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1. INTRODUCTION

1.1 BACKGROUND

In 1993, the National Academy of Sciences (NAS) released Pesticides in the Diets of Infants and Children (NAS, 1993), which highlighted that important differences can exist between children and adults with respect to risks posed by pesticides. Because of physiological and behavioral differences, exposures among children are expected to be significantly different than exposures among adults. Children may be more exposed to some environmental toxicants because they consume more food and water per unit of body weight and have a higher ratio of surface area to volume than adults. Equally important, rapid changes in behavior and physiology during childhood may lead to differences in exposure during childhood as a child grows up. In 1995, EPA established a policy "to consider the risks to infants and children consistently and explicitly as a part of risk assessments generated during its decision making process, including the setting of standards to protect public health and the environment"(U.S. EPA 1995) . Recognizing that exposures among infants, toddlers, adolescents, and teenagers can vary significantly, the U.S. Environmental Protection Agency (EPA) recently 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, 2002) is designed specifically to complement 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) 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). Dust and tracked-in soil accumulates most effectively in carpets, where young children spend significant amount of time (Lewis et al., 1999). Children living in agricultural areas may experience higher exposures to

pesticides than do other children. 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 breast 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 (for example, when exposures occur during periods of enhanced periods of susceptibility) and/or toxicokinetic differences (i.e., differences in absorption, excretion, and metabolism) (U.S. EPA, 2000c). Toxic contaminants in the environment can cause neurodevelopmental disabilities. The developing brain and nervous system can be particularly sensitive to environmental contaminants. For example, elevated blood lead levels and prenatal exposures to even relatively low levels of lead result in behavior disorders and reductions of intellectual function. Exposure to high levels of methylmercury can result in developmental disabilities (Myers and Davidson, 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). With respect to contaminants which are carcinogenic via a mutagenic mode of action, 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 help implement the Order, 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 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, have 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, ORD developed a Strategy for Research on Environmental Risks to Children (EPA, 2000c). The goal of this research strategy was to improve the quality of risk assessments

for children. This *Child-specific Exposure Factors Handbook* is further intended to support EPA's efforts to improve exposure and risk assessments for children (U.S. EPA 2002).

In 1997, 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. OCHP's child-related risk assessment policy and methodology guidance document survey (U.S. EPA, 1999a) highlighted the *Exposure Factors Handbook* as a source of information on exposure factors for children. EPA's *Children's Environmental Health Yearbook* (U.S. EPA, 1998) also lists the *Exposure Factors Handbook* as a source of exposure information for children. However, the EPA Program Offices identified the need to consolidate all children's exposure data into a single document. The goal of this *Child-specific Exposure Factors Handbook* is to fulfill this need. This Handbook provides non-chemical-specific data on exposure factors that can be used to assess doses from dietary and non-dietary ingestion exposure, dermal exposure, and inhalation exposure among children.

This handbook provides generic exposure factors data for the EPA recommended set of childhood age groups in the following areas:

- breast milk ingestion;
- food ingestion, including homegrown foods and other dietary-related data;
- drinking water ingestion;
- soil ingestion;
- hand-to-mouth and object-to-mouth activity;
- dermal exposure factors such as surface areas and soil adherence;
- inhalation rates;
- activity duration and frequency in different locations and various microenvironments;
- duration and frequency of consumer product use;
- body weight data; and
- duration of lifetime.

It is a compilation of available data from a variety of sources. Most of these data have been described in detail in 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 here 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. EPA made every attempt to clearly label the statistics presented. 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 age groups used in this handbook. Every effort has been made to reallocate source data into the age groups recommended by the EPA in the report entitled *Guidance on Selecting Age Groups for Monitoring and Assessing Childhood Exposures to Environmental Contaminants* (U.S. EPA, 2005a), when sufficiently detailed data are available. Within the constraint of presenting the original material as accurately as possible, 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.

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*, 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).

