

# **Guidance on Selecting the Appropriate Age Groups for Assessing Childhood Exposures to Environmental Contaminants**

## **Risk Assessment Forum Technical Panel**

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## EXECUTIVE SUMMARY

The purpose of this document is to provide guidance to Environmental Protection Agency scientists on the appropriate age groups to consider when assessing childhood exposure and potential dose to environmental contaminants. A consistent set of childhood age groups, supported by an underlying scientific rationale, will improve Agency exposure and risk assessments for children and will assist the Agency in implementing such regulatory initiatives as Presidential Executive Order 13045.

After a brief introduction, the second and third sections of this guidance summarize discussions held during the EPA Risk Assessment Forum July 2000 workshop on developmental change (see U.S. EPA, 2000) and a subsequent expert analysis of existing exposure factors data (Versar, 2001). From these efforts, the Risk Assessment Forum workgroup on childhood exposure has concluded that the following age groups should be recommended for consideration in Agency exposure assessments for children, and used as a guide for future exposure data collection.

**Table E-1 Recommended Set of Childhood Age Groups for Agency Exposure and Risk Assessments**

<b>Age Groups &lt; 1 Year<sup>a</sup></b>	<b>Age Groups ≥ 1 Year</b>
birth to < 1 month	1 to < 2 years
1 to < 3 months	2 to < 3 years
3 to < 6 months	3 to < 6 years
6 to < 12 months	6 to < 11 years
	11 to < 16 years
	16 to < 18 years
	18 to < 21 years <sup>b</sup>

a) for purposes of evaluating exposure or potential dose but not internal dose, it may be acceptable to combine some of these groups (e.g., the first three groups could be combined to encompass “birth to < 6 months”)

b) to be considered on a case-by-case basis

These age groups reflect a consideration of developmental changes in various behavioral and anatomical characteristics that impact exposure and potential dose, and physiological characteristics that impact potential dose, internal dose and effects. Some examples of the characteristics that were discussed during the July 2000 workshop are summarized in Table E-2. It should be noted that the participants in the July 2000 workshop concluded that, ideally, developmental change should be presented as a continuous function over time. However, they supported the idea that age groupings are useful in the development of exposure scenarios.

**Table E-2 Examples of Characteristics Considered in Deriving the Recommended Set of Childhood Age Groups**

Age Group	Behavior/Anatomy/Physiology Characteristics
birth to < 1 month	<p><b><u>Behavior Related</u></b> time spent sleeping or sedentary; breast and bottle feeding</p> <p><b><u>Physiology Related</u></b> rapid growth and weight gain; increasing proportion of body fat; high skin permeability; high oxygen requirements (increased breathing rate); deficiencies in hepatic enzyme activity; immature immune system; more alkaline stomach; increases in extracellular fluid; renal function less than predicted by body surface area</p>
1 to < 3 months	<p><b><u>Behavior Related</u></b> time spent sleeping or sedentary; breast and bottle feeding</p> <p><b><u>Physiology Related</u></b> rapid growth and weight gain; increasing proportion of body fat; high oxygen requirements (increased breathing rate); deficiencies in hepatic enzyme activity; immature immune system; more alkaline stomach; increases in extracellular fluid; renal function less than predicted by body surface area</p>
3 to < 6 months	<p><b><u>Behavior Related</u></b> solid foods may be introduced into diet, especially toward the end of this stage; contact with surfaces increases; mouthing of hands and objects increases; more time spent in breathing zone close to floor</p> <p><b><u>Physiology Related</u></b> rapid growth and weight gain; increasing proportion of body fat; deficiencies in hepatic enzyme activity; immature immune system functions; increases in extracellular fluid; renal function less than predicted by body surface area</p>
6 to < 12 months	<p><b><u>Behavior Related</u></b> food consumption expands; floor mobility increases (surface contact); children are increasingly likely to mouth non-food items; children develop personal dust clouds</p> <p><b><u>Physiology Related</u></b> rapid growth and weight gain; body fat increases begin to moderate; deficiencies in hepatic enzyme activity; immature immune system; rapid decrease in extracellular fluid; can begin predicting renal function by body surface area</p>
1 to < 2 years	<p><b><u>Behavior Related</u></b> full range of foods consumed; participation in increased play activities coupled with extreme curiosity and poor judgment; breast and bottle feeding cease; children walk upright, run, and climb; children occupy a wider variety of breathing zones and engage in more vigorous physical activities; frequency of mouthing hands and objects is high</p> <p><b><u>Physiology Related</u></b> some hepatic enzyme activities peaks at a level exceeding adult's; most immune system functions have matured; extracellular fluid becomes more consistently related to body size</p>

**Table E-2 Examples of Characteristics Considered in Deriving the Recommended Set of Childhood Age Groups**

<b>Age Group</b>	<b>Behavior/Anatomy/Physiology Characteristics</b>
2 to < 3 years	<p><b><u>Behavior Related</u></b> frequency of mouthing hands and objects begins to moderate; occupancy of outdoor spaces increases; children begin to wear adult-style clothing</p> <p><b><u>Physiology Related</u></b> hepatic enzyme activity level falls back to the adult range</p>
3 to < 6 years	<p><b><u>Behavior Related</u></b> continued increases in the occupancy of outdoor spaces</p> <p><b><u>Physiology Related</u></b> entering a period of relatively stable weight gain and skeletal growth (as opposed to a period marked by growth spurts)</p>
6 to < 11 years	<p><b><u>Behavior Related</u></b> decreased oral contact with hands and objects as well as decreased dermal contact with surfaces; children spend time in school environments and begin playing sports</p> <p><b><u>Physiology Related</u></b> period of relatively stable weight gain and growth but may be entering period of rapid reproductive and endocrine system changes (especially for females)</p>
11 to < 16 years	<p><b><u>Behavior Related</u></b> smoking may begin; increased rate of food consumption; increased independence (more time out of home); workplace exposures can begin</p> <p><b><u>Physiology Related</u></b> rapid skeletal growth; rapid reproductive and endocrine system changes</p>
16 to < 18 years	<p><b><u>Behavior Related</u></b> high rate of food consumption; independent driving begins; expanded work opportunities</p> <p><b><u>Physiology Related</u></b> rapid skeletal growth (may see epiphyseal closure); rapid reproductive and endocrine system changes</p>
18 to < 21 years	<p><b><u>Behavior Related</u></b> high rate of food consumption; increased time in work environments; may move away from home environment</p> <p><b><u>Physiology Related</u></b> reproductive growth continues (especially for males); epiphysial closure may take place</p>

Note: Many of the behavioral and physiological characteristics listed in this table are repeated across age groups (especially for ages up to <12 months; e.g., rapid growth and weight gain). In determining the range of ages to include in a particular age group, the rate of change in these characteristics was often a key factor discussed at the workshop.

The Risk Assessment Forum workgroup acknowledges that there may be instances where combining some of these age groups (e.g., combining the first three groups into one representing birth to <6 months) may be considered when estimating exposure or potential dose, especially if little variation might be expected. In addition, there may be instances where it is not necessary to address every age group listed above, because the focus of the exposure and risk assessment may be on a health effect for which only one or two of the above groups represent a critical window. Where there is a lack of exposure data for a particular age group of potential importance, the assessment could still include a rough estimate based on exposures of other age groups and consideration of how these age groups differ. It is recommended that if age groups are combined or excluded, the underlying scientific rationale should be provided in the exposure assessment. It is important for exposure assessors to engage in an iterative dialogue with toxicologists and other health scientists to determine the age groups (or portions of age groups) that will be the focus of any particular assessment. The Risk Assessment Forum workgroup recommends that the discussion of combining/eliminating age groups include the following elements.

- The basis for determining which age groups should be combined (or which groups can be dropped from the analysis) and why.
- A description of the scientific uncertainties and potential biases introduced when combining or excluding age groups (e.g., is an age group described as less than 1 year more representative of 6 to <12 months of age than younger age groups?)
- A discussion of the types of data and information that, if available, would allow combined age groups to be separated (or omitted age groups to be addressed) in future analyses.

To address the age groups recommended in this guidance, it will be necessary for Agency scientists to exercise their best scientific judgment in using existing data and models (e.g., the Interim Final Child-Specific Exposure Factors Handbook). Experts participating in the July 2000 workshop on developmental change provided the following observation concerning existing data.

“Data for both behavioral and anatomical exposure factors are limited in terms of both quality and coverage. The adequacy of current data sets is highly variable, and some of the data may not be useful because they were gathered using outdated methods or because lifestyle changes since the study was conducted make the results less relevant to today’s conditions. More up-to-date data would be useful for refining distributions of critical developmental periods.”

This guidance highlights a number of areas for short term analysis and longer term research that will assist in addressing the recommended age groups in future Agency assessments. These areas of further analysis and research are summarized in Table E-3. Some of the short term analyses described in Table E-3, are likely to be incorporated in an update to the Child Specific Exposure Factors Handbook (expected to be completed within the next year).

The longer term research identified in Table E-3 can be accomplished through the EPA Office of Research and Development *Strategy for Research on Environmental Risks to Children* (U.S. EPA, 2000b). The development of data on childhood activity patterns and exposure factors was ranked as a high priority research need in the strategy.

**Table E-3      Summary of Recommendations for Further Analysis and Research on Exposure Factors Data for Children**

Exposure Factor	Recommendation for Further Analysis and Research
Breast Milk Intake	<ul style="list-style-type: none"> <li>collect data on the distribution of breast milk intake across the U.S. population including major ethnic groups</li> <li>collect data on maternal nutrient status and its effect on the fat content of breast milk</li> </ul>
Food Intake	<ul style="list-style-type: none"> <li>analyze the combined 1994-1996 and 1998 Continuing Survey of Food Intake by Individuals (CSFII) to develop estimates for the recommended childhood age groups</li> <li>conduct research on the contamination of food resulting from contact with surfaces and hands</li> </ul>
Water Intake	<ul style="list-style-type: none"> <li>analyze the combined 1994-1996 and 1998 Continuing Survey of Food Intake by Individuals (CSFII) to develop estimates for the recommended childhood age groups</li> </ul>
Soil Ingestion	<ul style="list-style-type: none"> <li>collect soil ingestion data on a broader range of childhood ages (e.g., 3 months to &lt;13 years)</li> <li>collect data that would allow estimation of variability and distributions of soil intake across geographic areas, race, economic status and other demographic variables</li> <li>collect data that would allow the characterization of seasonal variation in soil intake; these data would support the development of distributional information for long term exposures</li> <li>explore new approaches to interpreting soil ingestion data</li> </ul>
Non-Dietary Ingestion	<ul style="list-style-type: none"> <li>systematic, probability-based studies of microactivities should be undertaken that address a broad range of childhood age groups (at least to &lt;6 years of age)</li> </ul>

