February 1994
Publication # 9285.7-15-1
EPA 540-R-93-081

1. BEFORE YOU START

1.1 BACKGROUND: PURPOSE AND DEVELOPMENT OF THE MODEL

The Integrated Exposure Uptake Biokinetic (IEUBK) Model for Lead in Children is a stand alone, PC compatible software package. It allows the user to estimate, for a hypothetical child or population of children, a plausible distribution of blood lead concentrations centered on the geometric mean blood lead concentration predicted by the model from available information about children's exposure to lead. From this distribution, the model calculates the probability that children's blood lead concentrations will exceed the user selected level of concern (default 10 μg/dL). The user can then explore an array of possible changes in exposure media that would reduce the probability that blood lead concentrations would be above this level of concern.

The model should be viewed as a tool for making rapid calculations and recalculations of an extremely complex set of equations that includes scores of exposure, uptake, and biokinetic parameters. This Guidance Manual concisely describes key features of the conceptual underpinnings of the IEUBK model, its evolution and development, its capabilities, and its limitations. The Manual then goes on to offer guidance on the use of the model as a risk assessment tool while cautioning against a number of possible misapplications of the model. A detailed description of the equations and parameters used in the model is provided in the Technical Support Document: Parameters and Equations Used in the Integrated Exposure Uptake Biokinetic Model for Lead in Children (a companion document to this Guidance Manual).

1.1.1 Description of the Model

The IEUBK Model is a simulation model. As a risk assessment tool, it can be a useful component of remediation strategies for lead in the human environment. The simulation of childhood lead exposure and retention is only one part of the risk assessment process. It is important to note that the model alone does not determine the level of cleanup required for a specific site. Rather, it predicts the likely blood lead distribution for children given the exposure to lead at that site, and the probability that children exposed to lead in that environment will have blood lead concentrations exceeding a health-based level of concern.

Blood lead concentrations are not only indicators of recent exposure, but also are the most widely used index of internal lead body burdens associated with potential health effects. Health effects of concern have been determined to be associated with childhood blood lead concentrations at or below 10 μg/dL (U.S. Environmental Protection Agency, 1986, 1990; CDC, 1991). The probability that children will have blood lead levels exceeding this level of concern is an important consideration for a risk assessor in compiling and evaluating all information applicable to a site to enable remediation decisions.

The IEUBK model can be applied at several different scales of application, but the interpretation of the model output and the form of the model or subsequent risk estimates is different for each application. In most uses of the model, a site is a spatial domain that is appropriate for remediation decisions, typically a residential yard with a single housing unit, or an equivalent area for multi-unit buildings or for undeveloped lots. The home and its surrounding yard is the basic unit for risk analysis because lead exposure for pre-school children commonly occurs within this domain. In Sections 1.4.4.2 and 4.2 we will describe an array of applications of the IEUBK model based on aggregating clusters of sites. The array is:

A: One location
- A1: one living unit, one child;
- A2: one living unit, more than one child;
- A3: more than one living unit, more than one child, homogeneous media concentrations;

B: Multiple locations, one neighborhood, homogeneous media concentrations

C: Multiple locations, one neighborhood, heterogeneous media concentrations;

D: Multiple locations, more than one neighborhood, heterogeneous media concentrations;

In category A, risk is calculated as the probability that, in a single child at a single site with the specified exposure scenario, the child's blood lead concentration will exceed the level of concern. The probability distribution describes the likely variability in blood lead for a child with a given exposure scenario. The best single-number prediction of blood lead concentration is the geometric mean of the distribution of blood lead concentrations that may occur for a child with the specified exposure scenario. This single-child assessment is used to evaluate remediation options on a house-by-house or yard-by-yard basis.

In categories B, C, and D, a frequency distribution of the individual risk of exceeding a blood lead level of concern is obtained. The percentage of children in multiple sites that are likely to have a blood lead concentration exceeding the level of concern can then be calculated. For category B, where all children of the same age have the same exposure scenario, this can be done with a single run of the IEUBK model. For categories C and D, where distinct subgroups have different exposure scenarios, risk must be calculated by aggregating the results from a number of model runs. Risk estimation for more than one neighborhood, for category D, has the added complication that a variety of model parameters may differ between neighborhoods, and within each neighborhood. Therefore, environmental lead concentrations may differ between neighborhood subgroups.

1.1.2 Simulation of Childhood Lead Exposure and Retention

Lead is a naturally occurring nonnutrient metal that follows environmental pathways similar to those of nutrient metals such as calcium. In the human environment, these pathways or routes of exposure transfer lead from sources such as food, drinking water, air, soil, and dust, to the human body by means of ingestion or inhalation. There are important analogies to be made between lead and calcium that contribute to our understanding of the biological behavior of lead. These analogies have aided in the formulation of the lead model. In particular, the nature of gut absorption of lead and calcium may be similar. Childhood growth and development of bone and soft tissue which require calcium influence the uptake of environmental lead from the gut. In addition to similarities in absorption, both lead and calcium are stored in quantity and subsequently released from bone tissue.

Shown conceptually on Figure 1-1, inhaled or ingested lead is absorbed through the lungs or gut into the blood stream where it is transferred to body tissues, including bone tissues. After a period of time, this lead returns to the blood stream where it is transferred to other tissues or eliminated with urine. Lead may also be eliminated from the body with sweat, hair or sloughed epidermal tissue, or it may be transferred through the liver and bile duct back to the gut where it passes out of the body with feces.

In Figure 1-1, the oval shapes show environmental lead media, and some of the pathways between them. The large rectangle shows the compartment that is central to lead distribution in the child, the blood plasma pool and associated extra-cellular fluid. Each lower rectangle shows a compartment in the child's body where lead may be retained. The excretion of lead from the body is shown by the circles.

