Training on the IEUBK Model, Adult Lead Methodology, and Recent Lead Risk Assessment Updates

TRW Lead Committee

Overview of Lead Model Training

- Introduction (why do we need models?)
- The IEUBK Model -- structure and components
- The U.S. EPA Adult Lead Methodology (ALM)
- Discuss IEUBK & ALM inputs (review data entry windows and input variables, and why some are controversial)
- Risk Assessment Issues and Guidance
- PbB calculation, risk calculation, & PRG

What is a Biokinetic Model?

- Biokinetic models assess the routes of environmental exposure to a substance and determine the distribution of this substance among the various body tissues in humans.

- Biokinetic models work best when there is a known effect that is associated with a specific tissue concentration in humans.
  - e.g., impaired nerve conduction velocity in children at 10 µg Pb/dL blood.

- Biokinetic models also enable the risk assessor to predict the relative effect of an increase in body tissue that might result from a specific increase in environmental exposure.
  - e.g., the expected blood lead concentration that would result from an increase in soil lead concentration of 500 mg/kg.

Lead Risk Assessment is Different

- In comparison to most other environmental contaminants, the degree of uncertainty about the health effects of lead is quite low.
- Some of these effects, particularly changes in the levels of certain blood enzymes and in aspects of children's neurobehavioral development, may occur at blood lead levels so low as to be essentially without a threshold.
- EPA decided that it was inappropriate to derive a Reference Dose (RfD) for lead.
- EPA regulates lead exposure by using a biomarker (blood lead concentration).
- Environmental exposures to lead are modeled to predict blood lead levels associated with those exposures.
- CDC established 10 µg/dL as the Federal level of concern in 1991.

OSWER Lead Risk Assessment Policy

- The IEUBK Model as the primary tool to generate residential risk-based soil cleanup levels.
- OSWER's risk reduction policy is for no child to have greater than a 5% probability of having a blood lead level >10 µg/dL.
- Modeling is used to associate environmental exposures with risk and inform cleanup decisions (relative to OSWER's risk reduction goal).
- In general, blood lead survey data should not be used as the only basis for cleanup decisions.

Purpose of the Lead Models

IEUBK (Integrated Exposure Uptake Biokinetic Model)

- Predicts the blood lead levels in children (under 7 years old) who are exposed to environmental lead from many sources
- Predicts the risk (probability) that a typical or hypothetical child exposed to specified media lead concentrations will have a blood lead level ≥10 µg/dL (the blood lead level of concern)
- Predicts PRG (cleanup levels) for various media for residential land use

ALM (Adult Lead Methodology)

- Predicts the risk of elevated blood lead levels in non-residential settings (adult exposure to soil; ultimate receptor is fetus)
- Predicts PRG (cleanup levels) for soil in non-residential land use

Characteristics of the IEUBK Model

- While IEUBK model risk assessments are more complex than the typical Superfund risk assessment approach, the IEUBK model is not as complex as variance propagation approaches (PRA)
- The IEUBK model employs more site-specific information than other EPA risk assessment models
- The IEUBK model performs well when comparing predicted and observed blood lead levels (*Hogan et al., 1998. Integrated Exposure Uptake Biokinetic Model for Lead in Children: Empirical Comparisons with Epidemiologic Data. Environmental Health Perspectives, Vol. 106 No. S6*)

Intake – Uptake – Biokinetic Relationship

Daily **Intake** of lead is calculated as follows:

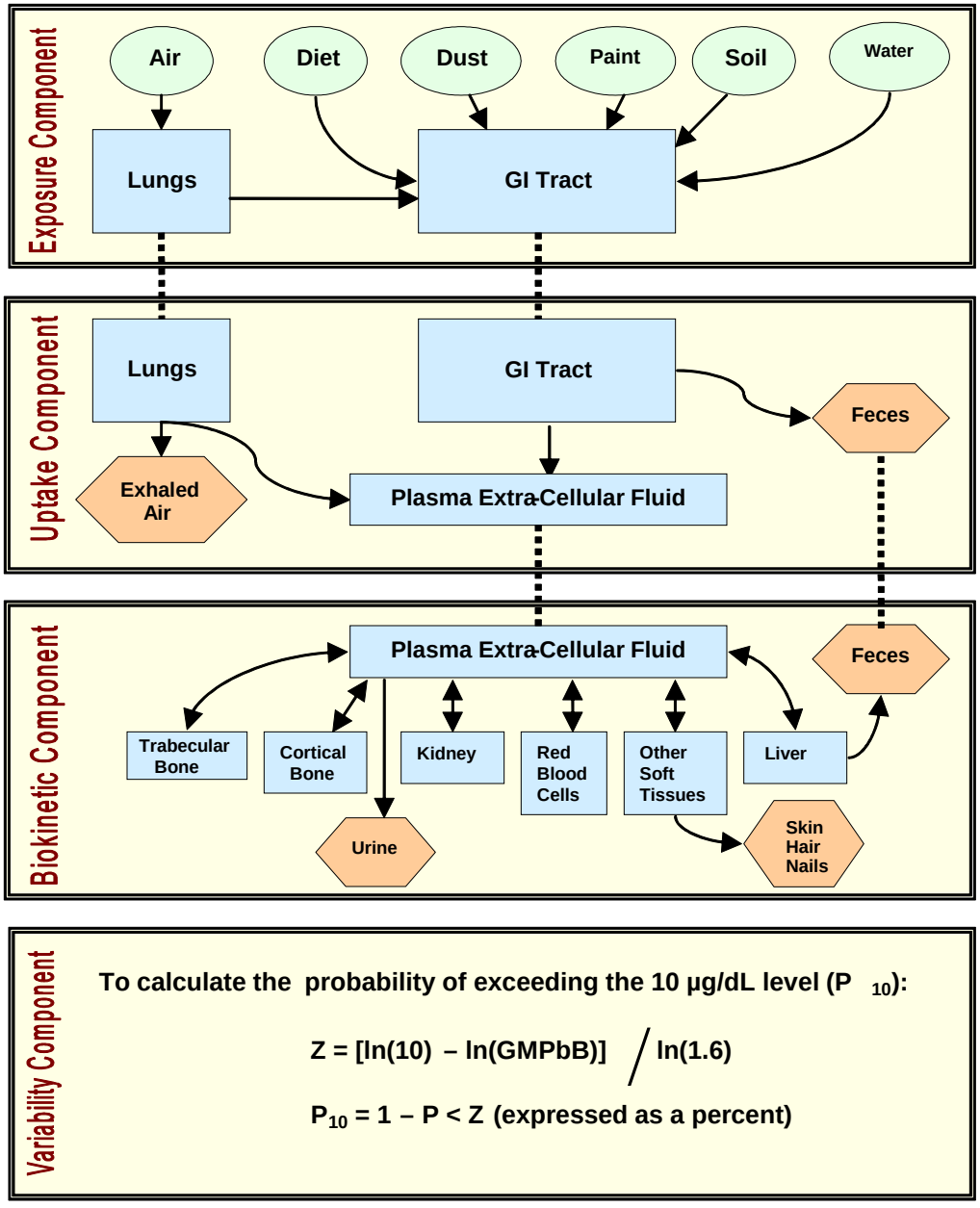
Intake = Media Concentration x Media Intake Rate

For example: µg lead/day = (µg lead / g of media) x (g of media / day)

Uptake is calculated based on media-specific absorption values (defaults are available): Uptake = Intake x Absorption Factor

Biokinetic module estimates transfer rates for Pb moving between compartments and through elimination pathways to derive a predicted long-term steady state geometric mean PbB concentration.

In the final step, the **Probability** module estimates a plausible distribution of PbB concentrations for a given GSD. The distribution is centered on the geometric mean PbB concentration calculated by the Biokinetic Module.


Exposure Component
Air
Diet
Dust
Paint
Soil
Water
Lungs
GI Tract
Uptake Component
Lungs
GI Tract
Feces
Exhaled Air
Plasma Extra-Cellular Fluid
Biokinetic Component
Plasma Extra-Cellular Fluid
Feces
Trabecular Bone
Cortical Bone
Kidney
Red Blood Cells
Other Soft Tissues
Liver
Urine
Skin Hair Nails
Variability Component
To calculate the probability of exceeding the 10 µg/dL level (P_{10}):
$Z = [\ln(10) - \ln(GMPbB)] / \ln(1.6)$
$P_{10} = 1 - P < Z$ (expressed as a percent)
Environmental Media
Body compartment or elimination pool required in more than one component
Elimination Pools of the Body
Body Compartments

History of the IEUBK Model Development

IEUBK is the product of many years of development

1985-89: Initially Office of Air Quality Planning Standards

1989: Development by Superfund following SAB review

1989-2001: DOS version (0.99d) development.

1994-2001: Release of 0.99d version by Superfund with input from EPA, ATSDR, CDC, and SAB.