1.2 PURPOSE

The purpose of this update and revision of the *Child-specific Exposure Factors Handbook* is to (1) most importantly, complement EPA's new set of recommended childhood age groups, as noted above, including a standardized way to define specific age groups (X to < Y); (2) to highlight changes in risk assessment practice first presented in the EPA's Cancer Guidelines regarding the need to consider children as lifestages rather than as subpopulations (U.S. EPA, 2005b); (3) emphasize a major recommendation in 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; and lastly, (4) to incorporate any new exposure factors data/research that have become available since the early 2000's.

As with the earlier version of the handbook, this new version will summarize key data on human behaviors and characteristics which affect children's exposure to environmental contaminants, and provide recommended values to use for these factors. These recommendations are not legally binding on any EPA program and should be interpreted as suggestions that Program Offices or individual exposure 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 which assessors should consider in assessing exposure among children of different ages, and may be used in conjunction with the EPA document entitled *Socio-demographic Data Used for Identifying Potentially Highly Exposed Populations* (U.S. EPA, 1999b).

This handbook is intended to be a continuously evolving document. Updates will be posted in the NCEA home page as new data become available.

1.3 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 EPA recommendations on numeric estimates for behavioral and physiological characteristics needed to estimate childhood exposure to toxic contaminants.

1.4 SELECTION OF STUDIES FOR THE HANDBOOK

The data presented in this handbook have been compiled from various sources, which include EPA's *Exposure Factors Handbook* (U.S. EPA, 1997a), government reports, and information presented in the peer-reviewed scientific literature. Studies were chosen that were seen as useful and appropriate for estimating exposure factors. The handbook contains summaries of selected studies published through June 2006.

General Considerations

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 were also included, as are new studies that became available after publication of the 2002 *Child-Specific Exposure Factors Handbook* (U.S. EPA, 2002). Key studies from the *Exposure Factors Handbook* were generally defined as the most useful for deriving exposure factors. The recommended values for most exposure factors are based on the results of these studies. As in the *Exposure Factors Handbook,* the key studies were selected based on the following considerations:

- *Level of peer review*: Studies were selected predominantly from the peer-reviewed literature and final government reports. Internal or interim reports were therefore avoided.

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

- *Reproducibility*: Studies were sought that contained sufficient information so that methods could be reproduced, or at least so the details of the author's work could be accessed and evaluated.

- *Focus on exposure factor of interest*: Studies were chosen that directly address the exposure factor of interest or address related factors that have significance for the factor under consideration. As an example of the latter case, one selected study contains useful ancillary information concerning fat content in fish, although it does not directly address fish consumption.

- *Pertinence of data to the U.S.*: Studies were selected that addressed the U.S. population. Data from populations outside the U.S. were sometimes included if U.S. data were limited for a specific exposure factor. Studies similar in methodology are also used to support or enhance the U.S. data.

- *Primary data*: Studies were deemed preferable if based on primary data, but studies based on secondary sources were also included when they offered an original analysis. For example, the handbook cites studies of food consumption based on original data collected by the U. S. Department of Agriculture (USDA) National Food Consumption Survey.

- *Currency of information*: Studies were chosen only if they were sufficiently recent to represent current exposure conditions. This is an important consideration for those factors that change with time. In some instances, recent data were very limited. Therefore, the data provided in these instances were the only available data. Limitations as to the age of the data were noted.

- *Adequacy of data collection period*: Because most users of the handbook are primarily addressing chronic exposures, studies were sought that utilized the most appropriate data collection techniques for the characterization of long-term behavior.

- *Validity of approach*: Studies that used experimental procedures or approaches that more likely or closely capture the desired measurement were selected. In general, 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 rely on validated indirect measurement methods such as surrogate measures (e.g., heart rate for inhalation rate) and 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.

- *Representativeness of the population*: Studies seeking to characterize the national population, a particular region, or sub-population were selected if they were

appropriately representative of that population. Studies with limitations in areas where little data exist were included and are noted as such.

