External Peer Review of
Child-Specific Exposure Factors Handbook:
EPA Response to Peer Review Comments

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This report is a summary of discussion points made during the External Peer Review Workshop of EPA's Draft Document *Child-Specific Exposure Factors Handbook,* held September 19-20, 2007, in Arlington, Virginia. This report captures the main points made by the peer reviewers at the workshop, and EPA's responses to the peer reviewer comments. It is not a complete record of all details discussed, nor does it embellish, interpret, or enlarge upon matters that may have been incomplete or unclear. Statements represent the individual views of meeting participants.

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1.0 INTRODUCTION

The responses to comments from the Recommendations and Conclusions Section of the Final *Report on the External Peer Review Workshop of EPA's Draft Document "Child-Specific Exposure Factors Handbook*" are addressed in this document. It is organized by specific chapter and the recommendations of the reviewers provided for each chapter. Following each comment is the response of the EPA. In addition, the responses to public comments are provided in Appendix A of this document.

2.0 RESPONSE TO PEER REVIEW COMMENTS

2.1 Chapter 1 (Introduction) and General Organizational Issues

Peer reviewers noted that Chapter 1 should serve as a "user's manual" for the handbook. To be more concrete and useful, reviewers suggested the following comments for Chapter 1:

Comment: Re-organized chapter 1 to more clearly lay out the document's background, purpose, rationale, and context, including what has changed in the current handbook compared to the previous exposure factors handbook.

Response: *The front matter and Chapter 1 (introduction) were edited to reflect the comment.*

Comment: Specify what is and is not covered in the document (e.g., toxicokinetics, pharmacokinetic modeling, fetal exposures, and exposure assessment details).

Response: *The front matter and introduction were edited to reflect the comment.*

Comment: Provide examples/scenarios showing how the document could be used (and a reference and subsequent link to Web-based documents on applications).

Response: *This is beyond the scope of the document. There is a separate effort to address this comment.*

Comment: Provide cautionary statements regarding potential pitfalls (e.g., limitations, data needs).

Response*: Data limitation discussions were revised and expanded in every chapter.*

Comment: Be placed online so that links to relevant topics and resources (e.g., "exposure-pedia") can be updated over time.

Response: *The handbook has been placed online on the NCEA homepage. Procedures for updating are being developed.*

Comment: Describe a consistent standardized approach for the subsequent chapters.

Response: *All chapters were revised for consistency of format, data presentation, and level of detail.*

In addition, the handbook's overall organization, presentation, and utility should be improved as follows:

Comment: In the executive summary, include a flow chart showing how this document fits into the overall scheme of a typical exposure/risk assessment sequence.

Response: *A figure was added that explains the exposure-dose effect continuum.*

Comment: In the executive summary, include summary tables that link to details in the subsequent chapters.

Response: *A table was added to the executive summary that summarizes the recommendations from the various chapters of the handbook.*

Comment: Explicitly define the grouping nomenclature used to compile the data in order to provide users with an unambiguous understanding of the eligibility criteria. Clear recommendations for grouping nomenclature are not only feasible but virtually required, since the handbook authors must make judgments in developing, assigning, and assessing the credibility of available exposure factors. This is particularly important given that the handbook is intended for use by a wide range of individuals with varying levels of expertise and sophistication.

Response: *Eligibility criteria were revised and discussions were expanded to make it more clear what key and relevant studies are.*

Comment: Edit all chapters for consistency in voice and presentation, since they currently read as a compilation of different papers.

Response: *The document has been extensively edited to ensure consistency.*

Comment: Reorganize the chapters to present the most important information first, followed by the background or historical information. For example, move the conclusions and recommendations to the beginning of each chapter, accompanied by any supporting tables to provide relevant background or support the conclusions.

Response: *The document has been reorganized to provide a summary of the recommendations for each factor at the beginning of each chapter. This includes a narrative description of the recommendations, a table of recommended values, and a table depicting EPA's confidence in recommended values.*

Comment: Provide a glossary of terminology.

Response: *A glossary was added to the document.*

Comment: The handbook currently uses inconsistent acronyms and parameter/variable notation conventions, reflecting the diversity of uses found in the literature. Use consistent notation throughout the handbook.

Response: *The document was edited for consistency.*

Comment: At the beginning of each chapter, summarize which studies are key to the chapter conclusions.

Response: *A summary of the recommendations for each factor have been moved to the beginning of each chapter, and the key studies used in developing these recommendation are identified.*

Comment: Where possible, standardize the summary tables (e.g., their titles, format, layout) and utilize consistent statistical parameters (e.g., number of subjects in groups, measures of central tendency, measures of variability). Tables should present the information the same way to make it easy to extract the most important information. Perhaps EPA could develop a table format for this document to highlight the information to the reader in the same way that Edward Tufte has written about constructing graphs.

Response: *EPA has standardized the table formats to the extent possible (e.g., where EPA has conducted its own analysis of a data set or where meta analyses of data from more than one study has been conducted). However, in some cases the raw data were not available to allow for the data to be standardized. In these cases, the data are presented in the way they were presented by the original authors. Data are presented for the standardized age groups.*

Comment: A number of tables, such as those in Chapter 9, although quite extensive, are presented without comment or much guidance about how they are to be used by risk assessors or the public. Users who are not embedded in or familiar with the EPA culture will likely find it difficult to apply these tables to their own needs. EPA should consider providing further guidance, perhaps in the form of examples or scenarios.

Response: *EPA is in the process of developing example scenarios that will illustrate the use of data from the Child-specific Exposure Factors Handbook. This document will be issued as a companion document to the handbook.*

Comment: In the chapters, many of the tables are separated into categories called "doers" or "non-doers," (or "consumers" or "non-consumers"), but these terms are not defined and it is left to the reader to create a definition. These terms should be defined in Chapter 1 and used consistently throughout the handbook.

Response: *These terms have been defined in the relevant chapters of the handbook and in the glossary.*

Comment: In each chapter, include a section on "data limitations" and "research needs."

Response: *Data limitation discussions were revised for consistency and expanded. The U.S. EPA decided against a research needs section because needs are better identified by the users. Instead the U.S. EPA has provided expanded discussions about data limitations.*

Comment: Develop an explicit procedure for updating the handbook, and then update it regularly to maintain the handbook as a dynamic document.

Response: *The U.S. EPA is in the process of developing options to best accomplish this task.*

Comment: In the executive summary, provide a table listing each chapter and the date of the latest revision (revision being defined as a change in quality of the substantive data provided).

Response: *This will apply to future revisions.*

Comment: With each update, provide in each changed chapter a paragraph statement detailing what updates were included and the date of currency.

Response: *This will apply to future revisions. The handbook states that it is current up to July 2008.*

Comment: Provide the handbook as a Web-accessible, hyperlinked document. This would have several advantages. It would (1) provide a flexible, dynamic, easily modifiable source of information for both EPA risk assessors and the wider public; (2) enable data such as those in Tables 9-1 to 9-73 to be included only as links to another source; (3) permit EPA to more easily update the document; and (4) make it possible for the public to provide immediate feedback to EPA on the document.

Response: *The U.S. EPA is in the process of developing options to best accomplish this task.*

2.2 Comments Related to Charge Question 2

Charge Question 2: Do the confidence ratings provide a clear rationale and adequately reflect the advantages and/or limitations of the studies addressed in the document? If not, please provide suggestions for alternative approaches for addressing confidence ratings. It has previously been suggested that the handbook provide a quantitative characterization of confidence in specific exposure factors.

Comment: In general, the reviewers agreed that some form of confidence rating was appropriate. They also agreed that quantitative confidence ratings were not appropriate given the underlying uncertainties in the exposure data.

Response: *Confidence ratings were revised to make them more transparent. No quantitative rating was provided.*

Comment: Reviewers discussed the appropriate form of the qualitative ratings. One reviewer suggested (and others concurred) that instead of low, medium, and high ratings, EPA should consider using language such as "increasing confidence" or "decreasing confidence." Another reviewer suggested fine-tuning the confidence ratings with additional categories such as Low-Medium, Medium-Medium, and High-Medium.

Response: *The table in the introduction was revised to address this comment.*

Comment: Reviewers generally agreed that EPA should provide a more thorough explanation of how it arrived at the overall confidence ratings.

Response: *Confidence ratings were revised to provide more transparency.*

Comment: EPA will likely require flexibility in deriving the overall confidence ratings, given the nature of the available data and the exposure factor being considered; these judgment calls should be transparent in the document.

Response: *Confidence ratings were revised to provide more transparency.*

Comment: Reviewers were generally concerned about the rating elements. They concurred that the ratings should get at the underlying validity of the data rather than relying on arbitrary metrics. While many of the rating elements already do this, some seemed arbitrary and should be revised. In particular, the rating of currency with an arbitrary cutoff date of 1990 is not appropriate, as a study's relevance depends on the variability of the exposure factor over time; there are many studies from well before 1990 that would still be considered "current" and others conducted more recently that are not. Similarly, study size should not be an arbitrary number: it should be based on the sample size needed to assess the underlying population distribution in the exposure factor of interest. Also, EPA should revise or eliminate the criteria on number of studies (3 = high, 1 = low).

Response: *Confidence ratings were revised to provide more transparency.*

Comment: Reviewers suggested that EPA consider collapsing the elements into fewer categories that get at the validity of the underlying data, including considerations such as the potential for bias and measurement error. They suggested that, when developing the confidence ratings, EPA should consider the number of literature citations to a particular study, using Science Citation or a similar approach.

Response: *Elements were collapsed into general categories to simplify.*

Comment: Reviewers did not agree that a study should be automatically downgraded because it was carried out and/or published in another country. A reviewer added the following post-meeting comment on this point: "EPA should officially reverse this policy of automatically downgrading studies from other countries. Many European countries maintain comprehensive databases linked to their national health care systems, so that in many instances their data are more reliable than those available in the U.S."

***Response**: Data from other countries were considered when there were reasons to believe that geographical, regional, and cultural differences would not affect the factor of interest.*

2.3 Comments Related to Charge Questions 3, 5, and 10

Charge Question 3: Please comment on whether data variability has been adequately addressed.
Charge Question 5: Please comment on whether or not the CSEFH document should present normative discussions about how to use data and uncertainty.
Charge Question 10: We acknowledge that there have been significant developments in the area of uncertainty analysis. The handbook refers to the 1997 Exposure Factors Handbook for more information in this area. Since we are in the process of updating the 1997 Exposure Factors Handbook, can you offer any suggestions for updating this section?

Comments: In some cases, there seemed to be ambiguity and perhaps some inconsistency in EPA's use of the term "upper percentile." A consistent and clear single definition of this term would be helpful.

The panel recognizes the caveat at the top of page 1-12 that "This handbook is not intended to provide complete guidance on probabilistic analyses." However, the update to both the 1997 Exposure Factors Handbook and this specific document can and should go further in alerting the reader that ultimately non-screening analyses should utilize probabilistic techniques. In addition, the document should highlight the non-obvious implications of using distributions of measured data for deriving risk-related variability and uncertainty distributions. For example, the reader needs to be aware that, other things being equal.

> Standard statistical descriptions of data (e.g., standard deviations) tend to overstate true (population) variability by including measurement errors. It is only the population variability (after excluding the spreading of the data from errors in the measurement techniques) that affects the spread of individual risks. For parameters where the measurement uncertainty has the same distributional form as the population risk-related variability, the "true" variability can be estimated by subtracting the variance attributed to measurement error from the total observed variance (Hattis and Silver, 1994):
>
> variance from true heterogeneity = observed variance – measurement error variance
>
> *(Hattis, D., and Silver, K. 1994. Human interindividual variability—a major source of uncertainty in assessing risks for non-cancer health effects. Risk Anal. 14: 421-431).*
>
> Standard descriptors of uncertainty (e.g., standard errors) tend to understate real uncertainty, often greatly, by omitting the effects of unsuspected systemic errors in both sample representativeness and such problems as miscalibration of measuring equipment. There are ways of correcting for this (Schlyakhter, 1994), but they have not yet been widely implemented for environmental exposure factor measurements,

and even the recognition of this problem is not yet widespread among statisticians and environmental scientists.

(Shlyakhter, A.I. 1994. An improved framework for uncertainty analysis: accounting for unsuspected errors. Risk Anal. 14: 441-447).

Response: *The term upper percentile was defined in the glossary and in the introduction. Other citations were added. The Exposure Factors Handbook will be revised and updated accordingly.*

Comment: When presenting distribution percentiles, a caveat should generally be included if the spread of the percentile values is implicitly based on a combination of variability and uncertainty. If should be noted if raw values have been compiled without adjusting for the spreading of the distribution due to measurement errors.

Response: *This issue is discussed in chapter 2.*

Comment: With respect to combining variability factors, EPA should discuss the caveats needed for the use of its summary descriptors of variability (e.g., upper percentiles) in analyses of different levels of sophistication. For example, it may not be appropriate to propagate multiple "upper percentile" estimates of different exposure factors in deriving realistic descriptions of full population distributions of exposure.

Response: *Discussions were added to describe limitations of the various studies.*

Comment: A frequent major issue in risk assessments for long-term effects is how to convert exposure variability distributions from short-term exposure factor observations to variability distributions appropriate for exposures and effects that occur over many months or years. Wallace et al. (1994) have developed and recently successfully tested (Wallace and Williams, 2005) an approach to address this problem.

(Wallace, L.A., Duan, N.; Ziegenfus, R.. 1994. Can long-term exposure distributions be predicted from short-term measurements? Risk Anal. 14: 75-85).

(Wallace, L.; Williams, R. 2005. Validation of a method for estimating long-term exposures based on short-term measurements. Risk Anal. 25: 687-69).

Response: *Both of these papers were added.*

Comment: Note that the panel recommends that EPA implement these revisions in discussions of variability and uncertainty in both the CSEFH and the Exposure Factors Handbook.

Response: *Chapter was revised and there are plans to revise the Exposure Factors Handbook.*

2.4 Comments Related to Charge Question 6

Charge Question 6: It was suggested by one of the internal reviewers that the CSEFH provide recommendations for acute, subchronic, and chronic exposures. Please comment on whether this is a feasible approach given that most of the data come from short-term studies.

Comment: Conceptually, acute, subchronic, and chronic exposures have established durations (see below); however, these durations should be placed in context of the disease outcomes. Given the rapid speed of growth and development during early childhood, the concepts of acute, sub-chronic, and chronic exposures do not really apply to this life stage. For example, a short-term exposure at 1 month may have long-lasting health impact(s) that may not become apparent until later in life. The life stage approach is valuable for addressing this concern. For example, a person-year's exposure (translated down to perhaps person-hours of exposure) could be used to address acute, sub-chronic, and chronic exposures.

[*EPA definitions: **Acute:** One dose or multiple doses of short duration spanning less than or equal to 24 hours. **Subchronic:** Exposure to a substance spanning approximately 10% of the lifetime of an organism. **Chronic:** Multiple exposures occurring over an extended period of time, or a significant fraction of the animal's or individual's lifetime.*]

***Response**: The U.S. EPA's definitions for acute, subchronic, and chronic were added. Life stage framework document was cited.*

Comment: Chapter 1 should discuss the meaning of each of these exposure periods (acute, subchronic, and chronic) and any specific differences that should be taken into account when assessing impacts in young children. For example: Are chronic exposures meaningful for the youngest age group (<1 month), since a child that young would only have had time to experience acute and sub-chronic exposure outside the uterus?

***Response:** Several papers are cited in the introduction that discusses windows of susceptibility and the importance of timing of exposure.*

Comment: It may not be feasible to examine subchronic exposures, since so few data are currently available. For example, subchronic exposure is rarely addressed in submissions for pesticide registrations. Subchronic exposure is a fertile area for future investigations.

***Response:** Agree no response necessary.*

Comment: The handbook should include a discussion on aggregating exposure from multiple exposure pathways. In addition, it may be valuable for the handbook to include a general discussion of other exposure-related issues, such as how to combine exposures due to soil ingestion (or some other ingestion) with distributions of contaminants among the exposure media. Such settings suggest the value in Monte-Carlo risk assessment schemes, and may identify the limitations of the approach using the exposure factors handbook.

Response: *This is a good idea for a supporting document, but it is outside the scope of the handbook.*

Comment: It would be useful to have recommendations for all these exposure types. Indeed, since many exposure studies are short-term, short-term exposure data are available and can be used directly or extrapolated to estimate long-term exposures. The more relevant issue is how to address short-term exposures with estimates of chronic toxicity.

Response: *This is an important issue, but outside of the scope of the handbook.*

Comment: The approach currently used in the handbook to present exposure factor data is guided by the available data, with some discussion of application. Detailed guidance for data extrapolation, such as developing alternate time estimates, or which exposure durations each factor in the handbook is appropriate or may be more appropriate in a separate document and specific for each chapter.

Response: *Agree, a companion document may be more appropriate.*

2.5 Comments Related to Charge Question 9

Charge Question 9: Every attempt was made to update the introduction with the latest guidance and developments in exposure assessment. Please comment on whether we have captured the major developments in the field.

"Exposure assessment" (or "exposure science") is a very broad field, whereas the CSEFH is specifically focused on selected exposure factors for children. Clearly, it is beyond the scope of the CSEFH to review and discuss the many important developments in the field; nevertheless, the panel feels that some of these developments and their potential for improving exposure assessment practices in the near future should be briefly mentioned in Chapter 1. For example:

Comment: Exposure science and assessment over the last decade has, to a great extent, changed its focus from environmental and micro-environmental quality characterization (i.e., the focus on contaminant concentrations in different media—air, water, soil, dust, food, etc.) to the individuals and populations experiencing the exposures, with emphasis on the behavioral and biological attributes (activity patterns coupled with temporally changing physiology/biochemistry) that determine contact with, and subsequent intake and uptake/dose of, environmental contaminants.

Response*: Chapter 1 was revised. Figure 1 was added, which addresses the change of focus mentioned by the reviewer. Advances in the field are discussed in each individual chapter.*

Comment: Exposure science is progressing rapidly beyond the simple characterization of "contact" with environmental and micro-environmental contaminants, by incorporating multi-scale biological concepts (from molecule to genome, cell, organ, organism) and related

quantitative methods as drivers for developing frameworks of comprehensive exposure analyses. References that provide estimates and data of exposure-related "biological parameters" include Price et al. (2003), Krishnan and Hattis (2005), EPA (2006a, b), Luecke et al. (2007), and Willmann et al. (2007).

(Price, P.S., Conolly, R.B., Chaisson, C.F., Gross, E.A., Young, J.S., Mathis, E.T., and Tedder, D.R. 2003. Modeling interindividual variation in physiological factors used in PBPK models of humans. Crit. Rev. Toxicol. 33(5): 469-503)

(Krishnan, K., and Hattis, D. 2005. Physiological Parameters in the Healthy and Diseased Aged Populations. U.S. Environmental Protection Agency, Office of Research and Development)

(EPA. 2006a. Approaches for the Application of Physiologically-Based Pharmacokinetic Models and Supporting Data in Risk Assessment. U.S. EPA National Center for Environmental Assessment. EPA/600/R-05/043A)

(EPA. 2006b. Use of Physiologically Based Pharmacokinetic Models to Quantify the Impact of Human Age and Interindividual Differences in Physiology and Biochemistry Pertinent to Risk. EPA/600/R-06/014A)

(Luecke, R.H., Pearce, B.A., Wosilait, W.D., Slikker, W., Jr., and Young, J.F. 2007. Postnatal growth considerations for PBPK modeling. J. Toxicol. Environ. Health A 70(12): 1027-1037)

(Willmann, S., Hohn, K., Edginton, A., Sevestre, M., Solodenko, J., Weiss, W., Lippert, J., and Schmitt, W. 2007. Development of a physiology-based whole-body population model for assessing the influence of individual variability on the pharmacokinetics of drugs. J. Pharmacokinet. Pharmacodyn)

***Response**: The chapter was revised to add language indicating that data on PBPK parameters and methods were not included in the handbook and referred the reader to sources of such data.*

Comment: Exposure factors should and will ultimately include those which extend from external dose to dose to target tissues, including biomarkers. Future research should focus on addressing all those factors. [*In a post-meeting comment, a reviewer suggested the following reference on this point: Ryan, P.B., Burke, T.A., Cohen Hubal, E.A., Cura, J.J., and McKone, T.E. 2007. Using biomarkers to inform cumulative risk assessment. Environ. Health Perspect. 115(5): 833-840. doi:10.1289/ehp.9334. Available via http://dx.doi.org/.*]

***Response:** Information about biomarkers of exposure is outside the scope of the handbook. Reference will be considered in future efforts.*

Comment: The spectacular enhancements in availability and usability of exposure-related databases (e.g., demographics, activity patterns, physiology, biomarkers, geographic information systems) have changed the face of exposure modeling in many ways; the most dramatic example is probably the increasing usage of EPA's CHAD (Consolidated Human Activities Database) in current practice. Though specific databases (CHAD, CSFII, NHANES, etc.) are mentioned in the

individual chapters, it would be useful to discuss the importance of the overall trend of online, publicly available databases within Chapter 1.

***Response**: This is being considered in the future plans for the handbook and Exposure Factors Program.*

Comment: While it does not currently appear feasible to provide adequate exposure factors that relate to exposure in (sometimes highly specific) microenvironments, Chapter 1 should briefly discuss the potential misclassification of exposure that can result from the use of larger-scale exposure factors instead of more appropriate micro-environmental measures. For example, significant gradients persisting in indoor air concentrations mean different relevant micro-environmental inhalation concentrations for adults and for children, who spend much of their time closer to the floor and in different locations within the home.

***Response**: This can be better addressed in a children's scenarios document, currently under development.*

2.6 Chapter 2 (Breast Milk Intake)

Comment: As with other chapters, the executive summary and recommendations should be moved forward, and the key studies should be clearly indicated.

***Response:** The recommendations section, recommendations table and confidence ratings table were moved to the front of each chapter. Two new sections were added to each chapter: the key studies section and the relevant studies section.*

Comment: The vast majority of data were for upper middle class white women; there may be difficulty in extrapolating to the population as a whole. If data are available by ethnic, geographic, or other subpopulations, they should be considered.

***Response:** Data were added when available from all studies cited.*

Comment: In Table 2-7, there appears to be a transcription error in the "1989" column for the "maternal age 20-24" row. The value of 4.2 given here seems inconsistent with other entries.

***Response:** Value was changed to 45.2.*

Comment: EPA should use scientific terminology: in particular, "human milk" rather than "breast milk" and "lactation" instead of "breast feeding." (All animal milk is "breast milk" and children can be fed human milk by bottle, from expressed milk, as well as directly from the breast.)

Response: *Human milk was added except for instances where changing it would lend to incorrect interpretation of the authors data. Lactation was also used, where possible.*

Comment: EPA should include additional information on how human milk composition changes over the lactation period and should expand on changes during a lactation event.

Response: *Milk composition is not within the scope of this document.*

Comment: Correlations between incidence, duration, and human milk composition should be investigated if available data can support this type of analysis.

Response: *Data are not available to support this analysis,*

Comment: If possible, social factors that may be important to initiation and duration of breast feeding, such as mother's work status, cultural differences, and socioeconomic status (SES), should also be considered.

Response: *Socio-demographic data were added where available.*

Comment: Reviewers discussed the use, in the tables, of the term "upper percentiles" without more specific characterization and recommended that EPA standardize the presentation if possible.

Response: *When upper percentiles were not available from a study, these were estimated by adding two standard deviations to the mean value. Recommendations for upper percentiles, when multiple studies were available, were calculated as the midpoint of the range of upper percentile values of the studies available for each age in months. This is described in the introduction to the chapter.*

Comment: The recommendation table should clearly indicate if the data are for infants exclusively fed human milk, as opposed to a formula-supplemented diet.

Response: *The document provided a summary of recommended human milk and lipid intake rates for exclusively breastfed infants. The distinction has been made in the chapter.*

Comment: Inconsistencies in the confidence table should be corrected.

Response: *A new confidence in recommendations table has been included with new assessment factors and inconsistencies have been addressed.*

Comment: The Arcus-Arth et al. paper submitted in the public comments is now published; (see below). EPA should add it to the chapter. Also, EPA should replace the outdated information on rates of lactation with more current data (see the peer reviewer comments for specific citations) and should consider other references cited in the peer reviewer comments.

(Arcus-Arth, A., Krowech, G., and Zeise, L. 2005. Breast milk and lipid intake distributions for assessing cumulative exposure and risk. J. Exp. Anal. Environ. Epidemiol. 15: 257-365)

Response: *This paper has been included in the revised chapter.*

2.7 Chapter 3 (Food Intake)

Comment: Study size rating. The recommended per capita estimates for fruit, vegetable, grain, meat, dairy, and individual intakes (Tables 3-16 and 3-17) were not based on the 1998 Children Supplemental Survey, but rather only on CSFII 1994–1996; therefore, they were only based on a small number of children. The total number of children <1 year in the CSFII 1994–1996 is 359 (see handbook Table 3-15), while the total number of children <1 year available in the CSFII 1994–1996 *and* 1998 data sets is 1,301 (see handbook Table 3-36). As such, the unweighted number of observations in CSFII 1994–1996 for population subgroups birth to 1 month, 1 to <3 months, 3 to <6 months, and 6 to <12 months is all well below 200 and inadequate for estimating upper percentile (90^{th} and higher) estimates (see statistical notes in Appendix 3E of the handbook). Therefore, the upper percentile estimates (90^{th} and above) for all age groups <1 year old in Tables 3-16 to 3-19, Tables 3-38 to 3-39, and the cells in Table 3-54 that refer to data in Table 3-16 are not statistically robust. For this reason, the confidence rating for the "study" size element that was noted in Table 3-55 as "high" based on the rationale that "the study was large and adequate" is misleading as it fails to consider the very small sample size for these population subgroups.

Response*: EPA conducted an analysis of the 1994-1996, 1998 CSFII. The results of this analysis are now included in the chapter. In addition, EPA revised the confidence ratings for the food chapters.*

Comment: Currency rating. The handbook indicates that the data were the most current publicly available at the time the analysis was conducted, and a "medium" rating was assigned. The data presented in the handbook are compilations of different analyses of the same or part of the same food consumption surveys (CSFII 1994–1996 or CSFII 1994–1996 and 1998) that were conducted at different times and for different age groups. More current national food consumption survey data, such as the NHANES 1999–2000, 2001–2002, and 2003–2004, have been released since the release of CSFII 1994–1996 and 1998. Given the availability of more updated national food consumption survey data, the currency rating should be lowered. By implication, it would make sense for EPA to incorporate the newer National Food Consumption Survey (NFCS) data into the CSEFH. It should be noted that these more recent survey years focused on obtaining more robust estimates of food consumption by children.