**Table E-3 Summary of Recommendations for Further Analysis and Research on Exposure Factors Data for Children**

Exposure Factor	Recommendation for Further Analysis and Research
Inhalation Rate	<ul style="list-style-type: none"> <li>the more recent CSFII data should be analyzed further to obtain food energy intake/energy expenditures for the recommended set of childhood age groups</li> <li>for short term, activity specific inhalation rate estimates, the approach of Allan and Richardson (1998) could be explored further but would need to be supported with the collection of additional activity data for children</li> <li>activity specific inhalation rate estimates could also be developed using the Layton (1993) approach as modified by McCurdy (2000); specifically, inhalation is calculated in the manner described by Layton but energy expenditure is estimated using a factorial approach in which an individual's activities are assigned energy expenditure values based on a multiplier of basal metabolic rate (termed a MET); daily estimates of energy expenditure derived from this method could be compared to estimates derived from the CSFII to lend insight into quality assurance issues</li> <li>a critical area of research (especially for children up to &lt;5 years of age) is the collection of ventilatory equivalence data for children; data collection efforts should consider susceptible populations such as asthmatic children</li> </ul>
Activity Patterns	<ul style="list-style-type: none"> <li>Analyze the most current version of the Consolidated Human Activity Database (CHAD) for activity pattern data applicable to the recommended age groups.</li> <li>develop methods for monitoring children's macroactivities</li> <li>collect population-based data on children's macroactivities and exposures to allow characterization as a function of age, gender, environmental setting (microenvironments), socioeconomic status, race/ethnicity, geographic location, and season; in particular, focus on young children (less than 4 years of age) and children aged 11 years and older</li> </ul>
Skin Surface Area	<ul style="list-style-type: none"> <li>update skin surface area estimates for children 2 years of age and older using the newer NHANES III data for height and weight; the analyses should support the recommended set of childhood age groups</li> <li>collect new height and weight data for children less than 2 years of age (for use in regression equations for determining skin surface area)</li> <li>more detailed studies of soil adherence to skin need to be conducted to determine variations among individuals and the effects of duration of activity, clothing use, and time of year on this factor</li> <li>explore the use of skin surface area in normalizing exposure estimates</li> </ul>
Body Weight	<ul style="list-style-type: none"> <li>further statistical analysis of the NHANES III data should be conducted to allow the derivation of multiple percentiles and distributional information for the recommended set of childhood age groups</li> <li>the NHANES III data should be analyzed further to develop body weight estimates that are specific for selected ethnic groups</li> <li>in addition to the relationship between age and weight, the existing data should be analyzed for other relationships (e.g., age and stature, body mass index, etc.) to develop a more complete understanding of body metrics that may have a bearing on exposures, doses, and risks</li> </ul>



## 1.0 INTRODUCTION

The 1993 National Academy of Sciences (NAS) report “Pesticides in the Diets of Infants and Children” highlighted important differences between children and adults with respect to risks posed by pesticides (NRC, 1993). Some of the principles in the NAS report provided the foundation for the Food Quality Protection Act of 1996 (FQPA) and the President’s Executive Order 13045, “Protection of Children from Environmental Health Risks and Safety Risk.” One of the provisions of the FQPA requires that children’s aggregate exposure be considered when establishing pesticide tolerances (legal limits for residues in food). Executive Order 13045 broadens consideration of impacts on children by stating that “each Federal agency: shall ensure that its policies, programs, activities, and standards address disproportionate risks to children that result from environmental health risks or safety risks”. Many of the comments the Environmental Protection Agency (EPA) received on the draft *Guidelines for Carcinogen Risk Assessment* (U.S. EPA, 1999) relate to the implementation of Executive Order 13045. In response to these comments and regulatory initiatives, EPA has been investigating ways to improve Agency risk assessments for children.

An EPA workgroup convened under the auspices of the Risk Assessment Forum has been exploring children’s exposure assessment issues. This workgroup has concluded that a major issue facing the Agency is how to consistently consider age-related changes in behavior and physiology when assessing early life stage exposure and potential dose. This issue is critical for scientists involved in preparing exposure assessments applicable to children and for use in evaluating integrated lifetime exposures.

Typically, Agency assessors have classified individuals under the age of 21 years as youth or children. However, how to subdivide this group in a consistent and scientifically supported manner has been somewhat elusive. Historically, Agency scientists have applied expert judgment to create age groups that capture periods of potentially high exposure or unusual exposure patterns (e.g., the frequency and duration of mouthing hands and objects during the 1 to <2 year old life stage). In some cases, expert judgment has been applied to capture vulnerable periods of development or critical windows when exposure to an environmental contaminant may be particularly damaging to a specific physiologic system (e.g., the effects of Pb on hemoglobin due to age related differences in iron deficiency). In many cases, the selection of age groups has been heavily influenced by the quality and quantity of existing data to support the development of exposure and potential dose estimates. The case-by-case application of these criteria has lead to cross-program variations in the specific age groups considered for assessing childhood exposure (see Figure 1).

The purpose of this paper is to provide guidance to Agency scientists on the appropriate age groups to consider when assessing childhood exposures and potential doses to environmental contaminants. The recommendations provided in this paper are based on discussions held during a July 2000 technical workshop on considering developmental changes when assessing exposures to children and a subsequent expert analysis of existing exposure factors data. This guidance provides a recommended set of childhood age groups to promote cross-program

consistency in Agency risk assessments for children. In addition, these age groups will guide future analyses of exposure factors data as well as new research and data collection efforts.

**Figure 1.**

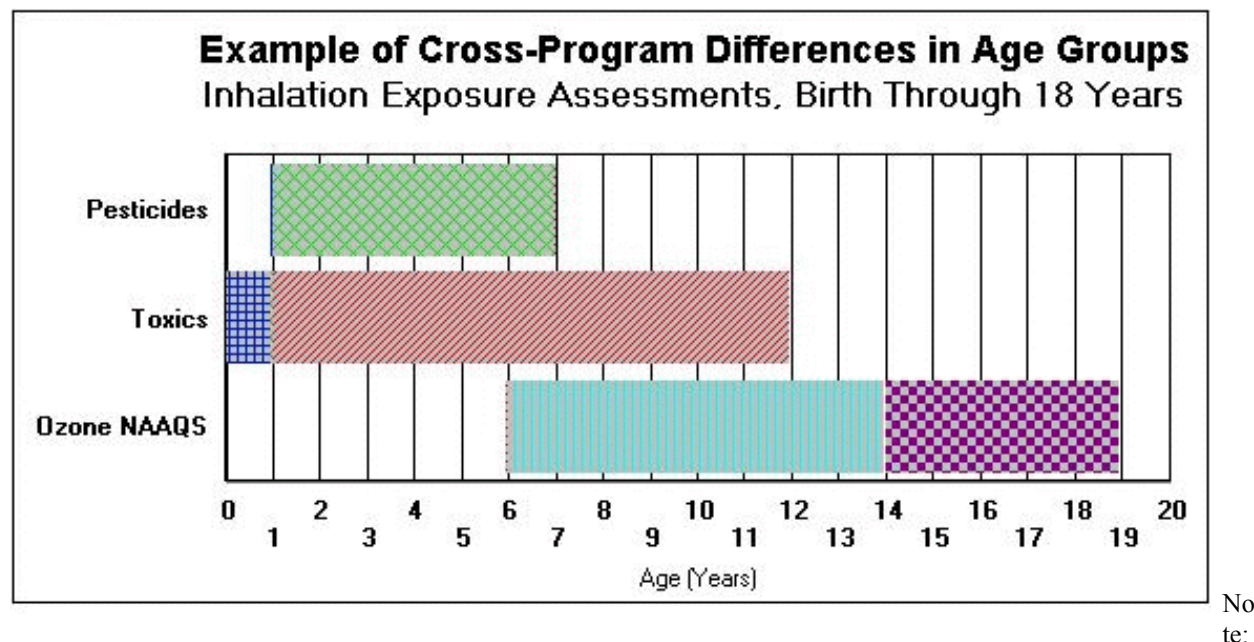


Figure 1 presents an example of the different childhood age groups that, in the past, have been considered in the exposure and risk assessments of three Agency programs. For inhalation exposures, the Office of Pesticide Programs typically assessed a childhood age group representing 1 to <7 years of age while the Office of Pollution Prevention and Toxics assessed groups representing birth to <1 year and 1 to <12 years and the Office of Air Quality Planning and Standards assessed groups representing 6 to <14 years and 14 to <19 years. These age groups may not reflect the current approach of any particular program.

## **2.0 AGE GROUPS TO CONSIDER WHEN ASSESSING CHILDHOOD EXPOSURES TO ENVIRONMENTAL CONTAMINANTS**

As noted in the introduction, children's behavior changes over time in ways that can have an important impact on exposure and potential dose. For example, crawling and mouthing of hands and objects during the 1 to <2 year stage of life can lead to dermal and oral potential doses that are appreciably higher than those of adults. Further, children's physiology changes over time in ways that can affect potential dose, internal dose, and susceptibility to certain health effects. The key issue is how to capture these changes in an assessment of risks from exposure to environmental contaminants.

On July 26 and 27, 2000, EPA held a workshop to examine developmental factors and how they influence the assessment of childhood exposure. Workshop participants included experts in the fields of pediatric medicine, toxicology, risk assessment, and public health. A summary of the workshop discussions is provided in the document *Summary Report of the Technical Workshop on Issues Associated with Considering Developmental Changes in Behavior*

*and Anatomy When Assessing Exposure to Children* (U.S. EPA, 2000). The discussions revealed that workshop participants preferred assessment approaches that could incorporate childhood development as a continuous function. However, recognizing the paucity of existing data, the participants concluded that age groupings (or bins) can be useful as guides for the development of environmental exposure scenarios. To that end, the workshop participants offered some preliminary advice on possible age groups related to developmental change. Note that prenatal development was outside the scope of the workshop discussions, but participants unanimously stressed the importance of including this lifestage in exposure and risk assessments.

