AUGUST 2007 FIFRA SCIENTIFIC ADVISORY PANEL RECOMMENDATIONS FOR SHEDS-DIETARY AND SHEDS-RESIDENTIAL MODULES (SUMMARIZED)

AND EPA RESPONSES

Background Material for July 20-22 2010 FIFRA Scientific Advisory Panel Meeting

TABLE OF CONTENTS

PREFACE

Over the past ten years, the Agency has requested the Panel to review several probabilistic dietary exposure software models.[1] These have included DEEM-FCID™, Calendex-FCID, CARES™, LifeLine™, and an earlier (specialized) version of SHEDS (SHEDS- Wood) designed to assess exposures and doses of wood preservatives. SHEDS-Wood was presented to the Panel on August 28, 2002 and December 3-5, 2003, and focused on children's dermal and non-dietary ingestion exposure to chromated copper arsenate (CCA) on treated decks and play sets.

In August 2007, SHEDS-Multimedia version 3 underwent review by FIFRA SAP.[2] This earlier version of SHEDS was an aggregate (single chemical) version that was able to assess residential post-application exposures. During that SAP, a conceptual approach to a planned dietary module for SHEDS-Multimedia was also presented to and reviewed by the Panel. At that time, the Agency directed a number of questions to the Panel regarding usability and potential improvements to the SHEDS-Multimedia residential module, as well as approaches to assessing dietary exposures, which would be coded into SAS and SHEDS in a future version. At this 2007 SAP, the Panel stated that it was generally "impressed with the current version of the SHEDS model and future plans for the model…" (SAP 2007, p.10), that "the model algorithms appear to be technically correct... [and that] the code is clear enough that the algorithms can be easily followed" (SAP 2007, p.10). In addition, the Panel stated that "the GUI is helpful and straightforward, but …could be improved by adding context specific information that is clearly available at all times" (SAP 2007, p.10). As part of its report, the Panel did have a number of suggestions on the organization, clarity, completeness, and usefulness of the model manuals.

Since that time, Agency staff from the Office of Pesticide Program (OPP) and the Office of Research and Development (ORD)'s National Exposure Research Laboratory (NERL) have continued to collaborate to develop and code the dietary module for the SHEDS-Multimedia software and to improve and update the residential module considering the Panel's 2007 suggestions. These efforts were geared toward producing a SHEDS-Multimedia Version 4.0 model, with both a residential and dietary module, that could be used to conduct an aggregate (single chemical) exposure assessment for a pesticide or other multimedia chemical, or a cumulative (multi-chemical) exposure assessment.

To date, this collaborative effort between ORD and OPP has produced separate SHEDS-Dietary and SHEDS-Residential exposure assessment software programs, each of which address a number of the 2007 Panels' ideas and concerns relating to user interface, algorithms, usability, utility, and documentation. The current (2010) SAP is being requested to review each of these two models, which are considered as modules of SHEDS-Multimedia version 4, and a proposed approach to merge them (i.e., calculate dietary and residential exposure for the same simulated individual after food consumption and activity pattern diaries are appropriately matched) for the next iteration of SHEDS-Multimedia.

The purpose of this background document is to recap and summarize for the current (2010) Panel the earlier 2007 comments and to provide the Agency's response to them. It is divided into two sections, with the first relating to the dietary module and the second relating to the residential module. These sections highlight research and development on the SHEDS-Multimedia dietary and residential modules that has occurred since the 2007 SAP; it is hoped that this document provides some background and context with respect to the Agency's continuing activities and efforts aimed at advancing SHEDS in particular, and exposure science in general, and that it will assist the Panel in its current deliberations.

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[1] Documentation for these models are listed in the April 2004 FIFRA SAP, Model Comparison. See website for meeting minutes and documents: http://www.epa.gov/scipoly/sap/meetings/index.htm.

[2] See http://www.epa.gov/scipoly/sap/meetings/2007/081407_mtg.htm for meeting materials and background documents

I. DIETARY EXPOSURE

The Agency's charge to the 2007 FIFRA SAP included five questions (3-1 to 3-5) regarding modeling dietary exposures to pesticides. Questions pertained to food residues, food consumption patterns; direct drinking water consumption patterns and the Bayer Drinking Water Consumption Survey; uncertainty analysis to better characterize exposure estimates; and aspects related to regional and seasonal differences in consumption.

Several questions asked of the Panel were partly motivated by the anticipated transition from using CSFII to using NHANES/WWEIA food consumption data in assessing dietary exposures to pesticides. The CSFII data were collected in 1994-1996, and 1998. The 1998 data were from a supplemental survey, conducted in large part to provide EPA with additional data for children. The NHANES/WWEIA database spans 1999-2006 and includes 53, 522 diaries; this is more up-to-date and includes approximately 12,000 more diaries than CSFII. The Agency's Office of Pesticide Programs has been developing food recipes for these new NHANES/WWEIA foods, so that the current dietary exposure models can be updated to include this more current food consumption survey data. The Agency anticipates a public release of those food recipes in summer 2010. SHEDS-Dietary v. 1.0 does not have those new recipes, but used instead a very rough form of these in anticipation of this information being received at a later date. OPP is working to have the NHANES/WWEIA data incorporated into all of the available dietary exposure models, including SHEDS-Dietary. The Agency hopes to conduct dietary exposure assessments using the newer these food consumption data in the near future, but a timeframe has not been developed for that transition.

Finally, the Agency has continued work on other topics noted in the dietary methods paper presented to the 2007 SAP, including Commodity-Specific (Eaters-only) Analyses, and some new contribution analyses. The Agency was not able to incorporate those features into this version of the SHEDS-Dietary GUI. The table in the Appendix to this document summarizes the status of a variety of features/options that are available in SHEDS-Dietary and how they relate to a number of 2007 FIFRA SAP questions, and the Panel may wish to refer to this as it reviews the 2007 SAP comments.

The following sections introduce, by topic area, the questions asked of the Panel in its 2007 review of the (planned) dietary aspects of SHEDS, followed by both a relevant excerpt of the Panel's responses to those questions, as well as EPA's 2010 corresponding responses that indicate how the 2007 SAP comments were – or sometimes were not – able to be incorporated into this version of SHEDS-Dietary. We believe that this background material will assist the Panel in its current review of SHEDS-Dietary v.1.0.

A. Eating Occasion Analyses: Food Residues

Question 3-1: As described in the SHEDS dietary background document, the timing information available in CSFII can be used to model food and indirect water intake throughout the day. With the ability to incorporate the timing of eating occasions in dietary exposure assessments, it is possible to assign either the same residue or a different residue to foods consumed on multiple eating occasions. In certain instances, the former seems logical (e.g., consumption of leftovers) while in other instances the latter appears appropriate (e.g., hash browns at home for breakfast and fried potatoes away from home for dinner). Please comment on developing simple decision rules – as described in the document – for assigning residue to commodities eaten on multiple eating occasions.

2007 Panel Comment: The Panel noted that the Agency's document did not include a clear list of rules for review, and suggested developing a decision diagram or flowchart to describe decision rules for assigning residues to commodities on multiple eating occasions. (p. 31)

***EPA 2010 Response*:** The Agency acknowledges that omission in the 2007 document. The default approach (e.g., DEEM-FCID™) for dealing with residues is to select a single residue for each commodity (RAC-FF) and apply that value to total daily consumption of that particular commodity (RAC-FF). The Agency considered modifying that decision rule based on the information contained in several data fields, including: (1) food item, (2) commodity (RAC-FF), (3) time of eating occasion, (3) source of food (e.g., store, restaurant, fast food, school, etc), and (4) if food was eaten at home or elsewhere. The 2007 background paper did not elaborate what data might be used nor depict a flowchart depicting how those responses would affect whether or not a new residue would be selected.

After having gained some experience assessing dietary exposures expressed on an eating-occasion basis and conducting some preliminary reviews of the food consumption data (see below), the Agency is generally comfortable with the default assumption of selecting a single residue for each modeled person-day for each commodity (RAC-FF). The SHEDS-Dietary module follows that particular assumption. The current version of SHEDS-Dietary includes an option in which separate residues are randomly selected when a person consumes a commodity (RAC-FF) via different food items. The two options available are as follows:

- Option not selected: For each new person-day, select a residue for each distinct Food-RAC-FF-TimeOfDay

- Option Selected: For each new person-day, select a residue for each distinct Food-RAC-FF

The example food diary in the 2007 paper (taken from the 1994-96/1998 CSFII) is reproduced below to illustrate the SHEDS-Dietary algorithm. The food diary indicates that the child consumed 'home fries' (food item=71403000) on two eating occasions: at 10:15 am and 6:00 pm, and fried eggs at 10:15 am; both foods contain the same commodity 'Pork Fat'. If the option "Same food-same residue" is selected, then SHEDS-Dietary will select a new residue for 'Pork Fat' consumed via Home Fries at the 6:00 pm eating occasion. If that option is not selected, the SHEDS-Dietary Module selects a new residue for each of the three eating events if the option is not selected. In either case, SHEDS-Dietary will select a new residue for the 'Pork Fat' in Fried Eggs since it is a different food than 'Home Fries'. [Note: DEEM-FCID will select the same residue for all 3 eating occasions since the Food-RAC-FF combination is the same at all three eating occasions.]

CSFII ID=28517-2-2: 1 yr, M, 13.6 kg			SHEDS-Dietary Option ("same food-same residue")	
Time of Day	Food (COM)	**Commodity** (RAC-FF)	Not Selected	Selected
10:15 am	Home Fries (7140300)	**Pork Fat** (25002930-213)	Residue1	Residue1
	Fried Eggs (3110500)	**Pork Fat** (25002930-213)	Residue2	Residue2
6:00 pm	Home Fries (7140300)	**Pork Fat** (25002930-213)	Residue3	Residue1

2007 Panel Comment: The Panel expressed several concerns regarding the use of such options: "Such level of refinement may not have added value especially when resolution in the food intake diary and residue data (each item in composite data does not contain the same level of residue) is lacking." (p.32)

EPA 2010 Response: The Agency agrees that it would be preferable to use consumption and residue data having similar resolution. We do not know what type of data the users might have available for use in any given dietary exposure assessment. Suppose for example, that there are two persons, one eating a single apple, and another eating four apples in a single day. If single serving residue data were used, then it would be appropriate to select a new residue for each apple that the second person ate, rather than applying a single residue to all four apples consumed that day. If composite residue data were used, then a single value from that composite distribution might better reflect the average residue for those four apples, although the model might underestimate exposures for the first person to whatever extent a composite residue may underestimate residue concentrations for single apples.

If a user had different types of residue data for different commodities, then one might want to apply a different algorithm based on the type of data being used. For example, if someone had concentration data representing single apples, and concentration data representing composited samples for oranges, then one might draw a new residue for each apple consumed, but would draw only one residue for multiple oranges that someone might have consumed on any given day. Implementing such an option would require another layer of programming. Since composite data are generally used by OPP in dietary exposure assessments, the SHEDS-Dietary model retains the option to select only a single residue value for each food item (e.g., raw uncooked apple) consumed on any given day.

2007 Panel Comment: "In addition, the Panel was concerned that making further assumptions without proper support data may introduce additional uncertainties in the exposure analysis. For example, the only way to determine whether the same food forms eaten at lunch and dinner are separate dishes or the same dish as leftovers for dinner may only be mere speculation." (p.32)

EPA 2010 Response: The Agency agrees that decision rules (simple or complex) may be based on limited or no information, but believes that: (i) decision rules can be beneficial in assessing uncertainty in the data and modeling algorithm(s); and (ii) that the information contained in the CSFII/NHANES surveys (food item) allow for educated guesses with respect to some of those uncertainties. In any case, the ability to model with "same food – same residue" option or not can be seen as a form of a sensitivity analysis to help evaluate how these assumption may affects the exposure and risk estimates. In the case of the food diary highlighted above, we do not know whether the 'home fries' that the person ate on the second occasion was a leftover from the morning consumption, or if a brand new batch was prepared using a different bag of potatoes. Since the person consumed the same food on both occasions, the SHEDS-Dietary model has the option to use – or not use -- the same residues for all four ingredients, including the fried potatoes (RAC-FF=0132990-213) to calculate total daily exposures for that person for that particular day. Such an assumption to use the same residue values may overestimate exposure to the extent that a different bag of potatoes (and new residue) may have indeed been used to prepare the second meal. Alternatively, if SHEDS-Dietary drew a new residue for each eating event in which the same Food-RAC-FF was consumed, then the model would underestimate the probability that such a person obtained high residues on both eating occasions if he indeed ate "leftovers". Whichever decision rule is implemented, some explicit modeling assumption will be made - even if the user is unaware of that assumption and resulting effects.

2007 Panel Comment: "For this issue, the first consideration is whether dietary exposure constitutes a major contributor to an overall multi-media exposure that exceeds a regulatory threshold. When dietary exposure is the focus for refinement, high contributing commodities are identified in the initial assessment and the impact of link-day residue for these commodities can then be assessed. .... Once the potential high contributing commodity-residue pairs are identified, the possibilities for repeated eating occasions could then be further investigated. Another generic decision process may be to evaluate how often people eat the same foods within a day or on different days based directly on food intake diary, e.g., CSFII data." (p.32)

> ***EPA 2010 Response:*** The Agency agrees that there is little value added to regulatory decision-makers by examining different residue assumptions in dietary exposure assessments for commodities that do not contribute significantly to an exposure estimate
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> The Agency has performed some analyses of food consumption patterns for selected fruits and vegetables and presented some of those findings to the research community (Nako, et. al., panel discussion at ISEA Conference, 2007). Two patterns that we observed were: (i) that people often consume fresh fruits and vegetables (e.g., apples, grapes, potatoes) on a single eating occasion, and (ii) fruit juices (apple juice, grape juice) are more likely to be consumed on multiple occasions throughout the day. For example, we found that over 90% (618/669) of children 1 to 2 years old eating fresh uncooked apples did so on a single eating occasion, while only 58% (1129/1957) of the children drinking apple juice did so on a single eating occasion. The Agency believes that such food consumption patterns help explain why recovery between exposure events ('eating occasions' analyses) often has limited effects upon the per capita 99.9th percentile for food-only exposure assessments. Accounting for recovery between eating occasions (exposure events) is important if a person obtains significant exposures on multiple occasions throughout the day, but concentration levels in food items that are often consumed on multiple eating occasions (e.g., apple juice, orange juice, bread, etc.), are often lower than those found on fresh fruits (apples, oranges) and vegetables.

2007 Panel Comment: "....the Panel was in general agreement that simple rules have the advantage of complex rules for clarity, uniformity of application, and transparency in operation. ... a simple set of rules in this case can be somewhat akin to a tier approach that is informed by a series of stepwise refinement analysis, progressing toward increasing complexity only when supported by data and the need for fine-tuning the analysis." (p.32)

> ***EPA 2010 Response:*** The Agency agrees that such refinements should only be explored when necessary. The Agency has found minimal effects on food-only analyses upon aggregate exposure at the per capita 99.9th percentile since a large fraction of consumers obtained much of their total daily exposures from a single food on a single eating occasion (e.g., NMC CRA).

2007 Panel Comment: "Since the upper tail is where the main interest lies in risk assessment, it is unlikely that there will be significant gain in changing into random draws of residues for multiple [within-day] eating occasions" (p.31)

> ***EPA 2010 Response:*** The Agency has found that accounting for intra-day recovery often has modest effects (10%-20%) on the per capita 99.9th percentile exposure for food-only exposure assessments, perhaps due to food consumption patterns and reasons noted above.

2007 Panel Comment: Finally, the Panel recommended that the Agency review several data sources that, including Child Development Supplement to Panel Study of Income Dynamics (PSID) and American Time Use Survey (ATUS).