Response: *EPA will incorporate an analysis of the NHANES data in future editions of the Handbook.*

Comment: Number of studies rating. This rating failed to discuss limitations of the 1987/88 NFCS from which the estimates of home-produced food intake were derived. This study is 20 years old (!) and the response rate for that survey was well below the response rates from the

preceding and/or following surveys. EPA should update this data table with more recent information.

Response: *As noted in the chapter on intake of home-produced foods, recent food consumption surveys conducted to estimate food intake among the general population (e.g., USDA's Continuing Survey of Food Intake among Individuals [CSFII] and the National Health and Nutrition Examination Survey [NHANES]) have not collected data that can be used to estimate consumption of home-produced foods. Thus, the 1987-1988 NFCS data set is currently the best available source of information for this factor.*

Comment: Assessment of acute/short-term exposure. Assessment of acute/short-term exposure is necessary for many of the toxicity endpoints pertinent to children. All of the intake estimates are provided on a per capita basis, which is more appropriate for chronic exposure scenarios. Per user estimates will be needed to assess acute/short-term exposure scenarios. EPA should develop "consumer-only" (or per "user") estimates (mean and upper percentiles) and include them in the handbook.

Response: *Consumer-only food intake rates are now included in the Handbook.*

Comment: Weakness of short-term survey data to predict long-term consumptions pattern for food infrequently consumed. This is an important weakness in general for foods that are infrequently consumed by a significant fraction of the population (e.g., many fruits and vegetables, such as rhubarb and berries, and meats such as liver and game). This is also a particular consideration for fish that tends to have characteristic contaminants. The two-day nature of the CSFII data will significantly over-represent the patterns of frequent consumers and significantly under-represent the patterns of infrequent consumers, as such data do not allow consumers to be assigned to one or the other group. If the two groups eat different fish, this will not be represented by the CSFII data. This is partially addressed by the NHANES 30-fish frequency from 1999–2000 and 2001–2002. These data have their own limitations given the long recall period, but should definitely be considered as a potential alternative and/or supplement to the CSFII data when selecting key studies.

Response: *Text indicating that short-term dietary data may not accurately reflect long-term eating patterns and may under-represent infrequent consumers of a given food has been added to all chapters that include short-term dietary data. In addition, EPA will incorporate NHANES 30-fish frequency from 1999–2000 and 2001–2002 in future revisions to the Handbook.*

Comment: The utility of short-term recall data for fish and other infrequently consumed foods can be improved by simultaneously collecting data on the usual frequency of consumption in future federal food consumption surveys. These data can then be used to re-weight the short-term data, since frequent and infrequent consumers can then be identified.

Response: *This information will be incorporated into the Handbook as it becomes available in future food consumption surveys.*

Comment: The tables do not provide data on fish intake by specific species. These data are critical because different fish species have different characteristic contaminant levels. It is not adequate to simply group fish by general categories (e.g., marine/freshwater).

Response: *The data for fish species have been incorporated in each study, where presented by the author. In some studies, these data were not available.*

Comment: Data on fish consumption by Native Americans is misleading, as different groups/tribes can have different patterns of fish consumption and consume different amounts of fish. Fish consumption data presented in the handbook for a specific Native American group applies only to that group.

Response: *Text indicating that fish intake data for a particular tribe may not be representative of other tribes was added to Chapter 10, Intake of Fish and Shellfish.*

Comment: It would be helpful for users to have some guidance on how to use the available data. With food consumption data, while the surveys are based on one- or two-day intakes, the analysis of the data on a *per capita* and *per user* bases allows a mean for estimating chronic and acute exposures. These discussion and recommended approaches may be best provided in a companion "user" guide.

Response*: A user guide is not available at this time for CSEFH. However, EPA has developed a standard scenarios document that provides scenarios presenting how the data can be used in assessments when site-specific data are not available. These scenarios illustrate the rationale used to select the appropriate data sets and to show how different data may be selected for the same scenario. A similar document is under development to address children's scenarios.*

Comment: The handbook should include data on autocorrelation within food groups for the two days of the CSFII (in order to refine variability estimates), as well as data on correlation across food groups (in order to allow modeling of overall contaminant intake in exposed populations).

Response*: EPA has not included these data at this time. This will require additional analysis and resources and it is beyond the scope of this document.*

Comment: The handbook should provide links to the U.S. Department of Agriculture (USDA) CSFII and to the NHANES data. It should also provide USDA's food intake data bibliography.

Response: *A link to USDA CSFII data was added to Chapters 9, 11, and 12. References are provided.*

Comment: Infant formula consumption data are missing and should be added.

Response: *Infant formula data were added.*

Comment: Fat content of meat and dairy products. The percent of lipids in meat and dairy products was based on a very old reference (USDA's 1979–1986 Agricultural Handbook No. 8) and should be updated. Updated fat content of foods, including meat and dairy products, are readily available from USDA and can be downloaded from the USDA Web site (http://www.ars.usda.gov/Services/docs.htm?docid=9673)

Response: *Updated information on fat content of foods, obtained from the USDA web site, was incorporated in Chapters 10 and11.*

2.8 Chapter 4 (Drinking Water Ingestion)

Comment: Overall, the panel thought that the tables of distributional information in Chapter 4 provided helpful information; however, for risk assessors, the chapter needs to present additional data on consumers ("users") only (together with information on the percentage of consumers in the overall population). In some cases, the presentation would benefit by clarifying some details:

Response: *Additional data have been added for consumers-only.*

Comment: In the tables that provided only a few summary statistics (e.g., the mean, 90^{th}, and 95^{th} percentile values in Table 4-1), EPA should also provide the geometric means and geometric standard deviations. These statistics will be helpful because the data would be much better described by skewed (such as lognormal rather than normal) distributions. Geometric means and geometric standard deviations can be estimated from the data provided, but the population distributions could be estimated with much greater accuracy and confidence if the geometric means and geometric standard deviations were explicitly provided. The panel also prefers the full distributional characterization format for the data, as used in Table 4-4, rather than the upper-half distributional presentation used for Table 4-7.

Response: *The tables in this chapter were revised to reflect the full distributions, where possible. Consumer-only data were also added. These data are based on a new analysis performed by the EPA - (Kahn, H.; Stralka, K.) supplemental data. Geometric means and standard deviations are not presented.*

Comment: As with the food ingestion chapter, EPA should include autocorrelation data derived from two-day observations to distributions of drinking water that allow analysis to estimate various percentiles of average intake over longer periods (weeks, months, years).

Response*: EPA has not included these data at this time. This will require additional resources and it is outside the scope of the document.*

Comment: This chapter should also include some tabulations of the locations of water consumption (e.g., home, school, day care center).

Response: *Data are not available for the location of water consumption (i.e., home, school, day care center, etc.)*

2.9 Chapter 5 (Soil Ingestion and Pica)

Comment: The introductory comments to this chapter are casual and seem more suited to a magazine article than a scientific document or handbook. Study reviews are not carefully worded and may appear confusing (e.g., as when discussing pica behavior as distinct from soil-pica on page 5-2).

Response: *The chapter has been edited thoroughly for wording tone and consistency of writing style.*

Comment: Studies of soil ingestion are nicely identified as "key studies," "relevant studies for primary analysis," "key studies of secondary analysis," and "relevant studies of secondary analysis." However, the criteria for including studies in these categories are not clearly stated. For example, key studies do not include reference to all the primary studies used in the data analysis (e.g., the Calabrese et al. 1988 study). Studies conducted outside the United States are discussed, but the reasons for not including them as key require more explanation (e.g., What are the considerations for excluding studies conducted outside the United States?). In general, the review of individual studies is uneven, with strengths and limitations not consistently provided. This makes it difficult to clearly understand the rationale for classifying studies as key.

Response: *The criteria for designating studies as "key" vs. "relevant" are now stated in section 5.3. Some studies conducted outside the United States have now been designated as "key." Individual studies' summaries have been edited for consistency, and to clarify the study's data collection design and methodology features that affect designation as "key."*

Comment: Several limitations of all soil ingestion studies emerge and deserve special attention. First, all studies were conducted in the summer/early fall. Data are not available for other seasons or time periods. Presenting results (as Table 5-13) that extrapolate over a year requires strong qualification and may not be appropriate.

Response: *Although the U.S. tracer element studies were conducted in the summer and early fall, a detailed review of the weather conditions that appear to have occurred during those studies' data collection periods (which were not always specified in published articles) reveals that cold and rainy conditions were present during one of the four studies. Table 5-13 was renumbered as Table 5-18, and the results are still presented. However, the central tendency soil, dust, and soil + dust recommendations are now based on an entirely different study, that does account for long-term seasonal and day to day variation in soil and dust ingestion.*

Comment: The role of soil-pica (a concept that EPA attempts to define on page 5-2 of the handbook) is difficult to assess in this chapter. A single subject in one study on two days was reported as having unusually high soil ingestion (soil pica). It is not clear whether there are other

data that can be drawn on to form recommendations, or whether a recommendation about a mean ingestion level is warranted.

Response: *The role of soil-pica continues to be difficult to ascertain. Review of both historic and more recent survey was used to extend information on soil pica behavior prevalence beyond what is known from the tracer element studies.*

Comment: The chapter attempts to distinguish soil ingestion from dust ingestion. Although a few articles have attempted to separate the sources, the review of this literature has not critically examined the assumptions underlying the analyses, which are usually not very strong and not supported by empirical data. The justification for averaging estimates of soil and dust is not given (in Table 5-20) or defended, and appears arbitrary. Obviously some proportion of dust is composed of soil (e.g., when outdoor soil on shoes is tracked into the house). Clearer guidance needs to be given on how to factor this into exposures assessments.

Response*: The U.S. EPA agrees that a critical examination of the assumptions underlying the tracer element studies' dust ingestion estimates is needed. To the U.S. EPA's knowledge, there are no published English-language articles that have performed such an examination. The central tendency dust and soil + dust ingestion recommendations rely on an assumption from the IEUBK modeling (ingested soil and dust is 45% soil and 55% dust), that has not yet undergone such a critical examination.*

Comment: The presentation of study data in Table 5-20 repeats analyses of the same basic data in different rows, and also repeats analyses of the same subjects over different time periods. The weighted estimates are difficult to interpret due to double counting of basic study data. Combining soil/dust ingestion for the 95 percentile requires substantial qualification and discussion, which are not provided. General concerns over separating variability from uncertainty, and different data collection periods in different studies, need to be given more prominence.

Response: *Table 5-20 has been removed from the chapter. A table that summarizes the soil and dust ingestion estimates from the key studies is included in the revised chapter (Table 5-19).*

Comment: Other recent mass-balance soil ingestion studies (in Germany and Japan) are not referenced; neither are other analyses of previous soil ingestion study data that may more appropriately account for issues such as study duration and uncertainty. These studies should be discussed, and reasons for inclusion or exclusion should be given. For example: Stanek, E.J., and E.J. Calabrese. 2000. Daily soil ingestion estimate for children at a Superfund site. Risk Anal. 20(5):627-635.

Response: *An extensive review of the English-language literature on soil ingestion failed to reveal either a German or a Japanese tracer element study (but did reveal a study of Kenyan children's geophagy). If translations from the original language are available, EPA will include these data in future revisions. In the revised chapter, some of the additional analyses of tracer element study data are included and discussed, but U.S. EPA did not consider every published*

secondary analysis as contributing substantially to the knowledge base on soil and dust ingestion. Stanek and Calabrese 2000 is now included in section 5.3.5.8.

Comment: One reviewer provided several comments on soil intake. He noted that he was familiar with many of the studies and authors. He discussed that variety of studies summarized in this chapter, and the Agency's categorization of key, relevant and secondary studies. He commented that the chapter is not clear as to why some studies are designated "key," while others are designated "relevant." He also expressed concern that the chapter included three studies (the Amherst, MA study, the Anaconda, MT study, and the Washington State study). He expressed concern that the Washington State study, published in 2006, was based on 1990 data. Additional data were subsequently collected around the same time, but not analyzed until 2006. The reviewer noted that the 1990 paper summarized the data collected and should be the key study. Later studies reanalyzed these data differently and combined data from different studies. He expressed concern that the handbook provided tables based on the later studies, and not the original study.

Response: *The criteria for designating studies as "key" vs. "relevant" are now stated in section 5.3. Both of the Washington State studies (original data collected in 1987 and 1988) were designated as "key." The potential problem with the 1988 data that were analyzed in the laboratory 12 years later (the 2006 study) is mentioned in that study's summary.*

Comment: One reviewer noted that the study's strengths were included at the end of a study summary, and expressed concern that a pica study (i.e., the 1989 study on a child eating a large amount of soil) was included in a table on children without pica. He also stated that key limitations were not dealt with equally in this chapter (e.g., fecal weight assumptions should be equally presented). He noted that one of his one-year studies was not included in this chapter. He also discussed the issue of soil versus dust, noting that not many studies have been performed in the context of separating soil and dust; therefore, the handbook's evaluation involved very strong assumptions. The reviewer also noted that one section of the chapter discussed a study on adults, and said that this study should not be included, since an adult study may confuse users.

Response: *Overall strengths and limitations of each data collection methodology are now described in a separate section, since restating those that are common to all studies using a given methodology in each study's summary is somewhat redundant. The issue of fecal weight assumptions is described in the overall methodology limitations section. See response to comment above regarding dust ingestion estimation assumptions. The chapter was revised to eliminate all references to adult soil ingestion except for a brief mention of the adult tracer element studies performed to validate the methodology used in children.*

Comment: Another reviewer commented that the chapter was well-thought-out for the soil ingestion discussion, but was not consistent in the pica discussion, resulting in confusion on the confidence levels of the pica studies.

Response: *As stated above, the role of soil pica, and estimated soil pica quantities for use in exposure assessment, is difficult to ascertain given the current state of knowledge.*

Comment: One reviewer remarked that soil ingestion is a challenging and complex area, and stated that the introduction needs to differentiate between soil and dust (e.g., suspended and suspendable dust). The reviewer expressed concern about the calculations and assumptions regarding fecal dry weights (i.e., using a factor that was different in different studies). He suggested that Chapter 5 should actually follow Chapter 6. He discussed the issue of soil versus dust (the amount of heavy metals and materials in each one, the amount of each one in carpets, etc.), and expressed concern that the handbook considered them together, which would lead users to assume that they are always similar. He stressed that the chapter should clarify that soil and dust are separate materials with different associate exposure issues. He also suggested that the chapter provide additional focus on dust. Another reviewer suggested that the handbook include one overarching chapter with different sections for soil and dust. A third reviewer remarked that further research is needed on soil versus dust.

Response: *The chapter's introduction was edited to define the terms "soil," "indoor settled dust," and "outdoor settled dust," and central tendency recommendations were developed for soil, dust, and a combination of soil and dust. The issue of fecal dry weights is described briefly in the methodology limitations section. The order of the soil and dust ingestion and non-dietary ingestion chapters has been reversed. Regarding the issue of soil versus dust, many users are likely to be familiar with the numerous technical issues that would pertain to differences between soil and dust exposures; the chapter revisions make it clear to users who are less familiar with these technical issues that there are likely to be differences between soil and dust exposures (although the current state of the science on this topic may limit the practical extent to which exposure assessors can distinguish between them).*

Comment: A reviewer requested that the chapter explain that dust contains soil-derived dust and, therefore, should be considered in exposure, since that might be the predominant exposure for some children. He questioned if studies have been conducted on the mineral content of smaller particles in soil. Another reviewer replied that such studies have been conducted, but not in the context of dust. He remarked that the bigger issue is whether children are ingesting soil or dust. A third reviewer recommended that the handbook mention this issue and provide some guidance.

Response: *The description of the tracer element methodology explains more clearly how dust ingestion estimates are calculated. In addition, one part of the methodology limitations section describes this issue and refers the reader to the secondary analyses that have been performed to try to illuminate this issue.*

Comment: A reviewer noted that most soil ingestion studies are conducted during the summer; however, the chapter based the soil ingestion evaluation on year-round ingestion, resulting in a conservative approach and an overestimation of exposure. Another reviewer commented that the duration differs for most of the estimates, and questioned how to interpret the resulting values. A reviewer noted on pages 5-30 and 5-31 that the best estimates of soil ingestion are likely to be overestimates, since the studies were conducted during the summer month. Alternatively, an annual best estimate could be calculated taking into account that ingested doses during cold, rainy/snowy months could be primarily based upon indoor dust as the primary exposure source.

Response: *See above response on the issue of seasonal variability in tracer element study estimates. Several places in the revised chapter mention the time period of the data collection for the various tracer element studies. The use of the biokinetic model comparison study (Hogan et al., 1998) as the basis for the central tendency soil, dust and soil + dust ingestion recommendations renders less important (but not moot) the matter of how to interpret the tracer element study estimates that are based on varying, and short-term, data collection periods.*

Comment: A reviewer noted the issue of indoor/outdoor factors, and remarked that a factor should not be evaluated in isolation from other factors (e.g., rain is more common in Seattle, which would affect soil and dust). She suggested that the chapter clarify how data are collected. Another reviewer commented that soil ingestion involves a range of different distributions, since it depends on season and locality. As an example he cited New York City, where most of the dust is from walls and carpets, not soil.

Response: *These limitations are discussed in the chapter. The comment that soil ingestion involves a range of different distributions dependent on season and locality appears to be quite accurate. An extensive review of the soil ingestion literature reveals a wide range of estimates that appear to be driven largely by locality. More important than the seasonality issue appears to be the issue of local attitudes and customs regarding either intentional or unintentional soil ingestion.*

Comment: A reviewer expressed concern about dust exposure in mouthing. Another reviewer responded that mouthing involves multiple types of materials, not specifically soil, and can result in exposure to dust from animal dander, consumer products, building materials, and paint. A third reviewer noted that toddlers do not spend much time outside. A reviewer commented that the handbook not make a blanket statement that the soil ingestion evaluation overestimates, but just draw attention to the issue. Another reviewer reiterated that the handbook should discuss the differentiation between soil and dust (and where it comes from).

Response: *See above responses regarding the issue of soil versus dust ingestion.*

Comment: A reviewer noted an editorial comment of concern on the introductory paragraphs of each chapter. The human milk chapter describes human mils as the best food for infants, and the food chapter describes the U.S. food supply as safe; however, the water chapter provides no such lead-in, and the soil chapter discusses soil ingestion as a "surprise." A reviewer recommended that the handbook be edited to eliminate these inconsistencies.

Response: *The wording has been changed.*

Comment: One reviewer requested clarification on the intake value of 10 to 14 grams per day given on page 5-31 of the handbook. This value was based on one child by an observer over a two-week period. The reviewer questioned the reliability of this database. Another reviewer responded that children will ingest a large amount of soil on occasion, and researchers are not sure how frequently this happens. He also remarked that some children eat more soil than others, and noted the difficulty in determining what constitutes a large amount. Therefore, the Agency used the one study available on this topic. Another reviewer noted the ethical concerns involved

in watching a child eat dirt, which explains why limited observational studies are available. The reviewer also noted that the study measured stool to determine the amount of soil ingested. A reviewer added: "A better and more complete rationale should be give for selecting an ingestion rate of 10 g soil/day for pica children. This value is taken from data on the intake of one child on the higher of 2 weeks of observation. The data base reviewed in the document is much richer than this."

Response: *The researchers did not observe children directly but rather assessed soil ingestion using tracer element quantities in children's stool samples. Rather than rely on the single study that included one child who obviously ate large quantities of soil (based on the child's stool tracer element content and the tracer element content of her yard soil and house dust), U.S. EPA undertook a careful review of the five tracer element studies' upper percentile data to determine which children appeared to have ingested more than 1,000 mg of soil per day during those studies' data collection periods. In addition, U.S. EPA undertook a careful review of survey response studies, and inferred, based on the bulk density of soils, that parent-reported observations of ingested soil indicated ingestion of soil-pica quantities (1,000 mg/day or more, inferring based on soil bulk densities) for at least some portion of children in those survey response studies. The consistent pattern of parent reports, or self-reports, of soil ingestion in numerous different demographic groups, numerous different locations, and over several decades, provides an indication of the prevalence of soil-pica behavior occurring in children (as soil-pica is defined in the revised chapter).*

Comment: A reviewer questioned whether a nutritional deficiency causes pica. A reviewer responded that nutritional deficiency causes pica in some cases (e.g., malnourished people will eat dirt).

Response: *Researchers have hypothesized different motivations for pica, soil pica, and geophagy behavior. Review articles in the literature regarding this issue have been included. Authors have concluded that there could be many different motivations, but no single hypothesis is explanatory. One pattern that consistently emerges in many cultures is geophagy practiced by pregnant women.*

Comment: Another reviewer explained the different types of hand-to-mouth contact; specifically, that pica involves intentional soil ingestion by putting soil material per se in the mouth, while mouthing involves accidental ingestion by putting foreign objects in the mouth. There are quantitative and qualitative differences between the two types. A reviewer suggested that the handbook include a broad statement explaining the differences.

Response: *Due to difficulties with understanding the motivations of children who place soil or dust materials in their mouths (see response to comment immediately preceding), and difficulties with distinguishing between intentional versus unintentional soil and dust ingestion by children, the revised mouthing and soil/dust ingestion chapters do not attempt to distinguish between these behaviors.*

Comment: On reviewer discussed two studies – a Japanese and German soil ingestion study – that evaluated soil ingestion using a mass balance approach (i.e., fecal studies). Another

reviewer noted a soil ingestion study from the Netherlands that was cited in the handbook, but ranked as low confidence because it was a foreign study. She thought the study could be relevant and the handbook should specify whether the study was ranked low for other reasons than being foreign.

Response: *An extensive review of the English-language literature on soil ingestion failed to reveal either a German or a Japanese tracer element study (but did reveal a study of Kenyan children's geophagy). These will be considered when translations become available. The two tracer element studies performed in the Netherlands were considered, and one of the two was designated as "key" because it included data for infants. Another study, of Jamaican children, was also designated as "key" because it provided considerable evidence of soil-pica behavior among institutionalized children. Studies of soil ingestion, including incidental soil ingestion, soil pica, and geophagy, that were conducted in other countries are difficult to evaluate for their relevance and applicability to U.S. children's soil and dust ingestion patterns, because cultural practices such as attitudes about soil ingestion may play a significant role in children's actual soil ingestion behaviors.*

Comments: (related to organization)

For Chapter 5, the studies for soil ingestion are presented in terms of Key and Relevant Primary and Key and Relevant Secondary studies. There is a logical approach consistent with the Introduction and previous presentations. The results are presented systematically in tables as the information allows (i.e., due regard is given for presentation of statistics associated with the data if these are available). Table 5-19 clearly identifies the studies used to recommendations.

The same is not true for the information on PICA, where a list of studies were presented in chronological order. A value from one of these is then presented (inconsistent with the approach in the introduction.)

Page 5-3, lines 10-19: Studies are classified as "key" or "relevant," and these terms are further described, but not self evident for the relevant studies. As a result, I don't understand why some studies are designated as "key" and others as "relevant." An example is the classification of the study by Calabrese et al. 1989 as relevant but not key. The reasons a study was classified as "relevant" rather than "key" should be clearly stated for each of the "relevant" studies.

The discussion highlights the importance of the terms "key" and "relevant." There is further description of the meaning of "key" in section 1.4. I'm not sure where the further description is of "relevance," or how it fits in the approach used to develop recommendations (in section 1.5). Since the conclusions depend on this classification I suggest that the decision rules be more clearly stated.

Response: *The Key and Relevant Primary and Key and Relevant Secondary Studies categories are retained in the final version. In general, studies that had a design that were a census of an entire area, or a randomized sample design (whether or not strict randomization was achieved in practice), were preferred over studies that were not of randomized or census design, so that the recommendations are based on data that ideally would contain fewer biases due to non-*

participation or non-randomized sample selection. Inevitably, studies used to develop recommendations are of relatively small sample sizes compared to the entire target population for the Child-Specific Exposure Factors Handbook. Thus, using key studies that include small samples in different parts of the country can serve the purpose of illuminating possible geographic variation in exposures.

Several studies were designated as "key", in spite of not achieving the desired design, implementation, and publication ideals, typically because they were the only study available that contained results for a particular age category, geographic location, or subpopulation.

Comments: (related to charge question #2)

For Chapter 5, the overall ratings for the recommendations on incidental ingestion appear appropriate from the summary table (5-22). However, there could be a much better explanations are needed for the recommendation for PICA. Indeed, it does not appear that there are any confidence ratings for the PICA recommendation in Table 5-22.

Response: *The confidence rating description has been revised to be more explicit about the considerations used to develop the confidence rating that applies to the central tendency, soil-pica, and geophagy recommendations.*

Comment:
page 5-15 line 29. There is no discussion of strengths and limitations of the Stanek et al (2001b) study, unlike other studies reviewed.

Page 5-22 line 5. There is no discussion of strengths and limitations of the Sedman study, unlike other studies reviewed.

Page 5-24 – line 6. There is no discussion of strengths and limitations of the Stanek (2001a) study, unlike the other studies reviewed.

Page 5-27 – line 3. There is no discussion of strengths and limitations of the Calabrese et al. (1991) study, unlike other studies reviewed.

Page 5-29 – line 16. There is no discussion of strengths and limitations of the Zartarian study, unlike other studies reviewed.

Response: *Methodological strengths and limitations have been discussed in the chapter.*

Comment: Page 5-29 lines 19-20. I find it somewhat confusing how a 'key' study is determined. In Table 5-19, a secondary analysis of data from the study by Calabrese et al. (1989) is identified as a key study, but it seems that the Calabrese et al (1989) study is not key. Why?

Response: *Calabrese et al (1989) is now classified as a "key" study, due to the fact that it is a study of primary analysis. The Table 5-19 identification of two secondary analyses as "key" studies has changed accordingly.*

Comment: Page 5-5 line 7. For Davis' 1990, study, when evaluating a 'soil + dust' estimate, soil and dust concentrations are weighted by the time outside to form a soil + dust concentration. This requires an assumption that the probability of ingestion of soil (or dust) is equal indoors and outdoors. I feel that this assumption should be stated in the study discussion, since it influences interpretation (and confidence) in the result.