To organize the workshop discussion, participants were divided into two subgroups according to their specific areas of expertise. One subgroup discussed behavioral development while the other focused on physiology and anatomical growth. Participants were asked to focus their discussion on those aspects of development that are particularly relevant to exposure and potential dose. These terms are defined in the EPA 1992 Guidelines for Exposure Assessment as:

*Exposure - Contact of a chemical, physical, or biological agent with the outer boundary of an organism. Exposure is quantified as the concentration of the agent in the medium [e.g., soil, water, air, food, etc.] in contact [with the organism], integrated over the time duration of that contact (EPA, 1992).*

*Potential Dose - The amount of chemical ingested, inhaled, or in material applied to the skin (EPA, 1992).*

*Internal Dose - The amount of chemical contained that has been absorbed and is available for interaction with biologically significant receptors (EPA, 1992).*

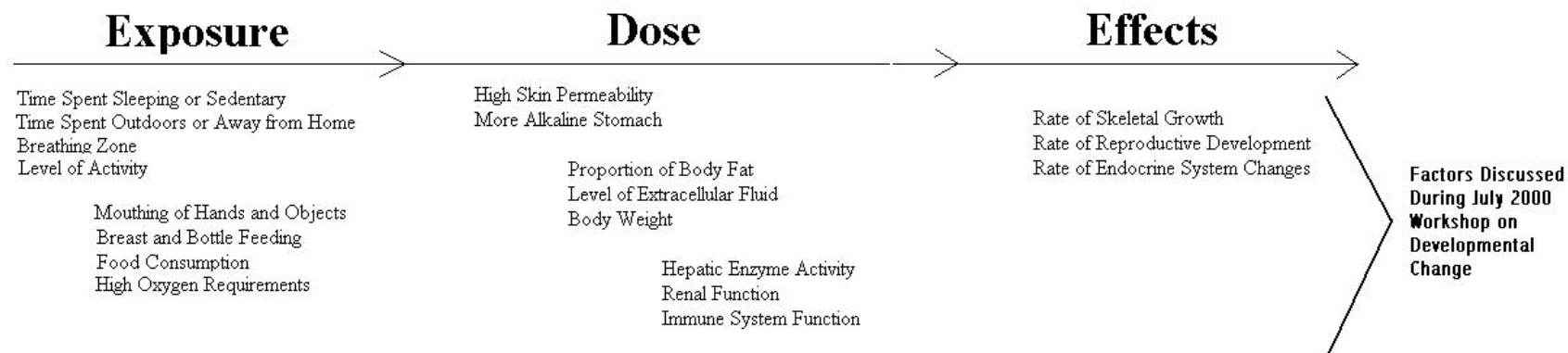
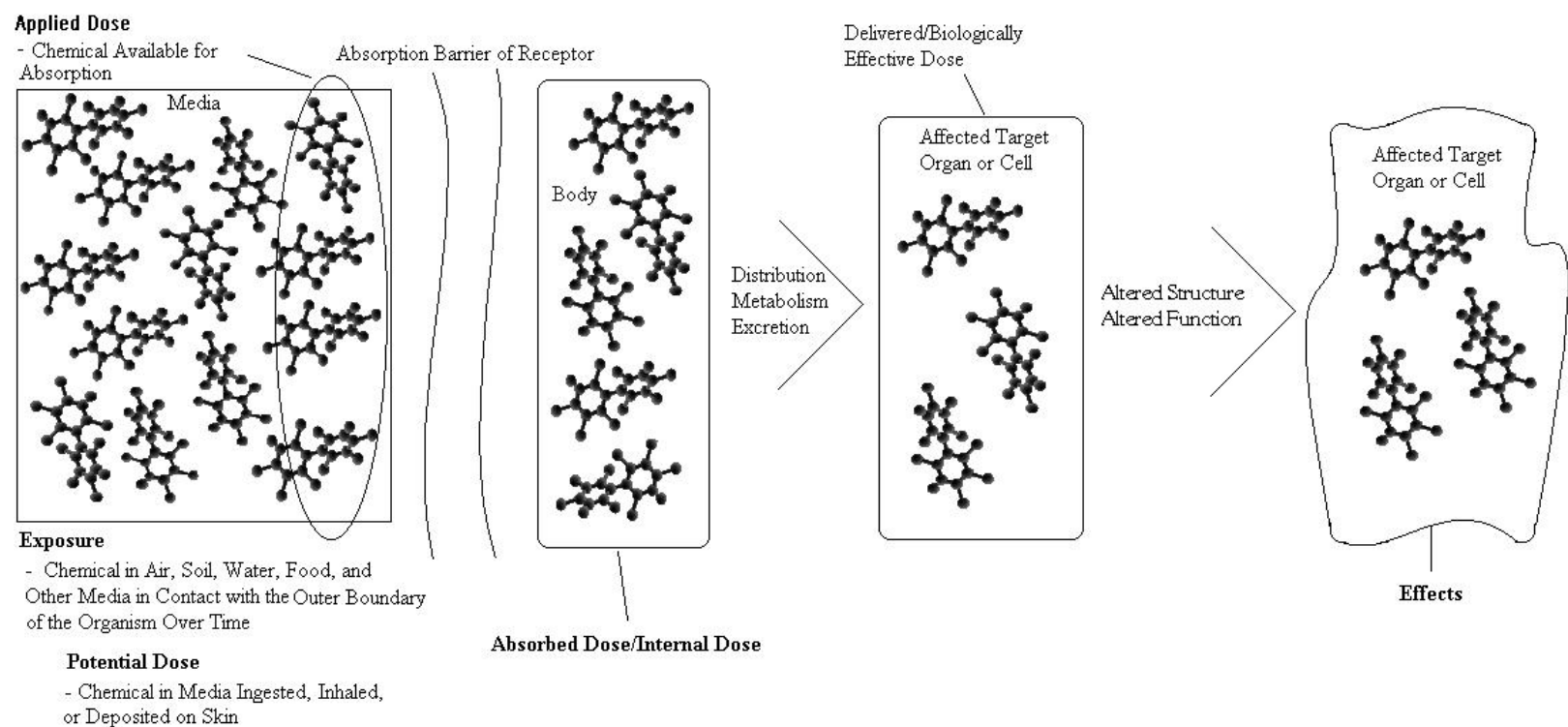
As will be noted below, some workshop participants found that the concepts of potential, internal dose, and effects are too interrelated to narrow the focus of the discussion to potential dose alone. The relationship between the 1992 Guidelines' definition of exposure and the related risk assessment concepts of dose and effects is portrayed in Figure 2. Figure 2 also lists some examples of characteristics that impact or otherwise provide an indication of exposure, dose, and possible susceptibility to effects. These example characteristics were discussed during the workshop.

The workshop subgroup addressing behavioral development recommended dividing the first year of life into three groups: 0 to <3 months, 3 to <6 months, and 6 to <12 months. After the first year of life, they recommended the following groups: 12 to <24 months, 2 to <6 years, 6 to <11 years, 11 to <16 years, and 16 to <21 years.<sup>1</sup> The participants in this subgroup arrived at

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<sup>1</sup> Note that a consistent language for describing age groups is lacking. The conventions that have been used (e.g., 1 to 2 years; 1-2 years; or simply 1 year, 2 year, 3 year, etc.) are imprecise in their meaning and have been inconsistently applied. For example, the behavior subgroup of the July 2000 workshop used 3 to 5 months to describe an age group spanning from the 1<sup>st</sup> day of the third month of life (day 90 post partum) through the last day of the 5<sup>th</sup> month of life (day 179). The physiology subgroup used the notation 3 to 6 months to describe the same time period. To avoid the confusion introduced by this linguistic imprecision, the Risk Assessment Forum workgroup has used the notation "x to <Y" in this paper (e.g., 3 to <6 months means day 90 through day 179).

**Figure 2. Relationship Between the Risk Assessment Concepts of Exposure, Dose, and Effects.**



these groupings by considering key factors or “major domains of behavioral development” for each route of exposure (U.S. EPA, 2000). For oral and dermal exposures, these factors included gross motor development, fine motor development, cognitive development, and social development. For inhalation exposures, the relevant factors included gross motor development, activity level, and breathing behavior (e.g., the transition from mouth to nasal breathing). Table 1 contains some examples of the specific considerations supporting the age groups derived by the behavior subgroup.

The subgroup addressing anatomy/physiological development recommended the following groupings: birth to <1 month, 1 to < 3 months, 3 to <6 months, 6 to <12 months, 1 to <3 years, 3 to <8 (female) or 9 (male) years, and 8 or 9 years to <16 (female) or 18 (male) years. The discussion that led to these age groups focused on anatomical characteristics (e.g., weight and proportion of body fat) and specific organ and physiological systems. These systems included: skin, skeleton, liver, immune system, reproductive system, endocrine system, lung and respiratory tract, gastrointestinal tract, circulatory system, renal system, cardiac system, central nervous system, muscle, and sensory organs. Table 2 contains some examples of the specific considerations supporting the age groups derived by the anatomy/physiology subgroup. The age groups listed in Table 2 were derived largely from considering the rate of change in the listed characteristics.

Early in the discussion of the anatomy/physiology subgroup, the participants concluded that developmental issues affecting exposure, potential dose, internal dose, and effects were too intertwined to allow an exclusive focus on potential dose. Therefore, their preliminary advice on possible age groups reflects some consideration of changes that impact internal dose and effects. For example, this subgroup discussed the maturity of hepatic enzyme activities (an indication of metabolic function affecting internal dose) and the rate of reproductive development (an indication of a susceptible period for effects) in developing their advice on age groups. Additional examples are noted in Table 2. While this subgroup’s recommendations do reflect some consideration of dose and effects issues, it should not be considered a comprehensive treatment of this subject. The Agency is currently considering childhood development and its relationship to dose and effects through other efforts.

**Table 1 - Examples of Factors Considered in Deriving Age Groups Reflecting Behavioral Development**

<b>Age Group</b>	<b>Characteristics Relevant to Oral and Dermal Exposure</b>	<b>Characteristics Relevant to Inhalation exposure</b>
Birth to <3 months	Breast and bottle feeding. Hand-to-mouth activities.	Time spent sleeping/sedentary.
3 to < 6 months	Solid food may be introduced. Contact with surfaces increases. Object/hand-to-mouth activities increase.	Breathing zone close to the floor.

**Table 1 - Examples of Factors Considered in Deriving Age Groups Reflecting Behavioral Development**

Age Group	Characteristics Relevant to Oral and Dermal Exposure	Characteristics Relevant to Inhalation exposure
6 to < 12 months	Food consumption expands. Children's floor mobility increases (surface contact). Children are increasingly likely to mouth non-food items.	Development of personal dust clouds.
12 to < 24 months	Children consume full range of foods. They participate in increased play activities, are extremely curious, and exercise poor judgment. Breast and bottle feeding cease.	Children walk upright, run, and climb. They occupy a wider variety of breathing zones and engage in more vigorous activities.
2 to < 6 years	Children begin wearing adult-style clothing. Hand-to-mouth activities begin to moderate.	Occupancy of outdoor spaces increases.
6 to < 11 years	There is decreased oral contact with hands and objects as well as decreased dermal contact with surfaces.	Children spend time in school environments and begin playing sports.
11 to < 16 years	Smoking may begin. There is an increased rate of food consumption.	Increased independence (more time out of home). Workplace exposure can begin.
16 to < 21 years	High rate of food consumption begins.	Independent driving begins. Expanded work opportunities.

