TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

This page is intentionally left blank

1 INTRODUCTION

1.1 PURPOSE

The purpose of the *Child-Specific Exposure Factors Handbook* is to provide exposure factors for children. The handbook highlights the changes in risk assessment practices that were first presented in the U.S. Environmental Protection Agency's (EPA) Cancer Guidelines, regarding the need to consider children as lifestages rather than as subpopulations (U.S. EPA, 2005b). It also emphasizes a major recommendation in U.S. EPA's *Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens* (U.S. EPA, 2005c) to sum exposures and risks across lifestages rather than relying on the use of a lifetime average adult exposure to calculate risk. This handbook also uses updated information to incorporate any new exposure factors data/research that have become available since the early 2000's, and is consistent with the U.S. EPA's new set of recommended childhood age groups (U.S. EPA 2005a), including a standardized way to define specific age groups.

As with the earlier version of the handbook, this new version summarizes key data on human behaviors and characteristics that affect children's exposure to environmental contaminants, and provides recommended values to use for these factors. These recommendations are not legally binding on any U.S. EPA program and should be interpreted as suggestions that Program Offices or individual exposure/risk assessors can consider and modify as needed. The decision as to whether to use site-specific or national values for an assessment may depend on the quality of the competing data sets as well as on the purpose of the specific assessment. The handbook has strived to include discussions of the issues that assessors may consider in assessing exposure among children of different ages, and may be used in conjunction with the U.S. EPA document entitled *Socio-demographic Data Used for Identifying Potentially Highly Exposed Populations* (U.S. EPA, 1999).

1.2 INTENDED AUDIENCE

The *Child-Specific Exposure Factors Handbook* may be used by exposure and risk assessors, economists, and other interested parties as a source for data and/or U.S. EPA recommendations on numeric estimates for behavioral and physiological characteristics needed to estimate childhood exposure to toxic contaminants.

1.3 BACKGROUND

Because of physiological and behavioral differences, exposures among children are expected to be different from exposures among adults. Children may be more exposed to some environmental contaminants, because they consume more of certain foods and water per unit of body weight and have a higher ratio of body surface area to volume than adults. Equally important, rapid changes in behavior and physiology may lead to differences in exposure as a child grows up. Recognizing that exposures among infants, toddlers, adolescents, and teenagers can vary significantly, the U.S. EPA published its "*Guidance on Selecting Age Groups for Monitoring and Assessing Childhood Exposures to Environmental Contaminants* (U.S. EPA. 2005a)." This update and revision of the 2002 interim final *Child-Specific Exposure Factors Handbook* (U.S. EPA, 2002a) is designed specifically to complement U.S. EPA's recommended set of childhood age groups:

? Less than 12 months old: birth to <1 month, 1 to <3 months, 3 to <6 months, and 6 to <12 months.

? Greater than 12 months old: 1 to <2 years, 2 to <3 years, 3 to <6 years, 6 to <11 years, 11 to <16 years, and 16 to <21 years.

Many studies have shown that young children can be exposed to various contaminants, including pesticides, during normal oral exploration of their environment (i.e., hand-to-mouth behavior) and by touching floors, surfaces, and objects such as toys (Eskenazi et al., 1999; Gurunathan et al., 1998; Lewis et al., 1999; Nishioka et al., 1999; Garry, 2004). Dust and tracked-in soil accumulate in carpets, where young children spend a significant amount of time (Lewis et al., 1999). Children living in agricultural areas may experience higher exposures to pesticides than do other children (Curwin et al., 2007). Pesticides may be tracked into their homes by family members. In addition, children living in agricultural areas may also play in nearby fields or be exposed via consumption of

contaminated human milk from their farmworker mother (Eskenazi et al., 1999).

In terms of risk, children may also differ from adults in their vulnerability to environmental pollutants because of toxicodynamic differences (e.g., when exposures occur during periods of enhanced susceptibility) and/or toxicokinetic differences (i.e., differences in absorption, metabolism, and excretion) (U.S. EPA, 2000a). The immaturity of metabolic enzyme systems and clearance mechanisms in young children can result in longer half-lives of environmental contaminants (Ginsberg et al., 2002, Clewell et al., 2004). The cellular immaturity of children and the ongoing growth processes account for elevated risk (AAP, 1997). Toxic chemicals in the environment can cause neurodevelopmental disabilities, and the developing brain can be particularly sensitive to environmental contaminants. For example, elevated blood lead levels and prenatal exposures to even relatively low levels of lead can result in behavior disorders and reductions of intellectual function in children (Landrigan et al., 2005). Exposure to high levels of methylmercury can result in developmental disabilities among children (Myers et al., 2000). Other authors have described the importance of exposure timing (i.e., preconceptional, prenatal, and postnatal) and how it affects the outcomes observed (Selevan et al., 2000). Breysse et al. (2005) suggests that higher levels of exposure to indoor air pollution and allergens among inner-city children compared to non-inner-city children may explain the difference in asthma levels between these two groups. With respect to contaminants that are carcinogenic via a mutagenic mode of action, the U.S. EPA has found that childhood is a particularly sensitive period of development, in which cancer potencies per year of exposure can be an order of magnitude higher than during adulthood (U.S. EPA, 2005c).

Executive Order 13045: *Protection of Children from Environmental Health Risks and Safety Risks*, signed in 1997, requires all federal agencies to address health and safety risks to children, to coordinate research priorities on children's health, and to ensure that their standards take into account special risks to children (EO, 1997). To implement the Order, the U.S. EPA established

the Office of Children's Health Protection (OCHP) (renamed the Office of Children's Health Protection and Environmental Education (OCHPEE) in 2005), whose job it is to work with Program and regional offices within the U.S. EPA to promote a safe and healthy environment for children by ensuring that all regulations, standards, policies, and risk assessments take into account risks to children. Legislation, such as the Food Quality Protection Act and the Safe Drinking Water Act amendments, has made coverage of children's health issues more explicit, and research on children's health issues is continually expanding. As a result of the emphasis on children's risk, the U.S. EPA Office of Research and Development (ORD) developed a *Strategy for Research on Environmental Risks to Children* (U.S. EPA, 2000a). The goal of the Strategy is to improve the quality of risk assessments for children. This *Child-Specific Exposure Factors Handbook* is also intended to support the U.S. EPA/ORD/NCEA's efforts to improve exposure and risk assessments for children.

In 1997, the U.S. EPA/ORD/NCEA published the *Exposure Factors Handbook* (U.S. EPA, 1997a). The handbook includes exposure factors and related data on both adults and children. Subsequently, the U.S. EPA Program Offices identified the need to consolidate all children's exposure data into a single document and the *Child-Specific Exposure Factors Handbook* was published in 2002 to fulfill this need. This handbook updates the 2002 edition of the *Child-Specific Exposure Factors Handbook* (U.S. EPA 2002a). It provides non-chemical-specific data on exposure factors that can be used to assess contributions from dietary and non-dietary ingestion exposure, dermal exposure, and inhalation exposure among children. Although the preconceptional and prenatal (fetal) life stages are important to consider they are not covered in this handbook. Preconceptional exposures are included in the *Exposure Factors Handbook* since they relate to maternal and paternal exposures, and exposure factors for pregnant and lactating women are being developed as part of a separate effort. This document does not include chemical-specific data or information on physiological parameters that may be needed for exposure assessments involving physiologically-based pharmacokinetic (PBPK) modeling. The U.S. EPA

has developed guidance on how to use PBPK information in risk assessment. More information on the application of PBPK models and supporting data is found in U.S. EPA (2006a, 2006b).

This handbook provides updated exposure factor information for children in the following areas:

- ingestion of water and other select liquids;
- non-dietary ingestion;
- soil and dust ingestion;
- inhalation rates;
- dermal exposure factors such as surface area and adherence;
- body weight;
- intake of fruits and vegetables;
- intake of fish and shellfish;
- intake of meat, dairy products, and fats;
- intake of grain products;
- intake of home-produced foods;
- total food intake;
- human milk intake;
- activity factors; and
- consumer products.

This handbook is a compilation of available data from a variety of sources. Most of these data have been described in detail in the U.S. EPA's *Exposure Factors Handbook* (1997a), but data published after the release of the *Exposure Factors Handbook* are also included here. This latest handbook updates the 2002 interim final *Child-Specific Exposure Factors Handbook* (U.S. EPA 2002). With very few exceptions, the data presented here derive from the analyses of the individual study authors. Because the studies included in this handbook vary in terms of their objectives, design, scope, presentation of results, etc., the level of detail, statistics, and terminology may vary from study to study and from factor to factor. For example, some authors used geometric means to present their results, while others used arithmetic means or distributions. Authors have sometimes used different age ranges to describe data for children. In most cases, the original data are unavailable, and the study results cannot be reallocated into the standard age groups used in this handbook. Every effort has been made to reallocate source data into the standard age groups

recommended by the U.S. EPA in the report entitled *Guidance on Selecting Age Groups for Monitoring and Assessing Childhood Exposures to Environmental Contaminants* (U.S. EPA, 2005a; see Section 1.7), when sufficiently detailed data are available. Within the constraint of presenting the original material as accurately as possible, the U.S. EPA has made an effort to present discussions and results in a consistent manner. The strengths and limitations of each study are discussed to provide the reader with a better understanding of the uncertainties associated with the values derived from the study.