1998: Independent Validation and Verification (IV&V)

1997-2001: IEUBK (0.99d) was converted to Windows

2001-present: IEUBKwin 1.0 and IEUBKwin 1.1

2005: NAS review

Independent Reviews of the IEUBK

The reviewers have generally found that the model was scientifically sound and useful for lead risk assessment

1990	SAB review for NAAQS
1992	SAB review and External Peer Review of model
1998	Independent Validation and Verification
1998	SAB review for TSCA Section 403 Regulation
2005	National Academies of Science (NAS) review for Coeur d'Alene site report

Evaluation and Validation of the IEUBK

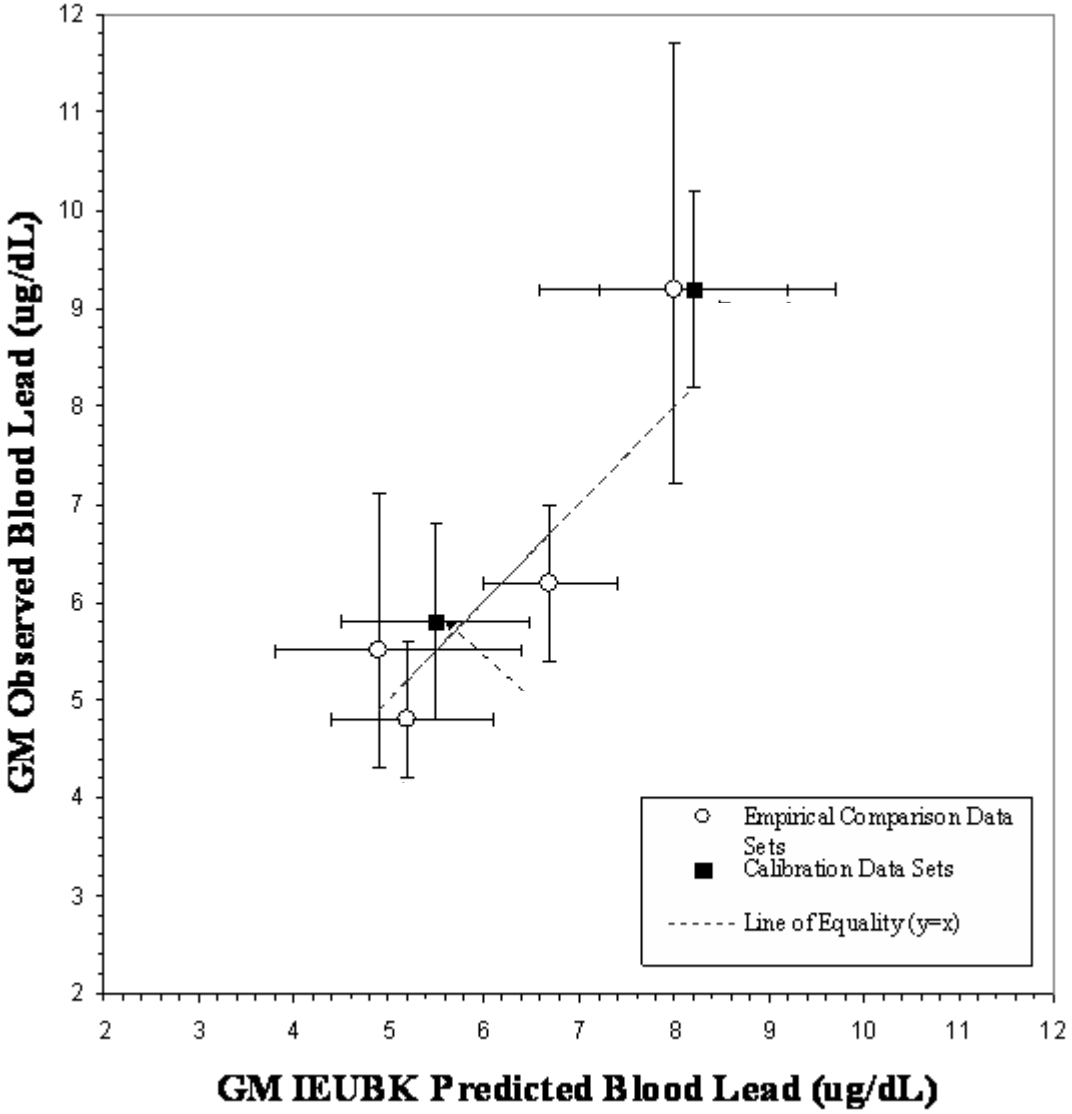
IV&V evaluated the following:

1. Scientific underpinnings of the model structure
2. Adequacy of parameter estimates
3. Mathematical relationships (as computer code)
4. Empirical comparisons (predicted vs. observed)

The process and results of the IEUBK validation are available online (TRW web site)

- 1994 Validation Strategy for the IEUBK
- 1998 Empirical Comparisons Manuscript (Hogan et al., 1998)

Comparison of IEUBK Predictions and Observed PbB



Correspondence of observed and IEUBK model-predicted blood lead concentrations by site: Kansas/Missouri, Illinois, Pennsylvania, 1991. The solid points are the GMs, whereas the open points provide 95% CIs for the GMs. Adapted from Hogan et al., 1998

Comparison of IEUBK Predictions and Observed PbB

Comparison of Observed and Predicted Geometric Mean Blood Lead and Risk of Exceeding 10 µg/dL for Three Community Blood Lead Studies

Dataset	N	Observed Blood Lead (µg/dL)		Model Predictions (µg/dL)	
		GM (95% CI)	Percent >10 (95% CI)	GM (95% CI)	Percent >10 (95% CI)
Galena, KA Jasper Co, MI[a]	111	5.2 (4.5-5.9)	20 (13-27)	4.6 (4.0-5.3)	18 (11-25)
Madison Co, IL[a]	333	5.9 (5.5-6.4)	19 (15-23)	5.9 (5.4-6.3)	23 (19-28)
Palmerton, PA[b]	34	6.8 (5.6-8.2)	29 (14-44)	7.5 (6.6-8.6)	31 (16-47)

Excerpts from Air Criteria Document for Lead (October 2006). Original data from Hogan et al. (1998)

CI, confidence interval; GM, geometric means
[a]Children away from home ≤10 hours/week
[b]Children away from home ≤20 hours/week

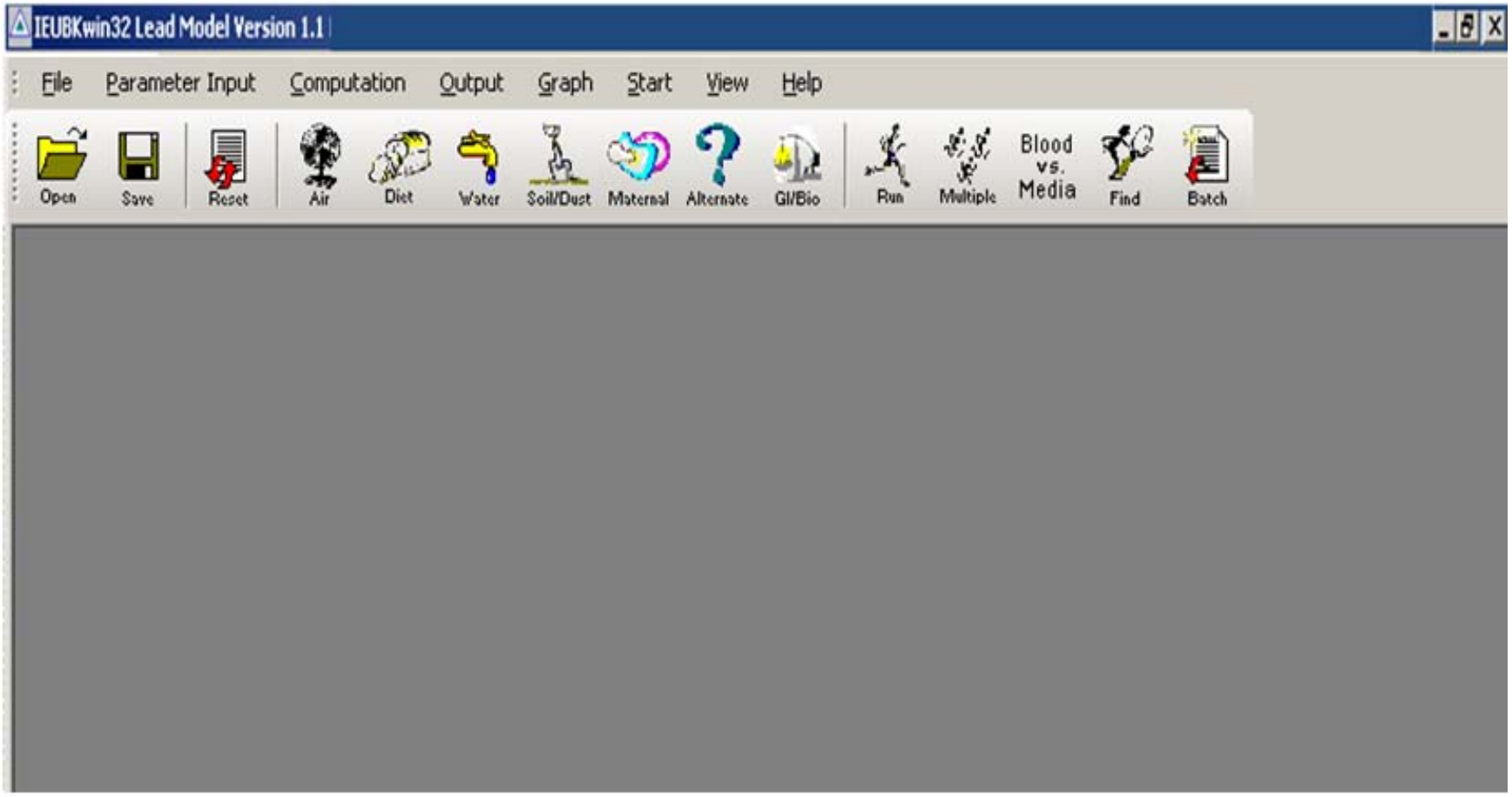
IEUBK Exposure Module Components

Media Concentrations for Input		
Soil	Soil must be sampled. Site-specific data required.	Refer to the IEUBK User's Guide and 1994 Guidance Manual for additional information on this input parameter.
Dust	Site-specific data or a value can be derived from soil concentration using multiple source analysis.	Refer to the IEUBK User's Guide and 1994 Guidance Manual for additional information on this input parameter.
Air (default)	0.1 µg/m^3	Ratio of indoor to outdoor air lead concentration is 30%. Site-specific data may be substituted.
Drinking Water (default)	4 µg/L	Site-specific data may be substituted.