- *Variability in the population*: Studies were sought that characterized any variability within populations (e.g., variability due to age, gender, ethnicity).

- *Minimal (or defined) bias in study design*: Studies were sought that were designed with minimal bias, or if biases were suspected to be present, the direction of the bias (i.e., an overestimate or underestimate of the parameter) is either stated or apparent from the study design.

- *Minimal (or defined) uncertainty in the data*: Studies were sought that have minimal uncertainty in the data, which was judged by evaluating all the considerations listed above. Studies that identify uncertainties, such as those due to inherent variability in environmental and exposure-related parameters or possible measurement error, were preferred. Studies that document quality assurance/quality control measures were also preferred.

1.5 APPROACH USED TO DEVELOP RECOMMENDATIONS FOR EXPOSURE FACTORS

As discussed above, EPA first reviewed all literature pertaining to a factor and determined key studies. These key studies were used to derive recommendations for the values of each factor for each of the childhood age groups discussed earlier. The recommended values were derived solely from 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. EPA's procedure for developing recommendations was as follows:

1. 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. 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. 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 lifestage or local population of interest.

3. The variability of the factor across the lifestage was discussed. This document attempts to characterize the variability of each of the factors. Variability refers to true heterogeneity or diversity in a population. Differences among individuals in a population are referred to as inter-individual variability, differences for one individual over time is referred to as intra-individual variability. Since most of the studies used to derive exposure factors data are short term in nature, they present the variability in short term exposures across a population sample and often do not allow analysis of either inter-temporal variability within individuals nor inter-individual variability of long term average exposures. Inter-individual variability in this handbook is characterized in one or more of the following 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.

4. Uncertainties were 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.

5. Finally, 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 EPA's judgment on the quality of the underlying data used to derive the recommendation.

This judgment was made using the guidelines shown in Table 1-1. Table 1-1 is an adaptation of the General Considerations discussed in Section 1.4. Clearly this is a continuum from low to high, and judgment was used to determine these ratings. Recommendations given in this handbook are accompanied by a discussion of the rationale for their qualitative rating.

Table 1-2 summarizes the principal exposure factors addressed in this Handbook and identifies the key tables that the reader may refer to when searching for a specific exposure factor.

It is important to note that the study elements listed in Table 1-1 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 depend on the exposure factor of interest. Also, the relative weights given to the elements for the various factors were subjective and based on the professional judgement of the authors of this handbook. In general, most studies would rank high with regard to "level of peer review," "accessibility," "focus on the factor of interest," and "data pertinent to the U.S."

These elements are important considerations for inclusion of a study in this handbook. However, a high score of these elements does not necessarily translate into a high overall score. Other elements in Table 1-1 were also examined to determine the overall score. For example, the adequacy of the data collection period may be more important when determining usual intake of foods in a population; on the other hand, 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 addition, some exposure factors are more easily measured than others. For example, soil ingestion by children is 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 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.

1.6 CHARACTERIZING VARIABILITY AND UNCERTAINTY

It is critical to note the distinction between uncertainty and variability. Uncertainty reflects our inability to be sure about the true value of a factor. Variability refers to the fact that children are not exactly alike - thus, for any given age, they may be different in terms of their weight, their behavior, what they like to eat and how much they eat, etc. These differences are important for exposure and risk assessors, as well as risk managers, to take into account if the range of exposures and risks faced by children are to be understood. For example, if one were to consider acute risks to US children under the age of 18 (about 73 million in 2005 - U.S. Census Bureau, the upper 99th percentile, while at the upper reaches of the range of variability, still accounts for 730,000 children on any given day - this may be important information for an exposure assessor to share with a risk manager. This document characterizes variability of each of the factors. Variability is characterized in one or more of the following 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 1-3. 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. A detailed presentation on variability and uncertainty for exposure factors and algorithms used in estimating exposure is presented in EPA's *Exposure Factors Handbook* (U.S. EPA, 1997a).