Most of the data presented in this handbook are derived from studies that target (1) the general population (e.g., USDA food consumption surveys) or (2) a sample population from a specific area or group (e.g., fish consumption among Native American children). If it is necessary to characterize a population that is not directly covered by the data in this handbook, the risk or exposure assessor may need to evaluate whether these data may be used as suitable substitutes for the population of interest or whether there is a need to seek additional population-specific data. If information is needed for identifying and enumerating populations who may be at risk for greater contaminant exposures or who exhibit a heightened sensitivity to particular chemicals, the reader is referred to *Socio-demographic Data Used for Identifying Potentially Highly Exposed Populations* (U.S. EPA, 1999).

Because of the large number of tables in this handbook, tables are presented at the end of each chapter, before the appendices, if any. In conjunction with the *Guidance on Selecting Age Groups for Monitoring and Assessing Childhood Exposures to Environmental Contaminants* (U.S. EPA, 2005a), this handbook is adopting the age group notation "X to < Y" (e.g., the age group 3 to < 6 years is meant to span a 3-year time interval from a child's 3rd birthday up until the day before his or her 6th birthday).

1.4 SELECTION OF STUDIES FOR THE HANDBOOK

Information in this handbook has been summarized from studies documented in the scientific literature and other available sources. Studies were chosen that were seen as useful and appropriate for

estimating exposure factors for children. The handbook contains summaries of selected studies published through July 2008.

Certain studies described in this handbook are designated as "key," that is, the most useful for deriving exposure factors. The recommended values for most exposure factors are based on the results of the key studies (See Section 1.5). Other studies are designated "relevant," meaning applicable or pertinent, but not necessarily the most important. This distinction was made on the strength of the attributes listed in the "General Assessment Factors" listed below.

1.4.1   General Assessment Factors

Many scientific studies were reviewed for possible inclusion in this handbook. Generally, studies identified in the *Exposure Factors Handbook* (U.S. EPA, 1997a) as key studies are also included in this handbook as key studies. Also included are new studies that became available after publication of the *Exposure Factors Handbook* and the 2002 *Child-Specific Exposure Factors Handbook* (U.S. EPA, 2002a). Key studies from the *Exposure Factors Handbook* were generally defined as the most useful for deriving recommendations for exposure factors. The recommended values for most exposure factors are based on the results of these studies. The Agency recognizes the need to evaluate the quality and relevance of scientific and technical information used in support of Agency actions (U.S. EPA 2002b, 2003a, 2006c). When evaluating scientific and technical information, the U.S. EPA's Science Policy Council (SPC) recommends using five General Assessment Factors (GAFs): (1) soundness, (2) applicability and utility, (3) clarity and completeness, (4) uncertainty and variability, and (5) evaluation and review (U.S. EPA 2003a). These GAFs were adapted and expanded to include specific considerations deemed to be important during evaluation of exposure factors data, and were used to judge the quality of the underlying data used to derive recommendations.

1.4.2   Selection Criteria

The confidence ratings for the various exposure factor recommendations, and selection of the key studies that form the basis for these recommendations, were based on specific criteria within each of the five GAFs, as follows:

(1) Soundness: Scientific and technical procedures, measures, methods or models employed to generate the information are reasonable for, and consistent with, the intended application. The soundness of the experimental procedures or approaches in the study designs of the available studies were evaluated according to the following:

> **Adequacy of the Study Approach Used:** In general, more confidence was placed on experimental procedures or approaches that more likely or closely captured the desired measurement. Direct exposure data collection techniques, such as direct observation, personal monitoring devices, or other known methods were preferred where available. If studies utilizing direct measurement were not available, studies were selected that relied on validated indirect measurement methods such as surrogate measures (such as heart rate for inhalation rate), and use of questionnaires. If questionnaires or surveys were used, proper design and procedures include an adequate sample size for the population under consideration, a response rate large enough to avoid biases, and avoidance of bias in the design of the instrument and interpretation of the results. More confidence was placed in exposures factors that relied on studies that gave appropriate consideration to these study design issues. Studies were also deemed preferable if based on primary data, but studies based on secondary sources were also included where they offered an original analysis. In general, higher confidence was placed on exposure factors based on primary data.

> **Minimal (or Defined) Bias in Study Design:** Studies were sought that were designed with minimal bias, or at least if biases were suspected to be present, the direction of the

bias (i.e., an over or underestimate of the parameter) was either stated or apparent from the study design. More confidence was placed on exposure factors based on studies that minimized bias.

(2) *Applicability and utility: The information is relevant for the Agency's intended* The applicability and utility of the available studies were evaluated based on the following criteria:

Focus on Exposure Factor of Interest: Studies were preferred that directly addressed the exposure factor of interest, or addressed related factors that have significance for the factor under consideration. As an example of the latter case, a selected study contained useful ancillary information concerning fat content in fish, although it did not directly address fish consumption.

Representativeness of the Population: More confidence was placed in studies that addressed the U.S. population. Data from populations outside the U.S. were sometimes included if behavioral patterns or other characteristics of exposure were similar. Studies seeking to characterize a particular region or sub-population were selected, if appropriately representative of that population. In cases where data were limited, studies with limitations in this area were included and limitations were noted in the handbook. Higher confidence ratings were given to exposure factors where the available data were representative of the population of interest.

Currency of Information: More confidence was placed in studies that were sufficiently recent to represent current exposure conditions. This is an important consideration for those factors that change with time. Older data were evaluated and considered in instances where the variability of the exposure factor over time was determined to be insignificant or unimportant. In some cases, recent data were very limited. Therefore, the data provided in these instances were the only available data. Limitations on the age of the data were noted. Recent studies are more likely to use state-of-the-art methodologies that reflect advances in the exposure assessment field. Consequently, exposure factor recommendations based on current data were given higher confidence ratings than those based on older data, except in cases where the age of the data would not affect the recommended values.

Adequacy of data collection period: Because most users of the handbook are primarily addressing chronic exposures, studies were sought that utilized the most appropriate techniques for collecting data to characterize long-term behavior. Higher confidence ratings were given to exposure factor recommendations that were based on an adequate data collection period.

(3) *Clarity and completeness*: *The degree of clarity and completeness with which the data, assumptions, methods, quality assurance, sponsoring organizations and analyses employed to generate the information are documented.* Clarity and completeness was evaluated based on the following criteria.

Accessibility: Studies that the user could access in their entirety, if needed, were preferred.

Reproducibility: Studies that contained sufficient information so that methods could be reproduced, or could be evaluated, based on the details of the author's work, were preferred.

Quality Assurance: Studies with documented quality assurance/quality control measures were preferred. Higher confidence ratings were given to exposure factors that were based on studies where appropriate quality assurance/quality control measures were used.

(4) Variability and uncertainty: The variability and uncertainty (quantitative and qualitative) in the information or the procedures, measures, methods or models are evaluated and characterized. Variability arises from true heterogeneity across people, places or time and can affect the precision of exposure estimates and the degree to which they can be generalized. The types of variability include: spatial, temporal, and inter-individual. Uncertainty represents a lack of knowledge about factors affecting exposure or risk and can lead to inaccurate or biased estimates of exposure. The types of uncertainty include: scenario, parameter, and model. The uncertainty and variability associated with the studies was evaluated based on the following criteria.

> **Variability in the population:** Studies were sought that characterized any variability within populations. The variability associated with the studies presented in this handbook is characterized as described in Section 1.5. Higher confidence ratings were given to exposure factors that were based on studies where variability was well characterized.

> **Uncertainty:** Studies were sought with minimal uncertainty in the data, which was judged by evaluating all the considerations listed above. Studies were preferred that identified uncertainties, such as those due to inherent variability in environmental and exposure-related parameters or possible measurement error. Higher confidence ratings were given to exposure factors based on studies where uncertainty had been minimized.

(5) Evaluation and review: The information or the procedures, measures, methods or models are independently verified, validated, and peer reviewed. Relevant factors that were considered included:

> **Peer review:** Studies selected were those from the peer-reviewed literature and final government reports. Unpublished and internal or interim reports were avoided.

