perfectly executed. In reality, these environments could have 'hot spots'. Children encountering these areas in the residence could have elevated exposures.*

We agree that this assumption is not necessarily health protective and may in fact be completely appropriate, particularly in light of data recently published by Van Dyke et al. (2009), who reported that two methamphetamine "cooks" generated a very fine particulate or vapor of the drug that remained airborne for many hours and ultimately deposited a residue layer on all interior surfaces of a small residence.

The legislation that provided funding for this project required us to develop a risk-based cleanup standard that would not result in significant health risks to the occupants of a former clandestine methamphetamine lab. We believe the reference dose and exposure assessment documents provide sufficient support for the proposed cleanup standard. We were not asked to determine how this standard would be achieved or whether it would be achievable under any circumstances. Consideration of potential contamination "hot spots" is essentially a "what if" proposal that is beyond the scope of our effort. The presence of unremediated or inadequately remediated areas would be a consequence of inadequacies in the cleanup process, not a shortcoming of the target cleanup standard.

2) Assumption #2 *(no source depletion) is health protective, as the authors indicate. It is most likely that residues would dissipate over time. However,*

whether dissipation over the relevant time period (3-4 months) would alter exposure estimates substantially is not known.

Dermal exposure involves the transfer of methamphetamine residues from surfaces to skin. Surface-to-clothing and surface-to-object transfers would also lead to depletion of dislodgeable residues on surfaces. Therefore, the daily activities of individuals living in a former clandestine methamphetamine lab would produce a slow decline in the surface methamphetamine concentration. Nevertheless, the rate of dissipation over the 90-day exposure period would be dependent on a number of factors that would be difficult to predict and would complicate the assessment significantly. Consequently, "no source depletion" was made as a simplifying yet health protective assumption.

3) ***Assumption #3*** *(no additional sources) is not health protective. It rules out any unforeseen sources or reservoirs of methamphetamine. The extent to which such sources might exist is unknown.*

We agree that this is not a health protective assumption, and we do not believe the draft report suggests that it is. The possible presence of contamination "hot spots" was addressed in our response to the comment on Assumption #1.

4) ***Assumption #4*** *(very young children) focuses on a realistic sub-population. It is not health protective for this population. The exposure analysis may be health protective for older children and adults.*

Again, we do not believe the draft report suggests that this is a health protective assumption. However, as Dr. Fenske points out, a cleanup standard based in part on a "most exposed" sub-population will ensure that populations that are less exposed (older children and adults) will be protected as well.

5) ***Assumption #5 (100 percent time in residence) is health protective. It is very unlikely that children would spend all of their time in a single residential environment.***

Please see the response to Dr. Wiegand's fifth comment (pages 5-6). Accounting for time spent away from the residence would reduce the estimated daily exposure, but only slightly. According to the *Exposure Factors Handbook* (U. S. EPA, 1999; Table 5-131), children 1-4 years of age spend on average about 84 percent of their time indoors at home (1212 out of 1440 minutes/day). The 95th percentile value is 1440 minutes/day.

6) ***Assumption #6*** *(no inhalation exposure) is not health protective. It rules out an exposure pathway, assigning it a value of zero in model exposure estimates.*

Please see our responses to Dr. Martyny's comments (pages 1-4). Our analysis provides an estimate of potential exposure that may occur in a post-remediation scenario, and we assume that the residual methamphetamine on all surfaces has been cleaned up to a specified target cleanup level. Data from a recent decontamination study by Martyny (2008) demonstrate that if the interior surfaces in a residence have been cleaned at least once, the amount of dislodgeable methamphetamine residue is substantially reduced. Furthermore, during the course of three workshops that we conducted in January 2008, contractors who have years of experience cleaning former clandestine methamphetamine labs informed us that the cleanup standard currently used in California and several other states (0.1 μg/100 cm^2) is a challenge because the last bit of methamphetamine residue is difficult to remove. Therefore, the routine activities of persons living in the structure are very unlikely to resuspend non-dislodgeable methamphetamine residue into the air. In addition, methamphetamine base (if present) would not be expected in indoor air of a remediated residence because it is volatile and would likely dissipate in a matter of days.

7) ***Assumption #7*** *(sub-chronic duration) defines exposure duration. It appears from the rationale provided on pages 11 and 12 that this assumption may be the opposite of health protective. That is, an assumption of a longer duration of exposure might be more protective.*

This assumption had no effect on the methamphetamine exposure calculations because (1) we assumes a non-depleting surface residue concentration, (2) we assumed that the target population is present in the home 24 hours/day, 7 days/week, and (3) exposure estimates were calculated in units of mg/kg-day. The rationale for not assuming a longer duration of exposure is also addressed in response to comments on pages 37 and

b) Identification of 6-month to 2-year-old children as the "most exposed" population

1) *This selection is appropriate when considering children and adults. However, as discussed in Section III, it is possible that in utero exposure to the fetus could result in the most serious health consequences. "Most exposed" is a relative term that must be judged against the relevant toxicological benchmark; e.g., reference dose. If the reference dose for the fetus is lower than that for very young children, then a lower exposure for this sub-population might still have greater health consequences. As detailed in Section III, the authors are encouraged to address this issue.*

Separate reference doses (RfDs) for different toxicity endpoints (e.g., chronic non-cancer toxicity, developmental toxicity or reproductive toxicity) were not calculated. Instead, a single RfD was calculated for an endpoint that we believe to be a sensitive indicator of methamphetamine toxicity: appetite suppression and consequent reduction in body weight gain. The study upon which the RfD was based was a three-dose, placebo-controlled, double blind study of weight gain during pregnancy involving a total of 84 women. An aggregate uncertainty factor was used in

combination with a Lowest Observed Adverse Effect Level (LOAEL) to calculate the RfD.

Appetite suppression is centrally mediated, well characterized neurological effect of the drug. Using the most sensitive indicator of toxicity is consistent with U.S. EPA's approach for developing an RfD, as any other manifestations of methamphetamine toxicity would, by definition, occur at higher doses.

Methamphetamine has been shown to be a developmental toxicant in rodents, but rodents appear to be considerably less sensitive to the drug than humans. The doses used in developmental toxicity studies of methamphetamine in laboratory animals are typically one order of magnitude higher than the lowest observed adverse effect levels (LOAELs) in humans (i.e., >1 mg//kg body weight in animals *vs.* <0.1 mg/kg body weight in humans). Furthermore, use of data from a rodent study would require an additional 10-fold uncertainty factor to account for animal-to-human extrapolation. The potential developmental toxicity of methamphetamine has also been investigated in women who took the drug during pregnancy. Our conclusions regarding the result of these studies were summarized in response to Mr. Morrison's first comment (page 13).

Our response to Mr. Morrison's first comment also noted that the proposed RfD for methamphetamine incorporates an additional three-fold uncertainty factor to account for potential neurodevelopmental toxicity. In addition, *in utero* exposure of a fetus could occur only as a result of the activities of the mother, and the SOP and SHEDS models both predicted that the daily exposure a woman would receive is approximately one-third lower than that of a young child. This provides an additional margin of safety where *in utero* exposure and potential neurodevelopmental toxicity are of concern.

c) Exposure estimation models

1) As indicated in the General Comments section, the authors are encouraged to consider whether a comparison of the exposure estimates from these two models is appropriate without modification of some of the SOP model parameters, and perhaps modification of one of the SHED parameter (surface-to-skin transfer efficiency).

Regarding the SOP model, we considered modifying the default value for a transfer coefficient for children based on the data published by Cohen Hubal et al. (2006). These data were collected from a study of two groups of children in relevant age ranges (6 to 12 months of age, and 2 to 3 years of age) in a day care center, which is an exposure scenario that is not unlike a residential exposure setting. However, the transfer coefficients were derived from indoor surfaces that had not been remediated, and our exposure scenario is based on a remediated indoor environment. Since remediation removes the majority of easily dislodged residue from the surface, the transfer coefficients calculated by Cohen Hubal et al. would probably over-estimate

actual exposures by a significant margin. Based on the results of the decontamination studies conducted by Martyny (2008), the degree of over-estimation may be as much as an order of magnitude. Therefore, we chose not to pursue a more intensive evaluation of the possible impact of incorporating the transfer coefficients developed by Cohen Hubal et al. into the SOP model.

Regarding the SHEDS model, we believe the distribution we used for surface-to-skin transfer efficiency (with a mean value of 7 percent) over-estimates the true transfer efficiency of methamphetamine from *remediated* surfaces. This conclusion is also based on the results of the decontamination studies conducted by Martyny (2008), as well as the recent analysis of experimentally determined transfer efficiencies published by Beamer et al. (2008), who found that the mean surface-to-skin transfer efficiencies of three different pesticides from carpet and vinyl surfaces ranges from 1 to 4 percent. Therefore, the distribution we utilized for surface-to-skin transfer in the SHEDS model is a health protective assumption that should over-estimate the actual exposure, producing a lower target cleanup level than otherwise would have been calculated.

d) Assumptions used to run SHEDS-Multimedia

Six assumptions are listed for the SHEDS-Multimedia analysis. Does the use of these assumptions lead to higher estimates of exposure than would have been calculated otherwise?

1) ***Assumption #1*** *(100 percent oral bioavailability): this is a realistic assumption; it is unlikely that it leads to higher estimates of exposure of any significance. See comments in Section 3.*

No response required.

2) ***Assumption #2*** *(dermal absorption efficiency of 57 percent): This assumption very likely underestimates the true dose. See comments in Section III.*

A detailed response to this comment is provided in Section 3.

3) ***Assumption #3*** *(maximum dermal loading): This assumption probably does not affect exposure estimates in any significant way, as indicated by the sensitivity analysis presented in the report (pp. 37-38).*

No response required.

4) ***Assumption #4*** *(residue-to-skin transfer efficiency of 7 percent): This assumption probably has the most substantial effect on exposure estimates, and is also the most problematic, as discussed in Section III. It is not clear whether this assumption raises or lowers exposure estimates.*

We believe assuming a mean surface-to-skin transfer efficiency of 7 percent likely overestimates the true exposure because the great majority of dislodgeable methamphetamine residue is removed from indoor surfaces when the residence is remediated. A detailed response to this comment is provided in Section III.

5) ***Assumption #5*** *(no depletion of residue): This assumption leads to higher exposure estimates.*

No response required.

6) ***Assumption #6*** *(residues are chemical film and not in house dust): This assumption should not have a material effect on exposure estimates, as the authors indicate.*

No response required.

e) Exposure parameter values adopted for SHEDS-Multimedia

1) *OEHHA should consider the extent to which it wishes to rely on unpublished scientific reports. Several unpublished reports are used for background information and context (Camann et al. (2000), Clothier 2000, Martyny et al. reports). One unpublished report (Hui and Maibach 2007) is used for a SHEDS model parameter input (4c). The results of this study need further clarification. Other SHEDS parameter values are based on personal communications (2i, 2j, 2m, 3a, 3b). I would encourage the authors to revisit these parameters and develop, where possible, more compelling scientific basis for these inputs.*

Our desire to utilize recent findings recent studies on the fate and transport of methamphetamine in indoor environments and adhere to a standard of citing only published, peer-reviewed scientific reports does indeed present a dilemma. Nevertheless, some of these reports, notably those conducted by Martyny and colleagues at National Jewish Hospital in Denver, are still being submitted for publication and others have recently been accepted for publication. The research described in the draft report by Hui and Maibach was conducted by researchers that have an unparalleled track record of research in the field of dermal exposure and transdermal absorption. These studies were conducted with funding provided by the Department of Toxic Substances Control and were carried out after detailed discussions with OEHHA. These results will be published once the documents supporting to proposed methamphetamine remediation standard are finalized.

In cases where important scientific findings were unpublished, we contacted the researchers directly, obtained copies of their reports and reviewed them in detail before deciding to cite them in our own report. This approach appears to be consistent with that taken by Beamer et al. (2008) who cited several unpublished research report in developing probability distributions for transfer efficiencies for

dermal exposure. Some of these studies were conducted under contract to U.S. EPA and unfortunately were never published in peer-reviewed journals.

Given constraints on time and resources, we of necessity relied on the analysis and scientific judgment of others, most notably Drs. Graham Glenn and Luther Smith of Alion Science and Technology who worked under contract to U.S. EPA on development of the SHEDS model. Drs. Smith and Glen have published numerous reports in the field of exposure assessment.

f) Use of exposure estimates from SHEDS-Multimedia to calculate a surface REL

1) The comparison of the SOP and SHEDS model was addressed in the General Comments section, and is also discussed in Section III. This issue should be revisited. The authors are encouraged to develop exposure estimates for an SOP model that incorporates the current science in this field.

