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Users Guide for the All Ages Lead Model (AALM) version 3.0 – Excel User Interface and Fortran Model Executable

Office of Research and Development
Center for Public Health and Environmental Assessment

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QUALITY ASSURANCE

This report was prepared by EPA with assistance from SRC, Inc. and ICF. EPA has an agency-wide quality assurance (QA) program that is outlined in the EPA Environmental Information Quality Procedure, CIO 2105-P-01.3, and follows specification outlined in EPA Environmental Information Policy CIO 2105.3. Quality assurance for this research is documented in a Quality Assurance Project Plan (QAPP), entitled All Ages Lead Model (AALM) Development, EPA QAPP ID: L-HEEAD-0033877-QP-1-0, August 10, 2023.

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I. A Brief History of the Leggett Model and an Introduction to the All Ages Lead Model

The Leggett biokinetic model (Leggett RW. 1993. Environ Health Perspect. 101(7):598-616) simulates the intake, exchange, and excretion of lead in humans from birth through adulthood using a series of body compartments with mass exchange between them. When the model was originally coded, it synthesized a wide variety of sometimes disparate sources of information related to the biokinetics of lead in humans. The Leggett model was informed by:

- Lead tracer studies of injection, ingestion, and inhalation in healthy adult humans,
- Measurements of lead in environmentally exposed men, women, and children at autopsy,
- Lead mass-balance studies on adult humans,
- Bioassay and autopsy measurements on occupationally exposed subjects,
- Lead studies in laboratory animals at different life stages
- Experimental, occupational, environmental, and medical data on the biokinetics of elements that serve as physiological analogues of lead, and
- Basic physiological information on the human body.

As such, the Leggett model structure is a minimal system of body compartments and mass exchange terms needed to synthesize all these data sets. The modular form of the model allows investigators to modify specific parameter values to address special problems in lead toxicology or to incorporate new information related to lead biokinetics. The original Leggett model included:

- **Input file:** an ASCII input file containing information describing the lead exposure scenario and the age-dependent lead transfer rates for each compartment, and
- **Model code:** an executable FORTRAN program which reads the input file, performs the prescribed calculations, and writes the outputs to an ASCII file.

This approach was designed to provide maximum flexibility and versatility rather than to be user-friendly.

1. The All Ages Lead Model and an Exposure Interface

The original Leggett model has, on several occasions, been translated onto other software platforms or into other programming languages. One notable example is the inclusion of the Leggett model in the Environmental Protection Agency's (EPA) All Ages Lead Model (AALM). In collaboration with EPA, SRC, Inc. recoded the model in the acslX programming language. Unlike FORTRAN, this programming language comes with off-the-shelf differential equation solvers supporting variable time steps, along with other functions (such as "TABLE") that easily allow input parameters to vary in time during the simulation.

SRC also added an Excel user interface that expanded the Leggett model to incorporate exposure estimation. The original Leggett model accepts inputs of inhalation and total oral intake in units of μg lead/day. The Excel user interface allows the user to enter time-varying air concentrations (μg lead/m^3 air); soil and dust concentrations (μg lead/g dust); water concentrations (μg lead/L water); inhalation rates (m^3 air/day); soil and dust ingestion rates (g dust/day); water ingestion rates (L water/day); and food and "other" intake rates (μg

lead/day).The user can also specify relative absorption factors for air, soil, dust, water, food, and "other" sources. The Excel interface writes input files for the acslX code and the acslX code incorporates the different media concentrations, media intake rates, and relative absorption factors to estimate total inhalation and total ingestion uptakes at each model time step. This feature greatly improved the versality of the model, and made it more user-friendly, since users could record and run a wide variety of exposure scenarios in a transparent way.

As part of coding and testing the AALM, EPA and SRC simulated a number of datasets, including adult and childhood datasets used during the original Leggett code calibration and validation as well as additional datasets identified during a literature search. Based on these tests, parameters were adjusted to ensure the best overall fit against all datasets. A full report documenting the datasets and parameter changes was provided to EPA and serves as a technical support document for this user guide.

2. Adapting the Exposure Interface for AALM

As noted above, acslX provides a number of benefits compared with a FORTRAN executable, and the AALM Excel interface improved versatility and made the model more user-friendly for estimating exposure profiles. However, acslX is proprietary software, limiting the availability to some stakeholders. Then, in 2015, makers of the acslX simulation language announced the language would be "sunsetted", meaning no new licenses would be sold. The EPA Office of Pollution Prevention and Toxics was already using the FORTRAN version as part of the Lead Renovation, Repair, and Painting analyses for public and commercial buildings; because of the number of simulations needed for this Monte Carlo analysis, acslX was not practical and EPA required the speed and efficiency inherent in the FORTRAN language to complete the analysis. As part of that project, EPA OPPT worked with EPA ORD to evaluate the differences between the AALM and the Leggett FORTRAN code and to harmonize the inputs. They re-evaluated the parameters against all datasets and also demonstrated that the acslX and FORTRAN versions, when configured with the same growth algorithms and input parameters, returned results to within +/- 5% of each other for a range of exposure scenarios in both children and adults. The final product included an acslX version of the All Ages Lead Model (AALM.CSL) and a harmonized FORTAN version (AALM.FOR), which was referred to as the All Ages Lead Model (AALM) version 2.0.

To help allow other researchers and regulators to use the FORTRAN version, particularly in the face of the acslX "sunsetting", EPA and ICF have created an Excel user interface. The goals of this user interface are:

1) To maintain the format and functionality of the AALM.CSL Excel interface, particularly with respect to exposure estimation,
2) To adapt the tool to create the input files for the AALM.FOR and to call the FORTRAN executable directly to allow the user to run the Leggett AALM algorithms without acslX, and
3) To provide a user's guide to help users to understand how to setup and run the simulations in this version.

3. User Interface and FORTRAN Updates

The AALM version 2.0 and associated technical documents were reviewed by an EPA Science Advisory Board (SAB). The SAB review of the AALM version 2.0 and associated documentation consisted of a two-day public meeting in October 17-18, 2019 and teleconferences on April 23 and June 23, 2020. The final August 2020 review report is posted on the SAB website: https://sab.epa.gov/ords/sab/f?p=100:0:8979490196190:APPLICATION_PROCESS=REPORT_DOC:::REPORT_ID:1086). The SAB provided Tier 1 (recommended revisions), Tier 2 (suggestions), and Tier 3 (future considerations). The AALM version 3.0 incorporates revisions in responses to all SAB Tier 1 and most Tier 2 comments, as well as some Tier 3 comments.

Beginning in April 2021 in response to SAB feedback, the user interface was updated to be more intuitive to use. Many of these updates included reorganization of tabs and information, increased use of macros and automation to guide the user through the tool, and introduction of processes to reduce how much the user needs to do to interact with the data. Further, the interface was updated to decrease visual clutter without content loss and to guide the user through providing acceptable, accurate data for the model, housed in FORTRAN.

The FORTRAN code was updated in several ways. First, a revised lung model was incorporated. Second, the contributions from the different inhalation and ingestion sources can now be tracked. This includes differing absorption and/or lung clearance rates by source. Third, explicit mass balance calculations have been added, both for total Pb and by source. Fourth, the code's processing time has been decreased through the introduction of several process efficiencies, including extensive vector and array processing. This also allows for more timesteps to be simulated. Details of these changes can be found in the AALM Technical manual. The AALM version 3.0 has been tested exclusively on computers with a Microsoft Windows operating systems. The AALM Fortran code and Excel Interface have not been used or tested on other systems (i.e., Apple, Linux) at this time.

II. Overview of the Excel User Interface and FORTRAN Model

The Excel user interface to AALM.FOR model consists of the following pieces:

- The Excel GUI:
  - Simulation control (Figure 1, Tables 1 and 2)
  - Growth Parameters (Growth Params; Table 3)
  - Time-dependent Physiological Parameters (Time Dep Phys Params; Table 4)
  - Time-independent Physiological Parameters (Time Ind Phys Params; Table 5)
  - Media (Figure 2, Table 6)
  - Lung (Figure 3, Table 7)
  - Fortran input file
  - Solution type (Figures 4 and 6, Table 8)
  - Transitions between Exposure Times (Table 9)
  - Binding to RBC (Table 10)

For quick start examples that can be loaded into the Excel GUI, see the Appendix.

    - Explore Data (Figures 6 and 7)
    - Summary
    - Output (Table 11)
    - Daily (Table 12)
- The Leggett executables:
    - These are 32- or 64-bit executables that are called by the Excel file to run the model. It is recommended that the default 64-bit executable is used.
- LeggettInput.txt:
    - This file is written with each simulation's FORTRAN inputs. It is a static reference for the file to retrieve these inputs.
- Supplementary files:
    - The user's guide (this document)
    - AALM Fortran code (AALM_20240209.f90): The Leggett model text file that was compiled to create the Leggett executable. It is not needed to run the model but may be needed by some researchers who wish to make future changes to the model algorithms.
    - Technical Support Document

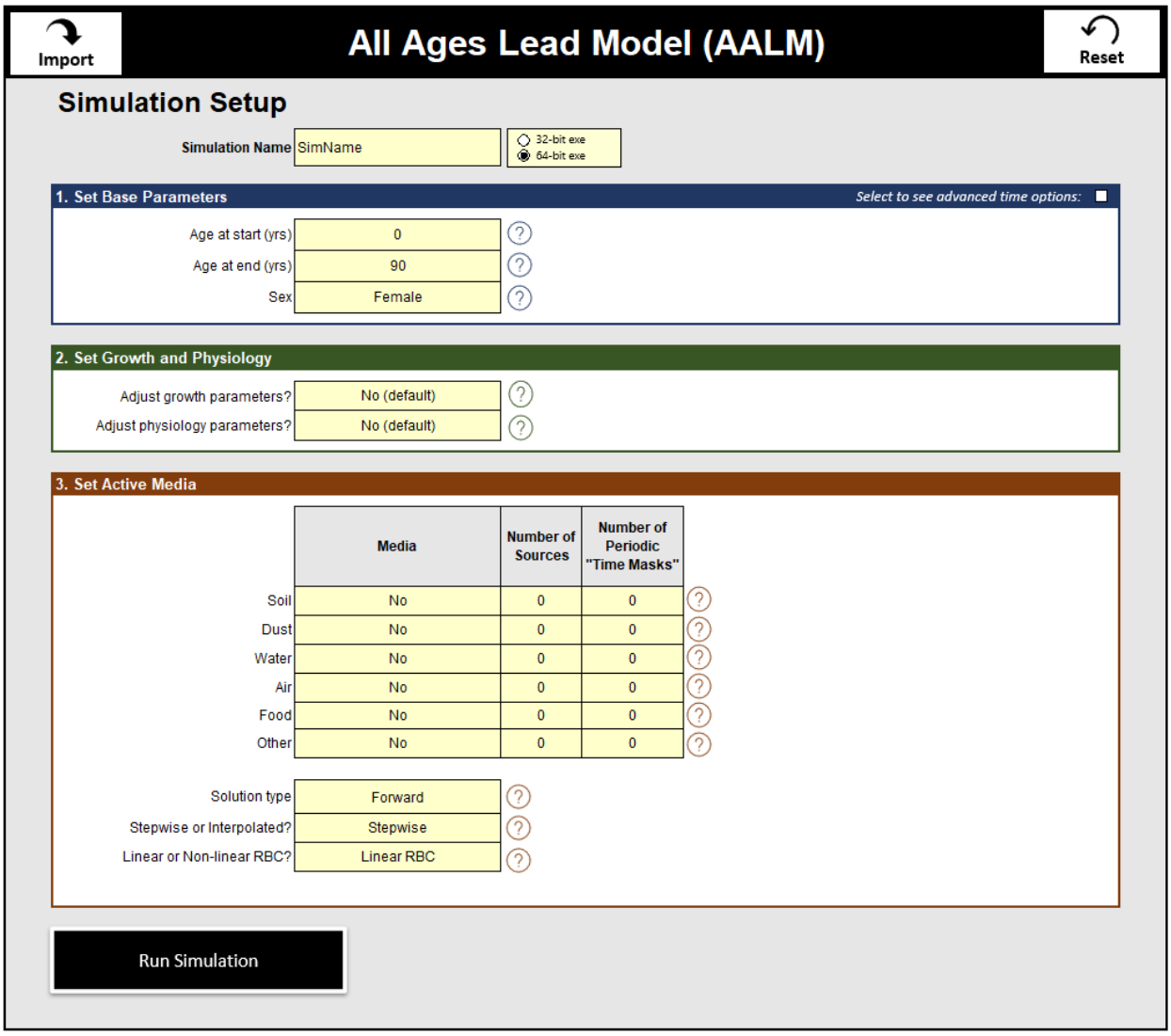


Figure 1 – Screenshot of Simulation Setup Screen

To run the model users must configure the Simulation Control tab variables. Based on which fields are indicated for adjustment, other tabs will appear for the user to navigate to in order to update the parameters under each heading. Follow the prompts until all fields are updated as desired. When ready, select “Run Simulation” at the bottom of the Simulation Control tab. This action will then:

1. Create the FORTRAN input file, which can be reviewed by the user,
2. Run the FORTRAN executable (32 or 64 bit as selected by the user), and
3. Import the results of the simulation back into Excel for interpretation and visualization.