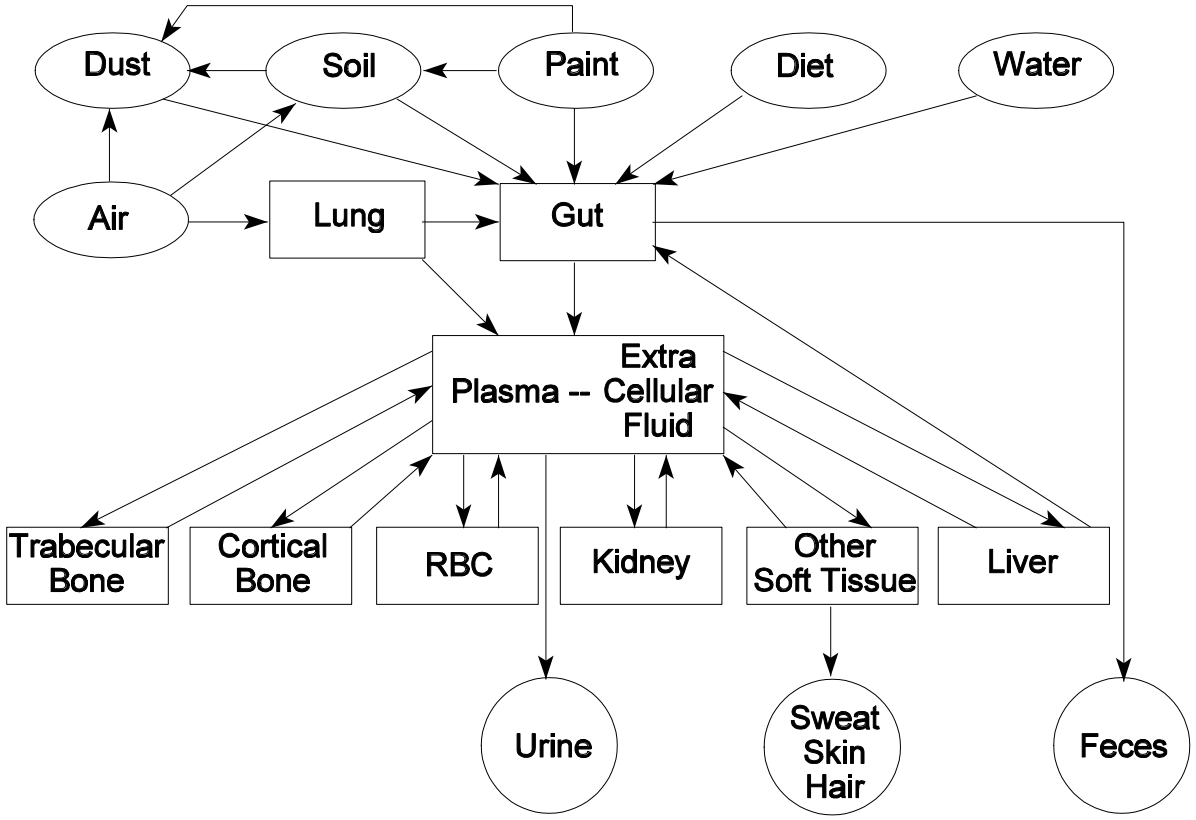

Figure 1-1. Conceptual diagram of the movement of environmental lead into and through the human body. The oval shapes show environmental media and the pathways of uptake. The large rectangle is the blood plasma compartment central to the distribution of lead in the body.

The foundation of the present IEUBK model is the construction of a detailed and thorough exposure scenario for children aged 0 to 84 months that can be adjusted to match the exposure of any child. The user starts with exposure information specific to these children and accepts generalized assumptions about any additional information required to complete the exposure scenario. The site-specific information usually consists of environmental media concentrations such as soil lead concentrations.

The model inserts default values whenever site-specific information is not used. The default values (e.g., dietary lead concentrations and consumption values) are typical of a child's environment in the sense that they are broad-based estimates of the expected

environment of a child. These default values are not necessarily appropriate for every site and should be reviewed by the user for every site-specific application.

This model uses standard age-weighted exposure parameters for consumption of food, drinking water, soil, and dust, and inhalation of air, matched with site-specific concentrations of lead in these media, to estimate exposure for the child. The model simulations represent chronic exposure and do not incorporate the variability in consumption patterns and media concentrations on a daily or seasonal basis. The model includes continuous growth of the child and simulates the changing environment of the child on a yearly basis. In theory, the exposure component of the model would apply to a single child or to any number of children with the same lead exposure scenario. With the proper substitution for media concentrations, the exposure component (but not the biokinetic component) would also apply to any other substance with sources and pathways of exposure similar to lead.

The model simulates lead uptake, distribution within the body, and elimination of lead from the body. The uptake portion of the model takes into consideration two mechanisms of absorption of lead in the digestive tract: saturable and non-saturable. Elimination of lead is modeled through several routes: urine, gastro-intestinal excretion, and sloughing of epidermal tissue, including hair and nails.

1.1.3 Historical Evolution from Slope Factor Models to the IEUBK Model

An explicit mathematical method for estimating the likely risk of elevated blood lead concentrations in young children has previously been used by the Environmental Protection Agency as one of its tools for developing the National Ambient Air Quality Standard for Lead and the National Primary Drinking Water Regulation for Lead. The method has historically been based mainly on an estimation of relationships between lead concentrations in children's blood and lead concentrations in specific individual environmental media such as air, water, soil and dust, based on empirical observations derived from experimentally controlled human exposure, animal toxicological studies, and epidemiological analyses. Such relationships also provide a basis for estimating the probability that elevated blood lead concentrations exceed a level of concern due to exposure to environmental lead in these media.

A mathematical approach of this type was used to evaluate potential alternative air lead standards based on health effects criteria (U.S. Environmental Protection Agency, 1977,

1978, 1989a). The relationship between blood lead and lead in environmental media was estimated statistically, both for adults and children (U.S. Environmental Protection Agency, 1986, 1989a). While the relationship was somewhat non-linear at blood lead concentrations above about 40 μg/dL in adults and 30 μg/dL in children, it was nearly linear at lower blood lead concentrations of interest. The relationship between blood lead and environmental lead concentrations in different media (air, water, soil, dust, food) was estimated using a model linear in lead concentrations. The linear regression coefficients between blood lead and lead in each of the environmental media have since become known as the slope factors for the media.

As more evidence has become available, it has become clear that these slope factors can not be regarded as universal constants that are the same everywhere, for all children at all sites. Some of the problems involved in the use of slope factors have been discussed by the U.S. Environmental Protection Agency (1989a) and by Brunekreef et al. (1984). In the development of improved lead models (U.S. Environmental Protection Agency 1986, 1989a), the following points were discussed:

(1) Slope factors are a function of many factors: media ingestion rates; bioavailability and absorption of lead from the medium; and biological kinetics of lead retention and elimination in the child. Biological and physical differences between sites and study populations cannot be incorporated explicitly and quantitatively into regression slope factors from different studies.

(2) Slope factors for a single medium, such as lead in air or lead in soil, may provide only a very incomplete picture of total lead exposure from a particular source, even if the source is identified with the medium. A single medium such as household dust may contain lead from many sources, and lead from a single source such as exterior lead-based paint may contribute to several exposure media pathways to the child.

Therefore, in 1985, the EPA Office of Air Quality Planning and Standards (OAQPS) initiated a project that would allow the calculation of blood lead concentrations in children exposed to differing arrays of concentrations of lead in air, soil, and dust. This model, called the Uptake/Biokinetic (or UBK) model for lead, was a computer simulation model based on the biokinetic model for lead in children developed by N. Harley and T. Kneip (1985). The biokinetic parameters for the UBK model were extrapolated from long-term feeding studies on infant and juvenile baboons (Mallon, 1983), autopsy data on human children, human infant feeding studies, and other sources. The exposure model that was coupled to the

biokinetic model was developed by OAQPS. Model calibration and validation was done using data from the 1983 EPA/CDC/Montana study on children in East Helena, Montana, who lived in the vicinity of a large primary lead smelter. The modeling approach was reviewed and approved by EPA's Clean Air Science Advisory Committee (CASAC) in 1990.

The overall framework of both the UBK and IEUBK models is shown in Figure 1-2. The oval shapes show environmental lead concentrations and the funnel-shaped symbols show lead intake from the environment at the portals of entry, the lung and the gut. These are the exposure/intake components of the IEUBK model. The next large rectangle shows the gut not only as the main portal of entry for lead from most exposure media, but also as the site for key absorption/uptake components of the IEUBK model for the evaluation of lead from soil, dust, diet, and drinking water. The very large rectangle shows the child's blood lead, partitioned into plasma-extracellular fluid and red blood cells. The two boxes to the right of the blood lead pool sketch the bone and soft tissue pools, and the elimination pathways are shown as circles. The right-hand box shows the blood lead concentration in the child, and the subdivisions show the estimated contribution of each medium to the child's blood lead concentration. In the example in Figure 1-2, we have assumed that all external lead media have been used in the IEUBK model, as have all internal lead sources. There is no unattributable component called "background". The attribution of specific fractions of blood lead to uptake from specific media is not as subject to statistical artifacts, since pathways from soil lead and air lead to dust lead are also included in the IEUBK model.

