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GUIDANCE MANUAL FOR THE IEUBK MODEL FOR LEAD IN CHILDREN

Office of Solid Waste and Emergency Response
U.S. Environmental Protection Agency
Washington, DC 20460

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U.S. ENVIRONMENTAL PROTECTION AGENCY
TECHNICAL REVIEW WORKGROUP FOR LEAD

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CHAIRPERSON

Region 8
Susan Griffin
Denver, CO

MEMBERS

Region 2
Mark Maddaloni
New York, NY

Region 3
Roy Smith
Philadelphia, PA

Region 5
Patricia VanLeeuwen
Chicago, IL

Region 8
Chris Weis
Denver, CO

NCEA/Washington
Karen Hogan

NCEA/Washington
Paul White

NCEA/Cincinnati
Harlal Choudhury

NCEA/Research Triangle Park
Robert Elias

NCEA/Research Triangle Park
Allan Marcus

ORD/Washington
Barbara Davis

GUIDANCE MANUAL FOR THE INTEGRATED EXPOSURE UPTAKE BIOKINETIC MODEL FOR LEAD IN CHILDREN

Prepared by

THE TECHNICAL REVIEW WORKGROUP FOR LEAD

for

THE OFFICE OF EMERGENCY AND REMEDIAL RESPONSE
U.S. ENVIRONMENTAL PROTECTION AGENCY

with Document Production Assistance from

THE ENVIRONMENTAL CRITERIA AND ASSESSMENT OFFICE
U.S. ENVIRONMENTAL PROTECTION AGENCY
RESEARCH TRIANGLE PARK, NC 27711

PREFACE

The Guidance Manual has been developed to assist the user in providing appropriate input to the Integrated Exposure Uptake Biokinetic (IEUBK) Model for Lead. The IEUBK Model is designed to model exposure from lead in air, water, soil, dust, diet, and paint and other sources with pharmacokinetic modeling to predict blood lead levels in children 6 months to 7 years old. This manual emphasizes the use of the IEUBK Model for estimating risks from childhood lead exposure to soil and household dust that might be encountered at CERCLA/RCRA sites, although other applications of the model are possible. The manual provides background information on environmental exposure parameters and recommends some useful approaches that allow flexibility for site-specific risk assessments, where possible. Default parameters are recommended unless there is sufficient data to characterize site-specific conditions. A separate Appendix on sampling is being developed and will be issued later. A Technical Support Document details the basis for the biokinetic parameters and equations in the IEUBK Model. In addition, EPA is continuing to compare the results of field studies with model predictions and will release these findings in a later document.

One of the proposed uses of this model will be support for the implementation of an Interim Directive of the Office of Solid Waste and Emergency Response (OSWER). This Interim Directive explains how the IEUBK Model results can be a tool for the determination of site-specific cleanup levels. In this context, the model is viewed as a predictive tool for estimating changes in blood concentrations as exposures are modified. The model is also viewed as a useful tool that should aid the Agency in making more informed choices about the concentrations of lead that might be expected to impact human health.

The development of the model has included the cooperative efforts of several EPA programs over nearly a decade. For the last three years, these efforts have been coordinated by the Technical Review Workgroup for Lead. During its development, the model has undergone review by outside scientists, and its usefulness has been evaluated by EPA staff, contractors, and other reviewers assessing site-specific risk. The current version of the IEUBK model and the Guidance Manual incorporates many of their recommendations.

The use of mathematical and statistical models for environmental risk assessment has become increasingly widespread because of the many practical difficulties encountered in controlling human exposure to toxicants with subtle and long-lasting effects. Exposure to lead during infancy and childhood increases the risk of irreversible neurobehavioral deficits at

levels of internal exposure as low as 10 to 15 µg Pb per 100 mL of blood (10 to 15 µg/dL). Lead has many known sources, and many pathways from its environmental sources into the child's body (U.S. Environmental Protection Agency, 1986). The Environmental Protection Agency has long been interested in methods for relating environmental lead concentrations to blood lead concentrations in children. Earlier approaches based on statistical correlations provided essential information on the existence and magnitude of childhood lead uptake from persistent exposure to different environmental sources, including lead in air, diet, drinking water, soil, dust, and lead-based paint. Unfortunately, these statistical relationships are limited in their ability to estimate the effects of alternative lead abatement methods that change pathways as well as sources.