Please note: to create the 32 and 64-bit executables, ICF used the proprietary Intel FORTRAN compiler. As such, the compiler itself is not provided as part of the package. This compiler version was needed to get the model to properly compile. ICF also attempted to compile the model using free FORTRAN compilers, including the GNU compiler. However, the code returned errors in the compilation during our testing.

III. How to Setup and Run the AALM version 3.0 Using the Excel Interface

1. This section of the User's Guide provides a brief description of how to configure the user interface (GUI) and run the FORTRAN model. Unzip the Model File Package

To begin to use the model, unzip the zip file and place the contents in any folder on your C:\ drive. You can save different Excel files for each of your different simulations, and these can be in different folders on your computer.

Each time you run AALM, the following files must be in the same folder:

1. AALM_32.exe and AALM_64.exe (the model executables)
2. AALM.xlsm

Next you can open the Excel GUI.

For some versions of Excel, the first time (or every time, depending on security settings) you use the tool, you may need to enable the macros within the file when you open it as well. When you open the tool, a yellow bar will appear at the top with a button "Enable Content?". Click the button to enable the macros. If this button does not appear, you can also do the following:

1. Click the Microsoft Office Button, and then click Excel Options.
2. Click Trust Center, click Trust Center Settings, and then click Macro Settings.
3. Click the options to enable the macros.

While not required, it is generally advisable to close other Excel files when running the AALM. Further, users should not have more than one instance of AALM open at a time. Users may compare the outputs of multiple simulations within the same instance of the tool, which should eliminate the need to have multiple workbooks open. As discussed in Section 3 of this document, an Excel csv file (Out_[*simulation name*].csv) contains the output of a simulation within a folder (*simulation name*) created by the AALM.

2. Complete the Simulation Control Tab and Modify Model Parameters as Needed

To run a simulation, begin with the Simulation Control tab. This tab will walk through each of the other tabs that should be changed based on which parameters are indicated as needing adjustment. All other parameters will remain hidden.

Yellow cells indicate values that can be adjusted by the user if desired. Other cells should not be edited.

Parameters which the user may change are in yellow throughout the GUI. These fields are also indicated in text.

Additionally, throughout the GUI, selecting "Reset" will set all parameters back to default values while

Reset buttons fill parameter values with default values while Clear buttons erase the parameter data.

selecting “Clear” will erase all the parameter data. Reseting is particularly useful for growth curves (Table 3), Time dependent parameters (Table 4), Time independent parameters (Table 5), and Solve for Allowable Concentration (Figure 6, Table 8).

Further, the “Import” buttons on the Simulation Control and Explore Data tabs can be used to import inputs and results of previously run scenarios, respectively.

Simulation Control primarily contains the Leggett input parameters that control the following:

The import buttons on the Simulation Control and Explore Data tabs allow users to load previously run inputs back into the GUI or analyze previously run data.

1. Simulation Name: The name optionally given by user that is associated with the current simulation. This will correspond to the input and output files generated.
2. Advanced Time Options:
    a. How often AALM calculates lead kinetics each day (timesteps per day).
    b. How often the calculations should be written to the output file (that is, how many time steps there are between each output).
3. Base Parameters:
    a. The age of the modeled individual at the beginning of the simulation, i.e., 0 years. Users do not have access to change this parameter.
    b. The age of the modeled individual at the end of the simulation.
    c. The sex of the modeled individual (for estimation of growth parameters).
4. Growth Parameters
5. Physiological Parameters
6. Media Parameters
7. Lung Parameters
8. Solution type, either forward or to solve for an allowable level.
9. Stepwise or interpolated transitions between exposures.
10. RBC binding (linear or non-linear allowing for saturation).

Simulation Name: The name of the output text files

The user can type in the name of the folder and files generated when a simulation is run. This name will be used for all simulation specific files tabs created. If the user does not create a unique name, Excel will overwrite the previous folder and files. It will warn the user before this happens so the user can revise the simulation name before the program overwrites previous outputs.

This field does not allow for special characters except for an underscore “_”. Users can use all letters and numbers in addition to this character. Spaces are not allowed as they are not interpreted correctly by FORTRAN. Additionally, this field does not allow for names longer than 20 characters. In the event that a simulation name that does not fit these parameters (special characters used or the length requirement is not met) is provided to the interface, users are reminded of these requirements with a descriptive error message.

Advanced Time Options

Unless the user selects “Select to see advanced time options” and alters the two parameters in that section, they will be set to the default values as noted in the table below and in the appendix Default Values.

If deviating from the default parameters, the user must decide what time steps to use and how often to export the model results. This will impact output specificity, which could impact analysis of the results. The interplay between these variables is explained in this section. The calculation is straightforward and uses a single time step for the full simulation.

Timesteps per day (steps_per_day)

Determine the number of timesteps to be used per day. In general, time steps should be shorter than the fastest biological process or the fastest rate of change in exposure. If exposure is varying quickly (e.g., due to an acute exposure scenario), the time step needs to be short and overall runtime becomes longer. The default for this parameter of 100 timesteps per day, which is one timestep every 14.4 minutes, is recommended.

PLEASE NOTE

Timesteps per day must not exceed 12 when using the 32-bit executable or 20 when using the 64-bit executable.

For use with the 32-bit executable, timesteps per day cannot exceed 12 (based on processing needs). For the 64-bit executable, timesteps per day have not been found to be limited in the same way, though greater than ~500 timesteps per day significantly slow down the processing time of the model.

Table 1 – Timesteps between outputs (outwrite): How Often the Outputs should be Written to the Output File

Parameter Prompt in User Interface	Name in FORTRAN Input File	Location	Default Value	Parameter Limits
Timesteps per day	steps_per_day	Simulation Control	100	Cannot exceed 12 when using the 32 bit executable.
Timesteps between outputs	outwrite	Simulation Control	100	Must be positive

The user may decide how often the model should write the output variables to the output file. This variable (outwrite) uses the number of time steps as its unit. If the time step is 0.5 days and the outwrite is 730, the outputs will only be written once every year (0.5*730). This helps to control the file size of the output file so that not every time step is saved.

The default for this parameter is 100, meaning one output will be written for every 100 timesteps, which if using the default value in timesteps per day (100) means one output is written per day.

Base Parameters

Age at start and Age at end (age_range)
Because lead accumulates in the body, it is generally necessary to model the entire lifetime exposure of an individual starting at birth. The Age at start parameter is 0 years (birth) and not accessible to users. The default end of the simulation is age 90, but this can be any value greater than the start age value, up to 100 years when using the 64-bit executable.

PLEASE NOTE
Age at end cannot exceed 8 years when using the 32-bit executable.

Sex: The sex of the modeled individual (for estimation of growth parameters)
Next the user specifies whether the modeled individual is a male or a female. The AALM uses growth algorithms that vary for males and females. Thus, the choice of sex does not control any biokinetics in the model, but it does affect the predicted concentrations by altering the volume of the modeled tissues/compartments over which the lead mass is distributed.

Table 2 – Base parameters

Parameter Prompt in User Interface	Name in FORTRAN Input File	Location	Default Value	Parameter Limits
Age at start (yrs)	age_range	Simulation Control	0	Set to zero, not adjustable by users
Age at end (yrs)	age_range	Simulation Control	90	Should not exceed 90 and must be greater than “Age at start”
Sex	sex	Simulation Control	Female	Binary; Female or Male

Growth Parameters

The Growth Parameter tab contains the different growth parameters used by the model such as weight, logistic constants, and the ratio of lean body mass to body mass. These parameters are used in the simulation to calculate the body weight at each age, which informs lead compartmentalization. The weight is calculated and graphed for easy visualization as:

$$BW = W_{birth} + \frac{age * W_{child}}{half + age} + \frac{W_{adult}}{1 + \kappa * e^{-\lambda * W_{adult} * age}}$$

After configuring the growth parameters, select “Done” to return to the Simulation Control tab and continue configuring the simulation.

Table 3 – Growth Curve Parameters

Parameter Prompt in User Interface	Name in FORTRAN Input File	Location	Default Value		Parameter Limits
sex	Sex	Growth Params	Female	Male	Binary; Female or Male
wbirth	Wbirth	Growth Params	3.3	3.5	Must be positive
wchild	wchild	Growth Params	22	23	Must be positive
half	half	Growth Params	3	3	Must be positive
wadult	wadult	Growth Params	34	50	Must be positive
kappa	po	Growth Params	600	600	Must be positive
lambda	lambda	Growth Params	0.017	0.0095	Must be greater than 0
LB	LB	Growth Params	0.85	0.88	Must be between 0 and 1

Physiological Parameters

The physiological parameters are broken out into time-dependent and time-independent parameters.

Time-dependent Parameters

It is highly recommended that no changes be made to any time-dependent parameter other than the gastrointestinal absorption fraction (F1). Altering any rate constants (unit: d^{-1}) or deposition fractions to compartments (unit: f) will alter mass balance. It is also recommended that number of ages for time-dependent parameters be left at the value of 11. Altering the number of ages could affect model mass balance.

Specified ages in this tab should be:

1. The minimum age of the simulation
2. Each age at which a parameter will *change* value

Before altering or filling in the time-dependent parameters, update the number of ages that should be displayed. This number should be each time the value of the parameters will change throughout the simulation time. Keep in mind this is across parameters, so the number should be high enough to represent all the parameter changes needed.

There are no limitations on the number of ages that must or must not appear other than requiring at least 1 age, so the parameters are represented in the inputs of the FORTRAN model. Additionally, the first age should be the minimum age being simulated.

For each age provided, the parameter value will be used until the next value is given. This age range can vary based on user preferences.

Table 4 – Time Dependent Model Parameters

Parameter Prompt in User Interface	Name in FORTRAN Input File	Location	Default Value	Parameter Limits
F1	f1	Time Dep Phys Params	Varied	Must be between 0 and 1
AMTBLD	amtbld	Time Dep Phys Params	Varied	Must be positive
FLONG	flong	Time Dep Phys Params	0.6	Must be between 0 and 1
GSCAL	gscal	Time Dep Phys Params	Varied	No longer used.
RBLAD	rblad	Time Dep Phys Params	Varied	Must be positive
RBRAN	rbran	Time Dep Phys Params	0.00095	Must be positive
RCORT	rcort	Time Dep Phys Params	Varied	Must be positive
RCS2B	rcs2b	Time Dep Phys Params	Varied	Must be positive
RCS2DF	rcs2df	Time Dep Phys Params	Varied	Must be positive
RDIFF	rdiff	Time Dep Phys Params	0.023105	Must be positive
RKDN2	rkdn2	Time Dep Phys Params	Varied	Must be positive
RLVR2	rlvr2	Time Dep Phys Params	Varied	Must be positive

Parameter Prompt in User Interface	Name in FORTRAN Input File	Location	Default Value	Parameter Limits
RRBC	rrbc	Time Dep Phys Params	Varied	Must be positive
RTRAB	rtrab	Time Dep Phys Params	Varied	Must be positive
RTS2B	rts2b	Time Dep Phys Params	Varied	Must be positive
RTS2DF	rts2df	Time Dep Phys Params	Varied	Must be positive
TBONE	tbone	Time Dep Phys Params	Varied	Must be between 0 and 1
TFRAC	tfrac	Time Dep Phys Params	Varied	Must be between 0 and 1
TOBRAN	tobran	Time Dep Phys Params	Varied	Must be between 0 and 1
TOSOF0	tosof0	Time Dep Phys Params	Varied	Must be between 0 and 1
TOSOF1	tosof1	Time Dep Phys Params	Varied	Must be between 0 and 1
TOSOF2	tosof2	Time Dep Phys Params	0.001	Must be between 0 and 1

Time-independent Parameters

Time independent parameters remain constant throughout the simulation or serve as a starting point for further calculation, so necessarily require less user setup than the time-dependent parameters.