**Table 2 - Examples of Factors Considered in Deriving Age Groups Reflecting Anatomical/Physiological Development**

Age Group	Anatomy/Physiology Characteristics
birth to < 1 month	Rapid growth and weight gain. Proportion of body fat increases. Increased skin permeability. Deficiencies in hepatic enzyme activity. Immature immune system functions. High oxygen requirements (leading to higher inhalation rates). Stomach more alkaline. Increases in extracellular fluid. Renal function less than predicted by surface area.
1 to < 3 months	Rapid growth and weight gain. Proportion of body fat increases. Deficiencies in hepatic enzyme activity. Immature immune system functions. High oxygen requirements (leading to higher inhalation rates). Stomach more alkaline. Increases in extracellular fluid. Renal function less than predicted by surface area.
3 to < 6 months	Rapid growth and weight gain. Proportion of body fat increases. Deficiencies in hepatic enzyme activity. Immature immune system functions. Increases in extracellular fluid. Renal function less than predicted by surface area.
6 to < 12 months	Rapid growth and weight gain. Body fat increase begins to level off. Deficiencies in hepatic enzyme activity. Immature immune system functions. Rapid decrease in extracellular fluid. Can begin predicting renal function by surface area.
1 to < 3 years	Some hepatic enzyme activities peaks, then falls back to adult range. Most immune system functions have matured. Extracellular fluid becomes more consistently related to body size.

**Table 2 - Examples of Factors Considered in Deriving Age Groups Reflecting Anatomical/Physiological Development**

Age Group	Anatomy/Physiology Characteristics
3 to < 8/9 years	Period of relatively stable weight gain and skeletal growth (as opposed to a period marked by growth spurts).
8/9 to < 16/18 years	Rapid skeletal growth. Epiphysial closure (may take until age 20). Rapid reproductive and endocrine system changes.

Prompted by the July 2000 workshop discussions, the Risk Assessment Forum workgroup developed an initial set of age groups that would serve as a starting point for the development of guidance. This initial set of age groups is presented in Table 3.

**Table 3 - Risk Assessment Forum Workgroup Initial Set of Childhood Age Groups**

Age Groups <1 Year	Age Groups ≥1 Year
birth to < 1 month	1 to < 3 years
1 to < 3 months	3 to < 6 years
3 to < 6 months	6 to < 11 years
6 to < 12 months	11 to < 16 years
	16 to < 18 years

These age groups were proposed as a reasonable interpretation of the July 2000 workshop recommendations. As a result of continuing deliberations and reviews of available exposure factors data, the Risk Assessment Forum workgroup concluded that it may be appropriate to further divide the 1 to < 3 years age group. An appropriate division would consider 1 to < 2 years and 2 to < 3 years as separate groups. This grouping is supported (in part) by the behavioral subgroup discussions from the July 2000 workshop (see Table 1). In addition, it is supported by existing exposure factors information (for example, consider the data for mouthing duration and frequency). The Risk Assessment Forum workgroup has further concluded that, in some cases, it may be appropriate to consider an additional age group spanning from 18 to < 21 years. It is unclear whether this age group should be considered part of the childhood lifestage or part of early adulthood. It is clear that it encompasses a period of continuing development and may capture important events such as a change in residence and epiphyseal closure (see Table 2). Therefore, *the Risk Assessment Forum workgroup is recommending the age groups presented in Table 4 as the set of age groups to consider when assessing childhood exposures to environmental contaminants.*

**Table 4 - Recommended Set of Childhood Age Groups for Agency Exposure Assessments**

<b>Age Groups &lt;1 Year<sup>a</sup></b>	<b>Age Groups ≥1 Year</b>
birth to < 1 month	1 to < 2 years
1 to < 3 months	2 to < 3 years
3 to < 6 months	3 to < 6 years
6 to < 12 months	6 to < 11 years
	11 to < 16 years
	16 to < 18 years
	18 to < 21 Years <sup>b</sup>

a) for purposes of evaluating exposure or potential dose but not internal dose, it may be acceptable to combine some of these groups (e.g., the first three groups could be combined to encompass “birth to < 6 months”)

b) to be considered on a case-by-case basis

The Risk Assessment Forum workgroup acknowledges that there may be instances where combining some of these age groups (e.g., combining the first three groups into one representing birth to <6 months) may be considered when estimating exposure or potential dose, especially if little variation might be expected. In addition, there may be instances where it is not necessary to address every age group listed above, because the focus of the exposure and risk assessment may be on a health effect for which only one or two of the above groups represent a critical window. Where there is a lack of exposure data for a particular age group of potential importance, the assessment could still include a rough estimate based on exposures of other age groups and consideration of how these age groups differ. It is recommended that if age groups are combined or excluded, the underlying scientific rationale should be provided in the exposure assessment. It is important for exposure assessors to engage in an iterative dialogue with toxicologists and other health scientists to determine the age groups (or portions of age groups) that will be the focus of any particular assessment. The Risk Assessment Forum workgroup recommends that the discussion of combining/eliminating age groups include the following elements.

- The basis for determining which age groups should be combined (or which groups can be dropped from the analysis) and why.
- A description of the scientific uncertainties and potential biases introduced when combining or excluding age groups (e.g., is an age group described as less than 1 year more representative of 6 to <12 months of age than younger age groups?)



- A discussion of the types of data and information that, if available, would allow combined age groups to be separated (or omitted age groups to be addressed) in future analyses.

### **3.0 PRELIMINARY REEVALUATION OF EXPOSURE FACTORS DATA FOR CHILDREN**

In the “Charge to Experts” for the July 2000 workshop (see U.S. EPA, 2000), several questions were posed to elicit discussion on whether existing exposure information is adequate to support a fine division of childhood age groups. The workshop participants provided the following general conclusion and recommendation:

“Data for both behavioral and anatomical exposure factors are limited in terms of both quality and coverage. The adequacy of current data sets is highly variable, and some of the data may not be useful because they were gathered using outdated methods or because lifestyle changes since the study was conducted make the results less relevant to today’s conditions. More up-to-date data would be useful for refining distributions of critical developmental periods.”

To explore this issue further, subsequent to the workshop, the Risk Assessment Forum workgroup commissioned an expert review and reevaluation of data available in the draft Child-Specific Exposure Factors Handbook (U.S. EPA, 2000a). The initial set of childhood age groups presented in Table 3 was used to guide this reevaluation. This reevaluation of exposure factors information contained a number of recommendations for short term analyses and longer term research to improve the database for childhood exposure. These recommendations were adopted by the Risk Assessment Forum workgroup and are summarized in the sections that follow.

#### **3.1 OVERVIEW**

The preliminary reevaluation of data available in the draft Child-Specific Exposure Factors Handbook (CSEFH) was accomplished through a panel of experts working under contract to Versar Inc. (Versar, 2001). Versar identified and selected experts based on their knowledge and experience working with specific exposure factors. The experts were asked to judge whether a reevaluation of the underlying exposure factors data would support new recommendations for the initial set of childhood age groups presented above in Table 3. In addition, the experts were asked to discuss quality assurance issues such as those considered in selecting key studies for the CSEFH. Some food intake data are available for the entire set of initial childhood age groups. Further, the expert providing the reevaluation analyzed these data using the same algorithms used for the draft CSEFH. Therefore, an example of how new food intake recommendations compare to recommendations from the June 2000 draft CSEFH is provided for per capita fruit in Appendix A, Table A-1.

The following discussion summarizes the recommendations for further analysis and research provided by the experts and adopted by the Risk Assessment Forum workgroup. For each route of exposure, single day exposure equations are provided to give some context for how

the exposure factors are used. Following the approach in the EPA Guidelines for Exposure Assessment (ISAPI, 1992), the exposure equations show calculation of potential dose (i.e., amount ingested, inhaled, or applied to the skin) or in one case, the absorbed dose (i.e., the amount crossing the exchange boundaries of skin, lung or digestion tract). The exposure equations are followed by summaries of the recommendations.

The single day exposure equations were selected for this discussion because of their convenience in presenting a context for the exposure factors. Depending on the health effects of concern, childhood exposures will need to be assessed for a variety of time horizons (e.g., from short term exposures lasting one to several weeks to longer term exposures lasting years). There are a number of issues related to using the recommended childhood age groups in various exposure models and time horizons. These issues will be discussed below in Section 4 of this guidance.

## 3.2 THE ORAL/INGESTION ROUTE OF EXPOSURE

Oral (ingestion) exposures are typically assessed by considering two major contributors: dietary exposures (from food, water, and breast milk intake) and incidental or non-dietary exposures (from mouthing hands and objects and from the deliberate ingestion of non-food items).

### 3.2.1 DIETARY EXPOSURES

The single-day potential dose of a contaminant associated with the consumption of one food item, water from one source, or breast milk can be estimated from the equation:

$$D_{pot(diet)} = C_{diet} \cdot IR_{diet} \quad \text{Equation (1)}$$

where:

$D_{pot(diet)}$	=	Single-day potential dose from ingestion of one food item, water from one source, or breast milk (mg/day)
$C_{diet}$	=	Concentration of contaminant in one food item, water from one source, or breast milk (mg/g)
$IR_{diet}$	=	Intake rate (mass) of food item, water, or breast milk (g/d)

Equation (1) can include terms for the contamination of food resulting from contact with surfaces and hands. However, in most cases there will be insufficient data to evaluate these terms. This is an area in need of further research.

### **3.2.1.1 *IR* FOR BREAST MILK**

Estimating potential dose for infants over longer time periods than a single day requires information on daily breast milk intake rates and the duration over which breast feeding occurs. In addition, information about the fat composition of breast milk is needed to estimate the possible concentration of chemical moieties in the milk. From the preliminary reevaluation of breast milk intake rate and fat composition using the existing data, recommendations can be derived for the initial set of childhood age groups for children 12 months of age and less (note that for breast milk fat/lipid composition, one estimate has traditionally been applied to all ages 12 months and less):

- Collect data that would allow estimation of the variability (i.e., estimation of distributions) across the population for milk intake as a function of age and/or infant weight. Studies should include consideration of the major ethnic groups in the U.S. population including Black, Asian, and Hispanic.
- Collect data that would allow estimation of the effect of a mother's nutrient status on the fat/lipid content of breast milk (both before and during lactation). Data are needed on the types of lipids that may change because of these variables and the mobility of such lipids in the milk during lactation.

The 6 to <12 month age group captures a period of rapidly decreasing breast milk intake. This observation is consistent with the July 2000 workshop discussion which noted the expanding variety of foods consumed during this time period. Therefore, future breast milk intake data collection efforts should consider that it may be appropriate to further divide the 6 to <12 month age group into two or three separate groups. In addition, it is believed that some infants older than 12 months continue to be breast fed. Data is needed to determine the frequency of breast feeding in older infants and to determine a reliable age, after which, it can be assumed that breast feeding has ceased.

### **3.2.1.2 *IR* FOR FOOD**

Children's exposure from food intake may differ from that of adults because of differences in the types and amounts of food eaten. Also, for many foods, the intake per unit body weight is greater for children than for adults. Based on the preliminary reevaluation of existing food intake data, recommendations can be derived for the initial set of childhood age groups for various food groups, individual foods, and the total diet. Food serving sizes and intake rates for home-produced foods were not included in this reevaluation because the data required to conduct such analyses are not readily available. In addition, fish intake was outside the scope of work for the preliminary reevaluation.