A detailed response to this comment is provided in Section 3.

g) *Use of sound scientific knowledge, methods, and practices*

1) *This report receives high marks in regard to the use of sound scientific knowledge, methods, and practices. The comments and suggestions provided in this review have highlighted areas in which there is scientific debate and room for improvement. The authors are encouraged to examine their exposure analyses in light of reviewer comments.*

h) Additional Scientific Issues

2) *None*.

No response required.

3. Detailed Comments

<u>To clearly identify the original text of the draft report, Dr. Fenske's comments, and OEHHA's responses to these comments, the original text of the December 2007 OEHHA report is in bold italics, Dr. Fenske's comments are in italics below each section of text, and OEHHA's response follows.</u>

a) Exposure Scenario Assumptions (pp. 9-12)

<u>Original text:</u>

1. All interior surfaces are uniformly contaminated, and the surface concentration of methamphetamine is equivalent to the specified cleanup standard.

The exposure scenario modeled in this report presumes a post-cleanup, residential exposure scenario. The maximum concentration of methamphetamine on all interior surfaces is assumed to equal the cleanup standard. This might be regarded as a health protective assumption since the synthesis of methamphetamine in a clandestine lab usually occurs in a specific location within the residence (typically the kitchen), and portions of the residence distant from the source of contamination (such as the bedrooms) may be uncontaminated or only lightly contaminated. Nevertheless, studies conducted by Martyny et al. (2004) suggest that methamphetamine residues are transported throughout the residence to locations distant from the site of synthesis. Therefore, assuming a post-cleanup scenario, a uniform maximum residue level throughout the residence is not entirely unreasonable.

Dr. Fenske's comment: *I would not necessarily characterize this assumption as health protective. The available data from Martyny et al. suggest that surface residues are fairly evenly distributed throughout the residence following a cook. Table IV shows an average residue on kitchen walls of 44 ug/100cm^2 13 hours post-cook, and an average residue on other walls of 33 ug/100cm^2. The difference is even less at 18 hours post-cook (45 and 38 ug/100cm^2, respectively). These levels are prior to any clean-up. We don't really know whether clean-up would reduce these levels proportionately, or whether it would tend to smooth out the differences. I would argue that this is a very reasonable assumption, and that it is not necessarily health protective.*

OEHHA's response: We agree with Dr. Fenske's analysis and conclusion. In response to this comment, a detailed review of published and unpublished research on the fate and transport of methamphetamine in indoor environments has been added to the exposure assessment report. In addition, the wording of the text that Dr. Fenske cited has been modified slightly to reflect our concurrence with his assessment of the data.

Original text:

2. ***The source concentration does not decline over time, i.e., there is no depletion of the surface methamphetamine concentration.***

Data from environmental studies of former clandestine methamphetamine labs (Martyny et al., 2004) clearly demonstrate that methamphetamine levels persist long after lab activities have ceased. Samples from abandoned clandestine methamphetamine labs collected years after drug synthesis activities have ceased indicate that methamphetamine residues can persist for years. These results support a non-depletion assumption when the residence is unoccupied.

Footnote 6 -- Martyny et al. (2004) state, "Even labs that had been busted several months prior to testing still had high contamination levels of methamphetamine present on many surfaces within the building."

Dr. Fenske's comment: *These statements need some revision. The Martyny et al. paper cited by the authors does not present such data. Rather, the statement quoted in footnote 6 is from the Discussion section of the paper. Martyny et al. are apparently referring to previous studies they have conducted, but they do not provide citations for these studies. Without reference to the original study, I don't believe it is appropriate to conclude that this point has been 'clearly demonstrated'. Similarly, footnote 7 is a personal communication with a Washington Department of Health official. Presumably there is evidence that residues can persist for years, but this statement should be qualified unless the studies that have generated this evidence can be obtained.*

Despite these concerns regarding the sources of information for this assumption, I would concur with the authors that a non-depletion assumption for unoccupied residences seems reasonable.

OEHHA's response: The Martyny et al. (2004) citation in the draft exposure assessment report was a pre-publication manuscript provided to us by Dr. Martyny. The report was published in 2007, and the citation in our report has been updated.

We agree that data demonstrating long-term persistence of methamphetamine on indoor surfaces is limited. While Martyny et al (2007) suggest that methamphetamine residues persist on interior residential surfaces for several months, data supporting this conclusion were not provided in their report. Anecdotal information based on personal communications also indicates longer-term persistence of the drug, but there are no data to support this conclusion. The wording in this section of the report has been changed to reflect a more careful analysis of the available information.

Original text:
However, as a practical reality, there are several mechanisms that will cause surface contaminant concentrations to decline over time. For example, cleaning with common household cleaning agents will reduce contaminant concentrations on surfaces. In addition, contact by the skin, clothing and shoes of persons living in the residence will result in transfer of methamphetamine residues away from contaminated surfaces. Slowly, these residues will be removed from the environment when the residents bathe, wash their clothing or leave the residence, the latter resulting in the transfer from the source area (the interior of the residence) to uncontaminated areas (outside the residence). Over the very long term, re-painting and replacement of carpets and linoleum will also reduce surface contaminant levels. Therefore, the assumption that methamphetamine concentrations are constant over time should be regarded as health protective insofar as it will lead to over-estimation of the time-weighted average daily exposure.

Dr. Fenske's comment: *It is interesting to note that McCauley and colleagues have found that attempts to clean Oregon farmworker homes tended to move*

pesticide residues around, but did not necessarily decrease surface residue levels [McCauley LA, Travers R, Lasarev M, Muniz J, Nailon R. 2006. Effectiveness of cleaning practices in removing pesticides from home environments. J Agromedicine 11(2):81-8)].

Nonetheless, it is reasonable to assume that surface residues would decrease over time for a variety of reasons. Lacking data on this process, however, means that this variable cannot readily be factored into exposure models. I would agree that this assumption is probably health protective, but I am not convinced that residue levels would decrease substantially over the relatively short sub-chronic exposure time period (90-120 days).

OEHHA's response: We are not convinced of this either. The results of recent decontamination studies conducted by Martyny (2008) indicate that cleaning with Simple Green® is a reasonably effective means of removing methamphetamine residues from a variety of surfaces, including semi-impervious materials such as painted plywood and wallboard and impervious materials such as sheet metal and glass. Given that the surfaces have been remediated (presumably using Simple Green® or a similar cleaning agent), little easily dislodgeable methamphetamine residue will remain on the surfaces. The observation that additional washings with the same agent are not particularly effective supports this conclusion. Consequently, the likelihood that post-cleanup residues can be removed by surface-to-skin or object-to-skin contact appears to be small. Therefore, while some of methamphetamine may be removed by transfer, the fraction removed is probably small, particularly over a 90-day exposure period.

Original text:

3. ***There are no additional sources or reservoirs of methamphetamine (e.g., contaminated air ducts) that would have the potential to elevate the concentration of methamphetamine on surfaces above the target cleanup standard.***

It is assumed that the cleanup standard will be applied to all surfaces in the residence, even those that are unlikely to be contacted directly by residents. Furthermore, assuming the presence of an unremediated source within in the residence would also add a significant layer of complexity to the exposure model, since it would require assumptions about the mass of contaminant present at the source, the efficacy of the release mechanism (e.g., air blowing through an air duct) and the rate of release, and contaminant dispersion and deposition within the residence.

Dr. Fenske's comment: *The primary justification for this assumption seems unsatisfactory. The authors state that the presence of an unremediated source within the residence would add complexity to the exposure model. The difficulties involved in adding such complexity should not be used as a reason for adopting an assumption that is not health protective.*

The example of contaminated air ducts is a very good one. I suggest the authors investigate whether current California cleanup procedures include decontamination of air ducts. I have encountered this same issue with residential structures that have been treated for termites; pest control applicators have sometimes inadvertently drilled into heating ducts. It has been my experience that this type of cleanup can actually be quite difficult and expensive.

OEHHA's response: The possible existence of unremediated sources of contamination does not simply enhance the complexity of the analysis. It requires that assumptions be made about the scale of the source, the mass of contaminants present on the surface, the dislodgeability of the residues, the nature of the release mechanism (air movement? vibration?), and the dispersion to "downstream" locations where human exposure can occur. We presently have no scenario-specific (i.e., clandestine methamphetamine lab) data to justify any of these assumptions. Any scenario we envisioned would be arbitrary and its relationship to any actual exposure scenario uncertain.

As noted in our response to a similar comment above, we do not believe it is our task to ensure that the cleanup standard has been achieved, or to assume that it has not been achieved. However, your point is important. We will pass it along to the Department of Toxic Substances Control, the agency responsible for developing cleanup guidance on the remediation of clandestine laboratories.

Original text:

4. ***The primary population of concern is children in the age range of 6 months to 2 years. These children, by virtue of age-specific behaviors and frequent contact with the floor, constitute a "most exposed" population in an indoor residential exposure scenario.***

Dr. Fenske's comment: *The population of very young children that is the focus of this exposure scenario is appropriate and very important for all of the reasons that authors indicate. However, there is a growing concern that even low level chemical exposures in utero can have profound and long-term effects on health (e.g., lead, PCBs, insecticides). There seems to be convincing evidence that in utero exposure the methamphetamine can have multiple and severe effects on the fetus (this is mentioned in the Discussion section of the Martyny et al. September 2005 report).*

The authors should discuss why they did not select in utero exposure as the "most exposed" population. The authors should also consider whether it would be feasible to model exposures to women during pregnancy living in these residences. Perhaps these exposures would be far below those for the 6-month to 2-year age range. But it may also be the case that the RfD for in utero exposure during pregnancy is lower than the RfD for children at this early stage of life.

OEHHA's response: Please see our response to Dr. Fenske's earlier comment on pages 22-23 and our response to Mr. Morrison's first comment (pages 12-14). Briefly, the proposed RfD for methamphetamine incorporates an additional 3-fold uncertainty factor to account for the potential neurodevelopmental toxicity that the drug might produce as a result of *in utero* exposure. The RfD is based on a sensitive, centrally mediated effect of the drug (appetite suppression), and the threshold dose was based on results of a placebo-controlled, double blind study in humans. A separate reference dose for potential development toxicity was not calculated because the available human data from studies of children born to mothers who took the drug during pregnancy are not adequate for this purpose (data on the amount of drug consumed and at what point(s) during pregnancy it was taken were at best imprecise). Doses used in developmental toxicity studies of methamphetamine in laboratory animals are typically one order of magnitude higher than the lowest observed adverse effect levels (LOAELs) in humans (i.e., >1 mg//kg body weight in animals *vs.* <0.1 mg/kg body weight in humans).

In utero exposure could only occur as a result of the activities and behavior of a pregnant adult female, and screening level estimates indicate that the exposure of an adult female population is approximately one-third less, on a mg/kg body weight basis, than the exposure of children 6 months to 2 years of age. This provides an additional margin of safety for the protection of children during development.

> Original text:
> ***Age-specific behaviors that greatly increase the exposure of young children to surface residues were recently summarized in a report by Firestone et al. (2007). Beginning at 6 months of age, children's "floor mobility" increases, leading to more frequent contact with surfaces. Also, children in this age bracket are increasingly likely to place non-food item in their mouth. Between 1 and 2 years of age, participation in play activities increase, and extreme curiosity and poor judgment (based in part on lack of knowledge of potential consequences) motivate exploratory and/or "risky" behaviors. The frequency of mouthing of hand and objects in children in this age range is high. Between ages 2 and 3, the frequency of mouthing of hands and objects begins to moderate and the amount of time spent outdoors increases.***
>
> Dr. Fenske's comment: *The Firestone article is an excellent source of information on children's behavior. The authors should also review material in EPA's Child-Specific Exposure Factors Handbook and recent updates to confirm, where possible, the information in the Firestone article. See PDF attachments.*

OEHHA's response: The most relevant data in the U.S. EPA's 2006 *Child-Specific Exposure Factors Handbook* are contained in Chapter 6 ("Other Non-Dietary Ingestion Factors"), particularly Section 6.2 ("Studies Related to Non-Dietary Ingestion"). Twelve studies of children's non-dietary ingestion were summarized and reviewed. Parameters evaluated included total mouthing times (minutes/day) as well as hand-to-mouth and object-to-mouth frequencies. The results of these studies

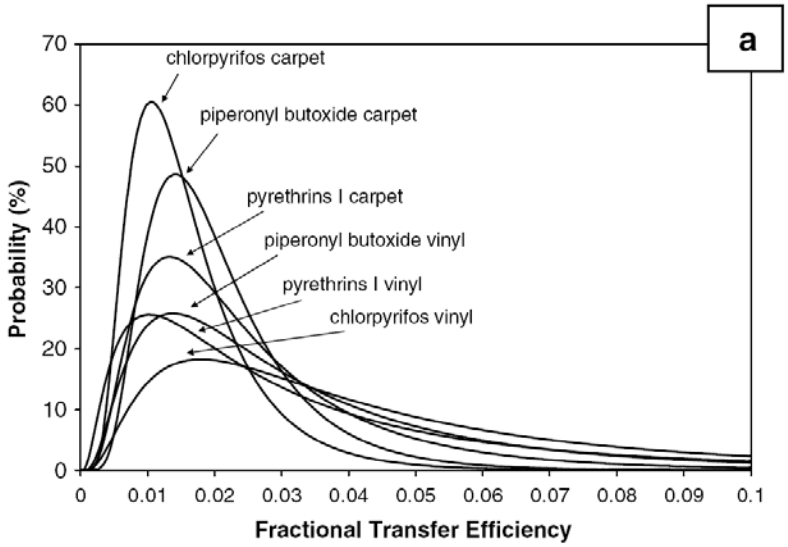
generally support the conclusion that mouthing behaviors (total mean mouthing time, total mean mouthing frequency and mean hand-to-mouth contact frequency) are highest in children 6 to < 12 months of age or 1 to < 2 years of age.