In the recommendations, 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 use of probabilistic analysis such as Monte Carlo requires a selection of distributions or histograms for the input parameters. This handbook is not intended to provide complete guidance on the use of probabilistic analyses. There are efforts in the Agency and elsewhere aimed at providing guidance on the use of these techniques.

1.7 USING THE HANDBOOK IN AN EXPOSURE ASSESSMENT

Some of the steps for performing an exposure assessment are (1) determining the pathways of exposure; (2) identifying the environmental media which transports the contaminant; (3) determining the contaminant concentration; (4) determining the exposure time, frequency, and duration; and (5) identifying the exposed populations and lifestages. Many of the issues related to characterizing exposure from selected exposure pathways have been addressed in a number of existing EPA guidance documents. These include, but are not limited to the following:

- *Guidelines for Exposure Assessment* (U.S. EPA, 1992a);
- *Dermal Exposure Assessment: Principles and Applications* (U.S. EPA, 1992b);
- *Methodology for Assessing Health Risks Associated with Indirect Exposure to Combustor Emissions* (U.S. EPA, 1990);
- *Risk Assessment Guidance for Superfund, Part A* (U.S. EPA, 1989);
- *Risk Assessment Guidance for Superfund, Part E* (U.S. EPA, 2004);
- *Estimating Exposures to Dioxin-Like Compounds* (U.S. EPA, 1994a);
- *Selection Criteria for Mathematical Models Used in Exposure Assessments: Groundwater Models* (U.S. EPA, 1988a);
- *Selection Criteria for Mathematical Models Used in Exposure Assessments: Surface Water Models* (U.S. EPA, 1987);
- *Standard Scenarios for Estimating Exposure to Chemical Substances During Use of Consumer Products* (U.S. EPA, 1986a);
- *Pesticide Assessment Guidelines, Subdivisions K* (U.S. EPA, 1984) *and U*, (U.S. EPA, 1986b);

- *Methods for Assessing Exposure to Chemical Substances, Volumes 1-13* (U.S. EPA, 1983-1989);
- *Guiding Principles for Monte Carlo Analysis* (U.S. EPA, 1997b);
- Policy for Use of Probabilistic Analysis in Risk Assessment at the U.S. Environmental Protection Agency, May 15, 1997 ;
- *Guiding Principles for Monte Carlo Assessments* (EPA/600/R-97/001) (http://www.epa.gov/ncea/monteabs.htm)
- *Options for Developing Parametric Probability Distributions for Exposure Factors* (EPA/600/R-00/058) July 2000 (U.S. EPA, 2000a)
- *Sociodemographic Data for Identifying Potentially Highly Exposed Populations* (U.S. EPA, 1999)
- *Framework for Cumulative Risk Assessment* (U.S. EPA, 2003a)
- *Example Exposure Scenarios* (U.S. EPA 2003b)
- *Guidance on Selecting Age Groups for Monitoring and Assessing Childhood Exposures to Environmental Contaminants* (U.S. EPA, 2005a)
- *Cancer Guidelines for Carcinogen Risk Assessment* (U.S. EPA, 2005b) *and Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens* (U.S. EPA, 2005c)

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.

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., Calabrese's et al. (1989) soil ingestion study using children from the Amherst, MA area). It is necessary for risk or exposure assessors characterizing a diverse population to identify and enumerate certain groups within the general population who are at risk for greater contaminant exposures or who exhibit a heightened sensitivity to particular contaminants. For further guidance on addressing susceptible populations, the reader is referred to *Socio-demographic Data Used for Identifying Potentially Highly Exposed Subpopulations* (U.S. EPA, 2001)

1.8 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 and Regional offices within the EPA. They depended on availability of data and were often based on professional judgement or historical use.