Response: *The published article briefly describes the methodology used to develop mean and median soil + dust ingestion estimates, and it apparently includes an implicit assumption that probability of ingesting soil outdoors is the same as the probability of ingesting dust indoors. This assumption is discussed in the study summary in the chapter.*

Comment: Page 5-29, lines 19-21 and Table 5-20, and also page 5-30, lines 16-24. I have a problem with the rational *[sic]* for the table, and the adequacy of the description of the results in the table. As discussed on page 5-30, some data are counted twice. The same data used for the Davis study and the Stanek and Calabrese 1995a studies were used in the Stanek and Calabrese 1995b study. Thus, the table double counts responses from these studies in terms of numbers of subjects. Second, the results cited in the Stanek and Calabrese 1995a study include the pica child, and hence have a mean much larger than would have occurred if the pica child had been excluded. It seems important this this be at least pointed out if these results are considered important. The inclusion of the pica child raises the mean estimate by about 70 mg/day for this study. It is not clear based on the discussion (see 5-30 lines 22-25) whether or not the pica children are included or not included.

There is a separate discussion of PICA (see page 5-31 lines 6-16), and this suggests that soil-pica is being treated as a separate issue. In fact, it appears that soil-pica behavior was included in Table 5-20.

Response: *The peer reviewer raises several intertwined issues with these comments. First, regarding consideration of soil-pica behavior and how it is incorporated into the soil and dust ingestion rate recommendations, the U.S. EPA reviewed the U.S. survey response studies published over several decades. The U.S. EPA observed a consistent pattern of a portion of young childrens' caregivers responding positively when questioned about observed soil and dust ingestion. This pattern, suggested that observable quantities of soil and dust ingested within a defined, relatively short, prior time period, may mean that observable quantities of soil and dust ingestion happen either continuously in a subset of children, or sporadically in many or most children (or some combination of the two situations). EPA is analyzing the raw data from NHANES 1 and 2 to develop estimates of the proportion of the population of children in the conterminous 48 states whose caregivers (and in the case of children age 12-20, who themselves) acknowledge ingestion of soil ("dirt" or "clay" in the terms used in these studies' questionnaires). Second, relying upon a reasonable assumption of soil bulk density, the U.S. EPA is inferring that an observable quantity of soil ingested by a young child could range in quantity anywhere from a few milligrams present on fingers, to several-grams-per-incident (since a teaspoon of soil with a typical bulk density is approximately 8 grams in weight). The combination of the soil bulk density information, together with the nationally representative sample of survey respondents acknowledging young childrens' observed ingestion of "dirt" or*

"clay," suggests that it is reasonable for EPA risk assessors to construct exposure scenarios in which at least some portion of a given population of children will at least occasionally ingest observable quantities (in either the milligrams or grams range) of dirt or clay per observation incident. Thus, the U.S. EPA does not view "soil-pica" behavior as though it is practiced by only a subset of children, and the recommendations have now been structured to account for at least some probability of large soil ingestion rates by at least some part of a given population of children. Regarding the inappropriate double-counting of study subjects' soil and dust ingestion estimates in the table from which the external peer review draft's recommended soil and dust intakes were developed, EPA agrees that the table's identification of key studies was flawed. This table has been replaced.

Comment: Page 5-32 lines 1-2. There is some evidence of absorption of trace elements via excretion in the urine in both Davis' studies, so that this result may not be as uncertain as suggested.

Response: *Agreed. The wording has been revised, and an extensive discussion of tracer element uptake has been included.*

Comments: (related to Charge Question # 3).

Page 5-3 line 27: Some wording can be made more clear to help identify where variability is averaged. In Davis's 1990 study, the average soil ingestion over 4 days was evaluated, not daily soil ingestion. The study was conducted over 7 days, but the food and fecal samples were aligned to match a 4 day ingestion period.

Page 5-4 line 24-28. Davis 1990 reports: "Attempts to relate demographic and behavioral characteristics to soil ingestion were disappointing. No consistent profile emerged. P120" The authors do mention the factors cited on lines 25-27, but do not 'observe that the following demographic characteristics were associated with high soil intake…." I think the study summary overstates the author's conclusions.

Page 5.5-line 6. I think this should be referred to as a 4-day study (not a week study).

Page 5.5 line 12. The trace elements are incorrectly identified, and confuse results between the Calabrese et al. 1989 study, and the 1997 study. Barium, manganese and vanadium were not used. Cerium, neodymium and lanthanum were used.

Page 5-6, line 7-8. The statement referring to dropping Ba, Mn and V is incorrect since they were not used.

Response: *The wording has been corrected.*

Comment: Page 5-6 lines 8-20. The results cited are 7-day averages. This is important to distinguish differences between studies, since soil ingestion is thought to be right skewed. Averages over longer time periods will increase the median of the soil ingestion distribution. A

more careful presentation will help distinguish inter-subject temporal variability from subject variability that occurs due to the different study time periods.

Response: *The results presentation has been modified.*

Comment: Page 5-6, lines 14-16. The combination of sentences is misleading and has been taken out of context. There are many differences between the Stanek and Calabrese 1995a study and the Calabrese 1997a study – perhaps one of which is that estimated soil ingestion in the 1997a study is for a 7-day average ingestion, whereas in the 1995a study, the quantity estimated is a 1-day ingestion. A difference is expected in these two due to inter-individual temporal variability. It is also true that the 1997 study subjects were on an EPA Superfund site. This is another factor to consider.

Response: *The results presentation has been modified.*

Comment: Page 5-7, line 8: The study data were collected 1 year after the Davis (1990) study, not prior to the study. Also, 20 families were selected for study, but one dropped out.

Response: *The study description has been modified.*

Comment: Page 5-7 line 15. Results are only given for children, not all family members.

Response: *The wording has been modified.*

Comment: Page 5-38, table 5-4. 'Family member' is child here.

Response: *The table's title has been modified.*

Comment: Page 5-7 lines 25-31. It is unclear what was meant by 'association' in the original articles, and so it is hard to know what is meant here. If the associations were based on Spearman rank associations, no p-value or test results were given.

Response: *The reviewer's comment is accurate. The wording in the chapter has been modified to limit the description to the associations found for children only, rather than children and adults. Data users would need to take into account the lack of transparency of the data analysis method when evaluating the utility of the information.*

Comment: Page 5-8 line 9. Isn't "sample population" the "study sample"?

Response: *Yes. The wording has been modified*.

Comment: Page 5-11, lines 23-24. The study design isn't clearly described. It consisted of two '3-day' studies, with intake collected in each week over 3 days, and fecal samples collected over 4 days.

Response: *The wording has been modified.*

Comment: Page 5-12, line 2, change 'confirmed' to 'concluded.'

Response: T*he description of the adult validation study was moved to the methodology limitations section, and the wording was modified.*

Comment: Page 5-12 – line 24. The idea of the analyses is not reflected in the summary. Excess trace element ingestion may be portioned to soil and dust. The idea is that 65% was estimated due to soil.

Response**:** *The wording has been modified.*

Comment: Page 5-33 line 24 and 27. These references should be 1992, and 1992b.

Response: *The reference dates have been corrected.*

Comment: Page 5-17, lines 6-10, and lines 20-28. I would suggest not including the 365 day extrapolation results in the handbook, or if they are to be included, to more severely emphasize the extent that the results depend on 'arbitrary' assumptions (such as log normal distributions), and may be quite uncertain.

Response: *The results are still included in the handbook, but the study is designated as "relevant" and the actual central tendency recommendation is based on a different study that does account for long-term (such as 365 day) exposures.*

Comment: Page 5-19 line 4. The use of the BMT does not address tracer metabolism. This is a separate issue. It addresses the relative concentrations of a trace element in soil and food.

Response**:** *The reviewer's comment is correct. The chapter now includes an extensive discussion of the issue of tracer metabolism in the methodology limitations section, and the study summary only refers to the Best Tracer Method's use of the relative concentrations of a trace element in soil and food.*

Comment: Page 5-20, line 7-8. I suggest re-writing: "defines the shape of soil intake distributions" by "defines a parametric distribution that is not inconsistent with the shape of the empirical soil intake distribution."

Response**:** *This summary was removed, as described above, based on a judgment that it added relatively little to the knowledge of soil ingestion patterns.*

Comment: Page 5-26, line 8-12. The sentence is not clear – the statement "only one child out of the more than 600 children involved in all of these studies ingested an amount of soil significantly greater than the range for other children" is obscure.

Response**:** *The wording has been modified.*

General Comments:
Certain statements and equations in the text of Chapter 5 need some clarification. For example:

- the "deposition in the respiratory system" mentioned in lines 13-14 of p. 15 needs to be clarified in terms of "location" etc.) in order for "subsequent ingestion" to make sense,
- Equation (5-2) on p. 5-4 is appears to be dimensionally incorrect, the issue of "standard fecal dry weight" has to be discussed further; maybe an appropriate, age-dependent, distribution (or set of distributions) needs to be defined: the differences in the values mentioned in the text (10 g/day on line 8 of p. 5-10, 15 g/day on line 9 of p. 5-13, 7.5 g/day on line 15 of p. 5-19) can cause substantial differences in corresponding exposure estimates.

Page 5-2: line 16. Can the term "recurrent" be clarified, or elaborated on.

Page 5-2, lines 27-29. The citation of Sayetta (1986) and statement that 50% of children have pica behavior is confusing. First, only for this sentence is pica behavior, as opposed to soil-pica used. The difference is not mentioned, nor is the more substantial literature on pica behavior (as opposed to soil pica). The sentence seems to focus on developmentally impaired children, but the 50% claim of pica is not qualified to developmentally impaired children. It seems like the inclusion is a "normative discussion" of pica, but the ideas can be more clearly stated.

Page 5-11 line 5-14. An additional limitation of the Clausing study is the assumption of constant fecal weights of 10 g/d.

Page 5-14, line 1-12. An additional limitation is the assumption of constant fecal weight of 15 g/d.

Page 5-14 line 27. This study also provides a partial explanation for differences in trace element specific soil ingestion estimates. Since concentrations of certain trace elements differ by particle size, such trace element may potentially help discriminate between ingestion of different particle sizes.

Page 5-15, line 27-28. The article states, "For soil ingestion, use of the median (as opposed to the mean) to estimate soil ingestion on a subject day is preferred because individual trace element estimate may be biased due to source error." This seems to contradict the limitation cited.

Page 5-29 lines 13-16. The description of a distribution and 95% does not seem to match the results in Table 5-20. I believe that the table referred to is missing in the report.

***Response*:** *The wording has been modified and the equation's units corrected. The issue of fecal weights is discussed briefly in the methodology limitations section, and the issue of particle sizes' influence on soil ingestion results can be discerned from the titles of the two secondary analyses on this topic. The Sayetta citation has been removed, and the wording modified to place into context the very limited research available on pica and soil pica behavior in children.*

Comments: (on whether or not the CSEFH document should present normative discussions about how to use data and uncertainty)
Please see corresponding answer to Question 5 for Chapter 1. This chapter has many problems.

Response**:** *Certain suggestions about how to use the recommended soil and dust ingestion values were provided to readers.*

Comment: (related to charge question #6) It was suggested by one of the internal reviewers that we provide recommendations for acute, subchronic, and chronic exposures. Please comment on whether this is a feasible approach given that most of the data come from short-term studies. The data is not sufficient to enable stable enough estimates of such time averages without sophisticated analysis. If such analyses are published elsewhere, then it may be worthwhile to comment on them.

Response**:** *Agree.*

Comment: (related to research gaps)
General comment: In some studies, adult results are given. The descriptions of the studies do not keep the focus on children's exposure, using the adult data to strengthen understanding of the children's results. For example, it is not clear what the relevance is of the discussion on page 5-7 lines 18-22.

Response: *The references to adult exposures have been removed.*

Comments: (based on if the literature search was complete enough and recommendations for studies or data that should be included).

Example references could include: Maertens et al., 2004; Rasmussen, 2004.
While the appropriate data appears to have been included, it would appear that some improvements in methodology by Stanek and Calabrese were not taken into account in making the recommendations. A clear explanation for this decision should be included.

Include: Stanek, E.J., III, Calabrese, E.J., Mundt, K., Pekow, P., Yeatts, K.B. (1998) "Prevalence of soil mouthing/ingestion among healthy children 1-6," Journal of Soil Contamination, 7:227-242.

An additional review reference may be: Steven L. Simon. 1998. Soil ingestion by humans: a review of history, data, and etiology with application to risk assessment of radioactively contaminated soil. Health Physics 74(6): 647-672.

Response**:** *U.S. EPA appreciates the suggested references. It did not appear that the Maertens citation contained any new information on dust ingestion estimates. The Rasmussen et al. research appears to be an example of additional studies that could be reviewed for further developing the knowledge base of relative incidental intakes of soil versus dust. We included the Stanek et al. (1998) reference in the revised chapter. The Simon article is useful as an*

overview of soil ingestion patterns worldwide (incidental soil ingestion as well as soil pica and geophagy), and potential relevance to risk assessment, but did not provide any new information..

Comments: (related to whether Chapter 5 is clear enough with respect to differentiating between soil and dust intake)

A clear definition of these terms (along with other terms appearing in chapters 5 and 6) is needed in the beginning of the discussion. The issue of suspended versus suspendable versus deposited dust has to be clarified. The physical (particulate) structure and the chemical compositions of (representative) soils and dusts need to be briefly discussed and compared. Issues such as differences in particle morphology, particle size distribution, organic and inorganic content, etc. of both soils and dusts need to be summarized; the corresponding effects of these properties on adhesion, intake, uptake, etc., should also be discussed with major uncertainties pointed out.

The introductory section clearly indicated that there is a difference between the two sources. However, the recommendation is based on the combined sources in the text and information tables but not in the final Table (5-21), which needs to be footnoted (see section 5-4 is not sufficient) to make this clear. In addition, separate line item recommendations (in Table 5-21) would be useful.

The Mickey Leland national Urban Air Toxics Research Center and Health Effect Institute sponsored research that could provide additional pertinent information on indoor particulates that originate outdoors.

This chapter does not clearly distinguish between soil and dust intake. I don't think that there is a critical assessment of the assumptions underlying the dust estimates in any study. It seems to me that the literature has assumed that the trace element ingested is from soil, and papers have been written under this assumption. Dust has been occasionally looked at, but not rigorously studied. As a result, the questions and assumptions needed to distinguish soil from dust ingestion haven't received careful attention. This issue is complicated, but potentially important. For example, some trace elements have different concentrations in soil based on particle size. Dust may be composed of a different particle size distribution than soil. Activity time has not been shown to be related to soil ingestion through exposure to outdoor soil. For this reason, the ability to separate soil from dust I consider to have "low" confidence. This clouds the use of the confidence ratings in Table 5-22.

Response**:** *The chapter was edited substantially to be more precise and clear about differentiating between soil and dust. The U.S. EPA was not able to find pertinent information on the Mickey Leland internet site. The complexities of separating soil ingestion estimates from dust ingestion estimates have not been explored thoroughly in the revised chapter, since that effort would require a substantial amount of time to review the available recent literature in detail and make informed judgments about the relative proportion of each that might be ingested.*

Comments: (related to the dividing line between Chapter 5 and Chapter 6 clear in terms of what questions the chapters are trying to answer)

The dividing line is not clear: the amount of soil/dust ingestion is a result of (mostly) the activity/behavior related factors discussed in Chapter 6. In this reviewer's opinion a somewhat modified version of Chapter 6 should follow the introductory material (containing the clarifications and definitions discussed above, in answer to Question 11) of Chapter 5. So, the presentation of estimates of soil/dust ingestion rates should follow presentation of the behavioral data, better reflecting the actual sequence of events in the exposure "continuum."

The distinction between the intent to the two chapters was clear to me.

There are two areas (non-soil/dust ingestion and other ingestion) may be separated as indicated.

***Response*:** *Both chapters have been revised to try to improve clarity in what the recommendations represent.*

Additional Comments for Chapter 5:

P. 5-3, lines 15 & 16: Why are foreign studies automatically classified as "relevant" rather than "key," if they are well designed, peer reviewed and pertain to cultures similar to those in the U.S.?

P 5-7, lines 8 – 10: See changes made in punctuation. I am assuming this was a study of a child and both parents/guardians.

P. 5-10, lines 11 & 12: Hygienic practices are likely to vary substantially between populations of underdeveloped and developed countries and between individuals in lower socioeconomic classes and middle classes. This "boiler plate" descriptor, however, should not be applied indiscriminately to every non-U.S. study. It is doubtful, for example, whether there is much of a difference in hygienic practices in most daycare centers in the Netherlands and in the U.S.

P. 5-30, lines 29-31, and p. 5-31, lines 1 – 5: It should be stated here that these best estimates of soil ingestion are likely to be overestimates, since the studies were conducted during summer months. Alternatively, an annual best estimate could be calculated taking into account that ingested doses during cold, rainy months should be primarily based upon indoor dust as the primary exposure source.

P. 5-31, lines 12 – 15: A better and more complete rationale should be given for selection of an ingestion rate of 10 g soil/day for pica children. The value is taken from data on the intake of 1 child on the higher of 2 weeks of observation. The data base reviewed in the current document is much richer than this.

The document's authors have done a thorough job of presenting and critiquing the most important investigations of soil ingestion by children. The evaluations and conclusions are quite reasonable, with the few exceptions noted above. Data from the key studies are clearly presented in tables at the end of the chapter. Information in the first column, entitled "Considerations" in

Table 5-22 is of very limited value. I believe it would be better to expand the Rationale. It may be preferable to present the overall confidence ratings for the major, or key studies.

Response**:** *See responses to earlier comments about soil ingestion studies conducted outside of the U.S., weather conditions during the U.S. tracer element studies, and soil pica evidence from the U.S. tracer studies combined with inferences about soil pica prevalence from the survey response studies.*

2.10 Chapter 6 (Other Non-Dietary Ingestion Factors)

Comment: Chapter 6 primarily covers "mouthing behavior," specifically:

- Mouthing time (duration with recommendations for mean mouthing time in min/day).
- Mouthing frequency (how often, with recommendations for mean contacts/hour).

The confidence in the rating is low, which is appropriate for the current evaluation. However, the chapter can be substantially improved as this area of study is receiving significant attention. Care is needed with interpretation, since much of the information is observational and some (e.g., parent's recall) is secondary.

Response: *The low confidence rating is retained, since chapter revisions did not result in substantial new data being added. Chapter editing attempted to highlight the care needed to interpret the existing data by emphasizing the data collection procedures used in each study.*

Comment: The data used for developing recommendations are relatively current (1999 to 2005). However, this field is rapidly developing, and a number of recent studies relevant to other non-dietary ingestion factors should be incorporated. Citations for these studies are provided in the reviewer pre-meeting comments (Appendix C). These comments also identify databases that include information on mouthing behavior. For example, the Health and Environmental Sciences Institute (HESI) Exposure Factors database (http://www.hesiglobal.org/NR/rdonlyres/EED82508-73D3-4405-A123-2E3BD5DCEB7A/0/HESIExposureData10Aug04.zip) provides ready access to mouthing data for all the studies quoted (and includes other studies) in a common downloadable format. Also, the ExpoFacts database (http://cem.jrc.it/expofacts) includes a UK study on mouthing.

Response**:** *All citations for additional studies were investigated; if accessible and pertinent, additional studies were added. The cited HESI database appears to be potentially useful for U.S. EPA risk assessors; it appears to be a compilation of many of the same data sets that are summarized in this chapter. However, as an independent, stand-alone database that may or may not have undergone peer review, it is unclear whether citing it as a reference would add useful information to the chapter. The UK study on mouthing was incorporated into the revised chapter.*

Comment: Chapter 6 could more logically be presented before Chapter 5. This would allow the current Chapter 6 to provide context for all types of non-dietary ingestion factors, including hand-to-mouth and object-to-mouth behavior.

***Response*:** *The chapter was moved ahead of the soil and dust ingestion chapter to provide the desired context.*

Comment: Based on the current study- and data-limited state of the field, total separation of the studies and factors (i.e., separate discussions of each of the studies for each of the factors) might not be useful. However, this should be considered in the future as the field develops. Clarification rather than separation is recommended for mouthing frequency and duration, since these are likely correlated.

Response: S*ome clarification (as well as separation, since studies all report mouthing frequency separately from duration) was provided in the chapter revisions.*

Comment: While the factors provided in Chapter 7 are consistent with those provided in EPA's 1997 Exposure Factors Handbook, the panel recommends that transfer factors (a research need) be included to make these factors useful for both documents, and that the handbook also include factors associated with microenvironments. Certain behaviors (e.g., mouthing) may be affected by ethnic and gender differences and these should be taken into account, as appropriate.

***Response*:** A*lthough needed to develop dose estimates, transfer factors are outside the scope of the exposure factors handbook. Transfer factors could vary significantly depending on substances mouthed and contaminants that are of concern, and U.S. EPA anticipates that risk assessors would develop information specifically for each risk assessment for which transfer factors are needed. Currently, data of sufficient quantity and quality for distinguishing mouthing behavior differences due to gender, ethnicity, or microenvironment are not available*.

Comment: Chapter 6 should be edited for consistent use of terms (e.g., "mouthing") and to present all information consistently with other chapters (e.g., have a summary at the chapter start, identify key and relevant studies), as discussed earlier.

***Response*:** *The chapter has been edited accordingly.*

Comment: Chapter 6 (Other Non-Dietary Ingestion Factors) – General and Specific Questions

A peer reviewer opened this discussion by noting that other non-dietary ingestion factors focuses primarily on mouthing behavior. She stated that mouthing behavior involves two factors: frequency (i.e., how often) and duration (i.e., how long). This subject area has recent data (i.e., mostly from 1998 to present); however, it is limited in the number of studies and in the number of subjects tested. Most of the studies are observational and involved weighted means based on hand-to-mouth and object-to-mouth activity. She commented that the confidence is low for the available data; however, she was willing to make some allowances, since this issue is a relatively new subject of study.

***Response*:** *The U.S. EPA agrees that confidence is low for the available data.*

Comment: A reviewer questioned how duration was counted. Another reviewer clarified that, for example, a duration of 15 seconds would count as one incidence in the mouth and then the incidences would be added up over a day and week.

***Response*:** *It appears that duration has been measured in different units by different researchers, and these different units are one source of difficulty when comparing results from different research groups or age categories. Further complicating the mouthing duration data is the issue of extrapolating from observation periods to times when children were not observed. These limitations were noted in the chapter.*

Comment: A reviewer expressed concern about the different issues related to different substances and different media (e.g., whether the substance occurs on the surface of the toy or within the toy). Another reviewer questioned if a dose estimate is possible. The original reviewer responded that EPA's pesticide office has conducted modeling of lead, but that such modeling is often hard to conduct. This reviewer also noted a concern about Table 6-15, which only presents numbers, and Table 6-10, which provides no information about numbers of subjects and does not give the user a sense of the distribution of the data.

***Response*:** *Table 6-15 was revised and renumbered as Table 4-19. Table 6-10 was removed in the revised chapter because of concern that readers might assume that the data in Table 6-10 were primary data observations (the data in Table 6-10 were the results from a statistical model developed using several assumptions). Information on the number of children in each study summarized in the chapter are provided in the individual tables for each study..*

Comment: Another reviewer commented that the Agency should analyze and discuss correlations.

***Response*:** *Presumably the commenter is referring to correlations between mouthing frequency and duration. It is logical to assume that mouthing frequency and duration are correlated. Of the very few studies found where both frequency and duration data were published, the studies are of sufficiently small numbers of children that this exercise did not appear to be justified at this point in time.*

Comment: A reviewer requested that EPA include a paragraph at the end of the chapter that would discuss the most significant findings, since the chapter currently provides details but no bottom line. He referred the panel to his pre-meeting comments for an example. Another reviewer suggested that a summary be provided at the beginning of each chapter.

***Response*:** *The chapter has been revised to summarize the overall state of the science on mouthing behavior. The recommendations table provides a "bottom line" in terms of quantitative estimates.*

Comment: One reviewer requested that EPA consider consistency or the lack thereof between all the analyses.

Response**:** *Consistency and lack of consistency, between studies that used the same and different data collection and data analysis methodologies was one of the considerations used to develop the confidence rating.*

Comment: A reviewer commented on measuring activities (and microactivities), and recommended that EPA add information from studies such as Black et al. (2005), Auyeung et al. (2006), Cohen-Hubal et al. (2006), Zartarian et al. (2006), Xue et al. (2007), etc. He disagreed with some of the terms EPA used in the handbook, and was surprised that recent developments that have been achieved through EPA initiatives were not mentioned. He requested that EPA include some information on these developments, and noted that the handbook needs more polishing.

Response**:** *The Xue et al. (2007) article was added to the revised chapter. AuYueng et al. (2006) was reviewed but excluded because it focused on hand contact rather than mouth contact. Similarly, Cohen-Hubal et al. (2006) and Zartarian (2006) did not include mouthing behavior data. Black et al. (2005) was already referenced in the chapter. The chapter revisions attempt to improve the handbook's consistency, completeness, accuracy and formatting.*

Comment: A reviewer noted that some studies involved children who were observed by a secondary source (e.g., parents) and emphasized the importance of including information in the handbook on whether the children were observed directly by the researcher or by parents who then reported the children's activities to the researcher. Another reviewer concurred that this information is very important; she cited Natalie Freeman's study, which reported that often children were not washing hands as often or as thoroughly as the parents reported.

Response**:** *The revised chapter now emphasizes each study's data collection method and its potential influence on the study results.*

Comment: The panel chair asked the panel if any newer studies on this subject exist. One reviewer noted two new studies and referred the panel to her pre-meeting comments. She also noted that there is a new ILSI database on mouthing studies. The chair asked the panel whether any studies on non-dietary ingestion in minorities or subpopulations. A reviewer responded that a pica study had not detected differences in subpopulations, but the study had limitations.

Response**:** *The studies identified as "key" in the revised chapter include children from various locations and socioeconomic strata, but it is unclear how well the existing U.S. demographic and racial/ethnic profile is represented among the small number of children in the key studies.*

Comment: A reviewer noted an inconsistency of how criteria in this chapter were rated compared to Chapter 1, and recommended that EPA review the document to make sure that criteria ratings are handled consistently among the chapters.