> **Number and agreement of studies:** Higher confidence was placed on recommendations where data were available from more than one key study and there was good agreement between studies.

1.5 APPROACH USED TO DEVELOP RECOMMENDATIONS FOR EXPOSURE FACTORS

As discussed above, the U.S. EPA first reviewed the literature pertaining to a factor and determined key studies. These key studies were used to derive recommendations for the values of each factor. The recommended values were derived solely from the U.S. EPA's interpretation of the available data. Different values may be appropriate for the user in consideration of policy, precedent, strategy, or other factors such as site-specific information. The U.S. EPA's procedure for developing recommendations was as follows:

(1) Study Review and Evaluation: Key studies were evaluated in terms of both quality and relevance to specific populations (general U. S. population, age groups, gender, etc.). The criteria for assessing the quality of studies are described in Section 1.4.

(2) Single versus Multiple Key Studies: If only one study was classified as key for a particular factor, the mean value from that study was selected as the recommended central value for that population. If multiple key studies with reasonably equal quality, relevance, and study design information were available, a weighted mean (if appropriate, considering sample size and other statistical factors) of the studies was chosen as the recommended mean value. If the key studies were judged to be unequal in quality, relevance, or study design, the range of means is presented and the user of this handbook must employ judgment in selecting the most appropriate value for the population of interest. Recommendations for upper percentiles, when multiple studies were available, were calculated as the midpoint of the range of upper percentile values of the studies for each age group where data were available.

(3) Variability: The variability of the factor across the population is discussed. For recommended values, as well as for each of the studies on which the recommendations are base, variability is characterized in one or more of three ways: (1) as a table with various percentiles or ranges of values; (2) as analytical distributions with specified parameters; and/or (3) as a qualitative discussion. Analyses to fit standard or parametric distributions (e.g., normal, lognormal) to the exposure data have not been performed by the authors of this handbook, but have been reproduced as they were found in the literature. Recommendations on the use of these distributions are made where appropriate based on the adequacy of the supporting data. The list of exposure factors and the way in which variability has been characterized throughout this handbook (i.e., average, median, upper percentiles, multiple percentiles, fitted distribution) are presented in Table 1-1.

In the providing recommendations for the various exposure factors, an attempt was made to present percentile values that are consistent with the exposure estimators defined in *Guidelines for Exposure Assessment* (U.S. EPA, 1992a) (i.e., mean, 50th, 90th, 95th, 98th, and 99.9th percentile). However, this was not always possible, because the data available were limited for some factors, or the authors of the study did not provide such information. It is important to note, however, that these percentiles were discussed in the guidelines within the context of risk descriptors and not individual exposure factors. For example, the guidelines state that the assessor may derive a high-end estimate of exposure by using maximum or near maximum values for one or more sensitive exposure factors, leaving others at their mean value. The term "upper percentile" is used throughout this handbook, and it is intended to represent values in the upper tail (i.e., between 90th and 99.9th percentile) of the distribution of values for a particular exposure factor.

(4) Uncertainty: Uncertainties are discussed in terms of data limitations, the range of circumstances over which the estimates were (or were not) applicable, possible biases in the values themselves, a statement about parameter uncertainties (measurement error, sampling error) and model or scenario uncertainties

if models or scenarios were used to derive the recommended value. A discussion of variability and uncertainty for exposure factors is presented in Chapter 2 of this handbook.

(5) Confidence Ratings: Finally, the U.S. EPA assigned a confidence rating of low, medium or high to each recommended value. This rating is not intended to represent an uncertainty analysis; rather, it represents the U.S. EPA's judgment on the quality of the underlying data used to derive the recommendation. This judgment was made using the General Assessment Factors (GAFs) described in Section 1.4. Table 1-2 provides an adaptation of the GAFs, as they pertain to the confidence ratings for the exposure factor recommendations. Clearly, there is a continuum from low to high, and judgment that was used to determine these ratings. Recommendations given in this handbook are accompanied by a discussion of the rationale for their rating.

It is important to note that the study elements listed in Table 1-2 do not have the same weight when arriving at the overall confidence rating for the various exposure factors. The relative weight of each of these elements for the various factors were subjective and based on the professional judgement of the authors of this handbook. Also, the relative weights depend on the exposure factor of interest. For example, the adequacy of the data collection period may be more important when determining usual intake of foods in a population, but it is not as important for factors where long-term variability may be small, such as tapwater intake. In the case of tapwater intake, the currency of the data was a critical element in determining the final rating. In general, most studies ranked high with regard to "level of peer review," "accessibility," "focus on the factor of interest," and "data pertinent to the U.S." because the U.S. EPA specifically sought studies for the handbook that met these criteria.

The elements in Table 1-2 were important considerations for inclusion of a study in this handbook. However, a high score for these elements did not necessarily translate into a high overall score. Other considerations went into determining the overall score. One such consideration was the ease at which the exposure factor of interest could be measured. For

example, soil ingestion by children can be estimated by measuring, in the feces of children, the levels of certain elements found in soil. Body weight, however, can be measured directly, and it is therefore a more reliable measurement. The fact that soil ingestion is more difficult to measure than body weight is reflected in the overall confidence rating given to both of these factors. In general, the better the methodology used to measure the exposure factor, the higher the confidence in the value.

(6) Recommendation Tables: The U.S. EPA developed a table at the beginning of each chapter that summarizes the recommended values for the relevant factor. Table ES-1 of the Executive Summary of this handbook summarizes the principal exposure factors addressed in this handbook and provides the confidence ratings for each exposure factor.

1.6 SUGGESTED REFERENCES FOR USE IN CONJUNCTION WITH THIS HANDBOOK

Some of the steps for performing an exposure assessment are: (1) identifying source of the environmental contamination and the media that transports the contaminant; (2) determining the contaminant concentration; (3) determining the exposure scenarios, and pathways and routes of exposure; (4) determining the exposure time, frequency, and duration; and (5) identifying the exposed population. Many of the issues related to characterizing exposure from selected exposure pathways have been addressed in a number of existing U.S. EPA documents. Some of these provide guidance while others demonstrate various aspects of the exposure process. These include, but are not limited, to the following references listed in chronological order:

- *Methods for Assessing Exposure to Chemical Substances, Volumes 1-13* (U.S. EPA, 1983-1989);

- *Standard Scenarios for Estimating Exposure to Chemical Substances During Use of Consumer Products* (U.S. EPA, 1986a);

- *Selection Criteria for Mathematical Models Used in Exposure Assessments: Surface Water Models* (U.S. EPA, 1987);

- *Selection Criteria for Mathematical Models Used in Exposure Assessments: Groundwater Models* (U.S. EPA, 1988);

- *Risk Assessment Guidance for Superfund, Volume I, Part A, Human Health Evaluation Manual* (U.S. EPA, 1989);

- *Methodology for Assessing Health Risks Associated with Indirect Exposure to Combustor Emissions* (U.S. EPA, 1990);

- *Risk Assessment Guidance for Superfund, Volume I, Part B, Development of Preliminary Remediation Goals* (U.S. EPA, 1991a);

- *Risk Assessment Guidance for Superfund, Volume I, Part C, Risk Evaluation of Remedial Alternatives* (U.S. EPA, 1991b);

- *Guidelines for Exposure Assessment* (U.S. EPA, 1992a);

- *Dermal Exposure Assessment: Principles and Applications* (U.S. EPA, 1992b);

- *Estimating Exposures to Dioxin-Like Compounds* (U.S. EPA, 1994a);

- *Soil Screening Guidance* (U.S. EPA 1996a);

- *Series 875 Occupational and Residential Exposure Test Guidelines - Final Guidelines - Group A - Application Exposure Monitoring Test Guidelines* (U.S. EPA 1996b);

- *Series 875 Occupational and Residential Exposure Test Guidelines - Group B - Post Application Exposure Monitoring Test Guidelines* (U.S. EPA 1996c);

- *Policy for Use of Probabilistic Analysis in Risk Assessment at the U.S. Environmental Protection Agency*, (U.S. EPA, 1997b);

- *Guiding Principles for Monte Carlo Analysis* (U.S. EPA, 1997c);

- *Sociodemographic Data for Identifying Potentially Highly Exposed Populations* (U.S. EPA, 1999);

- *Options for Developing Parametric Probability Distributions for Exposure Factors* (U.S. EPA 2000b);

- *Risk Assessment Guidance for Superfund, Volume I, Part D, Standardized Planning, Reporting, and Review of Superfund Risk Assessments* (U.S. EPA, 2001a);

- *Risk Assessment Guidance for Superfund Volume III, Part A, Process for Conducting Probabilistic Risk Assessments* (U.S. EPA, 2001b);

- *Framework for Cumulative Risk Assessment* (U.S. EPA, 2003b);

- *Example Exposure Scenarios* (U.S. EPA, 2003c);

- *Risk Assessment Guidance for Superfund, Volume I, Part E, Supplemental Guidance for Dermal Risk Assessment* (U.S. EPA, 2004);

- *Guidance on Selecting Age Groups for Monitoring and Assessing Childhood Exposures to Environmental Contaminants* (U.S. EPA, 2005a);

- *Cancer Guidelines for Carcinogen Risk Assessment Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens* (U.S. EPA, 2005b);

- *Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens* (U.S. EPA, 2005c);

- *Protocol for Human Health Risk Assessment Protocol for Hazardous Waste Combustion Facilities* (U.S. EPA, 2005d);

- *A Framework for Assessing Health Risk of Environmental Exposures to Children* (Final). (U.S. EPA 2006d); and

- *Concepts, methods, and data sources for cumulative health risk assessment of multiple chemicals, exposures and effects: a resource document* (Final) (U.S. EPA, 2008).