In 1985 the EPA Office of Air Quality Planning and Standards began to develop an alternative approach for estimating the effectiveness of alternative National Ambient Air Quality Standards for lead, particularly around point sources of air lead emissions such as smelters. This was a computer simulation model with two components: (1) a model of the biokinetics of lead distribution and elimination whose parameters vary with the child's age, and (2) a multi-source and multi-media lead exposure model in which air lead concentrations change over time. The biokinetic model was based on studies at New York University by Naomi Harley, Theodore Kneip, and Peter Mallon. The U.S. Environmental Protection Agency Clean Air Science Advisory Committee (CASAC) reviewed and found acceptable the OAQPS staff report documenting the model in 1989. A subsequent OAQPS staff paper reviewing the National Ambient Air Quality Standard for Lead, which included results of applying the model to point sources of air lead such as smelters and battery plants, was also evaluated by CASAC in 1990 (U.S. Environmental Protection Agency, 1990B).

Those who had been involved in developing the lead model then received a large and growing number of requests on applications of the model in a wide variety of other contexts not originally intended for model use. The largest number of these requests involved the use of the model to estimate the effects of soil lead abatement at Superfund sites.

The air model was further developed to include enhancements in absorption and biokinetics. In November, 1991, the Indoor Air Quality and Total Human Exposure Committee (IAQTHEC) of EPA's Science Advisory Board (SAB) reviewed the Uptake Biokinetic Model for Lead (version 0.4) and evaluated its use in assessing total lead exposures and in aiding in developing soil cleanup levels at residential CERCLA/RCRA sites. The Committee's Report was transmitted to EPA Administrator William K. Reilly in

March, 1992. The Committee concluded that while refinements in the detailed specifications of the model would be needed, the approach followed in developing the model is sound. The Committee stated that the model can effectively be applied for many current needs even as it continues to undergo refinement for other applications, based upon experience gained in its use.

The Committee was concerned that the reliability of the results obtained using the model is very much dependent on the selection of the various coefficients and default values that were used. In particular, the Committee identified the need for guidance on the "proper" geometric standard deviation (GSD) and the use of default values for other parameters. In addition to these general comments, specific comments were included in the Report. The comments of the SAB and other reviewers have been considered in this revision of the Guidance Manual.

Since the SAB review, EPA has further refined the model. The four main components of the current IEUBK model are: (1) an exposure model that relates environmental lead concentrations to age-dependent intake of lead into the gastrointestinal tract; (2) an absorption model that relates lead intake into the gastrointestinal tract and lead uptake into the blood; (3) a biokinetic model that relates lead uptake in the blood to the concentrations of lead in several organ and tissue compartments; and (4) a model for uncertainty in exposure and for population variability in absorption and biokinetics. A Technical Support Document that details the selection of parameters and equations in the model is available.

As with any multicompartmental model, pools in the compartmental analysis can be identified with specific organs or organ systems only if biological concentrations of the compartments are known. For some compartments, the biological concentrations have been measured at a number of time points so that the movement of lead from one compartment to another can be estimated. The biokinetic and absorption components of the model, however, are not observed directly but are inferred from accessible data.

In developing the IEUBK Model, EPA has learned much from "real world" comparisons of blood lead and predicted values—not only that the model works, but also that it can be made to work better. Guidance on the appropriate use of the model is based on our experiences, where possible, and on the experiences of many users and reviewers of the model. Many of the most useful parts of the Guidance Manual have been suggested by these reviewers.

While the model has been used to support the NAAQS for Lead, the Clean Water Act national regulations, and several other regulatory and enforcement issues, EPA is continuing its validation of the IEUBK Model with detailed evaluation of additional data collected from different types of sites. Comparison of predicted and empirical blood lead concentrations will be described in the Field Study Data Set Comparisons Document described in Section 1.2.2.

Although EPA is releasing version 0.99d of the IEUBK Model to ensure consistent application among users, the Agency will continue to evaluate the results of validation exercises and different applications of the model. The Environmental Protection Agency will determine periodically whether refinements to the model are warranted, considering scientific advancements and the development of alternative approaches.

The Environmental Protection Agency welcomes the suggestions of those using the IEUBK model. Questions regarding the site-specific application of the IEUBK Model should be raised with the appropriate Regional Toxics Integration Coordinator. Comments on the technical content of the manual or suggestions for its improvement may be brought to the attention of the Technical Review Workgroup for Lead, whose current addresses are listed on page xxi.