Response**:** *U.S. EPA has performed a review to ensure consistency of application of the confidence rating criteria.*

Comment: A reviewer expressed concern about the limited number of studies in this chapter. Another reviewer concurred, noting that EPA omitted some studies. She emphasized that EPA needs to follow through with the precedent set in Chapter 1.

Response**:** *U.S. EPA has added several studies suggested by reviewers and others identified since the peer review was performed***.**

Comment: A reviewer suggested that EPA consider gender differences, since different genders could have different mouthing behaviors.

Response**:** *One meta-analysis (Xue et al., 2007) looked at this issue and did not find statistically significant differences between genders. The reliability of data collection and analysis methodologies may improve in the future such that this issue and others like it can be explored in greater depth.*

Comment: A reviewer expressed concern about the way EPA described "normal child behavior" in the handbook. She emphasized that mouthing is a normal part of development, and said that the beginning of the chapter presents mouthing in a negative light. She suggested that EPA portray mouthing as a part of normal healthy child development by including a discussion on the progression of mouthing and the sequence of developmental stages.

Response**:** *The chapter was revised and is now neutral with respect to children's mouthing behavior. A short description of mouthing behavior in infancy and beyond is included in the introduction*.

Comments: (related to the organization of the handbook, including whether the data provided in the tables, in a clear, easily understood, and usable format)

For Chapter 6, which deals with "mouthing behavior", the presentation of the studies was done in chronological order with no clear discussion of which were considered key or relevant. Key studies should be clearly identified (consistent with the discussion in the Introduction), as far as possible. The summary tables, which provide the recommendations, do provide the studies that were used to calculate weighted means where this statistic is provided.

Response**:** *The chapter was revised to clearly identify the key vs. relevant studies, consistent with other chapters, and present them in chronological order by publication date. U.S. EPA judged that, for the data users' needs, separating mouthing frequency and duration data, and hand to mouth versus object to mouth categories for both frequency and duration, would be most useful, and thus revised the chapter to perform this separation. The reviewer's point about clarifying correlations between frequency and duration will probably be resolved in the future when more data, of better quality, become available for each age group.*

Comments: (related to the confidence ratings)

For Chapter 6, the overall ratings for the recommendations on mouthing behavior (both mouthing tome and frequency) are appropriately low (Table 6-22). It is understandable that this

set of factors is important but the document correctly advocates for using caution in using the data. This could be better emphasized. Also, how this information is translated to actual exposures (e.g., transference factors) are needed.

***Response*:** *The "low" confidence rating has been retained in the revised chapter. The text accompanying the recommendations should provide data users with appropriate caveats regarding use of the data. Transference factors are outside the scope of this document and would likely be addressed on a case-by-case basis in each risk assessment.*

Comments: (related to data variability)

Based on the limited data, much of the presentation appropriately focuses on qualitative discussions.

Page 6-10 lines 1-4. Mention that response was based on recall from parent or guardian.

Page 6-13 lines 11-21. The description of what was done is not clear from the write-up. I don't think the writer understood the role of the bootstrap method in the development.

Page 6-14 and Table 6-12. Does the time included add up to 5 hours? I think presentation of the table results can be improved, maybe just by adding the time period.

Page 6-42. Table 6-20. Include the SE if possible.

Response: *Data limitations were discussed throughout the chapter. Tables were revised and chapter was reorganized.*

2.11 Chapter 7 (Inhalation Route)

Comment: (related to organization of the Handbook – Charge Question 1)**:** In Chapter 7 (as in other chapters), the studies reviewed were presented in chronological order, with no clear up-front discussion of which were considered key or most relevant. Key studies should be clearly identified (consistent with the discussion in the introduction), as early as possible within the chapter.

Response: *Two new sections were added to Chapter 7: the key studies section and the relevant studies section.*

Comment: The terminology for Tables 7-3 to 7-5 is confusing and inconsistent with the other tables in Chapter 7.

Response: *These tables were revised as needed to eliminate inconsistent terminology.*

Comment: (related to confidence ratings – Charge Question 2)**:** Given the current status of the inhalation rate data specific to children's exposures, the use of confidence ratings would appear to be a reasonable compromise for the estimates presented in Chapter 7. The inhalation rate

recommendations provided in Chapter 7 are based on a single relatively new study: Lordo et al. (2006). Neither this study nor the data on which it is based have undergone peer review yet. While the confidence rating is subjective (and characterized as medium), there are substantial questions regarding the study outcomes that should be adequately addressed to justify why this study should be used to replace the current values. For example, the handbook does not incorporate (or even reference) very recent studies [Brochu et al., 2006a, b, c; (Although these references provide only daily mean inhalation rates for different age groups (rather than activity-dependent rates), they can be used for comparison and cross-evaluation with the corresponding mean rates proposed in the CSEFH) Arcus-Arth and Blaisdell, 2007].

The mean daily inhalation rate estimates developed through the Lordo et al. (2006) study and specifically recommended for use in CSEFH are substantially higher (almost by a factor of 2, for the younger children) than values previously recommended by EPA in its 1997 Exposure Factors Handbook, as well as the corresponding values in other studies, including the two recent ones mentioned above. When the draft CSEFH was released for review, the Lordo study was not publicly available; (the Lordo et al., 2006, study was subsequently made available to the public and EPA requested comments on it. These comments were not made available to the CSEFH peer review panel) therefore, it is not clear why it was rated as the single key study, while other studies that were previously used as the basis for inhalation rate recommendations were no longer considered valid. These issues, and in particular the questions regarding the newly recommended values for the younger children, should be addressed in finalizing the handbook.

Response: *Brochu et al. (2006), Arcus-Arth and Blaisdell (2007), and Stifelman (2007) were added to the chapter as key studies. Recommendations were revised accordingly.*

Comment: References should be provided to other available databases (and computer programs) for inhalation dosimetry (and for related parameters), such as the ICRP and P3M models. The handbook should compare the data and predictions from these databases and models to the rates calculated in Chapter 7 (and recommended by EPA through the CSEFH).

Response: *References to the ICRP were included in the chapter. Comparisons using PBPK models such as P3M were not deemed appropriate or necessary.*

Comment: (related to data variability – Charge Question 3) Chapter 7 is a good example of "deterministic" variability being introduced explicitly with respect to activity level within an age/gender group. Nevertheless, there should be a discussion of what other factors may affect breathing rates (e.g., weight, body mass index [BMI]), how these factors affect variability, and how large the effects might be. Dependencies between BMI and inhalation rate should be addressed, if possible. Information about subpopulations, such as obese children and ethnic groups, should be added, if possible.

Response: *Based on available information, discussion of other factors affecting inhalation rates has been included in the introduction section of the chapter.*

Comment: (related to additional issues not adequately addressed in the document – Charge Question 4) Inhalation rate and volume are the only respiratory parameters considered in

Chapter 7. Other major factors that determine the extent of systemic absorption of inhaled gases and vapors are pulmonary surface area for absorption, pulmonary blood flow rate (i.e., cardiac output), and air:blood partition coefficients (Bruckner et al., 2008). These factors are an integral part of physiologically based pharmacokinetic (PBPK) modeling. Relatively lipid-soluble gases are primarily absorbed in the alveoli, so alveolar surface area is a key determinant of their absorption. There is a substantial base of published data showing a linear relationship between alveolar and body surface areas. The rate of pulmonary/alveolar blood flow is also very important in absorption of chemicals that readily diffuse across cell membranes. Diffusion is "driven" by the difference in chemical concentration between the alveolar air and capillary blood (i.e., the more rapidly blood carries the chemical from the lung, the greater the concentration gradient). There are complete data sets, utilizing state-of-the-art technologies, on the age-dependence of cardiac output. However, published data on the age-dependence of air:blood partition coefficients are probably limited. Factors that influence the toxicokinetics and, in turn, the susceptibility of infants, children, and adolescents to toxicity have been addressed in a number of publications (e.g., Bruckner, 2000; Bruckner and Weil, 1999; Clewell et al., 2004; Gentry et al., 2003; Ginsberg et al., 2004a, b; Scheuplein et al., 2002). A brief statement mentioning these factors, along with PBPK modeling, would enhance this handbook.

Response: *Discussion of respiratory parameters as suggested is outside the scope of this Handbook.*

Comment: (related to the use of data and uncertainty – Charge Question 5**):** One source of uncertainty in ventilation rate distributions is the assumptions embedded in Energy Expenditure (EE) based estimation procedures. These assumptions and uncertainties should be presented in this document.

Response: *Discussion of uncertainties associated with Energy Expenditure (EE) has been added to the chapter and factored into the overall confidence rating for the inhalation rate recommendations.*

Comment: (related to data gaps – Charge Question 7) Research is needed (starting from literature surveys of potentially available data) to develop databases on estimates for inhalation rates through techniques that are not based on the EE approach; these data would be used in cross-evaluations of EE-derived estimates.

Response: *Inclusion of research gaps as suggested is outside the scope of this handbook.*

Comment: (related to literature search – Charge Question 8)**:** At a minimum, per the discussion above, additional references should include Brochu et al. (2006a, b, c) and Arcus-Arth and Blaisdell (2007).

Response: *The following references were added to the chapter:*

Arcus-Arth, A., and Blaisdell, R. 2007. Statistical distributions of daily breathing rates for narrow age groups of infants and children. *Risk Anal.* 27: 97-110.

Brochu, P., Ducré-Robitaille, J.-F., and Brodeur, J. 2006a. Physiological daily inhalation rates for free-living individuals aged 1 month to 96 years, using data from doubly labeled water measurements: a proposal for air quality criteria, standard calculations and health risk assessment. *Hum. Ecol. Risk Assess.* 12(4): 675-701.

Brochu, P., Ducré-Robitaille, J.-F., and Brodeur, J. 2006b. Physiological daily inhalation rates for free-living individuals aged 2.6 months to 96 years based on doubly labeled water measurements: comparison with time-activity-ventilation and metabolic energy conversion estimates. *Hum. Ecol. Risk Assess.* 12(4): 736-761.

2.12 Chapter 8 (Dermal Route)

Comment: Chapter 8 introduces the concepts and importance of applied (external) dose. The diagram of the concept presented in the chapter is too simplistic. Nonetheless, *only* body surface area and skin loading with soil are addressed in the chapter. Other key determinants of percutaneous absorption should be noted, and their role in local (skin) and systemic exposure to toxicants briefly described. These determinants include:

- The thickness of the stratum corneum (SC) (the barrier to absorption) varies markedly over different parts of the body. Thus, the extent of percutaneous absorption varies significantly, depending on the body surface that is exposed to a chemical.
- The thickness of the SC in full-term newborns and adults is comparable. Therefore, dermal absorption studies show no substantial age-dependence. Skin of premature newborns has a thinner, more immature SC and exhibits greater absorption of chemicals.
- Conditions common to children (e.g., abrasions, diaper rash, lesions from eczema, chicken pox, and other childhood diseases) can compromise the integrity of the SC and enhance absorption.
- Diapers and tight-fitting clothing aid in percutaneous absorption by keeping a chemical in direct contact with the skin and inhibiting evaporation of perspiration, resulting in increased hydration of the SC. This can solubilize water-soluble chemicals and enhance absorption. The scrotum, which has the thinnest SC, is covered by a diaper.
- Use of lipophilic creams and lotions can solubilize lipid-soluble chemicals on the skin's surface and permeate the SC with lipids. This enhances the absorption of lipid-soluble chemicals. Such creams and lotions are frequently used on infants and young children, especially in diaper areas.

***Response*:** *The focus of this chapter is on measurements of body surface area and dermal adherence of solids to the skin. Detailed discussion of all parameters that influence dermal absorption is outside the scope of the Handbook. For information on factors that influence dermal exposure, the readers are referred to Dermal Exposure Assessment: Principles and Applications (U.S. EPA, 1992b) and Risk Assessment Guidelines for Superfund (RAGs) Part E (U.S. EPA, 2004).*

Comment: It is well established and clear from data included in the chapter that infants and young children have a greater surface area:body weight ratio than do adults. Body surface area is usually considered to increase in direct proportion to lean body mass. It is not clear how surface area is affected by the increasing incidence of childhood obesity.

Response: *The U.S. EPA searched for information on this issue and no data were found.*

Comment: Increasing body weight and obesity in the population result in increased subcutaneous fat. Percutaneous absorption as a function of body surface area may not be linear with increasing body weight due to the subcutaneous fat. This fat can act as a depot for lipophilic chemicals, which will delay their systemic absorption. This implies that increasing body weight in the population may result in a decreased rate of systemic absorption per cm^2 of skin surface areas.

Response: *The U.S. EPA searched for information on this issue and no data were found.*

Comment: Dermal exposure of children to gases/vapors and chemicals in water (bathing, playing in water, swimming) should also be considered.

Response: The handbook does not provide chemical-specific data. Surface area data that can be used in these scenarios are provided in the chapter.

2.13 Chapter 9 (Activity Factors)

Comment: Like many of the other chapters, Chapter 9 suffers from a surfeit of older data that do not reflect contemporary trends. The panel recommends that EPA strive to obtain more recent information about the activities of children. For example:

During the past decade, video games and other electronic devices have become extremely popular among children. The implications are far reaching. Does the fascination with electronic games translate into more time spent indoors?

Response: *Agree, but the U.S. EPA did not find data to support this.*

Comment: A second deficiency, again noted in other chapters, is the lack of information about the variety of subpopulations that now make up the bulk of the U.S. population. Activities surveys based on white, middle class families cannot easily or straightforwardly be extrapolated to other ethnic and cultural subpopulations.

Response*: Data for activities by demographics to include ethnicity were added when available.*

Comment: A third deficiency is the absence of information about variations among socioeconomic subpopulations and changes in activity patterns in families. During the course of the meeting, we noted the need to take account of both ethnic and socioeconomic differences. Future versions of the handbook should place much greater emphasis on these differences, especially because other EPA initiatives, particularly that on cumulative risk assessment, explicitly include such variables."

Response: *Agree, but data were not available. The U.S. EPA does not have future plans at this point to collect such data.*

Comment: Chapter 9 should provide more specific explanations of the data. For example, Table 9-8 is described tersely as "Provides information on time spent in a car." Such a description is so compressed as to be uninterpretable. Instead, the chapter should provide sufficient detail to make the table useful to the reader—for example, how the data were acquired and over what time period, the characteristics of the population surveyed (e.g., their SES), and in what part of the country the data were collected. The terse descriptions on pages 9-6 though 9-9 provide a cogent argument for placing these data in an Internet- or Web-accessible format, which would allow a much fuller description of their source.

Response: *The data do not allow for providing further details.*

Comment: Per the general recommendation made above for all chapters (see Question 1), Tables 9-75 and 9-76 (upon which the conclusions and recommendations are based) should be moved, along with the conclusions and recommendations and other tables used to provide background (Table 9-74 and 9-77) or support the conclusions. The previous tables should play perhaps a reference role, rather than one in which they are primary. All the tables from 9-1 to 9-73 are preludes to the final three tables.

Response: *Recommendations were moved to the front.*

Comment: Table 9-75 should include sample sizes.

Response: *Sample sizes were added to all tables where available.*

2.14 Chapter 10 (Consumer Products)

Comment: The panel highly commends EPA for including a chapter on consumer products in the Handbook, as these products are likely to be a major source of exposure for young children. Home is where young children spend most of their time and, as vividly illustrated in Table 10-1, the numbers of products potentially used in the home are large. Further, data from a variety of sources, including Whyatt et al. (2007) and Lewis (2005), indicate that contaminants can be much more persistent in the indoor environment than in the ambient environment and that indoor concentrations can exceed ambient levels. Also, there is little regulation of exposures from consumer product use, and the requirements for toxicity testing of many products prior to marketing are limited. Thus, the handbook does a great service in calling attention to this exposure source. The panel highly concurs with the handbook's recommendation that "further data are needed on the frequency and duration of use and kinds of consumer products used by children." Products used around children also need further data, along with information about where such products are used (e.g., homes, daycare centers, school, and vehicles).

Response: *The data are limited on the use of consumer products by children.*

Comment: Of the available data, a minimal number of items were selected for presentation in Chapter 10 and do not reflect the major potential exposures to consumer products in the child's environment. Moreover, it not clear why some data were selected (e.g., microwave oven use) while others were not (e.g., gas stove use). Much existing data are missing from the chapter. For

example, the Consumer Products Safety Commission and various industry groups collect this kind of information and make much of it publicly available. There is additional information in the National Human Activity Pattern Survey (NHAPS) that was included in EPA's Exposure Factors Handbook but not in the CSEFH. Those who market such products (e.g., cosmetics and fragrances, soap and detergents) have considerable expertise in assessing their use, and much of these data are publicly available or could be made available at a sufficiently general level of detail.

***Response**: The data from NHAPS and other data from the EFH were added. Market data on cosmetics and toiletry were also added. The studies presented represent readily available surveys from which data were collected on the frequency and duration of use and amount of use of cleaning products, household solvent products, cosmetic and other personal care products, and pesticides. For a more detailed presentation of data on the use of consumer products among the general population, the reader is referred to the Exposure Factors Handbook (U.S. EPA, 1997). In the revision, a link is also provided for further information from Soaps and Detergents Association, EPA Source Ranking Database and the National Library of Medicine Household Products database.*

Comment: The data need to be better documented. For example, Tables 10-5 and 10-6 provide frequencies without indicating the time period. Also, separate statistics should be provided for "doers" and "non-doers," (i.e., as the data are presented in Table 9-26). Per the recommendation given above for Chapter 1, these terms need to be defined.

***Response:** Time periods have been added. A separate statistic for doers and non-doers were added, where possible (e.g., NHAPS data).*

Comment: The panel disagrees with the overall conclusion that "due to the large range and variation among consumer products and their exposure pathways, it is not feasible to specify recommended exposure values as had been done in other chapters of the handbook." It should be possible to identify major categories of consumer products (rather than attempting to go after the wide range of products) and to provide data on the frequency of their use, at least for activities that are common to many households. Additionally, the panel would like to see more data on consumer product usage among minority groups, rural households, and households in different regions of the country.

***Response:** EPA believes that the overall conclusion previously reached is a valid one and chose to not make recommendations for consumer products.*

Comment: Chapter 10, on consumer products, needs to include ethnic differences in cosmetic use. For example, African-American women use a much greater variety of hair products than Caucasian women, a difference that will impact children in the home. Some Hispanic women use skin lighteners that contain mercury, as a result of which their children are exposed.

***Response:** The data are limited for use by ethnicity. Two studies presented the study group demographics including ethnicity, but the use data are compiled by total study group.*

2.15 Chapter 11 (Body Weight Studies)

Comment: The panel recommends that EPA utilize more up-to-date birthweight information for its data on infants 0–1 months of age. EPA has used Hamill et al. (1979) as the basis for the recommended values for body weights in the birth to <2-month age category. Use of data published in 1979 is not acceptable because there has been a steady shift downward in average birthweight in the United States, as well as a shift toward a higher percentage of babies that are low birthweight. This has been well documented by the National Center for Health Statistics through their analyses of annual vital statistics data, which are published, peer-reviewed, national and readily available.

Response: *The NHANES data have been used for the recommended values. Data from the following reference have also been included:* Martin, J.A., Hamilton, B.E., Sutton, P.D., et al. 2006. Births: final data for 2004. *National Vital Statistics Reports* 55(1).

Comment: Also, via the vital statistics system, EPA has available and should use race-/ethnicity-specific data on birthweight. This is particularly important for newborns (because, for example, African American and Native American children are much more likely to be born low birthweight and are on average smaller than white babies). Likewise, the handbook should provide birthweight distributions for babies born preterm.

Response: *Data for preterm babies have been added from Martin, J.A., Hamilton, B.E., Sutton, P.D., et al. 2006. Births: final data for 2004. National Vital Statistics Reports 55(1).*

Comment: Second, the data used to calculate child weights are old (1988–1994). Much newer vital statistics data, drawn from birth certificates, are almost certainly available. This is a major problem because the United States has experienced an upward trend in average child weights, as well as overweight and obesity rates. Recent NHANES data are available for calculating body weights for the recommended age bins, and these newer NHANES data could be analyzed quickly. The 2005–2006 data will also be available soon. Like the vital statistics system, NHANES includes information on ethnicity which should be used.

Response: *NHANES data have been added. EPA performed an analysis using the most current data. The EPA analysis was based on 4 data sets of NHANES data covering 1999-2006.*

Comment: Third, the handbook should include estimates not only for weight but also height (or length) and BMI (or, at birth, ponderal index).

Response: *The CDC data for Height and BMI have been added.*

Comment: It also is of concern that EPA is utilizing an unpublished study (EPA, 2000) documented in an internal memorandum that is not available and seems not to have been peer reviewed. The Agency should not continue this practice.

Response: *The recommendations are no longer based on this memorandum. They are based on the EPA analysis of NHANES, 1999-2006 data*

Comment: The panel would encourage EPA to establish a process whereby these parameters can be kept up to date on a frequent basis, given that vital statistics and NHANES are reanalyzed periodically.

***Response*:** *Agree, but will be determined by the available resources.*

Comment: The high confidence ratings are inappropriate given that the data are out of date.

Response: *The confidence rating in the revised chapter is high because of use of the most current NHANES data.*

Comment: Variability should be addressed in a uniform fashion. For example, all tables could present percentiles. Also, confidence intervals would be useful. The tables should include numbers of subjects per category.

Response: *The number of subjects has been added, when available; confidence intervals were not available.*

2.16 Research Recommendations

Comment: See the list of recommendations below:

Response: *EPA acknowledges the research recommendations below and acknowledges that this type information would be useful. However, obtaining and incorporating the information is outside the scope of this document and the resources set aside for its development at this time.*

The peer reviewers had the following research recommendations.

Research to address exposure factors extending from external dose to dose to target tissues, including biomarkers.

Subchronic exposures.

Transfer factors.

Trans-placental transfer of environmental contaminants.

With respect to breast milk intake, maternal activities (e.g., possible correlation between work status and breast feeding practices).

Water ingestion data for infants less than 1 month old.

Research to better differentiate soil versus dust ingestion.

Development of databases on estimates for inhalation rates through techniques that are not based on the Energy Expenditure approach; these data would be used in cross-evaluations of EE-derived estimates.

The relationship of increased body weight to the skin's absorptive capacity.

Coordinated work with the BLS to leverage data-gathering opportunities associated with their U.S. time-use survey that includes data for adolescents down to 15 years.

Reviewers had also made several research recommendations in their pre-meeting comments. These included:

Additional research is needed in the areas of current activity patterns of exposure (spatially, temporally, physically, and subjectively). Many of the historical national data sets on which activity pattern data are based have become potentially obsolete, due to the rapid penetration of computer technologies (including Web-surfing, podcasting, and video gaming) into many levels of society, as well as the changing nature of children's extra-curricular activities (limited by safe neighborhoods, outdoor areas, and societal changes in the nature of the economy, industry, and service sector operations). Additionally, societal changes in the home environment (including multiple-income families requiring more day care or early-life care of children in locations other than their own home by individuals other than immediate family members, as well as longer commuting times between residential and work locations brought about by families seeking affordable housing) are likely to be misclassified by the use of earlier exposure factors related to previous conventional nuclear family, single-income-earner lifestyle assumptions.

More research is needed on children's exposures to consumer products and products manufactured for children, such as toys and arts and crafts products—not just the frequency and duration of use of these products but also the potential for transfer of exogenous substances from such products to hands and mouth, and perhaps also skin.

An important consideration might be to determine how "age groupings" comport with exposure and effects timing.

Soil ingestion studies have been conducted in limited populations and geographic regions. Expanding the range of the population covered (e.g., to the southern United States) is a need.

More data are needed on breast milk consumption and use of infant formula. Data are also needed on human lactation among ethnic minorities, since almost all the data presented in the handbook are for white upper class women.

Further studies are needed covering:

- A more diverse population of breast-feeding women.
- A larger population of breast-feeding women.
- A longer period, with continuous data collection as opposed to snapshots.

Research is needed on consumption rates for fish for different age groups, and to separate out store-bought fish from recreationally caught fish.

More and better use of longitudinal studies of dietary data would be helpful to develop and check methods for estimating longer-term exposures.

There is a real need for a long-term (e.g., 365-day) investigation involving a fairly large population. It is not known, for example, whether long-term correlations in dietary intake are evident in populations due to geographic location, ethnicity, age, or other criteria. Such a study would result in a major increase in knowledge of dietary intake and would prove invaluable for exposure assessors everywhere.

Studies are needed that focus on fish consumption and provide unbiased data on the patterns of infrequent consumers, among whom children are disproportionately represented. Studies combining short-term information (preferably seven-day recall as opposed to two-day recall) with questions related to usual patterns of fish consumption would be useful in addressing these concerns.

More research and data are needed for water intake for ages less than 1 year. The handbook's recommendations for the different age groups in that range are based on a database whose sample size is very small.

Estimation of distributions for longer-term exposures than the two days covered in the CSFII surveys is a key issue. Longitudinal data studying the same individuals over week-long periods in the course of a year (one week per season, as done in some recent studies of air exposures by Wallace, cited earlier) would be most helpful.

The following studies are needed:

- High-activity level water intake studies.
- Hot-climate studies.
- Longitudinal investigations of one-month to one-year duration.

Additional analysis is needed of age-specific water intake dependence on factors such as activity level, climate, etc.

Additional research is needed in the areas of current activity patterns of exposure (spatially, temporally, physically, and subjectively). Many of the historical national data sets on which activity pattern data are based have become potentially obsolete, due to the rapid penetration of computer technologies, podcasting, and video gaming into many levels of society, as well as the changing nature of children's extra-curricular activities (limited by safe neighborhoods, outdoor areas; societal changes in the nature of the economy, industry, and service sector operations) and societal changes in the home environment (including multiple-income families requiring more day care or early-life care of children in locations other than their own home by individuals other than immediate family members, as well as longer commuting times between residential and work locations brought about by families seeking affordable housing).

Research is needed on activity patterns among minority groups, especially African Americans, Hispanic Americans, Native American/Alaskan Natives, and Asian Americans; among rural children (vs. urban children); and among children in different regions of the country.

Data are needed on use of personal care products that are directly marketed to children (e.g., lip gloss, nail polish).

Another recommended research area is the large amount of time spent in automobiles. There is a need for more information on indoor air exposures in cars, particularly cars on the freeway in heavy stop and go traffic.