The development of standardized age bins was the subject of discussion in a 2000 EPA workshop titled "Issues Associated with Considering Developmental Changes in Behavior and Anatomy When Assessing Exposure to Children" (U.S. EPA, 2000b). The purpose of this workshop was to gain insight and input into factors that need to be considered when developing standardized age bins and to 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 the 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 contaminant 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 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 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:

<u>Age grouping based on behavioral characteristics</u>

0-2 months
2 - 6 months
6-12 months
1-2 years
2-6 years
6-11 years
11-16 years
16-21 years

<u>Age grouping based on physiological characteristics</u>

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 consideration of age groupings depend not only on behavioral and physiological characteristics, but also on the specific scenario being studied and contaminant of concern.

Based upon consideration of the findings of the technical workshop, as well as analysis of available data, EPA developed guidance which established a set of recommended age groups for development of exposure factors for children entitled "*Guidance on 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 EPA's recommended set of childhood age groupings.

The recommenced age groups 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; and 16 to < 21 years (U.S. EPA, 2005a).

1.9 CONSIDERING LIFESTAGE WHEN CALCULATING EXPOSURE AND RISK

A key component of 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, 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 should calculate chronic exposures by summing time-weighted exposures that occur at each lifestage; this handbook provides data arrayed by childhood age in order to support this new guidance. 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 as compared with those for adults, calculated risks could either decrease or increase as 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.

Table 1-4, 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) = Σ (Exposure x Duration x Potency x ADAF) summed across all the age groups presented in Table 1-4. 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 long term adult dose.

1.10 GENERAL EQUATIONS FOR CALCULATING DOSE

The definition of exposure as used in the Exposure Guidelines (U.S. EPA, 1992a) is the "contact of a chemical, physical, or biological agent with the outer boundary of an organism." 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 contaminant entering the body can be described in two steps: contact (exposure) followed by entry (crossing the boundary). The dose is the amount of agent available at human exchange boundaries (skin, lungs, gut) where absorption takes place during some specified time. An example of exposure and dose for the oral route as presented in the EPA Exposure Guidelines is shown in Figure 1-1. Starting with a general integral equation for exposure (U.S. EPA, 1992a), several dose equations can be derived depending upon boundary assumptions.

Average Daily Dose (ADD) has been used when assessing risks for many noncancer effects - this metric averages doses over the period of time over which exposure occurred. The ADD can be calculated by averaging the potential dose (D_{pot}) over body weight and an averaging time.

$$ADD_{pot} = [C \times IR \times ED] / [BW \times AT] \qquad (1\text{-}1)$$

Where:

C = Contaminant Concentration

IR = Intake Rate

ED = Exposure Duration

BW = Body Weight

AT = Averaging Time

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 1.9 above, EPA is now recommending that risks should be calculated by integrating exposures or risks throughout all lifestages.

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 that affect dermal exposure are the amount of material that comes into contact with the skin and the rate at which the contaminant is absorbed.

The exposure duration is the period of time over which exposure occurs. The length of time a person lives in an area, frequency of bathing, time spent indoors versus outdoors, etc., all affect the exposure duration. Chapter 9, Activity Factors, gives some examples of population behavior/activity patterns that may be useful for estimating exposure durations.

When the above parameter values intake rate (IR) and exposure duration (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.

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 contaminant per kg of body weight per day (mg/kg-day)). The dose is usually expressed in terms of mg/kg-day or other mass/mass-time units.

In most cases (inhalation and ingestion exposure), the dose-response parameters for carcinogen 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 the food ingestion and water intake data presented in chapters 3 and 4 respectively, 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/d/kg body weight. 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. Body weight data presented in chapter 11 may be used in other instances when the intake rate has not been normalized by body weight.