EPA 2010 Response: The Agency has some familiarity with the PSID and ATUS surveys, but has not analyzed those data due to limited time and resources. The Agency is aware that those surveys contain additional data on time use (activity patterns) and may use these data to update the CHAD data base (residential scenarios), but believes those data contain limited information on within-day food consumption patterns. The Agency plans to incorporate the CDC NHANES-WWEIA food consumption data into its dietary exposure models (more on that below - Q5) before exploring other food consumption data sources.

B. Food Consumption Patterns

Question 3-2: Please comment on the 8-record approach in SHEDS-dietary and the selection of age group, gender, season and day-type from which to create the "diary pools". What other approaches does the Panel recommend? Can the Panel suggest any "bounding approaches" that may – based on knowledge of actual eating patterns – provide upper and lower limits for longitudinal exposure estimates (e.g., yearlong consumption of the same diary throughout the year vs. random daily selection of CSFII diaries).

2007 Panel Comment: "The majority of the Panel is convinced that given the data and analysis presented by the Agency, it is not sufficient to construct the longitudinal dietary consumption pattern based on the 8-day eating occasions." (p.33)

EPA 2010 Response: The Agency plans to drop the 8-record approach for some of the reasons cited by the Panel, as well as limited data in the CDC NHANES/WWEIA survey which are restricted to two non-consecutive days. Specifically, the NHANES/WWEIA survey does not disclose the specific dates on which food consumption data (24 hr recall) were collected; therefore, this option cannot be implemented using the NHANES/WWEIA data.

The NHANES/WWEIA data in the current SHEDS-Dietary module contains a DATE field that was randomly generated – those Calendar dates are NOT real since the NHANES/WWEIA publically available datasets do not contain date information. These date values were created since it was difficult to modify the GUI such that users could use the 8-record approach for the CSFII data, but not the NHANES/WWEIA data. Since the Agency is dropping the 8-record option for use with the NHANES/WWEIA survey data, that Calendar date field will be deleted in future versions of the SHEDS-Dietary module.

2007 Panel Comment: The Panel noted that recent findings (Givens et al., 2007 Env. Research), suggests that a minimum of 6 consecutive days' of food consumption in each of 4 seasons would be adequate to represent an individual 1 year dietary consumption pattern. (p.33)

EPA 2010 Response: The Agency agrees that more information per person would be most beneficial for modeling food consumption patterns over medium term durations (1 year). One of the Panel members that also co-authored the Givens et al. paper recently provided the Agency with longitudinal consumption data for a small group of persons. The Agency appreciates these data, and plans to consider them to develop and evaluate methods for generating longitudinal consumption patterns.

2007 Panel Comment: "Some Panel members suggested that the Agency pay attention to the tails, as well as the median of the distribution in terms of consumption patterns. The Agency should treat with skepticism apparent good prediction of upper tail without concurrent good prediction of median. Such a situation assumes that the tail was accurately estimated in the absence of accurate prediction of the distribution or sources of variance." (p.33-34)

EPA 2010 Response: The Agency agrees. Efforts to develop and evaluate longitudinal consumption patterns for the SHEDS-Dietary model will focus on both the overall distribution including median and upper tail.

While modeled results of the upper tail are often robust to simulation uncertainty, the Agency hopes to get good predictions of the median since those are more amenable to use in model evaluation. As noted above, the Agency was provided food consumption data patterns for a small group of persons. These data contain more diaries per person (~40/person/year) than either the CSFII or NHANES/WWEIA surveys, perhaps allowing for evaluation of modeled food consumption patterns against actual consumption patterns for actual persons, although not at the extreme tails.

2007 Panel Comment: "The Panel recommends that the Agency should conduct analysis similar to those already performed with subsets of CHAD database, and see if the D-statistic may be useful for longitudinal implementation."(p.33)

EPA 2010 Response: The Agency has pursued this suggestion. The SHEDS-Dietary module contains this option (D&A method) using total caloric intake to develop longitudinal (multi-day) consumption patterns using the food consumption diaries in the corresponding age and sex cohort for the modeled person (See SHEDS-Dietary Technical Manual.)

2007 Panel Comment: "…the Panel generally agreed that significant value would likely be added to the SHEDS model development by collecting longitudinal dietary consumption, as well as individual behavior/activity data, particularly the activities at the microenvironment level from a small group of study participants stratified by age and gender. … Other Panel members have suggested the possibility of nesting a separate study within the proposed National Children's Study, and that this option should be considered by the Agency." (p.34)

EPA 2010 Response: The Agency agrees with the general message that new and better data, including longitudinal data, can add tremendous value to the development of aggregate exposure models. Agency scientists (ORD and OPP) have also been and will continue to be involved with the NCS study. The Agency also recognizes that scientists in other Agencies (e.g., NIH), and abroad (e.g., EFSA) have addressed longitudinal and other exposure assessment issues (e.g., Q4 Uncertainty Analyses), and aims to keep informed of those efforts through scientific meetings and publications.

C. Drinking Water Patterns

Question 3-3: Please comment on the advantages and disadvantages of providing an option to use the Bayer DWCS data in SHEDS. Please include in your comments any statistical concerns or issues associated with the design and conduct of the DWCS study. [*Clarification to Charge Question 3. EPA recognizes that is has provided each of the Panel members with only background information on the Bayer DWCS….and has not provided Panel members with the Bayer submission itself….EPA will use the thoughts and ideas presented by the Panel in its discussion of this topic and, if warranted at a later date, may present the study and our analysis to the Panel, along with our proposed use of the study as an available option.]*

2007 Panel Comment: The Panel appeared to consider the fixed option as a reasonable method to allocate total 'direct' water intake over the modeled day. However, the Panel noted: "The FIFRA SAP (2005) suggested allocating (direct) water amount to five events – with three occasions during meals

(25% of total per occasion) and two occasions in between meals (12.5% of total per occasion)"; not 6 fixed events as stipulated in the Agency's Eating Occasion analyses.

EPA 2010 Response: The Eating Occasions analyses currently employed by SHEDS-Dietary (and the DEEM-based approach) allocate direct drinking water consumption in 6 equal amounts, and at fixed times: 6 am, 9 am, 12 pm, 3 pm, 6 pm and 9 pm.[3] Our decision to use fixed times vs. the specific meals as recommended by the Panel was made to facilitate programming this option. Specifically, not everyone reported eating three meals (breakfast, lunch, dinner). Trying to determine 'three' primary eating occasions and times for two drinking water events between those eating occasions for all reported food diaries would require additional and likely complex programming (and decision rules).

2007 Panel Comment: In attempting to answer this question the Panel raised 8 questions of its own (resorted and grouped):

1. "Do DWCS drinking water patterns differ very much from the current implementation? The limited analysis made available to the Panel indicated that most individuals have 5 or fewer drinking water events during the day with a modal value of 3 (Figure 4). Distribution is very uniform throughout the 16 hours measured (Figure 5). This would seem to suggest that the approach currently implemented in SHEDS is representative and there is little here to support implementing the 2005 FIFRA SAP recommended allocation."

EPA 2010 Response: Drinking water patterns are as varied as food consumption patterns. Children generally consume more water per kilogram of bodyweight than adults, and as a result, infants and children often have the highest total dietary (food+water) exposures when expressed on a body weight basis at the per capita 99.9th percentile across all age groups.

The observation that drinking water consumption patterns vary considerably across individuals suggests that using a single distribution (i.e., 5 or 6 fixed events) may not capture such variability. The SHEDS-Dietary model includes a second option that allows the total direct water intake as reported by that (CSFII or NHANES/WWEIA) respondent to be allocated over the day, in proportion to the empirical distributions reported in the Bayer DWCS diaries. For a modeled person, the 'drinking water bins' were based on similar age, gender and season (information 'synthesized' in NHANES), as noted in the Technical Manual.

2007 Panel Comment:

2. Can a minor modification of the current implementation move the drinking water pattern closer to the DWCS without having to fully implement the DWCS into the simulation? (p. 35)
3. Can individuals be grouped into drinking water pattern types that are internally homogeneous and externally varied, allowing individuals to be selected to a drinking water pattern "type"? (p. 35)
4. Can "typical" drinking water patterns be discerned from the data that would lead to pattern types that would be easier to model and interpret? (p. 36)

EPA 2010 Response: The Agency concurs that various types of statistical analyses (e.g., cluster or principal components) on the Bayer DWCS data could help identify different 'types' of drinking water profiles. Reducing the number of the reported drinking water patterns into a few 'types' would simplify modeling drinking water exposures and discussing those predicted outcomes. The Agency has not conducted such analyses to date.

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[3] The use of 6 vs. the 5 events as recommended by the Panel was an oversight on the part of the Agency.

The Agency notes that the exposure model would still have to assign each modeled person to one of those 'types'. The food diaries (CSFII or NHANES/WWEIA) and drinking water diaries (Bayer DWCS) reflect behavioral patterns of different people on different days, and merging the information introduces new issues – e.g., a person may have been asleep in one diary at a given time and awake at that time in the other diary. This is a similar problem to using time activity data (CHAD) and food consumption data (NHANES/WWEIA) to combine potential exposures from residential and food uses. The issue is apparent only when the time of day for each behavioral activity (time spent playing on turf) from those corresponding diaries.

The Agency has not conducted further statistical analyses of the Bayer DWCS data as suggested by the Panel. The Agency notes that the NHANES/WWEIA survey recently began collecting information on the precise timing and amounts of direct drinking water consumption, and those food diaries will not require modeling within-day water consumption using either method (fixed approach nor Bayer DWCS data).

2007 Panel Comment:

5. Can the DWCS database be properly weighted to produce population relevant information? This question was voiced by a number of Panel members who were concerned about a number of the sampling aspects of the study. In particular, there is the potential for bias in study results because of the low response rate and high fraction of incomplete diaries. An attempt should be made to compute sampling weights to better match study results (the demographics of study responders) with the (demographics of the) US population. In particular, the Panel wondered which age, race, ethnicity, geographical or other groups were not adequately sampled or whether some of these groups are not represented in the dataset at all. (p. 36)

EPA 2010 Response: Yes, the Bayer DWCS sampling results can be weighted to some degree. The documentation to the Bayer DWCS indicates that the sponsors and primary investigator employed the services of the National Product Database Group (NPD), a marketing firm that maintained a National Home Testing (NHT) panel of 250,000 households. The document stated:

> The NPD group was chosen to conduct this survey because of its experience in tracking the consumption habits of the US population since 1980 through its National Eating Trends (NET®, 2004) service." "The NET maintains a diary panel of 2,000 households to track consumption habits of the US population.
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> "Two nationally represented samples (one for each wave) were extracted" from the NHT panel. "The sample for wave 1 included 3,000 households…randomly selected from the core sample of 250,000 households, while in an effort to increase the number of children in the survey, the sample for wave 2 included 650 households randomly selected from households with children less than 6 years of age in addition to 3,000 households randomly selected from the core sample." (p.9)

The Bayer DWCS data did not include sampling weights (i.e., oversampling households with children), but did include various demographic data, including census region, household income, head of household education, race, date (DD-MM-YY), as well as age and gender of subjects which could be used to weight the sample respondents. While there might be some bias with respect to low response rate and/or under-sampled groups, the direction of such bias is unclear. The Agency does not anticipate using the Bayer DWCS data once the timing of direct drinking water consumption data becomes available in the NHANES/WWEIA survey (2005/2006 onward).

2007 Panel Comment:

6. Will allocation of direct drinking water consumption via an empirical use of the Bayer DWCS data, say via some form of bootstrap sampling methodology, produce results that are markedly different

from a modified fixed drinking water pattern? Preliminary simulation results seem to suggest that it does not (p. 28).

EPA 2010 Response: The Agency has found that the Bayer DWCS option tends to produce slightly higher estimates at the per capita 99.9th percentile than the fixed (6 event) approach. For example, (Nako and Xue, 2006) compared the two methods for several drinking water scenarios for a particular chemical. The Bayer DWCS option provided slightly higher estimates than did the fixed approach for the US population and most age groups (within 10%). As noted in the document, the Bayer DWCS did not collect data for infants, and therefore, the option does not affect estimated exposures for infants. The infant subpopulation often produces the highest drinking water exposure due to their relatively high intake of water (ml/kg bw); however, many of the high consumption diaries reflect indirect water consumption (infant formula) for which eating occasion data (time of day and amounts consumed) are available.

SHEDS-Dietary (and DEEM-Based EO) Estimated Exposure at Per Capita 99.9th Percentile[a]

	Total Daily Exposure SHEDS-Dietary (DEEM-Based EO)		6 Fixed Events (2 hr half-life) SHEDS-Dietary EO (DEEM-Based EO)		Bayer DWCS (2 hr half-life) SHEDS-Dietary EO	
	Food Only	Food+ Water	Food Only	Food+ Water	Food Only	Food+ Water
US Population	37% (35%)	116% (119%)	35% (34%)	55% (58%)	35%	66%
Infants	41% (42%)	278% (285%)	41% (41%)	139% (147%)	-	-
1-2 yrs	82% (77%)	144% (145%)	77% (72%)	91% (95%)	77%	100%
3-5 yrs	60% (64%)	131% (135%)	57% (60%)	71% (77%)	57%	101%
6-12 yrs	45% (50%)	84% (87%)	43% (46%)	46% (48%)	43%	62%
13-19 yrs	32% (30%)	88% (91%)	31% (28%)	44% (46%)	31%	53%
20-49 yrs	31% (30%)	91% (94%)	30% (29%)	52% (54%)	30%	64%
50Plus	33% (35%)	70% (72%)	32% (34%)	45% (47%)	32%	46%
Females 13-49 yrs	31% (30%)	89% (92%)	30% (29%)	50% (50%)	30%	55%

[a] From Nako and Xue (2006). The DEEM-Based EO (Eating Occasion) results as provided in this table are similar to the Cross-Sectional SHEDS-Dietary Eating Occasion results, but that procedure does not allow empirical use of the Bayer DWCS data. They are presented here for comparison purposes.

2007 Panel Comment:

7. Is it true that all water consumed in a day must have the same concentration? "A note in Section 3.5 suggests that all water consumed in one day has the same concentration, regardless of source. This may have been true in the past but can this really be the case when many individuals drink water from multiple sources each day (bottled, tap, filtered, etc)? One situation mentioned was the scenario where contaminants in the water occur only at one specific time in the year (a pulse) with concentrations the rest of year being zero. Another situation mentioned is where the water used in cooking food is the contamination pathway. It is possible that factors related to drinking water source, municipal versus private, ground versus surface, chlorinated versus not, may influence consumption rates. Individuals may not be fully aware of many of these factors, but they will know

where the water they pay for comes from and this may also affect consumption. Finally we should not lose sight of the information available on residue data in drinking water as available in the Office of Drinking Water." (p.36)

EPA 2010 Response: People often drink water from different sources on any given day (e.g., tap: home, office/school; bottled; travel, etc.), and water from different sources may contain different concentrations. The CSFII survey asked the following questions regarding this issue:

- "What is the main source of the water used for cooking in the home? {Community water supply, Well or cistern, Spring (HH or public), Bottled water, Other, Don't know}" (RT15, H20_COOK)
- "What is the main source of the water used in your home for preparing beverages such as coffee, tea, juices, and baby formula? {same responses as above}" (RT15, H20_BEVR)
- "What is the main source of plain drinking water in your home?" (RT15, H20_DRNK

The next two questions refer to the amount of direct water consumption reported in the food diary:

- "How much of this plain drinking water came from your home? Would you say all, most, some, or none?" (RT25, D1_H2O_)
- "What was the main source of plain drinking water that did not come from your home? Was it tap water, water from a drinking fountain, bottled water, or something else?" (RT25, D1_H2O_A)

The Agency used responses to some of those questions to decompose both direct and indirect drinking water by four sources; tap, bottled, other, source not specified; indirect drinking water is further decomposed over 19 different food forms (e.g., uncooked, cooked-boiled, etc.). The documentation for those allocations is contained in the FCID food recipes. Other aggregate exposure models (e.g., DEEM-FCID™, CARES™, Lifeline™) allow users to assign different drinking water concentrations based on those four different sources; however, the Agency's risk assessments have **not** used that option to refine drinking water exposures. There are no plans to incorporate such an option into the SHEDS-Dietary model.