Longitudinal studies are needed showing how activity changes across time for a child. More data from children in younger age groups would be useful.

The consistency of individual activity patterns over time, especially as subjects age, would be a useful adjunct. If patterns change markedly over time in individuals, it would provide less confidence in calculating the average daily dose. More information about factors such as SES and ethnicity are needed to determine the extent of population variability in exposure factors.

EPA should explore the possibility of conducting small-scale studies to assess whether the activities for a given age group have changed significantly (with, say, power = 80 percent and *p*-value set at a predetermined level). Resources could thus be targeted just on updating activity for those age groups that have changed. For example, activity patterns may not have changed appreciably for the very young but are likely to have changed for older children.

The lack of data presented suggests that there are significant gaps in the understanding of children's exposures to consumer products. At least two issues need to be addressed to significantly close apparent data gaps: (1) a current listing of likely consumer products exposures for children needs to be updated, developed, and presented; (2) a current listing of available exposure factors as a function of age group needs to be updated, developed, and presented.

EPA should identify major categories of consumer products (rather than attempting to go after the wide range of products) and at least provide data on frequency of their use, at least for activities that are common to many households. (For example, how frequently do people wax their cars, paint their walls, clean the toilets?) EPA may want to consider a partnership with the Consumer Products Safety Commission and with industry to collect this kind of information. Those who market such products have a considerable amount of expertise in assessing their use; although they could not provide proprietary data, they probably could share methods and approaches.

Research is needed on household product usage among minority groups, especially African Americans, Hispanic Americans, Native American/Alaskan Natives, and Asian Americans; among rural households; and among households in different regions of the country. Such updated surveys should ask more specifically about time of usage of products, given the problem with the wording of the NHAPS questions. For the same reasons cited above for consumer products, EPA

may want to consider a partnership with the Consumer Products Safety Commission and with industry to collect this kind of information.

NHAPS needs to be brought up to date.

Given the recent changes in childhood obesity trends, a methodology for incorporating timely and current weight data into the national database (perhaps by collecting height and weight measurements currently made in public schools most school years) would seem valuable.

More information is needed on the change in body weight over time and also the impact of using BMI data.

EPA should consider preparing an additional handbook on fetal exposures and should consider as a research need that data be gathered on trans-placental transfer of environmental contaminants.

APPENDIX A

RESPONSE TO PUBLIC COMMENTS

A.1 General Comments

A.1.1. Comments from the American Chemistry Council

Comment: The alignment of the data presentation with recommended child specific age categories is also very helpful. It is important, however, that the data quality assessment consider that sample size for these individual age categories sample size can be relatively small. It is not clear if the data quality has been assessed based upon overall study sample population size, or the sample size of the subcategories for which data are presented. The quality assessment should be aligned with the data presentation.

***Response*:** *Agree that the sample size can be small for some age categories, however these are the age bins set by the EPA to promote consistency in data collection and presentation. It also serves the purpose of highlighting data gaps. EPA recognizes that the data quality can not always be assessed. Limitations of the data are presented for the studies.*

Comment: Also, we suggest reviewing the information in the handbook in totality, to gain an even greater understanding of children's exposure factors. For example, in Chapter 6 it is indicated that Davis (1995) found children age 0 to 48 months are awake approximately 8.9 hours per day; information on time awake can also be found in Groot *et al.* (1998) although not presented in the handbook. This type of information is also relevant to the time activity information presented within Chapter 7 (inhalation) and Chapter 9 (time activity). An integrated assessment of the data contained within the handbook may find additional opportunities for maximizing data utilization.

***Response*:** *This is a good idea, but it was considered resource intensive and will most likely not result in any new key information.*

Comment: The draft indicates that an existing research need is for additional data on child intake of ethnic foods. Depending upon the type of ethnic food for which this information is needed, a potential information source could be child food ingestion data in the European exposure factors database ExpoFacts or additional reference information posted on its internet site (http://envi.uku.fi/expofacts2006/). While any data would not be representative of the US population, it may be possible to develop an estimated range of child intake.

***Response*:** *This will be considered in future updates.*

Comment: The Council previously conducted an extensive analysis and developed and filed comments on the Agency's *Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens* (ACC comments filed May 5, 2003; EPA Docket Number OAR-2003-0008). With respect to the *Supplemental Guidance*, there are severe shortcomings with the datasets EPA relied on (see Attachment 2 (R.A. Becker, 2005, Society for Risk Analysis annual meeting, Challenges to Implementing EPA's New Supplemental Guidance for Assessing Cancer Risks from Early Life Exposures (SGAC)). For example, of the 515 ratios evaluated by EPA from acute exposure studies of 42 chemicals, 45% showed equal or less sensitivity of the early

life exposure period compared to exposure later in life. Of the 45 ratios of susceptibility derived from repeat dose studies, 58% showed equal or less sensitivity of the early life exposure period compared to exposure later in life. Based on the datasets EPA relied on, Becker (Attachment 2) has pointed out that, in fact, the scientific evidence to support EPA's hypothesis that exposure to carcinogens early in life leads to increased probability of tumor development, compared to exposure commencing later in life, is weak. Furthermore, making age-adjustments for both exposure and cancer potency would result in radically new age-specific 'annualized' cancer risk estimates. For example, using the *Supplemental Guidance*" method to calculate risk (Σ (Exposure x Duration x Potency x ADAF), for a given concentration (in air or water etc.), the amount of risk accumulated per year from age 0-2 is roughly 30 to 35 fold greater than in any one of the years from age 16-70 (Attachment 2). Such a risk accumulation rate has not been shown to be supported by scientific data. ACC believes the current practice of EPA carcinogen risk assessment is already health protective and very conservative.

Response**:** *This comment refers to guidance provided in the Cancer Supplemental Guidance and not data presented in the handbook.*

A.1.2. Comments from Department of Defense (DoD)

Comments: The External Review Draft version of the Child-Specific Exposure Factors Handbook (CSEF) provides non-chemical specific data on various exposure factors used in assessing children's exposures from dietary and non dietary ingestion, dermal contact, and inhalation. These child-specific exposure factors will be used by risk assessors to estimate children's potential health risk. The updated CSEF indicates that one reason for this update was to highlight changes in risk assessment practice first presented in the EPA's Cancer Guidelines (ref [a]) regarding the need to consider children as life stages rather than a single subpopulation. Another purpose was to follow a major recommendation in EPA's guidance in ref (b) to sum exposures and risks across life stages rather than using a lifetime average adult exposure to estimate carcinogenic risk.

Considering that the panel members in the 2000 EPA workshop titled "Issues Associated with Considering Developmental Changes in Behavior and Anatomy When Assessing Exposure to Children" indicated that age grouping/bins are only a crude approximation of an underlying distribution, and that the adequacy of existing exposure data is highly variable, we think that this revision of the CSEF is premature. We concur with the workshop participants warning that age bins, if used uncritically by individuals unfamiliar with the behavioral development that those bins crudely represent, could lead to significant errors of exposure assessment. Premature application of these 'age bins' can drive standard setting initiatives under corrective action cleanups, permit limits issued in new or renewed air and water permits, and waste cleanup requirements under the CERCLA and state CERCLA-like statutes. This may also have a compounded effect on the classification of chemicals that potentially may affect a wide variety of environmental, health, and safety standards currently in place.

Response**:** *EPA disagrees with the reviewer that revisions using standard age groupings were premature. Although EPA acknowledges that the child development occurs along a continuum,*

the use of standard age groups is useful in identifying data gaps and providing some consistency in the presentation of data.

Comment: We also believe that this document has not considered the significance of the growth of ethnic populations which may influence the lifestyles and therefore actual exposure factors among their key studies. For example, according to the US Census Bureau, Hispanics, who may be of any race, accounted for about one-half of the national population growth of 2.9 million between July 1, 2003, and July 1, 2004. The Hispanic growth rate of 3.6 percent over the 12-month period was more than three times that of the total population (1.0 percent). The Hispanic/Latino population 80 and older is expected to increase from 3% in 1990 to 14% in 2050.

Response**:** *Factor data have been added for ethnic groups in each chapter, where the data are available (human milk, consumer products, food intake, activity factors).*

Comment: Another factor that has not been considered among the key studies in this report is the increase in child obesity in recent years (ref [c] and [d]). The prevalence of juvenile obesity has risen in the last decade to exceed 20% in the United States (ref [c]), and the condition appears particularly prevalent among Hispanic and African-American girls. Additionally, results from the 2003-2004 National Health and Nutrition Examination Survey (NHANES) on child weight are available but were not evaluated in the CSEFH. We recommend that the data cited in ref (d) be evaluated and included in the final version of the CSEFH.

Response**:** *BMI data have been added, and for ethnic groups, where the data were available. NHANES data have been added based on EPA analysis of data covering 1999-2006.*

Comment: Section 1 describes the approach used to develop recommendations for exposure factors. The approach described in this section is similar to the approach presented in ref (e), in which exposure factors are based on certain "key" studies, and data from other "relevant" studies may be considered as supporting evidence. However, unlike ref (e), when the studies are being presented, they are not identified upfront as either "key" or "relevant." For example, Chapter 7 (Inhalation) presents all the studies that were reviewed in a single section (i.e., Section 7.2 "Inhalation Rate Studies"). It is not until the reader reaches Section 7.3 (Recommendations), that they are told that only one of six studies described in Section 7.2 was considered a "key" study and therefore the first five studies presented in Section 7.2 were not considered in the derivation of the recommended inhalation rates. The format used in ref (e), where the studies are described in 'subsections' as either "key" or "relevant" is a more transparent way to organize the document so the readers immediately understand the level of importance given by EPA to each study in deriving the exposure factors. We recommend that for clarity, EPA adopts the format used in ref (e) so that in each section the studies are presented in subsections and are clearly labeled as either "key" or "relevant" studies.

[References:

(a) USEPA, 2005. Guidelines for Carcinogen Risk Assessment. Risk Assessment Forum, Washington, DC; EPA/630/P-03/001F.

(b) USEPA, 2005. Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens. Risk Assessment Forum, Washington, DC; EPA/630/R-03/003F.
(c) Troiano, RP, and KM Flegal. Overweight children and adolescents: description, epidemiology, and demographics. Pediatrics 1998;101(3):497-504.
(d) Ogden, CL, et al. Prevalence of overweight and obesity in the United States. JAMA 2006;295:1549-1555.
(e) USEPA, 1997. Exposure Factors Handbook. Washington, DC: Office of Research and Development. EPA/600P-95/002F.
(f) USEPA, 2004. Risk Assessment Guidance for Superfund Volume I: Human Health Evaluation Manual (Part E, Supplemental Guidance for Dermal Risk Assessment). EPA/540/R/99/005.
(g) Summary Report for the ATSDR Soil-Pica Workshop, June 2000, Atlanta, Georgia. Prepared by Eastern Research Group]

***Response*:** *Eligibility criteria were revised and discussions were expanded to make it more clear what key and relevant studies are. Studies have been noted as key or relevant throughout the document.*

A.1.3. Comments from the Office of Environmental Health Hazard Assessment – California EPA

Comment: We suggest that each chapter be reviewed for consistency of terms (e.g., intake, ingestion, consumption).

***Response*:** *The chapters have been extensively edited for consistency.*

A.2 Chapter 1 (Introduction)

A.2.1. Comments from the American Chemistry Council

Comment: In Chapter 1, all of the tables and figures have apparently been inadvertently left off of the draft document that has been posted on EPA's website (http://oaspub.epa.gov/eims/eimscomm.getfile?p_download_id=458967). Therefore, we could not review Table 1-4.

***Response*:** *The error was corrected.*

A.2.2. Comments from the Department of Defense (DoD)

Comment: Page 1-1, Section 1.1 Background (lines 21 – 24) - The EPA's recommended set of childhood age groups increases the level of complexity for risk-assessment calculations. Use of these childhood age groups increases the number of age group calculations from the current two (i.e., 0-6 year old children and adults) to eleven (i.e., ten child age groups, plus one adult age group). Use of these numerous childhood age groups implies a level of precision for the exposure data that is not presently available.

***Response*:** *EPA acknowledges that there may be data gaps, but that there is value in considering all the age groups as a starting point in a risk assessment.*

Comment: Chapter 1, Introduction, Table of Contents - The Table of Contents for Chapter 1 lists four tables and figure that should be included in Chapter 1. However, these tables and figure were not included in the online version of the document that was downloaded. Therefore, this information could not be reviewed.

***Response*:** *Agree. Error was corrected.*

A.2.3. Comments from the Office of Environmental Health Hazard Assessment – California EPA

Comment: p. 1-3: The estimates for duration of lifetime were not found in the handbook.

***Response**: Lifetime was not intended to be included as a chapter in this handbook. A chapter is included in the Exposure Factors Handbook.*

Comment: p. 1-4 lines 16-21, and p. 1-16 lines 7-9: We suggest that this information be made more easily accessible by including it in a separate chapter or Appendix. Perhaps the chapter or Appendix could be titled "Basic methods and definitions used in CEFH". The line 16-21 is important information, especially for 0<12 month old infants. Some authors have classified infants as being X-months of age when their birthday falls anywhere between the 15th day of the prior (X-1) month and the 15th of the X-month. There can be significant differences in estimated exposures based on such differences in defining "age" for infants.

***Response**: A Glossary has been added to the Handbook.*

Comment: p. 1-6, lines 10-19: The water consumption and inhalation rate chapters recommend values that are from studies that have not been published and that we cannot find as being available from U.S. EPA.

***Response**: Recommendations have been revised in both chapters based on data that have been peer reviewed.*

Comments:

- p. 1-6, lines 18-19. Some chapters did not provide sufficient detail to allow the reader to reproduce the methodology (e.g., standard errors for food consumption estimates).
- p. 1-23: A methodology to extrapolate from short-term to long-term exposures would be helpful but well conducted longitudinal studies may provide the desired long-term exposure estimates without the uncertainty of extrapolation and methodology errors.

***Response**: Food intake chapter has been revised and separated into separate chapters. Standard deviation values have been added when available, especially in the study used for the recommendations. The Recommendations have been revised.*

A.3 Chapter 2 (Breast Milk Intake)

A.3.1. Comments from the Department of Defense (DoD)

Comment: Page 2-2, Section 2.2.2 Pao et al., 1980 (lines 14 – 15) - These lines state that data regarding the actual length of time an infant continues to be breast fed beyond 5 or 6 months are limited. For this reason, it seems appropriate to limit the evaluation of chemical exposure through breast milk to infants age 0 – 6 months. Limiting evaluation of breast milk ingestion to this age group is also supported by the Neville study (page 2-4, line 18), which states that solid foods are introduced at a mean age of 7 months. This position is further supported by the NAS study (page 2-5, lines 24 – 26) that states that the lipid content of breast milk varies according to the length of time that an infant nurses, and increases from the beginning to the end of a single nursing session. It is reasonable to assume that an infant receiving solid food would nurse for a shorter period of time, thereby lessening the exposure to potential chemical-containing lipids in breast milk.

***Response*:** *Data on human milk intake are available for infants up to 12 months old. It is also consistent with AAP recommendations.*

Comment: Page 2-5, Section 2.2.5 Dewey et al., 1991 a,b (line 12)
The sentence "*This decline is associated with the intake of solid food*" is out of place.

***Response*:** *Agree, the sentence was moved to the appropriate place.*

A.3.2. Comments from the Office of Environmental Health Hazard Assessment – California EPA

Comments: A paper was recently published by Arcus-Arth et al. (2005) that presents means and percentiles of daily breast milk intake rates in g/kg-day. Though the estimates presented in this paper are for the 0-6 and 0-12 month periods, reliable milk intake estimates could be derived for the established CEFH age periods (i.e., 0<1, 1<3, 3<6, and 6<12 month periods) from the Arcus-Arth et al. data. We welcome the opportunity to discuss the possibility of deriving rates for the CEFH age groups from the Arcus-Arth et al. data with the U.S. EPA. The Arcus-Arth et al. paper is attached for your convenience (Appendix A). For further information and discussion, please contact: Amy Arcus-Arth, aarcus@oehha.ca.gov, (510) 622-3199.

Also, Michaelsen et al. (1997) is not mentioned in the Arcus-Arth et al. paper but may have data that may be of interest to CEFH.

***Response*:** *The Arcus-Arth paper has been added to the chapter.*

Comment: P. 2-2, paragraph 2, sentence 2: which Exposure Factors Handbook?

***Response*:** *This text has been revised.*

Comment: p. 2-2, paragraph3, sentence 2: define "completely". How does this differ from "exclusively" used by Dewey and Lonnerdal, and Butte et al.?

Response: *Completely breast fed is not defined in the Pao reference. The chapter now defines exclusively breast fed and partially breast fed.*

Comments:

- p. 2-3, paragraph 2, sentence 2: when were the five infants given formula – after 3mos age?
- p. 2-3, paragraph 3: another limitation of this study is that intake is not on a bodyweight basis
- p. 2-3, paragraph 3: see Arcus-Arth et al., last paragraph p.363 continued to p. 364. Milk intake may not be much affected by nutrition, SES or other demographics of the mother except in cases of severe malnutrition
- p. 2-3, last sentence continued to next page: was this insensible water loss value used to adjust intake of the rest of the infants in the study? what is the interpretation or use of this number?

Response*: More descriptive text has been added to these studies.*

Comment: p. 2-5, paragraph 2, sentence 3: We suggest that the sentence be reworded as "…with the progressive intake of …".

Response: *The sentence was moved to the appropriate place.*

Comment: p. 2-5, paragraph 3: A significant limitation is that intake is not on a body weight basis.
p. 2-6, paragraph 2, sentence 2: Lipid content can be quite variable. There is a lack of consensus on the correlation between lipid content and milk volume (e.g., Michaelsen et al., 1990 reports a positive correlation while Arcus-Arth et al., 2005 report a negative correlation). Jenness (1979) and Jensen et al. (1978) report no significant affect of maternal nutrition on milk lipid content

Response: *The correlation research is outside the scope of this document.*

Comment: Population of Nursing Infants: p. 2-7 continued to 2-8: Newer data are available from Ross Laboratories. Here are some statistics from the Mothers Survey (Ross Division, Abbott Laboratories, 2001).

Table 3. Percent of infants breast feeding from 2000 Ross Laboratories Mothers Survey[a].

Survey	In hospital	At 6 months	At 12 months
Nationwide	68.4	31.4	17.6
Pacific States	81.8	41.2	26.2

[a]Source: Abbott Laboratories (2001).

We obtained data for the table directly from Abbott Laboratories but statistics through 2000 are available at: http://www.ross.com/aboutRoss/Survey.pdf

Response: *New data from CDC have been added.*

Comment: p. 2-8, paragraph 2, sentence 2: To avoid confusion, this sentence should be reworded to show that Maxwell and Burmaster (1993) estimated that 22% of all infants who are under one year of age would be breast feeding on any given day. As currently worded, the sentence could be mistakenly interpreted as Maxwell and Burmaster are estimating that 22% of infants have ever been breastfed.

Response: *These data are old and have been superseded by more recent information. No change in the sentence was done.*

Comments:

- p. 2-9, paragraph 2, sentence 2: It would be helpful to clarify that the intake referred to is not on a body weight basis (i.e., ml/day or g/day). Breast milk intake and energy requirements have been extensively evaluated by Butte and colleagues, and others. Good references on this topic are:

  (1) FAO Food and Nutrition Technical Report Series 1, Human energy requirements, Report of a Joint FAO/WHO/UNU Expert Consultation, Rome, 17-24 October 2001, United Nations University, World Health Organization, Food and Agriculture Organization of the United Nations Rome, 2004, available at: http://www.fao.org/docrep/007/y5686e/y5686e05.htm#TopOfPage - see Table 3.2 for energy requirements at each month age from 0-12 months in kcal/day and kcal/kg-day.

  (2) Butte, N.F., Wong, W.W., Hopkinson, J.M., Heinz, C.J, Mehta, N.R., & Smith, E.O. (2000). Energy requirements derived from total energy expenditure and energy deposition during the first 2 y of life. *Am J Clin Nutr*, 72(6):1558-1569. (available online as a pdf file: http://www.ajcn.org/cgi/reprint/72/6/1558).

- p. 2-9, 2nd paragraph, bottom: calculations. Are the infants considered "x-months of age" based on reaching the x-month birthday and up to but not including the x+1 month-birthday? In the past, some authors would assign an infant to "x-month of age" based on if the infant age was from the mid-point of (x-1) month to the mid-point of x-month.

Response: *The recommendations section has been revised and updated. A consistent set of age groups have been used throughout the handbook.*

Comment: References for Chapter 2

Arcus-Arth A, Krowech G, Zeise L. Breast milk and lipid intake distributions for assessing cumulative exposure and risk. J Expo Anal Environ Epidemiol. 2005 Jul;15(4):357-65.

Ferris A.M., Neubauer S.H., Bendel R.B., Green K.W., Ingardia C.J., and Reece E.A. Perinatal lactation protocol and outcome in mothers with and without insulin-dependent diabetes mellitus. Am J Clin Nutr 1993: 58: 43–48.

Jenness R. The composition of human milk. Semin Perinatol. 1979 Jul;3(3):225-39.

Jensen RG, Haggerty MM, McMahon KE. Lipids of human milk and infant formulas: a review. Am J Clin Nutr. 1978 Jun;31(6):990-1016.

Michaelsen KF, Skafte L, Badsberg JH, Jorgensen M. Variation in macronutrients in human bank milk: influencing factors and implications for human milk banking. *J Pediatr Gastroenterol Nutr*. 1990;11:229-239.

Michaelsen KF. Nutrition and growth during infancy. The Copenhagen Cohort Study. Acta Paediatr Suppl. 1997 May;420:1-36.)

Neubauer S.H., Ferris A.M., Chase C.G., Fanelli J., Thompson C.A., Lammi-Keefe C.J., Clark R.M., Jensen R.G., Bendel R.B., and Green K.W. Delayed lactogenesis in women with insulin-dependent diabetes mellitus. Am J Clin Nutr 1993: 58: 54–60.

L., Perheentupa J., and Siimes M.A. Exclusively breast-fed healthy infants grow slower than reference infants. Pediatr Res 1985: 19: 307–312.

Stuff J.E., and Nichols B.L. Nutrient intake and growth performance of older infants fed human milk. J Pediatr 1989: 115: 959–968.

***Response*:** *Stuff, Neubauer et al., and Salmenpera et al. were added to the chapter. Other references were examined, but did not provide relevant data.*

A.4 Chapter 3 (Food Intake)

A.4.1. Comments from Drs. Michael Shannon (Harvard Medical School) and James Roberts (Medical University of South Carolina)

Comment: While we understand that this resource is meant not to be chemical-specific, this section could be improved with the inclusion of basic information regarding pesticide residues in food. For example, the chapter could acknowledge the fact that the U.S. Department of Agriculture operates a respected pesticides data program that provides information on pesticide residues in food. A table listing the most commonly consumed foods by children and their pesticide residues would be extremely useful to health care providers.

***Response*:** *Data have been added to show the most commonly eaten foods for some food groups*

A.4.2. Comments from the Department of Defense (DoD)

Comment: Page 3-2, Section 3.1 Introduction (lines 14 – 15) - These lines state that total fruit and vegetable intake refers to the sum of all fruits and vegetables consumed including canned, frozen, dried, and fresh. Inclusion of all of these sources may greatly overestimate the intake of home-grown produce, which is the only relevant source of fruits and vegetables to consider in a human health risk assessment.

***Response*:** *The section was not intended to represent consumption of home produced foods. The sentence is defining what "total fruits" and "total vegetable" includes. Consumption of homeproduced foods are in a different chapter. No revision is necessary.*

Comment: Page 3-3, Section 3.1, Introduction (line 1) - The statement (line 1) that cooking "can increase the mass of contaminant in food" from formation reactions is misleading. Numerous studies that have been conducted tend to show contaminant levels in pre-cooked food either decrease or remain unchanged after cooking. Was the statement intended to suggest that reaction products may be formed during the cooking process (e.g., thermal reaction), and that these reaction products may be comparatively higher in concentration than the original contaminants?

***Response*:** *The text has been revised.*

Comment: Page 3-7, Section 3.2.2 U.S. EPA, 2003 (line 13) - Since infants less than six months of age receive most, if not all of their nutrition from breast milk and formula, we recommend making the lowest childhood age group be infants 6 months to < 1 year. Incorporation of infants under the age of 6 months may artificially lowers the ingestion rate of the age group 6 months to < 1 year.

***Response*:** *The age bins presented are those set by EPA and are intended to provide consistency among exposure factors data presentation. While it may make sense to consider children older than 6 months for food intake, it may not make sense and may miss high intakes for other factors (e.g., water intake).*

Comment: Page 3-7, Section 3.2.2, (line 24) - This section advises users to use body weights presented in Chapter 10 to convert from g/day to g/kg/day. However, this recommendation is inconsistent with intakes listed in tables that report data in both g/kg/day and g/day. These tables apparently used actual body weights reported by study subjects to make units adjustments; see for example, page 3-19, line 28, which indicates fish intake rates were converted from g/day to g/kg/day using body weights reported in the study. If study-specific body weights are available, and line 21, page 3-6 suggests they were collected, then like all other tables, Tables 3-16 to 3-19 should also report intake rates in g/kg/day. Although body weights for each age group is not expected to differ vastly from those reported in Chapter 10, using study-specific body weights reduces uncertainty and would be consistent with intakes reported elsewhere.

***Response*:** *This section states the following: "Converting these intake rates into units of g/day by multiplying by a single average body weight is inappropriate, because individual intake rates were indexed to the reported body weights of the survey respondents. However, if there is a need to compare the intake data presented here to intake data in units of g/day, a body weight for the age group of interest, as presented in Chapter 10 of this Handbook, should be used." Tables 3-16 through 3-19 are in g/kg-day.*

Comment: Page 3-121, Table 3-54. Summary of Recommended Values for Per Capita Intake of Foods, As Consumed - As seen in this table, the recommended intake rates are very similar between all age groups for all food categories other than dairy intake. In addition, there is a lack of data for fish ingestion for children under the age of 14. Review of this data lends further support to the conclusion that separate risk evaluations for each of the EPA's childhood age subgroups, based on the available exposure data, are not warranted.