The SOP algorithms and the SHEDS model both indicated that non-dietary ingestion accounts for less than 10 percent of a child's total exposure to methamphetamine residues on indoor surfaces. Therefore, more precise estimates of mouthing behavior in very young children are unlikely to alter the total methamphetamine exposure calculated for a post-remediation residential scenario.

> Original text:
> ***In justifying specific values for individual exposure parameters, age-specific exposure and behavioral data for children in the 6 months to 2 years age range are frequently limited. Nevertheless, a number of published reports have investigated the exposure of children in this approximate age range to surface contaminants (e.g., Cohen-Hubal et al., 2006), and additional studies are currently underway. In conducting the exposure assessment presented in this report, an attempt was made to utilize parameter values specific for the 6 months to 2 years age range when age-specific supporting data were available.***
>
> Dr. Fenske's comment: *The use of the most currently available data seems appropriate. The Cohen-Hubal et al. (2006) article is a very good source, but the SHEDS model does not use data from this article. A recent paper by Beamer et al. develops probability distributions for transfer efficiencies for dermal exposure (JESEE, 2008, April 2, Epub ahead of print). Although this paper does not examine transfer coefficients, it may prove of value with the SHEDS model, as this model currently requires input of transfer efficiencies.*

OEHHA's response: As noted earlier, SHEDS can utilize transfer efficiencies or transfer coefficients as input variables. Beamer et al. (2008)[58] identified 35 studies that evaluated surface-to-skin transfer efficiency. Of these, nine were used to fit transfer efficiency distributions for three pesticides (chlorpyrifos, piperonyl butoxide and pyrethrin I) on different types of surfaces (carpet, vinyl and foil). Lognormal distributions for fractional transfer efficiency are shown in the graph below.

[58] Beamer, P., Canales, R.A., and Leckie, J.O. (2008). Developing probability distributions for transfer efficiencies for dermal exposure. *Journal of Exposure Science and Environmental Epidemiology*, advance online publication.



Data analysis by Beamer et al., 2008. Fractional transfer efficiency distributions (lognormal) developed for chlorpyrifos, piperonyl butoxide and pyrethrin I on carpet and vinyl, based on data from published and unpublished research reports.

The geometric means of these distributions ranged from 0.01 (transfer of chlorpyrifos from carpet to skin) to 0.04 (transfer of chlorpyrifos from vinyl to skin). The authors stated, "Caution should be used when extending these distributions to other chemicals and surface types." Nevertheless, it is worth noting that all six geometric means are well below the mean surface-to-skin transfer efficiency that we assumed for methamphetamine (0.07) as a parameter value for the SHEDS model.

Furthermore, in none of these studies evaluated by Beamer et al. was the surface cleaned before surface-to-skin transfer was assessed. This is justifiable because it represents the typical exposure scenario for pesticides that are applied indoors. However, it does <u>not</u> represent the post-remediation re-occupancy scenario that we are attempting to model. Because cleaning a surface significantly reduces the amount of dislodgeable residue, we assume that transfer efficiencies determined using non-remediated surfaces over-estimate the transfer efficiencies that would be have been obtained had the surfaces been cleaned.

Based on this information, we believe the value for the transfer efficiency that was used for the SHEDS model overestimates the true value for this parameter, potentially by a substantial margin.

<u>Original text:</u>

5. ***The exposed individual spends 100 percent of his/her time in the remediated former methamphetamine lab environment.***

In a residential exposure scenario, it is appropriate to account for the time spent away from the residence. For an adult with a job away from the home, it would be reasonable to assume that this individual spends 9-10 hours/day, 5

days/week at his/her job, with 2 weeks of vacation each year. However, it is not unreasonable to assume that a 6 month to 2 year old child will spend most if not all of his/her time indoors, particularly if the period of residence coincides with the cold winter months or the hot summer months.

Dr. Fenske's comment: *I concur with this assumption, since there is a need to develop a clean-up standard that is protective for children who spend virtually all of their time in their own residences. However, some additional discussion of this assumption would be helpful. It is well documented that children this age do spend most of their time indoors, but they may spend time in multiple residences or in day care. The authors should explain why it is not feasible to include this time-location variable in a probabilistic analysis.*

OEHHA's response: Please see our response to Dr. Wiegand's comment on page 6. Accounting for time spent away from the residence would reduce the estimated daily exposure, but only slightly. According to the *Exposure Factors Handbook* (U. S. EPA, 1999; Table 5-131), children 1-4 years of age spend on average about 84 percent of their time indoors at home (1212 out of 1440 minutes/day). The 95th percentile value is 1440 minutes/day.

Including a time-location variable in our analysis would be feasible and straightforward, but it would have the effect of reducing the estimated exposure. In light of comments we have received formally and informally from other reviewers, we believed it would be best to assume that a child spends all of his/her time in the remediated residence. This was simply a health protective assumption, and children who spend significant time away from the residence would be less exposed and therefore even less likely to experience any adverse health effects from living in a remediated former methamphetamine lab.

Original text:

6. ***Inhalation of airborne methamphetamine residues does not represent a significant exposure pathway.***

While inhalation of airborne methamphetamine is likely to occur during the operational, discovery and removal, and cleanup and verification phases in the life of a clandestine methamphetamine lab, it is unlikely to be a significant exposure route during the post-cleanup reoccupancy phase. During this phase, surface methamphetamine residues have been remediated to the designated cleanup standard, so the mass of contaminant available for re-suspension is exceedingly small.

Dr. Fenske's comment: *I agree that the mass of contaminant available for re-suspension or volatilization is small. However, the air concentrations are likely to be proportional to the total mass of contaminant in the environment. If small amounts of surface residues are of concern, then the corresponding air concentrations may also be of concern.*

OEHHA's response: Based on the results of the decontamination study conducted by Martyny (2008), we believe the dislodgeability of methamphetamine residues is significantly reduced by remediation. After a surface has been cleaned one time with water and Simple Green®, subsequent washes are relatively ineffective at removing additional methamphetamine residue. Simple Green® is a moderately aggressive cleaning agent that contains 2-butoxyethanol. We believe it is unlikely that a significant amount of the methamphetamine remaining on a previously cleaned surface would be physically dislodged and re-suspended in air by the routine activities of the occupants of the residence.

The results of studies conducted at UC San Francisco indicate that the volatilization rate of the free base form of methamphetamine is sufficiently rapid that it should evaporate completely in a few days.

> Original text:
> ***Additionally, methamphetamine base has a relatively low octanol:water partition coefficient (log P = 2.07), suggesting that it does not readily adsorb to soil and dust particles. Therefore, resuspension of soil and dust by normal activities such as walking and vacuuming is unlikely to generate significant levels of airborne methamphetamine.***
>
> Dr. Fenske's comment: *The basis for this conclusion is not clear. The August 11, 2005 report by Martyny and colleagues indicated that human activities can have a significant effect on airborne methamphetamine (e.g., heavy activity produced a 3-fold increase in air concentration when compared to no activity; Table IV). Martyny et al. attribute the increase to re-suspension from contaminated surfaces. The authors of this report use the term "significant levels" of airborne methamphetamine, but do not define what would constitute a significant level. If we knew that air concentrations were responsible for less than 5 percent of the absorbed dose, for example, we could draw this conclusion. However, we know from long-term structural pest control studies that air concentrations of compounds like chlordane and chlorpyrifos can be found in indoor residential air for years after treatment, even though the applications did not occur within the residence, but rather in soil around and beneath the structure. In the scenario we are considering the chemical has been "applied" inside the residence. It seems reasonable to assume that some of the remaining residue will become airborne. Whether the levels are "significant" or not remains to be determined.*

OEHHA's response: [Note: The 2005 report by Martyny et al. was a pre-publication manuscript provided to us by Dr. Martyny. The report has just been published in *Journal of Occupational and Environmental Hygiene*. It is cited as "Van Dyke et al., 2009" in the newly added section on fate and transport of methamphetamine in indoor environments.]

The report describes a "worst case" environment that exists within the first 18 hours following two methamphetamine "cooks." Sources of contamination still remained in the residence and no remediation was conducted whatsoever. This is not the same exposure scenario as the one we attempted to model. Analogy to studies of long-term structural pest control is also inappropriate because, in these situations, the sources of contamination have not been removed and no attempt was made to remediate contaminated surfaces.

We modeled potential exposure in a post-remediation re-occupancy scenario. In this scenario, the sources of contamination have been removed and all previously contaminated media are expected to meet the designated target cleanup level for methamphetamine. Since surfaces have been cleaned, the dislodgeable residue – the mass of contamination that is potentially available for re-suspension – has been substantially reduced. Smooth, impervious surfaces such as glass and metal are likely to have no detectable methamphetamine residues (Martyny, 2008). Methamphetamine base will evaporate long before the residence is re-occupied. On the basis of this information, we do not believe that inhalation of airborne methamphetamine represents a significant exposure pathway for this scenario.

Original text:
Data characterizing airborne methamphetamine concentrations in former clandestine labs after the labs have been remediated are lacking. Martyny et al. (2005) measured airborne methamphetamine concentrations in a small single story residence during two methamphetamine "cooks" and 13-18 hours thereafter. Concentrations detected at the later time points were approximately 10-30 percent of the concentrations detected during synthesis, suggesting that airborne methamphetamine dissipates quickly once the source of indoor emissions has been eliminated.

Dr. Fenske's comment: *It is difficult to apply the data in the Martyny et al. article cited above to the post-cleanup scenario. Air concentrations did decrease over time in the Martyny et al. study, but I am not sure that 'quickly' describes the pattern observed. That 10-30 percent of the air concentrations measured during the actual cook are still present the next day is somewhat surprising. Also, the role of human activity, as noted above, can have a substantial impact on air concentrations. My view is that these data are not really useful for understanding likely air concentrations for the scenario under study.*

In summary, I am not persuaded that inhalation is an insignificant exposure pathway for this scenario. The evidence provided is very circumstantial. Would it be possible to include inhalation exposure in the SOP and SHED models to determine its contribution to total dose? Alternatively, it might be possible to examine some of the residential pesticide studies that are the basis for many of the model parameters to see what role inhalation played in terms of total dose.

OEHHA's response: [Note: A detailed summary and review of this study, now cited as "Van Dyke *et al*., 2009," is provided in a newly added section of the exposure assessment report titled "Investigation of the Fate and Transport of Methamphetamine in an Indoor Residential Environment."]

Justification for the conclusion that inhalation of airborne methamphetamine does not represent a significant exposure pathway in a post-remediation exposure scenario is provided in our response to the previous comment.

There are several conservative assumptions that were incorporated into this exposure assessment. These assumptions were made when the available information was judged insufficient to support a clear conclusion based on scientific data. Here, however, we believe the available information is sufficient to support the conclusion that inhalation does not represent a significant exposure pathway.

Original text:

7. A sub-chronic duration of exposure (3-4 months) is assumed.

In the quantitative analysis presented below, two methods are used to estimate daily exposure to surface methamphetamine residues in units of mg methamphetamine per kilogram body weight (mg/kg-day). Both estimates are based on the assumptions that the source concentration is constant (non-depleting) and that the exposed child spends 100 percent of his/her time in the remediated environment. For this reason, the duration of exposure does not affect the estimates of daily exposure to methamphetamine.