The units of intake in this handbook for some of the exposure factors (e.g., breast milk intake) are not normalized to body weight. In this case, the exposure assessor needs to use (in Equation 1-1) the average weight of the exposed population during the time when the

exposure actually occurs. If the body weight of the individuals in the population whose risk is being evaluated is non-standard in some way (e.g., children may be smaller than the national population) and if reasonable values are not available in the literature, then a model of intake as a function of body weight must be used. One such model is discussed in Appendix 1A of the *Exposure Factors Handbook* (U.S. EPA, 1997a). Some of the parameters (primarily concentrations) used in estimating exposure are exclusively site specific, and therefore default recommendations could 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 (HEC) on which inhalation unit risks, and reference concentrations, are based (U.S. EPA, 1994b). 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 ventilation 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 recently discussed at a peer involvement workshop hosted by EPA in 2006 (workshop results and references to be published in 2007).

Consideration of lifestage-particular physiological characteristics in the dosimetry analysis may result in a refinement to the human equivalent concentration (HEC) to insure

relevance in risk assessment across lifestages, or might conceivably conclude with multiple HECs, and corresponding inhalation unit risk values (e.g., separate for childhood and adulthood) (U.S. EPA, 2005b, c). 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/lifestage-specific assumptions in to the models.

There are no specific exposure factor assumptions in the derivation of 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 contaminant. 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. However, the Food Quality Protection Act (FQPA) of 1996 states that for threshold effects,

> *"an additional tenfold margin of safety for the chemical residue and other sources of exposure shall be applied for infants and children to take into account potential pre- and post-natal toxicity and completeness of data with respect to exposure and toxicity to infants and children. Notwithstanding such requirement for an additional margin of safety, the Administrator may use a different margin of safety for the pesticide chemical residue only if, on the basis of reliable data, such margin of safety will be safe for infants and children."*

In addition, FQPA lists several factors that must be considered when assessing risks to children, such as available information concerning the special susceptibility of children to pesticide chemical residues, neurological differences between children and adults, and effects of *in utero* exposure.

1.11 CUMULATIVE RISK

EPA recognizes that children may be exposed to mixtures of contaminants both indoors and outdoors. Exposure may also occur through more than one pathway. New directions in risk assessments in EPA put more emphasis on total exposures via multiple pathways (U.S. EPA, 2003a). Over the last several years, EPA has developed a methodology for assessing risk from

multiple contaminants. For more information, the reader is referred to EPA's *Framework for Cumulative Risk Assessment* (U.S. EPA, 2003a).

1.12 RESEARCH NEEDS

The data for several exposure factors for children are limited. The following list is a compilation of areas for future research related to childhood exposure factors:

- More recent information is needed on breastmilk consumption and the incidence and duration of breastfeeding.

- Information on children's food handling practices that might exacerbate exposure is needed to better characterize exposures among children.

- Further research on fish intake among children, particularly recreational and subsistence populations, is needed.

- Further research is needed on consumption of ethnic foods by children.

- Research is needed to better estimate soil intake rates, particularly on how to extrapolate short-term data to chronic exposures. Research is also needed to refine the methods to calculate soil intake rates (i.e., inconsistencies among tracers and input/output misalignment errors indicate a fundamental problem with the methods). In addition, there are no data for children <1 year or >7 years of age. Additional information on soil ingestion among children that provides better estimates of upper percentile rates is needed, in particular. Research is also needed to better understand the relative contribution of soil vs. dust ingestion.

- Further research is needed on dermal and non-dietary ingestion exposure factors, including the microenvironments in which children spend time and the types of materials that they contact, as well as information on the rate at which they

contact contaminated surfaces, the fraction of the contaminants that are transferred to skin and object surfaces, and the amount of the object/skin entering the mouth.

- Further research is needed to obtain better soil adherence rates for additional activities involving children.

- Further data is needed on the frequency and duration of use and kinds of consumer products used by children.

- Additional data on inhalation dosimetry and modeling, including inhalation rates that are specific to children's activities.

- Research is needed to derive a methodology to extrapolate from short-term data to long-term or chronic exposures.