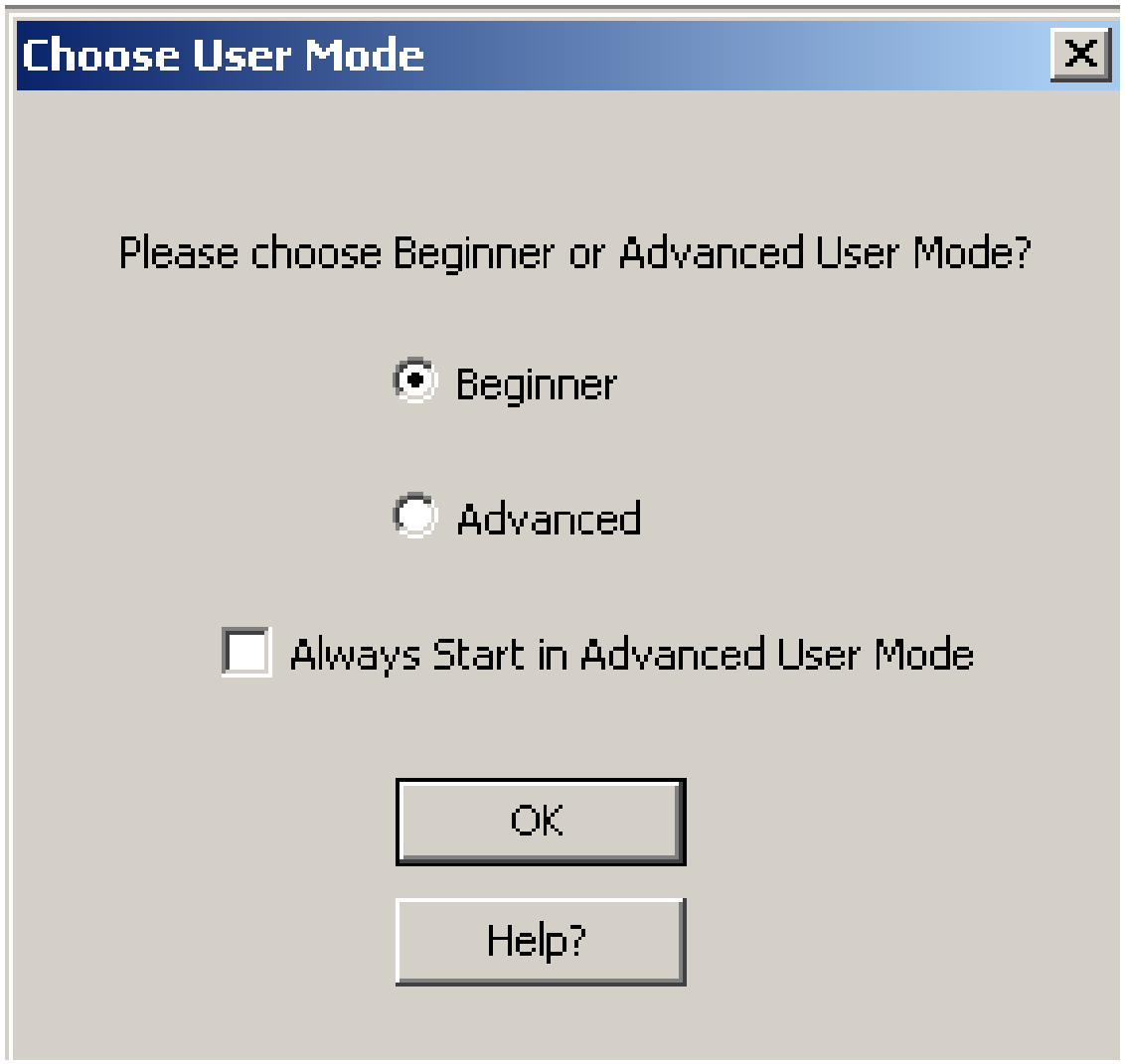
IEUBK Components (continued)

Media	Age-specific Intake Rates							Comments
	0-1 year	1-2 yrs	2-3 yrs	3-4 yrs	4-5 yrs	5-6 yrs	6-7 yrs	
Soil/dust (mg/day)	85	135	135	135	100	90	85	Default values recommended. Intake is apportioned 55% dust & 45% soil
Air (m^3/day)	2	3	5	5	5	7	7	Default values recommended
Drinking Water (L/day)	0.2	0.5	0.52	0.53	0.55	0.58	0.59	Default values recommended
Diet (µg Pb/day)	2.26	1.96	2.13	2.04	1.95	2.05	2.22	Site-specific data may be used to assess exposure to fish, game, or home-grown produce.
Alt. Source	Site-specific data may be used to account for intake of lead in other sources							Refer to the IEUBK User's Guide and 1994 Guidance Manual for more information

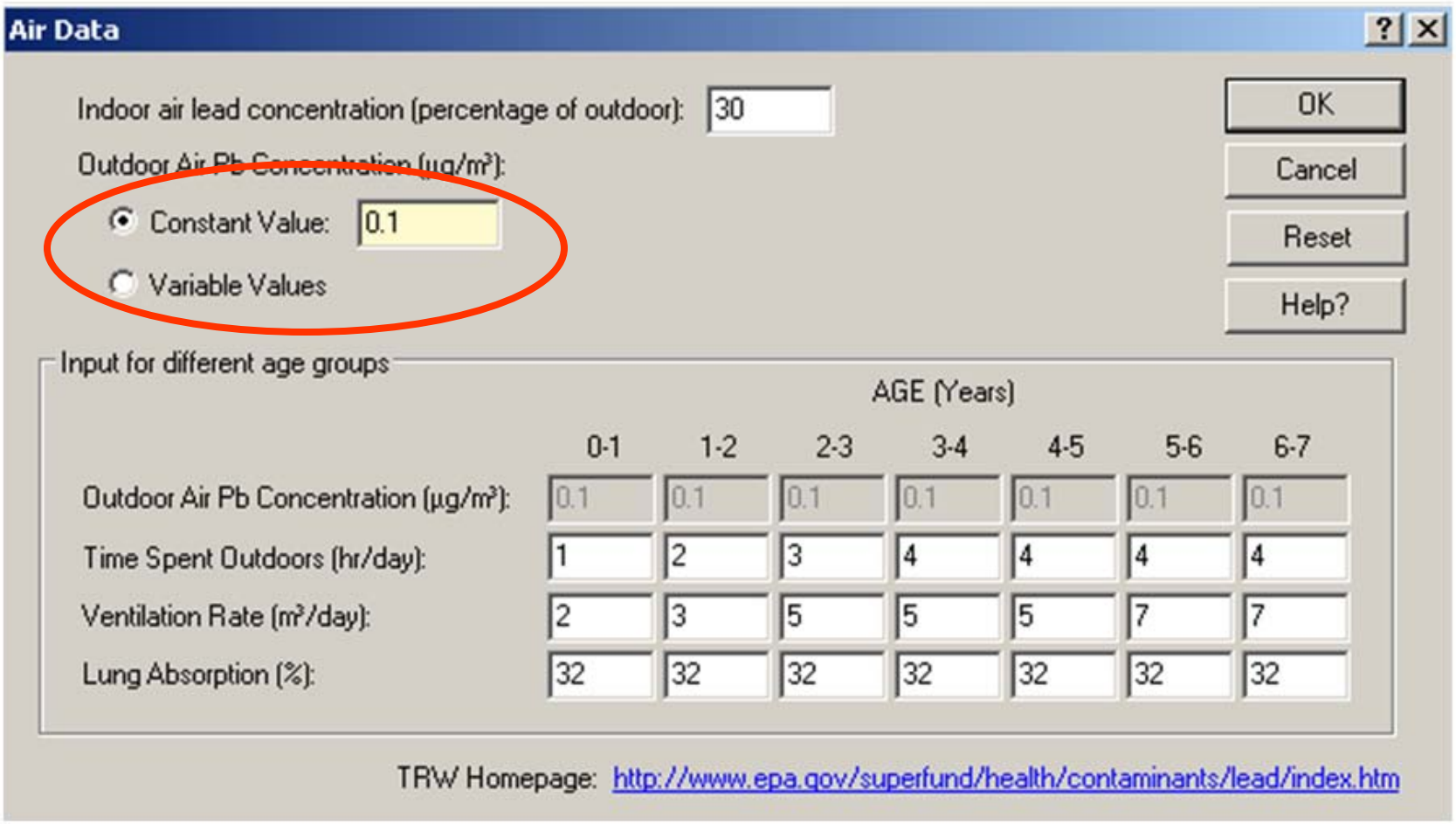
IEUBK Model screenshot showing input icons for pathways