Dr. Fenske's comment: *The two assumptions that the authors have adopted – surface residues do not dissipate over time (#2) and the exposed child is in the remediated environment 100 percent of the time (#5) – means that duration of exposure does not affect estimates of daily exposure, as the authors state. The question is, to what reference dose should these estimates be compared?*

OEHHA's response: Justification of a reference dose for methamphetamine was provided in the document, *Development of a Reference Dose (RfD) for Methamphetamine* (OEHHA, 2007; revised 2008). The toxicity endpoint for the RfD was appetite suppression and reduction in body weight gain – well characterized, centrally mediated indicators of methamphetamine's pharmacological activity. The primary study was a three-dose, placebo-controlled, double blind investigation of weight gain during pregnancy involving a total of 84 women. The mean duration of dosing was 15-17 weeks, although one quarter of the women in the three methamphetamine dose groups received the drug for 20-21 weeks. An aggregate uncertainty factor of 300 was used in combination with a Lowest Observed Adverse Effect Level (LOAEL) of 5 mg/day (0.08 mg/kg-day) to calculate the RfD (0.3 µg/kg-day). Basing an RfD on the most sensitive indicator of toxicity is consistent with the methodology developed by U.S. EPA, as any other manifestations of methamphetamine toxicity would occur at higher doses.

Original text:
We recognize that the activities of the individuals living in the residence will reduce surface methamphetamine concentrations over time. As discussed earlier, mechanisms of contaminant depletion include routine cleaning and contact with uncontaminated skin, clothing and other objects. In reality, these removal processes will cause the daily exposure to decline over time. This reality was taken into consideration in the decision to develop a sub-chronic reference dose (RfD) for methamphetamine, insofar as an additional uncertainty factor that would routinely be used to extrapolate to a chronic RfD from the results of a sub- chronic exposure study was not incorporated into the calculation.

Dr. Fenske's comment: *It is not clear how development of a sub-chronic reference dose is related to residue dissipation. The authors state that an additional uncertainty factor would routinely be used for a chronic RfD. Why? They also state that such an uncertainty factor was not incorporated for the sub-chronic RfD. Why not? A more detailed explanation of these points would be helpful. It does not seem appropriate to select a particular RfD or a particular set of uncertainty factors in order to offset the potential impact of what may be a dubious assumption.*

More importantly, the rationale provided for Assumption #7 does not address why a subchronic duration was adopted. The authors should address their selection of the reference dose at the outset of the report, and provide a compelling rationale for that selection. I suggest that this assumption be moved to the top of the list, and that the rationale include a discussion of the pros and cons of possible reference doses.

OEHHA's response: As noted in the response to the previous comment, justification for an RfD for methamphetamine was provided in a separate document. Consistent with U.S. EPA risk assessment methodology, extrapolation of data from a sub-chronic toxicity study to a chronic exposure duration generally requires incorporation of a 10-fold safety factor. For example, if the No Observed Effect Level (NOEL) from a 90-day sub-chronic toxicity study was 5 mg/kg-day, the estimated chronic NOEL based on the same data set would be 0.5 mg/kg-day. The additional uncertainty factor is included as an additional precaution in case the chemical is capable of producing adverse effects over the long term that would not be observed in a shorter-term (i.e., 90-day) study.

The RfD for methamphetamine was based on a subchronic study of the drug's effects on weight gain in humans. The average duration of exposure was 15-17 weeks, although some subjects were dosed for as long as 21 weeks. Since exposure duration in this study was approximately the same as the assumed duration of exposure that was assumed in OEHHA's exposure assessment, an additional uncertainty factor that

would account for potential adverse effects that may arise from longer-term exposure was not warranted.

The decision to assume a sub-chronic duration of exposure was based on two considerations. First, while we assumed that the concentration of methamphetamine residues on surfaces would not decline over time, we recognize that depletion – via various mechanisms that have discussed in response to previous comments – will occur. Exposure cannot occur without surface-to-skin transfer, which in turn leads to depletion of the surface concentration. The "non-depletion" assumption was made in part because (1) we have no data on the "natural attenuation" of methamphetamine residues in a residential environment, (2) it simplifies the analysis and renders it more transparent, and (3) it is health-protective, since the average daily dose over a 90-dauy period is greater under this assumption than it would be if we incorporated a source depletion rate.

The second reason for assuming a sub-chronic exposure duration is related to the target population of concern in this assessment: children 6 months to 2 years of age. As discussed on page 10 of the draft report, children in this age range are more likely to spend time indoors, have more frequent contact with the floor, and are much more likely to place their hands, toys and other objects in their mouths. Between the ages of 2 and 3, the frequency of mouthing begins to moderate and the amount of time spent outdoors increases. Therefore, the "critical window" for exposure to residues on indoor surfaces appears to last about one and a half years. This is approximately equivalent to a sub-chronic duration of exposure.

The RfD was not discussed as in this section of the exposure assessment document because it is not an exposure scenario assumption. A detailed presentation of the rationale for the RfD for methamphetamine is provided in the document cited above.

> Original text:
> ***Footnote 8 -- While the output from the SHEDS-multimedia model was based on a 90-day exposure duration, the surface concentration of methamphetamine was assumed to be constant. Therefore, the 90-day exposure estimates simply reflect variation in the behavior (surface contact rates, mouthing frequencies, etc.) of children in the 1-2 year old age range.***
>
> Dr. Fenske's comment: *This footnote should probably say "children in the 6 month to year old age range" to be consistent with Assumption #4.*

OEHHA's response: The change suggested by Dr. Fenske was made to the document.

b) Exposure Estimation Models (pp. 12-13)

Original text:
During methamphetamine synthesis, the fate and transport processes that lead to deposition of methamphetamine on interior surfaces have yet to be completely characterized. Clearly, additional studies in this area are warranted. Based on current knowledge, it appears that one or more steps in the methamphetamine synthesis process generate an aerosol or vapor of airborne methamphetamine which is transported widely throughout the interior of a residence (Martyny et al., 2005). When the vapor contacts a surface, it condenses and forms a film, similar to film that deposits on surfaces when pesticides are applied using broadcast spraying or an indoor fogger. Since the film of methamphetamine generated during clandestine methamphetamine synthesis is physically similar to the chemical film produced by indoor application of pesticides, models that have been developed to estimate indoor exposure to pesticide residues can also be used to estimate indoor exposure to methamphetamine residues. A central assumption in this report is that the pathways and mechanisms of exposure to pesticide residues on surfaces are the same as the pathways and mechanisms of exposure to surface methamphetamine residues.

Dr. Fenske's comment: *In this section the authors draw a direct analogy between transport processes for methamphetamine and pesticides in residences. This argument needs substantial revision and additional documentation if it is to be credible. The Martyny et al. studies indicate that methamphetamine is vaporized during the cooking process. In contrast, indoor foggers generally release semi-volatile insecticides in an emulsion rather than as a vapor, and this mixture deposits on surfaces within the treated area. Broadcast applications are quite different. They involve spraying of a water-based solution on carpets and furniture. Over time the semi-volatile pesticides in the solution can move to the vapor state and can be deposited on non-treated surfaces. The authors could strengthen their argument by providing some evidence that "the film of methamphetamine generated during methamphetamine synthesis is physically similar to the chemical film produced by indoor application of pesticides."*

Since the authors consider this analogy to be a "central assumption" in their analysis, I would suggest that they move this material into the previous section, and present this information as one of the "Exposure Scenario Assumptions".

The assumption that pesticide residue data can be used to represent methamphetamine residues introduces a new uncertainty factor into the exposure analysis. Can this uncertainty accounted for quantitatively in the modeling exercises? If not, how will the authors adjust their exposure estimates based on pesticide residue studies to address this uncertainty?

OEHHA's response: Our description of how methamphetamine becomes airborne is based primarily on research conducted by Dr. Martyny. At this point, however, the information we have is limited. We don't even know if the material released is the hydrochloride salt, the free base, or (most likely) a combination of the two. The relative amounts of the two forms probably depend on the mechanism of release. For example, if a solution of the free base were spilled it would evaporate and produce a vapor, while the salting out process might generate an aerosol containing both the free base and the hydrochloride salt.

While Martyny et al. have suggested that methamphetamine is released during the cooking process, it should be recognized that release of the drug during the cook is potentially highly hazardous – even lethal – to anyone in the immediate vicinity because of the production of phosphine gas. For this reason, cooks who have produced methamphetamine more than once generally attempt to seal their equipment very well and vent all fumes away from the building where the drug is made. Therefore, release of methamphetamine during the actual cook may not happen that often.

Van Dyke et al. (2009) have stated,

> *The size distribution of [airborne] methamphetamine is consistent with a condensation aerosol. This suggests that the methamphetamine is released as a vapor from the "salting out" process and condenses into very small particles. The predominantly small particle size of the aerosol also explains how it is able to migrate to nearly all areas of a residence.*

At this point, it appears that we have several testable hypotheses about when and how methamphetamine is released, and the form that it is released in.

The analogy between the release of methamphetamine during the synthesis process and release of a pesticide from an indoor fogger is based on the fact that both materials are released from a fixed location and rely on transport via indoor air to become dispersed throughout a residence. This results in a film of chemical that coats interior surfaces. (Dr. Martyny has suggested that interior surfaces become "plated" with methamphetamine when the drug is synthesized.) A pesticide fogger also produces a film on chemical on interior surfaces. In both cases, the amount of chemical on surfaces can be determined by collecting wipe samples. The primary difference between the two may be that the particle size distribution of methamphetamine appears to be very small – smaller than the emulsion particles generated by an indoor fogger. Consequently, a significant fraction (~15 percent) of methamphetamine is airborne 13 hours after synthesis and the drug has dispersed throughout the residence.

We did not make an analogy between the release of methamphetamine during synthesis and broadcast application of a pesticide.

The primary point here is that methamphetamine has been shown to form a relatively stable film of contamination on indoor surfaces (Martyny et al., 2007). Exposure will occur primarily via contact and subsequent surface-to-skin transfer, absorption across the skin, and inadvertent ingestion resulting from hand-to-mouth activity. As a consequence, we believe that the exposure models that have been developed to estimate exposure via these pathways are applicable to our exposure scenario, even though they were originally developed with a particular class of chemicals (pesticides) in mind.

Original text:
Two models were used to calculate estimates of exposure.

Dr. Fenske's comment: *Descriptions of the U.S. EPA guidance document for residential exposure assessment and the U.S. EPA SHEDS model are accurate, clearly written and very useful.*

OEHHA's response: No response required.

c) Exposure Estimates based on Algorithms Presented in Standard Operating Procedures for Residential Exposure Assessments (pp. 14-19)

Original text:
In an indoor residential environment, certain types of pesticide applications produce the same widespread surface contamination that results when methamphetamine is synthesized. For example, an indoor fogger is an effective means of applying a pesticide indoors because it disperses a film of pesticide on interior surfaces. Similarly, emissions from methamphetamine synthesis deposit a film of chemical residue throughout an entire house or apartment. For this reason, SOPs that were developed to estimate residential exposure to pesticides applied using an indoor fogger may be adopted to estimate residential exposure to post-cleanup methamphetamine residues on interior surfaces. The following calculations are based on SOP algorithms to estimate

- ***Dermal exposure following contact with contaminants on carpet***
- ***Dermal exposure following contact with contaminants on hard surfaces (floors and counter tops) in the kitchen or bathroom***
- ***Incidental non-dietary ingestion following hand-to-mouth transfer***

Dr. Fenske's comment: *This section relies on the assumption that methamphetamine and pesticide deposition are comparable. As indicated earlier, this argument needs to be strengthened. It is reasonable to say that a 'film' is deposited on surfaces in each case, but the chemical characteristics of these deposited films may be quite different in terms of volatilization and contact-transfer. We don't really know.*

OEHHA's response: We agree that, physically, methamphetamine forms a relatively stable film or layer of contamination on indoor surfaces. We also agree that the chemical characteristics of methamphetamine and various pesticide formulations are not similar. The lack of chemical similarity between methamphetamine and pesticides may or may not be a significant issue. We don't know for certain because data describing the chemical nature of surface methamphetamine contamination is not available.

Methamphetamine base has been shown to volatilize readily. Therefore, in a post-remediation exposure scenario where several months will have passed before the residence is ready for re-occupancy, it would not be expected to generate an airborne vapor. The hydrochloride salt of methamphetamine – or perhaps another salt that may form as a result of contact with indoor surface materials – appears to be the environmentally persistent form of the drug. Certainly, some form of the drug is persistent because it can be detected in wipe samples collected from the surface months after drug making activity has ceased.

Regarding contact transfer, the most important consideration is that in our exposure scenario all contaminated surfaces have been remediated and the dislodgeable residue has been reduced significantly (Martyny, 2008). The mean surface-to-skin transfer efficiencies calculated by Beamer et al. (2008) for transfer of three different pesticides from *unremediated* surfaces ranged from 1-4 percent. By comparison, when we ran the SHEDS model, the mean surface-to-skin transfer we assumed for transfer of methamphetamine from remediated surfaces was 7 percent. This alone suggests we may have over-estimated the actual exposures that would occur in this scenario.