In all particulars, the present version of the model, the IEUBK model, may be considered an enhancement and extension of the UBK model. Theoretically, in situations where the child has constant long-term or chronic lead exposure, both the slope factor approach and the UBK model (now the IEUBK model) should produce similar results when sufficient data exist to correctly characterize lead exposure, absorption, and biokinetics.

The IEUBK Model addresses three emerging paradigms of environmental risk assessment.

(1) Assessments that recognize the multimedia nature of exposures to environmental toxicants are a significant improvement in assessing health risks. Assessments restricted to single pathways of exposure can overlook situations where integrated multimedia exposures are high enough to trigger health concerns. The lead model is structured to integrate exposures occurring through air, water, food, soil, and dust in estimating the blood lead levels in children in realistic environmental settings.

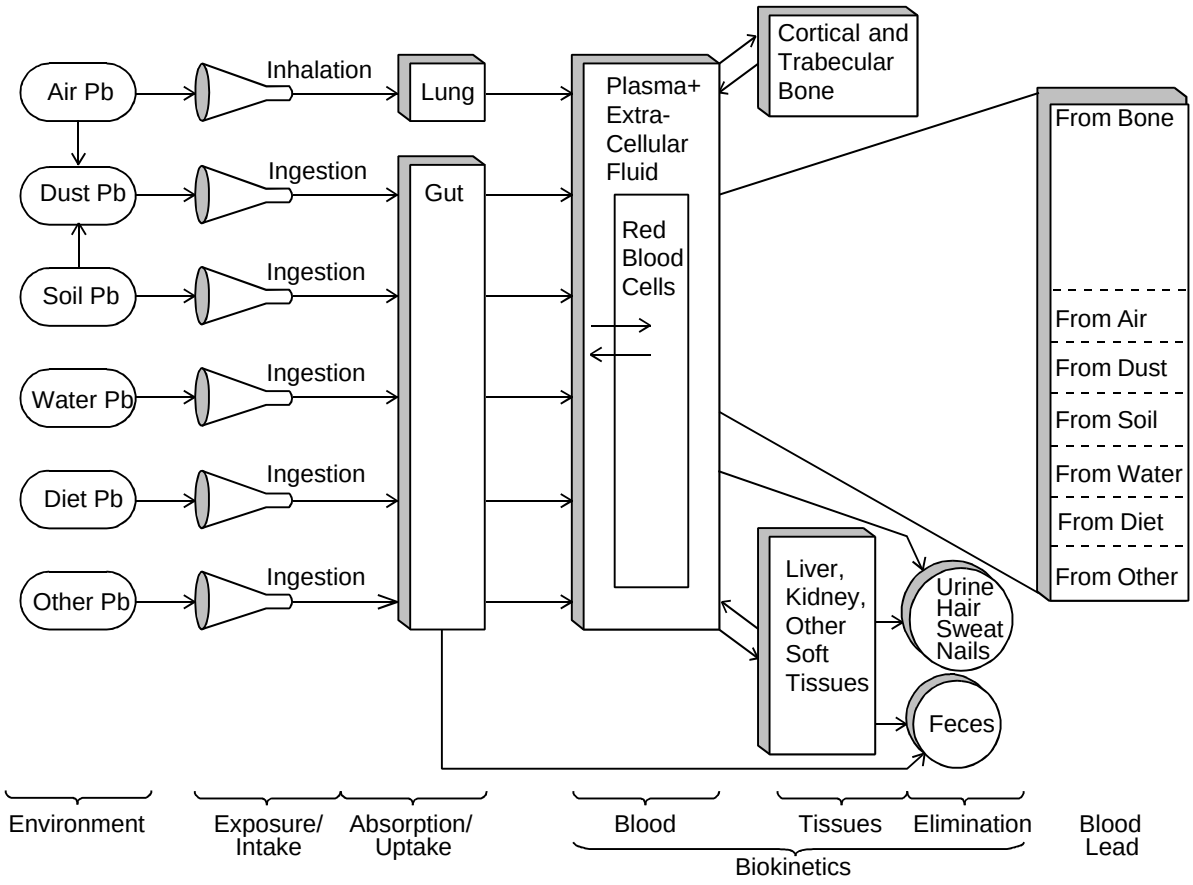

Figure 1-2. Components of the IEUBK Model, showing environmental exposure sources and pathways, absorption compartments, critical body tissue compartments, and elimination pathways.

(2) Pharmacokinetic information can strengthen the validity of environmental health assessments in comparison with more traditional methods that address only external dose or intake of a compound. Internal measures of dose that are pertinent to the biological effects exerted by a compound form an improved metric for risk assessment. The IEUBK estimates of blood lead concentrations as an internal indicator of potential health risk are based on pharmacokinetic modeling of lead absorption, transport, redistribution, and elimination.

(3) Environmental assessments need to address the substantial variability in exposure and risk resulting from these factors. Single point estimates of exposure or risk are of limited utility. Individuals differ in their surroundings, behavior, and physiological status. The Lead Model addresses variability through the estimation of probability distributions of blood lead levels for children exposed to similar environmental

concentrations of lead. Through systematic application of the model, data on the variability of levels of environmental lead contamination can be translated into estimates of the distribution of blood lead levels within populations of children.

1.1.4 Using the IEUBK Model for Risk Estimation

The IEUBK Model for lead is designed to facilitate: (a) rapid delineation of the relationship between environmental lead and blood lead in children; and (b) calculation of the risk of elevated blood lead (i.e., the probability of a given child or a group of children having blood lead concentrations exceeding a specified level of concern). As such, the IEUBK Model provides a tool for site-specific risk assessment for young children exposed to lead from different media and through different pathways in their environment, with particular emphasis on lead in air, water, soil, and household dust. Many other applications are possible. The intended applications of the IEUBK model are to:

(1) Provide a summary of children's long-term, primarily residential, exposure to lead;

(2) Provide a best estimate of the geometric mean blood lead concentration for a typical child aged 6 to 84 months, assumed to reside at a given residence;

(3) Provide a basis for estimating the risk of elevated blood lead (i.e., for exceeding a designated blood lead concentration of concern) for a hypothetical child of specified age with given site-specific residential lead exposure;

(4) Provide a basis for estimating the risk of elevated blood lead concentrations among early pediatric populations in a given neighborhood by aggregating the individual residential risk estimates;

(5) Predict likely changes in risk of elevated blood lead concentrations from exposure to soil, dust, water, or air lead following abatement actions designed to reduce exposure levels from one or more environmental media;

(6) Provide assistance in determining appropriate soil or dust lead target cleanup levels at specific residential sites;

(7) Provide assistance in estimating blood lead concentrations associated with soil or dust lead concentrations at undeveloped residential sites that may be developed in the future.

Each of these applications is discussed in more detail in Chapters 2, 4, and 5. The IEUBK model has been used for many purposes in addition to those for which it was originally intended. We are sure that the IEUBK model will continue to be used in many unintended and unexpected applications, just like any other new tool that has multiple uses. Some of these new applications are valid, others are demonstrably invalid, and the validity of many applications is simply unknown.

The risk estimates are calculated for a hypothetical child or a hypothetical population of children who could be occupying the specific household at the time of the measurements or at some future time. The IEUBK model can therefore be used to estimate the risk of elevated blood lead even when there are no children currently living at a house, or if there exist only environmental lead data for the dwelling unit. The model does not require that a neighborhood or community blood lead study be carried out. The user should be aware that a site-specific risk assessment requires site-specific soil and dust concentrations, and some of the absorption parameters may depend on specific characteristics of the soil and dust at the site. The IEUBK model accepts user inputs for site-specific differences in bioavailability of lead in different media, and site-specific differences in environmental lead pathways for different lead sources.