1.13 ORGANIZATION

The handbook is organized as follows:

Chapter 1	Provides the overall introduction to the handbook.
Chapter 2	Provides factors for estimating exposure through ingestion of breast milk.
Chapter 3	Provides factors for estimating human exposure through ingestion foods, including fish.
Chapter 4	Provides factors for estimating exposure through ingestion of drinking water.
Chapter 5	Provides factors for estimating exposure as a result of ingestion of soil.

Chapter 6	Presents factors for estimating exposure to environmental contaminants from other non-dietary ingestion such as hand-to-mouth and object-to-mouth activity.
Chapter 7	Provides factors for estimating exposure as a result of inhalation of vapors and particulates.
Chapter 8	Provides factors for estimating dermal exposure to environmental contaminants that come in contact with the skin.
Chapter 9	Presents data on activity factors (activity patterns, population mobility, and occupational mobility).
Chapter 10	Presents data on consumer product use.
Chapter 11	Presents data on body weight.

1.14 REFERENCES FOR CHAPTER 1

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Table 1-1. Considerations Used to Rate Confidence in Recommended Values		
CONSIDERATIONS	**HIGH CONFIDENCE**	**LOW CONFIDENCE**
Study Elements		
Level of peer review	The studies received high level of peer review (e.g., they appear in peer review journals).	The studies received limited peer review.
Accessibility	The studies are widely available to the public.	The studies are difficult to obtain (e.g., draft reports, unpublished data).
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.
Focus on factor of interest	The studies focused on the exposure factor of interest.	The purpose of the studies was to characterize a related factor.
Data pertinent to U.S.	The studies focused on the U.S. population.	The studies focused on populations outside the U.S.
Primary data	The studies analyzed primary data.	The studies are based on secondary sources.
Currency	The data were published after 1990.	The data were published before 1990.
Adequacy of data collection period	The study design captures the measurement of interest (e.g., usual consumption patterns of a population).	The study design does not very accurately capture the measurement of interest.
Validity of approach	The studies used the best methodology available to capture the measurement of interest.	There are serious limitations with the approach used.

Study sizes	The sample size is greater than 100 samples. The sample size depends on how the target population is defined. As the size of a sample relative to the total size of the target population increases, estimates are made with greater statistical assurance that the sample results reflect actual characteristics of the target population.	The sample size is less than 20 samples.
Representativeness of the population	The study population is the same as population of interest.	The study population is very different from the population of interest.[a]
Variability in the population	The studies characterized variability in the population studied.	The characterization of variability is limited.
Lack of bias in study design(a high rating is desirable)	Potential bias in the studies are stated or can be determined from the study design.	The study design introduces biases in the results.
<u>Response rates</u> In-person interviews Telephone interviews Mail surveys	 The response rate is greater than 80%. The response rate is greater than 80%. The response rate is greater than 70%.	 The response rate is less than 40%. The response rate is less than 40%. The response rate is less than 40%.
Measurement error	The study design minimizes measurement errors.	Uncertainties with the data exist due to measurement error.
Other Elements		
Number of studies	The number of studies is greater than 3.	The number of studies is 1.
Agreement between researchers	The results of studies from different researchers are in agreement.	The results of studies from different researchers are in disagreement.

[a] Differences include age, sex, race, income, or other demographic parameters.

Table 1-2. Summary of Exposure Factor References and Confidence Ratings

EXPOSURE FACTOR	**REFERENCE**	**CONFIDENCE RATING (mean/upper percentile)**
Breast milk intake rate	Table 2-11	Medium/Medium
Drinking water intake rate	Table 4-7	High/High
Food Intake- General Population *(fruit, vegetables, meats, dairy products, grains, fats, fish)*	Table 3-50	High/Low
Fish intake - Recreational	Table 3-50	Low/Low
Fish Intake - Native American Subsistence Population	Table 3-50	Low/Low
Home produced food intake	Table 3-50	Low/Low
Soil ingestion rate	Table 5-21	Medium/Low
Mouthing behavior	Table 6-21 (mouthing time) Table 6-22 (mouthing frequency)	Low/Low
Inhalation rate	Table 7-21	Medium/Medium
Dermal Factors	Surface Area Whole Body: Tables 8-6, 8-7, 8-8 Body Parts: Table 8-3 Solid Adherence Tables 8-9, 8-10, 8-16	Medium/Medium
Body Weight	Age 0 to <2 months: Table 11-1 Older Infants and Children: Tables 11-9, 11-10, 11-11	High/High
Activities (Showering, Swimming, Time Indoors/Outdoors, etc.)	Tables 9-75 and 9-76	Medium/Medium