2007 Panel Comment:

8. Because exposure from drinking water sources is a very small fraction of total exposure, is there a need to further model drinking water in the SHEDS model? "A number of Panel members felt that because of its low contribution to total exposure (e.g., 1-2 orders of magnitude less than food exposures), further modeling of drinking water consumption would not noticeably change model results" – this view was also mentioned at a previous SAP; "other Panel members felt that in some exposure scenarios the contribution from drinking water could represent a large fraction of total exposure and in those cases different water allocation models could produce quite different results" (p.36)

EPA 2010 Response: The Agency has found that drinking water contributions can often 'drive' total dietary (food+water) exposures, and therefore, the eating occasions' analyses may have a significant effect upon aggregate exposures at the per capita 99.9th percentile.

When relatively high predicted drinking water concentration values are included in the dietary assessment and water is the primary contributor, infants (newborns) often have the highest total dietary (food+water) exposures. Otherwise, children (1 to <3 years old or 3 to <6 years old) often have the highest total dietary exposures when fresh fruits and vegetables are the primary contributors. The infants having the highest water intake generally obtained much of their total

daily water intake through infant formula. Since infant formula is a food item, the time and amounts consumed throughout the day (24 hr recall) are provided in the CSFII and NHANES/WWEIA surveys. The Bayer DWCS and Fixed option focuses on allocating only the 'direct' portion of total drinking water intake over the particular day. The Bayer DWCS survey did not collect information on infants, but that information is not critical for most of the high-end exposures since the CSFII (and NHANES/WWEIA) survey captured the timing and amounts of their indirect water (infant formula) intake.

Relatively little time and resources have been devoted to refining the SHEDS-Dietary drinking water exposure algorithm. The focus on refining dietary exposures from food is largely due to the developers' experience that there is relatively less uncertainty in food residue inputs. The predicted drinking water concentrations used in those analyses are often derived from environmental fate models using conservative inputs (e.g. prevalence of land use, percent of watershed planted to crop, scope and magnitude of pesticide use, percent of crop treated and labeled use rates). A risk characterization of those parameters may better address uncertainties regarding such predicted drinking water exposures than other refinements to the drinking water exposure algorithm (e.g., by source, etc.).

2007 Panel Comment: "Previous SAP consultations on this topic remarked at the lack of adequate information on drinking water consumption patterns to properly analyze the fraction of exposures from this source. A good portion of the Panel do not think that the issue related to exposure from drinking water sources are likely to be less in the future and would like to see drinking water's impact examined in more detail. Issues such as water sources, use in cooking, temporal changes in contamination levels, methods of disinfection, etc., all seem to need further discussion and examination." (p.36-37)

EPA 2010 Response: The Agency concurs that more data should be sought, and further examination of those data should be made when drinking water exposures pose concerns. We note that we do not expect drinking water exposures to be a concern for pyrethroids.

2007 Panel Comment: "Water consumption patterns in the US seem to have changed since CSFII data were collected and, due to the wide use of bottled water, water is now a consumer product." (p.37)

EPA 2010 Response: The Agency agrees. The Agency presented some preliminary analyses comparing drinking water consumption in the CSFII and NHANES/WWEIA data (1999-2004) at a scientific conference (Xue, J. Nako, S. and Zartarian, V. 2007; International Society of Exposure Analysis). Those analyses provided several findings, including: (i) no significant differences of Indirect DW consumption, but (ii) Direct drinking water consumption rates is ~20 - 30% higher in the NHANES/WWEIA data.

2007 Panel Comment: "The current PDP data on finished water can be used in the reanalysis for drinking water contribution when needed." (p.37)

EPA 2010 Response: The Agency has not used the PDP data to model drinking water exposures to pesticides. Except for a few exceptions, the Agency has used predicted drinking water concentrations from environmental fate models, such as PRZM-EXAMS and SCIGROW to assess drinking water exposures. There are various science and policy reasons for this practice (e.g., the community water systems sampled may not reflect the most conservative sources for specific pesticides (i.e., highest predicted concentrations), and the number of samples collected were not designed to capture annual peak concentrations). The Agency may consider using the PDP data in future work on pyrethroids to evaluate the SHEDS-Dietary model.

D. Sensitivity and Uncertainty Analyses

Question 3-4: Sensitivity and contribution analyses are a routine part of OPP risk assessments. These analyses help inform the risk manager how exposures may change when certain model inputs are modified. These modifications to the model inputs are typically performed "one at a time" to permit isolation of the effect. In a typical risk assessment, all the dietary consumption data (i.e., reported CSFII diaries) are used along with the best available pesticide residue data. OPP risk assessors specify a sufficiently large number of Monte Carlo iterations such that exposure estimates are stable with respect to the random seed.

The Agency has not conducted formal quantitative uncertainty analyses. The Agency presented a simple bootstrapping procedure for conducting uncertainty analyses, utilizing only a subset of the consumption and residue data inputs. That procedure was designed to provide some insight into the question, "How much better would our exposure estimates be if we had more data?" by conducting the uncertainty analysis in the other direction. (a) Please comment on the scientific soundness and utility of the proposed bootstrap uncertainty approach. (b) Can the Panel recommend alternative approaches – and how they might be interpreted and used –for conducting uncertainty analyses of dietary exposure estimates?

2007 Panel Comment: "One index of uncertainty suggested, the ratio of the 95^{th} percentile to the 5^{th} percentile, is actually a measure of distributional spread. The median of this measure was proposed as one way of quantifying the potential impact on model results of inadequacies in the diet or residue data. An alternative measure suggested is the median of some important upper percentile; say the 99^{th} percentile, across the set of simulated response distributions." (pp. 37-38).

> ***EPA 2010 Response:*** The Agency believes that some Panel members may have misinterpreted the ratio ($95^{th}/5^{th}$), and would like to clarify how that ratio was calculated. First, the uncertainty analyses presented in the document dated 7/25/07 is based on the cross-sectional option SHEDS-Dietary model (not the D&A or 8-Diary longitudinal method). One hundred iterations were performed on all food diaries, and the total dietary exposure at some per capita percentile (99^{th}) is computed from those outcomes. This procedure is repeated 200 times with subsets of residue and/or consumption data by the bootstrap method, providing 200 values of estimated exposure at the per capita 99^{th} percentile. The 5^{th} and 95^{th} percentile of those 200 values of 99^{th} percentile are calculated, and the ratio is based on those two values. If the 99^{th} percentile over those 200 replicated samplings ranged from 2 ug/kg bw-day (5^{th}) to 4 ug/kg bw-day (95^{th}), then the ratio is 2 (=4/2). Note that the GUI for the SHEDS-Dietary does not allow the user to conduct the uncertainty analyses method presented in the 2007 analyses at this time, although it can be done by programming in the underlying SAS code and will be done in the next version.

2007 Panel Comment: "…the proposed method will not indicate the true value of enlarging the database. It will be useful for showing the uncertainty associated with re-sampling from a finite set of consumption and residue inputs." (p.38)

> ***EPA 2010 Response:*** The Agency concurs.

2007 Panel Comment: "Some Panel members had suggestions for other analyses approaches, including: (i) Measuring impact of changes to p1 and p2, (ii) post hoc power analysis, (iii) inter- and intra-run variability and (iv) alternate indices." (pp. 38-40)

> ***EPA 2010 Response:*** The Agency has not yet been able to carefully consider the Panel's recommendations or conduct/evaluate uncertainty analyses in the SHEDS-Dietary module.

2007 Panel Comment: "One Panel member indicated that the figures used in the report are transposed with respect to what is typically seen in publications, in this case with the probability axis on the horizontal and amount on the vertical axis. From a communication standpoint it would be preferable to make that change." (p.38)

> ***EPA 2010 Response:*** The Agency has incorporated the Panel's suggestion regarding axes configuration when presenting the results for some outputs, and will consider this recommendation further in future versions of SHEDS.

E. NHANES: Seasonal and Regional Effects

Question 3-5: Please suggest statistical or other methods that might be used to determine the extent to which region- and season- specific dietary consumption amounts and patterns might be important in developing dietary exposure estimates. Please consider in your response whether and how quantitative uncertainty methods could be used in addressing this issue.

2007 Panel Comment: "Statistical methods alone cannot resolve the uncertainties that arise due to regional and seasonal variations. The issue of the regional and seasonal differences can be addressed through analyzing the population and region- or season-stratified datasets, such as data from, for example, CSFII. For example, the CSFII dataset has the information on season and region, and CSFII was designed to represent the whole population. Using bootstrap methods, the percentiles of the exposure estimates can be computed for each region, each season, and region and season combination. The 50^{th}, 95^{th}, and 99^{th} percentiles can be compared to evaluate the impact of regional and/or seasonal differences in diaries, consumption, and exposure on the exposure estimates." (p.41)

> ***EPA 2010 Response:*** The Agency conducted limited analyses on food consumption patterns based on the CSFII food consumption survey information, and provided some of those results to ORD/NCEA to update the Agency's draft Exposure Factors Handbook (EFH 2009). For example, there are differences in consumption by region: e.g., consumption of okra is more prevalent among people living in the South (1.2 % on any given day) than Midwest (0.4%); and by season: e.g., more people eat pumpkins during the fall (2.8% on any given day) than during the spring (0.3%)[4].

2007 Panel Comment: "One Panel member raised a question of whether commodity consumption differs regionally, pointing out that diaries might be different from region to region, but commodities are likely to be from national or international sources. Exposure analyses that were presented at the previous SAP meetings indicated that seasonal and regional variations do not generally contribute significantly to the high end dietary exposures when a large number of commodities are included in the dietary exposure estimation. However, without seasonal- and regional- specific analyses, this conclusion is not apparent in light of the intuition that seasonal and regional variations of consumption likely exist." (p.40-41)

> ***EPA 2010 Response:*** The Agency recognizes two aspects of this issue: (i) calculation of per capita 99.9^{th} percentile, by region and/or season, and (ii) modeling dietary exposures based on

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[4] These values are somewhat different than the 2.6% in the South and 0.4% in the Midwest for okra and the 4.9% in the fall and 0.4% in the spring for pumpkins reported in the EFH. The EFH reports two-day averages and the percentages there reflect percent of population reporting consumption of the commodity of interest on at least one of the two reporting days. (The draft 2009 EFH is available at the following website: http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=20563)

national-level residues or 'binning' residues by region and/or season. With regards to calculating population-based statistics, the Agency notes that current aggregate exposure models (e.g., DEEM-FCID^{TM}) can calculate aggregate exposure at the per capita 99.9th percentile by region or season. The user can also perform similar calculations using the SHEDS-Dietary module (by region, season or both) since SHEDS retains all simulated outcomes and the demographics of the corresponding persons (at least for CSFII since seasonal and regional information is not available for the NHANES/WWEIA survey). The 99.9th percentile exposures for the highest season or region will generally be higher than the overall 99.9th percentile since it is based on a subset of all outcomes; however, the Agency has focused on the overall per capita 99.9th percentile, for specific age groups (infants, 1-2 yrs olds, 3-5 yrs olds, 6-12 yrs old, 13-19 yrs old, 20-49 yrs old, 50+ yrs old), and females 13-49 years old for reproductive and developmental toxicity endpoints.

The second aspect concerns whether the aggregate exposure model bins and selects residues based on source (origin and/or season). Such a refinement could produce slightly different effects if there is correlation between consumption and residues. For example, if high consumption and high residues occur in particular seasons (binge eaters at pick-your-own farm), then having one distribution for all residues may underestimate the occurrence of such exposure events. On the other hand, if low consumption often occurs with high residues (e.g., less purchases and consumption of higher priced imports during off-season), then assuming national-level residues may generate exposures that never occur. The model currently used by the Agency (DEEM-FCID^{TM}) does not permit such refinements; we are considering plans for developing such an option in the SHEDS-Dietary module.

2007 Panel Comment: "Panel strongly recommends that the Agency should be involved in the study design stage for the future NHANES to address those missing data/information issues. The Panel supports a better and stronger sharing of these data among the Agencies.

EPA 2010 Response: The Agency has developed strong working relationships with staff and managers at CDC and USDA regarding the NHANES study (both food consumption as well as biomonitoring data).

2007 Panel Comment: The Agency is encouraged to continue looking into collecting more updated dietary survey data, especially for building longitudinal patterns…If possible, the further study that the Agency will conduct should be reviewed by a separate SAP prior to the initiation of data collection."

EPA 2010 Response: The Agency will consider review of science and ethical issues (protocol, etc.) by a separate SAP if resources are available for future data collection efforts.

II. RESIDENTIAL EXPOSURE

The Agency's charge to the 2007 FIFRA SAP included eight questions regarding the aggregate residential module of SHEDS. Questions pertained to model code, approaches, and algorithms; the graphical user interface (GUI); documentation; and diary assembly methods. The Panel was asked to "try out" and test the software and many good suggestions regarding this aspect of the model were made. Other questions asked of the Panel at that time reflected various specialized issues such as the fugacity approach and Sobol's method for sensitivity analysis.

The purpose of this section of this background document is to recap and summarize for the current Panel the earlier 2007 comments with respect to the residential exposures assessed by SHEDS v.3 and to provide the Agency's 2010 response. The following sections introduce, by topic area, the questions asked of the Panel in its 2007 review, followed by both a relevant excerpt of the Panel's responses to those questions, as well as EPA's 2010 corresponding responses indicating how the comments were, if possible, able to be incorporated into this version of SHEDS-Residential. We believe that this background material will assist the Panel in its current 2010 review of SHEDS-Residential v.4.0.

A. Code

Question 1-1 a) Were Panel members able to load the software on to their computers? What, if any, difficulties were encountered in loading or running the software?

2007 Panel Comment: "The Panel recommends…that the prerequisite of SAS version 9.1.3 needs to be clearly stated in the introduction and installation instructions up front." (p.15)

> ***EPA 2010 Response:*** The SHEDS-Residential version 4.0 Technical Manual and User Guide both state that SAS version 9.1 or higher is needed. In the Technical Manual, the notice appears in sections 1.1 and 1.3 of the Introduction. In the User Guide, the notification appears in section 1.1, "Considerations for New Users of SHEDS-Residential."

2007 Panel Comment: "…the SHEDS installation program should check for SAS and abort installation if SAS is not installed." (p.15)

> ***EPA 2010 Response:*** As noted above, the user is informed of the need for SAS 9.1 (or higher) in both manuals.

2007 Panel Comment: "Panel members also noted a bug in the Installation Process: the batch file, "multimedia.bat" in the installation folder, contains incorrect information on the installation folder location, and hence does not run. It should be fixed with the correct folder location." (p.15)

> ***EPA 2010 Response:*** This is not a bug. The manual makes it explicit that you need this directory and that it may need to be renamed. The appropriate text is now in Section 7.1 of the user's guide, "Installing Batch Capability." The file is now named 'SHEDS.bat'.