These documents may serve as valuable information resources to assist in the assessment of exposure. The reader is encouraged to refer to them for more detailed discussion.

1.7 THE USE OF AGE GROUPINGS WHEN ASSESSING EXPOSURE

When this handbook was first published in 2002, no specific guidance existed with regard to which age groupings should be used when assessing children's exposure. Age groupings varied from case to case and among Program Offices within the U.S. EPA. They depended on availability of data and were often based on professional judgement. More recently, the U.S. EPA has endeavored to establish a consistent set of age groupings and publish guidance on this topic (U.S. EPA 2005a). This revision of the handbook attempts to present data in a manner consistent with the U.S. EPA's recommended set of age groupings.

The development of standardized age bins was the subject of discussion in a 2000 workshop sponsored by the U.S. EPA Risk Assessment Forum. The workshop was titled "Issues Associated with Considering Developmental Changes in Behavior and Anatomy When Assessing Exposure to Children" (U.S. EPA, 2001c). The purpose of this workshop was to gain insight and input into factors that need to be considered when developing standardized age bins and identify future research necessary to accomplish these goals. Panelists were divided into two groups. One

group focused their discussions on defining and characterizing the important facets of behavioral development during childhood, while the other group focused on defining and characterizing physiological development during childhood. During the workshop, it was recognized that the ultimate goal of exposure assessment is to develop a day-to-day model of human life that can predict the chemical exposures an individual is likely to face at any point in life. However, this is not likely to be accomplished in the near future, and assessors often need to classify individuals into age bins in order to simplify the exposure model. The recommendations listed below are those of the panel members and were considered by the U.S. EPA in the development of age groupings:

- Panelists agreed that child development is a series of discrete events, but these events occur along a contiuum.

- Age grouping/bins are a useful guide to fulfill the Agency's immediate need, but are only a crude approximation of an underlying distribution. Ultimately, sufficient data should be gathered to develop a continuous multivariate model that can replace bins.

- Adequacy of existing exposure data is highly variable.

- A considerable amount of additional information already exists, but it is dispersed in the literature. It was recommended that the U.S. EPA consults with experts in developmental biology, physiology, pharmacology, and toxicology and conducts an in-depth review of the literature.

- Long term research should include the development of integrated data sets that combines information about the exposure factors with biomarkers of exposure and effects.

- The definition of age groups/bins for childhood exposure assessment are

inextricably linked to toxicokinetic and toxicodynamic issues.

- The two break out groups (i.e., behavioral and physiological) offered the following preliminary ideas for age groupings:

Age grouping based on behavioral characteristics
        0-2 months
        2 - 6 months
        6-12 months
        1-2 years
        2-6 years
        6-11 years
        11-16 years
        16-21 years
Age grouping based on physiological characteristics
        0-1 month
        1-6 months
        6-12 months
        1- 3 years
        3-9 years
        9-21 years

One can observe that there was fairly good agreement among the two groups with regard to the age groupings that are important for infants and toddlers. However, there was some disagreement with regard to the older children. Appropriate age groupings depend not only on behavioral and physiological characteristics, but also on the specific scenario being studied and chemical of concern.

Based upon consideration of the findings of the technical workshop, as well as analysis of available data, U.S. EPA developed guidance that established a set of recommended age groups for development of exposure factors for children entitled "*Guidance for Selecting Age Groups for Monitoring and Assessing Childhood Exposures to Environmental Contaminants*" (U.S. EPA, 2005a). This revision of the handbook was developed specifically to present exposure factors data in a manner consistent with U.S. EPA's recommended set of childhood age groupings. The recommended age groups (U.S. EPA, 2005a) are as follows:

        Birth to <1 month

1 to <3 months
3 to <6 months
6 to <12 months
1 to <2 years
2 to <3 years
3 to <6 years
6 to <11 years
11 to <16 years
16 to <21 years

1.8 CONSIDERING LIFESTAGE WHEN CALCULATING EXPOSURE AND RISK

A key component of U.S. EPA's *Guidance on Selecting Age Groups for Monitoring and Assessing Childhood Exposures to Environmental Contaminants* (U.S. EPA 2005a) involves the need to sum age-specific differences in exposure across time when assessing long-term exposure, as well as integrating these age-specific exposures with age-specific differences in toxic potency in those cases where information exists to describe such differences: an example is carcinogens that act via a mutagenic mode of action (*Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens* - U.S. EPA, 2005c). When assessing chronic risks (i.e., exposures greater than 10 percent of human lifespan), rather than assuming a constant level of exposure for 70 years (usually consistent with an adult level of exposure), the Agency is now recommending that assessors calculate chronic exposures by summing time-weighted exposures that occur at each lifestage; this handbook provides data arrayed by childhood age in order to follow this new guidance (U.S. EPA 2005a). This approach is expected to increase the accuracy of risk assessments, because it will take into account lifestage differences in exposure. Depending on whether body-weight-adjusted childhood exposures are either smaller or larger compared to those for adults, calculated risks could either decrease or increase when compared with the historical approach of assuming a lifetime of a constant adult level of exposure.

The *Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens* also recommended that in those cases where age-related differences in toxicity were also found to occur, differences in both toxicity and exposure would need to be integrated across all relevant age intervals. This guidance describes such a case for carcinogens that act via a mutagenic mode of action, where age dependent potency adjustments factors (ADAFs) of 10x and 3x are recommended for children ages birth < 2 years, and 2 < 16 years, respectively when there is exposure during those years and available data are insufficient to derive chemical-specific adjustment factors.

Table 1-3, along with Chapter 6 of the "*Supplemental Guidance*" have been developed to help the reader understand how to use the new sets of exposure and potency age groupings when calculating risk through the integration of lifestage specific changes in exposure and potency.

Thus, Lifetime Cancer Risk (for a population with average life expectancy of 70 years) = ? (Exposure x Duration/70 yrs x Potency x ADAF) summed across all the age groups presented in Table 1-3. This is a departure from the way cancer risks have historically been calculated based upon the premise that risk is proportional to the daily average of the long term adult dose.

1.9 FUNDAMENTAL PRINCIPLES OF EXPOSURE ASSESSMENT

The definition of exposure as used by the International Programme on Chemical Safety (IPCS, 2001) is the "contact of an organism with a chemical or physical agent, quantified as the amount of chemical available at the exchange boundaries of the organism and available for absorption." This means contact with the visible exterior of a person such as the skin, and openings such as the mouth, nostrils, and lesions. The process of a chemical entering the body can be described in two steps: contact (exposure) followed by entry (crossing the boundary). In the context of environmental risk assessment, risk to an individual or population can be represented as a continuum from the source through exposure to dose to effect as shown in Figure 1-1 (U.S. EPA, 2003d; IPCS, 2006). The process begins with a chemical or agent released from a source into the environment. Once in the environment, the chemical or agent can be transformed and transported through the environment via air, water, soil, dust, and diet. Individuals become in contact with the chemical through inhalation,

ingestion, or skin/eye contact. The individual's activity patterns as well as the concentration of the chemical will determine the magnitude, frequency, and duration of the exposure. The exposure becomes an absorbed dose when the chemical crosses an absorption barrier. When the chemical or its metabolites interact with a target tissue, it becomes a target tissue dose, which may lead to an adverse health outcome. The text under the boxes in Figure 1-1 indicates the specific information that may be needed to characterize each box.

1.9.1   Dose Equations

Starting with a general integral equation for exposure (U.S. EPA, 1992a), several dose equations can be derived depending upon boundary assumptions.