***Response*:** *The analyses were redone for the age groups recommended by EPA. The lack of fish consumption data for children under the age of 14 does not support the conclusion that separate risk evaluations for each age category are unnecessary. However, it, highlights data gaps for certain age categories. EPA disagrees that consumption for all food categories is similar between age groups. For example, per capita intake of vegetables is three times higher for children 6 to < 12 months old than those of children 3 to < 6 months. Similarly, per capita intake of grains for children 6 to < 12 months old is five times higher than those of children 3 to < 6 months. These differences cannot be observed if age groups are lumped into larger age categories.*

Comment: Page 3-4, Section 3.1 Introduction (line 3) - Typographical error- "and" should be "an."

***Response*:** *corrected.*

Comment: Page 3-6, Section 3.2.2 U.S. EPA, 2003 (line 11) - Typographical error – "breadfast" should be "breakfast."

Response: *corrected.*

Comment: Page 3-15, Section 3.3.3.2 Toy et al., 1996 (line 17) - Typographical error – "insifficient" should be "insufficient."

Response**:** *corrected.*

Comment: Page 3-121, Table 3-54. Summary of Recommended Values for Per Capita Intake of Foods, As Consumed - Please include units for the data reported on the first page of this table.

Response**:** *corrected.*

A.4.3. Comments from the Office of Environmental Health Hazard Assessment – California EPA

Comment: It would be very helpful to have food intake estimates for consumers-only This would help to identify the degree to which highly exposed individuals may be at risk and the number of individuals who may be at increased risk (for a given contaminant in a food item). We would highly recommend that analysis of consumers-only food intake be conducted at least for the broad categories of fruit, vegetables, grain, meat, and dairy.

Response**:** *Additional data have been added for consumers-only.*

Comment: It would be very helpful to include CSFII 1998 data with the CSFII 1994-96 data for analysis. For small cell sizes, the inclusion of CSFII 1998 data would increase the precision and reliability of estimates, especially very low and high percentiles. For example, for the 0<3 month age group (breastfed infants excluded) from the 1998 CSFII dataset would increase the sample size from 65 to 182. We highly recommend that U.S. EPA consider such an analysis (i.e., including CSFII 1998 data), particularly since the data are readily available, and weighting and other statistical methodology should basically be the same as that used for analyzing just the CSFII 1994-98 data.

Response**:** *EPA conducted an analysis of the 1994-1996, 1998 CSFII. The results of this analysis are now included in the Handbook.*

Comment: p. 3-6, line 29 and p. 3-7, line 9: The methodology to derive standard errors is not given. Proper methods to derive variance estimates (e.g., standard errors) for complex multistage studies is very important. The method used to derive the SE's should be explained.

We are pleased that the recommended estimates are on a body weight basis.

Response**:** *Detailed descriptions of the methodologies to derive SE are provided in the internal documentation of data analysis. This handbook is meant to be a summary.*

Comments:

- p. 3-4: The study is listed as "USDA 1999". It is unclear what office or agency was responsible for the analysis and what methodologies were used to analyze the data.
- p. 3-5, line 8-10: It is not clear why day-1 intake was used.
- p. 3-5, line 12: unsure which analysis
- p. 3-5, line 13: "1 day" – is this day-1 or one day of intake?
- p. 3-5, line 18-19: We suggest to reword the sentence to include that the sampled population is not representative of the U.S. but when properly weighted and analyzed the results are considered to be representative of the U.S.
- p. 3-5, line 22-23: We suggest to add the words "usual or" between "reflect" and "long-term".
- p. 3-6 lists the study as US EPA 2003 while Table 3-54 (recommendation table) lists the study as EPA analysis of CSFII 94-96 data.
- p. 3-21, line 18. Table 3-36 is estimates of fat.

- Total Dietary Intake: does this analysis exclude breastfed infants? In Table 3-39, it is presumed that 40% of the infants were breastfed.
- p. 3-59 and 3-82, and Table 3-39: in some cases there are no estimated intake values for the 0<1, 1<3 and 3<6 month age groups (even when up to 16% of infants in this age group consumed that food type). Were only intake values that were greater than 1.0E-2 listed?

***Response*:** *Food intake chapter has been revised and separated into separate chapters. The chapters have been extensively edited for consistency.*

A.4.4 Comments submitted by the International Lead Zinc Research Organization

Comments: Throughout this chapter an important limitation is cited for the various data sets used to obtain food intake data.

P.3-5 **USDA, 1999** "One limitation of this data set is that it is based on a two-day survey period. Short-term dietary data may not accurately reflect long-term eating patterns. This is particularly true for the tails (extremes of the distribution of food intake. Other limitations of this study are that it only provides mean values of food intake rates, consumption is not normalized by body weight, and presentation of results is not consistent with EPA's recommended age groups."

P.3-7 **USEPA 2003 "**The *distribution* of average daily intake rates using short-term data (e.g., 2-day) do not necessarily reflect the long-term distribution of average daily intake rates."

Although there may not be any better available U.S. data at present, the following should be noted: The WHO (1985) provides Guidelines for the determination of chemical contaminants. Three basic approaches are described, namely: total diet (i.e. market or shopping basket studies; selective studies of individual foodstuffs; and, duplicate portion (duplicate diet) studies. "It is essential to have food consumption data for the first two methods in order to estimate a total intake. Records of a twenty-four hour period have been undertaken but a record of intake over 4-10 days should give a reasonable record of actual intake…the food diary approach can be used advantageously to determine food consumption for either individuals or large populations… Diaries of up to 1 month in length have been used when one or two specific items of foods in the diet are of interest." (IPCS, 1985).

If any long-term data are available it would be advantageous to include it.

***Response*:** *The only long term data found was for fish consumption frequency from NHANES. EPA is in the process of analyzing these data. The results of that analysis will be included in future editions of the handbook.*

A.5 Chapter 4 (Drinking Water Ingestion)

A.5.1. Comments from the Department of Defense (DoD)

Comment: Page 4-13, Table 4-7. Summary of Recommended Community Drinking Water Ingestion Rates - Review of the recommended water ingestion values on this table indicates that there is not a large difference in ingestion rates between the EPA's ten suggested childhood age groups. For example, there is less than a 2-fold difference between the mean ingestion rate of an infant age birth to < 1 month and a child age 1 to < 2 years. Similarly, there is approximately a 2-fold difference between the mean ingestion rate of a child age 2 to < 3 years and a child age 16 to < 21 years. We recommend that these age groupings should be combined to create a smaller number of groupings.

***Response*:** *The reviewer's observation is true if data are in mL/day. Differences are more significant when presented on a body weight basis. Age bins used are those chosen by the EPA for consistency and the recommendations are now based on the new analysis of Kahn and Stralka. The user can lump age groups if there are no differences in consumption per unit of body weight.*

A.5.2. Comments from the Office of Environmental Health Hazard Assessment – California EPA

Comment: The recommended water consumption rates are a great improvement over the traditionally used child default values of 1 liter consumption and 10 kg body weight. Normalizing consumption to body weight will reduce variability in consumption that stems from variability in body weight and avoid the underestimation of consumption of infants and young children. Additionally, we concur with the selection of the U.S. EPA 2004 analysis of the CSFII data as the basis for the recommended drinking water ingestion rates.

***Response*:** *No response needed.*

Comment: We strongly recommend that this section include drinking water ingestion rates for *consumers-only*. A review of the U.S. EPA 2004 document reveals that in the adult population, approximately 5% of the people consume no community water whatsoever. However, that proportion of non-consumers swells to over 25% in the youngest population of children – neonates and infants under six months of age. Even at 1 year of age, approximately 10% of the children surveyed receive no water from community sources. The result is that for the youngest of children, use of the all-individual data can result in a 25% or greater underestimation of what exposed children receive. Inclusion of consumer-only data, as available, is similarly appropriate for all other age groups as risk assessors are responsible for protecting exposed populations and not those who are unexposed. Therefore, we strongly recommend that consumer-only tables be added to this section of the document and that U.S. EPA provide a "Summary of Recommended Community Drinking Water Ingestion Rates" for children that is based exclusively on consumer-only data from the US EPA 2004 document.

***Response*:** *Drinking water ingestion rates for consumers-only have been added.*

Comment: The study design, methodology and analysis of the "EPA Analysis of CSFII (USDA, 1998)" is not described in the draft document or in a published report/paper. The reader does not know how the data were weighted, how the percentiles were calculated, etc. and therefore cannot independently replicate or verify the results. We recommend that the analysis methodology be published in the document, as an EPA report, or in a journal so that the reader is assured that the study has been peer-reviewed and could be replicated by the reader, ensuring transparency of the process.

Response**:** *EPA's analysis of the CSFII data were published by Kahn and Stalka 2008 in the Journal Exposure Analysis Environmental Epidemiology, which is now included in the chapter.*

Comment: The CSFII documentation recommends flagging parameters according to the FASEB/LSRO (1995) convention to alert the reader to parameters that may tend to be statistically less reliable due to small cell sizes. We recommend that water consumption parameters be flagged using the CSFII guidelines (see the guidance in Appendix 3E of this draft CEFH).

Response**:** *EPA has noted when the sample size does not meet LRSO, 1995.*

Comment: Patrick Levallois *et al*. (Institut National de Santé Publique du Québec, Sainte-Foy, Québec, email: patrick.levallois@msp.ul) presented an abstract at the ISEA/ISEE meeting this past summer which provided estimates of water intake for 2-month old infants in rural Canada. The abstract suggests that the Canadian estimates may support the infant water intake rates reported in by the Office of Drinking Water (U.S. EPA, 2004).

Response**:** *No response needed.*

Comment: We believe that the correct citation for the 1994-1996, 1998 CSFII database would be USDA (2000).

Response**:** *The correct citation is USDA, 1998.*

Comment: Page 4-3, 1st full paragraph: "…(3) that the sample size (more than 20,000)" – it would be helpful to include the sample size of *only* the children. Similarly, elsewhere in this chapter where sample size is identified, clarification of the number of children sampled would be beneficial.

Response**:** *Sample sizes of each age group have been added with the new Kahn and Stralka analysis.*

Comment: Page 4-4, 3rd paragraph, 3rd sentence: The sample of individuals surveyed in the CSFII is not representative of the U.S. population. However, sample and jackknife replication weights for each individual in the survey were created so that proper analysis of the data using the weights would provide results most representative of the U.S. population, including

subpopulations based on age groups, gender, and other demographics. We recommend that the sentence in the CEFH be reworded to reflect this difference in the representativeness of the data versus the results.

Response**:** *The CSFII 1994-96, 1998 was validated as demographically representative****.***

A.6 Chapter 5 (Soil Ingestion and Pica)

A.6.1 Comments from the Department of Defense (DoD)

Comments:
The information presented in this document does not appear to support the recommended mean value for soil pica ingestion. Furthermore, it appears that the methodology used to determine the recommended value for soil pica is inconsistent with the guidelines outlined in this document.

The text on page 5-31 reports that for soil pica, "An ingestion rate of 10 g/day is a reasonable value for use in acute exposure assessments…" (emphasis added). This page continues to explain that, "This value is based on only one pica child observed in the Calabrese et al. (1989) study where the intake ranges from 10-14 grams/day during the second week of observation."

The language in the above statement suggests that 10 g/day soil ingestion for pica should be considered a high-end estimate and would not be representative of the general population. However, Table 5-21 reports 10 g/day soil ingestion as the recommended mean intake rate for soil pica. We recommend that it seems inconsistent to characterize a value described as appropriate for acute exposures as defensible for mean, chronic exposures.

Response**:** *In contrast to the external peer review version of the handbook (September 2007), in which a separate recommendation for soil-pica behavior was published, the revised handbook characterizes "soil-pica" behavior as a soil ingestion rate that occurs at an unknown point on the upper end of the distribution of soil ingestion values. U.S. EPA believes that this approach is consistent with the sparse quantitative estimates that exist for soil pica behavior.*

Regarding whether the 10 gram per day reported mean value for one child is appropriate for short term, "acute" exposures versus for longer term, chronic exposures, the issue of time-averaging arises, with its influence on the magnitude of a soil ingestion value that is appropriate for exposures of differing durations. The 10 to 14 gram per day "mean" estimate is an average that was calculated over four days of data collection, and represents two days of extremely high soil ingestion interspersed with two days of significantly lower soil ingestion. The actual one day estimates for this child, on two separate days, were in the range of 19 to 20 grams on one day, and 23 to 36 grams on another day. When averaged across eight days of data collection, the same child's eight day "average" soil ingestion dropped to about 6 grams per day. Thus, it is clear that the averaging period is an important factor in the magnitude of the value chosen to represent the behavior. U.S. EPA believes that any of these estimates (6 grams per day averaged over eight days, 10 grams per day averaged over 4 days, or 19 to 36 grams per day for a single day) could be appropriate for an 8-, 4- or 1-day exposure duration, respectively. In reviewing the available tracer element data on soil-pica behavior, a wide range of averaged-over-four-or-more-days estimates emerged – anywhere from approximately 500 mg/day to 41,000 mg (41 grams) per day. The range is sufficiently wide, the available data are sufficiently sparse, and there are enough case reports in the medical literature describing children with habitual soil pica behavior, that it would appear that using a 1,000 mg/day (1 gram per day; about one-eighth of a teaspoon) value to represent soil-pica behavior over a relatively long time frame, such as a year, may be a reasonable approach.

Comment: Furthermore, the definition provided for soil-pica on page 5-2 includes an estimated range of 1,000-5,000 mg/day. While we recognize that this range is not a "bright line" and is only a means to characterize this phenomenon, it seems inconsistent that the recommended mean intake rate for soil-pica is two times greater than the high end of the definitional range.

Response**:** *The revised soil-pica behavior recommendation can be used on a longer-term basis to represent habitual soil-pica occurring over days, weeks, or months. The revised recommendation is now at the lower end (1,000 mg/day) of the open-ended definitional range of 1,000 to 5,000 mg/day or more.*

Comment: Additionally, we note that the soil-pica studies presented in this document were all performed over short time periods (e.g., two weeks) and thus do not adequately characterize chronic, long-term exposure. Since this report does not present evidence that supports the occurrence of soil-pica over intermediate or long-term exposures, we recommend that EPA include a discussion of the exposure duration/frequency which is appropriate to evaluate based on the available data. The omission of this important component of this exposure pathway could lead to inappropriate application of the soil-pica ingestion rates which would not necessarily be reflective of reality and could result in costly remedial actions.

Response**:** *U.S. EPA agrees that the available data on prevalence and frequency of U.S. children's soil-pica behavior continue to be very sparse. Review of the existing survey response studies published over several decades, and the NHANES 1 and 2 unweighted survey responses on dirt and clay ingestion, indicates a consistent pattern of a certain proportion of positive parent or caregiver responses to questions about soil ingestion by young children. These data suggest that there is at a minimum, sporadic, and at a maximum, habitual, ingestion of observable quantities of soil by at least some children, and the 1,000 mg/day lower bound on the open-ended definitional range of soil-pica behavior is probably fairly close to the range of observable quantities of soil (approximately 1/8 teaspoon). The tracer element studies' data suggest that on those occasions where larger quantities of soil are ingested, considerably more than 1,000 mg/day is ingested by many of the children who appear to exhibit the soil-pica behavior. Although the U.S. tracer element studies were of limited duration data collection periods, one study of Jamaican children occurred on four separate data collection days spread over 4 months, and found a similar pattern of soil-pica occurring over this longer time frame. Between the prevalence data from the survey response studies, and the tracer element data, U.S. EPA believes that there is support for a precautionary stance that children who exhibit soil-pica behavior might be expected to ingest significant quantities on certain days, over a time period of days, weeks, or months, and the 1,000 mg/day recommendation for soil-pica behavior may underestimate soil ingestion for certain children.*

Comment: Furthermore, at a 2001 workshop where ATSDR solicited input on its evaluation of soil-pica, the subject matter experts chose to be on the review panel, "…noted that ATSDR's assumption that soil-pica children ingest 5,000 milligrams (mg) of soil per day appears to be supported by only a few subjects in soil ingestion studies….[and]…some panelists thought that ATSDR's assumed ingestion rate for soil-pica children was high. Other panelists agreed, however, that ATSDR should err on the side of being protective and should use 5,000 mg until

more data are collected. They also stressed the need for validating the 5,000 mg soil ingestion rate" (ref(g)). We recommend that EPA take into account that the subject matter experts felt that ATSDR's soil pica ingestion rate of 5,000 mg/day was elevated, and therefore the EPA's recommended mean soil pica ingestion rate of 10,000 mg/day may also be elevated.

***Response*:** *As noted previously, the magnitude of a daily soil ingestion estimate is dependent on the averaging period used. A 6,000 mg/day or 10,000 mg/day ingestion rate that is based on either an 8-day average or 4-day average of the child in the Calabrese et al. (1989) study does not appear to be significantly elevated when compared to the actual single day ingestion estimates for this child, that ranged from 19,000 up to 36,000 milligrams per day. Risk assessors who need to assess a short-term, high magnitude exposure might use such values (6,000, 10,000, 19,000, or 36,000 mg/day), while risk assessors who need to assess a longer-term exposure might take into account the intra-individual day-to-day variability that may exist for many children who exhibit soil-pica behavior (based on the sparse data that are available), and use the recommended 1,000 mg/day ingestion rate to represent a soil-pica behavior occurring over a longer term exposure period.*

Comment: Finally, page 5-12 states, "Intake of soil and dust was estimated using a weighted ingestion for one child in the study ranged from approximately 10 to 14 grams/day during the second week of observation. Average soil ingestion for this child was 5 to 7 mg/day, based on the entire study period." Based on the guidance provided by the EPA in Section 1.5 (page 1-9), "If only one study was classified as key for a particular factor, the mean value from that study was selected as the recommended central tendency value for that population." However, by recommending 10 g/day as the mean value for soil-pica, it seems that EPA has not followed the guidelines that it laid out for itself.

***Response*:** *The revised chapter makes use of the entire range of soil ingestion estimates of all of the children who appeared to exhibit soil-pica behavior during the six tracer studies (Calabrese et al. (1989), Davis et al. (1990), Calabrese et al. (1997), Davis and Mirick (2006), Stanek et al. (1998)/Calabrese et al. (1997) and Wong 1988/Calabrese and Stanek (1993)) data collection periods. The current definition of soil-pica used in the handbook sets a lower bound on the range of soil ingestion estimates that are called "soil-pica," and due to averaging over data collection periods, soil ingestion estimates that are lower than the 1,000 mg/day lower end of the soil-pica definitional range might still represent soil-pica behavior. The range of soil ingestion estimates in the five studies was between 400 and 41,000 mg/day. The recommendation, 1,000 mg/day, is not the average of the "soil-pica" observations, but instead is a judgment of a reasonable, supportable value that represents an estimate of daily soil ingestion in soil-pica children over the time frames that are often assessed in U.S. EPA risk assessments.*

Comments:
Page 5-5, Section 5.2.1.2 Calabrese et al., 1997a (lines 10-11)
Page 5-6, Section 5.2.1.2 Calabrese et al., 1997a (lines 3-4 and line 12)
Page 5-6, Section 5.2.1.2 Calabrese et al., 1997a (lines 11-17)
Page 5-7, Section 5.2.1.2 Calabrese et al., 1997a (lines 1-2)

Comment: This study estimated soil ingestion for children residing on a Superfund site. It is unclear why this study was identified as a "key" study, and why it was used to help develop the recommended ingestion rates for the following reasons:

a. The families in this study were aware that they lived on a Superfund site, and they likely limited the exposure of the children involved in the study. In fact, this was mentioned as a potential reason for the low median soil ingestion rate of 7 mg/day, which may be an artificially-lowered exposure estimate.
b. The authors reported a net residual negative error, which may have resulted in underestimation of soil ingestion rates. The authors continue by stating they believe this error is not likely to affect the median by more than 40 mg/day. Since the median ingestion rate using the four best tracers was 20 mg/day, an impact of 40 mg/day seems significant.
c. The authors determined that a soil ingestion rate of 200-500 mg/day could be detected in a reliable manner using their tracer methodology. In comparison the mean ingestion rate derived from the study was 66 mg/day, which is well below the level deemed reliable to measure.

***Response*:** *We agree that parents' knowledge that the children were living on a Superfund site may have affected the children's soil ingestion. The net residual negative error is described in the revised chapter in the context of limitations of the tracer element methodology. The revised handbook uses this study only as a basis for the soil-pica recommendation, since U.S. EPA agrees that the tracer element methodology may be more reliable at higher soil ingestion rates.*

Comment: Table 5-19 lists the key studies that were used to determine the recommendations for soil ingestion. However, this table does not list any of the studies described in Section 5.3.2 (Soil Pica Among Children). Therefore, it seems that the EPA has made a recommendation for soil pica that is not based on any key studies. We recommend including the key studies that were evaluated to make the soil pica recommendation on this table so that the assumptions and methods used to make the recommendations are clearly described.

Response: *The handbook has been revised to clearly delineate the key vs. relevant soil ingestion studies.*

Comments:
Page 5-52, Table 5-20. Summary of Estimates of Incidental Soil and Dust Ingestion by Children (1-7 years old) from Key Studies (mg/day)

a. This table reports that the data reported from the Staneck [*sic*] and Calabrese (1995b) study are based on the use of aluminum and silicon as tracers. However, information that describes this study on page 5-18 reports that, "*Stanek and Calabrese (1995b) recalculated ingestion rates that were estimated in three previous mass-balance studies….using the Best Tracer Method (BTM)*" which involved selecting either the three or four tracers that had the lowest food/soil ratios for the each of the studies that was reevaluated by the authors. Although we did not have the original studies available to review, based on the discussion that the best three or four tracers were used, it seems incorrect to indicate that these values were based

solely on use of aluminum and silicon as tracers. We recommend confirming the tracers that were used.

***Response*:** *The Stanek and Calabrese (1995b) study is no longer designated as a key study. The commenter is correct in that aluminum and silicon were not the only two tracers used.*

b. The median value reported on this table for soil ingestion from the Stanek and Calabrese 1995a study is reported as 31 mg/day. Based on our review from the summary data provided in this section, it seems that this value should be 25 mg/day. We recommend ensuring that the appropriate value is reported in the text and on this table.

***Response*:** *The difficulty in determining an appropriate median value reported in this study is understandable given the complex data presentation in the published article. U.S. EPA's view is that the procedures used to "trim" the data prior to calculating the median are not supportable, given the apparent limitations of the tracer element methodology.*

c. A median value is not reported on this table for the Davis and Mirick 2005 study, although this information is discussed in Section 5.2.1.3 and on Table 5-4. Please explain why this information was not used to estimate the median soil ingestion for all the key studies evaluated.

***Response*:** *The revised chapter reports the range of estimated median results from the Davis and Mirick (2006) study in the study summary, and the estimated medians themselves in Table 5-11.*

d. As with other chapters in the CSEFH, ingestion rates are only available for a portion of the EPA's recommended childhood age subgroups. The EPA should reconsider the utility of having so many different age subgroups. If the proposed groupings are retained, this document should provide guidance to users on how to estimate exposure factors for the subgroups that are not supported by the available studies.

***Response*:** *The revised handbook provides guidance to users on recommended values for the age groups that were not included in the key studies. In most cases, it is reasonable to expect that a recommended value for a particular exposure factor/age group combination represents a point on a continuum, and that a lack of specific data for a particular age group does not mean that members of that age group have no exposure.*

Comment: Page 5-53, Table5-21. Summary of Recommended Values for Soil Ingestion
We recommended that the following clarifications should be made regarding use of the ingestion rates shown on this table:

a. The table should clarify if the ingestion rates include the ingestion of household dust.
b. Direction should be given regarding when it is appropriate to use the 400 mg/day soil ingestion rate.

***Response*:** *The revised handbook clarifies recommended quantities of soil versus household dust. The comment refers to a 400 mg/day soil ingestion rate that was the recommended upper*

percentile soil ingestion value in the September 2007 external peer review draft, which the revised handbook has altered to two separate recommendations: one for soil-pica behavior, and one for geophagy behavior. The revised handbook provides guidance on when it is appropriate to use each recommendation.

A.6.2 Comments from General Electric

Comment: The Draft CSEFH recommends soil ingestion values of 100 mg/day (mean) and 400 g/day (95th percentile) for children between 1 and 7 years old. These values are not based upon the "best available science."

First, these values are the weighted average of soil and dust ingestion values derived from five soil/dust ingestion papers that were judged to be "key." Some of those studies have been superseded by more recent, and more sophisticated, studies of soil ingestion by the same authors who published the earlier studies. The Draft CSEFH cites only one of these more recent studies; it gives it extremely short shrift (one paragraph at page 5-15 of the CSEFH) and does not explain why the study is not considered "key." If EPA considered all of the newer studies and gave them appropriate weight, the recommended soil ingestion values would, of necessity, be reduced substantially.

Response**:** *U.S. EPA believes the secondary analysis soil/dust ingestion papers sometimes shed light on important factors that affect the magnitude and uncertainty of soil ingestion estimates. However, in some cases, these secondary analyses are no more sophisticated than the original published studies, and they usually rely heavily on statistical theory to explain the tracer element studies' results. A careful review of the tracer studies reveals the presence of significant methodological problems that render the data unreliable except perhaps the higher values (and for titanium, it appears that all of the values may be unreliable). U.S. EPA has not found the statistical theory secondary analyses to sufficiently or adequately explain the apparent methodological problems. Nor has U.S. EPA found that the tracer element soil ingestion research base has expanded to include significant developments in the nutrition, anatomy and physiology literature that may provide more plausible explanations of some of the tracer element studies' methodological problems than the statistical theory explanations.*

Comment: Second, although the CSEFH recognizes that all of the soil ingestion studies relied on data from short periods that might not be representative of "usual" exposure, the CSEFH does nothing to address this issue. In fact, all of the data used in the soil ingestion studies were collected during the summer, the period likely to be associated with the highest rates of soil exposure and ingestion. Extrapolation of such data to include periods with lower rates of exposure inevitably leads to substantial overestimation of longer term exposure. For these two reasons, the Draft CSEFH soil ingestion values should be reevaluated and lowered substantially.

Response**:** *The revised CSEFH relies on other, non-tracer-element studies to develop the recommendations that can be used for "usual" or long term, exposures. A detailed review of the exact weather patterns and data collection times of the original tracer element studies found that a wide range of weather conditions appear to have occurred during the four U.S. tracer element studies' data collection periods (a fifth tracer element study gave no indication of the month(s)*

or year(s) during which data collection occurred). Although two of the studies did occur during summer months, and high temperatures and dry weather conditions occurred for these two studies, the other two studies appeared to have occurred during fall months in locations in the northern U.S. where temperatures below freezing, and/or significant precipitation, occurred.