2007 Panel Comment: "Cross-platform compatibility was one issue that the Panel felt should be addressed in future iterations of the program. Therefore, it may benefit users of other operating systems if the installation package is also provided as a zip archive (i.e., the users can then extract the folder and change the SAS invocation based on the requirements of their operating system). This facilitates, with a minimal amount of effort, use of SHEDS on other operating systems. Such a package could be provided through EPA's ftp servers." (p.15-16)

EPA 2010 Response: This was not done for version 4. This would be a major development effort, especially for the GUI, that would require significant QA and resources.

2007 Panel Comment: "It appears that the uninstall program simply removes the underlying SHEDS program and all the simulations the user may have defined and run until that point. This should be clearly noted, and the user should be provided detailed information and prompted about this step." (p. 16)

EPA 2010 Response: Uninstalling is a function of the installation wizard and Windows, and because of this, no prompt message has been added. However, in the User Guide, two warnings appear about the loss of files that may have been previously created. A warning box is in Section 3.2, "Installation under MS Windows" and boldface type appears in Section 3.2.5 "Removing SHEDS-Residential."

2007 Panel Comment: "They also felt it was useful to add utilities to make the model more accessible and useful, e.g., code to review input values and note extreme or illogical combinations, or a script generator to run designed experiments on the model."

EPA 2010 Response: Checks on illogical combinations would be impractical to do comprehensively given available resources, so no major additional checks or review opportunities have been added. After considering this suggestion, however, verification of the legitimacy of inputs was improved slightly. For example, checks have been added that variables representing fractions or probabilities do not exceed one. Also, checks to prevent negative values have also been implemented.

Regarding a script generator, the user cannot submit multiple variability runs simultaneously via the GUI; however, design of experiments may be assisted in that the user can now submit sensitivity and uncertainty runs through the GUI. Multiple variability runs could be prepared in advance via the GUI, and then simultaneously submitted in batch mode (for example, to run over a weekend). See Section 7 "SHEDS-Residential: Batch Mode" of the User's Guide.

2007 Panel Comment: "… the naming of the variables within the SHEDS code can be significantly improved."

EPA 2010 Response: Variable naming has been improved for version 4.0, as detailed in Appendix B of the SHEDS-Residential version 4.0 Technical Manual.

2007 Panel Comment: "Autocorrelation can have an important effect on the tails of the exposure distributions."

EPA 2010 Response: This was considered for v. 4, but given available resources, data, and the number of inputs that would be required for this option, and considering relative importance of this option compared to other priorities, autocorrelation between events was not implemented. If the D&A method is chosen for the longitudinal diary method in v.4, however, then the user can implement autocorrelation on the key exposure variable between diaries for each simulated individual, as detailed in the SHEDS-Residential version 4 Technical Manual, section 2.5.1.

2007 Panel Comment: "It is important that the developers anticipate future data sets, especially longitudinal, and try to keep the code scalable."

EPA 2010 Response: We agree with the Panel's comments, and have implemented flexibility and scalability in the SHEDS SAS code and input data. However, we are still exploring options of these aspects for longitudinal analyses because we are refining the methodology.

B. Graphical User Interface (GUI)

Question 1-1 b) The SHEDS-Multimedia version 3 graphical user interface (GUI) was designed to be user-friendly to exposure modelers and risk assessors. Please comment on the organization and usability of the GUI, any difficulties you encountered, which features and output capabilities were most useful, and whether any additional options would be helpful. Please also comment or offer suggestions for improving the GUI/model interface.

2007 Panel Comment: "The Panel identified three major issues that should be addressed in future versions of the software. First, the Panel felt that there was need for a substantive case study to guide novice users, preferably using realistic data.

A novice user, without appropriate data sets, will have significant difficulty or be overwhelmed by the number of inputs to provide, even for a simple case. This highlights the need for an example case that will also allow users to make minor customizations and not have to develop a case from scratch." (p. 16)

EPA 2010 Response: Both dietary and residential case study simulations were conducted with version 4, and are provided in the Technical Manual and User Guides. The case studies in the User Guides (dietary and residential) were designed to lead a novice user through the GUI screens. Also, the Technical manual contains default suggestions for non-chemical specific inputs in Appendix G, and provides some guidance on running the model with fewer relevant inputs by disabling user-selected pathways.

2007 Panel Comment: "Second, Panel members noted that there were many hard-wired approaches in the model, and these need to be clearly identified in the program and the manual and preferably open to adjustment by advanced users from within the program." (p. 16)

EPA 2010 Response: SHEDS developers used what we feel are best available approaches, and provide several options to the user in some cases (e.g., dermal method, concentration generation). The longitudinal diary assembly and sensitivity options have been expanded in version 4. These are discussed in the SHEDS-Residential Technical manual, sections 2.5 and 5.5, respectively. In addition, the interface now provides a utility for sub-setting the CHAD database (see Section 5.4 "Specify Population and Sampling" of the User's Guide). Because the SAS code and GUI are available to the user, advanced users can make additional changes. We minimized hard-wired inputs and documented them clearly in the Technical Manual (see beginning of section 2).

2007 Panel Comment: "Error checking and reporting need to be improved within the program in terms of the number of simulations that can or should be run. At present the system allows the input of an unreasonably large number of individuals to simulate (on the order of 10^{200}: higher numbers are reset to 10), without checking or reporting disk space or processing time requirements." (p. 16-17)

EPA 2010 Response: Both the Technical Manual and User Guides now provide estimates of run time based on the number of simulated individuals. The notice appears within the first three paragraphs of the User's Guide. The information appears in Section 1.3 "SHEDS-Multimedia Version 4 Overview" of the Technical Manual. An advisory on storage requirements appears in

both Section 1.3 of the Technical Manual and Section 3.1 "Requirements" in the User's Guide. The user is now also provided an on screen estimate of the run time.

2007 Panel Comment: "Similarly the specification of run names needs to be made more systematic. When a run name is not specified, instead of a quick error message, the application goes to the next screen and provides a cryptic error message. Later, a blank case is created. It is probably better to have a default such as "untitled" following the conventions used in many applications." (p. 17)

EPA 2010 Response: This has been implemented for Version 4.

2007 Panel Comment: "When checking for errors (using the "Check for Errors" button), the application gave very cryptic messages such as: "deleted", "library not found", etc., and then finally reported "no errors found." The error messages are likely due to outputs of some underlying operations that do not impact the specific case, so they should be appropriately filtered out." (p. 17)

EPA 2010 Response: No change was implemented in this regard, as other revisions had greater priority.

2007 Panel Comment: "Additional major features that would be desirable for SHEDS are 1) "the ability to specify alternative locations or folders for storing simulations;" (p. 17)

EPA 2010 Response: This has been implemented in Version 4.

2007 Panel Comment:
2) "the application should allow the user to specify different folders for storing simulations (this will often be dictated by disk space constraints, etc.) and allow a user to organize simulations in a hierarchical manner. A major advantage of this approach is that the previous simulations are saved even when SHEDS is uninstalled;" (p. 17)

EPA 2010 Response: This has been implemented in Version 4.

2007 Panel Comment:
3) "the model documentation should clarify what is meant by some terminology within the program, for example: the use of terminology such as "Application Scenarios" versus "Run Files" can be confusing;" (p. 17)

EPA 2010 Response: Wording has been changed in both the User's Guide and Technical Manual to improve clarity. Terminology revision was a particular focus in the transition to version 4.

2007 Panel Comment:
4) "the interface should include a "tool tip" for each menu item which provides descriptive information while being unobtrusive; (p. 17)

EPA 2010 Response: Help text is now available in the Version 4 GUI. It appears in the SAS Help Bar at the bottom of the SAS screen.

2007 Panel Comment:
5) "the application should include functional help buttons." (p. 17)

EPA 2010 Response: Help buttons are now available in the Version 4 GUI.

2007 Panel Comment: "Desirable additional minor features noted by the Panel include having the "Run Name" shown on the title bar of the pop-up windows at all stages. This is even more important in the context of the following software bug noted by one Panel member: when the user asks to overwrite an existing run with the one he/she is editing, an error message is displayed (saying that the run already exists), and the application loads up the existing old run. The user is not provided an opportunity to force the change, and has to cancel the operation. However, upon canceling the operation, the old run becomes the "current run", and any further changes made will be reflected in that run. Having the run name displayed prominently will alert the user right away." (p. 17)

> ***EPA 2010 Response:*** The number of allowable characters for the run name has been limited to 32. The run name now appears on each title bar in Version 4.

2007 Panel Comment: "The GUI is helpful and straightforward, but most Panel members felt it could be improved by adding context specific information clearly available at all times. One of the major issues with the program is that it places great responsibility on the user to make sure that the inputs are logical. The user can, for example, assume an exponential distribution for the value of a parameter, with no suggestion that it has to be between 0 and 1. The Panel also felt that there should be a more convenient way to see a summary of the inputs to facilitate checking that all values are logical." (p. 16)

> ***EPA 2010 Response:*** In the version 4 GUI, the user has the option of exporting all inputs for a given run to Excel for printing. Checks have been added that variables representing fractions or probabilities do not exceed one. Checks to prevent negative values have also been implemented.

2007 Panel Comment: "One Panel member wanted to focus on modeling female subpopulations, and then changed the inquiry to include both sexes, only to have the program lock up with no ability to return to previous screens. Since there was no option to cancel, the user needed to restart SAS. The user should be allowed to return to previous selections or the screen revised to include a running output of the selections made. For example, it would be useful to be able to return to the "specify exposure scenario details" screen easily from submenus." (p. 16)

> ***EPA 2010 Response:*** The problem encountered by the panel member was traced to a nonfunctioning "Cancel" button. This has been remedied.

2007 Panel Comment: "…Panel members expressed concerns about the quality of the graphics and plots generated by the program. Although this is a problem associated with SAS itself, providing systems and/or advice to the user on methods to provide reasonable quality graphics and plots is important for promoting SHEDS usage." (p. 16)

> ***EPA 2010 Response:*** The option to export output files into CSV format, which can then be imported into other graphical packages outside of SAS, exists within SAS, and the procedure for using it is described in Section A.5 "Exporting SAS Datasets" in Appendix A of the User's Guide. Text in Section 5.11.1 "Additional Outputs and Files" refers the user to this appendix.

2007 Panel Comment: "The Panel noted a need for clearer instructions on run times…"

> ***EPA 2010 Response:*** Both the Technical Manual and User Guide now provide estimates of run time based on the number of simulated individuals. The notice appears within the first three paragraphs of the User's Guide. The information appears in Section 1.3 "SHEDS-Multimedia Version 4 Overview" of the Technical Manual. The user is now also provided an on screen estimate of the run time.

2007 Panel Comment: "...it is important that units of input variables be displayed because specification of units fosters better user understanding. Units of input variables should be clearly stated in all cases because specification of units is important to user understanding."

> ***EPA 2010 Response:*** In reviewing SHEDS-Multimedia in response to this comment, some instances were found where units did not appear on the screen. This has been remedied.

C. User Guide

Question 1-1 c) Please comment on the organization, clarity, completeness, and usefulness of the User Guide document and provide any suggestions for improvement.

2007 Panel Comment: "The Panel recommends, however, that the prerequisite of SAS version 9.1.3 needs to be clearly stated in the introduction and installation instructions up front. Furthermore, it would be helpful to provide users with some idea as to run time expected in the documentation. ...

- "The SAS log window will accumulate numerous unessential messages, so it might be useful to have a separate SHEDS window to show progress of a simulation." (p. 17)

EPA 2010 Response: The prerequisite of SAS version 9.1 or higher is now clearly stated in the documentation up front, as suggested. A run progress indicator is now displayed on the screen. In addition, text has been revised in Section 5.5.8 "Save the Log File" in the User's Guide. The revised wording clarifies that when the log screen is saved to an external file, this "turns off" the log on the screen and allows the user to check the status of the run via accessing the external file.

2007 Panel Comment:

- "The issue of truncation of distributions is important for the user to be able to review. The program should warn the user when inappropriate values are selected." (p. 18)

EPA 2010 Response: In the GUI, a plot of the specified distribution is available for many inputs. Truncated values are "stacked up" at the truncation point. It is visually clear when this becomes excessive. Additional options for handling inputs that are sampled "out of bounds" have been added to version 4; these are discussed in Section 3.1.4.1 "Truncation of Distributions" in the Technical Manual.

2007 Panel Comment:

- "The overview of the SHEDS interface, shown in Figure 1 of the User Guide, is inconsistent with the flow of the program" (p. 18)

EPA 2010 Response: This figure has been revised for Version 4 and is now designated Figure 2.1. It was not intended as a detailed flowchart, but rather as an overview of the program's operation. Text has been revised to alert the user that not all screens are represented in the figure and therefore this figure is not meant to lead one through individual screens as they are encountered in the interface.

. **2007 Panel Comment:**

- "The installation documentation should provide information relevant to Windows Vista, especially given that in a time frame of one or two years, a significant portion of the user community may be using Vista." (p. 18)

EPA 2010 Response: With Windows Vista being superseded by Windows 7, this comment would seem to be less relevant than at the time of the last SAP. However, the point has been investigated with SAS. Vista Professional is supported by SAS, but Vista Home is not. SAS did indicate that some problems have been reported when using SAS on the latter version. As noted in the User's Guide, SHEDS-Residential version 4 has been developed and quality assured under the Windows XP environment. Consultation with SAS directly has indicated that the model and interface should operate correctly under Windows 7, but quality assurance has not been conducted for Version 4 within this operating system. SAS does support Windows 7 Professional and Home Premium (but only 'Premium' for the home).

2007 Panel Comment:

- "The minimum requirements for running SHEDS, as described in the User Guide, appear unrealistically low (e.g., the actual requirements for Windows XP and SAS may actually exceed the requirements described in the manual). The actual requirements for running the model are unlikely to be met by most of the commonly used computers. Specifying more realistic requirements for a "reasonable performance" or just specifying the requirements as "a computer that runs SAS (version x)" are two possible alternatives." (p. 18)

EPA 2010 Response: We reviewed the minimum requirements. We disagree that commonly used computers cannot run the model, and most 2007 Panel members had no problems running SHEDS. No change was made to the documentation in regard to specific requirements. However, as noted elsewhere in the responses, the requirement of SAS 9.1 or higher and the estimate of run time and storage requirements have been made more prominent.

2007 Panel Comment:

- "Sections should be numbered, and additional cross-referencing should be included, including hyperlinks between the User Guide and Technical Manuals and a substantive glossary." (p. 18)

EPA 2010 Response: Sections have been numbered for the SHEDS-Residential version 4 User's Guide and Technical Manual. However, other topics had higher priority than cross-referencing and hyperlinking.

2007 Panel Comment:

- "The captions for figures and tables in the User Guide should be more descriptive." (p. 18)

EPA 2010 Response: This comment was taken into account in developing the table and figure captions for the Version 4 User's Guide and Technical Manual.

2007 Panel Comment:

- "The User Guide also should contain some of the technical details of the probability distributions (can be directly copied from the Technical Manual). As written, the manual expects users to understand the type of distribution they are using." (p. 18)

EPA 2010 Response: Both the version 4 User Guide and Technical Manual now contain the detailed probability distribution descriptions in an appendix.

2007 Panel Comment:

- "Other models developed by EPA and revised over the years have addressed many user issues in a readable manner. A review of the IEUBK (Integrated Exposure Uptake Biokinetic Model for Lead) interface and User Guide will address some of the challenges faced by new users." (p. 18)

EPA 2010 Response: The IEUBK documentation was examined for ideas on how to orient new users. The User Guide now contains a new initial section, "Considerations for New Users of SHEDS-Residential."