These parameters are summarized below and summarized in more detail in the Appendix as well as in the GUI.

PLEASE NOTE

It is highly recommended that no changes be made to any time-independent parameter other than the maternal blood lead concentration (BLDMOT).

Table 5 – Time Independent Model Parameters

Parameter Prompt in User Interface	Name in FORTRAN Input File	Location	Default Value	Parameter Limits
ASHWT	ashwt	Time Ind Phys Params	2800	Not currently used in the Leggett code.
BLDMOT	bldmot	Time Ind Phys Params	0.62	Must be positive
BONIN	bonin	Time Ind Phys Params	0.32	Must be between 0 and 1
BRANIN	branin	Time Ind Phys Params	0.045	Must be between 0 and 1
BRATIO	bratio	Time Ind Phys Params	0.85	Must be between 0 and 1
CRTWT	crtwt	Time Ind Phys Params	4000	Must be positive
H1TOBL	h1tobl	Time Ind Phys Params	0.45	Must be between 0 and 1
H1TOH2	h1toh2	Time Ind Phys Params	0.1	Must be between 0 and 1
H1TOSI	h1tosi	Time Ind Phys Params	0.45	Must be between 0 and 1
HCTA	hcta	Time Ind Phys Params	0.41 (female) 0.46 (male)	Must be between 0 and 1
HCTB	hctb	Time Ind Phys Params	0.52	Must be between 0 and 1
HEPIN	hepin	Time Ind Phys Params	0.055	Must be between 0 and 1

Parameter Prompt in User Interface	Name in FORTRAN Input File	Location	Default Value	Parameter Limits
IFETAL	ifetal	Time Ind Phys Params	1	Binary, 0 or 1
KWT	kwt	Time Ind Phys Params	310	Must be positive
PLSVOL	plsvol	Time Ind Phys Params	30	Must be positive
POWER	power	Time Ind Phys Params	1.5	Must be positive
RBCIN	rbcin	Time Ind Phys Params	0.07	Must be between 0 and 1
RBCNL	rbcnl	Time Ind Phys Params	20	Must be positive
RBCVOL	rbcvol	Time Ind Phys Params	22	Must be positive
RENIN	renin	Time Ind Phys Params	0.01	Must be between 0 and 1
RKDN1	rkdn1	Time Ind Phys Params	0.139	Must be positive
RLLI	rlli	Time Ind Phys Params	1	Must be positive
RLVR1	rlvr1	Time Ind Phys Params	0.0693	Must be positive
RPLAS	rplas	Time Ind Phys Params	2000	Must be positive
RPROT	rprot	Time Ind Phys Params	0.139	Must be positive
RSIC	rsic	Time Ind Phys Params	6	Must be positive
RSOF0	rsof0	Time Ind Phys Params	2.079	Must be positive
RSOF1	rsof1	Time Ind Phys Params	0.00693	Must be positive

Parameter Prompt in User Interface	Name in FORTRAN Input File	Location	Default Value	Parameter Limits
RSOF2	rsof2	Time Ind Phys Params	0.00038	Must be positive
RSTMC	rstmc	Time Ind Phys Params	24	Must be positive
RULI	ruli	Time Ind Phys Params	1.85	Must be positive
S2HAIR	s2hair	Time Ind Phys Params	0.4	Must be between 0 and 1
SATRAT	satrat	Time Ind Phys Params	350	Must be positive
SIZEVF	sizevf	Time Ind Phys Params	3	Must be between 0 and 1
SOFIN	sofin	Time Ind Phys Params	0.5	Must be between 0 and 1
TBONEL	tbonel	Time Ind Phys Params	0.08	Must be between 0 and 1
TEVF	tevf	Time Ind Phys Params	0.5	Must be between 0 and 1
TOFECE	tofece	Time Ind Phys Params	0.006	Must be between 0 and 1
TOKDN1	tokdn1	Time Ind Phys Params	0.025	Must be between 0 and 1
TOKDN2	tokdn2	Time Ind Phys Params	0.0004	Must be between 0 and 1
TOLVR1	tolvr1	Time Ind Phys Params	0.04	Must be between 0 and 1

Parameter Prompt in User Interface	Name in FORTRAN Input File	Location	Default Value	Parameter Limits
TOPROT	toprot	Time Ind Phys Params	0.0004	Must be between 0 and 1
TORBC	torbc	Time Ind Phys Params	0.25	Must be between 0 and 1
TOSWET	toswet	Time Ind Phys Params	0.0035	Must be between 0 and 1
TOURIN	tourin	Time Ind Phys Params	0	Must be between 0 and 1
TRBWT	trbwt	Time Ind Phys Params	3000	Must be positive
VBLC	vblc	Time Ind Phys Params	0.067	Must be positive
VKC	vkc	Time Ind Phys Params	0.0085	Must be positive
VLC	vlc	Time Ind Phys Params	0.025	Must be positive
VLUC	vluc	Time Ind Phys Params	0.015	Must be positive

Media Parameters

After defining the configuration of Media, select “Go to Media” to update the page with the defined selections.

PLEASE NOTE

Data other than that defined in the Simulation Control tab and appearing in the Media tab will **not** be included in the simulation inputs for FORTRAN.

Binary switches (Yes/No) to include or exclude a certain exposure media

These switches allow the user to easily include or exclude exposure from a given pathway (air, dust, water, food, soil, and other). Please be aware that parameters other than those defined on the simulation control tab will NOT be included in the simulation when inputs are defined for the FORTRAN files (e.g., if data was entered on the Media tab for Soil, but the Soil pathway is switched to “No” on Simulation Control tab before running simulation). Users must ensure Simulation Control is accurate.

Number of Sources

Sources can be used to model varied environments (or sources) of exposure. Each media is allowed up to three different sources of exposure.

Examples of sources could be school, work, home, playgrounds, etc. These exposures can then be turned on or off to mimic realistic exposure patterns using “masks” as outlined below.

The number of sources should be greater than zero if masks are to be used. However, if sources is set equal to zero, when users select “Go to Media” all options for sources (i.e., 3) and masks (i.e., 9) will appear.

After all sources are defined (i.e., active) and if no masks are applied, select “Go to Media” to configure the page.

Number of Periodic “Time Masks”

Time masks temporarily block or “turn off” the exposure from the given source from occurring during the desired time period.

Masks are used in simulations to temporarily “turn off” exposure from a specific source. This process temporarily turns off the source specified for the defined length of time. Below is an example of how masks could be used to assess high lead concentrations in drinking water at a weekend camp. In this example Source 1 is the camp exposure, which is “masked” (turned off, or blocked) 5 days of the week when the child is at home or school. As setup in the example, exposure is turned off on days 2, 3, 4, 5, and 6 (i.e., first day blocked is 2 and the last day blocked is 6). Hence, the camp exposure source is only active (i.e., turned on) during days 1 and 7. The days turned off by a mask are always within the same period (e.g., 7 days for a week). Hence the “first day blocked” must be less than or equal to the “last day blocked”. Applying the mask correctly in the below example requires that the first and last day blocked be consecutive days of the week (e.g., 1 and 2 or 6 and 7).

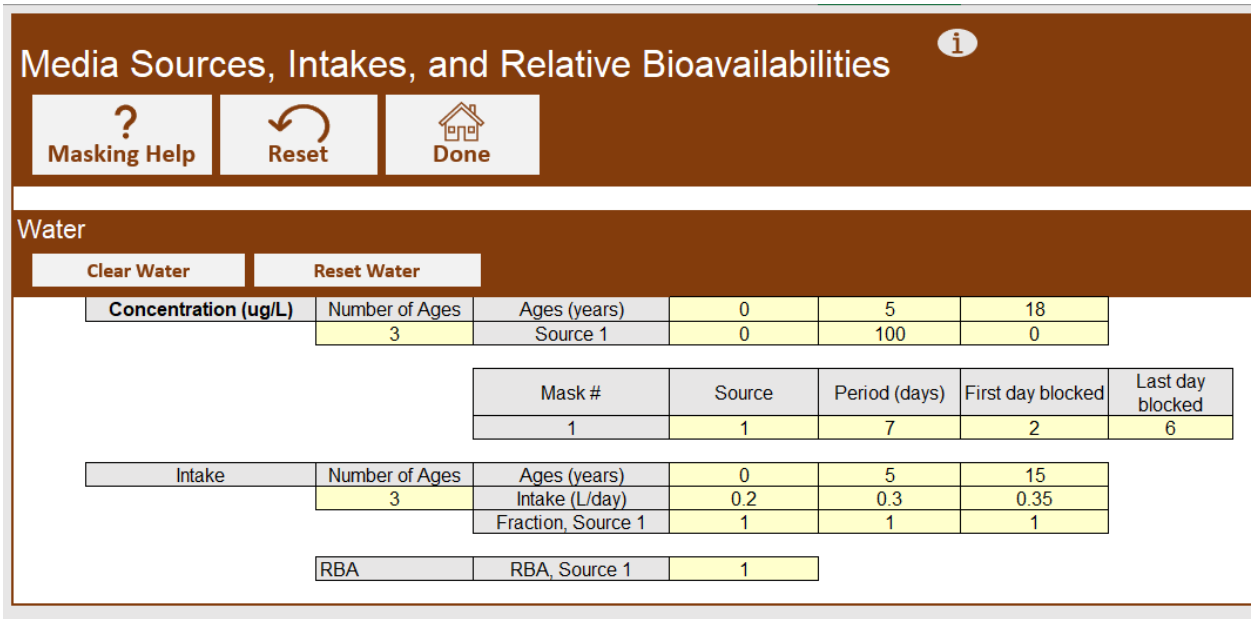


Figure 2 – Screenshot of Water setup in Media tab

Special use cases and additional examples of how to use these masks appropriately are provided in the Appendix in Mask Examples.

Users may choose masks for any of their 3 sources per media. This tool allows for up to 9 masks per media type. Each mask is specific to one source.

For each of the media defined by the user, the following parameters are provided to FORTRAN. Additionally, some parameters such as masks and concentrations are repeated as needed provided by user inputs.

Filling in Media

After defining the configuration of the Media tab in Simulation Control, define the number of ages needed for both concentration of lead in the media and intake. The Number of Ages is limited to 20. Specific ages in this tab should be the minimum age of 0 years and the age at which a parameter will change value.

PLEASE NOTE

For recommended media concentrations and intake rates as a function of age refer to Appendix C of the Technical Support Document (TSD) for the AALM v3.0. Users may also refer to the AALM Example Scenarios (Example 1 and 1a) in the Appendix of this User Guide for defaults related to the IEUBK model v2.0 for children.

The number of ages set by the user should depend on how often the concentration or intake changes by age. This number should be each time the value of the parameters will change throughout the simulation time. Keep in mind this is across sources, so the number should be high enough to represent all the changes needed. The first age should be the minimum age of the simulation followed by each age at which the concentration or intake will change. If only one concentration is used (e.g., for soil or water), that concentration only needs to be set for a single age starting of 0 years. The number of desired changes in media intake rates can differ from the number of changes in concentration.

Table 6 – Parameters used in Media Tab

Parameter Prompt in User Interface	Name in FORTRAN Input File	Location	Default Value	Parameter Limits
Number of Sources	sources	Simulation Control	0	Values allowed: 0-3
Concentration: Number of ages	conc_ages	Media	Varied	Maximum 100 ages can be defined
Concentration (by source and age)	concs#	Media	Varied, site-specific, refer to Appendix C of the TSD for the AALM v3.0 for recommendations	Must be positive

Parameter Prompt in User Interface	Name in FORTRAN Input File	Location	Default Value	Parameter Limits
Intake: Number of ages	intake_ages	Media	Varied	Must be positive
Intake	intake_amt	Media	Varied, refer to Appendix C of the TSD for the AALM v3.0 for recommendations	Must be positive
Fraction	frac#	Media	1	Must be between 0 and 1; Automatically set to 1 when there is only 1 source
Mask	mask#	Media	None	Four numbers describing the mask (source #, period length (days), first day masked, last day masked)
RBA	RBA	Media	Soil: 0.6 * Dust: 0.6 * Water: 1 Air: 1 Food: 1 Other: No default	Relative bioavailability of each media specific source #, applied only to fraction transferred to GI tract.