1.1.5 Validation of the IEUBK Model

What does it mean to say that a computer simulation model is "valid"? In general, we interpret this to mean that:

- the model is biologically and physically plausible and incorporates the best available empirical data on parameters;
- the model uses numerically accurate algorithms and the accuracy of the computer codes for these algorithms has been verified;
- the model provides some satisfactory empirical comparisons of model output with real-world data.

We believe that the scientific basis and computational correctness of the IEUBK Model is sound, and that the IEUBK model provides valid prediction of observed blood lead

concentrations from representive populations of children with typical exposure. The empirical comparisons in which there are differences between observed and predicted blood lead concentrations underscore the importance of valid exposure scenarios as input. They also show the importance of valid blood lead data from truly representative population sampling methods when interpreting these empirical comparisons.

1.1.5.1 The Model Is Biologically and Physically Plausible

The parameters and equations used in the model are documented in the Technical Support Document: Parameters and Equations Used in the Integrated Exposure Uptake Biokinetic Model for Lead in Children. The exposure model component is based on data for human children in most instances, with lead exposures that are characteristic of children in the U.S. since about 1980. The ingestion parameters are based on surveys for drinking water and tap water (Ershow and Cantor, 1989), market basket estimates of dietary intake (Pennington, 1983; Gartrell, 1986), and on observational studies of soil and dust ingestion for children in the U.S. (Binder et al., 1986; Calabrese et al., 1989, 1992a,b, 1993; Davis et al., 1990). While these studies have not resolved all of the uncertainty in childhood lead exposure, especially from sources such as lead-based paint, they have provided a much more realistic basis for quantitative modeling. The exposure component of the IEUBK model extends the UBK model assumptions (U.S. Environmental Protection Agency, 1989a) that have been reviewed by CASAC (1990).

An absorption component was developed for the IEUBK model based on evidence discussed in Section 4.1. This evidence includes in vivo data in infant and juvenile baboons and human infants whose intake of lead is observed and known (Mallon, 1983; Sherlock and Quinn, 1986). The model has two modes for absorption, saturable and non-saturable. In the non-saturable mode, absorption of lead is a constant fraction of the total lead ingested for a specific medium. The saturable mode follows the Michaelis-Menten kinetics for saturable absorption as proposed by Aungst and Fung (1981). Development of the algorithm is also based on data from lead balance and feeding studies in human infants and children (Alexander, 1974a,b; Ryu et al., 1983, 1985; Ziegler et al., 1978).

The compartmental structure of the earlier biokinetic model is based on compartmental models for lead in adults as discussed in detail in the Air Quality Criteria Document for Lead (U.S. Environmental Protection Agency, 1986). The model was verified and extended based on studies in infant and juvenile baboons (Mallon, 1983) whose age (5 to 26 months) and size (2.5 to 6 kg) are only slightly smaller than those of human children. The biokinetic distribution and elimination parameters use ratios of lead concentrations in tissues and blood

following chronic exposure. The ratios of lead concentrations in tissues of human children from autopsy data (Barry, 1975, 1981) were used to adjust the baboon's biokinetic distribution parameters to human infants and children (Harley and Kneip, 1985). The biokinetic parameters for baboons were re-estimated using the compartmental structure of the current IEUBK model (Marcus, 1992). The tissue-to-blood concentration ratios from the human child autopsy data were incorporated in the IEUBK model, assuring complete consistency with the best available data.

1.1.5.2 The Model Is Computationally Accurate

The IEUBK model uses a fast and accurate one-step numerical integration method known as 'backward Euler', with user-adjustable time steps to verify numerical accuracy of the solution. Coding of the model equations was verified by a separate recoding of the model in another programming language. Independent code verification will be described in forthcoming Technical Memoranda (see Section 1.2.2).

1.1.5.3 Empirical Comparisons of the Model

Comparison of the IEUBK model output with empirical human blood lead data has two requirements. The first requirement is that the child's total lead exposure is completely and accurately characterized by the empirical data, including site-specific data on environmental lead concentration, media ingestion, and bioavailability. The second requirement is that the blood lead data from the field study are accurate and typical for that exposure scenario. A typical child may not have the exposure described by the measured and default parameters of the model, or a child may also respond atypically to the measured and default parameters. The solution is to find the correct set of parameters (measured or site-specific alternatives to default) that describes the child's site-specific exposure or response to exposure.

Environmental lead concentrations and blood lead measurements are subject to measurement errors such as repeat sampling variability and analytical error. Without careful attention to quality assurance/quality control (QA/QC) procedures, there may be systematic biases in blood lead measurements. The results of the blood lead field study may also differ from the model predictions for typical children if the blood lead sample is not representative of the population being sampled.

Validation by empirical comparisons with paired data sets of good quality is an ongoing process. In earlier versions of the model, empirical comparisons indicated satisfactory agreement between observed and predicted blood lead concentrations. Several data sets have been identificed that are of adequate data quality for evaluating the validity of the IEUBK

Model, and more data sets are expected to become available in the future. The Field Study Data Set Comparisons document referred to in Section 1.2.2 will discuss the results of these analyses. Comparisons of empirical data with the IEUBK model require appropriate site-specific exposure scenarios, valid assumptions about bioavailability, and demonstrated representativeness of the sample of children recruited into the study in relation to the target population from which they were drawn.

Our preliminary analyses of several data sets so far indicate that the model satisfactorily predicts blood lead concentrations for the overall sample populations in specific neighborhoods. Further analyses will be needed to determine if empirical comparisons are as strong for subpopulations defined by factors such as differences in age, differences in contact or behavior that affected the amount of soil ingested, suspected or possible differences in bioavailability, differences in contribution of soil to household dust, and identifiable biases in recruitment of children. More extensive evaluation of these data sets will be described in the Field Study Data Set Comparisons document described in Section 1.2.2.

Careful determinations should be made by users with regard to how well default values specified by this manual for key exposure and demographic parameters apply to the particular sample of children (or subpopulations) being evaluated. Appropriate adjustments made in pertinent default values may notably improve the fit of the model to empirical data. We caution the user not to arbitrarily select alternate values for the default parameters, but rather to obtain site specific or population specific data on important parameters.

1.2 ORGANIZATION OF THE MANUAL

1.2.1 Increasing Levels of Guidance and Technical Assistance

This manual is designed to provide you with the information you need at several levels of detail. The further you read into manual the more specific guidance you will find for using the model. By the time you have finished reading Chapter 1, you should have a general understanding of how the model works and what it can do. You may want to install the model and then work your way through Chapter 2 as you become more familiar with each feature of the model. Instructions for installing the model are found in Section 2.4.

As you explore the various features of the model, you will become familiar with the menus and their options. An overview of the menu system is in Section 2.1, and a detailed

description of these menus can be found in Section 2.2. This is the section that the novice user will want to follow closely. In a guided tour through the menu system, you will find that each menu option becomes a part of the process of constructing a model "run," and that these runs may be as simple as determining the blood lead concentration using only default exposure conditions, or as complicated as neighborhood risk estimation calculated as the sum of individual risks. Many of these options were suggested by comments received during the extensive review of drafts of this Guidance Manual.