2007 Panel Comment:

- "Specify Application Exposure Scenarios" does not include the option to add new exposure scenarios relevant to pesticide application. The model should allow assessment of non-standard application methods." (p. 18)

EPA 2010 Response: This can be done with the SHEDS-Residential SAS code. Also, the GUI now allows the creation of a user-defined scenario and/or chemical, as explained in Sections 5.7.1.1 and 5.6.1, respectively, of the User Guide.

Question 1-2 a) Please comment on whether the descriptions of specific model components are scientifically sound and whether the algorithms described in the Technical Manual represent the state of the science for performing exposure assessments. Please also comment or offer suggestions for improving or modifying these algorithms or other aspects of the model construct.

2007 Panel Comment: "In general the model is scientifically sound and appears to represent the state-of-the-science, with the notable exception of the dermal exposure analysis section, as discussed below. The larger overlying issue is the quality and the transparency of "hard-wired" approaches within the model. The representation of some of these issues, e.g., hand to mouth contact, are in existing EPA documents or peer-reviewed publications, but are largely invisible to the user and not clearly identifiable without careful examination of the underlying SAS code. While it is not necessary to present this data in the Technical Manual, several of the suggestions about the transparency of processes and equations noted by the Panel are important for understanding the functioning and reasonableness of the model. Equations, units, and key decision points should be clearly stated and, if needed, hyperlinked to important decision variables." (p. 18-19)

EPA 2010 Response: The equations, assumptions, hard-wired approaches and input, and units are explicitly stated in the Technical Manual. The user's guide now contains a new initial section, "Considerations for New Users of SHEDS Multimedia.," that presents an overview of the capabilities of the model, its underlying processes, distributions, and configuration options; these are expanded on in the User Guide and the Technical Manual.

2007 Panel Comment: "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." (p. 19)

EPA 2010 Response: Version 4 supports both the TE and TC methods. The current documentation does not favor either method.

2007 Panel Comment: "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." (p. 19)

EPA 2010 Response: The Panel's issue appears to be with whether the transfer efficiency or transfer coefficient approach (Cohen Hubal et al., 2000, EHP, 108(6): 475-486) is preferable.

There is no consensus in the scientific community as to which approach is best to use. As before, SHEDS-Residential version 4 allows the user the choice of either the TE or TC approach. However, the Technical Manual explicitly states that internally the model utilizes a user-supplied TC, or calculates a transfer coefficient as a function of TE, as part of estimating dermal exposure. The dermal exposure algorithm has been modified in version 4 to incorporate reduced transfer of chemical to the skin as the amount of pesticide on the skin increases. With respect to absorption of the chemical, the model moves the pesticide into the stratum corneum and thence to the blood, as opposed to directly into the blood. These aspects are discussed in Sections 2.7.2.1-2.7.2.4 of the Technical Manual.

2007 Panel Comment: "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. As an example, one Panel member noted that one oft-cited use of a TE approach (Gurunathan et al., 1998) violates conservation of mass. Therefore, the Panel urges caution in use of this approach, as it needs to be anchored with and compared to other relevant data, such as biomonitoring." (p. 19)

EPA 2010 Response: The issue is more with what value to select for transfer efficiency, not with the SHEDS dermal equation. The SHEDS user has the responsibility to select the appropriate study/values. Version 4 allows different TE or TC values for different surfaces. A variable "chemfrac" is provided in version 4 as a check against any violations of conservation of mass.

2007 Panel Comment: "The Panel noted that the paragraph at the bottom of page 43 is incorrect in its assertions about the rate of dermal transfer. Dermal absorption (at least in the sense of binding to stratum corneum as opposed to systemic absorption) is not necessarily slow relative to diary events in the context of residential exposure scenarios." (p. 19)

EPA 2010 Response: There appears to be confusion over the dermal exposure/absorption terminology in the SHEDS documentation. We believe that the clarified terminology regarding exposure and dose in version 4 addresses these concerns. Specifically, we now define dermal exposure at the external skin surface. Section 2.7.2 of the SHEDS-Residential Technical Manual explicitly discusses dermal exposure and dose in version 4. A new feature in version 4 is that the chemical now moves into the stratum corneum first and later is absorbed into the blood.

2007 Panel Comment: "For example, Fenske & Lu (1994) showed apparent rapid uptake of chlorpyrifos at low skin loadings. Failure to account for dependence of absorption efficiency on skin loading is a significant weakness of current practice." (p. 19)

EPA 2010 Response: SHEDS includes a simple PK model, but allows for exporting to PBPK models that can include more realistic absorption rates. As noted above, the dermal exposure algorithm has been modified in version 4 to incorporate reduced transfer of chemical to the skin as the amount of pesticide on the skin increases and with respect to absorption of chemical into the stratum corneum as opposed to directly into the blood. These aspects are discussed in Sections 2.7.2.1-2.7.2.4 of the Technical Manual.

2007 Panel Comment: "The age grouping in SHEDS is slightly different from the dietary exposure analysis default groups. Operationally, this may not be a major problem as long as it is possible for the user to conduct model runs for a custom population of choice. However, since the apparent differences in age cohort pooling has underlying emphasis that is specific to certain key parameters of interest, it would help to include a brief explanation for the basis of the SHEDS specific age cohort system. The same should be presented for dietary and water components when they are added to the next version of

SHEDS. For practicality, the Agency may want to consider consolidating the two different age cohort systems, and informing the user of the rationale." (p. 19)

EPA 2010 Response: The SHEDS version 4 GUI provides the following options for age groups:

Residential GUI
Inputs:
The user has the option to use either the "EPA Age Groups" (1,2,3-5,6-10,11-15,16-20,21-29,30-49,50-69,70+ years) or "Optional Age Groups" (0,1-2,3-5,6-12,13-19,20-49,50+ years). This is selected via a button on the Population and Sampling screen.

Outputs:
The user has the option to select a max and a min age for displaying outputs (tables and graphs) in the GUI. Thus, output age groups are completely at the discretion of the user; any summary statistics are calculated on the fly based on the selections.

Dietary GUI
Inputs:
(U.S. Population, 0,1-2,3-5,6-12,13-19,20-49,50+ years, Females 13-49 years)

Outputs:
Same as Inputs.

2007 Panel Comment: "The current model construct allows only pair-wise correlations although more complex multivariate dependencies may exist. The Panel noted that techniques of partial correlation coefficients could be used to allow for multiple correlations." (p. 19)

EPA 2010 Response: We recognize the validity of the comment, but at this point there does not seem to be much of a demand nor available databases for addressing complex multivariate dependencies. Allowing pair wise correlations of inputs in version 4 is a significant enhancement from existing exposure models.

2007 Panel Comment: "The system also could be augmented by allowing default correlations such as low, medium, or high correlations." (p. 19)

EPA 2010 Response: Allowing default low, medium, or high correlations with subjective assignment of correlation numbers would introduce more uncertainty into the model. In the input data set (via SAS not GUI), the user can enter/construct functional relationships to address complex correlations among multiple variables.

2007 Panel Comment: "The Agency is encouraged to consider providing default shapes of continuous probability distributions for user specified input parameters. The Agency scientists have invested substantial effort in reviewing these data and appear to be in a good position for suggesting default distribution types, while still allowing the user to deviate from them. Having defaults has the advantage of more easily comparing different runs by different users, making the deviation from defaults more readily identifiable and more transparent." (p. 20)

EPA 2010 Response: In the version 4 User Guide, the second and third paragraphs of Section 1.3 "Configuring SHEDS to the Scenarios of Interest" inform the user that the distributions in the demonstration files may be used to familiarize oneself with the model and its operation, but that runs must be customized by the user for a specific application. As noted above, a case study for permethrin was conducted with version 4. The associated files are provided as the demonstration

input files, as noted in Section 2.2 of the User's Guide. The Technical Manual also contains default suggestions for non-chemical specific inputs in Appendix G.

2007 Panel Comment: "The description of embedding a simple PK model on SHEDS version 3 was not sufficient to allow Panel members to make constructive comments. Estimated absorbed dose is an outcome many would like to see as part of a SHEDS run. Panel members were aware that the Agency has separate groups working on various PBPK models. Instead of developing their own simple PBPK model specifically for SHEDS, the Panel recommended that the SHEDS development staff keep abreast of developments by these other PBPK model teams with the idea of integrating SHEDS with these PBPK models at some future point." (p. 20)

EPA 2010 Response: Version 4 retains a simple PK dose model that is intended to provide a quick screening level of blood and urine doses. Version 4 also contains the capability to output exposures to a more comprehensive PBPK dose model. The developers of SHEDS have followed the Panel recommendations in keeping abreast of PBPK modeling. One case study, dietary arsenic, is included in the materials for Panel review. The linkage with SHEDS and PBPK modeling with a permethrin case study will be presented to the July 2010 SAP.

2007 Panel Comment: "Verifying the precision and accuracy of SHEDS predictions is not described in the materials provided to the Panel for either version 3 or 4 of the model, except for the proposed sensitivity and uncertainty analyses. The Panel felt that before implementing SHEDS or other models in risk assessment, it is critical to understand how the model predicted values compare to the reasonable range of exposures that can be measured in the general population, or in important population sub-groups. SHEDS offers a very flexible platform for users to input variables and parameters and other characteristics that will affect the outcomes of the simulations. Evaluating predictions from SHEDS using exposure measurements is one exercise that will inform the Agency about the accuracy and robustness of the model. Extremely wide or extremely narrow distributions of predicted exposures compared to observed values are suggestive of problems with the model that could lead to questions of its ultimate utility in describing a situation." (p. 20)

EPA 2010 Response: EPA has conducted a case study for permethrin, linking SHEDS with EPA/ORD's PBPK model, and comparing results against the NHANES biomarker data. Part of this case study has included evaluating SHEDS and its individual modules where possible, using available measurements (e.g., duplicate diet intake data). These results are being presented to the July 20-22, 2010 SAP.

2007 Panel Comment: "Given the centrality of the CHAD diaries and human activities for developing model runs, it would be extremely helpful if the User Guide presented a typical diary of one weekday and one weekend day as part of the example case study." (p. 20)

EPA 2010 Response: The text of Section 2.5 "Generating Longitudinal Activity Patterns for a Simulated Individual" and Figure 2-5 describe how the model constructs longitudinal activity diaries and follows simulated individuals through them. The version 4 Technical Manual now contains an Appendix D "Summary of the CHAD Database" that includes summary information by individual study, diary counts by age/gender cohort, an example diary excerpt, and complete listings of all CHAD activities and locations. The user may use the GUI to select or deselect particular studies from the CHAD database.

D. Technical Manual

Question 1-2 b) Please comment on the organization, clarity, completeness and usefulness of the Technical Manual and provide any suggestions for improvement.

2007 Panel Comment: "The Panel had a number of suggestions on the organization, clarity, completeness, and usefulness of the Technical Manual. In general the Panel felt that the audience and scope should be more clearly defined sooner in the manual." (p. 20)

> ***EPA 2010 Response:*** We agree with these recommendations. The new introductory section of the User Guide "Considerations for New Users of SHEDS-Residential" attempts to better orient users to the model's scope.

2007 Panel Comment: "The most important issue identified by the Panel was the need for a comprehensive case study that would illustrate the strengths and limitations of the model. A second issue identified by the Panel was the need for a standard data set that could be used to orient various model clients; users, reviewers, Agency risk managers, and stakeholders are all important audiences, and a comprehensive example is important for explaining the utility of the model as well as serving as a benchmark for evaluating future changes to SHEDS." (p. 20)

> ***EPA 2010 Response:*** We included illustrative case studies for both the dietary and residential modules in the version 4 documentation. The User Guides provide step-by-step instructions to walk through these case studies using provided data and settings. Regarding a standard data set, we have provided a default file for non-chemical specific inputs, based on available literature data, in the SHEDS-Residential package and Technical Manual Appendix G.

2007 Panel Comment: "As part of these improvements, the manual needs an early statement as to what the user can and cannot change in the model. A fuller description of the fixed inputs and decisions embedded in the model is needed: particular datasets (e.g., CHAD, the contacts data base for dermal exposure) need fuller explication to achieve user understanding and model transparency. Because the manual lacks a description of the strength of the underlying datasets, risk assessors have no way of estimating confidence in the output distributions. As the Agency does with weight of evidence descriptors in toxicology studies and confidence qualifiers in IRIS, this would allow the assessor to understand whether exposure estimates are based on studies or diaries that capture the characteristics of the exposure of the population or individuals being evaluated. It also provides an understanding of data gaps and can be used to prioritize resources, both human and financial." (p. 20-21)

> ***EPA 2010 Response:*** We minimized hard-wired approaches and inputs in version 4, and documented them clearly in the Technical Manual. Data sets used in SHEDS runs are CHAD, U.S. Census, and NHANES as assumed underlying databases. Other data are supplied by the user. The Version 4 Technical Manual now contains an Appendix D "Summary of the CHAD Database" that includes summary information by individual study, diary counts by age/gender cohort, an example diary excerpt, and complete listings of all CHAD activities and locations. In version 4 the GUI allows sub-setting of the CHAD database. In addition, a note has been added in Section 3.8.1 of the Technical Manual explaining that NHANES was designed as a nationally representative study. No elaboration on the U. S. Census has been added. The user may alter or replace any of these databases using SAS.

2007 Panel Comment: "The Technical Manual has to serve as a detailed reference guide and should inform on technical issues associated with installing and running the program. It should address the limits of the model, ways to avoid common mistakes and errors, the process of obtaining results, modification and extensions of the program, and interpretation of results." (p. 21)

> ***EPA 2010 Response:*** Most of this information is in the User Guide. We do not discuss interpretation of results or modification and extensions of the program in the SHEDS manuals.

2007 Panel Comment: "As presently constructed it [The Technical Manual] has no central logic in terms of variable names and definitions: the Panel noted that it would be useful to have a central definitions list that consolidates this information in one location." (p. 21)

> ***EPA 2010 Response:*** In the revised version 4 Technical Manual, SAS variable names and definitions are provided in Appendix B "Selected SAS Variable Nomenclature" and Appendix F "Description of SHEDS Multimedia Input Files." Macro names and definitions are provided in Appendix C "The SHEDS Code Residential Modules and their Functions." In addition, some naming information is also contained in Appendix A "Terminology Used in SHEDS-Residential."

2007 Panel Comment: "The document should provide a table detailing representative run times and disk space requirements for a set of population and uncertainty run sizes. This can help in planning for a simulation beforehand." (p. 21)

> ***EPA 2010 Response:*** Both the Technical Manual and User Guides now provide estimates of run time based on the number of simulated individuals. The notice appears within the first three paragraphs of the User's Guide. The information appears in Section 1.3 "SHEDS-Multimedia Version 4 Overview" of the Technical Manual. An advisory on storage requirements appears in both Section 1.3 of the Technical Manual and Section 3.1 "Requirements" in the User's Guide. The user is now also provided an on screen estimate of the run time through the GUI.

2007 Panel Comment: "In general, the Panel felt that the description of CHAD data could be expanded and improved. Although several criteria are listed in the manual, the following factors should also be considered in the random selection of representative activity patterns for an individual: temperature, season, and employment status. Some of the criteria for selecting activity diaries (e.g., diaries that have non-zero sleep time) can be strengthened. For example, selecting a diary with "sleep > 0" is reasonable for a short-term simulation. However, repetition of such a diary for an extended period will likely result in unrealistic scenarios." (p. 21)

> ***EPA 2010 Response:*** The version 4 Residential Technical Manual now contains an Appendix D "Summary of the CHAD Database" that includes summary information by individual study, diary counts by age/gender cohort, an example diary excerpt, and complete listings of all CHAD activities and locations. The criteria for selecting diaries may be altered by editing the "Diary QA rules" input file.