The CSEFH and the new recommendations provided through the preliminary reevaluation are based on the 1994-1996 CSFII. Analyses of the 1998 Continuing Survey of Food Intake by Individuals (1998 CSFII) will substantially improve the estimates of childhood

food intake. The 1998 CSFII is a supplemental study that specifically targeted childhood food consumption patterns. Combining the 1998 data with the 1994-1996 data dramatically increases the number of observations for some age groups. For example, for children less than 1 year of age, use of the 1998 study quadruples the number of observations compared to using the 1994-1996 study alone. Use of the 1998 study should improve overall confidence in the food intake estimates for children.

### 3.2.1.3 *IR* FOR WATER

The legislative mandates of the Safe Drinking Water Act (SDWA) Amendments of 1996 require EPA to gather up-to-date information on water ingestion and to identify subpopulations that may be at elevated risk of health effects from exposure to contaminants in drinking water. To fulfill this mandate, EPA's Office of Water (OW) uses estimates of per capita water ingestion found in the dietary and demographic data from the 1994-1996 CSFII (note that OW is currently evaluating the use of the 1998 CSFII). The CSEFH recommendations are based on the OW analysis, supplemented with additional studies that support recommendations for special subpopulations and probability distributions. Based on the preliminary reevaluation of existing water intake data, recommendations can be derived for the initial set of childhood age groups for direct ingestion (e.g., ingestion of tap water as a beverage), indirect ingestion (e.g., ingestion of tap water added during food preparation), and the total of direct and indirect ingestion.

More research on the water intake of children and further analysis of the CSFII data are recommended. The 1998 CSFII may substantially improve the estimates of childhood water intake. The 1998 CSFII is a supplemental study that specifically targeted childhood consumption patterns. Combining the 1998 data with the 1994-1996 data would likely increase the number of observations for some age groups. As noted above, the EPA OW is currently evaluating these data. Use of the 1998 study should improve overall confidence in the water intake estimates for children.

## 3.2.2 NON-DIETARY EXPOSURES

Incidental or non-dietary ingestion exposures result from the mouthing of contaminated hands and objects and from the deliberate ingestion of non-food items (also known as pica behavior). Currently, two approaches to estimating potential dose are commonly employed.

The first approach is used where data exist on the intake rate (*IR*), notably for ingestion of soil or a combination of soil and indoor dust. This approach uses a variation of equation 1 where the non-food vehicle (e.g., soil or dust) is substituted for the food item:

$$D_{pot(non-diet)} = C_{non-diet} \cdot IR_{non-diet} \quad \text{Equation (2)}$$

where:

$D_{pot(non-diet)}$	=	Single-day potential dose from ingestion of one non-dietary substance (e.g., soil) from one source (mg/day)
$C_{(non-diet)}$	=	Concentration of contaminant in substance (mg/g)
$IR_{(non-diet)}$	=	Intake rate (mass) of substance (g/d)

The second approach is used when data on  $IR$  do not exist and are generally not obtainable. It involves looking at the specific locations and activities that bring a child into contact with a contaminant. In this approach, locations are divided into microenvironments, which are defined as surroundings that can be treated as homogeneous or well characterized in the concentrations of an agent ( e.g., home, office, automobile, kitchen, store). Behaviors are defined as macroactivities and microactivities. Macroactivities are general activities such as watching television, sleeping, and showering. Microactivities are detailed actions that occur within a macroactivity, such as mouthing of objects and moving around on the floor while playing.

Ingestion of contaminants present on surfaces in product formulations, adsorbed to dust, and in neat form are usually assessed using a microactivity approach, embodied in an equation of the following type:

$$D_{pot(non-diet)} = CL_{h/o} \cdot TE_{mouth} \cdot SA_{h/o} \cdot EF_{mi} (ort_{mi}) \quad \text{Equation (3)}$$

where

$D_{pot(non-diet)}$	=	Single-day potential dose from ingestion of contaminant for a given microactivity (e.g., mouthing hands; mouthing objects) over a 24-hour period (mg/day)
$CL_{h/o}$	=	Total contaminant loading on hand or object (mg/cm <sup>2</sup> ). For hands, $C_{h/o}$ can be estimated from a microactivity approach to dermal exposure assessment if sufficient data are available
$TE_{mouth}$	=	Transfer efficiency - fraction transferred from hand or object to mouth (unitless).
$SA_{h/o}$	=	Surface area of hand or object that is mouthed (cm <sup>2</sup> /event or cm <sup>2</sup> /minute)
$EF_{mii}$	=	Frequency of microactivity (e.g., number of mouthing events) over a 24-hour period (events/day)

$t_{mi}$  = Total time spent engaged in microactivity over a 24-hour period (minutes/day).

The following discussion addresses  $IR$  for soil,  $EF_{mi}$  and  $t_{mi}$ . Skin surface area is addressed in the section discussing the dermal route of exposure (object surface area is case specific) while transfer efficiencies ( $TE_{mouth}$ ) are chemical/media specific and will not be addressed in this document. As noted above, contaminant loading on hands ( $CL_{h/o}$ ) can be estimated from a microactivity approach to dermal exposure assessment if sufficient data are available (see discussion in section 3.4).

### 3.2.2.1 $IR$ FOR SOIL

Children's exposure to contaminants in soil and dust differs from that of adults primarily because of differences in behavior patterns. Several studies have been conducted to estimate the amount of soil ingested by children. Most of the early studies attempted to estimate the amount of soil ingested by measuring the amount of dirt present on children's hands and making generalizations based on behavioral assumptions. More recently, soil intake studies have been conducted using a methodology that concurrently measures trace elements in feces and soil. The selected trace elements are believed to be poorly absorbed in the gut. This approach is referred to as the mass balance approach. The preliminary reevaluation of mass balance soil intake data indicates that, using the existing data, recommendations can be derived for the initial set of childhood age group ages 1 to < 3 years, 3 to < 6 years and 6 to < 11 years.

There is a paucity of data for estimating childhood soil ingestion rates. A broad research program in soil ingestion is needed to fill this data gap. Components of such a program could include:

- Collecting soil ingestion data on a broader range of childhood ages (e.g., 3 months to < 13 years).
- Collecting data that would allow estimation of variability and distributions of intake across geographic areas, race, economic status and other demographic variables.
- Collecting data that would allow the characterization of seasonal variation in soil intake. These data would support the development of distributional information for long term exposures.

### 3.2.2.2 $EF_{mi}$ and $t_{mi}$

Children contact potentially contaminated surfaces and objects with their hands more frequently than adults as they explore their environment. Further, children have the urge to mouth objects or their fingers as a sucking reflex and as a habit. Data on these behaviors (referred to as microactivity data) are sparse. The majority of information comes from small studies, many of which were designed to test methodologies for monitoring microactivities. The

limited data focus on the frequency of and time spent mouthing hands and objects (as noted above if mouthing time [minutes/day] is used to estimate exposure,  $SA_{h/o}$  in Equation (3) must be presented per unit time [i.e., cm<sup>2</sup>/minute], not per event). Given the paucity of existing data, no new microactivity recommendations can be made at this time.

A research program, including a comprehensive data collection effort is needed to improve estimates of microactivities for non-dietary exposure assessment. Existing studies are small and include a variety of methodologies. Systematic, probability-based studies should be undertaken that address a broad range of childhood age groups (at least to < 6 years of age).

### 3.3 THE INHALATION ROUTE OF EXPOSURE

Children may be more highly exposed than adults through inhalation of environmental contaminants. Infants and young children have a higher resting metabolic rate and rate of oxygen consumption per unit body weight than adults because they have a larger area for heat loss and they are growing rapidly (see Table 2). The following discussion summarizes the expert reevaluation of exposure factors data relevant for the inhalation route of exposure.

A 24-hour potential dose from inhalation exposure to environmental contaminants in a microenvironment during a macroactivity can be estimated from the following equations:

$$D_{pot(inh)} = C_{me} \cdot IR_{air/ma} \cdot t_{me/ma} \quad \text{Equation (4)}$$

where

$D_{pot(inh)}$	=	Inhalation potential dose over a 24 hour period for one macroactivity in one microenvironment (mg/day)
$C_{me}$	=	Average concentration of contaminant in the air of the microenvironment in 24 hour period (mg/m <sup>3</sup> )
$IR_{air/ma}$	=	Air intake rate (inhalation or respiration rate) associated with macroactivity (m <sup>3</sup> /hour)
$t_{me/ma}$	=	Time spent in microenvironment pursuing macroactivity in 24 hour period (hours/day)

The following discussion addresses *IR* and *t*. Note that *t* is also used in some dermal exposure models. Therefore the section on the dermal route of exposure will refer back to the discussion provided in this chapter for *t*

### 3.3.1 *IR* FOR INHALATION

Three basic techniques are used for estimating intake rate for inhalation. The first technique uses direct measurements of breathing rates during various activities. A measured average breathing rate can be used. Or if data are available, breathing rates can be assigned to various activities and daily values can be calculated as the sum of the activity-specific breathing rates, weighted by activity durations. In contrast, a metabolically based approach determines breathing rate as a function of the oxygen demand needed to provide the metabolic energy for sustaining a given lifestyle. The third approach is a hybrid of the first two. A physiological measure of oxygen consumption, such as heart rate, is used along with activity data to estimate how much air is inhaled during an individual's daily activities. The preliminary reevaluation focused on the metabolic approach of Layton (1993) which estimates daily inhalation rate as follows:

$$IR_{air} = E \cdot VQ \cdot H \cdot CV \quad \text{Equation (5)}$$

where

$IR_{air}$	=	Air intake rate (m <sup>3</sup> /day or m <sup>3</sup> /hour)
$E$	=	Energy expenditure or intake (kcal/day or kcal/hour)
$VQ$	=	Ventilatory equivalent (i.e., the ratio of the minute volume to oxygen uptake at body temperature, ambient pressure, and water vapor saturated air [unitless])
$H$	=	Volume of oxygen at standard temperature and pressure (dry air) consumed in the production of 1 kcal of energy (0.21 L O <sub>2</sub> /kcal)
$CV$	=	Unit conversion factor = 0.001 m <sup>3</sup> /L

To solve Equation 5, age specific data are needed to estimate *E* and *VQ* (*H* and *CV* are constants). Age specific estimates of *E* (food energy intake) can be determined from the national food consumption studies. The draft CSEFH recommendations are based, in part, on the analyses of Layton (1993) who used the 1977-1978 National Food Consumption Survey (NFCS). Estimates of *E* based on the more recent food consumption studies are approximately 10% higher.