As you begin to apply the model to a specific risk assessment situation, you will find that Section 2.3 contains detailed recommendations for building an exposure scenario. This section also contains a helpful worksheet for planning model runs. Follow this section closely, as it contains many helpful suggestions on the appropriate use of the model, as well as warnings of improper applications. In Chapter 4, you will find a detailed discussion on assessing the relationship between soil/dust lead and blood lead. This chapter also describes the biokinetics of the model and specific issues in the use of the model for the ingestion of paint chips. If you need more help, turn to Chapter 5, where several specific examples are available to guide you through some of the more complicated procedures. As you become more experienced, you will find Chapter 3 a quick and ready reference to the various menu options. This chapter also contains a comprehensive review of default parameters.

1.2.2 Additional Documentation

Additional technical documents are or soon will be available to supplement the IEUBK Model and this Guidance Manual. These are:

- Technical Support Document: Parameters and Equations Used in the Integrated Exposure Uptake Biokinetic Model for Lead in Children—a description and documentation of all equations and parameters in the model;

- Field Study Data Set Comparisons—a description of several validation exercises that have been or will shortly be carried out;

- Sampling Manual—approaches and protocols for environmental and biological sampling for collection of data compatible with the IEUBK Model;

- Technical Memoranda—occasional technical updates that will be released to explain some features in greater detail or to alert the user to possible misapplications of the model.

1.3 GETTING READY TO USE THE MODEL

1.3.1 Preparing a Site-Specific Exposure Scenario

The use of the IEUBK model requires input data that are appropriate to the site(s) and subject(s). The most convenient way to do this is to construct a multi-media, site-specific exposure scenario using the exposure scenario worksheet (Figure 2-11; see Section 1.4.3).

For most assessments of lead-contaminated soils, the minimal site-specific data are the soil lead and indoor dust lead concentrations for the residential exposure unit. Additionally, it would be helpful to include estimates of specific exposures from diet, drinking water, air, maternal exposure, or other sources that could replace the default exposure parameters believed to be of concern at the particular site.

There may be potentially important differences among sites, and predictions of blood lead values are expected to become more accurate as more site-specific data are added. Children at highest risk are those with the highest exposures to some lead-containing medium. Data should be collected at a site so as to identify locations in the residence or community where young children may be exposed to elevated levels of lead in soil, dust, water, or air. Household-level data are useful because proposed soil, dust, and paint abatements are usually based on the house and yard as the most likely sources of lead exposure in preschool children. High exposures from lead in the household water distribution system are also possible, and this source has been identified in some childhood lead poisoning cases (Cosgrove et al., 1989). The preferred level of environmental input data for the model can be derived from a comprehensive multimedia household environmental lead study.

The households studied should be representative of housing or sites where young children currently reside, as well as the places where young children may live in the future. In many applications, you will also need to include existing homes not occupied by children. These can usually be addressed in the same manner as housing currently occupied by children, using specific measurements of various environmental media lead concentrations. Risk assessments addressing as yet unbuilt housing should use existing residential site soil concentration data.

Predictions of blood lead concentrations may improve with better information on lead concentrations where the child spends time during the day, or on child-specific behavior.

Activity pattern analysis, based on data taken from questionnaires and family interviews, can be useful in identifying children currently at risk, and in determining site-specific differences in behavior or access to lead sources that may differ in bioavailability. Public education and parental awareness of lead hazards may reduce the amount of lead in soil and dust ingested by the child, and quantitative studies of the effects of such actions are currently in progress.

Exposure of children in day care centers, playgrounds or open areas may substantially affect total exposure to lead when potential lead exposures in such areas are high. These cases need to be considered in site risk assessment. The IEUBK Model allows dust and drinking water ingestion components to be separated into household and non-household sources by allocating a percentage of dust and water intake outside the home to sources with other concentrations. Time-weighted average air lead exposures are believed to be adequate indices of lead intake by inhalation in home and non-home settings under most circumstances and are used in the model. However, there is presently little information on the use of time-weighted averages for ingestion of soil, dust, or water away from the home. Soil and dust ingestion depends on children's activities, on hand-to-mouth behavior, and on intensity of soil contact related to sources and pathways away from home.

In addition to exposure, the IEUBK Model also allows site-specific information on the bioavailability of lead from various sources to be taken into account. Bioavailability describes the relationship between the potentially available lead intake from environmental media and the amount of lead entering the body through the lungs or the gut and then into systemic circulation.

You should be alert to the possibility that there may be site-specific differences in bioavailability of lead at different sites, particularly with respect to soil and paint. Some factors that may affect bioavailability include chemical speciation of lead in soil or paint, size of particles, mineral matrix of the particles, and whether the particles are likely to be ingested by the child along with meals or on an empty stomach. These are discussed in Section 4.1. Many of the issues are subtle and should be referred to the EPA Technical Review Workgroup for Lead.

In some cases, relatively non-available environmental lead in soil or paint can be converted into readily available lead particles in household dust by physical and chemical processes in the environment. A housing unit with lead in paint or soil will continue to generate household dust lead exposure as long as paint deteriorates or is disturbed by

remodeling, and as long as outside soil and surface dust are moved into the house by pets and by human activities like gardening and remodeling.

The model default value for the Geometric Standard Deviation (GSD) (reflecting variability among individuals who have contact with a fixed lead concentration) is based on analyses of data from neighborhoods having paired sets of environmental concentration and blood lead data. The recommended default GSD of 1.60 is believed to be very widely applicable. Only when reliable site-specific paired data from a sufficiently large study are available, should the substitution of a site-specific GSD be made using guidance given in Section 4.2.

1.3.2 Understanding How the Biokinetic Component of the Model Works

The general term "biokinetic" is used to describe the movement of lead through various parts of the human body as a kinetic process. Current blood lead concentrations depend on prior exposure history as well as present exposure. With constant lead exposure, a near steady-state blood lead concentration level is achieved because there is a dynamic near-equilibrium between lead moving out (from blood plasma to peripheral tissues and through excretory routes), and lead moving in (to plasma from gastrointestinal uptake and remobilization into plasma from peripheral tissues and long-term bone storage).

The IEUBK Model assumes that skeletal lead turnover occurs relatively more rapidly in children than in adults. The lead in a child's blood is thus a mixture of lead taken up from recent environmental exposure and lead released from skeletal stores that reflect historical exposures. However, the faster turnover time assumed for children compared to adults implies that the lead burden in the skeleton is a smaller fraction of total body burden in children than in adults. The skeletal contribution to blood lead thus increases as the skeletal fraction of total body burden of lead increases.

The blood lead concentrations in children achieve nearly a steady state relationship with exposure within a period of months after changes in exposure. The situation in children is more complicated than in adults because the kinetic parameters also change with the child's growth and with changes in behavior that affect lead intake, absorption, distribution, and elimination. The model is adequate to estimate childhood blood lead concentrations in near-equilibrium or in slowly changing exposure settings, as may be attained some time (months) after abatement occurs. The gradual phase down of lead in gasoline would be an example of

changes that occurred slowly enough in most urban areas to permit accurate modeling of blood lead concentration changes accompanying the air lead concentration changes.

1.3.3 Understanding Limitations of the Model

The IEUBK Model is designed to evaluate relatively stable exposure situations, rather than rapidly varying exposures. The model does not report each iterative calculation; rather, it reports one-year average blood lead concentrations. Because the IEUBK Model allows changes in exposure to environmental lead concentrations only at one year intervals, and provides output at only one year age intervals, changes in exposure are smoothed over one year. The model cannot be used to predict the effects of short term exposure episodes, such as exposure over a few days or weeks to lead dust and airborne particles that may be generated during lead paint abatement. The IEUBK Model should provide reasonable accuracy for blood lead concentration prediction as long as the changes in these environmental lead concentrations can be approximated by annual average values.