2007 Panel Comment: "The Technical Manual should also list the intermediate files generated, provide relevant details so that users can write scripts for assessing model correctness." (p. 21)

> ***EPA 2010 Response:*** This would require significant effort because intermediate variables are overwritten, and this is not a high priority to the Agency. An advanced user could directly modify the SAS code to output the particular desired intermediate variables of interest, if interested.

2007 Panel Comment: "Information on restarting a simulation from an interrupted portion should also be provided." (p. 21)

> ***EPA 2010 Response:*** Development of this "restart" feature has been initiated but is not yet completed.

2007 Panel Comment: "The Technical Manual should also provide details on weighting population based on the distribution in a simulated population region (e.g., a county or a state), i.e., sufficient

documentation should be provided for sampling from "study specific" population characteristics." (p. 21)

EPA 2010 Response: No change in this regard has been made. The default population file may be replaced with one tailored to the specific application desired, or alternatively specific inputs may be so tailored.

2007 Panel Comment:

- "The Quality Assurance section should be moved to the end of the Technical Manual." (p. 21)

EPA 2010 Response: Quality Assurance is now discussed in Section 8 of the version 4 Technical Manual.

2007 Panel Comment:

- "The captions for the figures and tables should be made more descriptive." (p. 21)

EPA 2010 Response: This comment was taken into account in developing the table and figure captions for the version 4 User's Guide and Technical Manual.

2007 Panel Comment:

- "The descriptions of the probability distributions should be moved to an Appendix." (p. 21)

EPA 2010 Response: Both the version 4 Residential User Guide and Technical Manual now contain the detailed probability distribution descriptions in an appendix.

2007 Panel Comment:

- "Numbering chapters and subchapters is strongly recommended to be used instead of the current, unnumbered heading-based organization." (p. 21)

EPA 2010 Response: Sections have been numbered for the version 4 Residential User's Guide and Residential Technical Manual.

2007 Panel Comment:

- "Formulae should be presented using mathematical notation, in contrast to the textual expansion of terms (e.g. F = ma versus Force = Mass x Acceleration), especially for complex equations. If common explanation is thought to be necessary, an informal presentation could be added." (p. 21)

EPA 2010 Response: We appreciate the panel's desire for standard, brief mathematical notation. However, we chose more expansive notation in the interest of clarity for the broad spectrum of users envisioned for SHEDS. The notation used also provides a more direct connection with the SAS code itself.

2007 Panel Comment:

- "The usage of some terms in the manuals differs slightly from their definition in statistical literature, e.g., interchangeable usage of the terms "variability distribution," "probability distribution," and "probability vector." These inconsistencies should be addressed." (p. 21-22)

EPA 2010 Response: Statistical terminology was reviewed and some changes made, particularly in the wording applying to discrete variables. A subsection on discrete variables has been added to Appendix E "Probability Density Functions," a footnote has been added to the first page of the

Introduction, and text has been added to section 3.1.5 "Probability vectors." Better distinctions are now made in the use of the terms "variability distribution," "probability distribution," and "probability vector." Because of the way the code handles them and one enters these values into the software, Bernoulli variables and multinomial variables are now discussed separately.

2007 Panel Comment:

- "The manual addresses at several instances the issues of accuracy, e.g., when sampling from a population and generating the population variability and then comparing the center of the distribution of an exposure endpoint with the extremes of the distribution, e.g., percentiles. A formal definition of accuracy would clarify the discussion of these issues. When addressing the characterization of the variability distribution the Panel noted that the population variability as an outcome of SHEDS is not different from the variability of endpoints investigated in an empirical study (e.g., a large epidemiological study). In both cases principles of statistical data analysis have to be applied. The document should refer to such general principles where possible. Similarly one may require that the exposure modeler set up a study design in a sort of study protocol before starting SHEDS for sensitivity and/or uncertainty analyses. This would then resolve some of the fallacies discussed on page 76. It might be reasonable, to combine the two issues identified in separate locations within the manual (on pages 47 and 75)." (p. 22)

EPA 2010 Response: Detailed results are kept in model runs; for both variability and uncertainty results, confidence intervals can be generated for model output results.

2007 Panel Comment:

- "The description of the probability vectors needs to be revised so that it covers also a variable with only two discrete outcomes; i.e., a Bernoulli variable with one single parameter p, the event probability, e.g., to parameterize existence of pet or lawn." (p. 22)

EPA 2010 Response: Because of the way the code handles them and one inputs them, Bernoulli variables and multinomial variables are discussed separately. Bernoulli variables are called "Binomial" variables in SHEDS version 4.

2007 Panel Comment:

- "The associated text on page 49 would benefit from more formal probabilistic and statistical terminology. If the authors think that would be too formal, that part could be moved to an appendix." (p. 22)

EPA 2010 Response: We prefer to leave the existing description in the text.

2007 Panel Comment:

- "Pages 51-54 on the distributions should go to an Appendix with mathematical formulae for the distributions described in a formal mathematical type, referring to the statistical literature, e.g., that of Johnson, et al. (1994, 1995, and 2004)." (p. 22)

EPA 2010 Response: As noted above, the detailed descriptions of the probability distributions now reside in Appendix E of the Technical Manual and have been augmented with a subsection on discrete distributions.

2007 Panel Comment:

- "On page 24 there are instances where no dust is contacted. The basis for this decision is unclear: is it for model internal consistency or based on empirical data?" (p. 22)

EPA 2010 Response: As a simplification measure, the separate modeling of dust contact has been eliminated from the exposure calculations in Version 4. When dust concentrations are provided, they are converted to surface loadings to be combined with other forms of the chemical. This point is explained in Section 1.6.2 "Dust and soil ingestion in version 4" and Section 2.6 "Contact Duration and Concentration averaging."

2007 Panel Comment:

- "The manual needs to clarify if and how the model addresses region-based seasonal events, such as spring-time applications, in calculation of the annual exposures." (p. 22)

EPA 2010 Response: A paragraph is included at the end of Section 1.3 "Configuring SHEDS to the Scenarios of Interest" in the User's Guide that indicates that to contrast explicitly exposures between two different regions or seasons, it would be better to conduct separate model runs with inputs specific to those given regions or seasons. Currently, seasonally-varying chemical usage inputs are supported. In addition, the text points out that advanced SAS users can conduct a single run that incorporates seasonal-variation in other inputs.

2007 Panel Comment:

- "There is insufficient description to determine how the calculation or estimation of application rates is determined. The manual should clearly state if this is proprietary information, and if so can they be updated over time with empirical data? Otherwise, the information should be presented in detail." (p. 22)

EPA 2010 Response: Application rates, amounts, usage frequencies, and locations are user-specified. A sentence has been added to Section 2.4.3 "Chemical usage patterns (applications)" to indicate that SHEDS contains no proprietary information, though the user may employ such data at his or her discretion. Regarding updating over time, the user can do another model run with revised application rates and usage information.

2007 Panel Comment:

- "Because this is a residential model, and because residents of multi-family dwellings have less control over their pesticide applications, the model should consider a multi family housing designation as a person level variable and address whether it is correlated with other microenvironments or parameters." (p. 22)

EPA 2010 Response: The user has the option of conducting a separate run for different subpopulations of interest to the user, with sub-population specific inputs. We did not make any code changes in SHEDS per this recommendation because it raises questions of adequate diary pools and whether code changes would need to be made for other special sub-populations.

2007 Panel Comment:

- "The Technical Manual and the User Guide provide a wealth of information and many details on SHEDS' construction and structure, on the approaches used and on their programming. One Panel member noted that the structural description of SAS procedures as given in SAS Manuals could be a template for the description of the various procedures of SHEDS." (p. 22)

EPA 2010 Response: The SAS manual style is for more advanced users than the anticipated end user of SHEDS.

Question 1-3: a) Please comment on whether the annotated code is sufficiently clear such that the algorithms can be followed and understood. b) Please also comment on whether these algorithms are technically correct and consistent with the descriptions provided in the Technical Manual.

2007 Panel Comment: "In terms of code readability, it is desirable to have adequate cross-referencing between the Users' Guide, Technical Manual, GUI, and the actual code. This would allow a user to check the underlying code for a given operation without reading the code file that contains multiple modules. This can be accomplished by providing hyperlinks in the electronic versions of the documents, and by providing the annotated code separately (e.g., in the form that can be easily used in a "code browser," or in the form of HTML with the comments as "tool tips"). Furthermore, separating the utility modules from the core modules in the current SHEDS code is relatively straightforward and recommended as this will enhance code readability." (p. 23)

> ***EPA 2010 Response:*** Given available time and resources, other topics had higher priority than cross-referencing and hyperlinking.

2007 Panel Comment: "The naming of the variables within the SHEDS code can be significantly improved. Currently, the code uses cryptic names such as washprob, absr_gr, absr_gm, bioavm, and bioavr, with subtle changes in variable names for different quantities – this can potentially lead to difficult to notice errors. The code can be improved by providing more informative names, and through the use of a "nested" or hierarchy of variables (e.g., through the use of objects/classes in SAS). The variable naming can also be improved by using a consistent naming scheme. For example, the current version of the SHEDS code uses variables such as washprob, has_lawn_p, timeofday_indoor, and re-entry_indoor, all denoting probabilities." (p. 23)

> ***EPA 2010 Response:*** Variable naming has been improved in Version 4. these variables are listed in tables throughout the Technical Manual and in Appendix B.

2007 Panel Comment: "The code changes across different versions should be adequately documented. In fact, it is desirable to have an archive of major versions of SHEDS available to interested researchers so that they can use simple text differences between different versions of the SHEDS code or individual modules." (p. 23)

> ***EPA 2010 Response:*** The differences between versions 3 and 4 are highlighted in Section 1.6 "Changes from version 3 to version 4" in the Residential Technical Manual.

2007 Panel Comment: "The technical documentation and code comments do not mention issues regarding the backward compatibility of the current version with earlier versions, which is very important." (p. 23)

> ***EPA 2010 Response:*** The input and output files from earlier versions are not compatible with version 4. Many of the variables used in version 3 are still used in version 4, although in several cases the variables have been re-named to improve consistency. Also, the exposure and dose boundaries have changed between versions 3 and 4. A list of the correspondences in outputs between the versions is provided in Table 7-1 in the Residential Technical Manual.

2007 Panel Comment: "Additionally, a bug tracking/reporting system is also desirable for users and developers." (p. 23)

> ***EPA 2010 Response:*** We will discuss designating a person(s) for ongoing SHEDS Technical Support via email and/or phone.

2007 Panel Comment: "The technical documentation or code comments should provide details on the intermediate variables in the SHEDS simulations, and on how a user can enable these to be stored and analyzed. Experienced users can then easily obtain summary statistics, improved visualizations, and other desired outputs." (p. 23)

> ***EPA 2010 Response:*** In general, intermediate variables are dropped or are eventually overwritten for space considerations. As noted earlier, advanced SAS users may alter the code to retain any intermediate variables desired. A new feature in version 4 is the ability to resubmit an earlier run using the same random numbers as previously. The user may now request output for selected persons from the earlier run. The intermediate variables for these persons may be saved without overwriting the values for other persons.

2007 Panel Comment: "… some suggestions for improving algorithms as well as for enhancing the consistency between the Technical Manual and code were made [by the Panel]. These include providing reproducibility of simulation results (by reusing a random "seed" if it is provided by the user), addressing or acknowledging issues associated with running stochastic programs on multiple machines and associated potential correlations in the random number generation process." (p. 24)

> ***EPA 2010 Response:*** Reproducibility by controlling the random seed has been implemented in version 4. The Panel's concern regarding correlations from runs on multiple machines has been addressed by using two levels of randomization involving different streams, so whenever the initial seeds for runs are different, the streams do not overlap.

2007 Panel Comment: "A minor comment from the Panel members includes documenting the descriptions of probability distributions used in the Technical Manual and User Guide, because the distributions are often parameterized in different ways, and it is important to clearly describe how these distributions have been parameterized in SHEDS." (p. 24)

> ***EPA 2010 Response:*** Both the Version 4 Residential User Guide and Technical Manual now contain the detailed probability distribution descriptions in an appendix.

F. Multiple Chemicals

Question 2-1: Please comment on the technical aspects and usefulness of the planned methodology for extending SHEDS-Multimedia version 3 to address multiple chemicals in version 4.

2007 Panel Comment: "The Panel focused its comments [on extending the application of SHEDS from single to multiple chemical assessments] on issues associated with tracking of mass of media and chemical, product co-occurrence, pesticide metabolites, programming issues, scenarios, database representativeness and absorption and bioavailability.

"The logic of extending the application of SHEDS from single to multiple chemical assessments is plausible and warranted. However the nature of such proposed work would be complex, time and resource consuming, and the process itself may pose significant challenges. The Panel expressed several concerns about the planned methodology.

"…Overall, the concept of going from aggregate to cumulative as described is useful. One important feature that is not mentioned in the document is the importance of input from risk managers and Agency scientists about the chemicals that are subject to cumulative assessments and the process used to make these determinations. Once this decision is made the focus shifts to model structure and outputs, and the

Panel focused its comments on mass tracking, product co-occurrence, pesticide metabolites, programming issues, scenarios, and absorption and bioavailability." (p. 24)

> ***EPA 2010 Response:*** The importance of input from risk managers and Agency scientists about the chemicals that are subject to cumulative assessments and the process used to make these determinations is not directly relevant to the SHEDS structure or manuals and does not need to be discussed in them.

2007 Panel Comment: "The process of tracking mass is unclear in Version 3, and many Panel members felt that future versions of the model should track mass in media because, for example, it makes it possible to track the mass that is lost through touching and subsequent washing of the hand, and allows tracking of mass in specific media over time. The Agency is encouraged to explore the feasibility of this mass balance step. The Panel noted that, in the document, the definition of "carrier" in SHEDS is somewhat overlapping with "media." For example, air (either indoor or outdoor, or in the treated or untreated rooms) is considered a carrier and a medium in some places in the manual. The manual is also unclear as to why "residue" itself would be considered as a carrier. Residue has to be associated with or adhered to the carrier before it can reach the simulated individuals in any of the media. As stated in the documentation, "When a person comes into contact with a contaminated MEDIUM, a certain amount of one of more carriers will be transferred onto or into the body" (page 7, SHEDS Version 4 Planning document, June 12, 2007 version). Care must be taken to correctly define and use the terms "carrier", "media" and "residue."" (p. 24-25)

> ***EPA 2010 Response:*** We are tracking mass of chemicals contacted in version 4 via loading and removal processes; however, we do not feel that the benefit obtained by a mass balance approach to tracking chemical mass in the various media would outweigh the effort needed and the computational difficulties that would arise. Our experience indicates that the adjustments needed to the environmental concentrations are insignificant. Terminology has been revised in the version 4 Technical Manual. The terms "carrier" and "residue" are no longer used. The model code now computes the chemical mass in the microenvironments and the amount transferred to the simulated individual, and reports the ratio as the "chemfrac" variable.

2007 Panel Comment: "A scenario (a child playing with uncontaminated soil) provided by the Agency further complicated this matter. As stated in the documentation, by taking into account such activity, the mass of the carrier, which is soil, will change on the hands, the body, and possibly in the GI tract. However, if the soil is not contaminated, the change of soil mass would not affect the model outputs. Since each diary is being considered as an independent event (with some autocorrelation), even if this child might come in contact with contaminated soil on a different occasion, the mass of the soil that will be transferred this time would not affect the mass of soil that is uncontaminated." (p. 25)

> ***EPA 2010 Response:*** The example cited was hypothetical and only intended to apply within the context of a "carrier" implementation for version 4, and assumed that all contact would be modeled to determine total "carrier" exposure (for example, a mixture of contaminated and uncontaminated soil). However, as a simplification measure, dust and soil exposure have been revised for the exposure calculations in version 4. This point is explained in Section 1.6.2 "Dust and soil ingestion in version 4" and Section 2.6 "Contact Duration and Concentration averaging."