* Default for smelter associated soil and dust Pb contamination.

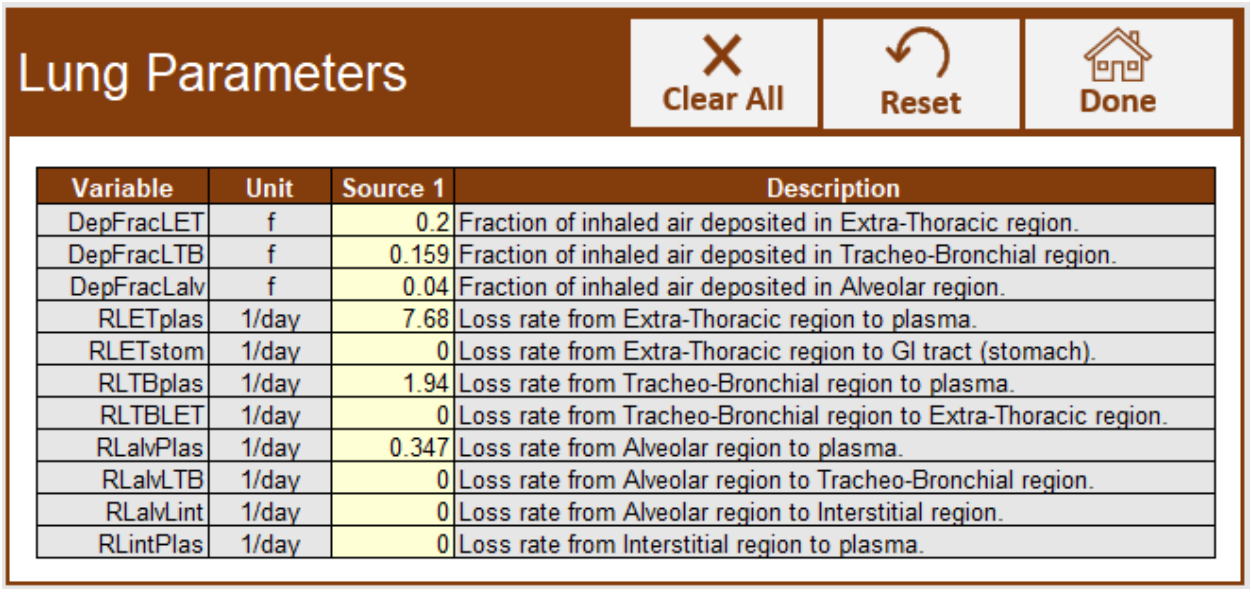
Lung Parameters

This tab houses the parameters needed for FORTRAN to run a simulation with Air media. Users are asked to update this data when Air is selected “Yes” on the Simulation Control tab.

Table 7 – Lung Parameters

Parameter Prompt in User Interface	Name in FORTRAN Input File	Location	Default Value	Parameter Limits
DepFracLET	DepFracLET	Lung	0.2	Must be between 0 and 1
DepFracLTB	DepFracLTB	Lung	0.159	Must be between 0 and 1
DepFracLalv	DepFracLalv	Lung	0.04	Must be between 0 and 1
RLETplas	RLETplas	Lung	7.68	Must be positive
RLETstom	RLETstom	Lung	0	Must be positive
RLTBplas	RLTBplas	Lung	1.94	Must be positive
RLTBLET	RLTBLET	Lung	0	Must be positive
RLalvPlas	RLalvPlas	Lung	0.347	Must be positive
RLalvLTB	RLalvLTB	Lung	0	Must be positive
RLalvLint	RLalvLint	Lung	0	Must be positive
RLintPlas	RLintPlas	Lung	0	Must be positive

As described in Section 2.3.3.1 of the Technical Support Document for the AALM v3.0, lung the parameters in Table 7 and Figure 3 are for lung deposition, absorption, and elimination kinetics are based on a study of human subjects. The subjects inhaled a clean (not excessively carbonaceous due to a fuel rich mixture) automotive exhaust from combustion of fuel containing ^{203}Pb-labeled tetraethyllead. The aerosol particles were reported to be 0.1 μm and below. As such, the lung kinetics (used in AALM v2.0 and v3.0) are most appropriate for near-ultrafine (around 0.1 μm in diameter) combustion aerosols. It is anticipated that a future version of the AALM will offer guidance on particle deposition fractions for other sized aerosols and for the lung kinetics parameters that are set to zero in AALM v3.0.



Variable	Unit	Source 1	Description
DepFracLET	f	0.2	Fraction of inhaled air deposited in Extra-Thoracic region.
DepFracLTB	f	0.159	Fraction of inhaled air deposited in Tracheo-Bronchial region.
DepFracLalv	f	0.04	Fraction of inhaled air deposited in Alveolar region.
RLETplas	1/day	7.68	Loss rate from Extra-Thoracic region to plasma.
RLETstom	1/day	0	Loss rate from Extra-Thoracic region to GI tract (stomach).
RLTBplas	1/day	1.94	Loss rate from Tracheo-Bronchial region to plasma.
RLTBLET	1/day	0	Loss rate from Tracheo-Bronchial region to Extra-Thoracic region.
RLalvPlas	1/day	0.347	Loss rate from Alveolar region to plasma.
RLalvLTB	1/day	0	Loss rate from Alveolar region to Tracheo-Bronchial region.
RLalvLint	1/day	0	Loss rate from Alveolar region to Interstitial region.
RLintPlas	1/day	0	Loss rate from Interstitial region to plasma.

Figure 3 – Lung Parameters screenshot

Switch to indicate solution type

The user can choose between “Forward” and “Solve for Allowable Concentration”. Forward solutions are calculated as normal with all the inputs feeding linearly into lead concentrations (by tissue type) in the outputs. The Solve for Allowable Concentration option allows users to calculate inputs iteratively to achieve the specified target BLL.

To run a Solve for Allowable Concentration simulation, make the selection on the Simulation Control and return to the Media tab (at the top of the sheet) to update the parameters there. When selecting “Solve for Allowable Concentration” a reminder will appear to help prompt the user back to the Media tab to update these parameters. Confirm that there is only 1 source for the specified media. If the background lead levels of the Allowable Concentration run are too high to achieve the target BLL no outputs will be produced as there is no data appropriate for the situation.

Table 8 – Model Options for Forward and Solve for Allowable Concentration Simulations

Parameter Prompt in User Interface	Name in FORTRAN Input File	Location	Default Value	Parameter Limits
Solution type	iterate	Simulation Control	Forward	Values specified in drop down menu
Media	media	Media	No default	Values specified in drop down menu

Parameter Prompt in User Interface	Name in FORTRAN Input File	Location	Default Value	Parameter Limits
Source	subtype	Media	No default	Values specified in drop down menu
Link Dust and Soil?	Dustsoil	Media	No	Binary
Target BLL	targetbll	Media	No default	Must be positive
Precision	precision	Media	0.01	Must be positive
Metric	metric	Media	Arithmetic Mean	Binary; Arithmetic Mean or Maximum value for BLL
Age Width	agewidth	Media	No default	Must be positive
Age Min	agemin	Media	No default	Must be positive
Max Iteration	maxiter	Media	5	Must be positive
GSD	gsd	Media	1.6	Must be positive
Tail Fraction	tailfrac	Media	0.05	Must be between 0 and 1

The screenshot provided in Figure 4 illustrates the parameter setup to solve for the Pb concentration in soil that will limit the probability to 5% for children (aged 1-6 years) from having a blood lead that exceeds a target BLL of 5 µg/dL. The metric is the arithmetic mean of predicted blood Pb concentration over a five-year period starting when the hypothetical child turns 1 year of age. Notice in Figure 4 that dust and soil concentrations are linked, whereas by default they are not linked. This linkage means that the Pb concentration of soil and dust will be increased or decreased by the same fraction of the originally entered concentrations until a solution is reached. This solution is slightly different from the approach used in the Integrated Exposure Uptake Biokinetic (IEUBK) model v2.0. If the IEUBK model v2.0 default “Multiple source analysis” is used, the model calculates an indoor dust Pb concentration (µg/g) that equals 0.7 times the soil Pb concentration (µg/g) plus 100 m^3/g times the air Pb concentration (µg/m^3). If users desire to solve for a soil Pb concentration in the same manner as the IEUBK model, an equation can be entered into Cell F39 as =0.7*F12+100*F93 to solve for the dust Pb concentration (Cell F39) as a function of the soil Pb concentration (Cell F12) and the air Pb concentration (Cell F93). Users will need to run the solver function iteratively two or three times. That is, after each run of the solver function, the user will enter the allowable soil Pb concentration obtained by the solver into Cell F12 of the Media tab, then rerun the solver function.

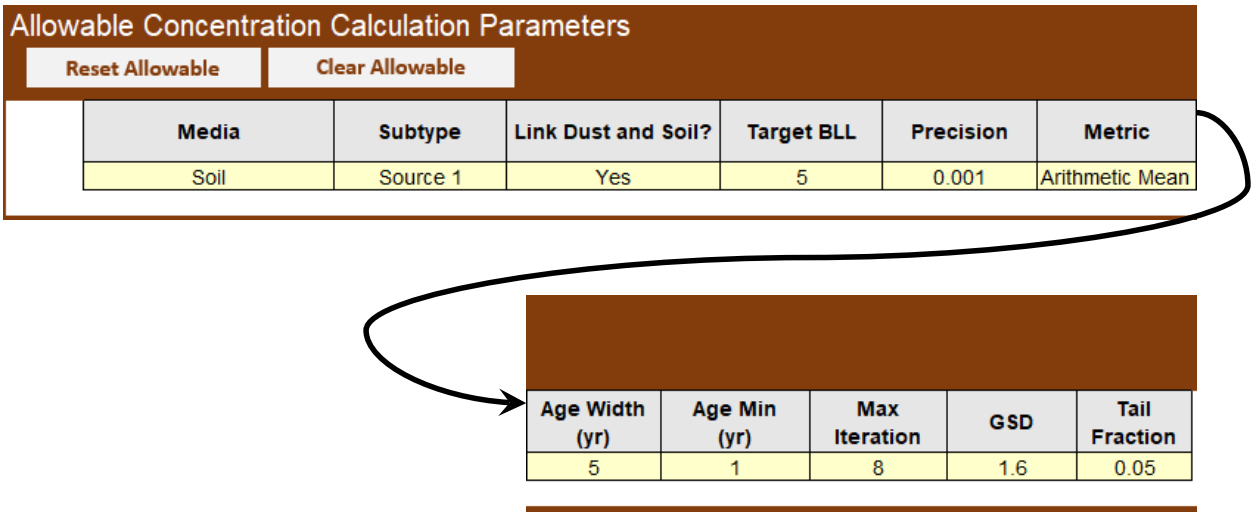


Figure 4 – Screenshot of Setup for Allowable Concentration Solution

Switch to indicate stepwise or interpolated transitions between exposures

The Stepwise or Interpolated switch allows users to calculate changes in the sources of lead exposure defined in Media in a stepwise manner or with linear interpolation between defined concentrations for each age. In the stepwise approach the exposure concentrations remain constant for the given age until defined for the next age, when they immediately change according to user inputs. With the interpolated approach the exposure concentrations change gradually over the given time period according to a linear formula between the concentrations at the ages provided.

Table 9 – Stepwise or Interpolated Transitions for Exposure Intakes

Parameter Prompt in User Interface	Name in FORTRAN Input File	Location	Default Value	Parameter Limits
Stepwise or Interpolated?	Interp	Simulation Control	Stepwise	Binary; Stepwise or Interpolated

Switch to indicate if red blood cell (RBC) should be linear or allow for saturation

The RBC switch allows users to define if the red blood cell parameter should be calculated linearly, or non-linearly which allows for saturation. For more information, see Section 2.3.4.3 (Red Blood Cells) in the Technical Support Document for the AALM v3.0.