The model is intended to describe a single residential-level exposure setting. The dwelling unit could be a detached single-family home, a separate home in a multiple-unit building such as a row house or duplex, or an apartment in a multiple-unit building. There is an implicit assumption that the input parameters characterize long-term residential exposure scenarios in such settings. While exposure changes daily in response to changes in the child's diet and activity, there is presumably a true mean exposure level that can, in principle, be estimated from real-life samples. For this reason, the IEUBK model allows changes in air, food, dust, and soil lead exposure input parameters only at 1-year intervals. Although water lead exposure could, in principle, be handled in similar detail, the IEUBK model does not allow annual changes in drinking water lead during the model run. The IEUBK model includes some capabilities for dealing with lead exposures outside the home, such as by use of separate dust ingestion parameters and concentrations at day care centers, schools, and secondary residences.

We recommend using a simple average or arithmetic mean of soil lead concentrations from a representative area in the child's yard, and an average of dust lead concentrations from representative areas frequented by children inside the house. This rationale is appropriate for areas that are sufficiently small so that any part of the area may be accessible to a typical child living at a random residence located within the area.

The IEUBK model calculates blood lead and tissue lead burdens for all ages from 0 to 84 months. However, the blood lead concentrations in children less than 6 months of age will still be affected by pre-natal lead exposure and are likely to show little influence from exposure to soil, dust, and paint, which are the media currently of greatest interest. The results of the model simulation are therefore not reported for children younger than 6 months.

There are many reasons why individual blood lead concentrations may differ from the predicted geometric mean blood even though the predicted mean accurately describes the population. Some of the components of individual differences are discussed in Section 4.2. The GSD is the only parameter in the model that characterizes the combined variability in blood lead attributable to inter-individual differences and "random" temporal variability in absorption and biokinetics, "random" behavioral changes and inter-individual differences affecting ingestion rate, and measurement errors in environmental lead concentration. The strength of this approach is that GSD estimates are based on empirical data on the variability of blood lead levels in children exposed to similar concentrations of lead. Other approaches to evaluating the effects of variability, such as Monte Carlo simulation, were deferred for the present version of the IEUBK Model, because they demanded excessive computation and require much greater amounts of model input data. Monte Carlo methods, however, are still being evaluated as a possible enhancement of the IEUBK model, as discussed in Section 1.5.

1.4 RUNNING THE MODEL

1.4.1 Your Responsibilities

The IEUBK model provides a great deal of flexibility in describing site-specific or age-dependent exposure scenarios. The price for this level of flexibility is that no exposure scenario is appropriate for every application of the IEUBK model, and this is particularly true of the "default" parameters. The responsible use of the IEUBK model requires input data that are appropriate to the site(s) and subject(s). The most convenient way to do this is to use the exposure scenario worksheet (Figure 2-11; see Section 1.4.3).

The most sensitive parameters for most applications involving soil lead exposure are the soil-to-indoor dust transfer coefficient, the soil and dust ingestion parameters, the soil lead absorption fraction, and the Geometric Standard Deviation. You should always review these parameters.

Factors affecting transport of soil lead into household dust should be noted when appropriate. For example, houses with very small grass-covered yards are likely to have a smaller contribution of the yard's soil lead concentration to household dust lead concentration than houses with large yards, no grass cover, and fine uncompacted surface soils that are easily blown or carried into the house by humans and outdoor pets. While the concentration of lead in exterior dust derived from the soil may be a useful measure of exposure, these data are not usually available because exterior surface dust samples are not usually collected. You are always responsible for the decision to use default values in place of either measured dust lead concentrations or dust lead concentrations estimated from soil lead concentrations.

The proportion of intake in the form of soil vs. dust should be considered carefully, as there may be differences in the bioavailability of lead in soil vs. lead in house dust even when much of the dust is derived from soil. In spite of considerable efforts to determine the ingestion intake of soil and dust by children, these values are still subject to uncertainty. Site-specific data on soil ingestion by children are rarely available, but would be valuable in modeling site-specific exposure to lead. Only limited information is available about the effects of the child's micro-environment on soil and dust ingestion, with evidence suggesting much larger intakes of soil for children in intrinsically dirty environments such as campgrounds, and lower soil intake for children who spend much of their time in cleaner environments such as day care centers.

You are responsible for the choice of non-default bioavailability parameters. Bioavailability parameters may differ among sites. Non-default bioavailability parameters may be justified by experimental studies with the actual site materials, assessments of other sites with similar materials, or site specific information on properties of particles that may affect bioavailability.

The Geometric Standard Deviation is not considered a highly site-specific parameter, and should normally be kept at its default value of 1.60. If you use some other value, you should document the reasons for this modification, since risk estimates are typically very sensitive to the GSD value used.

1.4.2 Exploring Model Options

The IEUBK model has a large number of options. You are encouraged to explore these options before doing any substantive analyses, because there are often several alternative methods that can be used to obtain model outputs. These options are identified in Chapter 2.

They include alternative source menus for soil and dust lead, dietary lead, and lead in drinking water. The soil/dust lead menu includes options for air-to-dust and soil-to-dust transfer coefficients, as well as for non-household sources.

There are options beyond single runs of the model. These include multiple runs for overlay plotting of probability curves, for plotting blood lead vs. environmental media lead concentration, and for multiple runs (batch mode input) for each of a group of individual children of different ages using child-specific data.

The multi-media bioavailability menu includes options for changing the passive vs. facilitated absorption of lead from all media. The half-saturation uptake, a parameter that determines the extent of non-linear or saturable absorption, may also be changed from the normal default value of 100 μg Pb/day.

Run options include the choice of an iteration time step. With low exposure and no year-to-year change in concentration, as used in the "Default" option, there should be no differences in output using other iteration time steps. Differences in blood lead of a few percent may occur with higher and rapidly changing exposures. For a single run, almost any PC (XT or later) will produce a solution within 60 seconds, even without a math coprocessor, with the default iteration time of 4 hours. However, with a batch mode input file of several hundred records, the simulation run may take many hours. In this case, you may select a longer iteration time and speed up the run for a preliminary analysis. If you use a longer time step, you should verify accuracy using records with high exposure or large changes in exposure.

1.4.3 Documentation of Input Parameter and Data Files

By reviewing every adjustable parameter in the model and noting which ones have been modified in a particular run, you have a permanent record of the input. An electronic copy of the exposure input parameters can be made using the parameter SAVE option. Distinctive names for parameter files ([name].SV3), input data files ([name].DAT), simulation run files (RESULTS.TXT), batch mode output files ([name].TXT and [name].ASC), probability plot overlay files ([name].LAY) and blood lead vs. media concentration files ([name].MED) may be used to document input specifications as well as output.

The worksheet provides a convenient format for noting reasons for use of non-default parameters, or justification for use of default parameters. For example, soil lead

concentrations and dust lead concentrations could be measured values at each house. Repeated values of household data would be used to weight the statistical results from batch mode files. Missing value imputation methods should be identified, for example, "KID ID = 17,22,35, missing dust lead concentration estimated by PbD = 180 + 0.28 * PbS." This is critical information in allowing other users to reproduce your results (including yourself, since it is unlikely that most users will be able to recall over one hundred model parameters after the passage of some months or years).