TABLE OF CONTENTS

TABLE OF CONTENTS (cont'd)

TABLE OF CONTENTS (cont'd)

TABLE OF CONTENTS (cont'd)

TABLE OF CONTENTS (cont'd)

TABLE OF CONTENTS (cont'd)

LIST OF TABLES

LIST OF TABLES (cont'd)

LIST OF TABLES (cont'd)

LIST OF TABLES (cont'd)

LIST OF FIGURES

LIST OF FIGURES (cont'd)

LIST OF SCREENS

LIST OF SCREENS (cont'd)

TECHNICAL REVIEW WORKGROUP FOR LEAD

Harlal Choudhury
U.S. Environmental Protection Agency
Environmental Criteria and Assessment Office
26 West Martin Luther King Dr.
Cincinnati, OH 45268

Barbara Davis
U.S. Environmental Protection Agency
(5204G)
401 M St. SW
Washington, DC 20460

Rob Elias
U.S. Environmental Protection Agency
(MD-52)
Environmental Criteria Assessment Office
Research Triangle Park, NC 27711

Susan Griffin (Chair)
U.S. Environmental Protection Agency
Region 8 (8 HWM-SM)
999 18th St., Suite 500
Denver, CO 80202

Karen Hogan
U.S. Environmental Protection Agency
(7404)
401 M St. SW
Washington, DC 20460

Mark Maddaloni
U.S. Environmental Protection Agency
Region 2
Emergency and Remedial Response Division
26 Federal Plaza
New York, NY 10278

Allan Marcus
U.S. Environmental Protection Agency
(MD-52)
Environmental Criteria and Assessment Office
Research Triangle Park, NC 27711

Roy Smith
U.S. Environmental Protection Agency
Region 3 (3 HW15)
Hazardous Waste Management Division
841 Chestnut St.
Philadelphia, PA 19107

Pat Van Leeuwen
U.S. Environmental Protection Agency
Region 5 (HSRLT-5J)
Waste Management Division
77 West Jackson Blvd.
Chicago, IL 60604

Chris Weis
U.S. Environmental Protection Agency
Region 8 (8 HWM-SM)
999 18th St., Suite 500
Denver, CO 80202

Paul White
U.S. Environmental Protection Agency
(8603)
Office of Health and Environmental Assessment
401 M St., SW
Washington, DC 20460

GLOSSARY OF MODEL TERMS

Absorbed dose - The amount of a substance penetrating an absorption barrier (the exchange boundaries) of an organism, via either physical or biological processes.

Absorption barrier - Any of the exchange barriers of the body that allow differential transport of various substances across a boundary. Examples of absorption barriers are the skin, lung tissue, and gastrointestinal tract wall.

Accuracy - The measure of the correctness of data, as given by the difference between the measured value and the true or standard value.

Ambient - Surrounding conditions.

Ambient measurement - The measurement (usually of the concentration of a chemical or pollutant) taken in an ambient medium, normally with the intent of relating the measured value to the exposure of an organism that contacts that medium.

Ambient medium - One of the basic categories of material surrounding or contacting an organism (e.g., outdoor air, indoor air, water, or soil) through which chemicals or pollutants can move and reach the organism. (See biological medium, environmental medium.)

Arithmetic mean - The sum of all the measurements in a data set divided by the number of measurements in the data set.

Background level (environmental) - The concentration of substance in a defined control area during a fixed period of time before, during or after a data gathering operation.

Bias - A systematic error inherent in a method or caused by some feature of the measurement system.

Bioavailability - The fraction of intake at a portal of entry into the body (lung, gut, skin) that enters the blood. Bioavailability is typically a function of chemical properties, physical state of the material that an organism ingests or inhales, and the ability of the individual organism to physiologically absorb the chemical. The absorption rate varies widely by type of substance and can greatly influence the toxicity of lead over that acute timeframe.

Biokinetics - processes affecting the movement of molecules from one internal body compartment to another, including elimination from the body.

Biological measurement - A measurement taken in a biological medium. For the purpose of exposure assessment via reconstruction of dose, the measurement is usually of the concentration of a chemical/metabolite or the status of a biomarker, normally with the intent of relating the measured value to the internal dose of a chemical at some time in the past.

(Biological measurements are also taken for purposes of monitoring health status and predicting effects of exposure). (See ambient measurement.)

Biological medium - One of the major categories of material within an organism (e.g., blood, adipose tissue, or breath) through which chemicals can move, be stored, or be biologically, physically, or chemically transformed. (See ambient medium, environmental medium.)

Body burden - The amount of a particular chemical stored in the body at a particular time, especially a potentially toxic chemical in the body as a result of exposure. Body burdens can be the result of long term or short term storage, for example, the amount of a metal in bone, the amount of a lipophilic substance such as PCB in adipose tissue, or the amount of carbon monoxide (as carboxyhemoglobin) in the blood.