Data for determining age specific estimates of  $VQ$  (a measure of breathing efficiency) are limited. Existing data do not support recommendations for children less than 3 years of age due to the lack of  $VQ$  data for these ages. Further, although the existing data may support a recommendation for children aged 3 to < 6 years, the data are very limited. The paucity of data for young children is a particularly important source of uncertainty given that the limited data (and the current understanding of childhood physiology) suggest that  $VQ$  will be higher for these age groups. The existing data do support recommendations for children aged 6 to < 11 years, 11 to < 16 years, and 16 to < 18 years.

The following are several recommended areas of further analysis and research:

- First, the more recent CSFII data can be analyzed further to obtain food energy intake/energy expenditures ( $E$ ) for the entire initial set of childhood age groups.
- For short term, activity specific inhalation rate estimates, the approach of Allan and Richardson (1998) could be explored further but would need to be supported with the collection of additional activity data for children.
- Activity specific inhalation rate estimates could also be developed using the Layton (1993) approach as modified by McCurdy (2000). Specifically, inhalation is calculated in the manner described above but  $E$  is estimated using a factorial approach in which an individual's activities are assigned energy expenditure values based on a multiplier of basal metabolic rate (termed a MET). Daily estimates of  $E$  derived from this method could be compared to estimates derived from the CSFII to lend insight into quality assurance issues.
- Finally, a critical area of research (especially for children less than 6 years of age) is the collection of  $VQ$  data for children. Data collection efforts should consider susceptible populations such as asthmatic children.

### 3.3.2 $t_{me/ma}$ TIME SPENT IN MICROENVIRONMENTS PURSUING MACROACTIVITIES

Childhood exposures to environmental contaminants are influenced by the locations where children spend their time and by the types of activities in which they engage. For example, the number of hours per day children spend indoors at home (a specific microenvironment), watching TV (a specific macroactivity) will be an important determinant in estimating their daily inhalation, dermal, and non-dietary ingestion exposures. Various studies available in the published literature examine these two facets of childhood activity patterns. To consider whether new recommendations for the initial set of childhood age groups can be derived, the draft CSEFH and a more recent publication by Hubal et al. (2000) which provides a preliminary evaluation of data available in EPA's Consolidated Human Activity Database (CHAD) have been considered. CHAD includes a compilation of data from several activity

pattern studies including: Human Activity Patterns in Cincinnati Ohio (1987), Activity Patterns in a Retirement Home in Baltimore County Maryland (1997 and 1998), California Air Resources Board Activity Patterns of California Residents (1988), California Air Resources Board Activity Pattern Survey for California Children (1990), A Study of Personal Exposure to Carbon Monoxide in Denver Colorado (1983), Los Angeles Area Studies: Development of Improved Methods to Measure Effective Doses of Ozone (1989 to 1992), the University of Michigan National Study (1997), the National Human Activity Pattern Studies (1992 to 1994), the Valdez Air Health Study (1991), and the Study of Carbon Monoxide Exposure of Residents of Washington DC (1984).

Given the paucity of existing data, new recommendations for children less than 1 year of age and 11 years of age and older cannot be made. Referring to Hubal et al. (2000), the expert providing the preliminary reevaluation stated that “the current database on children’s macroactivities is sparse and data are insufficient to adequately assess exposures to environmental contaminants. However, the results of the Hubal et al. (2000) evaluation of CHAD data for children less than 12 years of age are sufficient to provide recommendations for time in microenvironments and participation in certain macroactivities for children in age groups of [1 to < 3 years], [3 to < 6 years], and [6 to < 11 years].”

The expert providing the preliminary reevaluation supported the conclusions and recommendations of Hubal et al. (2000) stating that the present state of knowledge regarding children’s exposures and activities are inadequate to assess exposures to environmental contaminants sufficiently. The expert recommended two specific areas of research.

- Develop methods for monitoring children’s activities and exposures.
- Collect population-based data on children’s activities and exposures to allow characterization as a function of age, gender, environmental setting (microenvironment), socioeconomic status, race/ethnicity, geographic location, and season. In particular, focus on young children (less than 4 years of age) and children aged 11 years and older.

### **3.4 THE DERMAL ROUTE OF EXPOSURE**

Dermal exposure to environmental contaminants can occur during a variety of activities involving different media and microenvironments. These include: swimming or showering in contaminated water; playing outdoors in contaminated soil and sediment; using commercial products (e.g., use of mosquito repellent); and playing indoors on contaminated floors or countertops. The magnitude of such exposures is influenced by age-specific behavioral factors such as time spent playing and crawling on contaminated surfaces and the amount of clothing worn during play activities.

The following discussion focuses on approaches to estimating childhood dermal exposure to contaminants in soil, on surfaces, and in water. Each approach uses different calculations and

requires different data (although there is some overlap). For dermal exposures to contaminants in soil, the following general equation can be used:

$$D_{pot(dermal)} = C_{soil} \cdot SA_{dermal/ma} \cdot ADH_{dermal/ma} \cdot EF_{ma} \quad \text{Equation (6)}$$

where

$D_{pot(dermal)}$	=	Dermal potential dose over a 24 hour period of contaminants in a single source of soil for a single macroactivity (mg/day)
$C_{soil}$	=	Contaminant concentration in a single source of soil (mg/g)
$SA_{dermal/ma}$	=	Total surface area of skin exposed to soil during macroactivity (cm <sup>2</sup> )
$ADH_{dermal/ma}$	=	Soil adherence to skin for macroactivity (g/cm <sup>2</sup> /event)
$EF_{ma}$	=	Frequency of macroactivity over a 24 hour period (events/day)

Given that soil adherence can vary across different regions of the body (e.g., hands versus legs), the above equation is often solved for individual body parts and total daily exposure estimated by summing. In such cases, surface area and soil adherence data for specific body parts is needed.

There are two approaches to calculating dermal exposure to contaminants on surfaces: a macroactivity approach and a microactivity approach. For the macroactivity approach (also referred to as the transfer coefficient approach), the following equation has been used:

$$D_{pot(dermal)} = CL_{surf} \cdot TC_{surf/ma} \cdot t_{me/ma} \quad \text{Equation (7)}$$

where

$D_{pot(dermal)}$	=	Dermal potential dose over a 24 hour period for a single microenvironment/surface/macroactivity combination (mg/day)
$CL_{surf}$	=	Total contaminant loading on a single surface in the microenvironment (mg/cm <sup>2</sup> )
$TC_{surf/ma}$	=	Dermal transfer coefficient for a specific surface and macroactivity combination (cm <sup>2</sup> /hour). $TC_{surf/ma}$ represents the surface area contacted per unit time that results in a transfer of contaminants to skin.
$t_{me/ma}$	=	Time spent in microenvironment pursuing macroactivity in 24 hour period (hours/day)

For the microactivity approach, the following equation is typical:

$$D_{pot(dermal)} = CL_{surf} \cdot TE_{surf} \cdot SA_{surf/mi} \cdot EF_{mi} \quad \text{Equation (8)}$$

where

$D_{pot(dermal)}$	=	Dermal potential dose over a 24 hour period for a given microenvironment/surface/microactivity (mg/day)
$CL_{surf}$	=	Total contaminant loading on a single surface in the microenvironment (mg/cm <sup>2</sup> )
$TE_{surf}$	=	Transfer efficiency - fraction of contaminant transferred from the surface to the skin per microactivity event (unitless)
$SA_{surf/mi}$	=	Area of surface that is contacted per microactivity event (cm <sup>2</sup> /event)
$EF_{mi}$	=	Frequency of microactivity (e.g., knee contact with floor) over a 24 hour period (events/day)

For dermal exposure to contaminants in water or other fluids in which the skin is immersed, a permeability coefficient is used to calculate uptake as an absorbed dose:

$$D_{abs(dermal)} = C_{water/ma} \cdot k_p \cdot SA_{dermal} \cdot t_{ma} \quad \text{Equation (9)}$$

where

$D_{abs(dermal)}$	=	Dermal absorbed dose over a 24 hour period of contaminants in a single source of water for a single macroactivity (mg/day)
$C_{water/ma}$		Concentration of contaminant in water
$k_p$	=	Permeability coefficient (cm <sup>2</sup> /hr) which is measured experimentally
$SA_d$	=	Total surface area of exposed skin (cm <sup>2</sup> )
$t_{ma}$	=	Time spent in macroactivity over a 24 hour period (hr/day)

Overall, the assessment of dermal exposures is an area that is ripe for research. The preliminary reevaluation for dermal exposure factors focused on two factors in the equation for estimating dermal exposure to contaminants in soil: total skin surface area ( $SA_{dermal}$  - also used in estimating exposure to contaminants in water) and soil adherence to skin ( $ADH_{dermal/ma}$ ).  $SA_{dermal}$  will be discussed below in section 3.4.1. Soil adherence to skin ( $ADH_{dermal/ma}$ ) is more closely related to activity than age and will not be evaluated further in this document.

Data on the frequency of macroactivities ( $EF_{ma}$ ) are sparse. Most studies have focused on the time spent in such activities (e.g.,  $t_{me/ma}$  - minutes/day) as opposed to the number of times the activities are performed each day. Exceptions include the frequency of swimming and showering events. Therefore, data on the frequency of macroactivities were not included in the preliminary reevaluation.

For the macroactivity approach to assessing dermal exposure to contaminants on surfaces, the data for time spent in microenvironments pursuing macroactivities ( $t_{me/ma}$ ) is discussed above in section 3.3.2. The data available for the development of dermal transfer coefficients ( $TC_{surf/ma}$ ) is extremely limited. The EPA Office of Pesticide Programs (OPP) has proposed an interim value of 10,000 cm<sup>2</sup>/hour for children playing outdoors on lawns and indoors on carpeted or hard flooring (U.S. EPA, 1997). This value was derived from a California EPA study in which adults mimicked the activities of children on a contaminated carpet. OPP applied a correction to account for the differences in body surface area between adults and children. The macroactivity approach would benefit greatly from further research providing activity and surface specific dermal transfer coefficients for children. The preliminary reevaluation did not include a review of this factor.

As with the macroactivity approach, few data exist to support the use of the microactivity approach to estimating dermal exposures from contaminated surfaces. The data for frequency of microactivities ( $EF_{mi}$ ) is discussed in section 3.2.2.2. Most of the available studies focus on the frequency of mouthing events in children. For this specific microactivity and others (e.g.,

specific body part contacts with surfaces) the data are extremely sparse. Further, data on the area of surface that is contacted during a microactivity event ( $SA_{surf}$ ) is virtually non-existent. As noted above in section 3.2.2.2, a systematic, comprehensive data collection effort is needed to support these exposure factors. The remaining factors in the microactivity dermal exposure equation are chemical/media specific.

For the estimation of dermal exposure from contact with contaminated water, skin surface area ( $SA_{dermal}$ ) will be addressed in the section that follows. For other factors in equation (9), consult the Superfund Dermal Guidance (add reference) for a complete discussion. One component, time spent bathing, showering, or swimming ( $t_{me/ma}$ ), is discussed above in section 3.3.2. As noted above for estimating dermal exposure to soil, data on the frequency of macroactivities ( $EF_{ma}$ ) were not included in the preliminary reevaluation.