One of the more useful of these derived equations is the Average Daily Dose (ADD). The ADD, which is used for many noncancer effects, averages exposures or doses over the period of time exposure occurred. The ADD can be calculated by averaging the potential dose over body weight and an averaging time.

$$ADD_{pot} = \frac{External\ Dose}{Body\ Weight\ \times\ Averaging\ Time} \quad (Eqn\ 1\text{-}1)$$

The exposure can be expressed as follows:

$$External\ Dose = C \times IR \times E \quad (Eqn\ 1\text{-}2)$$

Where:
C = Contaminant Concentration
IR = Intake Rate
ED = Exposure Duration

Contaminant concentration is the concentration of the contaminant in the medium (air, food, soil, etc.) contacting the body and has units of mass/volume or mass/mass.

The intake rate refers to the rates of inhalation, ingestion, and dermal contact, depending on the route of exposure. For ingestion, the intake rate is simply the amount of food containing the contaminant of interest that an individual ingests during some specific time period (units of mass/time).

Much of this handbook is devoted to rates of ingestion for some broad classes of food. For inhalation, the intake rate is the rate at which contaminated air is inhaled. Factors presented in this handbook that affect dermal exposure are skin surface area and estimates of the amount of soil that adheres to the skin.

The exposure duration is the length of time of contaminant contact. The length time a person lives in an area, frequency of bathing, time spent indoors versus outdoors, etc., all affect the exposure duration. Chapter 16, Activity Factors, gives some examples of population behavior/activity patterns that may be useful for estimating exposure durations.

When the above parameter values IR and ED remain constant over time, they are substituted directly into the exposure equation. When they change with time, a summation approach is needed to calculate exposure. In either case, the exposure duration is the length of time exposure occurs at the concentration and the intake rate specified by the other parameters in the equation.

Note that the advent of childhood age groupings means that separate ADD's should be calculated for each age group considered. Chronic exposures can then be calculated by summing across each lifestage-specific ADD.

Cancer risks have traditionally been calculated in those cases where a linear non-threshold model is assumed, in terms of lifetime probabilities by utilizing dose values presented in terms of lifetime ADDs (LADDs). The LADD takes the form of the Equation 1-1, with lifetime replacing averaging time. While the use of LADD may be appropriate when developing screening level estimates of cancer risk, as discussed in Section 1.8 above, the U.S. EPA is now recommending that risks should be calculated by integrating exposures or risks throughout all lifestages (U.S. EPA, 1992a).

For some types of analyses, dose can be expressed as a total amount (with units of mass, e.g., mg) or as a dose rate in terms of mass/time (e.g., mg/day), or as a rate normalized to body mass (e.g., with units of mg of chemical per kg of body weight per day (mg/kg-day)). The LADD is usually expressed in terms of mg/kg-day or other mass/mass-time units.

In most cases (inhalation and ingestion exposures), the dose-response parameters for carcinogenic risks have been adjusted for the

difference in absorption across body barriers between humans and the experimental animals used to derive such parameters. Therefore, the exposure assessment in these cases is based on the potential dose, with no explicit correction for the fraction absorbed. However, the exposure assessor needs to make such an adjustment when calculating dermal exposure and in other specific cases when current information indicates that the human absorption factor used in the derivation of the dose-response factor is inappropriate.

For carcinogens, the duration of a lifetime has traditionally been assigned the nominal value of 70 years as a reasonable approximation. For exposure estimates to be used for assessments other than carcinogenic risk, various averaging periods have been used. For acute exposures, the doses are usually averaged over a day or a single event. For nonchronic noncancer effects, the time period used is the actual period of exposure (exposure duration). The objective in selecting the exposure averaging time is to express the exposure in a way which can be combined with the dose-response relationship to calculate risk.

The body weight to be used in the exposure Equation 1-1 depends on the units of the exposure data presented in this handbook. For example, for food ingestion, the body weights of the surveyed populations were known in the USDA surveys, and they were explicitly factored into the food intake data in order to calculate the intake as g/kg body weight-day. In this case, the body weight has already been included in the "intake rate" term in Equation 1-2, and the exposure assessor does not need to explicitly include body weight.

The units of intake in this handbook for the incidental ingestion of soil and dust are not normalized to body weight. In this case, the exposure assessor will need to use (in Equation 1-1) the average weight of the exposed population during the time when the exposure actually occurs. When making body weight assumptions, care must be taken that the values used for the population parameters in the dose-response analysis are consistent with the population parameters used in the exposure analysis. Intraspecies adjustments based on lifestage can be made using a scaling factor of $BW^{3/4}$ (U.S. EPA 2006d, 2006e). Some of the parameters (primarily

concentrations) used in estimating exposure are exclusively site specific, and therefore default recommendations should not be used. It should be noted that body weight is correlated with food consumption rates and inhalation rates.

The link between the intake rate value and the exposure duration value is a common source of confusion in defining exposure scenarios. It is important to define the duration estimate so that it is consistent with the intake rate:

- The intake rate can be based on an individual event (e.g., serving size per event). The duration should be based on the number of events or, in this case, meals.

- The intake rate also can be based on a long-term average, such as 10 g/day. In this case the duration should be based on the total time interval over which the exposure occurs.

The objective is to define the terms so that, when multiplied, they give the appropriate estimate of mass of contaminant contacted. This can be accomplished by basing the intake rate on either a long-term average (chronic exposure) or an event (acute exposure) basis, as long as the duration value is selected appropriately.

Inhalation dosimetry is employed to derive the human equivalent exposure concentrations on which inhalation unit risks, and reference concentrations, are based (U.S. EPA, 1994b). U.S. EPA has traditionally approximated children's respiratory exposure by using adult values, although a recent review (Ginsberg et al., 2005) concluded that there may be some cases where young children's greater inhalation rate per body weight or pulmonary surface area as compared to adults can result in greater exposures than adults. The implications of this difference for inhalation dosimetry and children's risk assessment were discussed at a peer involvement workshop hosted by the U.S.EPA in 2006 (Foos et al., 2008).

Consideration of lifestage-particular physiological characteristics in the dosimetry analysis may result in a refinement to the human equivalent concentration to insure relevance in risk assessment across lifestages, or might conceivably conclude with multiple human equivalent concentrations, and

corresponding inhalation unit risk values (e.g., separate for childhood and adulthood) (U.S. EPA, 2005b). The RfC methodology, which is described in *Methods for Derivation of Inhalation Reference Concentrations and Applications of Inhalation Dosimetry* (U.S. EPA, 1994b), allows the user to incorporate population-specific assumptions into the models. The reader is referred to U.S. EPA guidance (U.S. EPA, 1994b) on how to make these adjustments.

There are no specific exposure factor assumptions in the derivation of Reference Doses (RfDs). The assessment of the potential for adverse health effects in infants and children is part of the overall hazard and dose-response assessment for a chemical. Available data pertinent to children's health risks are evaluated along with data on adults and the no-observed-adverse-effect-level (NOAEL) or benchmark dose (BMD) for the most sensitive critical effect(s), based on consideration of all health effects. By doing this, protection of the health of children will be considered along with that of other sensitive populations. In some cases, it is appropriate to evaluate the potential hazard to children separately from the assessment for the general population or other population subgroups.

1.9.2 Use of Exposure Factors Data in Probabilistic Analyses

Although this handbook is not intended to provide complete guidance on the use of Monte Carlo and other probabilistic analyses, some of the data in this handbook may be appropriate for use in probabilistic assessments. The use of Monte Carlo or other probabilistic analysis requires characterization of the variability of exposure factors and requires the selection of distributions or histograms for the input parameters of the dose equations presented in Section 1.9.1. The following suggestions are provided for consideration when using such techniques:

- The exposure assessor should only consider using probabilistic analysis when there are credible distribution data (or ranges) for the factor under consideration. Even if these distributions are known, it may not be necessary to apply this technique. For example, if only average exposure values are needed, these can often be computed accurately by using average values for each of the input parameters unless a non-linear model is used. Probabilistic analysis is also not necessary when conducting assessments for screening purposes, i.e., to determine if unimportant pathways can be eliminated. In this case, bounding estimates can be calculated using maximum or near maximum values for each of the input parameters. Alternatively, the assessor may use the maximum values for those parameters that have the greatest variance.

- It is important to note that the selection of distributions can be highly site-specific and dependent on the purpose of the assessment. In some cases the selection of distributions are driven by specific legislation. It will always involve some degree of judgment. Distributions derived from national data may not represent local conditions. The assessor needs to evaluate the site-specific data, when available, to assess their quality and applicability. The assessor may decide to use distributional data drawn from the national or other surrogate population. In this case, it is important that the assessor address the extent to which local conditions may differ from the surrogate data.

- It is also important to consider the independence/dependence of variables and data used in a simulation. For example, it may be reasonable to assume that ingestion rate and contaminant concentration in foods are independent variables, but ingestion rate and body weight may or may not be independent.