1.4.4 Documentation of Model Output

1.4.4.1 Selecting Output Alternatives

Results of IEUBK model simulations may be saved in several forms. You should select in advance the most useful of these forms, since the results of some interactive simulations cannot be recovered once you have bypassed the opportunity to save the results. Choices are:

(1) A sequence of single simulation runs. Sequential runs can be interactively appended to the file named RESULTS.TXT. The average of the geometric mean blood lead concentrations for children in sequential one-year age intervals, the input concentrations for several media, and the media-specific daily lead uptake for each year are saved. You must use the "Save" option at the end of each run to be saved, but this allows you to drop results from non-informative runs rather than save them.

(2) A sequence of graphics overlay simulation runs. The multiple plot option saves input data for blood lead probability plots for a range of evenly spaced media lead concentrations. For example, you may generate plot data for soil lead concentrations of 250, 500, 750, and 1000 ug/g, for children of ages 12 to 24 months. The data in the [name].LAY overlay file includes the geometric mean blood lead for children in the age range, the lead concentration in soil and in other media. The actual plots of probability density or cumulative distribution functions depend on the GSD value selected, and these plots include the probability of exceeding the user-specified LOC for use in risk estimation. Probability plots may be printed on standard laser printers.

(3) A sequence of blood lead vs. media lead simulation runs. The media range option saves input data for blood lead vs. media lead plots for a range of evenly spaced media lead concentrations. For example, you may generate plots of blood lead vs. soil lead concentrations smoothly interpolated from calculated values at 250, 500, 750, and 1000 ug/g, for children of ages 12 to 24 months. The data in the [name].MED overlay file includes the geometric mean blood lead for children in the age range

at the selected media lead concentrations, the lead concentration in soil and in other media. Plots may be printed on standard laser printers.

(4) Batch mode simulation runs. The batch mode option requires an input data file, as described in Chapter 2. Output consists of user-named files [name].ASC and [name].TXT that contain predicted blood lead concentrations for each case or record (child) in the input data file. The output files also document the missing value imputations when some of the input data on residential lead concentrations in air, water, soil, or dust are missing. The files may be used as input for the statistical analysis programs in the companion PBSTAT program, which produce statistical and graphical comparisons of the observed and predicted blood lead concentrations.

1.4.4.2 Understanding the Output

You should carefully review the output options described in Section 1.4.4.1. Each option allows you to examine a different aspect of the IEUBK simulation. The numerical simulation component of the IEUBK model produces an estimate of a geometric mean blood lead concentration for children of a given yearly age. This is the average of the estimates for children during that one-year interval. The IEUBK model arrives at these estimates by calculating at each time step an updated estimate of all compartment lead masses, or equivalent tissue lead concentrations. The update algorithm combines uptake of lead from the environment with all of the movements of lead into each compartment from another compartment, or out of each compartment, either into another compartment or by elimination from the child's body. In this version of the IEUBK model, the output consists of the daily uptake rate (intake rate times fraction absorbed) for each medium, and the blood lead concentration, as annual averages.

The output from a single simulation run may be displayed in several forms. Most users wish to see the variability associated with a predicted blood lead concentration. This range can be demonstrated graphically by selecting the intrinsic variability GSD and then plotting a cumulative probability distribution. The range of plausible blood lead values may be determined graphically as defined by upper and lower percentiles of the distribution. For example, the 5th and 95th percentiles of the distribution will include 90 percent of the children with the given site-specific or household-specific exposure scenario. Since "plausible range" requires a subjective choice of percentiles, you are free to choose any appropriate values. Since the predicted geometric mean blood lead concentration is based on

an a priori mathematical simulation and not on a data-driven statistical estimate, this plausible range should never be considered as equivalent to a confidence interval.

The other output characteristic that many users wish to see is the estimated probability of exceeding the specified blood lead level of concern, corresponding to the given exposure scenario or scenarios (for multiple runs in a given medium). This also requires a GSD value. This probability may be interpreted as the percentage of children with the given household-specific exposure scenario who are expected to exceed the level of concern. If applied to a single site or residence, it may also be interpreted as the probability of exceeding the level of concern for any single child who may reside at that site in the future.

1.4.4.3 Interpreting the Output and Communicating the Results

The model calculates the probability that a blood lead concentration derived from the model's specified parameters will exceed a level of concern specified by the user. There are two valid interpretations for the output:

(1) The output of the model may be considered to be the best estimate of a plausible range of blood lead concentrations for a hypothetical child with a specific lead exposure scenario. The range of values is centered on the geometric mean blood lead concentration expected for a typical child with this exposure scenario. The upper tail of the probability distribution provides an estimate of the risk of exceeding some blood lead level of concern for a typical child of that age residing in the same household and with the same exposure history.

(2) The output of the model may also be considered to be the predicted geometric mean blood lead of a *population* of children with the same lead exposure scenario, and the upper tail of the probability distribution to be the fraction of children exceeding the chosen blood lead level of concern when all of these children have the same exposure history.

The array of applications for which the IEUBK model can be validly used is:

A: One location
- A1: one living unit, one child;
- A2: one living unit, more than one child;
- A3: more than one living unit, more than one child, homogeneous media concentrations;

B: Multiple locations, one neighborhood, homogeneous media concentrations

C: Multiple locations, one neighborhood, heterogeneous media concentrations;

D: Multiple locations, more than one neighborhood, heterogeneous media concentrations;

A single run of the IEUBK model is sufficient for categories A and B. A classification or disaggregation of the neighborhood into distinct exposure subgroups is required in categories C and D, with the possibility of different ingestion or absorption parameters for different neighborhoods in category D. Neighborhood-scale and community-scale risk estimation requires aggregating the risk estimates for individuals or subgroups.

The differences between these levels is sketched in Figure 1-3. Category A requires calculating only a single blood distribution. Category B requires calculating a blood lead distribution for each child, but since each child of the same age has the same exposure scenario in category B, a single run of the model is sufficient to characterize risk for this subgroup. In category C, there are different exposure scenarios for each subgroup. Risk estimates must be calculated for each such subgroup, then added up across sites and children.

The model output in category A: Single child, single site of exposure, includes a blood lead concentration, a distribution of blood lead concentrations, and a probability of exceeding the blood lead level of concern. Since children in environments with the same lead exposure may have a range of blood lead concentrations, we describe the likely variability in blood lead for a child with a given exposure scenario by a probability distribution. The predicted blood lead concentration is the geometric mean of the distribution of blood lead concentrations that may occur for a typical child with the specified exposure scenario. Risk is calculated from this distribution as the probability that a hypothetical child living at this site, with the specified exposure scenario, will have a blood lead concentration exceeding the blood lead level of concern. This single-child assessment is necessary in order to use the model to evaluate remediation options on a house-by-house or yard-by-yard basis. The single-child assessment also provides a criterion for model testing and validation using epidemiology data.