Table 10 – Choice of Linear or Nonlinear binding to RBC

Parameter Prompt in User Interface	Name in FORTRAN Input File	Location	Default Value	Parameter Limits
Linear or Non-linear RBC?	irbc	Simulation Control	Non-linear RBC	Binary; Linear or Non-linear

3. Run the Model and Review the Results

Figure 5 – Button to Run a Simulation

Finally, run the simulation by selecting Run Simulation (Figure 5) found at the bottom of the Simulation Control tab (Figure 1). The Excel file will create the text version of the input file, create a .xlsm of the input file for user records, run the model, and import the results. If you have an error, ensure that the executable file requested (32 or 64-bit) and User Interface (or GUI) are saved in the same folder.

PLEASE NOTE
Simulation outputs are housed within the parent directory in a folder with the same name as the user-defined simulation name.

The outputs of the FORTRAN executables are written to a folder within the directory housing the Excel GUI with the same name as the user provided simulation name. These files are:

- **Day_[Simulation Name].csv**
  This output displays intake, uptake, and excretion data sums by day of the simulation. This information is then displayed in the GUI in [Simulation Name]_Daily. This data can be used for further analysis or could be read back into the GUI for visualization using the “Import” button on the Explore Data tab.
- **[Simulation Name]_FortranInput.xlsm**
  This output serves as a record of the inputs of the simulation provided to FORTRAN. Values that deviate from the default are bolded and highlighted for the user in yellow.
- **LeggettInput.txt**
  This output serves as a secondary record of the inputs provided to FORTRAN that could be used to manually re-run the simulation if needed by replacing the file of the same name in the parent directory and opening the FORTRAN executable or could be read back into the GUI using the “Import” button on the Simulation Control tab.
- **Log_[Simulation Name].csv**
  This output serves as a full log of the source data at each timestep.
- **Out_[Simulation Name].csv**

The **import** buttons on the Simulation Control and Explore Data tabs allow users to load previously run inputs back into the GUI or analyze previously run data.

This output displays concentration and mass data sums by tissue for each user-defined output timestep. This information is then displayed in the GUI in [Simulation Name]_Output.

- **Src_[Simulation Name].csv**
  This output displays the source defined exposure data (including total lead intake, body burden, and amount eliminated) by each user-defined output timestep.
- **RunInfo_[Simulation Name].csv**
  This output displays information about the simulation especially when the simulation solves for an allowable concentration. When that selection is chosen this file is used by the GUI to display the calculated allowable concentrations.

These outputs are then imported into the GUI and displayed or summarized in the following tabs:

- **Output Summary**: Acts as a menu to access outputs and displays allowable concentration data as applicable.
- **Explore Data**: Presents data visualizations and allows for blood lead exceedance calculations.
- **Detailed Outputs**: Presents user-defined timestep-level data from the model.
- **Daily**: Presents data from the model at a daily interval.

Output Summary

This tab houses basic analysis of the simulation and directs the user to the two raw output files imported into the GUI. This tab has five buttons for users to select:

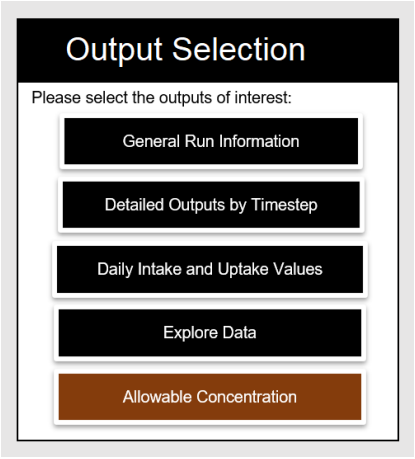


Figure 6 – Output Section Screenshot

- **General Run Information**
  This button displays brief summary data of the simulation such as the runtime and duration, simulation timespan, type of run, and an indication of any errors or warnings encountered.
- **Detailed Outputs by Timestep**
  This button takes the user directly to Detailed Outputs, described below.
- **Daily Intake and Uptake Values**
  This button takes the user directly to Daily, described below.
- **Explore Data**
  This button takes the user directly to the Explore Data tab, described below.
- **Allowable Concentration**
  If the solution type was a Solve for Allowable Concentration, the button displays the Solve for Allowable Concentration input data, along with the solution of when the target BLL was reached in the user-defined Media.

Explore Data

Before analyzing and visualizing data in Explore Data, update the page to ensure the data from the simulation name defined on the Simulation Control page is displayed. To display previously run simulation data, the “Import” buttons on the Simulation Control and Explore Data tabs can be used to import inputs and results of previously run scenarios, respectively.

In the Explore Data tab, users can select which data summaries are most valuable for them in their analysis by selecting each desired data summary with the check boxes to the left of each compartment.

As in the rest of the GUI, yellow cells indicate fields which should be updated or altered by the user. The white fields will calculate automatically based on these updates.

PLEASE NOTE

Throughout the GUI, yellow fields indicate cells which should be altered by the user. The white fields will calculate automatically based on these updates.

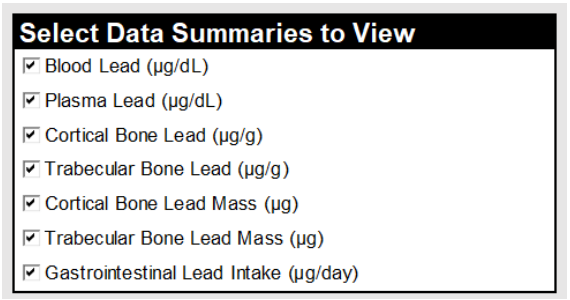


Figure 7 – Graphs that Users may Select to Display

For each data summary, the GUI calculates:

- Compartment-specific lead statistics, for a user-defined age range
  - Percent exceedance of the average, for a user-defined limit and geometric standard deviation (GSD)
- Compartment-specific lead values, for a user-defined age
  - Percent exceedance at the user-defined age, for a user-defined limit and geometric standard deviation (GSD)
- Compartment-specific Area under the curve (AUC), for a user-defined age range

Uses of these parameters may vary depending on the reason for the simulation, but in general, the calculations of age-defined exposure values are expected to be useful for those users which may be performing site-specific risk assessments or otherwise assessing risk. The AUC value may be useful in calculation of a time-weighted average for each compartment.

Further, the x- and y- axes of the graphs can be altered to view a smaller portion of the graph in greater detail as desired.

Detailed Outputs

This tab displays the output data as defined in the advanced time options and base parameters. Each output field (described below) is quantified at each timestep as defined by the user. These timesteps are then calculated into days and years to aid the user with analysis.

Table 11 – Output Parameters Displayed on the Detailed Outputs Tab

Variable	Data description
timestep	Timestep number, with 0 being the start of the simulation
days	Age in days since birth
years	Age in decimal years since birth (=age/365)
Cblood	Total Blood Pb concentration (BLL)
Cplas	Blood plasma Pb concentration
Ckidney	Kidney Pb concentration
Cliver	Liver Pb concentration
Ccort	Cortical bone Pb concentration
Ctrab	Trabecular bone Pb concentration
Cbone	Total bone Pb concentration
Ablood	Pb mass in blood (plamsa + RBC). Same as in original Leggett code, this does not include plasma-protein Pb.
Aplas	Pb mass in plasma
ARBC	Pb mass in red blood cells (RBC)
Akidney	Pb mass in kidneys
Aliver	Pb mass in liver
Acort	Pb mass in cortical bone
Atrab	Pb mass in trabecular bone
Abone	Pb mass in bone (sum of P+Q)
Asoft	Pb mass in soft tissue (sum of 3 tissue types)
Abrain	Pb mass in brain
ART	Pb mass in lungs (sum over compartments)
Astom	Pb mass in stomach
AGI	Pb mass in GI tract (sum of SI, ULI, LLI)
Aprot	Pb mass in protein-bound plasma
AEVF	Pb mass in extra-vascular fluid (EVF)
Ablad	Pb mass in bladder
Aflow	Pb mass traveling between compartments
Tbody	Total Pb mass in body

Variable	Data description
Aurine	Total Pb mass excreted via urine (summed over time)
Afecal	Total Pb mass lost via feces (summed over time)
Asweat	Total Pb mass lost via sweat (summed over time)
Ahair	Total Pb mass lost to hair (summed over time)

Daily

This tab displays output parameters summarized as daily values for intake, uptake, and excretion for each media.

Table 12 – Output Parameters Displayed on the Daily Tab

Variable	Data description
InAirTot	Total Pb mass inhaled (summed over each day)
InAirDep	Total inhaled Pb mass deposited (summed over each day). *This variable is currently only showing deposition in the ET region, not TB or PU.*
InIngest	Total ingested Pb mass (summed over each day)
InDust	Total Pb mass from dust ingestion (summed over each day)
InSoil	Total Pb mass from soil ingestion (summed over each day)
InWater	Total Pb mass from water ingestion (summed over each day)
InFood	Total Pb mass from food ingestion (summed over each day)
InOther	Total Pb mass from other ingestion (summed over each day)
UpTotal	Total Pb uptake in plasma (summed over each day)
UpAir	Total Pb plasma uptake from air (summed over each day)
UpLung	Total Pb plasma uptake in lungs (summed over each day)
UpGIAir	Total Pb plasma uptake from air in GI tract (summed over each day)
UpGITotal	Total Pb plasma uptake in GI tract (summed over each day)
UpIngest	Total Pb plasma uptake from ingestion (summed over each day)
UpGIDust	Total Pb plasma uptake from dust (summed over each day)
UpGISoil	Total Pb plasma uptake from soil (summed over each day)
UpGIWater	Total Pb plasma uptake from water (summed over each day)
UpGIFood	Total Pb plasma uptake from food (summed over each day)
UpGIOther	Total Pb plasma uptake from other (summed over each day)

Variable	Data description
ExAir	Total inhaled Pb not deposited in lungs (summed over each day)
ExUrine	Total Pb mass excreted in urine (summed over each day)
ExFeces	Total Pb mass excreted in feces (summed over each day)
ExSweat	Total Pb mass excreted in sweat (summed over each day)
ExHair	Total Pb mass excreted in hair and nails (summed over each day)

4. QA Step: Confirm the Intake Results Give the Correct Time Series

As a final QA step, the user is encouraged to inspect the output and verify that the intake time-varying profiles match what was intended. Remember that if the simulation exposure is varied over a very brief time period but the output interval was longer than that time period, the actual intake change won't be recorded in the output (e.g., an exposure from age 1.25 to 1.75, but outputs only saved every year).

IV. Troubleshooting

Table 13 – Troubleshooting Questions and Answers

Question	Answer
Setup	
I'm having trouble getting the model to run.	Ensure all the files from the zip file are in the same folder and none have been deleted. If needed unzip the original file again and export the original files.
My Media tab isn't set up the way I defined it in Simulation Control.	Navigate to the Media tab through "Go to Media" this will update the formatting of the tab.
Running AALM	
Some of my data isn't populating.	Check the Simulation Control. Any data outside the parameters set in this tab are ignored when writing the input files for FORTRAN.
Reviewing the Results	
Where are my output files?	Outputs and a copy of the FORTRAN inputs for the run are written to a folder with the same simulation name within the folder housing the GUI.

Question	Answer
My Explore Data tab looks like it has old data.	Before using, select “update” at the top of Explore Data to ensure the data has updated to the run name specified on Simulation Control.
The output file is blank but the daily file generated correctly.	If an allowable concentration run results in background lead too high to reach the target BLL, there are not results to show, so they are not displayed in the GUI but the files are still generated.

V. Appendix

The sections in this appendix are meant to serve as a reference sheet for users to summarize the user-defined parameters in this tool as well as give more instruction to users about how to implement various scenarios.