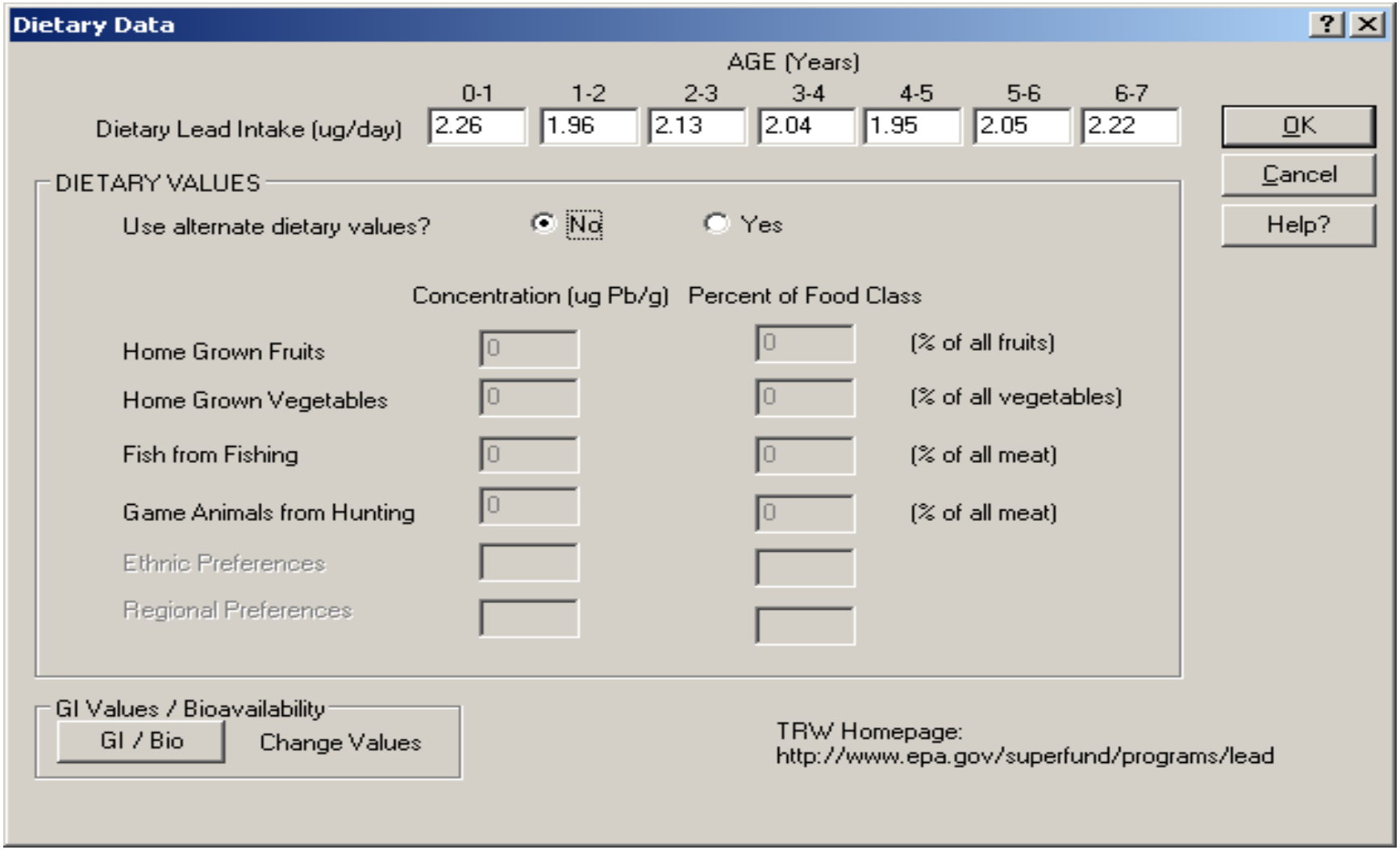
Choosing the User Mode



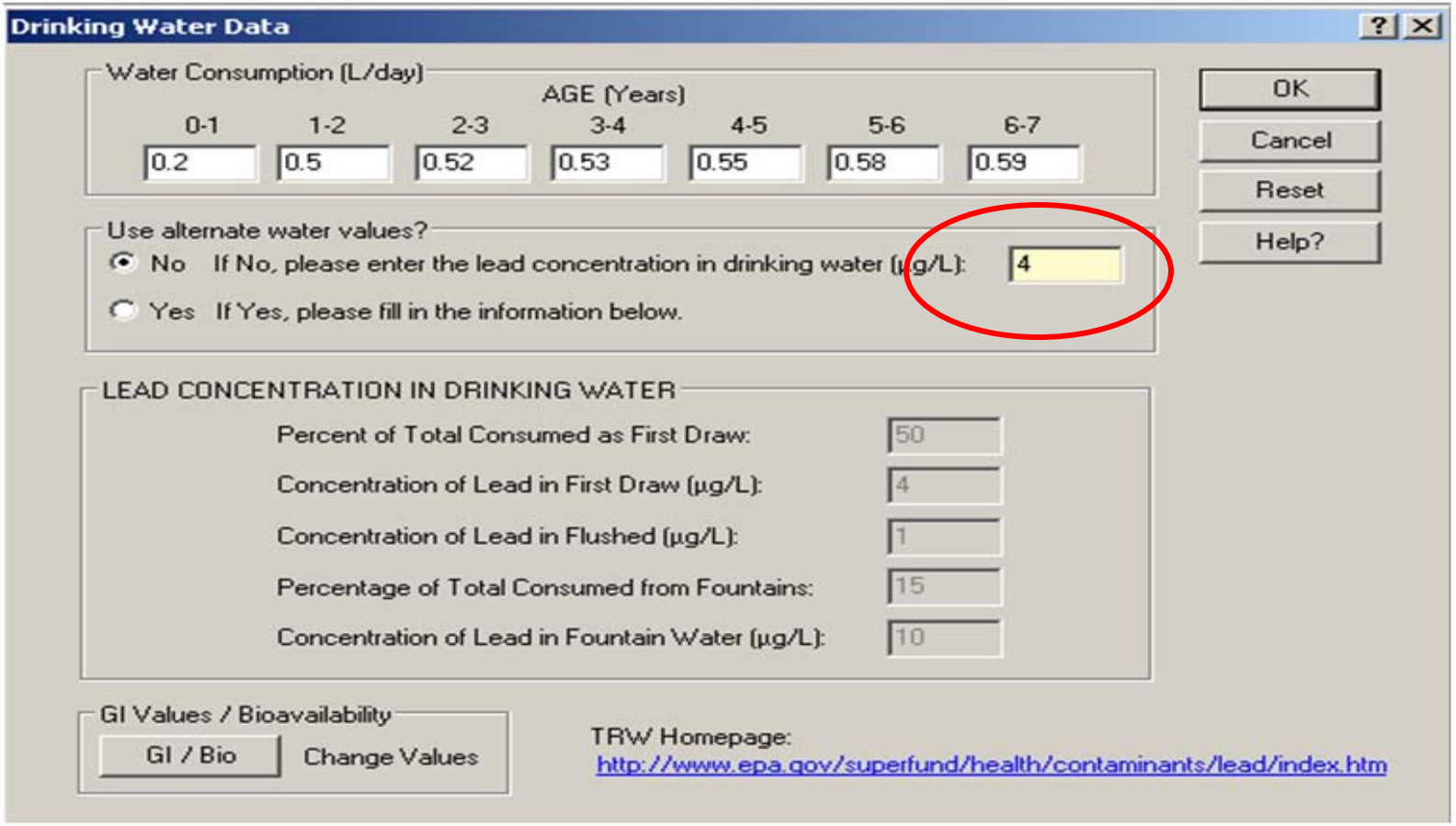
Air Exposure Input



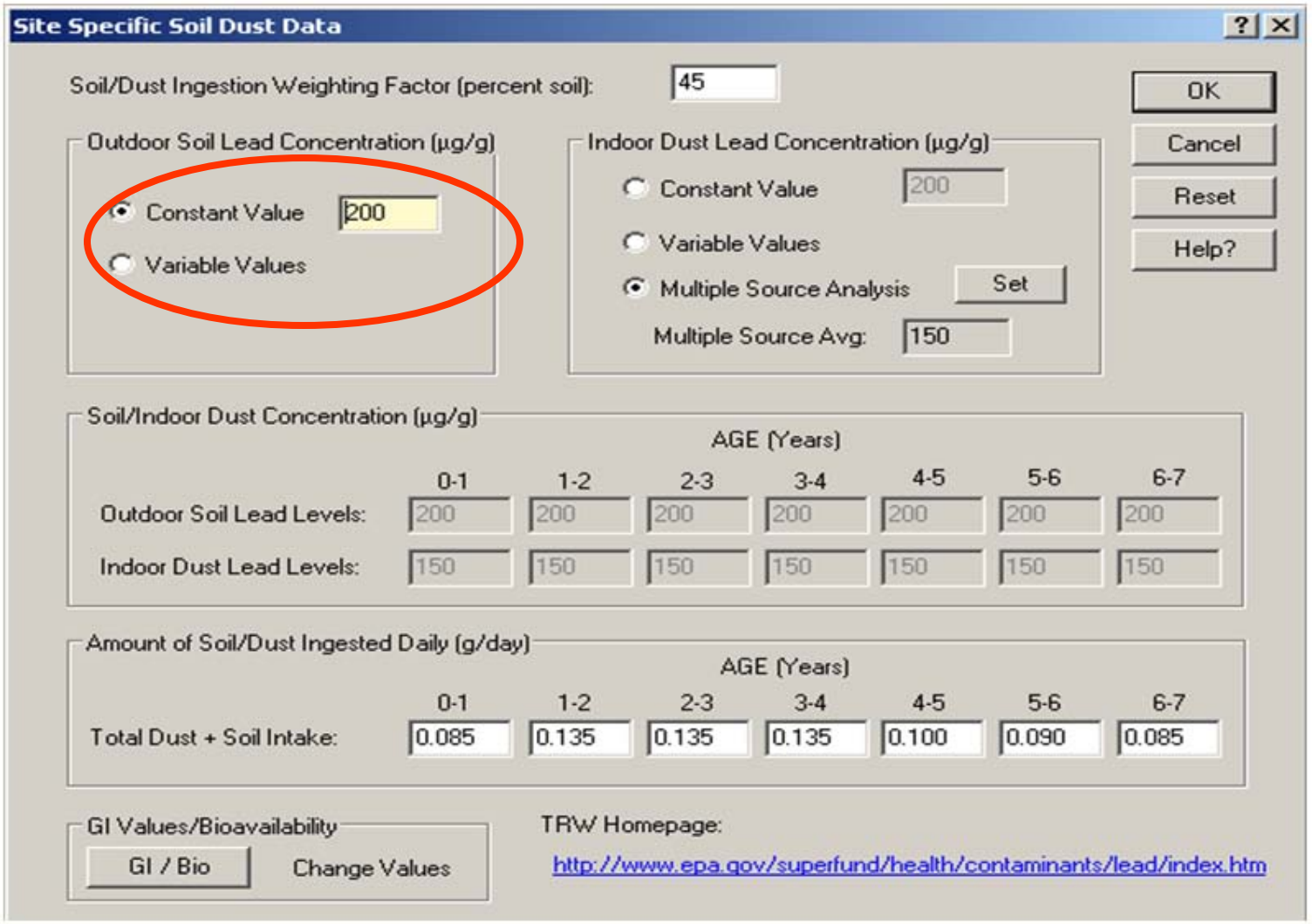
Dietary Exposure Input



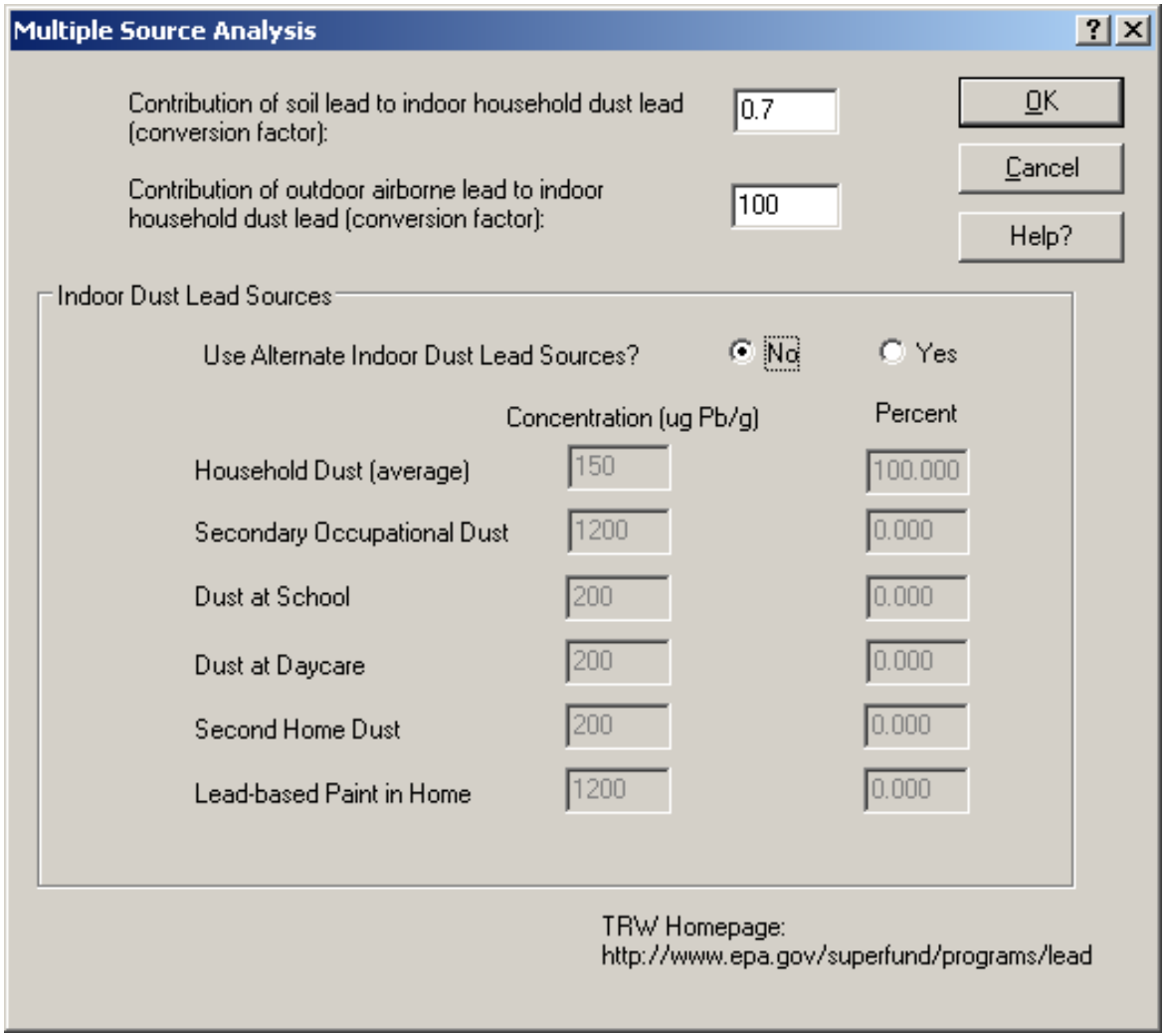
Drinking Water Exposure Input



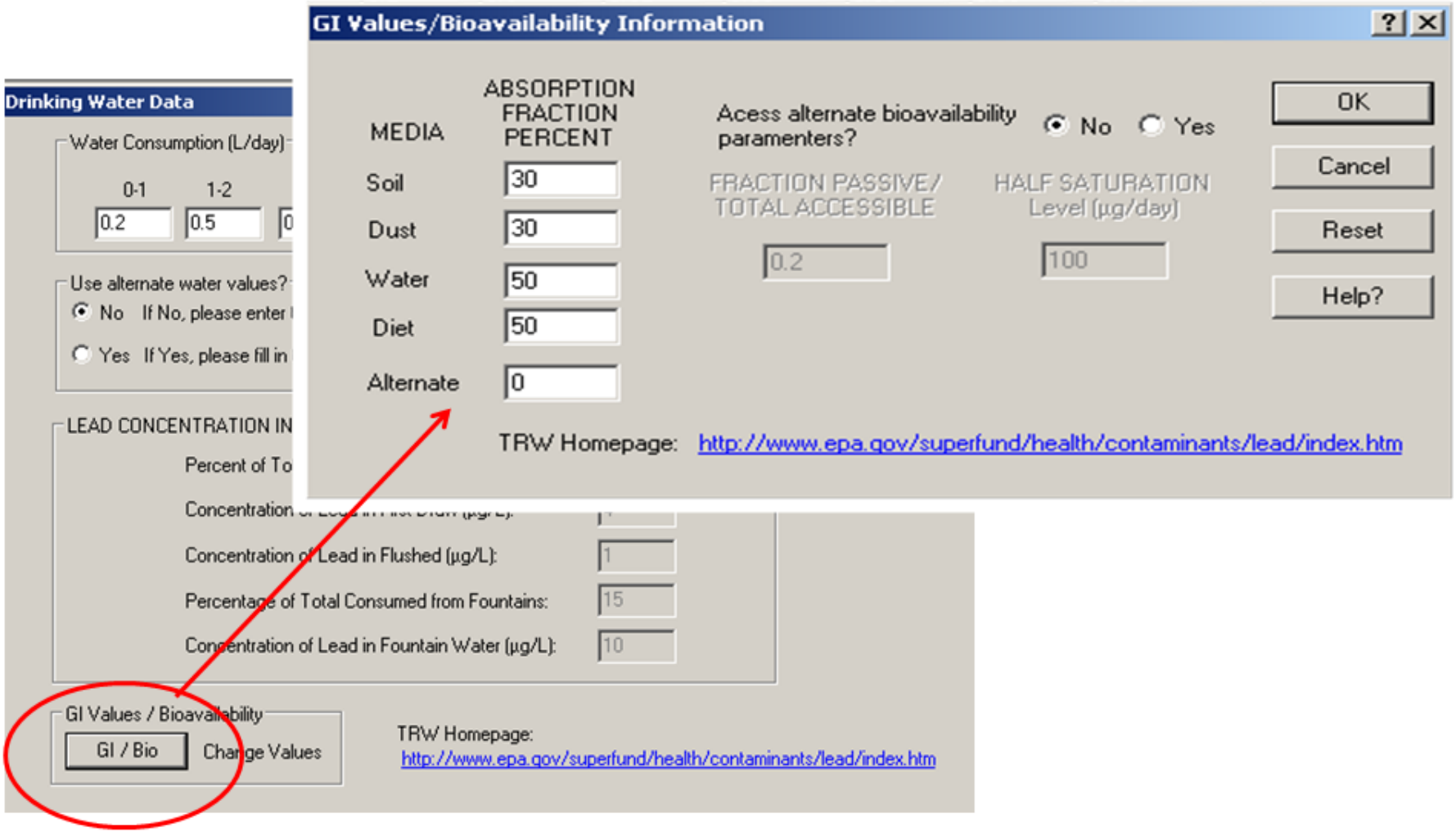
Soil and Dust Exposure Input



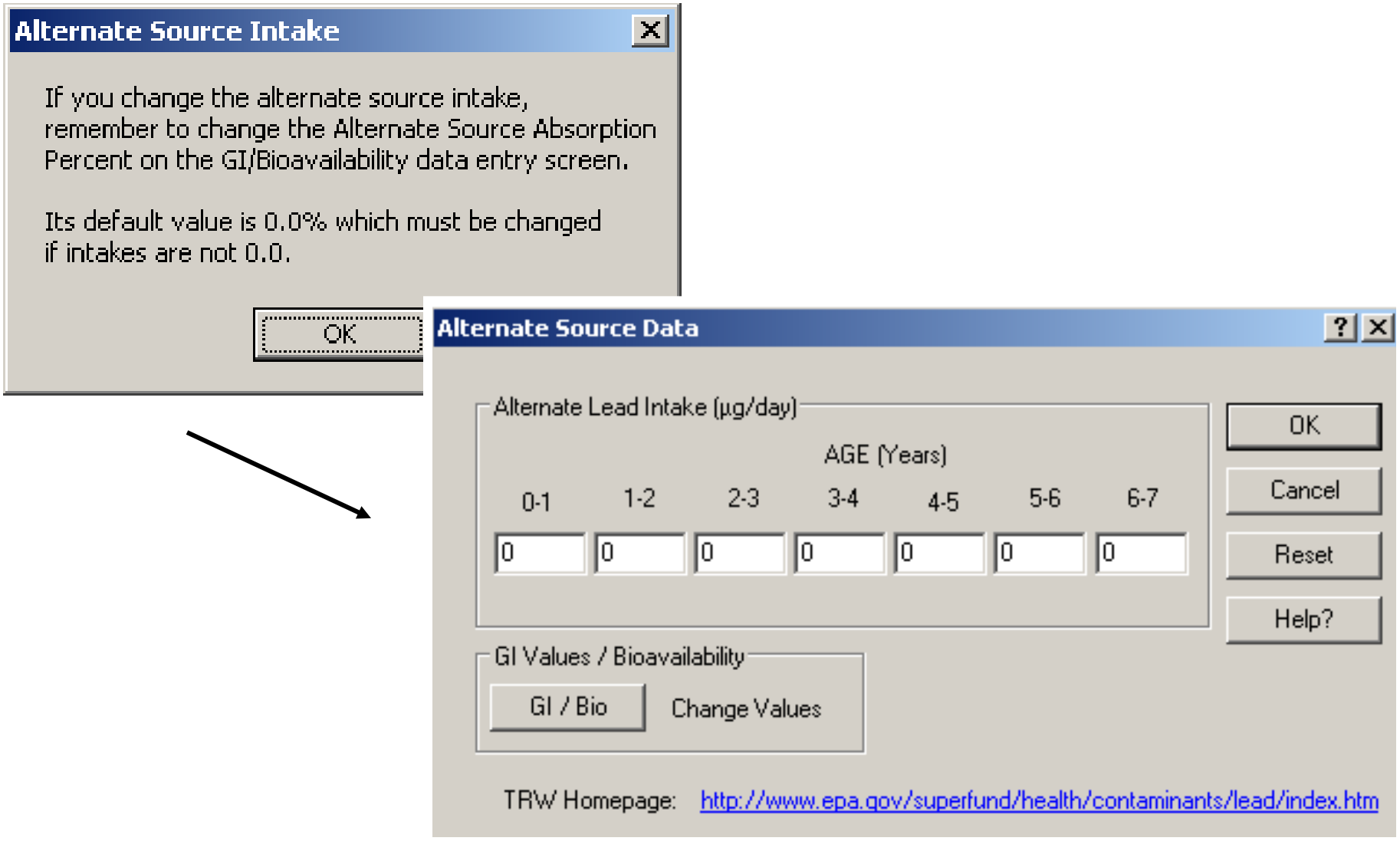