Comparability - The ability to describe likenesses and differences in the quality and relevance of two or more data sets.

Compartment - A distinct anatomical organ, tissue, fluid pool, or group of tissues within the body that are regarded as "kinetically homogeneous."

Dose - The amount of a substance available for interaction with metabolic processes or biologically significant receptors after crossing the outer boundary of an organism. The potential dose is the amount ingested, inhaled, or applied to the skin. The applied dose is the amount of a substance presented to an absorption barrier and available for absorption (although not necessarily having yet crossed the outer boundary of the organism). The absorbed dose is the amount crossing a specific absorption barrier (e.g., the exchange boundaries of skin, lung, and digestive tract) through uptake processes; internal dose is a more general term denoting the amount absorbed, without respect to specific absorption barriers or exchange boundaries. The amount of the chemical available for interaction by any particular organ or cell is termed the delivered dose for that organ or cell.

Environmental medium - One of the major categories of material found in the physical environment that surrounds or contacts organisms (e.g., surface water, ground water, soil, or air) and through which chemicals or pollutants can move and reach the organisms. (See ambient medium, biological medium.)

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 in contact integrated over the time duration of that contact.

Exposure pathway - The physical course a chemical or pollutant takes from the source to the organism exposed.

Exposure route - The way a chemical or pollutant enters an organism after contact (e.g., by ingestion, inhalation, or dermal absorption).

Exposure scenario - A set of facts, assumptions, and inferences about how exposure takes place that aids the exposure assessor in evaluating, estimating, or quantifying exposures.

Geometric mean - The nth root of the product of n values. Also, the exponential function of the mean or expected value of the natural logarithm of a variable.

Geometric standard deviation (GSD) - The exponential function of the standard deviation of the natural logarithm of a variable.

Guidelines - Principles and procedures to set basic requirements for general limits of acceptability for assessments.

Intake - The process by which a substance crosses the outer boundary of an organism without passing an absorption barrier (e.g., through ingestion or inhalation). (See also "potential dose").

Internal dose - The amount of a substance penetrating across the absorption barriers (the exchange boundaries) or an organism, via either physical or biological processes.

Matrix - A specific type of medium (e.g., surface water, drinking water) in which the analyte of interest may be contained.

Median value - The value in a measurement data set such that half the measured values are greater and half are less.

Monte Carlo technique - A repeated random sampling from the distribution of values for each of the parameters in a generic (exposure or dose) equation to derive an estimate of the distribution of (exposures or doses in) the population.

Pathway - The physical course a chemical or pollutant takes from the source to the organism exposed.

Pharmacokinetics - The study of the time course of absorption, distribution, metabolism, and excretion of a foreign substance (e.g., a drug or pollutant) in an organism's body.

Potential dose - The amount of a chemical contained in material ingested, air breathed, or bulk material applied to the skin.

Precision - A measure of the reproducibility of a measured value under a given set of conditions.

Probability samples - Samples selected from a statistical population such that each sample has a known probability of being selected.

Random samples - Samples selected from a statistical population such that each sample has an equal probability of being selected.

Range - The difference between the largest and smallest values in a measurement data set.

Reasonable worst case exposure or risk range - The lower portion of the "high end" of the exposure, dose or risk distribution. The reasonable worst case conceptually should be targeted at above the 90th percentile in the distribution, but below about the 98th percentile ("maximum exposure or risk range").

Representativeness - The degree to which a sample is, or samples are, characteristic of the whole medium, exposure, or dose for which the samples are being used to make inferences.

Risk - The probability of deleterious health or environmental effects.

Route - The way a chemical or pollutant enters an organism after contact (e.g., by ingestion, inhalation, or dermal absorption).

Sample - A small part of something designed to show the nature or quality of the whole. Exposure-related measurements are usually samples of environmental or ambient media, exposures of a small subset of a population for a short time, or biological samples, all for the purpose of inferring the nature and quality of parameters important to evaluating exposure.

Scenario evaluation - An approach to quantifying exposure by measurement or estimation of both the amount of a substance contracted, and the frequency/duration of contact, and subsequently linking these together to estimate exposure or dose.

Structural Equations Model - A statistical model of a process in which several regression equations are solved simultaneously, and outputs or responses from one equation may be used as inputs or predictors in another equation. Useful in pathway modeling.

Surrogate data - Substitute data or measurements on one substance used to estimate analogous or corresponding values of another substance.

Uptake - The process by which a substance crosses an absorption barrier and is absorbed into the body.