2007 Panel Comment: "As stated by the Agency, the run-time and the storage space for the model output may significantly be hampered by the proposed approach, if all the chemicals in the formulation are included in developing the variables. However, if the intent of developing SHEDS version 4 is to cumulatively assess exposures to a group of chemicals that has the same toxicological endpoint, the concern about resources may not be warranted. One Panel member noted that it is uncommon to have a single product containing more than 2 active ingredients that cause the same health concern. So instead of n=10 as proposed for use in the algorithms in version 4, the actual sample size might be no more than 3." (p. 25)

EPA 2010 Response: While we agree that is useful to have an upper bound on the number of chemicals, we cannot in the model development process rule out the ability of the model to address several chemicals simultaneously. We recognize that there may be a need for more than 10 chemicals within a single simulation.

2007 Panel Comment: "The document available for the Panel to review is brief and lacks detail on a number of issues. The Panel noted that the current product-related co-occurrence system may be problematic if there are substantial future changes in product formulation. This also implies that intentional product co-occurrence is more important than unintentional "random" product co-occurrence, an assumption that needs close inspection. The document was unclear, but during the presentation the Agency indicated that it will consider addressing both multiple products that contain multiple chemicals and multiple chemicals with a common mode of action that are not necessarily present in a single product. The Agency should explore using different data sources for assessing multiple chemical co-occurrences: for example, pesticide use data could potentially be useful for assessing multiple chemicals for different purposes (e.g., garden versus indoor versus lawn). In addition, the considerations for co-occurrence for residue in food is another complex issue to be explored (e.g., number of pesticides found in one food commodity versus multiple chemicals in a salad) that is not fully explicated in the document." (p. 25)

EPA 2010 Response: We appreciate the Panel's concern regarding the brevity of the documents describing these model extensions. The version 4 Residential Technical Manual provides a complete explanation of the revised model. The Panel's concern with respect to co-occurrence between different scenarios is not an issue in version 4 – users may specify intentional co-occurrence or leave the probabilities as independent. This is described in Section 2.4.3 "Chemical usage patterns (applications)" with more specific discussion in Sections 2.4.3.1 "Usage frequency" and 2.4.3.2 "Usage dates and co-occurrence" and 3.4.3 "Co-occurrence Factors" in the Technical Manual. When multiple chemicals of interest are present in the same residential model run, SHEDS automatically calculates co-occurring exposures based on the user-specified co-occurrence pattern mentioned above. Regarding the dietary module, SHEDS accounts for co-occurrence by preserving the structure of PDP residue data, which captures co-occurrence by analyzing each sample for multiple chemicals.

2007 Panel Comment: "The Panel noted that the ability to model compound metabolites should be included in the multiple chemical model, but this will require development of a module to quantify metabolite production. One Panel member noted that one important lesson from the Agency's CTEPP (Children's Total Exposure to Persistent Pesticides and Other Persistent Organic Pollutants) Study is that tracking of metabolites is necessary for mass balance. In the absence of full accounting for metabolites, evaluation of model performance will be limited to a small number of compounds, such as PCP and 2,4-D, for which the urinary biomarker is the parent compound." (p. 25)

EPA 2010 Response: The Panel has recommended that SHEDS does not need an improved PK model (for example, that may include metabolism) but rather focus on linking with existing dose models for this purpose.

2007 Panel Comment: "The current document states that using a single efficiency for washing removal of soil/dust from the skin regardless of compound is an advantage of the multiple chemical model. Uniform washing efficiency may be reasonable for soil or dust-borne chemicals. However, a single removal efficiency is also apparently assumed for "residues" (i.e., for free chemical on the skin). Since chemical washing efficiency is likely to be tied to the physical-chemical properties of a given chemical, this could be a disadvantage. Relatively lipophilic compounds are less likely to be efficiently removed by washing than relatively water soluble compounds." (p. 25-26)

> ***EPA 2010 Response:*** As noted in the response to the Panel's earlier comment regarding dermal absorption, we believe that this recommendation arises from unclear terminology. In SHEDS, residues are not free chemical on the skin. We assume that the amount of "free chemical" is negligible in practice and that all chemical will be bound in some matrix or carrier. Terminology has been improved in the Technical Manual. Chemical-specific washing removal rates can be specified, if desired, using the SAS data set editor.

2007 Panel Comment: "While this move from aggregate to cumulative assessment provides an opportunity to use an "object oriented" programming approach for encapsulation of variables, it is also possible that users can be overwhelmed by the number of parameters that they have to provide. Therefore, the Panel envisions that GUI modifications may be substantial (e.g., moving from pesticide-specific interface to general multimedia interface) even though the underlying code changes may be relatively minor. Therefore, it is desirable to have one underlying code base and different interfaces." (p. 26)

> ***EPA 2010 Response:*** A true object-oriented approach is not compatible with the SAS programming language. As noted earlier, variable naming has been improved in version 4. Also, the GUI allows users to retrieve and edit chemical-specific input data defined in an earlier run. In addition, the user can load chemical-specific data for permethrin into a new run. In the future, data for other chemicals will be available in SHEDS.

2007 Panel Comment: "One Panel member noted that the memory requirements of such a system may be large due to the increase in the number of chemicals to be simultaneously modeled. The temporal resolution of the simulation will potentially be dictated by the fastest simulation time and the lowest time scale to be modeled." (p. 26)

> ***EPA 2010 Response:*** If a large number of chemicals are to be run simultaneously, then this is a potentially serious issue. The version 4 code loops over chemicals and overwrites temporary variables and files specific to each chemical, thus reducing storage needs. While the quantity of output grows with the number of chemicals, this is limited by the space on the hard drive, not by memory. Changing the temporal resolution from the current CHAD diary event level would require substantial changes in the exposure algorithm. So far, there is no indication that the temporal resolution must be altered to permit runs with many chemicals.

2007 Panel Comment: "An additional feature that is desirable but not included in the written plan is scenarios for home applicator exposure. This was presented at the meeting as one potential added component for version 4, and includes both professional and home applicators, and the Panel felt that this was an important addition that needs careful consideration." (p. 26)

> ***EPA 2010 Response:*** Handler exposure by home applicators is available in version 4. However, this is designed to simulate exposure of a resident who applies pesticides, not a pest control professional.

2007 Panel Comment: "One Panel member noted that the description of absorption efficiency and bioavailability for non-dermal pathways in the Technical Manual is unclear, and therefore the state of science cannot be evaluated because equations and model inputs are not available. The Panel cautions that, like dermal absorption, GI and lung bioavailability estimations and assumptions are dependent upon factors such as medium, particle size, material thickness on exposure surfaces, and other factors that need careful attention in a multi-pathway, multi-media, and multi-chemical model." (p. 26)

> ***EPA 2010 Response:*** Terminology has been revised for Version 4. Regarding the Panel's caution with respect to absorption, the focus of SHEDS is on the exposure to the chemical(s). As recommended by the Panel and noted elsewhere, SHEDS will be linked to a more sophisticated dose model. This linkage with ORD's PBPK model, illustrated with a permethrin case study, will be presented at the 2010 July SAP meeting.

G. Fugacity

Question 2-2: Please comment on the technical aspects and usefulness of the planned methodology for incorporating a fugacity-based source-to-concentration module into SHEDS-Multimedia version 4. Does the Panel recommend additional efforts with the fugacity module (e.g., modeling more realistic multi-room dwellings) given available information?

2007 Panel Comment: "The Panel believes that the fugacity approach is well suited to treatment of multiple chemicals and is therefore compatible with other development goals for SHEDS, but the Panel had less unanimity about whether the fugacity option would provide more useful results than approaches currently used in the model. The Panel expressed a desire to see example calculations and sensitivity analyses that illustrate the performance of the fugacity-based approach."

> ***EPA 2010 Response:*** A fugacity model can be useful to help guide the determination of some version 4 inputs. Such a model has been developed for use with SHEDS, and was presented to the August 2007 SAP. However, this is currently external to SHEDS version 4, not a module within it. Future research could include sensitivity analyses that illustrate the performance of the fugacity-based approach. Depending on those results, the Agency may consider incorporating the fugacity module as an integral part of the SHEDS code.

2007 Panel Comment: "The Panel notes that EPA proposes to evaluate the fugacity module using chemical transport data from a 1-house study. While this is a reasonable place to start, the Panel encourages more extensive testing including application to cases in which both environmental data and biomonitoring data are available." (p. 27)

> ***EPA 2010 Response:*** There are other existing sources of input data that we plan to assess, in addition to the 1-house study, for conducting sensitivity analyses as recommended by the Panel.

2007 Panel Comment: "The Panel expressed less unanimity with respect to the actual likely utility of the fugacity option and expressed a desire to see example calculations that might better illustrate the performance of this option. Only through sensitivity analysis can the question of value be determined. In particular, the effect of time scale being simulated should be examined. The Panel also asked for clarification regarding whether the fugacity approach will be limited to indoor environments." (p. 26-27)

> ***EPA 2010 Response:*** See above. The Agency will conduct additional analyses on the utility and performance of the fugacity model before considering making it an integral part of SHEDS.

2007 Panel Comment: "With respect to the second part of the charge question, the Panel agrees that simulation of a multi-room house is certainly feasible mathematically. Mixed opinions were expressed

regarding the value of moving beyond a two-zone (treated/untreated) model. Clearly there is some point at which lack of data necessary to describe more complicated systems will prevent derivation of added benefit by increasing complexity. The Panel therefore suggested that EPA start with a simple (two-zone) version and more thoroughly investigate and document performance at that level before considering multi-room systems." (p. 27)

> ***EPA 2010 Response:*** We agree that a 2-zone house is adequate for now, but could in the future consider multi-room residences.

2007 Panel Comment: "Under this charge question, there was discussion of whether SHEDS should account for removal of contaminant residues from environmental compartments via absorption by occupants. It was suggested that EPA compare predicted mass absorbed to assumed mass applied for various scenarios to provide more information on this topic. Although the term did not arise explicitly in the discussion, in effect the Panel suggested that EPA include routine computation of Intake Fraction (Bennett et al., 2002a,b) in SHEDS output." (p. 27)

> ***EPA 2010 Response:*** As noted above, SHEDS-Residential version 4 now performs the calculations regarding the fraction of chemical mass that is transferred to the simulated individual. However, the environmental concentrations are not adjusted for this transfer, for two reasons. First, most houses have multiple individuals in them and the removal of chemical by all persons should be considered, as should removal by pets or by cleaning. The simulated individual will generally be a small part of the total removal, and SHEDS already reduces the amount of chemical present on an hourly basis in the decay/dispersion calculations. The second reason is the modularity of SHEDS; the program assumes the activity diary and concentrations are independent and it would complicate the program to have feedback between the diary module and concentration module.

H. New Longitudinal Diary Assembly Method

Question 2-3: Please comment on the technical aspects, potential utility, and added value of the planned methodology for longitudinal diary assembly in SHEDS-Multimedia version 4. Does the Panel believe that this new method will create an assemblage of diaries that better simulates reality and provides more accurate estimates of exposures related to within-individual time-activity patterns? Please suggest procedures and/or longitudinal data which could be used to select factors (the "D" factor intra-class correlation coefficient, and the 1-day lag autocorrelation) or refine/evaluate this method in SHEDS.

2007 Panel Comment: "The Panel believes that it is likely that the current activity database (CHAD) may not contain enough diaries to allow random draws using the new longitudinal diary assembly method and several members raised concerns about the representativeness of the US population in the CHAD dataset. Since a significant number of CHAD diaries were excluded for various reasons, further proposed decisions that reduce an already small dataset might be problematic for accurately determining the within-subject variation. Furthermore, as stated in the documentation, two of the most important pieces of information, chemical usage patterns and contact possibilities, are not included in the diary database. These concerns dampened the enthusiasm of the Panel for implementing this new longitudinal diary assembly method in the upcoming revision of SHEDS." (p. 28)

EPA 2010 Response: The Panel's concerns with respect to small diary pools and the representativeness of CHAD are equally applicable to any diary assembly method, and are related to the user's intended objective. Ideally, the user should customize the diary database to match the target population. For example, CHAD could be restricted to the NHAPS study (approximately 9300 diaries), which is nationally representative. For another example, the diary database was restricted to 1 to 6 year-old children with a minimum amount of outdoor time for a study of exposure to chemicals on decks and play sets. But again, these issues apply to the underlying database, not the assembly method. As noted earlier, improvements in the description of CHAD and how to better customize it to the user's application will be explored.

Small diary pools do make it problematic to model within-subject variation. However, this applies to all diary assembly methods and the new method is better at characterizing within-person variation.

It is true that the main drivers of dermal exposure are not included on the diaries. However, the method is simple to implement and requires little additional input by the user. The new method is now available as an option in version 4.

2007 Panel Comment: "The Panel concurs that including a lag autocorrelation function (currently set at 1-day) would be necessary to eliminate repetitive activities from the longitudinal diaries that are likely unrealistic (such as pumping gas into an individual's car on successive days). However, the Panel suggests that the Agency's efforts should focus on behaviors relevant to potential residential pesticide use, such as frequency of gardening activity, rather than examples related to air pollution exposure assessment." (p. 28)

EPA 2010 Response: One of the advantages of introducing autocorrelation in the diary assembly is that it allows the user to determine the degree of repetitiveness present for the key exposure variable. The Panel is correct in noting that the key variable used in the new method must be relevant to the specific pesticide exposure being modeled. Some suggestions for key variables are listed in Section 5.5.4 "Diary Assembly Method" of the User's Guide.

2007 Panel Comment: "The use of realistic and well documented scenarios in the model is, in the Panel's judgment, as high or higher in priority as further refinement of the diary assembly and autocorrelation methods. For the explicit purpose of estimating the individual and population exposures, it may be more constructive for SHEDS 4 to suggest defaults for key variables and allow for deviation from these defaults as needed by informed users to display the strengths and limitations of the future versions of the model."

EPA 2010 Response: As noted earlier, key variables are listed in Section 5.5.4 "Diary Assembly Method" of the User's Guide and a case study was conducted.

2007 Panel Comment: "The Panel believes that the concept behind the new longitudinal diary assembly method has scientific merits, and the technical aspects of the proposed method based on the D-statistic and 1-day lag autocorrelation is sound. However, the application of this method in the interest of predicting aggregate human exposures to environmental chemicals may be somewhat limited. This is particularly true for activities that may lead to potential exposures that are either difficult or implausible to track as continuous "key variables." For example, it is useful to use the D-statistic for tracking how long a person spent outdoors for studying human exposure to air pollutants (like the "Southern California Ozone Exposure Study" cited by the Agency) because the time spent outdoors is correlated with the amount of ozone being inhaled by the subjects. However, it might not be as feasible to implement the D-statistic approach in compiling longitudinal exposure data sets, such as the frequency of hand contact on a contaminated surface, when multiple factors need to be considered before the

exposure scenario can be confirmed. Such a limitation is inherited from the concept of incorporating the within and between-subject variation in order to better control the longitudinal properties of the final assembled diary. The key variable(s) also needs to be ranked in order to generate the x-score. Those theoretical requirements constrain the utility of this proposed method for predicting longitudinal exposures in which inhalation exposure is not the predominate pathway. In other words, unless the longitudinal diaries do not encompass a great number of human micro-activities (such as potential exposures other than inhalation) in which time spent in the area where the contaminant is present is the only and the ideal key variable, the incorporation of this new longitudinal diary assembly method in SHEDS version 4 may not add significant value. Based on Glen et al. (2007), it appears that there is also a possibility to choose more than one key variable for creating a longitudinal diary and therefore the Agency is encouraged to explore this possibility."