Default Values

Table 14 – Default Model Values

Parameter Prompt in User Interface	Name in FORTRAN Input File	Location	Default Value	Parameter Limits	Description
Timesteps per day	steps_per_day	Simulation Control	100	Cannot exceed 12 when using the 32-bit executable	Number of times lead loading and distribution should be calculated in the simulation each day
Timesteps between outputs	outwrite	Simulation Control	100	Must be positive	Frequency of output written containing lead loading and distribution calculations
Age at start (yrs)	age_range	Simulation Control	0 – Not accessible for change by users.	Must not be greater than 0 and must be less than “Age at end”	Age of the simulated individual at the start of the simulation
Age at end (yrs)	age_range	Simulation Control	90	Must not exceed 100 and must be greater than “Age at start”. Cannot exceed 8 years when using the 32-bit executable.	Age of the simulated individual at the end of the simulation
Sex	sex	Simulation Control	Female	Binary; Female or Male	Sex of the simulated individual
wbirth	wbirth	Growth Params	3.3	Must be positive	Weight at birth

wchild	wchild	Growth Params	22	Must be positive	Maximum weight for early hyperbolic growth period
half	half	Growth Params	3	Must be positive	Age at which weight is half WCHILD
wadult	wadult	Growth Params	34	Must be positive	Maximum weight for logistic growth period
kappa	kappa	Growth Params	600	Must be positive	Logistic constant kappa
lambda	lambda	Growth Params	0.017	Must be greater than 0	Logistic constant lambda
LB	LB	Growth Params	0.85	Must be between 0 and 1	Ratio of lean body mass to body mass
ASHWT	ashwt	Time Ind Phys Params	2800	Not used	Skeletal ash weight
BLDMOT	bldmot	Time Ind Phys Params	0.62	Must be positive	Maternal blood lead concentration
BONIN	bonin	Time Ind Phys Params	0.32	Must be between 0 and 1	Fraction of body lead, at birth, in bone
BRANIN	branin	Time Ind Phys Params	0.045	Must be between 0 and 1	Fraction of body lead, at birth, in brain
BRATIO	bratio	Time Ind Phys Params	0.85	Must be between 0 and 1	Fetal: maternal blood lead concentration ratio

CRTWT	crtwt	Time Ind Phys Params	4000	Must be positive	Cortical bone weight
H1TOBL	h1tobl	Time Ind Phys Params	0.45	Must be between 0 and 1	Fraction of transfer out of liver compartment 1 that goes to diffusible plasma
H1TOH2	h1toh2	Time Ind Phys Params	0.1	Must be between 0 and 1	Fraction of transfer out of liver compartment 1 that goes to liver compartment 2
H1TOSI	h1tosi	Time Ind Phys Params	0.45	Must be between 0 and 1	Fraction of transfer out of liver compartment 1 that goes to the small intestine
HCTA	hcta	Time Ind Phys Params	0.41	Must be between 0 and 1	Adult hematocrit (sex dependent)
HCTB	hctb	Time Ind Phys Params	0.52	Must be between 0 and 1	Birth hematocrit
HEPIN	hepin	Time Ind Phys Params	0.055	Must be between 0 and 1	Fraction of body lead, at birth, in liver
IFETAL	ifetal	Time Ind Phys Params	1	Binary, 0 or 1	Switch for starting tissue Pb from maternal blood (1)
KWT	kwt	Time Ind Phys Params	310	Must be positive	Adult kidney weight

PLSVOL	plsvol	Time Ind Phys Params	30	Must be positive	Plasma volume
POWER	power	Time Ind Phys Params	1.5	Must be positive	Exponent for RBC deposition
RBCIN	rbcin	Time Ind Phys Params	0.07	Must be between 0 and 1	Fraction of body lead, at birth, in red blood cells
RBCNL	rbcnl	Time Ind Phys Params	20	Must be positive	Threshold concentration in RBC for non-linear deposition from diffusible plasma to RBC
RBCVOL	rbcvol	Time Ind Phys Params	22	Must be positive	Red blood cell volume
RENIN	renin	Time Ind Phys Params	0.01	Must be between 0 and 1	Fraction of body lead, at birth, in kidney
RKDN1	rkdn1	Time Ind Phys Params	0.139	Must be positive	Transfer rate from kidney compartment 1 to urinary pathway
RLLI	rlli	Time Ind Phys Params	1	Must be positive	Transfer rate from lower large intestine to feces
RLVR1	rlvr1	Time Ind Phys Params	0.0693	Must be positive	Transfer rate out of the liver compartment 1, including to small intestine and diffusible plasma

RPLAS	rplas	Time Ind Phys Params	2000	Must be positive	Total transfer rate from diffusible plasma to all compartments
RPROT	rprot	Time Ind Phys Params	0.139	Must be positive	Transfer rate from bound plasma to diffusible plasma
RSIC	rsic	Time Ind Phys Params	6	Must be positive	Transfer rate from small intestine to upper large intestine
RSOF0	rsof0	Time Ind Phys Params	2.079	Must be positive	Transfer rate from soft tissue compartment 0 to diffusible plasma
RSOF1	rsof1	Time Ind Phys Params	0.00693	Must be positive	Transfer rate from soft tissue compartment 1 to diffusible plasma
RSOF2	rsof2	Time Ind Phys Params	0.00038	Must be positive	Transfer rate from soft tissue compartment 2 to diffusible plasma
RSTMC	rstmc	Time Ind Phys Params	24	Must be positive	Transfer rate from stomach to small intestine
RULI	ruli	Time Ind Phys Params	1.85	Must be positive	Transfer rate from upper large intestine to lower large intestine
S2HAIR	s2hair	Time Ind Phys Params	0.4	Must be between 0 and 1	Deposition fraction from soft tissue compartment 1 to other excreta

SATRAT	satrat	Time Ind Phys Params	350	Must be positive	Maximum (saturating) concentration of lead in RBC
SIZEVF	sizevf	Time Ind Phys Params	3	Must be between 0 and 1	Relative volume of the EVF compartment compared to plasma (EVF/Plasma)
SOFIN	sofin	Time Ind Phys Params	0.5	Must be between 0 and 1	Fraction of body lead, at birth, in soft tissue
TBONEL	tbonel	Time Ind Phys Params	0.08	Must be between 0 and 1	End value of TBONE-age array
TEVF	tevf	Time Ind Phys Params	0.5	Must be between 0 and 1	Deposition fraction from diffusible plasma to extravascular fluid
TOFECE	tofece	Time Ind Phys Params	0.006	Must be between 0 and 1	Deposition fraction from diffusible plasma directly to the small intestine (not including the transfer from biliary secretion, specified by RLVR1)
TOKDN1	tokdn1	Time Ind Phys Params	0.025	Must be between 0 and 1	Deposition fraction from diffusible plasma to kidney compartment 1
TOKDN2	tokdn2	Time Ind Phys Params	0.0004	Must be between 0 and 1	Deposition fraction from diffusible plasma to kidney compartment 2

TOLVR1	tolvr1	Time Ind Phys Params	0.04	Must be between 0 and 1	Deposition fraction from diffusible plasma to liver compartment 1
TOPROT	toprot	Time Ind Phys Params	0.0004	Must be between 0 and 1	Deposition fraction from diffusible plasma to protein-bound plasma
TORBC	torbc	Time Ind Phys Params	0.25	Must be between 0 and 1	Deposition fraction from diffusible plasma to red blood cells, below non-linear threshold
TOSWET	toswet	Time Ind Phys Params	0.0035	Must be between 0 and 1	Deposition fraction from diffusible plasma to sweat
TOURIN	tourin	Time Ind Phys Params	0	Must be between 0 and 1	Deposition fraction from diffusible plasma to urine
TRBWT	trbwt	Time Ind Phys Params	3000	Must be positive	Trabecular bone weight
VBLC	vblc	Time Ind Phys Params	0.067	Must be positive	Total blood volume
VKC	vkc	Time Ind Phys Params	0.0085	Must be positive	Kidney volume in the adult
VLC	vlc	Time Ind Phys Params	0.025	Must be positive	Liver volume in the adult

VLUC	vluc	Time Ind Phys Params	0.015	Must be positive	Lung volume in adult
F1	f1	Time Dep Phys Params	Varied	Must be between 0 and 1	GI-tract absorption fraction which are applied to Pb ingested from all sources. (based on Leggett 1993)
AMTBLD	amtbld	Time Dep Phys Params	Varied	Must be positive	Age-scaled amount of blood
FLONG	flong	Time Dep Phys Params	0.6	Must be between 0 and 1	Age-scaled fraction of total transfer from the exchangeable bone directed to non-exchangeable bone
GSCAL	gscal	Time Dep Phys Params	Varied	Not used	Age scaling factor for GIT transfer
RBLAD	rblad	Time Dep Phys Params	Varied	Must be positive	Age-scaled transfer rate from urinary bladder to urine
RBRAN	rbran	Time Dep Phys Params	0.00095	Must be positive	Age-scaled transfer rate from brain to diffusible plasma
RCORT	rcort	Time Dep Phys Params	Varied	Must be positive	Age-scaled transfer rate from non-exchangeable cortical bone to diffusible plasma
RCS2B	rcs2b	Time Dep Phys Params	Varied	Must be positive	Age-scaled transfer rate from cortical bone surface to diffusible plasma

RCS2DF	rcs2df	Time Dep Phys Params	Varied	Must be positive	Age-scaled transfer rate from cortical bone surface to exchangeable cortical bone
RDIFF	rdiff	Time Dep Phys Params	0.023105	Must be positive	Age-scaled transfer rate from the exchangeable bone, including transfer to surface and non-exchangeable bone
RKDN2	rkdn2	Time Dep Phys Params	Varied	Must be positive	Age-scaled transfer rate from kidney compartment 2 to diffusible plasma
RLVR2	rlvr2	Time Dep Phys Params	Varied	Must be positive	Age-scaled transfer rate from the slow liver compartment 2 to diffusible plasma
RRBC	rrbc	Time Dep Phys Params	Varied	Must be positive	Age-scaled transfer rate from red blood cell to diffusible plasma
RTRAB	rtrab	Time Dep Phys Params	Varied	Must be positive	Age-scaled transfer rate from non-exchangeable trabecular bone to diffusible plasma
RTS2B	rts2b	Time Dep Phys Params	Varied	Must be positive	Age-scaled transfer rate from trabecular bone surface to diffusible plasma
RTS2DF	rts2df	Time Dep Phys Params	Varied	Must be positive	Age-scaled transfer rate from surface trabecular bone to exchangeable trabecular bone
TBONE	tbone	Time Dep Phys Params	Varied	Must be between 0 and 1	Age-scaled deposition fraction from diffusible plasma to surface bone

TFRAC	tfrac	Time Dep Phys Params	Varied	Must be between 0 and 1	Bone deposition-scaled fraction of diffusible plasma-to-bone deposition that goes to trabecular surface bone; 1-TFRAC is the fraction that goes to cortical surface bone.
TOBRAN	tobran	Time Dep Phys Params	Varied	Must be between 0 and 1	Age-scaled deposition fraction from diffusible plasma to brain
TOSOF0	tosof0	Time Dep Phys Params	Varied	Must be between 0 and 1	Age-scaled deposition fraction from diffusible plasma to soft tissue compartment 0
TOSOF1	tosof1	Time Dep Phys Params	Varied	Must be between 0 and 1	Age-scaled deposition fraction from diffusible plasma to soft tissue compartment 1
TOSOF2	tosof2	Time Dep Phys Params	0.001	Must be between 0 and 1	Age-scaled deposition fraction from diffusible plasma to soft tissue compartment 2
Number of Sources	sources	Simulation Control	0	Values allowed: 0-3	Sources of lead exposure per each type of media (ie. soil, dust etc.)
Concentration: Number of ages	conc_ages	Media	Varied	Maximum 100 ages can be defined	Number of ages at which the user wishes to define lead concentration for the given sources; concentration should be defined each time the concentration will change for each of the sources defined
Concentration (by source and age)	concs#	Media	see Appendix C of the TSD for the AALM v3.0	Must be positive	Lead concentration to be simulated by each source varied by age as needed

Intake: Number of ages	intake_ages	Media	Varied	Must be positive	Number of ages at which the user wishes to define intake for the given sources; intake should be defined each time the concentration will change for each of the sources defined
Intake	intake_amt	Media	Varied. See Appendix Table Media Source Intake Values by Age	Must be positive	Intake of the given media to be simulated by each source varied by age as needed
Fraction	frac#	Media	1	Must be between 0 and 1; Automatically set to 1 when there is only 1 source	Fraction of exposure of each source in intake
Mask	mask#	Media	None	Four numbers describing the mask (source #, period length (days), first day masked, last day masked)	A period of temporary period of non-exposure from a given lead source
RBA	RBA	Media	Soil: 0.6 * Dust: 0.6 * Water: 1 Air: 1 Food: 1 Other: No default	Must be positive	Relative bioavailability of each media specific source #, applied only to fraction transferred to GI tract
DepFracLET	DepFracLET	Lung	0.2	Must be between 0 and 1	Fraction of inhaled air deposited in Extra-Thoracic region.