With the SOPs and the SHEDS model, we assumed that a fraction of the methamphetamine residue on a remediated surface is transferrable to skin if the surface is contacted. It may not be transferrable at all, and it certainly should not be as easily transferrable as pesticides are from a non-remediated surface.

d) Post-Application Dermal Dose from Pesticide Residues on Carpets

Original text:
Exposure scenario: Pesticide residues are transferred to the skin of adults, toddlers and infants who come in contact with treated carpets for recreation, housework and other occupant activities.

Dr. Fenske's comment: *The authors need to be careful here. Previously, they used the analogy between methamphetamine vapors and indoor fogger treatments. Now they are basing their analysis on broadcast or crack and crevice treatments. These treatments are quite different. Foggers emit an emulsion, whereas broadcast and crack-and-crevice treatments involve dilution of the formulated product in water. Are all of these application methods comparable to the methamphetamine exposure scenario? Please clarify.*

The list of assumptions includes information on adults, but the focus of this analysis is on very young children. I found this confusing.

Assumption 1 states that 5 percent of the application rate is available on the carpet as dislodgeable residue. Assumption 1 on page 17 states that 50 percent is available. Which is correct?

The authors make an assumption of 8 hours per day for this exposure pathway. They should explain at the outset of this section that the total exposure time for this scenario is 12 hours per day: 8 hours per day on carpets and 4 hours per day on hard surfaces.

Footnote #11 cites U.S. EPA, 1996, but this is not listed in the references. I think this is the Exposure Factors Handbook. Please check the Child-Specific Exposure Factors Handbook to make sure that the appropriate dermal transfer coefficients are being used.

A body weight of 15 kg will underestimate exposure for crawling infants (6-12 months). Footnote #12 states that the original SOP document provided separate transfer coefficients and body weights for these very young children, but that the revised document did not include these. Why did this change occur? Were the original values incorrect?

A dermal absorption value of 60-70 percent is presented in this section, but with no citation. Please explain and document or omit from this section.

<u>OEHHA's response:</u> We made analogy between the production of methamphetamine vapors and aerosol during synthesis of the drug and the release of pesticides by indoor foggers. Both processes produce a film of contamination on indoor surfaces. We made no analogy between the chemical composition of various pesticide formulations and the chemical composition of the contaminants originating from the synthesis of methamphetamine.

Chapter 8 of the SOP document specifically addresses crack and crevice and broadcast treatment. Indoor fogger treatment is not specifically addressed in the document. We agree that crack and crevice and broadcast treatment will probably produce a more variable distribution of pesticide residues on indoor surfaces than fogger treatment. However, the mechanisms of exposure to surfaces residues will be the same.

We have modified the wording in this section of the report to avoid confusion between the different modes of pesticide application that can be used indoors.

Exposure parameter values for adults were kept in the report because we received several comments concerning potential exposure of pregnant women, and these were addressed in our response by calculating an adult exposure.

The 1997 version of the SOPs assumes that 50 percent of the applied pesticide is available on carpet as dislodgeable residue. This value was changed to 5 percent (10 percent for hard surfaces) in the 2001 revisions to the SOPs. The 50 percent value in the draft exposure assessment document was an error that has been corrected.

Wording reflecting the 12 hour total exposure duration (8 hours' contact with carpets and 4 hours' contact with hard surfaces) has been added to the report.

The 1996 U.S. EPA citation refers to a report prepared by Versar, Inc. for the Office of Research and Development, National Exposure Research Laboratory. This reference has been added to the report.

Chapter 8 of the *Child-Specific Exposure Factors Handbook, External Review Draft* (U.S. EPA; September, 2006) addresses adherence of "solids" to skin. Most research in this area has been focused on soils adherence, although other solid residues such as household dust can also adhere to skin. The report focuses on adherence factors, the amount of material that adheres to the skin per unit of surface area. It does not provide any information on transfer coefficients. We do not believe that studies of soil adherence to skin are useful in estimating surface-to-skin transfer and dermal exposure of chemical residues on indoor surfaces.

In the 2001 update of the SOP parameter values, U.S. EPA did not provide rationale or justification for the eliminating parameter values for very young children.

A reference to the draft report by Hui and Maibach (2007) has been added to this section of the exposure assessment report. The mean dermal absorption value was changed to 57 percent. This value was taken from Table P-4 of the draft report. These data were obtained with skin samples pre-treated with pH 4.5 buffer and pH 5 receptor fluid, ensuring that the pH of the skin sample would also be 5 throughout the duration of the experiment. Normal skin pH is 4.5 to 6. Under these conditions, <1 percent of the ^{14}C-labeled methamphetamine evaporated.

> <u>Original text:</u>
> ***For former meth labs, the post-cleanup concentration of methamphetamine residues on surfaces (i.e., the indoor surface residue) is the target cleanup level, which in most states is 0.1 µg/100 cm^2 (0.001 µg/cm^2).***
>
> <u>Dr. Fenske's comment:</u> *This target cleanup level should be documented by referencing the relevant state documents. Also, it would be helpful if the report included a discussion of the rationale for this cleanup level. Is the only basis for this level the limit of analytical detection? If so, that limit has likely changed by now.*

OEHHA's response: A list of current target cleanup levels utilized in different states was recently compiled by U.S. EPA (2008). This document is now cited in the revised exposure assessment report. The version we have is a pre-decisional draft for review only. However, we were informed by U.S. EPA staff that the document should be generally available in December 2008.

The current cleanup standard was based on analytical detection limit and was developed by the state of Washington several years ago. Martyny (2008) reported a detection limit of 0.05 µg/100cm^2. The detection limit may have changed but the target cleanup standard has not.

e) Post-Application Dermal Dose from Pesticide Residues on Hard Surfaces

Original text:
The exposure scenario and assumptions are identical to those specified for calculating the dermal dose from residues on carpets, although the duration of exposure is assumed to be just 4 hours/day. The latter value is justified on the basis that it represents the mean of the 90th percentile values for time spent on the kitchen and bathroom for all age groups (adults and children).

Dr. Fenske's comment: *The comments presented above for carpets are relevant to this analysis as well.*

OEHHA's response: The assumption regarding the percentage of dislodgeable residue was changed to 10 percent, per the 2001 revisions to the SOPs.

f) Post-Application Dose Estimate for Toddlers from Incidental Non-Dietary Ingestion of Pesticide Residues on Indoor Surfaces from Hand-to-Mouth Transfer

Original text:
Exposure scenario: Pesticide residues are transferred to the skin of toddlers during post-application contact with treated indoor areas and are subsequently ingested as a result of hand-to-mouth transfer. The 3 year-old age group was selected for this scenario because, at the time the SOP was written, this was the youngest age group for which data on hand-to- mouth activity were available.

Dr. Fenske's comment: *It appears that there are no hand-to-mouth transfer data available for the age group of interest. The use of data for 3 year old children seems to be the only option. If additional data have become available since the SOP was written, please use these new data.*

It is not clear why the duration of exposure to indoor surfaces is 4 hours/day. The last two calculations have assumed 8 hours/day and 4 hours/day, respectively, for a total for 12 hours/day.

OEHHA's response: Newer data for hand-to-mouth activity for children approximately near the target age range (6 months to 2 years) are available (Xue et al., 2007). Based on data from four studies of children 6 to ≤ 12 months of age, the mean indoor hand-to-mouth frequency was 18.9 contacts/hour. Data from three studies of children 1 to ≤ 2 years provided a mean of 19.6 contacts/hour. 95th Percentile estimates for both age groups were 52 and 63 contacts/hour, respectively.

Exposure via incidental ingestion was re-calculated using an average hand-to-mouth contact frequency of 19 contact/s hour and an average body weight of 12 kg (U.S.EPA, 1997; Table 7-3). The net effect of these two changes is discussed in the "Analysis and Interpretation" section of the revised exposure assessment report.

g) Total Estimated Exposure via All Three Pathways

Original text:

Dermal Dose from Pesticide Residues on Carpets:	***0.0032 mg/kg-day***
Dermal Dose from Pesticide Residues on Hard Surfaces:	***0.0016 mg/kg-day***
Incidental Ingestion Dose from Hand-to-Mouth Activity:	***0.00015 mg/kg-day***
TOTAL:	***0.00495 mg/kg-day***

For comparison, using the same surface residue level, the SHEDS model estimated an average total absorbed dose of 0.000015 mg/kg-day, or 330 times less than the residential SOPs. If the experimentally determined dermal absorption efficiency for methamphetamine had been used in the SOP equations, the dose estimates for the two dermal absorption pathways would have been reduced by approximately one-third, but the estimate of total dose still would have been 220 times greater than the dose estimate generated by the SHEDS model.

Dr. Fenske's comment: *Comparison with the results from the SHEDS model is out of place here, since the SHEDS analysis has not yet been presented. I suggest that the above paragraph be moved to the final section of the report, after the SHEDS model analysis.*

OEHHA's response: Per Dr. Fenske's suggestion, we have reserved discussion comparing results from the SOP algorithms and the SHEDS model to the section at the end of the report that evaluates the output from the two models.

h) Analysis and Interpretation

Original text:

Based on the SOP algorithms, 97 percent of total exposure for a child results from dermal contact with "soft" surfaces such as carpet and hard surfaces such as linoleum. Ingestion, which occurs secondarily to dermal contact with

contaminated surfaces and subsequent hand-to- mouth activity, accounts for just 3 percent of total exposure. These results are largely driven by the default value for the dermal transfer coefficient for a child 1 to 6 years of age (6,000 cm^2/hour). The guidance document does not provide justification for this value. However, the results of a recent study conducted by Cohen Hubal et al. (2006) suggest that this default value appears to be very health protective. In this study, children's exposure to surface pesticide residues was evaluated in a childcare center where the pesticide esfenvalerate had been applied the previous day. Transfer coefficients were based on surface sampling data and pesticide loadings on cotton body suits that the children wore to monitor their dermal exposure.

Dr. Fenske's comment: *I don't believe that it has been established that cotton body suits properly mimic the human skin in regard to contact and transfer of surface residues. There is good evidence to indicate that wet skin will collect more residue than dry skin. The cotton garments used by Cohen Hubal were presumably dry. The authors might wish to explore this issue more carefully, using the current scientific literature.*

OEHHA's response: We agree that the validity of using cotton fabric as a surrogate for human skin has not been demonstrated. However, many of the children in the Cohen Hubal et al. study were in approximately the age range as our target population, and the exposure scenarios (children in a day care center *vs.* children at home) were similar as well.

Nevertheless, our scenario and the scenario evaluated by Cohen Hubal et al. differ significantly insofar as the surfaces in our scenario have been remediated prior to occupancy. Remediation reduces the amount of dislodgeable residue from surfaces, and the surface to skin transfer efficiency is correspondingly reduced. In the Cohen Hubal et al. study, pesticides were applied one day and the study was transfer coefficients were determined the next, with no cleaning in the interim. The authors did not indicate the type of pesticide application, but the range of surface wipe loadings (0.47 to 120 ng/cm^2) suggests crack and crevice application. This represents another significant difference between this scenario and the post-remediation scenario we addressed. In a post-remediation scenario, we do not anticipate that dislodgeable surface loadings will vary over a 250-fold range because the residue that is easiest to dislodge will have been removed.

Original text:
Dermal transfer coefficients calculated using the data obtained from this [Cohen Hubal] study ranged from 10 to 6,000 cm^2/hour. Therefore, the SOPs specify a default value for the transfer coefficient for a child that is equivalent to the maximum value obtained by Cohen Hubal et al. The authors of this study concluded, "...results of this work suggest that the default assumption used by the U.S. EPA OPP [i.e., the SOPs] is reasonable." An alternative interpretation would be that dermal transfer coefficients for children have a

wide range of variability, and that dermal exposures would be more appropriately estimated using a stochastic model, such as SHEDS Multimedia, which accounts for the wide range of children's behaviors and activities. The algorithms and default parameter values prescribed by the SOPs appear to be appropriate for obtaining very health protective, screening level estimates of exposure.

Dr. Fenske's comment: *The U.S. EPA residential SOP approach uses a deterministic model. It uses a relatively conservative value for the dermal transfer coefficient. The Cohen Hubal study demonstrates that the SOP value of 6,000 cm^2/hour is a plausible, upper bound value.*

The authors then introduce their own interpretation of the Cohen Hubal study as a justification for using a stochastic approach. The insertion of this language at the end of the SOP model analysis is awkward. The authors should explain at the beginning of this report that they are going to contrast the deterministic SOP model with the stochastic SHEDS model. This would be more effective than the current approach, which uses the findings of the SOP model to justify the stochastic approach. It is generally acknowledged within the exposure science community that stochastic models are preferred to deterministic models. This point should be made early on in the report.

OEHHA's response: It is worth noting that transfer coefficients calculated by Cohen Hubal et al. incorporate an adjustment factor of 40 percent (upward) to account for transfer of pesticide residue to he hands and feet, which were not covered during their study. The 40 percent factor was obtained from an earlier study by Ross et al. (1990), who evaluated surface-to-skin transfer of pesticides to human subjects engaged in Jazzercise® exercise. We believe the validity of applying a correction factor developed from a study of adults engaged in vigorous physical activity to children in a day care setting is open to discussion.