Multiple Source Analysis Detail



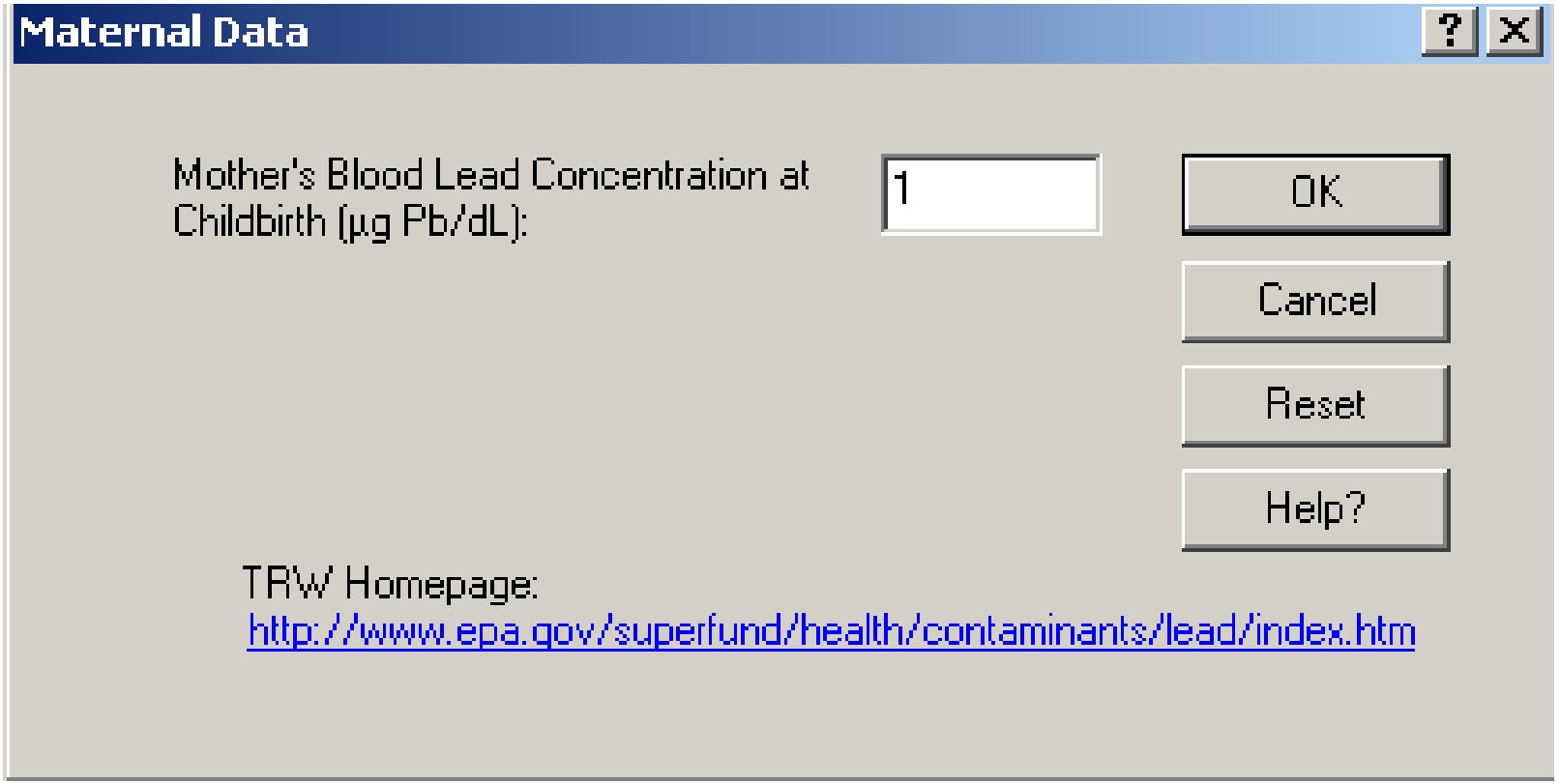
Bioavailability Information Input



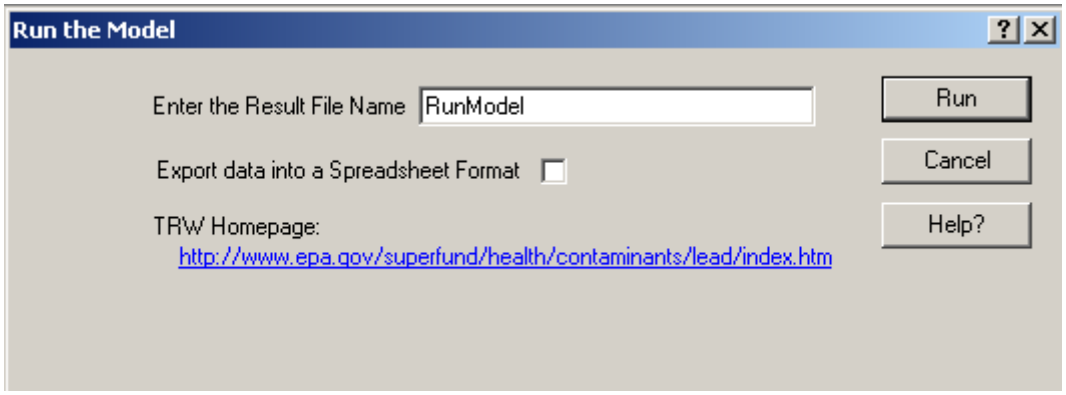
Alternate Exposure Input

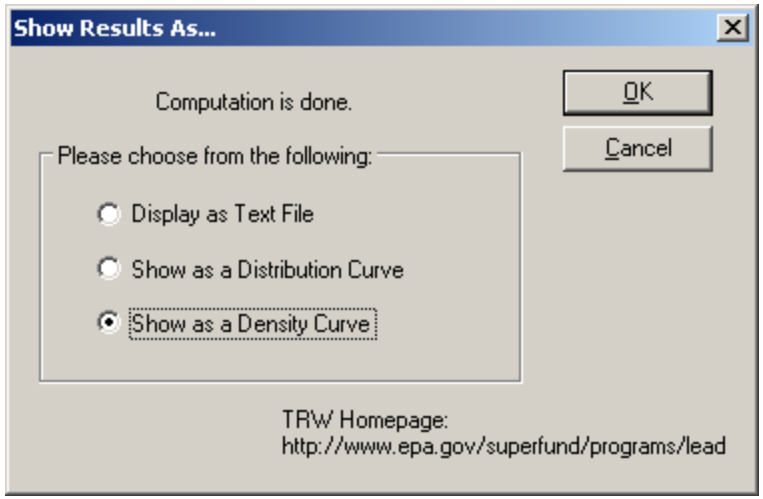


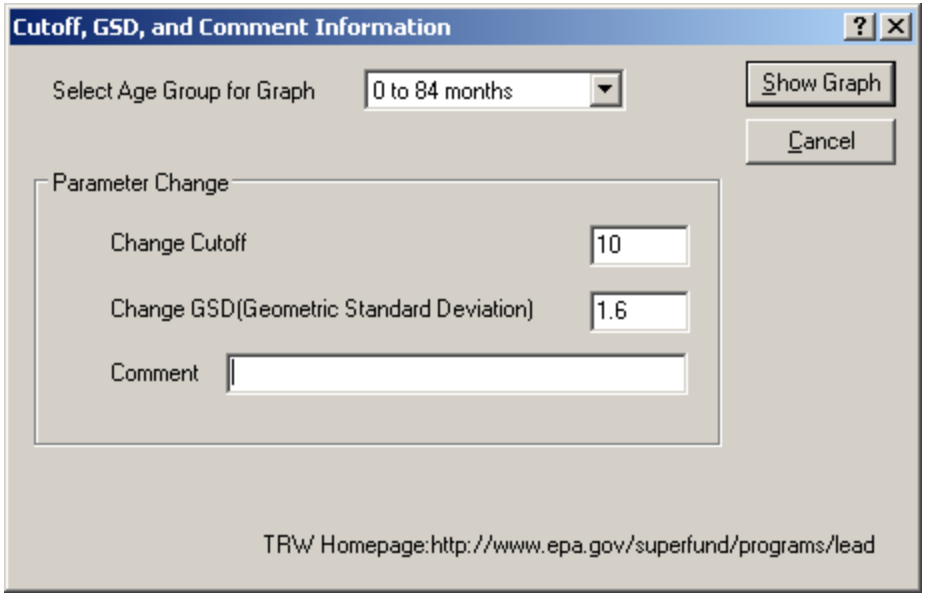
Maternal Exposure Input



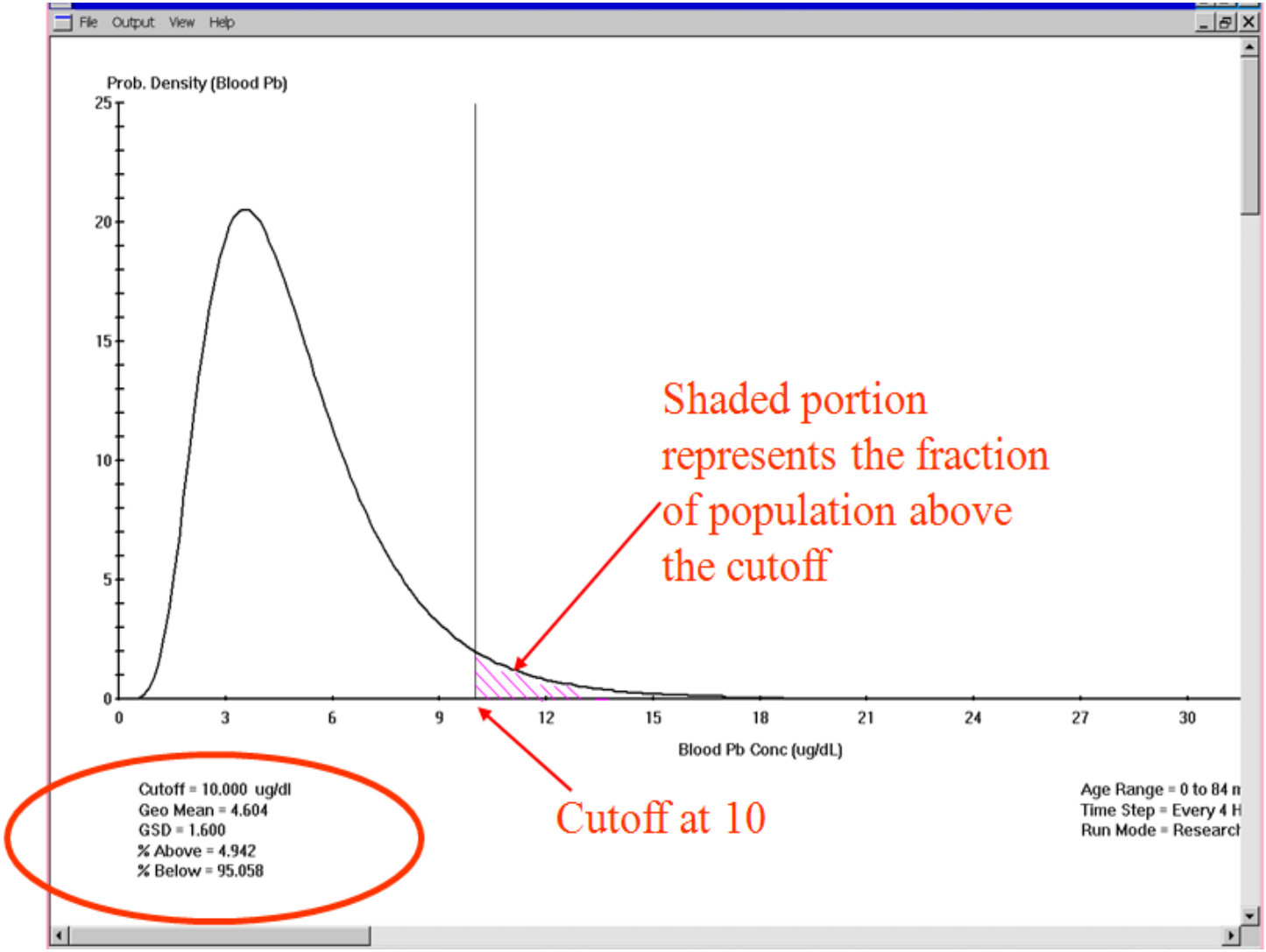
Run Risk Calculation (forward equation)