### **3.4.1 $SA_d$ OR SKIN SURFACE AREA**

Dermal exposures can be estimated using the skin surface area of the total body (as in estimating dermal exposure during showering) or using the skin surface areas of specific body parts (as noted above for estimating dermal exposure from contaminants in soil). In either case, the skin surface areas are typically based on estimates derived from the relationship between height, weight, and surface area. Historically, regression equations have been derived from analyzing the concurrent height/weight/surface area measurements made by Boyd (1935). Then, distributions of measured values of height and weight available in the National Health and Nutrition Examination Surveys (NHANES) are used in the regression equations to develop distributions of skin surface area for the U. S. population. This is the approach employed by EPA in the CSEFH.

NHANES III data could be used to provide new recommendations for estimates of skin surface area for the initial childhood age groups 2 years of age and older (EPA used the NHANES II data for children > 2 years of age in the draft CSEFH).

For further analysis and research on skin surface area, new height and weight data for children less than 2 years of age are needed. Further, although dermal soil adherence ( $ADH_{dermal/ma}$ ) is more activity specific than age specific, more detailed studies of  $ADH_{dermal/ma}$  could be conducted to determine variations among individuals and the effects of duration of activity, clothing use, and time of year on this factor.

In addition, there is a need to update skin surface area estimates for children 2 years of age and older using the newer NHANES III data for height and weight. The analyses should support the recommended initial set of childhood age groups provided in Table 4 of this document.

#### ***A Final Note on Skin Surface Area***

In calculating dose, it has been common practice at EPA to divide the daily potential or absorbed dose estimates by human body weight (in kg). This will be discussed further in the

next section. This calculation (referred to as normalizing the exposure estimate) facilitates comparisons between exposures and the various measures of toxicity.

In the discussion of water intake (*IR* for water), the expert providing the preliminary reevaluation quoted an observation by J. D. Current (1998): “it is a frequent practice in anesthesiology and critical care medicine to use estimates of human body surface area to reflect the body’s metabolic functions, such as ventilation rate [inhalation rate], fluid requirements, and extracorporeal circulation” (Versar, 2001). This observation is supported by the discussions of the physiology subgroup of the July 2000 workshop on developmental change. It appears that this subgroup considered the ability to predict renal function using body surface area to be an important determinant in grouping children by age (see Table 2). The subgroup indicated that such predictions begin to be reliable at 6 months of age and beyond.

The expert providing the preliminary reevaluation recommended that exposures from water intake should be normalized by body surface area. This recommendation could apply equally to other exposure estimates (e.g., exposure from food intake). However, a corresponding change in the approach to normalizing the various measures of toxicity would also be needed. This issue needs to be explored further.

### **3.5 HUMAN BODY WEIGHT (BW)**

As noted above, human body weight is used to normalize daily exposure estimates in the calculation of daily potential doses. For dietary exposures, the studies used to derive intake rates for food and water (namely the CSFII 1994-1996 and 1998 studies) include body weight information for each individual surveyed. Therefore, the food and water intake for a specific individual can be normalized by the body weight for that individual to yield potential doses in units of g/kg-day. For breast milk ingestion, non-dietary ingestion, inhalation, and dermal contact, such concurrent collection of body weight information is absent from the relevant exposure factors data. Therefore, these exposures must be normalized by body weight information from other sources. Typically, these exposures are normalized by average body weight estimates for the general U. S. population derived from data available in the NHANES studies. The following discussion conveys the results of the preliminary reevaluation of human body weight data for the initial set of childhood age groups and areas identified for further research

- Further statistical analysis of the NHANES III data will allow the derivation of multiple percentiles and distributional information for the initial set of age groups.
- In addition to the relationship between age and weight, the existing data should be analyzed for other relationships (e.g., age and stature, body mass index, etc.) to develop a more complete understanding of body metrics that may have a bearing on exposures and risks.

- The NHANES III data should be analyzed further to develop body weight estimates that are specific for selected ethnic groups.

#### **4.0 THE RECOMMENDED SET OF CHILDHOOD AGE GROUPS, EXISTING EXPOSURE MODELS AND TEMPORAL ISSUES**

This guidance provides a recommended set of childhood age groups for consideration in Agency exposure and risk assessments. The purpose in providing these recommendations is to introduce a consistent starting point for program specific assessments and research initiatives for children. In addition, this guidance provides a preliminary review of existing exposure factors data for children to determine how well current data will support the use of the recommended groupings and to provide some initial guidance on research areas.

In addition to the issues summarized above, exposure assessors using the recommended set of childhood age groups will encounter issues related to the structure and function of existing exposure models and issues related to addressing various time horizons for exposure and risk assessment. The following discussion highlights some of these issues to help the assessor make more informed decisions when using the recommended age groups.

#### **4.1 EXISTING EXPOSURE MODELS FOR AGGREGATE AND CUMULATIVE RISK ASSESSMENT**

Currently, there are several models under development for assessing aggregate and cumulative exposure and risks. These include Calendex, developed by Novigen Sciences, Inc., the LifeLine Model Version 1.1, developed under a cooperative agreement between EPA's Office of Pesticide Programs and Hampshire Research Institute, the Stochastic Human Exposure and Dose Simulation Model (SHEDS), under development by EPA's Office of Research and Development, the Cumulative and Aggregate Risk Evaluation System (CARES), under development by member companies of the American Crop Protection Association, and the Residential Exposure Year Model (RexY), under development by Infosciences.com. Generally, these models are being developed to address the aggregate exposure/cumulative risk mandates for pesticides under the Food Quality Protection Act of 1996 (FQPA). Each of these models involves combining exposures to an individual or population of individuals across sources, pathways and routes and presenting the exposure results at a given time or as time profiles. These models use well established exposure algorithms along with probabilistic sampling techniques and survey instruments to estimate daily exposure and simulated longitudinal exposure patterns. Establishment of criteria ( e.g. age) to match data from multiple survey instruments is essential to the construct of these models. It is important for the exposure assessor to develop a full understanding of the model construct. Such an understanding will allow the model outputs to be interpreted in light of the recommended childhood age groups described in this document and will allow for a more complete characterization of uncertainties. Figure 3 helps to illustrate this point.

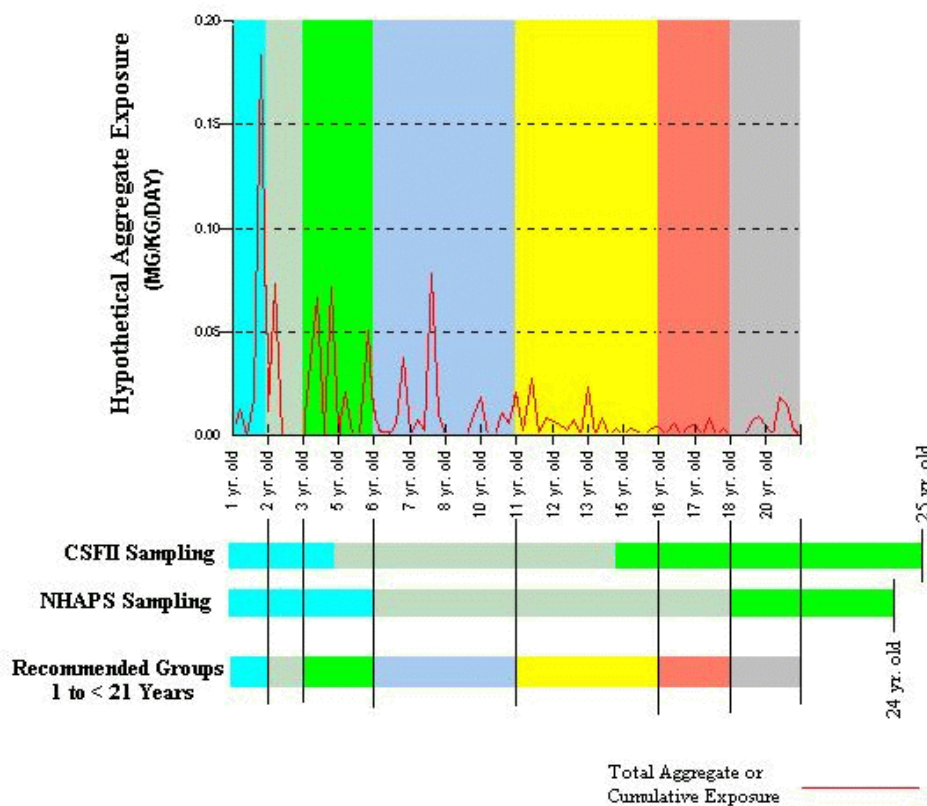
To develop time profiles of aggregate and cumulative exposures, each of these models randomly samples the existing exposure factors data. It is important for the exposure assessor to



develop a full understanding of the sampling algorithms used by each model. Such an understanding will allow the model outputs to be interpreted in light of the recommended childhood age groups and will allow for a more complete characterization of uncertainties. Figure 3 helps to illustrate this point.

Figure 3 portrays an example aggregate/cumulative time profile of single day exposures for ages 1 to <21 years. It should be noted that, although the existing models estimate single day exposures, they may not provide profiles of single day exposures as portrayed in Figure 3. Instead they provide profiles of seasonal averages or seasonal maximum exposures. This is done to conserve computing resources. To construct the profile in Figure 3, the example model randomly sampled food consumption data from the Continuing Survey of Food Intake by Individuals (CSFII) and activity pattern data from the National Human Activity Pattern Survey (NHAPS). Random samples were drawn from bins defined by certain age ranges. As can be seen in Figure 3, the ages represented by the sampling bins do not align with the childhood age groups recommended in this guidance. For example, daily food consumption estimates for children aged 3 to <6 years were drawn partly from a CSFII bin representing 1 to <5 years (for the 3 to <5 year olds) and partly from a CSFII bin representing 5 to <15 years (for the 5 to <6 year olds). The activity pattern estimates for this age group (3 to <6 years) were drawn from a NHAPS bin representing 1 to <6 years. There may be sound statistical reasons for the age bins used in the example model. For example, achieving a particular sample size within each bin may have driven the selection of ages that were included. However, such circumstances illustrate the need for additional exposure factors data for children. In the case of the daily food consumption estimates, use of the CSFII 1998 survey may allow the sampling bins in this model to be refined to more closely align with the recommended childhood age groups.

**Figure 3. Example Time Profile of Aggregate/Cumulative Exposure Comparing Model Sampling Algorithms with Recommended Childhood Age Groups.**



Note: The time profile of exposure depicted in Figure 3 is adapted from a model that is currently under development. Therefore, the profile and sampling algorithms may not represent the current functioning of any particular model but serve to illustrate the issue discussed in this section.