As noted above, we have revised this portion of the report and eliminated reference to the SHEDS model and the results we obtained with it. An Executive Summary explaining the overall organization and analytical strategy has been added to the report.

i) Exposure Estimates based on the Stochastic Exposure and Dose Simulation Model for Multimedia, Multipathway Chemicals (SHEDS-Multimedia), Version 3 (pp. 20-22)

Dr. Fenske's comment: *The SHEDS model relies on the U.S. EPA's Consolidated Human Activity Database (CHAD). This source should be referenced in the report. Do the authors have any comments to offer concerning the utility of CHAD? Does it provide adequate information for the subpopulation of interest? Is it up to date?*

OEHHA's response: We did not evaluate the CHAD database to determine whether or not it is completely up-to-date. Given that new research that is relevant to this exposure assessment is being published all the time, we suspect it is not. However, we attempted to utilize new information on critical exposure factors if it was available. For example, we utilized the age-specific hand- to-mouth contact frequency distributions published by Xue et al. (2007). Similarly, we incorporated the dermal uptake efficiency for methamphetamine that was determined experimentally by Hui and Maibach (2007).

Original text:
SHEDS-Multimedia can also be run as a two-stage Monte Carlo model (also called an "uncertainty run"), which consists of a series of variability runs with the input variables modified between each variability run to represent uncertainty in the input parameters of the variability runs. However, two stage Monte Carlo simulations were not completed for this report.

Dr. Fenske's comment: *The authors should provide an explanation as to why two-stage Monte Carlo simulations were not conducted for this analysis.*

OEHHA's response: We had two primary reasons for not pursuing a two-stage Monte Carlo analysis. First, we felt that basing a proposed health-based cleanup standard on a more complicated analysis would reduce the transparency of the process we used to generate the standard. In workshops held in California in January and February 2007, explaining one-stage Monte Carlo analysis to health care providers, child protective services personnel, hazardous waste cleanup specialists, fire protection personnel and law enforcement officers was a challenge. Second, we did not believe we had sufficient chemical- and scenario-specific information to pursue a more intensive analysis. For example, we have no information on the surface-to-skin transfer of methamphetamine residues from remediated surfaces. We have relied on a conservative interpretation of the results of surface-to-skin transfer of fluorescent tracers and pesticides, and believe we have over-estimated the value for this parameter. Nevertheless, we have no way of knowing this for certain. Under these circumstances, a two-stage Monte Carlo analysis appears unwarranted.

j) Additional Exposure Assumptions for SHEDS-Multimedia (pp.22-26)

Original text:

1. ***The oral bioavailability of ingested methamphetamine residues following hand-to- mouth or object-to-mouth movements was assumed to be 100 percent.***

An oral bioavailability of 100 percent may be regarded as somewhat health protective because few chemicals are completely absorbed following ingestion. Nevertheless, methamphetamine is known to be well absorbed by all routes of exposure, including ingestion. In addition, its rapid rate of dermal absorption suggests the drug passes readily through biological membranes.

Dr. Fenske's comment: *This is not an additional exposure assumption. The residential SOP model also assumes 100 percent oral bioavailability. Do the authors have any information to indicate that the oral bioavailability of very low levels of methamphetamine is less than 100 percent? If not, then this is a very reasonable assumption. I don't believe that it should be considered 'health protective' unless there is evidence that indicates absorption substantially less than 100 percent. I would refer to this as a simplifying assumption necessary due to lack of data.*

OEHHA's response: We agree with Dr. Fenske's comment, although we do not believe that the original text actually suggests that we regard this to be a health protective assumption. Nevertheless, we made minor changes to this section to ensure that this point was made clear. Oral bioavailability is discussed here because it was not specifically addressed in the discussion of the SOP algorithms.

Original text:
Since the post-remediation surface concentration of methamphetamine is anticipated to be extremely low (the prevailing default cleanup standard is 1 ng/cm^2) and the residue-to-skin transfer efficiency is assumed to have a mean value of just 7 percent, the mass of the drug transferred to the mouth via hand-to-mouth activities is anticipated to be extremely small.

Dr. Fenske's comment: *The authors have not yet discussed this transfer efficiency assumption (assumption 4 later in this section), yet they use it to help justify the oral bioavailability assumption. This is awkward and should be avoided, as discussed previously.*

OEHHA's response: Reference to the assumed value for the surface-to-skin transfer efficiency of methamphetamine residues was omitted from this portion of the text.

Original text:
Therefore the extremely low rate of intake of the drug is not expected to limit its absorption efficiency.

Dr. Fenske's comment: *I am not sure what this sentence is trying to convey. Please clarify.*

OEHHA's response: For some chemicals, oral absorption may less efficient if the rate of intake of the chemical is high. Here, however, the rate of intake is extremely small and would not be expected to affect the bioavailability of methamphetamine.

Original text:
2. ***Based on experimental data, the mean dermal absorption efficiency of methamphetamine was estimated to be 57 ± 7.6 percent (mean ± SD).***

In vitro studies of the dermal absorption of methamphetamine were recently completed by Drs. Xiaoying Hui and Howard Maibach at the University of California San Francisco (UCSF). These studies, which were based on a standard protocol utilizing Franz diffusion cells and human skin samples, indicate that methamphetamine is well absorbed across the skin. Experimental details are provided in a draft report of the UCSF studies, included as an appendix to this report.

Dr. Fenske's comment: *I was not able to find the dermal absorption value (57 +/- 7.6 percent) that the authors cite in the report by Dr. Hui. If the authors intend to use this value they should provide a specific reference to its location in the report.*

I view the 57 percent value as too low for the exposure scenario presented in this report, and suggest that an absorption value of 100 percent would be more appropriate.

By my calculations, considering chemical found in the epidermis, dermis, edge skin, and receptor fluid to be absorbed, Table P-1 in Dr. Hui's report indicates dermal absorption values of 35 percent for 4.10 µg loading, 40 percent for 2.07 µg loading, and 54 percent for 1.09 µg loading. Consistent with many other studies of this kind, the percent absorbed increases as skin loading decreases, and the function is non-linear. The lowest loading in the Hui study is 1.09 µg over 1 cm^2, or approximately 1 $\mu g/cm^2$. In contrast, the maximum skin loading that the authors permit in the SHEDS model is 0.01 $\mu g/cm^2$. Thus, the skin loadings of concern for this report are at least two orders of magnitude lower than those used in the Hui study. The August 2007 SAP minutes included the following observation (page 19): "Failure to account for dependence of absorption efficiency on skin loading is a significant weakness in current [dermal exposure analysis] practice."

At the very low loadings anticipated in this exposure scenario, we can expect a very high percent absorbed. Hughes and colleagues demonstrated this effect quite convincingly for dermal absorption of halogenated compounds (Hughes et al. 2001. Food Chem Toxicol 39:1263-1270). It seems likely that absorption of the very low loadings anticipated for this exposure scenario would approach 100 percent. Thus, a value of 100 percent dermal absorption would appear to be most appropriate for this analysis.

OEHHA's response: The value for dermal absorption efficiency was taken from the first column of data in Table P-4 of the draft report (Hui and Maibach, 2007). The amount of drug remaining in the skin was combined with the amount in the receptor fluid to obtain total dermal absorption. The data from table P-1 were obtained using a receptor fluid pH of 7.4, and most of the drug was lost to evaporation because the hydrochloride salt of methamphetamine was converted to the free base. The data from Table P-4 were obtained with a receptor fluid pH of 5, which is within the range

of normal skin pH. (The normal range is 4.5 to 6.) With the exception of certain solvents such as glycol ethers and dimethyl sulfoxide, few chemicals have an efficiency of dermal absorption as high as methamphetamine.

We disagree with the hypothesis that dermal absorption should be 100 percent at very low skin loadings. Using this logic, the skin would provide no barrier to absorption of any chemical if the concentration were low enough. In fact, the opposite is true: if the skin loading is low enough, the skin will provide a complete barrier to absorption because the mass of chemical will not be sufficient to penetrate the stratum corneum.

Original text:

3. ***The maximum dermal loading of methamphetamine residues on the skin (body and hands) was assumed to be ten times greater than the target cleanup concentration for methamphetamine on surfaces.***

SHEDS-Multimedia incorporates separate variables for maximum dermal loading on the hands and body, although the values for the two variables are usually identical. They are included in the model to prevent multiple contacts from adding to the dermal load indefinitely. Therefore, when the maximum dermal loading is obtained, no additional contaminant can be transferred to the skin.

The target cleanup standard first proposed by the state of Washington and subsequently adopted by several other states is 0.1 µg/100 cm^2, or 1 ng/cm^2. Since the surface cleanup standard is so low, we have assumed that the skin can accumulate up to ten times the state of Washington's cleanup standard. This assumption, combined with methamphetamine's high rate of dermal uptake and an assumed average residue-to-skin transfer efficiency of 7 percent, strongly suggests that dermal loading is the limiting factor in the mass of methamphetamine taken up via the dermal pathway.

Dr. Fenske's comment: *The SHEDS model requires the analyst to input a maximum dermal loading. The decision to limit dermal loading to 10 times the cleanup standard appears to be arbitrary. That is, no scientific justification is provided. Nonetheless, it seems to be a reasonable upper bound value for this exposure analysis. I consider it a good judgment call.*

The authors tend to cloud the discussion of this assumption by introducing information on an assumption (7 percent transfer efficiency) that has not yet been presented. Mention of this latter assumption is not necessary.

OEHHA's response: Reference to the assumed surface-to-skin transfer efficiency has been omitted from this portion of the report.

Original text:

4. ***The mean surface residue-to-skin transfer efficiency for methamphetamine was estimated to be 7 percent for all types of surfaces.***

Residue-to-skin transfer efficiency is likely dependent on the chemical properties of the contaminating substance and (if applicable) the carrier in which the chemical is present. Nevertheless, the transfer efficiencies reported by Camann et al. (2000) for chlorpyrifos, pyrethrin I and piperonyl butoxide – three chemically distinct substances – were not remarkably different in most cases.

Dr. Fenske's comment: *The Camann citation is a set of PowerPoint slides. I question whether it is appropriate to use these unpublished data in this analysis. Also, I am not sure what the report authors mean when they say that transfer efficiencies "were not remarkably different in most cases." Does this mean that they were remarkably different in some cases?*

OEHHA's response: The last sentence here was changed to reflect the fact that the range of transfer efficiencies for these three chemicals was generally less than 2-fold under a wide variety of conditions (dry palms, palms wetted with water, palms wetted with saliva, and palms wetted with the surfactant dioctyl sodium sulfosuccinate). As noted in response to a previous comment (page 32), Beamer et al. (2008) also concluded that the surface-to-skin transfer efficiencies for these three chemicals varied over a relatively narrow range. A reference to the Beamer et al. paper has been added to the revised exposure assessment report.

Original text:
The default distributions for the transfer efficiency parameter (beta distribution; shape 1: 0.6; shape 2: 8.4; mean 0.07) that were supplied with the SHEDS model is based on two references, one conducted by Nishioka (2003) under contract to U.S. EPA and the other published by Cohen Hubal et al. (2005).

Dr. Fenske's comment: *The Nishioka (2003) citation is not listed in the references at the end of the report. I was not able to find the specific values listed above in the Cohen Hubal article. Presumably, these values were calculated by the SHEDS scientists.*

The surface residue-to-skin transfer efficiency parameter is probably the weakest element of the SHEDS model and therefore of this exposure analysis. The sensitivity analysis presented on pages 37-38 of the report makes it clear that this parameter is the most critical element of the exposure analysis.

The FIFRA SAP August 2007 minutes include the following statements (page 19): "The Panel's greatest concern was about dermal exposure analysis. SHEDS appears to use both the transfer efficiency (TE) and transfer coefficient (TC) approaches in its assessments. The Panel noted that, at present, the

documentation appears to favor the use of the TE over TC approach. The Panel urges use of a scientifically defensible approach to dermal exposure estimation, and notes that the current state-of-the-practice of dermal modeling in the regulatory sphere is weak. The SHEDS dermal protocol is regarded as state-of-the-practice, not state-of-the-science. The Panel noted that the TE approach is misnamed, as it does not represent efficiency, has no inherent internal logic (it merely represents observed similarities), and cannot incorporate different types of surfaces or those with varying degrees of contamination. . . . Therefore, the Panel urges caution in use of this approach. . . . "

In my view, these concerns raised by the SAP indicate the need for a careful revisiting of the use of the SHEDS model for this exposure analysis, with particular scrutiny on the transfer efficiency parameter. I am uncomfortable with the fact that this parameter relies on a single laboratory study. We should have several studies that confirm this parameter before declaring it a valid representation of transfer efficiency. I also note that this study used a relatively novel method for quantification of skin exposure -- fluorescent imaging. My work in the 1980's was the first to quantify skin exposure using fluorescent imaging; I have visited the Battelle laboratory where the Cohen Hubal et al. work was conducted; I also served as a peer reviewer of the Ivancic et al. paper that describes the quantitative method for fluorescent imaging. I believe Dr. Ivancic has moved this field forward significantly with his very meticulous work. Nonetheless, my own experience in this field warns me that it is quite possible to under-predict skin exposure with such methods due to fluorescent quenching. It would be reassuring to have these results corroborated by a more traditional method such as chemical extraction and analysis.