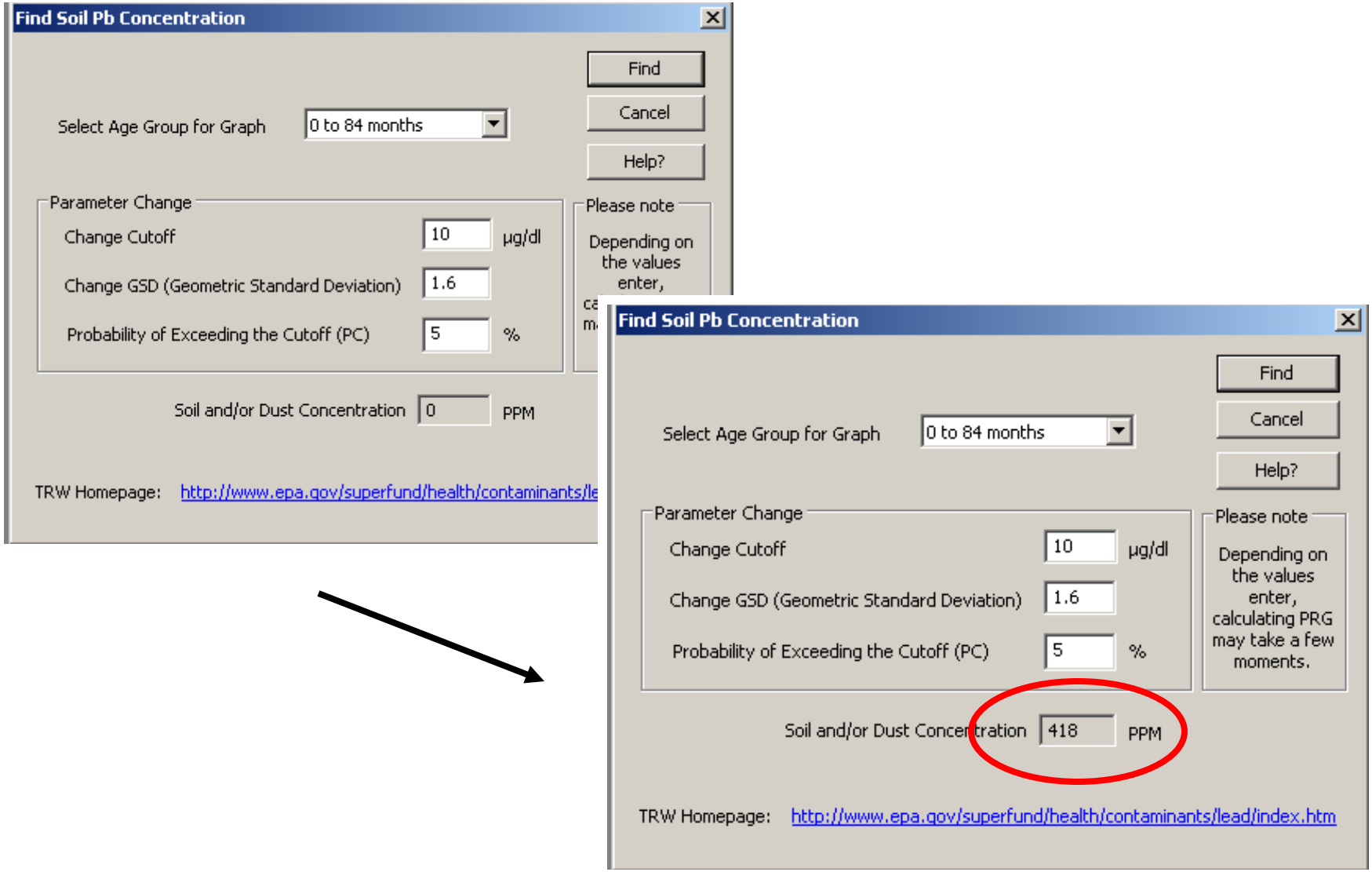




Output from the IEUBK Model



Run PRG Calculation (backward equation)



Sensitivity Analysis

- Predicted PbB and total lead uptake were most sensitive to the amount of soil/dust ingested per day.
- Predicted PbB and total lead uptake were moderately sensitive to the following (listed in decreasing relative sensitivity):
  - absorption fraction for soil dust and diet,
  - soil lead concentration,
  - indoor dust lead concentration,
  - dietary lead concentration,
  - contribution of soil lead to indoor dust lead, and
  - half-saturation absorbable intake (based on output-input ratio).
- The predicted probability of exceeding a specified level of concerns is very sensitive to changes in the GSD.