Comment: In addition, the Draft CSEFH fails to make clear that the recommended "values for soil ingestion" include household dust ingestion. The Draft CSEFH requires amendment in several respects to remove any ambiguity regarding this matter.

***Response*:** *The revised handbook has been amended throughout to be explicit regarding when ingestion estimates refer to soil, dust, or a combination of soil and dust.*

Comment: Finally, the Draft CSEFH should clarify that soil pica is not a common behavior. Moreover, the Draft CSEFH should not contain any soil ingestion value for the pica child. Currently, the draft recommends a soil ingestion value of 10 g/day for such a child. As discussed below, there is virtually no support for this value.

***Response*:** *U.S. EPA agrees that the available data on prevalence and frequency of U.S. children's soil-pica behavior continue to be very sparse. Review of the existing survey response studies published over several decades, and the NHANES 1 and 2 unweighted survey responses on dirt and clay ingestion, indicates a consistent pattern of a certain proportion of positive parent or caregiver responses to questions about soil ingestion by young children. These data suggest that there is at a minimum, sporadic, and at a maximum, habitual, ingestion of observable quantities of soil by at least some children, and the 1,000 mg/day lower bound on the open-ended definitional range of soil-pica behavior is probably fairly close to the range of observable quantities of soil (approximately 1/8 teaspoon). The tracer element studies' data suggest that on those occasions where larger quantities of soil are ingested, considerably more than 1,000 mg/day is ingested by many of the children who appear to exhibit the soil-pica behavior. Although the U.S. tracer element studies were of limited duration data collection periods, one study of Jamaican children occurred on four separate data collection days spread over 4 months, and found a similar pattern of soil-pica occurring over this longer time frame. Between the prevalence data from the survey response studies, and the tracer element data, U.S. EPA believes that there is support for a precautionary stance that children who exhibit soil-pica behavior might be expected to ingest significant quantities on certain days, over a time period of days, weeks, or months, and the 1,000 mg/day recommendation for soil-pica behavior may underestimate soil ingestion for certain children.*

Comment: <u>EPA Should Give More Weight to the More Recent Studies of Soil Ingestion</u>

As noted above, the Draft CSEFH recommends soil ingestion values of 100 mg/day (mean) and 400 mg/day (95^{th} percentile) for children between 1 and 7 years old. These values were derived from five "key" soil/dust ingestion papers. Three of the five papers were published by Edward Calabrese, Edward Stanek, and colleagues. The same investigators have published improved, more recent studies of soil ingestion by both children and adults. The newer studies indicate that the daily soil ingestion rates included in the CSEFH are overestimated. Specifically, the newer studies indicate that a reasonable mean soil ingestion rate for young children is around 30

mg/day, and a reasonable upper-bound soil ingestion rate for such children is approximately 100 mg/day.

Because of improvements in study methodologies, the results of the newer studies are more representative of potential exposures for children. The two recent studies (discussed below) provide the most objective information for use in deriving both mean and high-end estimates of daily soil intake.

The Draft CSEFH recommends a soil ingestion rate of 400 mg/day to estimate upper bound exposures for 1 to 7 year old children. CSEFH, Table 5-21. This recommendation is based solely on tracer studies in children that were undertaken by Calabrese and his coworkers (Stanek and Calabrese, 1995a & 1995b), and particularly on Calabrese et al. 1997, which supported a higher 95th percentile exposure value than the authors' previous papers. See CSEFH, Table 5-20. In addition, the Draft CSEFH recommends a mean soil ingestion rate of 100 mg/day. CSEFH, Table 5-21. This recommendation is based on tracer studies that were reported in the same Calabrese and coworkers studies cited above, as well as studies by Davis et al. 1990 and Davis and Mirick 2006. Updated analyses by Calabrese and coworkers, conducted using improved methodologies and published before the Draft CSEFH was published, indicate that these previous estimates should be refined and improved.

The most recent such analysis was reported in Stanek et al. (1999) (not cited by the draft CSEFH) and Stanek and Calabrese (2000) (described in a single paragraph in the CSEFH, at p. 5-15). As described by Stanek and Calabrese (2000), this study implemented several improvements in analytical procedures and data analysis that were developed since the publication of their earlier papers. These improvements led to refined estimates of both the mean and 95th percentile soil ingestion estimate for younger children. The advantages of this recent analysis included: (1) a relatively large study group (n=64 children); (2) improved particle size measurements that focused attention on soil of smaller particle size (3) randomized selection of participants (4) the use of a relevant age group (1 to 4 year old children); (5) use of a random sample of the population for that age group; and (6) better control for input/output error. The soil ingestion rates reported by Stanek and Calabrese (2000) for these children are:

A 95th percentile rate of 106 mgday (when extrapolated over a 365-day period);
An arithmetic mean ingestion rate of 31 mg/day; and
A median (50th percentile) ingestion rate of 17 mg/day.

Stanek and Calabrese (2000) also calculated the best linear unbiased predictors of the 95th percentile of soil ingestion over different time periods and reported the following results:

Over a 7-day exposure period, the 95th percentile soil ingestion rate was 133 mg/day;
Over a 30-day exposure period, the 95th percentile soil ingestion rate was 112 mg/day;
Over a 90-day exposure period, the 95th percentile soil ingestion rate was 108 mg/day; and
Over a 365-day exposure period, the 95th percentile soil ingestion rate was 106 mg/day.
This evaluation of the data suggests that, as the length of time that the children are studied increases and as the precison of the analysis improves (i.e., reduced uncertainty), the daily ingestion rates decline. This is reasonable due to the fact that daily fluctuations in soil ingestion

rates will tend to average out over time. This narrowing of the distribution of soil ingestion estimates when daily variability and uncertainty are reduced is not unexpected and is referred to as "regression to the mean" (Stanek and Calabrese 2000). As noted by Stanek and Calabrese (2000), use of these longer-term estimates is more appropriate when assessing risks associated with chronic exposures.

In a presentation to EPA Region 1 in May 2002, Dr. Calabrese explained these points and recommended, based on this more recent study, that the soil ingestion rates to be used for young children in recreational scenarios should be 100 mg/day for the upper bound and 20 mg/day (based on this median in this study) for the central tendency estimate. Dr. Calabrese reiterated these recommendations in a 2003 letter to GE, a copy of which is attached as an Exhibit.

There is no apparent reason for not treating the newer studies as "key." Accordingly, EPA should either revise the recommendations regarding soil ingestion in the Draft CSEFT [*sic*] to reflect the newer studies, or should explain the scientific basis for not doing so.

***Response*:** *See the response to the earlier comment, disagreeing that some of the more recent secondary analyses of the tracer study results are necessarily an improvement, refinement, or "more sophisticated" than the original published results. The Stanek et al. (1999) study is now summarized as a relevant study in the revised chapter. The revised handbook (Chapter5) explains in detail the U.S. EPA's position that the tracer element methodology appears to contain limitations for its usefulness as the basis for central tendency soil ingestion estimates.*

Comment: Soil Ingestion Rates for the Older Child Should be Set Equal to Those for Adults

The Draft CSEFH does not contain recommended soil ingestion rates for older children, despite the fact that pre-adolescents and teenagers are sometimes specifically evaluated in risk assessments. This omission is likely due to the fact that mouthing behavior generally stops by the time a child reaches the age of six and soil ingestion behavior by older children and teenagers is similar to the soil ingestion behavior of adults. It is recommended that the CSEFH specifically state that there is similarity in the soil ingestion behaviors of older children and adults and, therefore, recommend that adult soil ingestion rates should be used to evaluate the potential exposures in this age group.

Response: *U.S. EPA agrees that soil ingestion estimates are a continuum between the age groups that are typically studied, and adult (>21 year olds) age groups. A careful review of the ages of children studied for each type of recommendation (soil only central tendency; dust only central tendency; soil + dust central tendency; soil-pica; and geophagy) suggests that it is possible that the commenter's view is correct, that the soil ingestion rates of older children are similar to those of adults. For the central tendency estimates, children in the key study ranged in age from 6 months up to 7 years old, and the soil-only central tendency recommendation for this age category happened to coincide with the current central tendency soil-only recommendation for adults (50 milligrams/day). Thus extrapolating the recommended soil-only central tendency recommendation for children up to 7 years old beyond that age group, up to 21 years old, did not cause any conflict with existing recommendations for adults. For dust ingestion, no such comparison is possible due to a lack of data on adult dust ingestion. For soil-pica, the study that*

included older children (up to 14 years old) included one soil-pica child in the older group of children; the published literature on pica behavior suggests that there may not be any basis for assuming that soil pica behavior ceases at a particular age or developmental stage. For geophagy, a study that included U.S. adolescents (Smulian et al., 1995 did not significant differences between adolescent and adult geophagy behavior when the study subjects were pregnant women.

Comment: The Recommended Ingestion Rates Should be Lowered Further to Reflect that the Data on Which They Are Based are Only Representative of Short Term, High Exposure, Periods

As repeatedly recognized by the Draft CSEFH, the short term studies which form the basis of the Draft CSEFH's estimates of soil ingestion are not representative of long term rates of soil ingestion. See Draft CSEFH, at 5-31 ("[I]ndividuals were not studied for sufficient periods of time to get a good estimate of usual intake. Therefore, the values presented ….may not be representative of long term exposures.") The 1997 Exposure Factors Handbook suggests, in fact, that annual soil ingestion exposure in many parts of the country is substantially lower than the values recommended for exposure by EPA's exposure factors guidance:

Although the recommendations presented below are derived from studies which were mostly conducted in the summer, exposure during winter months when the ground is frozen or snow covered should not be considered as zero. Exposure during these months, although lower than in the summer months, would not be zero because some portion of house dust comes from outdoor soil.

Exposure Factors Handbook, Section 4.7. While exposure in the winter might not zero [*sic*], it would be significantly lower than during the summer.

The data presented by all of the "key" exposure studies referenced in the Draft CSEFH are representative of short term exposure in periods of good weather, when soil exposure, and therefore soil ingestion, are certain to be substantially higher than at other times of the year. Accordingly, it is highly likely that the Draft CSEFH's recommended child soil ingestion values substantially overpredict soil ingestion.

The following table illustrates the extent of this problem The table considers only those key studies that provided original data, not the "key" studies that provided further analysis of previously-published data.

Study	Place of Study	Duration	Time of Year
Davis et al. 1990	Washington State	7 days	"primarily during the summer"
Calabrese et al. 1997	Montana	7 days	"during a two week period in…September"
Davis and Mirick, 2006	Washington State	7 days	"primarily during the summer"

These studies, which were all conducted during the summer, are likely to have gathered soil ingestion data at the high end of the range for such data. Moreover, given the locations of these studies – all in northern states with long and cold winters – the study data are not likely to be representative of children's soil exposure for the vast majority of the year. Thus it is important that the CSEFH acknowledge that its recommended ingestion rates may only be representative of soil ingestion behaviors on those days or during those times of year when children are expected to have direct contact with outdoor soil during play activities.

***Response*:** *See the response to the previous comment on this topic. A detailed review of the weather patterns during the key tracer element studies' data collection periods indicates that for two of the four studies for which data collection periods are discernible, periods of low temperatures and precipitation occurred. The central tendency soil and dust recommendations do not rely on the tracer element study results, but instead rely on a study that did account for seasonal and day to day variability in soil and dust intakes.*

Comment: <u>The Draft CSEFH Fails to Make Clear that the Recommended "Values for Soil Ingestion" Include Household Dust Ingestion</u>

EPA's 1997 Exposure Factors Handbook makes clear that the term "soil ingestion" refers to ingestion of both soil and household dust. For example, in discussing winter exposure, the EFH states:

> Although the recommendation presented below are derived from studies which were mostly conducted in the summer, exposure during winter months when the ground is frozen or snow covered should not be considered as zero. Exposure during these months, although lower than in the summer months, would not be zero because *some portion of house dust comes from outdoor soil.*

Exposure Factors Handbook, Section 4.7 (emphasis added). The Draft CSEFH itself states that the recommended 95th percentile ingestion rate is "based on soil and dust ingestion." Draft CSEFH at 5-31 (describing final adopted values). However, in other instances, it is clear that the Draft CSEFH values are based on ingestion of both soil and dust. For example, in describing the final mean ingestion value, the Draft CSEFH states that it is "the best estimate of mean soil ingestion." In addition, while Table 5-20 makes it clear that data on both soil and dust ingestion were used to derive the final ingestion values, other tables do not. For example, table 5-21,

which sets forth the final values for mean and 95th percentile ingestion, is titled "Summary of Recommended values for Soil Ingestion," and makes no mention of dust ingestion.

The text and the tables of the CSEFH should be reviewed carefully and the document should be edited to make clear that the recommended values for "soil ingestion" include ingestion of dust. That should prevent risk assessors from "double counting" soil and dust ingestion. Alternatively, the CSEFH should provide discrete recommendations for rates of outdoor soil ingestion and indoor dust ingestion in order to assist risk assessors who may be separately evaluating outdoor and indoor exposures, respectively

Response**:** *The revised handbook has been carefully reviewed and edited to ensure that recommended values for soil, dust, and soil + dust are clearly stated.*

Comment: The CSEFH Should Make Clear that Pica Soil Ingestion Is Not a Common Behavior and Should Make No Recommendation Regarding Pica Soil Ingestion Rates

The discussion of pica soil ingestion by children is somewhat misleading in that it leads the reader to believe that 50 percent of children engage in pica behavior. Draft CSEFH, at 5-2. This statistic, however, is actually related to total pica behavior (including ingestion of all types of foreign objects and materials such as paper, hair, cloth and other items) rather than soil pica. While the CSEFH does qualify this statement by discussing the difference between pica behavior and soil pica, that discussion is belated, not appearing until page 5-25. Thus, if individuals do not read the entire section on pica, they would assume that the guidance is reporting that 50 percent of children engage in soil pica. In fact, the incidence of soil pica is not very high. EPA acknowledges this where it reports that of 600 children involved in "key" soil ingestion studies, only one individual engaged in pica behavior. CSEFH, at 5-26. Thus the actual prevalence of soil pica may be closer to 0.2 percent than the 50 percent implied on page 5-2. This discussion needs to be clarified much earlier in the document in order to avoid confusion about the frequency of pica behavior. It is also important to clarify, in that discussion, that the pica behavior most frequently occurs in 1 to 3 year old children and does not generally occur in older children.

The recommended soil ingestion value for the pica child of 10 g/day is based on one child from the Calabrese et al. 1991 study whose soil ingestion was far outside the range of the other study participants. Draft CSEFH, at 5-31. See 1997 Exposure Factors Handbook, Table 4-23. As discussed previously, the Draft CSEFH itself points out that the one child from the Calabrese study was the only one of more than 600 children involved in the key soil ingestion studies who exhibited pica behavior. This incidental data on one child should not form the basis for an EPA recommendation. For all that EPA knows, 10 g/day could be substantially underestimating what a pica child would ingest. Moreover, that single data point, even if it were representative of pica behavior, is of no use without sufficient data on the frequency of pica among American children. If the Draft CSEFH retains the pica ingestion value, it should explicitly acknowledge that no reliable data exist on pica frequency among children in the United States and that a risk assessment should include a risk estimate for the pica child only where such behavior is known exist [*sic*] in the population at issue.

***Response*:** *The revised handbook has been edited substantially to clarify the known extent of soil-pica behavior, as reported by parents or other caregivers. The Sayetta citation has been removed, and the wording modified to place into context the very limited research available on pica and soil pica behavior in children. The commenter's contention, that pica behavior occurs most frequently in 1 to 3 year old children and does not generally occur in older children, has not been substantiated in the literature. Regarding the single soil-pica child's soil ingestion estimates as the basis for the soil-pica recommendation, see responses to previous comments on this topic..*

References:

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Davis, S.; Waller, P.; Buschbom, R.; Ballou, J.; White, P. (1990) Quantitative estimates of soil ingestion in normal children between the ages of 2 and 7 years: population based estimates using aluminum, silicon, and titanium as soil tracer elements. Arch. Environ. Hlth. 45:112-122.

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Stanek, E.J.; Calabrese, E.J. (1995a) Daily estimates of soil ingestion in children. Environ. Health Perspect. 103(3):276-285.

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Stanek, E.J., and E.J. Calabrese. 2000. Daily soil ingestion estimates for children at a Superfund Site. Risk Analysis 20(5):627-635.

Exhibit E.1

Letter from Dr. Edward Calabrese Re: Soil Ingestion Rates

July 23, 2003

Kevin W. Holtzclaw
Manager – PCB Issues
General Electric Company
3135 Easton Turnpike
Fairfield, CT 06431

Re: Soil Ingestion Rates

Dear Mr. Holtzclaw:

The General Electric Company (GE) has asked for my opinion on the soil ingestion rates used by the U.S. Environmental Protection Agency (EPA) for general residential and recreational exposures in its June 2003 draft of the Human Health Risk Assessment (HHRA) for the Housatonic River. For upper bound exposures, those rates are 200 mg/day for young children and 100 mg/day for older children and adults. The central tendency estimates are 100 mg/day for young children and 50 mg/day for older children and adults. These rates are based on prior studies by our group – Calabrese et al. (1989) and Stanek and Calabrese (1995a, b) for young children, and Calabrese et al. (1990) for adults.

As explained in a presentation that I made on this subject to EPA Region 1 in May 2002, I believe that these rates are overstated and can be significantly improved by reliance on newer soil ingestion studies from our group, which used improved methodologies. I have reviewed the discussion of this topic in the document entitled "Attachment E: Selection of Soil Ingestion Rates," which GE sent me and which I understand will be part of GE's comments on the HHRA. I entirely agree with that discussion. To summarize:

1. Soil Ingestion Rates for Young Children. Our most recent study of soil ingestion rates in young children (Stanek and Calabrese, 2000) included several improvements over our prior studies. These included: 1) a relatively large study group (64 children); 2) improved particle size measurements that focused attention on soil of smaller particle size; 3) a longer study duration (365 days); 4) the use of a relevant age group (1 to 4 year old children); 5) use of a random sample of the population for that age group; and 6) better control for input/output error. The results of this study showed a 95^{th} percentile soil ingestion rate of 106 mg/day (when evaluated over a year), a median (50^{th} percentile) ingestion rate of 17 mg/day, and an arithmetic average ingestion rate of 31 mg/day. Based on these results, I recommend that the most appropriate soil ingestion rates to use for chronic exposures to young children would be an upper bound rate of 100 mg/day (based on the year-long 95^{th}

percentile value from our study) and a central tendency estimate of 20 mg/day (based on the median value from our study).

2. Soil Ingestion Rates for Adults and Older Children. Our most recent study of soil ingestion rates in adults (Stanek et al., 1997) likewise included a number of improvements over our prior (1990) study. These included: 1) a large number of subjects (10) and days (28) of participation; 2) an improved study design that considered seven consecutive days of fecal sampling; 3) improved selection of soil tracers; 4) a broader range of soil ingestion validation; and 5) an enhanced capacity for additional assessments including particle size of the soil ingested. In this study, one of the participating adults had an unusually high soil ingestion estimate (2 grams) on the first day of the study week. In fact, on that day, this subject had 4 times higher freeze-dried fecal weight than on any other day of the study, suggesting that his excretion on that day reflected a 3-4 day accumulation, instead of just one day, as assumed in the calculations. In consequence, the 95th percentile ingestion rate from this study (331 mg/day), which is driven by that result for one subject, is uncertain, unstable, and artificially inflated. In these circumstances, I recommend that EPA use the upper 75th percentile value from this study, which was 49 mg/day, as the basis for an upper bound soil ingestion rate of 50 mg/day for adults and older children. For the central tendency estimate, I recommend use of an ingestion rate of 10 mg/day. This is consistent with the mean soil ingestion rate observed in our 1997 study (6 mg/day) and would represent half of the central tendency rate that I have recommended for young children.

I appreciate the opportunity to review these materials. Please do not hesitate to contact me if you have any further questions.

Sincerely,

/s/

Edward J. Calabrese, Ph.D.

Professor of Toxicology

Director of the Northeast Regional

Environmental Public Health Center

EJC/ps

References for Letter

Calabrese, E.J., R. Barnes, E.J. Stanek, H. Pastides, C.E. Gilbert, P. Veneman, X.R. Wang, A. Lasztity, and P.T. Kostecki. 1989. How much soil do young children ingest: An epidemiologic study. *Regul. Toxicol. Pharmacol*. 10:123-37.

Calabrese, E.J., E.J. Stanek, C.E. Gilbert, and R.M. Barnes. 1990. Preliminary adult soil ingestion estimates: Results of a pilot study. *Regul. Toxicol. Pharmacol*. 12:88-95.

Stanek, E.J., and E.J. Calabrese. 1995a. Daily estimates of soil ingestion in children: *Environ. Health Perspect*. 103(3):276-85.

Stanek, E.J., and E.J. Calabrese, E.J. 1995b. Soil ingestion estimates for use in site evaluations based on the best tracer method. *Hum. Ecol. Risk Assessment*. 1:133-156.

Stanek, E.J., E.J. Calabrese, R.Barnes, and P. Pekow. 1997. Soil ingestion in adults – Results of a second pilot study. *Toxicol. Environ. Safety* 36:249-257.

Stanek, E.J., and E.J. Calabrese. 2000. Daily soil ingestion estimates for children at a Superfund Site. *Risk Analysis* 20(5):627-635.

A.6.3 Comments submitted by the International Lead Zinc Research Organization

Comments:
On p. 5-30 and p. 5-31 of this chapter, the following is stated:

Therefore, the recommended soil ingestion values are based on soil and dust estimates. Rounding up to the nearest hundred, 100 mg/day is the best estimate of the mean soil ingestion for children under 7 years of age…Rounding to the nearest hundred, the recommended 95th percentile soil ingestion rate for children is 400 mg/day based on soil and dust ingestion.

EPA's 1994 guidance manual is clear that an average, or central estimate, of soil ingestion should be used.
"The reader should also note that there are statistical problems in interpreting an observed median value from these studies (Davis et al. 1990, Calabrese 1989). For example, in a population of children who all ingested very small amounts of soil on most days but occasionally ingested larger quantities, the median from a short term measurement study will be below the average daily quantity ingested by any of the children. The mean value is not subject to bias, and therefore is judged to be a more meaningful measure of ingestion. It should be noted that the 200 mg/d ingestion value presented in Superfund guidance can be supported as roughly, an upper bound on mean ingestion considering the values seen in different ingestion studies. The values recommended for use in the model (85 to 135 mg/d) represent a more central value within the range of values seen in different studies." (EPA, 1994).

Staneck [*sic*] and Calabrese subsequently published (1995) a re-analysis of the data EPA relied on to develop the Agency's original guidance ie., the Calabrese et al. (1989) data and the Davis and Waller et al. (1990) data. The revised analysis calculated an average soil ingestion rate for each child then formed a distribution of soil ingestion rates at percentiles of this distribution, e.g., for the 50th percentile child (50% of children have an average soil ingestion rate below this value). It would appear that the data for the 50th percentile child is perhaps the most relevant estimate for use in exposure assessment.

Since the recommendations in section 5.4 are based on Table 5-20 p. 5-52, it may be advisable to also include a bold-faced statement about the 50th percentile value of 60 mg ingestion of soil and dust being a more central value seen in the soil ingestion studies and a value that is more relevant for use in exposure assessment. The mean is also a central value, but probably within the upper limit of that central range. It then becomes clear that the 400 mg/day is an upper range limit outside of the central range and not necessarily applicable to a wide range of children.

Response**:** *The revised handbook does not rely solely on the tracer element study soil and dust ingestion estimates, and thus the comment is somewhat moot. Interestingly, one of the key studies for the soil and dust ingestion estimates (Hogan et al., 1998) provides a geometric mean soil and dust intake of 113 mg/day (averaged over children ages 1 to <7 years old), and the resulting model predictions appear to slightly underestimate (geometric mean) these children's blood lead levels. If the tracer study 50th percentile value of 60 mg/day (soil and dust) cited by the commenter was a more accurate representation of children's central tendency soil and dust intakes than the 113 mg/day default value in the IEUBK model (averaged over several years),*

one would expect that the several hundred children in the Hogan et al. (1998) study would have had correspondingly lower measured blood lead levels, unless there was a different reason for the discrepancy.

Comment: Also, on p. 5-30 there is a brief discussion of dust and soil ingestion rates for infants <1 year of age suggesting that infants may spend most of their time indoors and dust concentration may be more appropriate for calculating ingestion rates for this group. Soil intake for adults and infants is poorly documented, but is unlikely to exceed that of children. Very young infants do not engage in behavior (crawling and other exploratory activity) that place them at risk for soil and dust ingestion. A provisional assumption of intake is incorporated into exposure assessment models on the understanding that intake for the very young child does not occur, but increases to 25 mg/day (typical), with a worst case estimate of 85 mg/day, by 12 months of age. Isotopic ratio studies have confirmed that the majority of blood lead in very young infants is derived from dietary sources (Gulson et al., 2001).

***Response*:** *The current state of science on soil and dust ingestion in very young (0 – 6 month old infants) is likely to evolve over time; U.S. EPA's judgment was that insufficient information is available at this point to develop recommended soil and dust values for 0 to <6 month old infants. The revised handbook incorporates a modified estimate for the 6 to <12 month old infants, who would be expected to engage in behaviors in which soil and dust ingestion would occur (crawling and other exploratory activity, along with hand to mouth behavior). The data in the Hogan et al. (1998) study appear to indicate that the 85 mg soil + dust ingestion per day, for 6 to <12 month olds, may be too high, and thus the recommended values for this age group have been modified (reduced) from the 85 mg soil + dust per day. It is possible that future research could again affect the recommended value for this age group.*

REFERENCES

Calabrese, E.J., R. Barnes, E.J. Stanek, H. Pastides, C.E. Gilbert, P. Veneman, X.R. Wang, A. Lasztity, and P.T. Kostecki. (1989). How Much Soil do Young Children Ingest: An Epidemiologic Study. Regu Toxicol Pharmacol 10:123.

Davis, S., Waller, P., Buschbom, R., Ballou, J., and White, P. (1990) Quantitative Estimates of Soil Ingestion in Normal Children between the Ages of 2 and 7 years: Population-Based Estimates Using Aluminum, Silicon, and Titanium as Soil Tracer Elements. Arch Environ Health 45(2):112-122.