In addition to a qualitative statement of uncertainty, the representativeness assumption should be appropriately addressed as part of a sensitivity analysis.

- Distribution functions to be used in probabilistic analysis may be derived by fitting an appropriate function to empirical

data. In doing this, it should be recognized that in the lower and upper tails of the distribution the data are scarce, so that several functions, with radically different shapes in the extreme tails, may be consistent with the data. To avoid introducing errors into the analysis by the arbitrary choice of an inappropriate function, several techniques can be used. One technique is to avoid the problem by using the empirical data itself rather than an analytic function. Another is to do separate analyses with several functions that have adequate fit but form upper and lower bounds to the empirical data. A third way is to use truncated analytical distributions. Judgment must be used in choosing the appropriate goodness-of-fit test. Information on the theoretical basis for fitting distributions can be found in a standard statistics text, (e.g., Gilbert, 1987, among others). Off-the-shelf computer software can be used to statistically determine the distributions that fit the data. Other software tools are available to identify outliers and for conducting Monte Carlo simulations.

- If only a range of values is known for an exposure factor, the assessor has several options.
  - keep that variable constant at its central value.
  - assume several values within the range of values for the exposure factor.
  - calculate a point estimate(s) instead of using probabilistic analysis.
  - assume a distribution. (The rationale for the selection of a distribution should be discussed at length.) There are, however, cases where assuming a distribution is not recommended. These include:
    -- data are missing or very limited for a key parameter;
    -- data were collected over a short time period and may not represent long term trends (the respondent usual behavior) - examples include: food consumption surveys; activity pattern data;
    -- data are not representative of the population of interest because sample size was small or the population studied was selected from a local area and was

therefore not representative of the area of interest; for example, soil ingestion by children; and
    -- ranges for a key variable are uncertain due to experimental error or other limitations in the study design or methodology; for example, soil ingestion by children.

1.10 CUMULATIVE EXPOSURES

The U.S. EPA recognizes that children may be exposed to mixtures of chemicals both indoors and outdoors through more than one pathway. New directions in risk assessments in the U.S. EPA put more emphasis on total exposures via multiple pathways (U.S. EPA, 2003d, U.S. EPA, 2008). Over the last several years, the U.S. EPA has developed a methodology for assessing risk from multiple chemicals (U.S. EPA, 1986b, 2000c). For more information, the reader is referred to the U.S. EPA's *Framework for Cumulative Risk Assessment* (U.S. EPA, 2003b).

1.11 ORGANIZATION

The handbook is organized as follows:

Chapter 1	Introduction
Chapter 2	Variability and uncertainty
Chapter 3	Ingestion of water and other select liquids
Chapter 4	Non-dietary ingestion
Chapter 5	Soil and dust ingestion
Chapter 6	Inhalation rates
Chapter 7	Dermal exposure factors
Chapter 8	Body weight
Chapter 9	Intake of fruits and vegetables
Chapter 10	Intake of fish and shellfish

Recommended values for exposure factors are presented at the beginning of each chapter, followed by detailed discussions of the data on which these recommendations are based. Because of the large number of tables in this handbook, tables are presented at the end of each chapter, before the appendices, if any.

1.12 REFERENCES FOR CHAPTER 1

AAP (1997) Child Health Issues for the Second Session of the 106th Congress. Environmental Health. American Academy of Pediatrics Department of Federal Affairs 601 13th Street, NW Suite 400 North Washington, DC 20005. AAP Washington Office Child Health Issues for the Second Session of the 106th Congress: Environmental Health. Available online at http://www.aap.org/advocacy/washing/chieh/htm.

Breysee, P.N.; Buckley, T.J.; Williams, D.; Beck, C.M.; Jo, S.; Merriman, B.; Kanchanaraksa, S.; Swartz, L.J.; Callahan, K.A.; Butz, A.M.; Rand, C.S.; Diette, G.B.; Krishman, J.A.; Moseley, A.M.; Curlin-Brosnan, J.; Durkin, N.B.; Eggleston, P.A. (2005) Indoor exposures to air pollutants and allergens in the homes of asthmatic children in inner-city Baltimore. Environ Res. 98:167-176.

Clewell, H.J.; Gentry, P.R.; Covington, T.R.; Sarangapani, R.; Teeguarden, J.G. (2004) Evaluation of the potential impact of age- and gender-specific pharmacokinetic differences on tissue dosimetry. Toxicol Sci. 79:381-393.

Curwin, B.D.; Hein, M.J.; Sanderson, W.T.; Striley, C.; Heederik, D.; Kromhout, H.; Reynolds, J.j.; Alavanja, M.C. (2007) Pesticide dose estimates for children of Iowa farmers and non-farmers. Environ Res. 105: 307-315.

EO (1997) Executive Order 13045. Protection of Children for Environmental Health Risks and Safety Risks. Available on line at http://yosemite.epa.gov/ochp/ochpweb.nsf/content/whatwe_executiv.htm.

Eskenazi, B.; Bradman, A.; Castriona, R. (1999) Exposure of children to organophosphate pesticides and their potential adverse health effects. Environ Health Perspect. 107(3):409-419.

Foos, B.; Marty, M.; Schwartz, J.; Bennet, W.; Moya, J.; Jarabek, A.M.; Salmon, A.G. (2008) Focusing on children's inhalation dosimetry and health effects for risk assessment: an introduction. J Toxicol Environ Health, Part A, 71(3):149-165.

Garry, V.F. (2004) Pesticides and children. Toxicol Appl Pharmaol. 198(2004):152-163.

Gilbert, R.O. (1987) Statistical methods for environmental pollution monitoring. New York: Van Nostrand Reinhold.

Ginsberg, G.; Hattis, D.; Sonawame, B.; Russ, A.; Banati, P.; Kozlak, M.; Smolenski, S.; Goble, R. (2002) Evaluation of child/adult pharmacokinetic differences from a database derived from the therapeutic drug literature. Toxicol Sci. 66:185-200.

Gurunathan, S.; Robson, M.; Freeman N.; Buckley, B.; Roy, A.; Meyer, R.; Bukowski, J.; Lioy, P.J. (1998) Accumulation of chloropyrifos on residential surfaces and toys accessible to children. Environ Health Perspect. 106(1):9-16.

IPCS (2001) Glossary of exposure assessment-related terms: a compilation. IPCS Exposure Terminology Subcommittee, International Programme on Chemical Safety, World Health Organization. Available on line at http://www.who.int/ipcs/publications/methods/harmonization/en/compilation_nov2001.pdf

IPCS (2006) Principles for Evaluating Health Risks in Children Associated with Exposure to Chemicals. Environmental Health Criteria 237. International Programme on Chemical Safety, World Health Organization.

Landrigan, P.J.; Sonawane, B.; Butler, R.N.; Transande, L.; Callan, R. (2005) Early environmental origins of neurodegenerative disease in later life. Environ Health Perspect. 113(9):1230-1233.

Lewis, R. G.; Fortune C.; Willis, R. D.; Camann, D. E.; Antley, J. T. (1999) Distribution of pesticides and polycyclic aromatic hydrocarbons in house dust as a function of particle size. Environ Health Perspect. 107(9):721-726.

Myers, G.J.; Davidson, P.W. (2000) Does methylmercury have a role in causing developmental disabilities in children? Environ Health Perspect. 108(3):413-419.

Nishioka, M.G.; Burkholder, H.M.; and Brinkman, M.C.; Lewis, R.G. (1999) Distribution of 2,4-dihlorophenoxyacetic acid in floor dust throughout homes following homeowner and commercial lawn application: quantitative effects of children, pets, and shoes. Environ Sci Technol. 33:1359-1365.

Selevan, S.G.; Kimmel, C.A.; Mendola, P. (2000) Identifying critical windows of exposure for children's health- monograph based on papers developed from the Workshop: Identifying Critical Windows of Exposure for Children's Health held September 14-15, 1999 in Richmond, VA. Environ Health Perspect. 108(3):451-455.

U.S. EPA. (1983-1989) Methods for assessing exposure to chemical substances. Volumes 1 - 13. Office of Toxic Substances, Exposure Evaluation Division, Washington, DC.

U.S. EPA. (1986a) Standard scenarios for estimating exposure to chemical substances during use of consumer products. Volumes I and II. Office of Toxic Substance, Exposure Evaluation Division, Washington, DC.

U.S. EPA. (1986b) Guidance for the health risk assessment of chemical mixtures. Risk Assessment Forum, Washington, DC.

EPA/630/R-98/002. Available on line at http://cfpub.epa.gov/si/si_public_record_Report.cfm?dirEntryID=20533

U.S. EPA. (1987) Selection criteria for mathematical models used in exposure assessments: surface water models. Exposure Assessment Group, Office of Health and Environmental Assessment, Washington, DC. WPA/600/8 87/042. Available from NTIS, Springfield, VA; PB-88-139928/AS.