IEUBK Strengths and Limitations

- Strengths:
  - Integrates multimedia exposure and relates it to a well characterized biomarker of effect
  - Risk predictions and PRG over a range of exposure scenarios
  - Inputs tailored to support Superfund site risk assessment
  - Risk information complementary to a public health (PbB) study or when no public health (PbB) study is available
- Limitations:
  - Cannot assess short-term, periodic or acute exposures (exposures must be for at least 1 day per week for 90 consecutive days)
  - Cannot assess pica exposures
  - Cannot assess dust exposures using loading data
  - Cannot assess age groups >7 years

EPA Adult Methodology (ALM)

- Adopted and modified from Bowers et al. (1994)
- Uses a simplified biokinetic slope factor (BKSF)
- Slope relates change in PbB (µg/dL) per µg/day Pb absorbed
- Exposure and other variables differ from IEUBK (IR, bioavailability, etc.)

ALM Spreadsheet (Risk Calculation)

Calculations of Blood Lead Concentrations (PbBs)
U.S. EPA Technical Review Workgroup for Lead, Adult Lead Committee
Version date 6/21/09

Variable	Description of Variable	Units	GSDi and PbBo from Analysis of NHANES 1999-2004	GSDi and PbBo from Analysis of NHANES III (Phases 1&2)
PbS	Soil lead concentration	ug/g or ppm	2240	1235
$R_{fetal/maternal}$	Fetal/maternal PbB ratio	--	0.9	0.9
BKSF	Biokinetic Slope Factor	ug/dL per ug/day	0.4	0.4
GSD_i	Geometric standard deviation PbB	--	1.8	2.1
PbB_0	Baseline PbB	ug/dL	1.0	1.5
IR_S	Soil ingestion rate (including soil-derived indoor dust)	g/day	0.050	0.050
IR_{S+D}	Total ingestion rate of outdoor soil and indoor dust	g/day	--	--
W_S	Weighting factor; fraction of IR_{S+D} ingested as outdoor soil	--	--	--
K_{SD}	Mass fraction of soil in dust	--	--	--
$AF_{S,D}$	Absorption fraction (same for soil and dust)	--	0.12	0.12
$EF_{S,D}$	Exposure frequency (same for soil and dust)	days/yr	219	219
$AT_{S,D}$	Averaging time (same for soil and dust)	days/yr	365	365
PbB_{adult}	**PbB of adult worker, geometric mean**	**ug/dL**	**4.2**	**3.3**
$PbB_{fetal,0.95}$	95th percentile PbB among fetuses of adult workers	ug/dL	10.0	10.0
PbB_t	Target PbB level of concern (e.g., 10 ug/dL)	ug/dL	10.0	10.0
$P(PbB_{fetal} > PbB_t)$	**Probability that fetal PbB > PbB_t, assuming lognormal distribution**	**%**	**5.0%**	**5.0%**

Recommended PbB_0 and GDS_i Input

Calculations of Preliminary Remediation Goals (PRGs)
U.S. EPA Technical Review Workgroup for Lead, Adult Lead Committee
Version date 6/21/09 EDIT RED CELLS

Variable	Description of Variable	Units	GSDi and PbBo from Analysis of NHANES 1999-2004	GSDi and PbBo from Analysis of NHANES III (Phases 1&2)
$PbB_{fetal,\ 0.95}$	95th percentile PbB in fetus	ug/dL	10	10 ←
$R_{fetal/maternal}$	Fetal/maternal PbB ratio	--	0.9	0.9
BKSF	Biokinetic Slope Factor	ug/dL per ug/day	0.4	0.4
GSD_i	Geometric standard deviation PbB	--	1.8	2.1 ←
PbB_0	Baseline PbB	ug/dL	1.0	1.5 ←
IR_S	Soil ingestion rate (including soil-derived indoor dust)	g/day	0.050	0.050
$AF_{S,D}$	Absorption fraction (same for soil and dust)	--	0.12	0.12
$EF_{S,D}$	Exposure frequency (same for soil and dust)	days/yr	219	219
$AT_{S,D}$	Averaging time (same for soil and dust)	days/yr	365	365
PRG		ppm	2,240	1,235

Guidance for the IEUBK and ALM

- Model documentation (user's guides and validation information)
- Short Sheets
  - MSD
  - Ingestion Rate
  - Sieving
  - Sampling Guidance
  - Small Arms Firing Range
  - Exposure Point Concentration
  - Residential Dust Guidance
- Residential Sites Handbook
- TRW Bioavailability Guidance
- Frequently Asked Questions (FAQs)

TRW Lead Committee Web Site: www.epa.gov/superfund/lead

Soil Lead Bioavailability Guidance

Guidance for Evaluating the Oral Bioavailability of Metals in Soils for Use in Human Health Risk Assessment

United States
Environmental
Protection Agency

OSWER 9285.7-80

Guidance for Evaluating the Oral Bioavailability of Metals in Soils for Use in Human Health Risk Assessment

EPA

OSWER 9285.7-77
May 2007

ESTIMATION OF RELATIVE BIOAVAILABILITY OF LEAD IN SOIL AND SOIL-LIKE MATERIALS USING *IN VIVO* AND *IN VITRO* METHODS

Assessing Risk Example Exposure Scenarios

1. Site exposure to lead for a residential community where single (arithmetic mean) media concentrations is available
   - Risk: IEUBK single run mode
   - PRG: IEUBK find media concentration

2. Residential exposure to lead in soil with individual residence media concentrations
   - Risk: IEUBK batch mode run
   - PRG: IEUBK find media concentration

3. Exposure to lead contaminated soil on an industrial property
   - Risk: ALM
   - PRG: ALM

4. Adolescent recreational exposure to contaminated soil
   - Risk: ALM
   - PRG: ALM

Case Studies

1. IEUBK: Single run with 500 ppm soil and default (old) dietary data. Risk calculation.

2. IEUBK: Single run with 500 ppm soil and new dietary data (attached). Risk calculation.

3. IEUBK: PRG calculation using new dietary data and modified drinking water value. Also saving and reloading a data file and reset all parameters.

4. IEUBK: Multiple runs for soil range using new dietary data and modified drinking water value. Plot of risk calculations.

5. IEUBK: Find media concentration for soil without and with new dietary data and interpretation of GM PbB output.

6. IEUBK: Creating a batch mode input file from a spreadsheet file (attached).

7. IEUBK: Running a batch mode to calculate risk.

8. ALM: Example data entry for non-residential scenario. Calculation of risk and PRG.

Case Studies

ALM example scenario: non residential exposure scenario for a soil-intensive contact scenario.

What is PRG?

Use PbB_0 & GSD_i from recent NHANES and IRs of 100 mg/day

PRG = Approx 620 ppm

Case Studies

Is the following health protective?
Residential soil PRG is 600 ppm for future use. PbA = 0.05 µg/m³, PbW = 1 ppb, Soil bioavailability = 21%.

Enter media data and use new dietary values

Use find media concentration

Yes, PRG is <5% NTE 10 µg/dL

Case Studies

Is the following health protective?
PRG of 2500 ppm for a fire monitoring station occupied by adults 7 days per week for 4 months (16 weeks) of the year.

Use ALM with EF = 112 days/year

IRs=50 mg/day

No, PRG is >5% NTE 10 µg/dL

Case Studies

Assuming that 2500 ppm is the selected soil lead concentration for those fire monitoring stations (occupied by adults), what is the maximum duration that they can be occupied (assuming continuous exposure)?

IRs = 50 mg/day

Reduce EF to achieve is <5% NTE 10 µg/dL

Approximately 15 weeks

Wrap up

EPA provides risk tools and guidance to assess lead exposure at hazardous waste sites. The TRW Lead Committee is available to support users when questions or when novel applications arise

- Evaluate & develop models and other risk tools
- Provide technical support for the development and implementation of EPA guidance on lead
- Review application of risk assessment tools
- Provide technical assistance to end users for use of non-standard (site-specific) values

TRW Lead Committee Members are EPA staff from Regions, Headquarters, and Labs

TRW Lead Committee

Co-Chairs

- Mary Ballew (Region 1)
- Mike Beringer (Region 7)
- Jim Konz (OSRTI HQ)

TRW Web page:

www.epa.gov/superfund/lead

Contact the TRW hotline

- Send an e-mail to pbhelp@epa.gov
- Call the toll-free TRW hotline at 1-866-282-8622