The example presented in Figure 3 represents an oversimplification in that it only portrays random sampling from two exposure factor databases (CSFII and NHAPS). In this case, the databases include consumption estimates for food and water ( $W_T$  for food and water) and time spent in microenvironments pursuing macroactivities ( $T_{me/ma}$ ). In reality, aggregate and cumulative exposure models will need to assign values to most (if not all) the exposure factors discussed in Section 3.0 above. Doing so could involve random sampling of empirical distributions, random sampling of theoretical probability models, and selection of fixed deterministic values. For example, to develop an estimate of aggregate exposure from the ingestion and dermal routes, the model could assign values to each exposure factor as described in Table 5.

**Table 5 Hypothetical Example of Assigning Exposure Factor Values in an Aggregate/Cumulative Model.**

Exposure Factor		Assigned Value
$IR_{diet}$	for Food and Water Consumption	Randomly Sampled from CSFII Data
$IR_{non-diet}$	for Soil Ingestion	Fixed Deterministic Value from CSEFH
$t_{me/ma}$	for Activity Patterns and Duration of Dermal Exposure to Surface Contaminants	Randomly Sampled from NHAPS Data
$TC_{surf/ma}$	for Dermal Transfer of Surface Contaminants	Fixed Deterministic Value from Residential SOPs.
$SA_{dermal}$	for Dermal Exposure to Water Contaminants	Randomly Sampled from NHANES Data for Height and Body Weight
$t_{ma}$	for Duration of Dermal Exposure to Water Contaminants	Randomly Sampled from a Theoretical, Parametric Distribution (e.g., Uniform).

It is important to understand the sampling approaches used in aggregate/cumulative models to fully characterize the uncertainty with respect to addressing different developmental stages or age groups. In the example portrayed in Figure 3, if the majority of food consumption observations in the 5 to <15 year old bin are actually from surveys of 10 to <15 year olds, these data may not be adequately representative of the 5 to <6 year olds. Risk assessments for childhood exposure should discuss such uncertainties and potential biases in the risk characterization.

#### 4.2 TEMPORAL ISSUES - TIME HORIZONS AND AVERAGING TIMES

In Section 3.0, exposure factors were presented in the context of the mathematical models for single day dose estimates. Converting the potential doses to a common metric, such as absorbed dose, where necessary, and summing doses across sources, pathways and routes of exposure would yield a single point on the aggregate dose profile depicted in Figure 3. Depending on the health effect of concern, these single day estimates may, or may not, be the correct metric for use in risk assessment.

A generic exposure assessment issue (i.e., broader than just childhood exposure assessment) is the integration of exposure estimates over time in a way that is meaningful for comparison to dose measures used in risk assessment (e.g., NOAELs, RfDs, slope factors, BMDs, etc.). Exposure estimates may be presented as peak doses or excursions occurring over a very short period of time (e.g., minutes), time weighted averages (e.g., TWA over 8 hours), single day doses (representing the sum over 24 hours), average daily doses (e.g., averaged over a month or a year), and lifetime average daily doses. A potential problem with the time integration of exposure estimates is that the pattern of exposure can be obscured. If the exposure pattern is

relatively continuous and at a constant level, then time averaged doses will be close in magnitude to single day dose estimates and will match actual human experience. However, when infrequent exposure events of high magnitude and short duration are averaged, they are equated with continuous, lower level exposures that do not match human experience. Such masking of the pattern of exposure may be a particular concern in assessing childhood risks. Children may experience unique exposure patterns that are important to consider in relation to their kinetic development and critical windows for effects. Therefore, the temporal scale for estimating exposures, doses, and risk in children needs to be considered carefully.

Selection of the appropriate temporal scale will be driven by the health effects of concern. For example, as explained in the EPA Proposed Guidelines for Carcinogen Risk Assessment, cancer risks are generally based upon the premise that risk is proportional to total lifetime dose and therefore the exposure measure used is the Lifetime Average Daily Dose (LADD). However the Proposed Guidelines also note that there may be assessments where the mode of action for a chemical indicates that dose rates are important in the carcinogenic process. In these cases, shorter term, less-than-lifetime average dose estimates may be more appropriate for risk assessment than the LADD.

In some cases it may be inappropriate to average doses. For example, the EPA Guideline for Developmental Toxicity Risk Assessment note that there is a possibility that a single exposure event may be sufficient to produce adverse developmental effects. In such a case, it would be inappropriate to use time averaged doses over a different time frame than the actual exposure experienced (e.g. averaging of a peak exposure over an 8 hour period). Often it will be important to examine the peak exposure as well as the average exposure over some specified time period to gain a full understanding of the potential for effects.

#### **4.2.1 CALCULATION OF TIME AVERAGED DOSES**

Approaches to calculating time averaged doses vary depending on the time frame of interest and the data and models being used. As noted above, the time frame (or temporal scale) of interest is determined from the health effects of concern. Therefore, the approach to time averaging dose estimates should be determined through a close and continuing dialogue between the exposure assessor and the toxicologist. One must also consider how the model constructs a longitudinal exposure profile and whether intra and inter-day exposure variability has been appropriately modeled.

Once the time frame of interest has been determined, the specific approach to calculating the time averaged dose will depend on the data and models used to estimate the single day doses that serve as the starting point. Often, data are too limited to estimate the day to day variations in exposures. In such cases, the single day dose equations in Section 3.0 ( $D_x$ ) are solved deterministically to represent a typical day of exposure under a given scenario (e.g., for a particular age group). To develop time averaged doses from such estimates, the typical single day estimates are multiplied by the number of days of exposure (assumed to be equivalent to the typical day) in the time frame of interest ( $Days_{Exposure}$ ) and then divided by the total number of days in the time frame ( $Days_{Total}$ ).

$$ADD = \frac{D_x \times Days_{Exposure}}{Days_{Total}} \quad \text{Equation (10)}$$

Probabilistic aggregate/cumulative models that use random sampling algorithms to generate a profile of doses (see Figure 3) provide day by day estimates of dose throughout the life of an individual. To develop time averaged doses from such models, the individual days of exposure are summed over the time frame of interest and then divided by the total number of days in the time frame.

$$ADD = \frac{\sum D_x}{Days_{Total}} \quad \text{Equation (11)}$$

As noted above, some of the existing probabilistic aggregate/cumulative exposure models present profiles of seasonal average daily doses (daily doses averaged over 90 days). In addition, some of these models offer the ability to calculate and present user defined profiles of moving time averages (also known as rolling averages or running averages). For example, the profile presented in Figure 3 may have represented 7 day averages (as opposed to single day estimates). In such a case, the point representing day 7 would be plotted as the average daily dose for days 1 through 7, day 8 would be plotted as the average daily exposure for days 2 through 8, day 9, the average of days 3 through 9, and so on.

The Lifetime Average Daily Dose (LADD) is a special case of the ADD where the time frame of interest ( $Days_{Total}$ ) is equal to the entire lifetime. For the LADD and other ADDs where the time horizon crosses multiple age groups, calculation of time averaged doses using the approach presented in Equation 10 may be better represented by the following equation:

$$ADD = \frac{\sum_{Groups=1toN} (D_x \times Days_{Exposure})_{Group}}{Days_{Total}} \quad \text{Equation (12)}$$

where *Group* refers to specific age groups for which a typical day of exposure has been assessed. The following example equation for the LADD further illustrates this approach.

$$LADD = \frac{(D_x \cdot Days_{Exposure})_{<1month} + \dots + (D_x \times Days_{Exposure})_{3to<6years} + \dots + (D_x \cdot Days_{Exposure})_{Adults}}{Days_{Lifetime}}$$

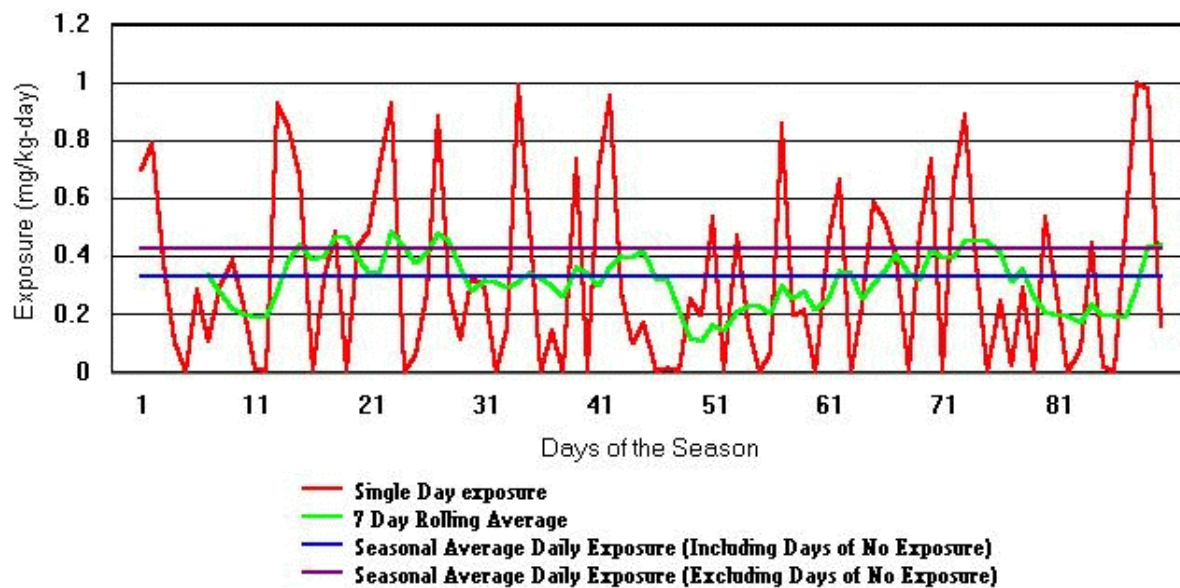
**Equation (13)**

In the above approaches to time averaging dose, days on which exposures occur are averaged together with days for which there are no exposures. As noted in the introduction to this section, this obscures the pattern of exposure and equates high, episodic exposures with lower level, continuous exposures. To moderate this effect, one could calculate a time averaged dose based only on the days exposed. For example, Equation 12 could be modified as follows.

$$ADD = \frac{\sum_{Groups=1toN} (D_x \times Days_{Exposure})_{Group}}{\sum_{Groups=1toN} (Days_{Exposure})_{Group}} \quad \text{Equation (14)}$$

Any approach to time averaging exposure needs to be informed by a consideration of dose kinetics (e.g., absorption, distribution, metabolism, and excretion) and effects (e.g., critical windows for effects, time to effect, etc.). Therefore, as noted above, the exposure assessor and toxicologist should work closely to determine the most appropriate approach. Figure 4 attempts to portray, graphically, the effect of different time averaging approaches.

**Figure 4. Comparison of Single Day Exposure Estimates to Various Time Averaged Exposures**



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