U.S. EPA. (1988) Selection criteria for mathematical models used in exposure assessments: groundwater models. Exposure Assessment Group, Office of Health and Environmental Assessment, Washington, DC. EPA/600/8 88/075. Available from NTIS, Springfield, VA; PB-88-248752/AS.

U.S. EPA. (1989) Risk assessment guidance for Superfund. Volume I Human health evaluation manual: Part A. Interim Final. Office of Solid Waste and Emergency Response, Washington, DC. EPA/540-1-89/002. Available online at http://www.epa.gov/oswer/riskassessment/ragsa/index.htm.

U.S. EPA. (1990) Methodology for assessing health risks associated with indirect exposure to combustor emissions. EPA 600/6-90/003. Available from NTIS, Springfield, VA; PB-90-187055/AS.

U.S. EPA. (1991a) Risk assessment guidance for Superfund. Volume I Human health evaluation manual: Part B, Development of preliminary remediation goals. Office of Solid Waste and Emergency Response, Washington, DC. EPA/540/R-92-003. Available online at http://www.epa.gov/oswer/riskassessment/ragsb/index.htm.

U.S. EPA. (1991b) Risk assessment guidance for Superfund. Volume I Human health evaluation manual: Part C, Risk evaluation of remedial alternatives. Office of Solid Waste and Emergency Response, Washington, DC. Publication 9285.7-01C. Available online at http://www.epa.gov/oswer/riskassessment/ragsc/index.htm.

U.S. EPA. (1992a) Guidelines for exposure assessment. Washington, DC: Office of Research and Development, Office of Health and Environmental Assessment. EPA/600/Z-92/001. Available at http://www.epa.gov/NCEA/raf/pdfs/exposure.pdf.

U.S. EPA. (1992b) Dermal exposure assessment: principles and applications. Washington, DC: Office of Health and Environmental Assessments. EPA/600/8-9/011F. Available online at http://www.epa.gov/ncea/pdfs/efh/references/DEREXP.PDF.

U.S. EPA. (1994a) Estimating exposures to dioxin-like compounds. Draft Report. Office of Research and Development, Washington, DC. EPA/600/6-88/005Cb.

U.S. EPA. (1994b) Methods for derivation of inhalation reference concentrations and applications of inhalation dosimetry Washington, DC. EPA/600/8-90/066F.

U.S.EPA (1996a) Soil screening guidance. Office of Solid Waste and Emergency Response, Washington, DC. EPA/540/F-95/041. Available online at http://www.epa.gov/superfund/health/conmedia/soil/index.htm

U.S.EPA. (1996b) Series 875 Occupational and Residential Exposure Test Guidelines - Final Guidelines - Group A - Application Exposure Monitoring Test Guidelines. EPA712-C96-261. Available online at http://www.epa.gov/opptsfrs/publications/OPPTS_Harmonized/875_Occupational_and_Residential_Exposure_Test_Guidelines/Series/875_000.pdf

U.S. EPA. (1996c) Series 875 Occupational and Residential Exposure Test Guidelines - Group B - Post Application Exposure Monitoring Test Guidelines. EPA712-C96-266. Available online at http://www.epa.gov/opptsfrs/publications/OPPTS_Harmonized/875_Occupational_and_Residential_Exposure_Test_Guidelines/Series/875-2000.pdf

U.S. EPA. (1997a) Exposure factors handbook. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. EPA/600/P-95/002Fa,b,c. Available online at http://www.epa.gov/ncea/efh/.

U.S. EPA. (1997b) Policy for use of probabilistic analysis in risk assessment at the U.S. Environmental Protection Agency. Science Policy Council. Available online at http://www.epa.gov/OSA/spc/pdfs/probpol.pdf

U.S. EPA. (1997c) Guiding principles for Monte Carlo analysis. Office of Research and Development, Risk Assessment Forum, Washington, DC. EPA/600/R-97/001. Available online at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=29596.

U.S. EPA. (1999) Sociodemographic data used for identifying potentially highly exposed populations. U.S. Environmental Protection Agency, Washington, DC. EPA/600/R-99/060. Available online at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=22562.

U.S. EPA. (2000a) Strategy for research on risks to children. Office of Research and Development, Washington, DC. EPA/600/R-00/068.

U.S. EPA. (2000b) Options for developing parametric probability distributions for exposure factors. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. EPA/600/R-00/058. Available on line at http://www.epa.gov/ncea/paramprob4ef.htm.

U.S. EPA. (2000c) Supplementary guidance for conducting health risk assessment of chemical mixutres. Risk Assessment Forum, Washington, DC. EPA/630/00/002F. Available on line at http://www.epa.gov/NCEA/raf/pdfs/chem_mix/chem_mix_08_2001.pdf

U.S. EPA. (2001a) Risk assessment guidance for Superfund. Volume I Human health evaluation manual: Part D, Standardized planning, reporting and review of Superfund risk assessments. Office of Solid Waste and

Emergency Response, Washington, DC. Publication 9285.7-47. Available online at

http://www.epa.gov/oswer/riskassessment/ragsd/tara.htm.

U.S. EPA. (2001b) Risk assessment guidance for Superfund. Volume III, Part A, Process for conducting probabilistic risk assessment. Office of Solid Waste and Emergency Response, Washington, DC. EPA/540/R-02/002. Available online at http://www.epa.gov/oswer/riskassessment/rags3adt/

U.S. EPA (2001c) Summary report of the technical workshop on issues associated with considering developmental changes in behavior and anatomy when assessing exposure to children. Office of Research and Development, Risk Assessment Forum, Washington, DC. EPA/630/R-00/005. Available online at http://cfpub.epa.gov/ncea/raf/recordisplay.cfm?deid=20680

U.S. EPA. (2002a) Child-Specific exposure factors handbook. Interim Final. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. EPA/600/P-00/002B.

U.S. EPA (2002b). Overview of the EPA quality system for environmental data and technology. Office of Environmental Information, Washington DC. EPA/240-R/02/003. Accessed online at http://www.epa.gov/quality/qs-docs/overview-final.pdf

U.S. EPA (2003a). A summary of general assessment factors for evaluating the quality of scientific and technical information. Science Policy Council, Washington DC. EPA/100/B-03/001. Accessed online at

http://www.epa.gov/osa/spc/pdfs/assess2.pdf

U. S. EPA. (2003b) Framework for cumulative risk assessment. Risk Assessment Forum, Washington, DC. EPA/630/P-02/001F. Available online at http://cfpub.epa.gov/ncea/raf/recordisplay.cfm?deid=54944.

U.S. EPA. (2003c) Example exposure scenarios. Office of Research and Development, Washington, DC; EPA/600/R03/036. Available online at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=85843.

U.S. EPA. (2003d) Human health research strategy. Office of Research and Development, Washington DC 20460. EPA/600/R-02/050. Available online at http://www.epa.gov/ORD/htm/researchstrategies.htm#rs01

U.S. EPA. (2004) Risk assessment guidance for Superfund. Volume I Human health evaluation manual: Part E, Supplemental guidance for dermal risk assessment. Interim. Office of Solid Waste and Emergency Response, Washington, DC. EPA/540/R/99/005. Available online at http://www.epa.gov/oswer/riskassessment/ragse/index.htm.

U.S. EPA. (2005a) Guidance on selecting age groups for monitoring and assessing childhood exposures to environmental contaminants. Office of Research and Development, Washington, DC. EPA/630/P-03/003F. Available online at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=146583

U.S. EPA. (2005b) Guidelines for carcinogen risk assessment. EPA/630/P-03/001F. Available online at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=116283.

U.S. EPA. (2005c) Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens. Risk Assessment Forum, Washington, DC. EPA/630/R-03/003F. Available online at: http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=116283.