> ***EPA 2010 Response:*** We agree that there may be situations for which the new method does not provide a significant benefit over existing methods. However, SHEDS is a general model designed to be applicable to multiple chemicals and multiple pathways. For some of these pathways, the variables in the CHAD database may be very relevant. Therefore, we felt that it is useful to add the new method as an option. Given the work detailed in Glen et al. (2007) and the fact that the method has been incorporated in another SHEDS model, the effort to include it in Version 4 was manageable. As a point of clarification, the Glen et al. reference suggested combining diary variables into a single key variable as opposed to having multiple key variables.

2007 Panel Comment: "One Panel member wanted to see how the longitudinal diary development using the D-statistic and the autocorrelation would impact exposure prediction. As presented by the Agency, there are several data sets that have the potential to be used for this purpose, and the Panel recommends that the Agency contact the PI of those studies to obtain permission to access their data sets." (p. 28-29)

> ***EPA 2010 Response:*** Exploration of some of these longitudinal datasets is currently underway. For example, EPA is analyzing 10 new longitudinal CHAD diaries collected by the Office of Research and Development. EPA has also recently obtained longitudinal dietary data from Dr. Alex Lu that was mentioned at the August 2007 SAP meeting. We plan to examine the D&A statistics from these datasets.

I. Sobol

Question 2-4: Please comment on the technical aspects and usefulness of the planned methodology for utilizing Sobol's method for sensitivity analysis in SHEDS-Multimedia version 4, and whether Sobol's method would be a useful supplement to the existing sensitivity analysis methods used for the SHEDS-Multimedia version 3 model.

2007 Panel Comment: "The Panel was divided on the utility of Sobol's method, and wondered whether the new sensitivity analysis method is needed. Several Panel members expressed concern that the required number of simulations for sensitivity analysis appeared to be very low. The Agency's view that a single sensitivity run can be considered to represent multiple "individual-days" of simulations is not correct, because a single variability run will ultimately produce a single population metric (e.g., the 95th percentile for population exposures). It appears that the proposed use of Sobol's method will allow the computation of "local sensitivity," without addressing the corresponding uncertainty. Global sensitivity analysis, on the other hand, allows the estimation of sensitivity as well as uncertainty, and thus would be a preferred approach.

"Several Panel members expressed concern that the required number of simulations (2N + 2) for sensitivity analysis involving N parameters appears to be very low. For example, if a single parameter has 10 levels of values, doing a sensitivity analysis with just 4 simulations (2*1+2) is impractical. The Agency's view that a single sensitivity run can be considered to represent multiple "individual-days" of simulations is not correct in this case, because a single variability run will ultimately produce a single population metric (e.g., the 95th percentile for population exposures).

"...Many of the Panel members were not convinced about the utility of the Sobol's method for SHEDS, and were also perplexed by the complexity of the method.

"...Since Sobol's method has not been used with a large scale probabilistic model before, the Panel urges caution in using the method. Furthermore, the number of changes to the model structure and code (e.g., by making a majority of the SHEDS code deterministic, with random parameters provided in one module) appear to be large, further reducing the usefulness of incorporating this methodology in SHEDS.

"However, some Panel members felt that since the Sobol method is an accepted method for sensitivity analysis it should be included, since in general it is a good idea to provide new techniques as alternatives to variability and uncertainty analysis." (p. 29)

EPA 2010 Response: We appreciate the Panel's difficulty in being able to evaluate a complex and unfamiliar method given the limited amount of material provided. There seems to be a misunderstanding of the method with respect to several points. More extensive explication of the approach is certainly desirable. A manuscript is in preparation on this, and a poster was presented on the topic at the 2007 ISEA conference (Glen G., Isaacs, K. Smith, L. Adapting Sobol's method of sensitivity analysis to stochastic models. The 17th Annual Conference of the International Society of Exposure Analysis. Durham, NC. October 14-18, 2007.). With respect to several specific points raised by the Panel, we offer the following comments. These brief comments are intended to clarify, but do not fully explain the method.

- Sobol's method does not target the sensitivity of any particular population summary statistic (such as the 95th percentile). Rather, it attempts to answer the question of why individuals differ in their ultimate exposure. Briefly, it quantifies the relationship between input settings and exposure through random variation of selected subsets of the inputs. Because the entire parameter space is explored, Sobol's method is a global sensitivity analysis method.

- The number of runs in Sobol's method is adequate to address sensitivity as described above. There may be confusion between the number of individuals simulated and the 2N+2 runs. The latter represents the number of selected subsets of inputs that are used. As with a variability run in SHEDS, the number of individuals is the user's choice and a larger number of individuals provides a better characterization of sensitivity.

- The panel is correct that Sobol's method does not address uncertainty explicitly. Sobol's method can address both variability and uncertainty by folding the two into a single distribution for each input. However, it is envisioned that the current SHEDS 2-stage approach will be maintained for uncertainty analysis.

- As the Panel noted earlier, it is quite desirable to control the random number seeds to allow reproducibility of the model runs. As noted earlier, this capability was not present in v.3 but this

was added in v.4. This is the key requirement in terms of implementing Sobol's method for the SHEDS code, and this is what was meant by making the SHEDS code deterministic.

- In their comments, the Panel suggested that Sobol's method is a variant of the FAST sensitivity analysis method. This is incorrect. Both are variance decomposition approaches, but otherwise are very distinct. Both were explored for use in SHEDS, but FAST had limitations that rendered it inapplicable to SHEDS. Briefly, FAST requires a number of incommensurate frequencies equal to the number of inputs. The number of available frequencies is limited, and the number of runs required to calculate the sensitivity quickly becomes infeasible. Another major limitation was that FAST provided no reasonable method for handling variables that must be re-sampled through time. In addition, Sobol's method handles discrete inputs better.

- The Panel also suggested the use of ANOVA for sensitivity analysis. In addition, at least one Panel member thought that Sobol's method was a reinvention of experimental design. It was not the intention to suggest that Sobol's method replace ANOVA. Quite to the contrary, we feel that Sobol's analysis can be a useful complement to helping design an effective ANOVA approach. Though Sobol's method does not provide a statistical significance test, it is extremely helpful in indicating which combinations of inputs are negligible and which inputs have important interactions associated with them. Thus, results from Sobol's analysis can provide very valuable input to the design of, for example, a fractional factorial ANOVA.

- Sobol's method has been added as an option for sensitivity analyses. This is described in the SHEDS-Residential version 4 Technical Manual, section 6.5, and also in the User Guide section 5.11.5.2. Sobol's method is an option to the user through the version 4 GUI.

J. Other Changes

Question 2-5 a) Please comment on (and prioritize, as appropriate) the technical aspects and usefulness of planned changes to the SAS code and GUI for SHEDS-Multimedia version 4 that are listed items in Section 5 of the above-referenced background document. b) Please comment on any additional modules, features, or capabilities that the Panel feels should also be high priorities for the next version of SHEDS including issues associated with the code, user interface/user friendliness, input, and output/output display. Are there modules, features, or capabilities of other human exposure models that should be considered for inclusion in SHEDS-Multimedia version 4 (e.g. simulation of individuals; longitudinal diary assembly?

2007 Panel Comment: "As a first suggestion the Panel felt that the developers should do everything that is simple and does not involve a major reorganization of the code. At the same time, a lot of effort should not be placed into options that will not make much difference in the overall conclusions drawn from the model. Most Panel members thought that PBPK modules should not be a high priority and should remain independent modules from the SHEDS model output."

> ***EPA 2010 Response:*** Version 4 incorporates exposure to multiple chemicals and addresses key comments from the 2007 SAP; it does not contain a detailed PBPK module.

2007 Panel Comment: "The Panel felt that the Agency should get more experience with the application of this model before getting into a major reorganization of the code. It is important that the developers anticipate future data sets, especially longitudinal, and try to keep the code scalable. Autocorrelation can have an important effect on the tails of the exposure distributions. Anything that helps the user understand uncertainty and variability is important. Several Panel members emphasized that improved graphics were important for wide model comprehension and acceptance. They also felt it was useful to

add utilities to make the model more accessible and useful, e.g., code to review input values and note extreme or illogical combinations, or a script generator to run designed experiments on the model. This is similar to sensitivity analysis but could be more general. The user could ask a series of questions about what factors and interactions are of interest, and then plan and implement a fractional factorial or response surface design to test hypotheses. Prior to adding additional functionality (modules, features, or capabilities), sensitivity analysis with the specific modeling assumptions should be conducted. This involves defining the population exposure metrics, and performing sensitivity analysis. It is possible that some proposed features can be discarded after this analysis, based on lack of sensitivity of the exposure metric to the new feature." (p. 30)

EPA 2010 Response: These summary comments have been addressed above.

2007 Panel Comment: "The Panel liked the idea of users being able to re-parameterize distribution mean, variance and shape so they can conveniently move between distributions without having to refer to statistics texts (e.g., Johnson, et al., 1994, 1995, and 2005) for the parameter definitions. Experience has shown, however, that unless a distribution has an extreme right tail, the choice of distribution does not make much difference." (p. 30)

EPA 2010 Response: The version 4 GUI reports summary statistics such as the mean when plotting distributions, but does not automatically parameterize different forms to match their moments.

2007 Panel Comment: "Some users of the model will not be constrained by EPA practice and will want to model non-compliant application, i.e., not following the pesticide label. It is important that the model provide an "application programming interface" definition that describes the format and the type of intermediate data, in a simple and easy to use manner. This will lead to the following advantages: a) users and developers can independently create input/output analysis modules, provided there is adequate documentation for developing such tools; b) this will overcome current issues with the quality of plots and graphs; and c) provide facility to input empirical distributions for specifying uncertainty and variability; d) plus provide sufficient number of examples, so the novice and expert users can utilize the system to the fullest extent." (p. 30-31)

EPA 2010 Response: With the changes to version 4, much of what the panel requests is available. The user may create a non-compliant scenario, if desired. This is accomplished simply via the choice of inputs. Also see Section 5.7.1.1 "Create User-Defined Scenario" in the User Guide. The output capabilities have been enhanced in version 4 so that the user may conduct their own analyses of model outputs.

The SAS language packages the input and output data in a form that can be manipulated by other SAS programs. Essentially, SAS data sets already have the API capabilities discussed above.

2007 Panel Comment: "The Panel felt that it would be useful if SHEDS provided better context-specific help files, the ability to calculate margins of exposure (MOEs), and other options for selecting and matching CHAD and food consumption diaries (e.g., by age, gender, season, weekday, region, race, METS/caloric intake)." (p. 31)

EPA 2010 Response: Help buttons on now provided throughout the GUI, and illustrative case studies are presented in the manuals. MOEs are now available in version 4. EPA is currently finalizing guidance to address such issues as differing exposure averaging times and the interpretation of population variability. We will explore other options for selecting and matching

CHAD and food consumption diaries, and seek the July 2010 SAP's input on linking dietary and residential modules.

APPENDIX

SHEDS-Dietary Option/Feature	Available in SHEDS-Dietary?	Notes [Option linked to 2007 FIFRA SAP Question]
Food Consumption Data Sources		
CSFII (1994-96, 1998 Children supplemental)	Yes	Data used in Agency risk assessments (e.g., DEEM-FCID™)
NHANES (1999-2006), Preliminary data	Yes	Food recipes not available for new foods
Modeling Longitudinal Consumption (Food, Water) Patterns		
Within Day Direct DW Consumption: 6 Equal Amounts, Fixed Times (6 am, 9, 12, 3, 6, 9 pm)	Yes	**[Q3 FIFRA SAP 2007]**
Within Day Consumption of Direct DW: Bayer DW Consumption Survey	Yes	**[Q3 FIFRA SAP 2007]**
2-Diary	Yes	Similar to Method used in Agency risk assessments (e.g., Calendex-FCID™)
8-Diary	Yes	**[Q2 & Q5 FIFRA SAP 2007**; option available but not recommended; will be dropped in next update since data not included in NHANES]
Diary Assembly (DA)	Yes	Currently based on Total Caloric Intake
Residues (Food & Drinking Water)		
Commodity (FCID) Residues	Yes	Method used in OPP risk assessments (e.g., DEEM-FCID™)
Food Residue (vs. Commodity)	No	Option used to assess Arsenic (Journal article); Case study assigns residues to FCID commodities; Difficult to Incorporate in GUI
Drinking Water Concentrations	Yes	Single Distributions only (e.g., DEEM-FCID™)
Drinking Water Concentrations – Calendar Year	No	Randomly Select Year, then apply to corresponding Modeled Day (e.g., Calendex-FCID™ and CARES™ use of 30 years of PRZM-EXAMS predicted DW concentrations)
Modeling Food Residues		
Select Single Residue for all Eating Occasions, by Commodity (RAC-FF)	Yes	Method used in Agency risk assessments (e.g., DEEM-FCID™)
Select New Residue for different Eating Occasions, by Food-RAC-FF	Yes	**[Q1 FIFRA SAP 2007**, 32; Option often has little effect for food-only analyses; may 'add' uncertainty]
Correlation across commodities, across multiple chemicals (products) applied to foods, and over subsequent days	No	Minimal data to implement; (FIFRA SAP 2007, p.25)
Multiple Distributions for Commodity (RAC-FF)	No	E.g., probability of 'Domestic' or 'Import';
Multiple Distributions for Commodity (RAC-FF), By Season	No	**[Q5 FIFRA SAP 2007]** E.g., linking food consumption with seasonal (and/or regional) residues
Modeling Drinking Water Concentrations		
Randomly select new DW concentration each day	Yes	Method used in Agency risk assessments (e.g., DEEM-FCID™)
Randomly select Year for each Person-iteration, then apply Predicted DW based on Calendar (365) date	No	Retain seasonal patterns (autocorrelation) in DW concentrations. Method used in Agency risk assessments (e.g., Calendex-FCID™, CARES™)
Sensitivity/Uncertainty Analyses		
Sensitivity Analyses	*	Requires supplemental routine (e.g., effect of consumption outliers on infant DW exposures – aldicarb memo)
Uncertainty Analyses	*	**[Q4 FIFRA SAP 2007]** Requires supplemental routine

SHEDS-Dietary Option/Feature	Available in SHEDS-Dietary?	Notes [Option linked to 2007 FIFRA SAP Question]
Compiling/Viewing Summary Statistics		
Total Daily Exposures (99.9th)	Yes	Measure used in OPP assessments
Average Daily Exposures (99.9th)	*	Need supplemental routine
Eating Occasions (99.9th) based on Maximum Exposure over all Eating Occasions	Yes	Method used to characterize exposures (NMC CRA)
Eating Occasions with Chemical-Specific Half-Life (99.9th)	*	Method used in DEEM-Based Eating Occasions analyses; Need supplemental routine. Supplemental program to calculate per capita 99.9th for single-chemical, single-day was recently incorporated into GUI; needs QC.
Plotting Person-Day Exposures	Yes	Visualize Exposure Patterns/Persisting Dose
Contribution Analyses: Shares of Total Exposure, by Commodity	Yes	Used to develop risk mitigation options
Contribution Analyses: Shares of Total Consumption, by Food (Commodity)	Yes	
Output Summary Results (99.9th, CEC, etc.) to File (MS Excel/MS Word)	*	SAS Editor/Wizard allow users to export results
View/Query Data (Food Diaries, Recipes, etc.)	*	SAS Editor allows users to view/query data
New Aggregate Contribution Analyses	*	Need supplemental routine

* not implemented in GUI but can be conducted using SAS code