This brings us to the later Cohen Hubal (2006) study. This was a real-world study in child care centers, with children wearing cotton garments that were extracted and analyzed for pesticides. Transfer coefficients (cm2/hr) rather than transfer efficiencies were reported, consistent with the SAP concerns. The authors discuss this study in the last section of their report (pp. 40-41). They note that Cohen Hubal study found transfer coefficients in excess of the 6,000 cm2/hr value used in the residential SOP model. However, they do not view these results as helpful in defining surface-to-skin transfer. Instead, they conclude that the default values in SHEDS are most appropriate for this analysis.

I would urge the authors to reconsider this decision. I was struck by the fact that the Cohen Hubal et al. (2006) study found median transfer coefficients for infants of 1,700 cm2/hr in one visit and 1,200 cm2/hr in another. Although 3-5 times lower than the 6,000 cm2/hr value used in the residential SOP model, these values are substantial, suggesting that transfer may be more efficient in these real-world environments than in the laboratory. I believe it would be worthwhile to run the SHEDS model using a transfer parameter derived from the Cohen Hubal child care center study.

OEHHA's response: The Nishioka (2003) reference has been added to the list of references. As noted earlier, the transfer efficiency distribution calculated by the developers of the SHEDS model provides a mean transfer efficiency of 7 percent. This is significantly higher than the range of mean values (1-4 percent) calculated by Beamer et al. (2008) based on an evaluation of multiple research reports on the transfer of three pesticides from two types of surfaces.

We recognize there are uncertainties associated with using transfer efficiencies as a basis for estimating dermal exposure. However, we also believe there are uncertainties associated with the use of transfer coefficients. There are summarized in our responses to Dr. Fenske's last comment (page 57) and the comment on pages 47-49. Despite these uncertainties, we believe we have over-estimated dermal exposure by over-estimating the efficiency of surface-to-skin transfer of methamphetamine residues *from previously cleaned surfaces*. The adoption of the transfer efficiency distribution calculated by the developers of the SHEDS model was a precautionary assumption that was made in response to the lack of chemical- and scenario-specific data, that is, the lack of data characterizing the transfer efficiency of methamphetamine residues from remediated surfaces.

While there were aspects of the study by Cohen Hubal et al. (2006) that are similar to ours, there were also significant differences. Foremost among these is the fact that the study did not involve dermal exposure to residue remaining after the surfaces had been cleaned. Rather than conduct a conduct a more intensive evaluation of data whose relevance to our exposure scenario was marginal, we chose instead to use age-specific behavioral data (e.g., surface contact frequencies and hand-to-mouth frequencies) in combination with a conservative (high) estimate of the actual surface-to-skin transfer efficiency. By over-estimating dermal exposure, the estimated target cleanup level is lower than it otherwise would have been.

Original text:

5. *Contact with uncontaminated surfaces or is assumed not to deplete methamphetamine residues from the skin.*

SHEDS allows the user to specify a value for contaminant depletion from the skin as result of contact with uncontaminated surfaces (parameter 3 (d), "removal efficiency during events without water"). The exposure scenario that this exposure analysis is based on assumes that all surfaces are uniformly contaminated with methamphetamine, so contact with uncontaminated surfaces would be unlikely to occur. We have conservatively assumed that contact with uncontaminated surfaces is not a mechanism of contaminant depletion from the skin; all the residue that adheres to the skin as a result of contact with contaminated surfaces is assumed to remain on the skin until removed (albeit partially) by washing.

Dr. Fenske's comment: *I agree that this is a health protective and reasonable assumption.*

OEHHA's response: No response required.

Original text:

6. ***Methamphetamine is assumed to be present on surfaces as a chemical film or residue; soil and dust inside the home were assumed not to be contaminated with methamphetamine.***

SHEDS-Multimedia has separate inputs for contaminant concentration as a "residue" on surfaces and as a constituent of soil and dust in the home. We have assumed that methamphetamine is only present as a surface residue; the concentration in soil and dust inside the residence is assumed to be zero. This assumption is based in part on the relatively low octanol:water partition coefficient of methamphetamine (log P = 2.07). In the outdoor environment, chemicals with partition coefficients this low do not adsorb readily to soil and translocate readily from the surface to groundwater if spilled onto soil. There are no data available on the physical form of methamphetamine as a contaminant inside a residence. A portion of the chemical may indeed be adsorbed to soil or dust particles, but there is no basis for estimating the percentage that is adsorbed to particles and the percentage that is not. Since a single distribution was used to characterize the surface-to-skin transfer of methamphetamine residues, this assumption should not have a material effect on the exposure estimates generated by the model.

Dr. Fenske's comment: *I agree with the authors' rationale for this assumption.*

OEHHA's response: No response required.

k) Justification for Parameter Values used in SHEDS-Multimedia

Dr. Fenske's comment: *I am generally in agreement with the parameter values used in SHEDS-Multimedia, with the exception of the surface-to-skin transfer parameter, as discussed above. Also, it may be necessary to include inhalation as an exposure pathway. I am concerned that a number of the parameters do not appear to be based on peer reviewed reports or articles. I suggest that the authors make a final review of the sources of the inputs in the model.*

OEHHA's response: As noted in our responses to previous comments, data describing the transfer efficiency of methamphetamine residues from surfaces to skin are lacking. Furthermore, to our knowledge, data describing the surface-to-skin transfer of *any* chemical *from a remediated surface* are also unavailable. Lacking this data, we have made the precautionary assumption that the transfer efficiency distribution calculated by the developers of the SHEDS model, which is based on transfer of fluorescent tracers from unremediated surfaces, very likely over-estimates the true transfer efficiency of methamphetamine from a remediated surface. The

analysis of experimentally determined transfer efficiencies for three pesticides from unremediated carpet and vinyl surfaces (Beamer et al., 2008) supports the contention that assuming a mean transfer efficiency of 7 percent most likely leads to over-estimation of actual exposure.

The conclusions of the report by Beamer et al. also appear to be consistent with the results of unpublished research that was conducted under contract to U.S. EPA (e.g., Camann et al., 2000). The studies conducted by Martyny et al. were provided to us prior to their submission for publication. One of these reports was published in April 2008 and another (Van Dyke et al., 2009) was just published. We anticipate that reports describing the results of the recently completed decontamination studies will be published in the near future.

Remediation removes the great majority of dislodgeable residue from surfaces (Martyny, 2008). If additional cleaning using a moderately aggressive cleaning techniques and a solvent-based cleaning agent (Simple Green®) is not a particularly effective means of removing additional methamphetamine residue from surfaces, we do not believe that the routine activities of individuals living in a remediated residence are likely to create significant levels of airborne methamphetamine. We believe conjecture about potential contamination "hot spots" should more rightly be directed toward the cleanup and verification procedures that are needed to demonstrate that a former clandestine methamphetamine lab meets the proposed target cleanup level and is fit for re-habitation.

l) Sensitivity Analysis: Evaluation of Changes in the Values of Individual Parameters on Estimates of Absorbed Dose

Dr. Fenske's comment: *This analysis was discussed previously in regard to surface-to-skin transfer.*

OEHHA's response: We agree that surface-to-skin transfer is a critical parameter in this analysis, and we believe that we have over-estimated its actual value because the surfaces in our scenario have been cleaned to meet the proposed target remediation standard before exposure can occur.

m) Comparison of Exposure Estimates based on SHEDS-Multimedia and the Standard Operating Procedures (SOPs) for Residential Exposure, and Rationale for Use of SHEDS-Multimedia to Derive a Risk-Based Cleanup Level for Methamphetamine

Dr. Fenske's comment: *The residential SOP model was designed to provide screening level exposure estimates in the absence of data, as the authors indicate. However, it is possible to refine the residential SOP model as data become available. If we accept the central assumption of this report – pesticide residue data can be used to estimate methamphetamine residue exposure – then new data from pesticide exposure studies could be used in the SOP model to produce more*

realistic exposure estimates. I would urge the authors to re-calculate exposure estimates with the SOP model, using the best available scientific data.

In summary, I am not convinced that the comparison of the results generated by the two models is a fair one. I came away with the impression that the Residential SOP model served as a 'straw man' for the SHEDS-Multimedia model. That is, the SOP model, which was published in 1997 and revised in 2001, was presented as is, with no new information added; whereas, the SHEDS model parameters were often based on the latest science available in this field. The report states (page 12), "the SOPs were intended to be used both as a screening tool, and for more refined risk assessments which chemical-specific data and information are available." If data and information from the more recent pesticide exposure studies were incorporated into the SOP model, I suspect that the gap between the models' estimates would narrow considerably.

The authors should also consider that the SHEDS model is not particularly transparent. There are so many variables and assumptions incorporated into the model that it is difficult, even for someone steeped in this scientific field, to feel complete confidence in the validity of the output. I can't imagine how this would appear to someone less familiar with dermal exposure analysis. In contrast, the residential SOP model is relatively simple and understandable. If it turns out that the results from these two approaches – after incorporation of the most current scientific information – are roughly comparable, then OEHHA might find some advantage to the SOP model in regard to communication with other state officials and with public stakeholders.

<u>OEHHA's response:</u> We too were concerned about transparency, and that was one of our reasons for not pursuing a two-stage Monte Carlo analysis using the SHEDS model. Furthermore, we believe the SOP algorithms might rightly be regarded as deceptively transparent because most of their uncertainty is distilled into a single parameter, the transfer coefficient. As noted in response to an earlier comment, a transfer coefficient incorporates contact frequency, contact area, exposure duration and transfer efficiency under a single "umbrella" term. It is an empirically derived ratio between dermal exposure, expressed in units of µg/hr, and surface loading, expressed in units of $\mu g/cm^2$ (Cohen Hubal et al., 2006), and is scenario-specific (Fenske, 1993). If its value changes under different exposure scenarios, it is difficult to determine which of the component parameters changed or how much they changed. For example, different transfer coefficients for 1-2 year olds *vs.* 10-12 year olds might be due to differences in contact rate and contact area, but additional studies would need to be conducted in order to validate this hypothesis.

With the SHEDS model, we chose to base our exposure estimates on transfer efficiency in combination with age-specific distributions characterizing the contact behaviors of children in our target age range. Therefore, age-specific distributions for the frequency of hand and body contact with surfaces (contact events/hr), the contact area associated with each event (cm^2/contact event), and the fraction of body surface

area that is unclothed could all be incorporated as separate variables into the analysis. Certainly, each of these parameters has uncertainty associated with it, but each is subject to experimental investigation and the distributions describing them will be improved as new data become available. Taking the approach, the only "residual" uncertainty (i.e., the uncertainty that is unlikely to be addressed experimentally in the foreseeable future) the distribution characterizing the surface-to-skin transfer efficiency of methamphetamine from a remediated surface. Given the lack of chemical- and scenario-specific data, we intentionally chose to over-estimate the value for this parameter, relying on a distribution that was developed from surface-to-skin transfer of chemical residues from unremediated surfaces. This was a precautionary decision that was taken to ensure that the proposed target remediation standard would not present a significant risk of adverse effects on the health of future occupants of a former clandestine methamphetamine lab.

Response to Comments on the Revised Draft Document, *Assessment of Children's Exposure to Surface Methamphetamine Residues in Former Clandestine Methamphetamine Labs, and Identification of a Risk-Based Cleanup Standard for Surface Methamphetamine Contamination* (OEHHA, December 2008)

I. Comments from Mr. Tony Ohrazda, Environmental Health Specialist II, Clandestine Drug Lab Remediation Program, Tacoma-Pierce County Health Department, Tacoma, Washington

1. Assumption number 6 essentially says that the source concentration does not deplete over time, and Assumption number 2 assumes a 3-4 month exposure due to a perceived depletion over time.

   Comment: These two assumptions appear to be contrary to one another.

   Response: The non-depletion assumption was made to provide a conservative estimate of the daily exposure a child would receive over a 90-day period. Had we assumed that the surface concentration declines over time, the average daily dose over the sub-chronic exposure period would have been lower. This assumption also simplifies the analysis and avoids the need to justify a particular algorithm that describes the rate of surface residue depletion over time.