U.S. EPA. (2005d) Protocol for human health risk assessment protocol for hazardous waste combustion facilities. EPA530-R-05-006. Available online at http://www.epa.gov/combustion/risk.htm

U.S. EPA. (2006a) Approaches for the application of physiologically based pharmacokinetic

(PBPK) models and supporting data in risk assessment. Office of Research and Development, Washington DC. EPA/600/R-05/043F. Available online at http://cfpub.epa.gov/ncea/CFM/recordisplay.cfm?deid=157668

U.S. EPA. (2006b) Use of physiologically based pharmacokinetic (PBPK) models to quantify the impact of human age and interindividual differences in physiology and biochemistry pertinent to risk (Final Report). Office of Research and Development, Washington, DC. EPA/600/R-06/014A. Available online at http://cfpub.epa.gov/ncea/CFM/recordisplay.cfm?deid=151384

U.S. EPA (2006c) Guidance on systematic planning using the data quality objectives process. Office of Environmental Information, Washington DC. EPA/240B/06/001. Availabel online at

http://www.epa.gov/QUALITY/qs-docs/g4-final.pdf

U.S. EPA. (2006d) A framework for assessing health risk of environmental exposures to children (Final). Office of Research and Development, Washington, DC. EPA/600/R-05/093F. Available online at

http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=158363

U.S. EPA (2006e) Harmonization in interspecies extrapolation: use of $BW^{3/4}$ as default method in derivation of the oral RfD (External Review Draft). Risk Assessment Forum, Washington, DC. EPA/630/R-06/001. Available online at http://cfpub.epa.gov/ncea/raf/recordisplay.cfm?deid=148525

U.S. EPA (2008) Concepts, methods, and data sources for cumulative health risk assessment of multiple chemicals, exposures and effects: a resource document (final). Office of Research and Development, Washington, DC. EPA/600/R-06/013F. Available online at

http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=190187

Table 1-1. Characterization of Variability in Exposure Factors				
Exposure Factors	Average	Median	Upper percentile	Multiple Percentiles
Ingestion of water and other select liquids	✓	✓	✓	✓
Non-dietary ingestion	✓	✓	✓	
Soil and dust ingestion	✓	✓	✓[a]	
Inhalation rate	✓	✓	✓	✓
Surface area Soil adherence	✓ ✓		✓	✓
Body weight	✓	✓	✓	✓
Intake of fruits and vegetables	✓	✓	✓	✓
Intake of fish and shellfish	✓	✓	✓	✓
Intake of meats, dairy products, and fats	✓	✓	✓	✓
Intake of grain products	✓	✓	✓	✓
Intake of home produced foods	✓	✓	✓	✓
Total food intake	✓	✓	✓	✓
Human milk intake	✓		✓	
Time indoors Time outdoors Time showering Time bathing Time swimming Time playing on sand/gravel Time playing on grass Time playing on dirt	✓ ✓ ✓ ✓ ✓ ✓ ✓ ✓	 ✓ ✓ ✓ ✓ ✓ ✓	 ✓ ✓ ✓ ✓ ✓ ✓	 ✓ ✓ ✓ ✓ ✓ ✓
[a] Soil pica and geophagy.				
✓ = Data available				

Table 1-2. Considerations Used to Rate Confidence in Recommended Values		
General Assessment Factors	**Increasing Confidence**	**Decreasing Confidence**
Soundness		
Adequacy of Approach	The studies used the best available methodology and capture the measurement of interest.	There are serious limitations with the approach used; study design does not accurately capture the measurement of interest.
	As the sample size relative to that of the target population increases, there is greater assurance that the results are reflective of the target population.	Sample size too small to represent the population of interest.
	The response rate is greater than 80 percent for in-person interviews and telephone surveys, or greater than 70 percent for mail surveys.	The response rate is less than 40 percent.
	The studies analyzed primary data.	The studies are based on secondary sources.
Minimal (or defined) Bias	The study design minimizes measurement errors.	Uncertainties with the data exist due to measurement error.
Applicability and Utility		
Exposure Factor of Interest	The studies focused on the exposure factor of interest.	The purpose of the studies was to characterize a related factor.
Representativeness	The studies focused on the U.S. population.	Studies are not representative of the U.S. population.
Currency	The studies represent current exposure conditions.	Studies may not be representative of current exposure conditions.
Data Collection Period	The data collection period is sufficient to estimate long-term behaviors.	Shorter data collection periods may not represent long-term exposures.
Clarity and Completeness		
Accessibility	The study data could be accessed.	Access to the primary data set was limited.
Reproducibility	The results can be reproduced or methodology can be followed and evaluated.	The results cannot be reproduced, the methodology is hard to follow, and the author(s) cannot be located.
Quality Assurance	The studies applied and documented quality assurance/quality control measures	Information on quality assurance/control was limited or absent.

Table 1-2. Considerations Used to Rate Confidence in Recommended Values (continued)		
General Assessment Factors	**Increasing Confidence**	Decreasing Confidence
Variability and Uncertainty		
Variability in Population	The studies characterize variability in the population studied.	The characterization of variability is limited.
Uncertainty	The uncertainties are minimal and can be identified. Potential bias in the studies are stated or can be determined from the study design.	Estimates are highly uncertain and cannot be characterized. The study design introduces biases in the results.
Evaluation and Review		
Peer Review	The studies received high level of peer review (e.g., they are published in peer review journals).	The studies received limited peer review.
Number and Agreement of Studies	The number of studies is greater than 3. The results of studies from different researchers are in agreement.	The number of studies is 1. The results of studies from different researchers are in disagreement.

Table 1-3. Integrating U.S. EPA's *Guidance on Selecting Age Groups for Monitoring and Assessing Childhood Exposures to Environmental Contaminants* (U.S. EPA, 2005a) with U.S. EPA's *Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens* (U.S. EPA, 2005c) For Those Contaminants Which Act Via a Mutagenic Mode of Action

Exposure Age Group[a]	Exposure Duration (yr)	ADAF (Age-Dependent Potency Adjustment Factor)
Birth to < 1 month	0.083	10x
1 < 3 months	0.167	10x
3 < 6 months	0.25	10x
6 < 12 months	0.5	10x
1 to < 2 years	1	10x
2 to < 3 years	1	3x
3 to < 6 years	3	3x
6 to < 11 years	5	3x
11 to < 16 years	5	3x
16 to < 21 years	5	1x
> 21 years (21 to < 70 yr)	49	1x

[a]   EPA's recommended childhood age groups (excluding ages >21 years).
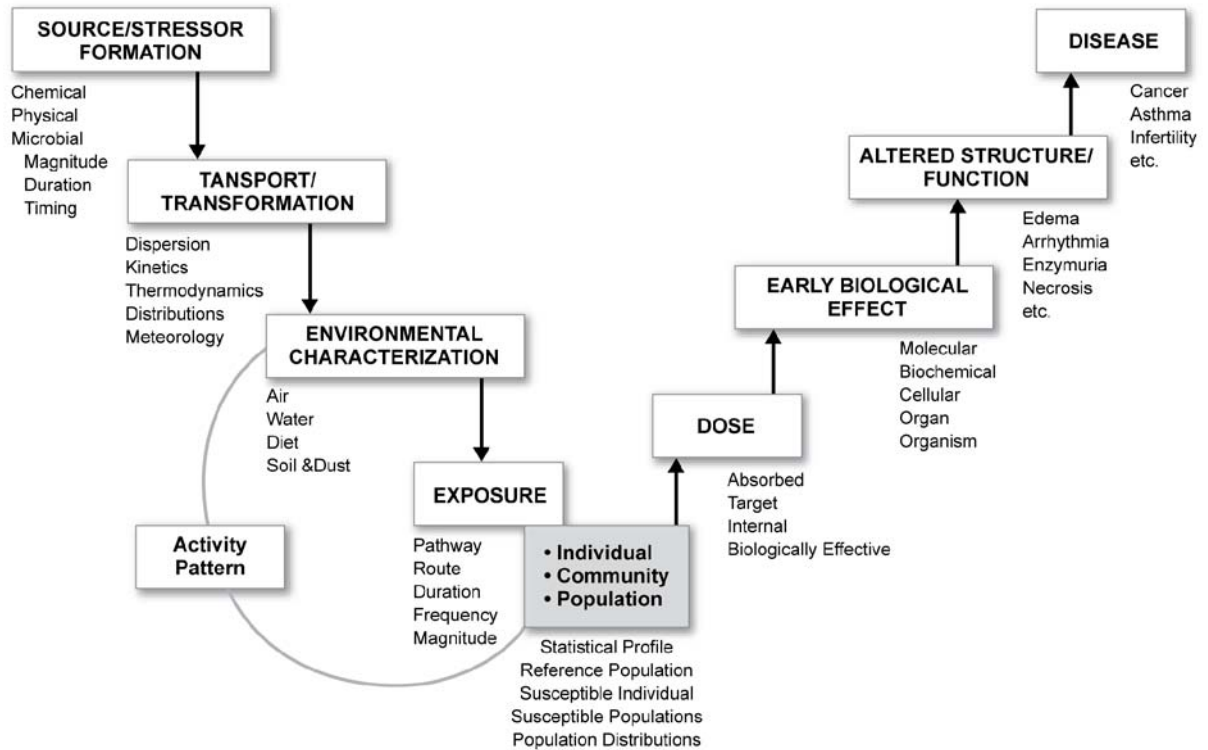
Figure 1-1 The Exposure-Dose-Effect Continuum

Source: U.S. EPA, 2003d; IPCS, 2006.