The model output in category B: Multiple children, single site or equivalent sites of exposure, is the predicted blood lead concentration for each child as the geometric mean of the distribution of blood lead concentrations that may occur for each child with the specified exposure scenario. Risk is calculated by aggregating the calculated risk for each child as the percentage of hypothetical children living at this site or at these sites, with the specified exposure scenario, that will have a blood lead concentration exceeding the blood lead level of

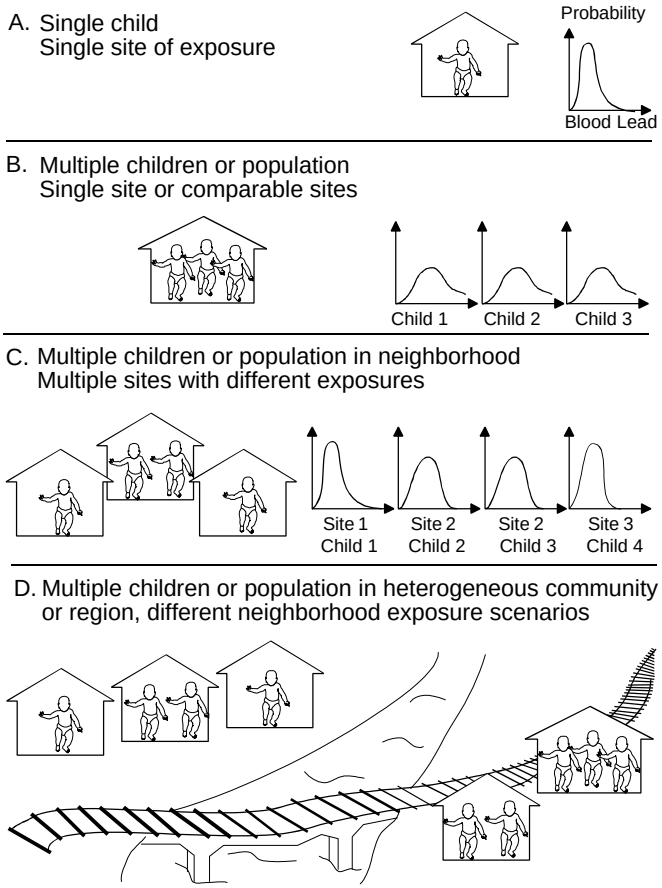

Figure 1-3. Categories of application of the IEUBK Model.

concern. The calculation is exactly the same as the single-child assessment, but there is an important shift in interpretation of the output.

There are situations in which a single site really can have multiple children of the same age with the same exposure scenario. A single housing unit may be occupied by several households with pre-school children of the same age. Rental properties may be occupied in succeeding years by different families, each of which may have a pre-school child of the same age with virtually the same exposure as occupants in other years. In general, the multiple-child or population exposure scenarios would be applied to a hypothetical population of occupants.

Neighborhood-scale risk estimation is discussed in Section 4.2, with examples. The model output in C: Multiple children, multiple sites with different exposure, cannot be

obtained by a single run of the IEUBK model. It is necessary to construct an exposure scenario for each distinct exposure subgroup in the population. For each child or exposure subgroup, risk is calculated in a single run of the IEUBK model with the specified exposure scenario. The risks for each exposure subgroup are aggregated across all subgroups, weighted by the number of children with that exposure scenario or by the percentage or likelihood of the exposure scenario.

There is no one-step method by which neighborhood-scale risk estimation can be done using this version of the IEUBK model. The problem of risk estimation for children in a large community or a region is even more difficult when different subgroups of children may have very different exposure scenarios, including differences in behavior that affect ingestion, and differences in lead absorption due to behavioral or nutritional differences.

A common misinterpretation of the IEUBK Model is that it predicts *community* geometric mean blood lead and the fraction of children at risk when the input is the mean or geometric mean of household-specific environmental lead concentrations. That mis-step can be misleading, particularly when the environmental variables have a wide distribution among the neighborhoods of the community. This misinterpretation is especially dangerous for post-abatement settings intended to eliminate the higher exposures when there are multiple exposure media. A correct approach requires applying the model to each individual home or site using the lead concentrations seen at that site and combining these results as an aggregate of sites in several neighborhoods to form an estimate of community risk. A second useful approach is based on subdividing a community into neighborhoods and clusters of residence units with similar media lead concentrations. Specific information on building appropriate neighborhood exposure scenarios is given in Section 2.3, *Building an Exposure Scenario*. Examples are provided in Section 4.2.

We should emphasize that the IEUBK model is intended to provide a best estimate of geometric mean blood lead. The IEUBK model is not intended to be used in a worst-case scenario, as the model does not apply any uncertainty factors or modifying factors in making risk estimates. If, as usual, there is some uncertainty about model parameters, these can be evaluated using sensitivity analyses. Remember that you are responsible for documenting plausible non-default values.

Uncertainty about parameters is not the same as the intrinsic variability in environmental data and blood lead responses. The components of variability are discussed in

Section 4.2 on the blood lead Geometric Standard Deviation (GSD), which plays a critical role in risk estimates.

1.5 REFINEMENTS AND ENHANCEMENTS

The biokinetic component of the IEUBK model is based on an age-dependent compartmental model with identifiable physiological compartments: red blood cells, plasma and extracellular fluids, kidney, liver, other soft tissues, trabecular and cortical bone (Figure 1-1). There are many compartmental models in the literature; some with fewer compartments (Rabinowitz et al., 1976), others with many more compartments (Leggett, 1993). The Technical Review Workgroup for Lead was aware of important research in the development of physiologically-based pharmacokinetic (PB-PK) models for lead in humans, primates and rats that took into account the slow diffusion of lead through the bone matrix (O'Flaherty, 1992a,b,c, 1993a,b). However, the Workgroup chose to develop a compartmental model that uses transfer times or transfer rates between compartments instead of physiologically based compartmental coefficients. The transfer rates can be estimated from data in non-human primates, especially the studies on infant and juvenile baboons that were done at New York University (Mallon et al., 1983; Harley and Kneip, 1985).

The IEUBK biokinetic model was based on:

(1) empirical kinetic data on blood lead in baboons of similar weight and developmental stage to human infants and young children;

(2) kidney, liver, tibia and femur lead concentrations in baboons after the end of the lead exposure study;

(3) autopsy data for lead levels in young children who died from causes not related to lead exposure;

(4) extrapolations from studies in human adults;

(5) lead feeding and lead balance studies in human infants.

There is, in principle, a degree of similarity between these approaches, since the compartments in the IEUBK model are defined by real anatomical and physiological properties. The transfer times from the PB-PK model can be calculated from blood flow rates to organs and tissue groups, volumes of these organs, partition coefficients across

membranes, and solid state diffusion coefficients for the bone matrix. The principal difference between the biokinetic components of the IEUBK and PB-PK models is that, in the absence of suitable physiological data, empirical data were used in estimating transfer times in the IEUBK model. Future development of the IEUBK Model is expected to continue in the direction of physiologically based biokinetic components similar to PB-PK models.

Many users have expressed interest in tools that allow a more detailed investigation of the effects of non-environmental variability on the distribution of blood lead concentration. The Monte Carlo approach would allow every parameter in the model to be assigned a random variation at every iteration of the computation. For example, each parameter could be multiplied by a random factor (mean value 1) at every iteration. This would require that adequate data would be available to support the input distributions. An extremely large amount of computing would be necessary. A substantial amount of additional study is needed before Monte Carlo methods can be added to the IEUBK model.

The IEUBK model currently evaluates children from birth to age 84 months. Many users have requested extension of the model to other populations, including older children and adults, with emphasis on populations at special risk. Both the physiological and biokinetic parameters of adults are at least as well known as those of children, with the possible exception of lead distribution within the human maternal-fetal unit. Transfer of lead from the mother to the neonate during lactation would also be of interest.

1.6 GETTING MORE HELP

As scientific knowledge advances, this Guidance Manual will be updated and revised. If you have questions regarding the site-specific application of the IEUBK Model, you may direct your inquiries to the appropriate EPA Regional Toxics Integration Coordinator. Comments on the technical content of the manual or suggestions for its improvement may be brought to the attention of members of the EPA Technical Review Workgroup for Lead listed in the front of this document.