DepFracLTB	DepFracLTB	Lung	0.159	Must be between 0 and 1	Fraction of inhaled air deposited in Tracheo-Bronchial region.
DepFracLalv	DepFracLalv	Lung	0.04	Must be between 0 and 1	Fraction of inhaled air deposited in Alveolar region.
RLETplas	RLETplas	Lung	7.68	Must be positive	Loss rate from Extra-Thoracic region to plasma.
RLETstom	RLETstom	Lung	0	Must be positive	Loss rate from Extra-Thoracic region to GI tract (stomach).
RLTBplas	RLTBplas	Lung	1.94	Must be positive	Loss rate from Tracheo-Bronchial region to plasma.
RLTBLET	RLTBLET	Lung	0	Must be positive	Loss rate from Tracheo-Bronchial region to Extra-Thoracic region.
RLalvPlas	RLalvPlas	Lung	0.347	Must be positive	Loss rate from Alveolar region to plasma.
RLalvLTB	RLalvLTB	Lung	0	Must be positive	Loss rate from Alveolar region to Tracheo-Bronchial region.
RLalvLint	RLalvLint	Lung	0	Must be positive	Loss rate from Alveolar region to Interstitial region.
RLintPlas	RLintPlas	Lung	0	Must be positive	Loss rate from Interstitial region to plasma.
Solution type	iterate	Simulation Control	Forward	Values specified in drop down menu	Switch indicating if the simulation should use forward calculation or solve for an allowable concentration

Media	media	Media	No default	Values specified in drop down menu	Media source of lead to be used in allowable concentration calculation
Source	subtype	Media	No default	Values specified in drop down menu	Switch indicating if concentration of lead should be linearly interpolated between user defined values or stepwise in calculation
Link Dust and Soil?	Dustsoil	Media	No	Binary	Switch indicating is red blood cells should be linear or non-linear (allowing for saturation)
Target BLL	targetbll	Media	No default	Must be positive	Target BLL to solve for
Precision	precision	Media	0.01	Must be positive	Allowable variation from the BLL
Metric	metric	Media	Arithmetic Mean	Binary; Arithmetic Mean or Maximum value for BLL	Calculation method to solve for target BLL
Age Width	agewidth	Media	No default	Must be positive	The number of simulation days to calculate BLL over
Age Min	agemin	Media	No default	Must be positive	Starting age of target BLL calculation
Max Iteration	maxiter	Media	5	Must be positive	Maximum number of interations used to calculate if target BLL is reached
GSD	gsd	Media	1.6	Must be positive	Assumed geometric standard deviation of the assumed lognormal distribution of BLL

Tail Fraction	tailfrac	Media	0.05	Must be between 0 and 1	Fraction of the lognormal distribution in the tail
Stepwise or Interpolated?	interp	Simulation Control	Stepwise	Binary; Stepwise or Interpolated	Switch indicating if concentration of lead should be linearly interpolated between user defined values or stepwise in calculation
Linear or Non-linear RBC?	irbc	Simulation Control	Non-linear RBC	Binary; Linear or Non-linear	Switch indicating is red blood cells should be linear or non-linear (allowing for saturation)

* Default for smelter associated soil and dust Pb contamination.

Mask Examples

Below are some examples of scenarios which were modeled with previous versions of AALM and how they might be implemented with this current system of masking.

Please note that the masking logic as currently implemented acts in a negative way, blocking sources in a regular periodic manner. The specific examples are more amenable to a positive "windowing" logic, where the sources are active only during the specified intervals. This process may be implemented on future iterations of AALM.

The current system allows multiple masks to be applied to the same source. If any mask is active the source is blocked.

Example 1: Children's camping over several years
Allow 2 weeks of exposure each summer from ages 10 to 18 years inclusive.

There are two ambiguous points here. First, the simulation could simply begin at age 10 and end when the person turns 19. Then the age range is automatically accounted for. The second point is that there is no seasonality in the simulation, except perhaps in the sources. Age is a matter of time since birth, and people can be born at any time of the year.

Suppose the simulation is over a lifetime and the person is assumed to be born in the summer. Turn on the camping source exposure (0.5 µg/g) when age 10 is reached (3650 days) and off after the age 18 exposure ends (say, 9*365 days later). Although the soil Pb concentration of 0.5 µg/g will not cause a noticeable change in blood Pb concentration, 500 µg/g would. Use stepwise so the source turns on and off abruptly. The mask has period 365 days because it repeats annually. It blocks all but the first 14 days of each year, for example:

Soil, mask1, 4, 1, 365, 15, 365

Soil

Reset Soil | Clear Soil

Concentration (ug/g)	Number of Ages	Ages (years)	0	10	19
	3	Source 1	0	0.5	0

Mask #	Source	Period (days)	First day blocked	Last day blocked
1	1	365	15	365

Intake	Number of Ages	Ages (years)	0	0.25
	2	Intake (g/day)	0.018	0.032
		Fraction, Source 1	1	1

RBA	RBA, Source 1	0.6

Figure 8 – Screenshot 1 for Applying Masks to Camping Scenario

This says that the mask applies to soil source #1 (the number after the "4", which is the number of values to be read from the row), has a period of 365 days, and starts on day 15 and ends on day 365 of each period.

Alternatively, the mask could exclude all but the last 14 days of the year as follows:

Soil, mask1, 4, 1, 365, 1, 351

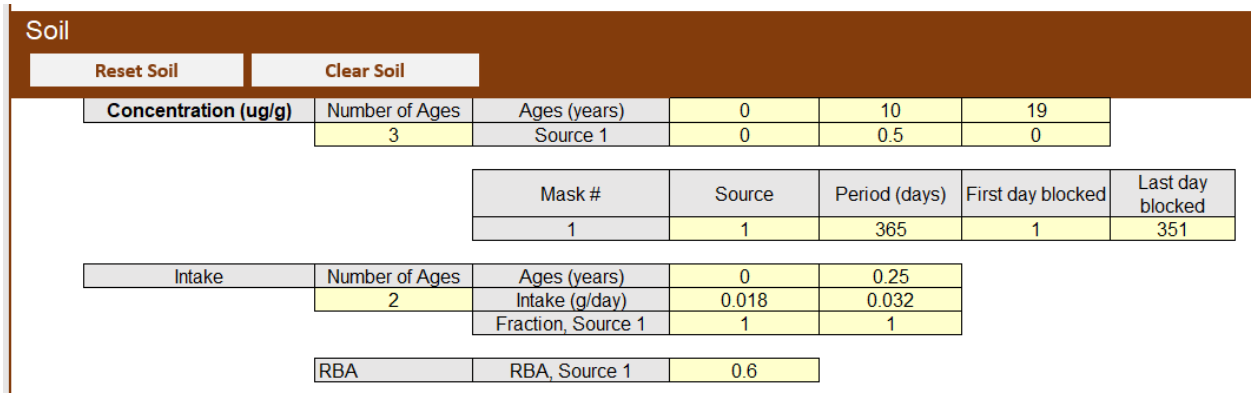


Figure 9 – Screenshot 2 for Applying Masks to Camping Scenario

To make the exposure time in the middle of the year is more difficult because two masks are needed: one to exclude the days before camping and the other for the days after, for example:

Soil, mask1, 4, 1, 365, 1, 180
Soil, mask2, 4, 1, 365, 195, 365

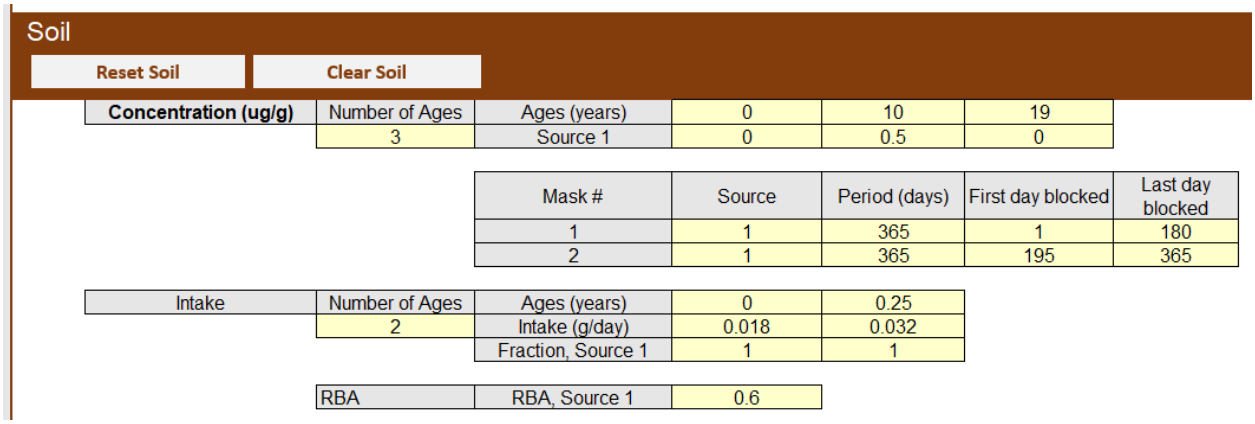


Figure 10 – Screenshot 3 for Applying Masks to Camping Scenario

This allows the source to operate on days 181 through 194 inclusive, each year.

Example 2: Youth summer day camp exposures from 6 to 19 years inclusive
Allow 8 weeks (excluding weekends) of exposure from age 6-19 (inclusive).

This is similar to example 1 except that the exposure is interrupted each week to exclude weekends. Although the soil Pb concentration of 0.5 µg/g will not cause a noticeable change in blood Pb concentration, 500 µg/g would. Turn the source on when the child reaches age 6 (6*365 days) and off 13 years later. Two masks are needed, one with a period of 365 days to create the annual repetitions and the other with a period of 7 days to create the weekly pattern.

Again, there is flexibility in when the day camp starts relative to the child's birthday. If it runs for the last 8 weeks that they are 6 years old, then the following works:

Soil, mask1, 4, 1, 365, 1, 309
Soil, mask2, 4, 1, 7, 6, 7

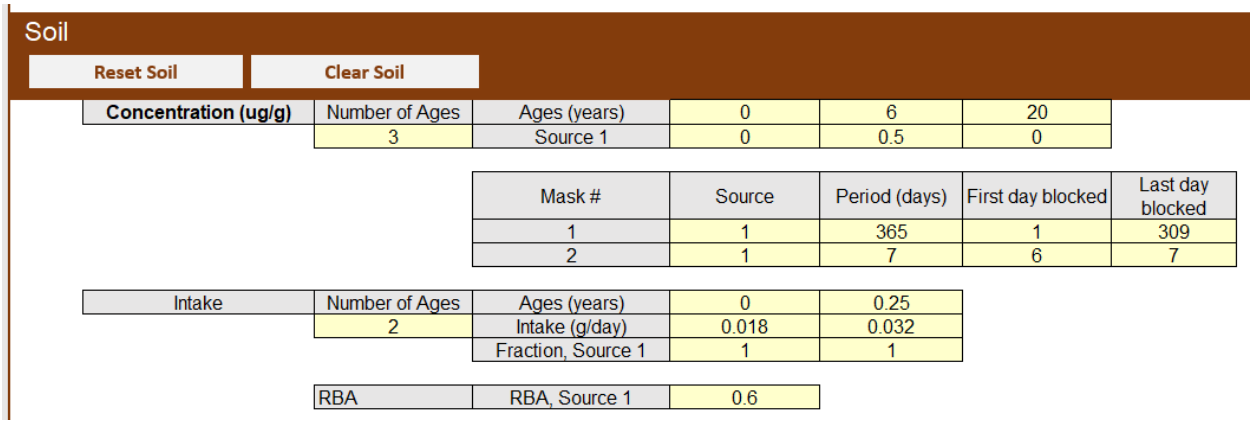


Figure 11 – Screenshot for Applying Masks to Summer Camp Scenario

Both masks apply to the same source (the "1" after the "4"). The first mask blocks all but the last 56 days of each year. The second mask blocks days 6 and 7 of each week. The result is 8 weeks of 5 days exposure each week, repeating each year for 13 consecutive years.