   However, exposure cannot occur without transfer of methamphetamine residue from contaminated surfaces to skin. It is reasonable to presume that transfer to clothing and other objects will occur as well, and additional residues will be removed whenever surfaces are cleaned. As a result of these removal processes, the concentration of methamphetamine residue on indoor surfaces will decline over time. Unfortunately, data describing the rate of decline are not available.

2. The risk-based cleanup standard was calculated by applying a sub-chronic RfD value.

   Comment: If the RfD had an additional uncertainty factor applied to extrapolate sub-chronic to chronic, how would that change the calculated risk based cleanup standard?

   Response: In general, an uncertainty factor of 10 is applied to extrapolate a chronic RfD from sub-chronic data. This is not always the case, however. As noted in the response to comments on the RfD document, the U.S. EPA's chronic RfD for the pesticide DDT is based on a 27-week feeding study in rats and an aggregate uncertainty factor of 100. A 10-fold uncertainty factor was used to estimate a NOEL observed in the rat study to a human NOEL, and a second 10-fold uncertainty factor was used to account for variation in human sensitivity to the pesticide. An uncertainty factor for subchronic to chronic conversion was not included because the toxicity database included a corroborating chronic study.

   We do not believe that a chronic exposure scenario is justified for the following reasons:

- The mass of methamphetamine contamination present on indoor surfaces in a remediated residence is finite.
- Multiple mechanisms for removal and consequent depletion of residue levels exist.
- The age-specific behaviors of young children that lead to increased exposure to chemical residues on surfaces are of limited duration.

3. Assumption number 3 states that the inhalation route of exposure does not represent a significant exposure pathway. Inhalation was not included in either of the two models used.

   Comment: Wouldn't the very same mechanisms (uptake and cleaning) used to justify the reduction of source (sub-chronic rationale) likely cause some re-suspension of methamphetamine?

   Response: Some resuspension may occur. However, we believe the concentration of resuspended residue in indoor air will be small for the following reasons:
   - The decontamination studies conducted by Martyny (2008) indicate that it is difficult to remove methamphetamine residue from a surface that has already been remediated. Therefore, the mass of methamphetamine resuspended by various mechanical processes (e.g., walking across cleaned vinyl flooring) is likely to be small.
   - Resuspended methamphetamine will be diluted in indoor air.
   - Additional dilution will occur as a result of the air exchange with uncontaminated outdoor air.

   Furthermore, re-suspension of surface residues will lead to depletion of surface residue levels, which in turn will reduce exposure via dermal contact and subsequent transdermal absorption and inadvertent ingestion. This is because the mass of methamphetamine available for exposure is finite.

   Comment: What affect would applying a very low factor to account for an inhalation route have on the calculated risk based cleanup standard?

   Response: Very little, if any. As noted above, assuming that a portion of the methamphetamine residue on surfaces is re-suspended and becomes airborne forces us to assume that the concentration of the drug on surfaces has been depleted, i.e., it is less that it would be otherwise. As a result, accounting for exposure via inhalation would reduce exposure via the other complete exposure pathways (dermal contact followed by transdermal absorption and inadvertent ingestion). Most of the airborne methamphetamine would not be inhaled because of dilution in indoor air and subsequent exchange of indoor air with uncontaminated outdoor air.

4. Using the SOP model for calculating dermal dose rates, the authors differentiate between carpet and hard surface flooring, and come up with two different dose rates. The variables in each equation are identical with the exception of duration. The assumption is that only kitchens and baths are hard surfaced, while all other areas of a house are carpeted. OEHHA uses the variable of 4 hours/day in a kitchen or bath, while 8 hours a day in a carpeted area. Therefore the dose rate for carpet is twice that of hard surface.

Comment: Carpets are generally removed in a post decontamination scenario. If the authors are going to make the assumption that all source material has been removed in a post decontamination scenario (i.e. HVAC) why not assume all carpet has been removed? Is it a correct assumption that only kitchens and baths are hard surfaced?

Response: For clarification, the equations used to estimate exposure via contact with carpet and hard surface flooring were taken directly from the SOP guidelines, which were developed by U.S. EPA. This is not a model that OEHHA developed. The assumptions that an individual spends 4 hours/day in a kitchen or bath and 8 hours/day in carpeted areas of the home were also taken directly from the SOP guidelines.

We did not assume that the HVAC system was removed prior to re-occupancy of a former clandestine methamphetamine lab. We assumed that the surfaces of the HVAC system had been evaluated and cleaned if necessary, and did not constitute an unremediated reservoir of methamphetamine contamination. In other words, we assumed that the cleanup contractor did the job he was hired to perform.

Our exposure scenario assumes that *all* surfaces are contaminated with methamphetamine at the designated cleanup level. If the cleanup contractor and property owner determine that replacement of flooring or any other interior surface material is appropriate, and the remaining surfaces meet the proposed cleanup standard, then the daily exposure will be less than what we have estimated. This would provide an extra margin of safety for future residents.

We do not believe it is correct to assume that only kitchens and baths have impervious flooring. This is not a critical assumption in the SOP model since the per hour dose rates for carpet and hard surfaces are identical in our exposure scenario.

5. SOP discusses hand to mouth transfer.

Comment: They (who are "they") use a 3-year old age group because "at the time the SOP was written, this was the youngest age group for which data on hand- to-mouth activity were available". The "3 year-old group" does not satisfy the most likely/susceptible population. This data is from the 1996 US EPA exposure Factors Handbook. In reading Dr. Fenske's comment (p-102) addressing this issue, OEHHA responds by stating "Exposure via incidental ingestion was re-calculated using an average hand-to-mouth contact frequency of 19 contacts/hour and an average body weight of 12 kg." The end result was an order of magnitude increase in the Total Estimated Exposure. OEHHA describes how this increase affects the SOP model in the "Analysis and Interpretation" section of the report. The range of exposure estimates used in the SHEDs model appears to be 1.4 -15 contacts per hour. Therefore the SHEDs model never reaches the average contact frequency determined by Xue et. al. (2007). It is not clear to me what OEHHA is implying in their analysis and interpretation. It is clear that OEHHA is comfortable with adhering to the original data rather than the Xue et. al. (2007) data, as the 1996 US EPA exposure Factors Handbook data remains in the revised draft.

Response: "They" are the U.S. Environmental Protection Agency. The SOP guidelines were originally prepared in 1997 and revised in 2001. Therefore, at the time these guidelines were written, the 1996 Exposure Factors Handbook reflected the most recent data available on a variety of exposure parameters.

The commenter has confused hand-to-mouth and object-to mouth frequencies. The SOP guidelines only provide an algorithm for estimating inadvertent ingestion via hand-to-mouth transfer. They do not address inadvertent ingestion via object-to-mouth transfer. The SHEDS model provides estimates of exposure via both pathways.

Using the SHEDS model to calculate inadvertent ingestion exposure via the hand-to-mouth pathway, we utilized the distribution published in 2007 by Xue et al. (mean of 19.6 contact events/hour). (See Table 3, page 37 of the Revised Draft.) To calculate inadvertent ingestion exposure via the object-to-mouth pathway, we utilized the distribution cited in Paromita Hore's 2003 Ph.D. dissertation (5 ± 4 contact events//hour, with a range of 1.4-15). (See Table 3, page 38 of the Revised Draft.)

Comment: What effect does applying 0.007 mg/kg-day instead of 0.00495 mg/kg-day have on the calculated risk based cleanup standard using the SOP Model?

Response: The estimated exposure and the cleanup standard are inversely proportional to one another. Therefore, if the proposed cleanup standard were based on the results of exposure estimate provided by the SOP model, increasing the estimated daily exposure by 41%[59] would produce a proportionate decrease in the cleanup standard.

Comment: What effect would an increase in the range of "Object-mouth contact rate" to conform to Xue et. al. (2007) data have on the SHEDs model?

Response: The commenter has confused hand-to-mouth and object-to mouth frequencies. Using the SHEDS model, the distribution describing the hand-to-mouth for 1-2 year old children (Xue et al., 2007; Table VI) was used to estimate inadvertent ingestion exposure via the hand-to-mouth pathway. This distribution for children 6 to 12 months of age (18.9 ±17.4 contacts/hour) was very similar to the distribution of 1-2 year olds (19.6±19.6 contacts/hour). Inadvertent ingestion exposure via the object-to-mouth pathway, we utilized the distribution cited in Paromita Hore's 2003 Ph.D. dissertation (5 ± 4 contact events//hour, with a range of 1.4-15).

Comment: Would the study be better served by utilizing the more recent and more applicable (target population) data? Would utilizing the more recent data be more health protective?

Response: Not necessarily. Parameter values used in the SHEDS model were based on review of the available data and consultations with Drs. Smith and Glen of Alion Science and Technology, U.S. EPA's contractor for development of the SHEDS model. Parameter values

[59] [(0.007-0.00495)/0.00495] x 100

specific for the population of greatest concern (6-18 month old children) were used where possible. When the data were published was not a consideration in our decision-making process.

Comment: What are the benefits of using the 1996 data?

Response: We assume this is a rhetorical question. We attempt to use the best data available, irrespective of when it was published.

6. The SHEDS model incorporates several assumptions. Assumption 3 states that the maximum amount of methamphetamine that can accumulate is 10X the cleanup level. They further state that the dermal loading is the "limiting factor" in the mass of methamphetamine taken via the dermal pathway.

   Comment: How was the 10X factor derived?

   Response: The assumption regarding the maximum amount of methamphetamine that can accumulate on the skin was based on best professional judgment, following consultation with Drs. Luther Smith and Graham Glen of Alion Science and Technology, U.S. EPA's contractor for development of the SHEDS model. Our primary objective was to ensure that the value we assumed for this parameter did not have a significant impact on the overall exposure estimate. As noted in the Sensitivity Analysis (Table 5, page 48 of the Revised Draft), reducing the assumed value for this parameter by two-thirds had a trivial impact on the overall exposure estimate.

7. The study indicates that dermal absorption of methamphetamine residues on the body is by far the most significant exposure pathway (excluding respiratory). The study also states that any increase in meth loading on the skin leads to a proportional increase in absorbed dose. Given these statements it seems that modifying the 10X CUL[60] dermal loading maximum would greatly affect the proposed CUL. However, the sensitivity analysis appears to indicate that no significant change occurs if the maximum dermal loading is *decreased* by a 3-fold factor.

   Comment: How would the SHEDs model be impacted if the dermal loading was *increased* by a 3-fold factor?

   Response: Dermal loading was examined in the SHEDS sensitivity analysis, summarized in Table 5 and discussed on page 47 of the Revised Draft. We noted that a 3-fold increase in surface-to-skin transfer efficiency led to approximately a 3-fold increase in the 95th percentile estimate of total exposure. The same table notes that a 3-fold decrease in the *maximum* dermal loading for hands and body produced no change in the total exposure estimate. Together, these results suggest that exposure via transdermal absorption is primarily affected by the surface-to-skin contact rate, contact area, exposed skin surface area, and the amount of time spent in the contaminated environment.

[60] We presume that "CUL" refers to cleanup level.

Comment: If bathing may increase absorption rates (Moody & Maibach, 2006) and infants typically get washed every other day, then shouldn't that be incorporated into the activity diary of the model has an increase of burden, not a decrease of burden?

Response: The paper by Moody and Maibach discusses the "wash-in" phenomenon for several chemicals including the mosquito repellant DEET. We have no data for methamphetamine. Washing the skin may increase transdermal absorption of methamphetamine or reduce it. Wash-in phenomenon has only been characterized for a handful of chemicals. (See Table 1 of the Moody and Maibach report.) Lacking experimental evidence that the wash-in effect is applicable specifically to methamphetamine, we believe it would be inappropriate to assume that it affects the transdermal absorption of the drug in our exposure calculations.

Our analysis assumed that 57% of the methamphetamine that is applied to the skin is absorbed, which is very high compared to the dermal absorption efficiencies of most chemicals.

8. The SHEDS model was run for a population of 100 children 1-2 years of age for 90 days.

Comment: How would the SHEDs model be impacted if it were run for a population of 0-1 year olds at a duration considered to be a chronic exposure?

Response: The SHEDS model does not estimate exposure for children 0-12 months of age. In this regard, the recent report by Firestone et al. (2007; cited on page 19 of the Revised Draft) indicates that floor mobility does not increase until about 6 months of age. Therefore, children 0-6 months of age are likely to be less exposed to surface contamination that children in the target age range selected for our analysis (6-18 month of age).

The output from the SHEDS model is an estimate of dose in units is mg/kg-day, based in part on the assumption that the concentration of methamphetamine on indoor surfaces remains constant for the entire duration of exposure. Therefore, running the model for a multi-year duration of exposure (and assuming no age-related changes in behavior over that time period) would not change the daily exposure estimate.