Table 1-3. Characterization of Variability in Exposure Factors

Exposure Factors	Average	Median	Upper percentile	Multiple Percentiles	Fitted Distributions
Breast milk intake rate	✓		✓		
Total intake rate for major food groups	✓	✓	✓ Qualitative discussion for long-term	✓	
Individual food intake rate	✓				
Drinking water intake rate	✓		✓	✓	✓
Fish intake rate for general population, recreational marine, recreational freshwater, and Native American	✓	✓	✓	✓	
Serving size for foods	✓		✓		
Home produced food intake rates	✓	✓	✓	✓	
Soil intake rate	✓	✓	✓ Qualitative discussion for long-term		
Mouthing Behavior	✓				
Inhalation rate	✓		✓	✓	
Surface area Soil adherence	✓ ✓		✓	✓	
Body weight	✓	✓	✓	✓	
Time indoors Time outdoors Showering time	✓ ✓ ✓	 ✓	 ✓	 ✓	

Table 1-4. Integrating EPA's *Guidance on Selecting Age Groups for Monitoring and Assessing Childhood Exposures to Environmental Contaminants* with EPA's *Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens* For Those Contaminants Which Act Via a Mutagenic Mode of Action

Exposure Age Group	**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
Note: Age groups for cancer potency adjustment (birth to < 2 years; 2 to < 16 years; and 16 years and above) are represented by the three colored bands of exposure age groups.		

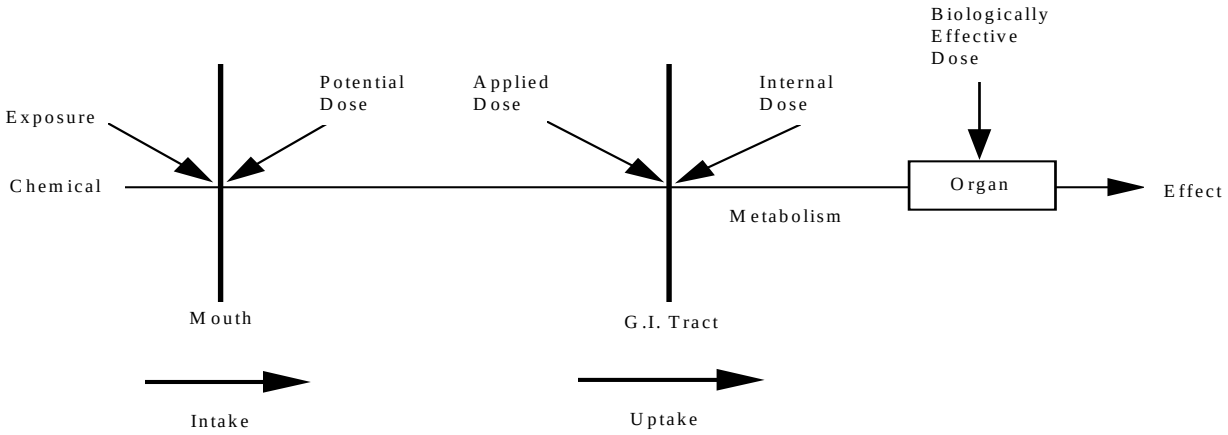

Figure 1-1. Schematic of Dose and Exposure: Oral Route

Source: U.S. EPA, 1992a