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International Programme on Chemical Safety (IPCS) (1995). Environmental Health Criteria 165 – Inorganic Lead. Published under the joint sponsorship of the United Nations Environment Programme, The International Labour Organisation and the World Health Organization; World Health Organization, Geneva.

Stanek, E.J. and Calabrese, E.J. (1995). Soil Ingestion Estimates for use in Site Evaluations Based on the Best Tracer Method. Hum Ecol Risk Assess 1(2):133-156.

United States Environmental Protection Agency (US EPA) (1994a). Guidance Manual for the Integrated Exposure Uptake Biokinetic Model for Lead in Children. Office of Emergence and Remedial Response. Washington, DC. Publication No. 9285.7-15-1. EPA/540/R-93/081. PB 93-963510. February.

WHO (1985) Guidelines for the study of dietary intake of chemical contaminants. Geneva, World Health Organization (WHO Offset Publication No. 87).

A.7 Chapter 6 (Other Non-dietary Ingestion Factors)

A.7.1. Comments from the American Chemistry Council

Comments: P. 6-6, first full paragraph: The handbook indicates the Groot et al. (1998) reference did not differentiate the types of objects mouthed. Groot et al. (1998) however, does provide data by object type (see pp. 27-28), which should be added to the handbook.

P. 6-42, Table 6-20: Would be informative to add N for each age group to the table.

P. 6-43, Table 6-21: The Reed et al. (1999) study included children age 2-6 years old, and should be included under that age category (the row above), rather than the 3-6 year category.

Response**:** *The summary of the Groot et al. (1998) study's limitations has been revised and no longer states that object types were not differentiated. The study's differentiation is limited to fairly general categories of object types (non toys, toys for mouthing, other toys, and fingers) that, in U.S. EPA's judgment, may be of somewhat limited use in risk assessments. One U.S. study contains detailed differentiation of a number of different types of objects and surfaces, and this study's data (AuYueng et al., 2004) has been included in the chapter. Table 6-20 is no longer included in the chapter.*

A.7.2 Comments from Department of Defense (DoD)

Comments:
The information in Chapter 6 (Other Non-Dietary Ingestion Factors) suggests several ways by which ingestion exposure could occur, but the information is not usable in a risk assessment context without the following supporting information:

- Methods for estimating contaminant concentration on toys and other smooth surfaces identified in the referenced studies;
- A suggested percentage of the contaminant concentration on a toy or other smooth surface that would be transferred to the mouth or from fingers-mouth.
- Justification for why the exposure times measured (e.g., 1-2 seconds per mouthing exposure) would contribute enough of a contaminant dose to warrant evaluation in a risk assessment when other exposures, such as inhalation and soil ingestion, are also present.

This chapter also mentions exposures such as soil-hand-mouth and dust-mouth. These exposures are more accurately soil ingestion exposures, which are covered in Chapter 5 (for an example, see page 6-9, lines 12-13). In general, a discussion on fate and transport of contaminants to indoor areas, and a discussion regarding how these exposures are different from soil and dust ingestion is warranted.

Response: *The scope of the document is limited to providing quantitative estimates of exposure factors. Methods for estimating contaminant concentration on toys and other smooth surfaces would need to be developed or obtained in the context of a particular risk assessment, since specific characteristics of different contaminants, or substances/objects that are mouthed, could*

affect contaminant transfer. Similarly, the specific characteristics of different contaminants, or substances/objects that are mouthed, could also affect whether extremely short duration mouthing contact events of 1 to 2 seconds are significant in the context of overall exposure from numerous sources. Quantitative estimates of such mouthing contact event frequencies and durations would be needed in order to compare potential exposures from mouthing behavior with potential exposures from other pathways.

A.8 Chapter 7 (Inhalation Chapter)

A.8.1. Comments from the American Chemistry Council

Comments:
The document includes one new inhalation reference (Lordo *et al*., 2006) which is chosen as the basis for new inhalation rate recommendations. The scientific merit of this study is difficult to assess at this point, as it is has not been published. This report developed under contract for EPA was not found in a search of EPA's website, publications, or exposure factors webpage, or in general internet searches performed with two different search engines. There are two concerns with the Lordo *et al*. estimates based upon the summary information presented:

> 1. The analysis, as presented, derives ventilation rates from activity-associated METS values from the CHAD database. Based upon age and gender only, activity patterns from the NHAPS data set are linked to NHANES body weight data, to develop distributions of ventilation rates. The analysis, as presented, does not appear to consider that activity patterns are likely dependent to some extent on body weight – that is, children with greater body weights are likely to have less active lifestyles. Thus, the analysis will overestimate ventilations rates if general age & gender activity patterns are applied to children regardless of body weights.
>
> The difference is likely to be significant, based upon ranges for time spent at various activity levels (Table 7-19). For example, for moderate activity, the difference between the 5th percentile and the maximum time spent can be up to 7 hours, depending upon age group. Similar differences are noted for time spent in sedentary and passive intensity activity and light intensity activity.
>
> 2. The information presented indicates that the METS values from the CHAD database are not child-specific. The basis of the METS values should be provided, along with an assessment as to whether they are appropriate for children. Thus, we feel at this time it is not appropriate to use the Lordo *et al*. reference as a basis for changing the current recommendations in the earlier draft Child Specific EFH, which are in agreement with those in the 1997 USEPA Exposure Factors Handbook.

Response**:** *Brochu et al. (2006), Arcus-Arth and Blaisdell (2007), and Stifelman (2007) were added to the chapter as key studies. Recommendations were revised accordingly.*

A.8.2. Comments from the Department of Defense (DoD)

Comment: Page 7-36, Table 7-20. Confidence in Inhalation Rate Recommendations
Page 7-37, Table 7-21. Summary of Recommended Values for Inhalation
Compared to the 1997 EHF, the overall confidence in the recommended inhalation rates has reduced from "high" to "medium" while some of the recommended inhalation rates have nearly

doubled (e.g., in 1997, the recommended rate for infants < 1 year for long-term exposure was 4.5 m^3/day compared to 8.76 m^3/day for males from birth to < 1 year).

For evaluating long-term exposures (those typically evaluated in a risk assessment), the range of recommended inhalation rates for children age 0 – 6 years is 9 – 13 m^3/day. This is a very small range, and suggests that there is no need to separate this group into the seven subgroups recommended by the EPA. This same comment holds true for children ages 6 – 21 years, who have a proposed inhalation rate range of 13 – 17 m^3/day. The EPA recommends that children in this age range be separated into three subgroups for risk evaluation.

Response**:** *These are the age bins set by the EPA. Recommendations based on more recent data show that infants < 1 month old have inhalation rates 2.5 times higher than 6 to <11 years old on a body weight basis.*

Comment: Page 7-14, Table 7-3. Distribution of Predicted Intake Rates by Location And Activity Levels For Elementary And High School Students

The reported mean and standard deviation for the elementary school children participating in medium activity levels is 0.96±0.36. However, when this same data was reported in the 1997 EFH, the mean and standard deviation were reported as 0.96±0.42.

Response**:** *The value in the Exposure Factors Handbook needs to be corrected.*

Comment: Page 7-15, Table 7-5. Distribution Patterns of Daily Inhalation Rates For Elementary (EL) And High School (HS) Students Grouped by Activity Level

a. The title for this table is printed in a separate page from the actual table. We recommend showing the table name on the same page as the table.

b. The values presented for the recommended inhalation rates are all rounded up so that each value is presented to the nearest tenth. This results in some values being presented to only one significant figure. We recommend showing at least two significant figures for each of these values so that when intake is calculated, rounding errors are not compounded.

Response**:** *No response needed. This table was deleted from the chapter.*

A.8.3. Comments from the Office of Environmental Health Hazard Assessment – California EPA

Comment: Arcus-Arth and Blaisdell have written a paper which has been accepted for publication (October 8, 2006 by the Journal of Risk Analysis) but the date of publication is unknown. The authors developed breathing rates for narrow age ranges of children (3 month age groups for 0<1 year, and each year for 1<19 years of age) using Layton's metabolic equation and energy intake data. Rates are in L/day and L/day-kg and were derived to be representative of the U.S. population. The rates differ from Layton's by the use of more recent energy intake data, rates normalized to body weight for each individual, deriving rates for narrow age ranges of

infants and children, the use of more child-specific conversion factors, and the adjustment of energy intakes to account for energy stored and not expended (infants). Though the Arcus-Arth and Blaisdell paper does not include breathing rates for the CEFH age groups, such rates could be derived by the authors (Arcus-Arth and Blaisdell), or by using the parametric information provided in the paper. The authors welcome the opportunity to work with U.S. EPA to develop breathing (inhalation) rates for the CEFH age groups. Please contact: Amy Arcus-Arth, aarcus@oehha.ca.gov, (510) 622-3199.

***Response*:** *The Arcus and Blaisdell paper has been added.*

Comment: The methodology used to derive the inhalation rates that are recommended in the handbook is not described in sufficient detail in the handbook for the reader to follow and replicate. This is important since the study (Lordo et al., 2006) that derived the recommended inhalation rates has not been published and, to our knowledge, is not otherwise available to the public. We suggest to either use a published study or to describe the Lordo et al. methodology in sufficient detail that it can be followed and replicated by the reader.

***Response*:** *Brochu et al. (2006), Arcus-Arth and Blaisdell (2007), and Stifelman (2007) were added to the chapter as key studies. Recommendations were revised accordingly*

Comment: The sentence on p. 7-10 lines 8-9, is not clear. The term "scaled down" could be more specifically described. Were the number of minutes in a day that each activity was performed averaged over the 20 days of activity patterns?

***Response*:** *The total number of minutes were averaged over the 20 days.*

Comment: For the Lordo et al. study, the NHANES body weights were matched to 20 sets of NHAPS 24-hour activity patterns based on age groups (0<1 year, 1<2 years, 2<3 years, 3<6 years, 6<11 years, 11<16 years, and 16<21 years) and gender. Though broad age and gender groups are typically associated with some activity patterns and a range of body weights, other factors may also be associated with activity patterns. Body weight itself is associated with activity patterns. But assigning a body weight to a random set of activity patterns presumes that there is no association between body weight and activity pattern. Especially with the current prevalence of obesity in children, it may be important to consider the association of an individual's body weight (e.g., an obese child) with activity patterns. The Lordo et al. methodology uses a BMR equation and body weight to predict a "basal" inhalation rate. If the child is obese, a very high inhalation rate would probably be predicted from the high body weight, when the likelihood is that the child is not physically active and therefore would actually have a very low inhalation rate. It is unfortunate that body weight data are not available from the NHAPS as then "basal" inhalation rates and activity (energy expended) based inhalation rates could be derived for each individual. This would remove the uncertainty associated with combining disparate data.

***Response*:** *EPA recognizes that this is a limitation of the approach.*

Comment: By deriving an "average 24-hour activity pattern" for each NHANES individual, important interindividual variability information is lost. This is because the activity pattern data are from different individuals. This should be noted, especially in reference to interpretation of percentiles of inhalation rates.

***Response*:** *EPA recognizes that this is a limitation of the approach.*

Comment: The differences in energy expended in physical activity during the day determine differences in inhalation rates for the same body weight person. Thus, it is very important to assess energy expenditures, both in terms of accuracy and in terms of variability.

***Response*:** *Data using energy expenditures are also presented.*

Comment: We are unsure how the percentiles in Table 7-19 are to be interpreted since for each individual data point, the individual daily inhalation rate is a compilation of body weight, activity pattern data averaged across persons (and activities??), and MET distributional information summarized from various ages of individuals. The percentiles in Table 7-19 are probably primarily a function of variability in body weight. Though body weight is generally correlated with inhalation rate, it is probably not the driver of interindividual inhalation rate variability (energy expenditure probably plays a greater role). It would be helpful to provide information with which to better interpret Table 7-19.

***Response*:** *It is unclear what the reviewer is requesting. Table 7-19 (now 6-15) is the distribution of time spent in each activity by individuals within an age group and not inhalation rates.*

Comment: The NHAPS activity pattern data were primarily collected for exposure (e.g., gas stoves) and location (e.g., inside) information. These activity data provide little if any information that describes the amount of energy expended for that activity. Since energy expenditure is the primary factor that determines inhalation rate (high energy expenditure activities can increase a "basal" inhalation rate 5-6 fold), activity-specific energy expenditure information is very important to the determination of inhalation rates. Though CHAD provides distributional parameters for MET values for various activities, these activities are grouped into very broad categories (e.g., general leisure) and categories that could include low and high energy expenditure activities (e.g., "perform music, drama, dance"). The lack of data with which to assign specific METS (or another energy expenditure level metric) to specific activities should be noted in the handbook.

***Response*:** *Activities were grouped into categories based on professional judgment.*

Comment: Though Schofield (1985) provides a detailed review of BMR studies and improves on prior BMR equation data and methods, there are still important limitations to the equations, especially for the 0<3 year age group. Schofield (1985) derived the BMR equations by compiling data from many disparate studies and regressing measured energy expenditures on bodyweight and height. Schofield grouped the data by bodyweight, but published the equations according to age groups. This resulted in Schofield's 0<3 year age group having average ages of

0.67 and 0.81 years, and body weights of 6.57 and 6.86 kg, for boys and girls respectively. Thus, the BMR equations developed for the 0<3 year age group may be more representative of children 0<1 year of age than 0<3 years of age. This BMR equation may not accurately predict BMR for all ages within the broad 0<3 year age group. Schofield notes that height significantly contributed to the regression for 0<3 year olds. Because the Lordo et al. study did not include height in determining BMR, there is uncertainty in the BMR estimates for 0<3 year olds. We acknowledge that there is a lack of data on BMR, and that Schofield probably presents the best available estimates. Nonetheless, the limitations of Schofield's equations should be considered and either noted in the study or adjusted if possible.

***Response*:** *EPA recognizes that this is a limitation of the methodology.*

Comments:

- p. 7-1, line 4: define inhalation rate (e.g., volume inhaled per unit time)
- It is suggested to use the term "body weight" Instead of "weight" to avoid confusion with "sampling weight" and other types of "weights".
- p. 7-9, line 17: what was the sample size of children?
- p. 7-9, line 25: from information in the CHAD manual, there are 1791 children 0<18 years of age in NHAPS. It would be more informative to list the number of children, rather than all individuals.
- p. 7-11, line 1: "five" conflicts with the "four" activity level ranges listed on page 7-10.
- Table 7-13 and 7-14: It would probably be less confusing for the reader if the same unit of measure (liter or m^3) were used throughout the tables. Though it is helpful to provide a note about the difference in the unit of time.
- p. 7-11, line 15: though the NHAPS and NHANES are each representative of the U.S. population (for NHANES, when properly weighted during analyses), combining values from one dataset with the other, will reduce the representativeness of the data.

Response: *The introduction to the chapter has been considerably expanded to describe inhalation rates and dosimetry. The chapter has been edited. Sample size data are included in the tables and the units have been made consistent to* m^3.

Comment: References for Chapter 7
Arcus-Arth A, Blaisdell RJ. Statistical distributions of daily breathing rates for narrow age groups of infants and children. J Risk Analysis (accepted for publication 8Oct 2006).

***Response*:** *This reference has been added.*

A.9 Chapter 8 (Dermal Route)

A.9.1. Comments from Drs. Michael Shannon (Harvard Medical School) and James Roberts (Medical University of South Carolina)

Comment: This section makes considerable use of 1985 data. Given the increasing weight of children and the relationship between weight and BSA, EPA may wish to revisit whether the estimates are accurate. Additionally, while skin characteristics are discussed in terms of BSA and "solids adherence," there is no review or discussion of skin permeability in children. Although the literature on skin permeability of children is not considerable, it may warrant examination for inclusion of some basic information in this chapter. For example, the U.S. Consumer Product Safety Commission has published well-established data on children's skin permeability and arsenic.

Response**:** *Limited discussion has been added and the reader is referred to EPA document Dermal Exposure Assessment: Principles and Applications. BSA data were derived from the more recent NHANES survey 1999-2006. The handbook does not contain any chemical specific data.*

A.9.2. Comments from Department of Defense (DoD)

Comment: The recommended values presented in Section 8 for soil adherence factors (AFs) are geometric means. However, when estimating dermal exposure, ref (f) recommends that when selecting an AF, the risk assessor can consider one of the following two options: *"(1) select a central tendency (i.e., typical) soil contact activity and use the high-end weighted AF (i.e., 95th percentile) for that activity; or (2) select a high-end (i.e., reasonable but higher exposure) soil contact activity and use the central tendency weighted AF (i.e., 50th percentile) for that activity*." Since in this document EPA only presents/recommends geometric mean values, it is unclear if the recommendation in ref (f) is no longer endorsed by EPA. Similarly, in Section 9, the recommended values for time children spend per day in the shower and bathtub are essentially half of the value recommended in ref (f). We recommend that EPA provide clear guidance as to how the information in this document relates to recommendations in other EPA guidance, such as ref (f).

References:

(a) USEPA, 2005. *Guidelines for Carcinogen Risk Assessment.* Risk Assessment Forum, Washington, DC; EPA/630/P-03/001F.

(b) USEPA, 2005. *Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens*. Risk Assessment Forum, Washington, DC; EPA/630/R-03/003F.

(c) Troiano, RP, and KM Flegal. *Overweight children and adolescents: description, epidemiology, and demographics*. Pediatrics 1998;101(3):497-504.

(d) Ogden, CL, et al. *Prevalence of overweight and obesity in the United States*. JAMA 2006;295:1549-1555.

(e) USEPA, 1997. *Exposure Factors Handbook*. Washington, DC: Office of Research and Development. EPA/600P-95/002F.

(f) USEPA, 2004. *Risk Assessment Guidance for Superfund Volume I: Human Health Evaluation Manual (Part E, Supplemental Guidance for Dermal Risk Assessment).* EPA/540/R/99/005.
(g) *Summary Report for the ATSDR Soil-Pica Workshop, June 2000, Atlanta, Georgia.* Prepared by Eastern Research Group.

***Response*:** *Geometric means are a measure of central tendency. Arithmetic means were not provided in the literature. As stated in the introduction, recommendations are not legally biding on any EPA program office. Superfund is generally interested in characterizing the reasonable maximum exposure (RME).*

Comment: Page 8-1, Section 8.1 Introduction (lines 16 – 18) - The potential dermal exposures listed for children are not relevant, or are unclear, as noted below:

a. Dermal exposure to commercial cleaning liquids is unlikely for a child, other than accidental exposure that is not typically considered in a risk assessment evaluation.

b. Dermal exposure to vapors and fumes is not typically evaluated due to the more likely exposure pathway of inhalation of vapors.

c. The indoor dermal exposure is unclear. Please clarify if this is equivalent to dermal exposure to indoor particulates. If so, this pathway is considered under evaluation of dermal exposure to soil, and does not need to be presented again.

***Response*:** *The Introduction has been revised.*

Comment: Page 8-12, Section 8.4.1 Body Surface Area - The recommended body surface area measurements are based on data obtained from 1988 – 1994, and may not reflect the current size of children in some age groups given the reported increased prevalence of childhood obesity as reported in refs (d) and (e). We recommend including the data evaluated in ref (e) to update these figures, as appropriate.

***Response*:** *Newer data for body surface area has been added. The data are from the EPA analysis of NHANES 1999-2006 data*

Comment: Page 8-1, Section 8.1 Introduction (lines 26 – 27)

The last sentence on this page refers readers to, "*…and Risk Assessment Guidelines (RAGs) Part E.*." This should be updated to refer to Risk Assessment Guidelines for Superfund (RAGS) Part E.

***Response*:** *Text was revised.*

Comment: Page 8-21, Table 8-6. Mean and Percentile Skin Surface Area (m^2) Derived from EPA Analysis of NHANES III (All Children)

Page 8-22, Table 8-7. Mean and Percentile Skin Surface Area (m^2) Derived from EPA Analysis of NHANES III (Male Children)

Page 8-23, Table 8-8. Mean and Percentile Skin Surface Area (m^2) Derived from EPA Analysis of NHANES III (Female Children)

The values presented for the recommended skin surface areas are all rounded up so that each value is presented to the nearest tenth. This results in some values being presented to only one significant figure. We recommend showing at least two significant figures for each of these values so that when intake is calculated, rounding errors are not compounded.

***Response*:** *The recommendations have been changed to reflect 2 significant figures.*

A.10 Chapter 9 (Activity Factors)

A.10.1. Comments from Department of Defense (DoD)

Comment: Page 9-9, Section 9.2.6 Funk et al., 1998 (lines 31 – 34) - This information would also be relevant to the inhalation exposure chapter, but was not found there.

***Response*:** *Cross references will be considered in future updates* .

A.11 Chapter 10 (Consumer Products)

A.11.1. Comments from Department of Defense (DoD)

Comment: The information in Chapter 10 (Consumer Products) describes exposures that are not typically associated with exposure to environmental releases. As such, these exposures do not have a direct application to typical risk assessments where chronic exposures are evaluated. It would be useful if the EPA included a discussion of how they envision this data being used in a baseline risk assessment, if at all.

***Response*:** *The chapter is not intended to provide information on environmental releases of consumer products. The chapter was edited and expanded. The data presented provides information on frequency of used of consumer products. These are typically used in chronic risk assessments. An example scenarios document is being developed.*

A.12 Chapter 11 (Body Weight)

A.12.1. Comments from Drs. Michael Shannon (Harvard Medical School) and James Roberts (Medical University of South Carolina)

Comment: The estimates of body weight rely on data that is 10-27 years old (e.g., NHANES data from 1976 to 1980). More recent data from NHANES 1999-2002 are also utilized, but for the most part the older data are emphasized. In addition, Figures 11-1 through 3 (weight by age percentiles) are based on 1979 data and should be deleted, based on the fact that this 27-year-old data cannot be considered valid or useful for current medical practice or research. Finally, this chapter contains no discussion about the evolving use of body mass index (BMI) instead of body weight to estimate the size of children. We consider this to be a significant oversight.

Response**:** *BMI data have been added.*

A.12.2. Comments from Department of Defense (DoD)

Comment: Page 11-1, Section 1.1 Introduction - It is stated here that the childhood body-weight measurements were taken from studies conducted in preparation of the 1997 Exposure Factors Handbook (ref [e]). It is likely that these values do not reflect the current rise in childhood obesity as reported in ref (c) and (d), and therefore may underestimate mean childhood weight. Since more recent data is available per ref (d), we recommend updating this section to include greater consideration of more recent data.

Response**:** *The introduction has been revised and newer data for body weight has been added. The data are from the EPA analysis of NHANES 1999-2006 data*

Comment: Page 11-15, Table 11-11. Summary of Recommended Values for Body Weight

There is an error in the "Table Reference" column for the age groups 2 to < 3 months up to 16 to < 21 years. The tables referenced in this cell should be Table 11-8 (all); Table 11-9 (males), and Table 11-10 (females).

Response**:** *The recommendations section has been updated based on new body weight data from an EPA analysis of NHANES 1999-2006 data.*

A.12.3. Comments from the Office of Environmental Health Hazard Assessment – California EPA

Comment: While this chapter does discuss the U.S. EPA analysis of the CSFII data from 1994-1996, it does not include the recent findings from the U.S. EPA 2004 analysis which includes the 1998 CSFII survey whose focus was to survey and collect data on children. We recommend the results of the U.S. EPA 2004 analysis be included in this chapter, and a discussion of its relative merits in comparison to the NHANES data be presented.

Response**:** *The data are from a new EPA analysis of NHANES 1999-2006 data*

Comment: We suggest that the CDC Growth Charts (2000) be considered for the 0<2 month old age groups. Birth certificate data were used to supplement data from NHES and NHANES. Though the NHES and NHANES data are from the 1970s and 80s, infant birth weight has probably not changed that much since then. The biggest change in body weights has probably been with non-infant children, where lifestyle changes have significantly changed body weights during the past two decades or so.

Response**:** *The CDC growth charts have been added.*

Comment: For body weights of young infants, it is important to discern between full-term and preterm infants. In 2004, there were 508,356 premature births in the U.S., which is 12.5% of all births, and an increase from 11% in 1994 (March of Dimes website, 2006, http://www.marchofdimes.com/peristats/). Because the subpopulation of pre-term infants is sufficiently large, and their sensitivity to environmental agents may be greater than children and adults, body weight parameters for this subpopulation should be considered for inclusion in CEFH as a separate "age" group or as a subpopulation with separate exposure parameters during their first six months (or so) of extra-uterine life.

Response**:** *Available data for pre-term infants and fetal growth have been added to the chapter.*

Comment: It would be helpful to know if estimated infant (0<12 months age) body weights in CEFH include data from infants exclusively breastfed or exclusively formula-fed.
Another factor that has been documented to affect infant body weight is the type of milk fed to the infant. Starting at about 2-4 months of age, infants who are formula fed tend to have greater rates of weight gain than breastfed infants. Subsequently breast fed infants may be "leaner" during the 6-12 month age periods relative to formula-fed infants (e.g., Ziegler, 2006.

Response**:** *These data were not available on weight comparison for exclusively breast and or formula fed infants. EPA may address this at a later time.*

Comment: Page 11-1, line 24-25. The Fels study collected infant body weight data from 1929–1975. Body weights of infants and young children from the 1930s are likely to be significantly different from today's infant and children's body weights due primarily to the high prevalence of formula feeding between the 1930s and the 1980s. These formulas likely led to iron deficiency of infants since iron fortified formula was not introduced until 1959 and hypernatremic dehydration associated with high levels of protein in formulas until the 1960s. Fomon (2001) is a good source of information on infant feeding practices during the 20th century.

References for Chapter 11

Fomon SJ. Infant feeding in the 20th century: formula and beikost. *Journal of Nutrition.* 2001;131:409S-420S (available at: http://jn.nutrition.org/cgi/content/full/131/2/409S).

Ziegler EE. Growth of breast-fed and formula-fed infants. Nestle Nutr Workshop Ser Pediatr Program. 2006;(58):51-9; discussion 59-63.

***Response**: These references are not included in the update of the chapter because they were not relevant. Fomon 2001 does not contain any data on human milk intake. Instead it is a review paper of the changes in infant feeding practices from the 1900 to 2000. Ziegler 2006 focuses on the differences in growth and nutrition between breast-fed and formula-fed infants. It does not contain data on human milk intake.*