Example 3: Dietary Supplements taken on regular schedule
Allow intake of dietary supplement on a daily basis from age 7 on.

This is a food intake, for which AALM requires input in total Pb/day (not separated into a product of food mass consumed and Pb concentration of food). In this example, only the mass of Pb in the dietary supplement is illustrated. Set up a constant source of the appropriate mass of lead consumed per day (corresponding to an intake of 1 tsp of supplement per day), starting at the age when the supplement is first administered. For this scenario it is assumed that a teaspoon of supplement has a mass of 5 grams and that the lead concentration in the supplement is 1.4 ppm, which gives a daily intake of 7 µg. Then mask it as follows in each of the cases:

a) 2 consecutive days per week:
- food, mask1, 4, 7, 3, 7

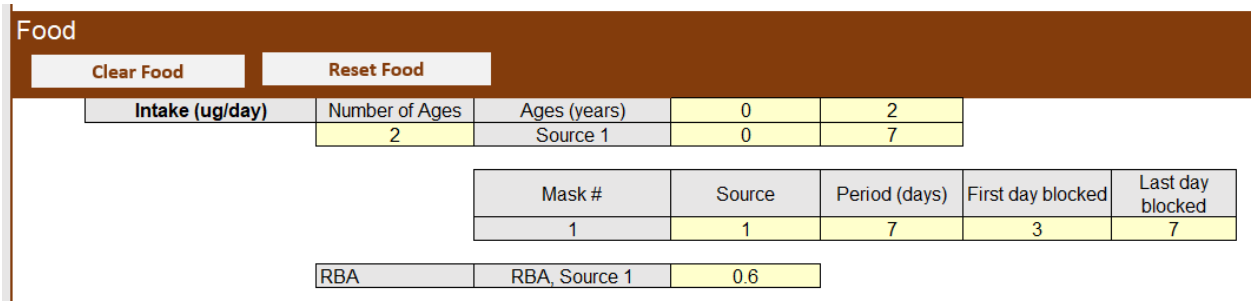


Figure 12 – Screenshot 1 for Applying Masks to an Adulterated Dietary Supplement

b) 2 non-consecutive days per week:
- food, mask1, 4, 7, 2, 3 and food, mask2, 4, 7, 5, 7

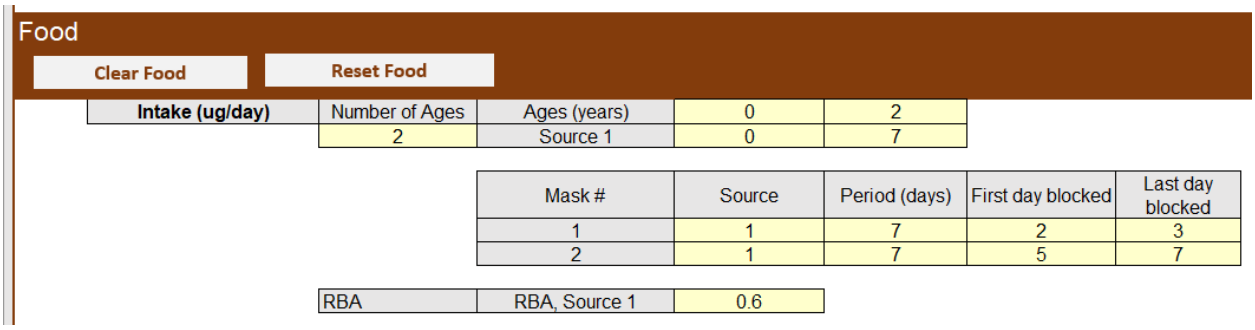


Figure 13 – Screenshot 2 for Applying Masks to an Adulterated Dietary Supplement

c) 2/7 tsp every day:

- No mask, just lower the source to 2/7 of above (i.e., 2 µg).

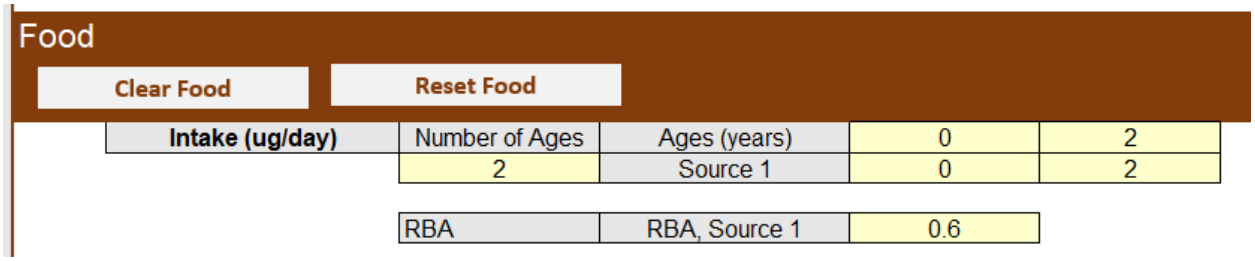


Figure 14 – Screenshot 3 for Alternative to Masks to an Adulterated Dietary Supplement

Example 4: Therapeutic home remedies

This would count as "other" media, which like food uses total Pb ingested per day without separating it into mass and concentration. Determine the Pb intake per day from this source and set up a constant source at that level.

a) 7 days per week for days 60 to 120 after the 20th birthday.

- Set up the source to start at age 20.16 (i.e., 20+60/365) and end at 20.33 (i.e., 20+120/365), using stepwise (Cell E34 of the Simulation Control tab). No mask needed.

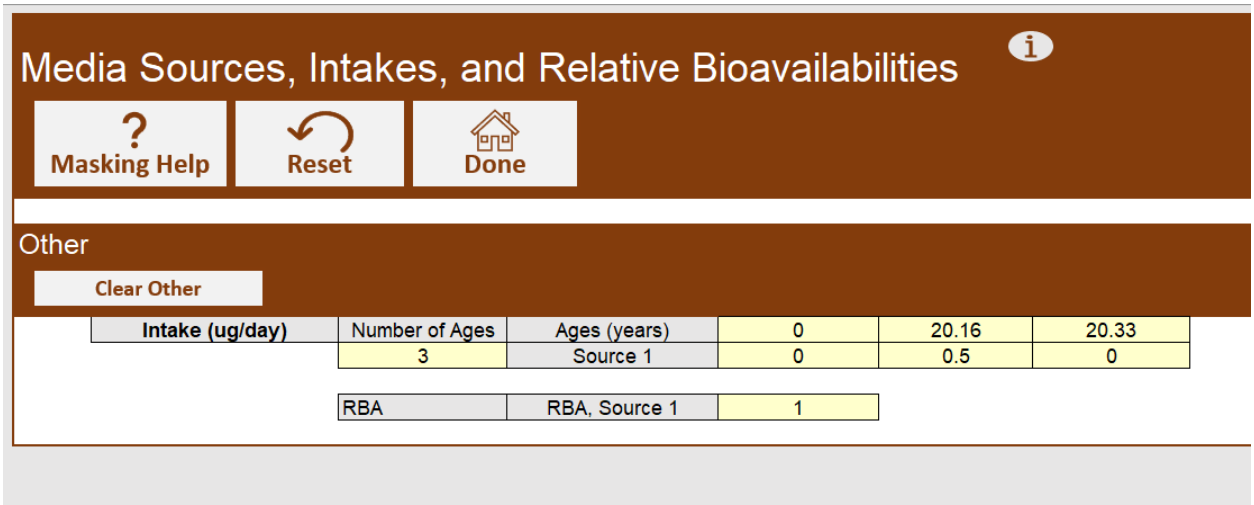


Figure 15 – Screenshot for Adulterated Therapeutic Home Remedies Scenario

b) 1 pill on 1 day per week for 4 months starting at 20 years of age.

- Set up the source to start at age 20 and end at 20.33 (i.e., 20+4*30/365), using stepwise (Cell E34 of the Simulation Control tab). Use the mask "other, mask1, 4, 1, 7, 2, 7". This allows the pill to be taken only on day 1 of each week.

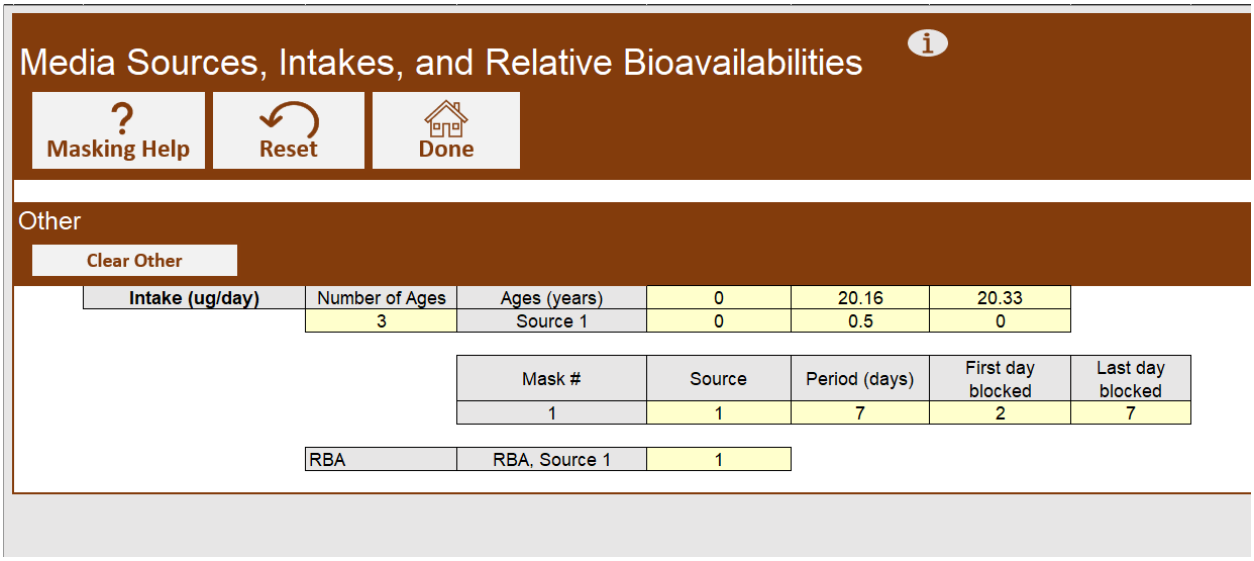


Figure 16 – Screenshot with Masks for Adulterated Therapeutic Home Remedies Scenario

AALM Example Scenarios

These scenarios were developed to give users some starting points in developing their own media exposure scenarios.

Example 1: IEUBK Exposure Scenario

Import: LeggettInput_Ex1.txt

This scenario details how users may replicate an Integrated Exposure Uptake Biokinetic (IEUBK) model v2.0 exposure scenario in the AALM. The scenario begins at birth and ends after 7 years and includes exposure to every medium except “Other” in the AALM or “Alternate” in the IEUBK. This scenario uses IEUBK v2.0 defaults to estimate blood lead levels in a female child. The IEUBK is not sex specific. To best match the IEUBK, it is recommended the simulations for a male and female be averaged.

After importing the file, users can see and adjust imported values from the “Simulation Control” tab by going down the screen to “Item 3”. Set Active Media” and pressing the <Go to Media> button. The soil and dust intake rows are 45 and 55%, respectively, of the IEUBK defaults for soil plus dust ingestion at each year of life. The scenario setup in this example is for an exposure to 200 mg/kg of lead in soil. Press <Done> to exit the “Media” tab. From the “Simulation Control” tab, press <Run Simulation>. After the simulation is complete, users will be on the “Output Selection” tab, press <Explore Data>. When viewing results, users may wish to zoom in on age ranges. To the side of each graph, the min and max value for an axis may be entered. To return to Excel defaults, a non-numeric value may be entered. Also, users should notice that some statistics are provided to the right of each graph. The age ranges can be adjusted by users. The top graph is for blood lead, the average blood lead from the age of 1 year until the child turns 6 years is 2.436 µg/dL with a 6.3% probability of exceeding 5.0 µg/dL. By comparison, the IEUBK model predicts an average blood lead from the age of 1 year until the child turns 6 years is 2.31 µg/dL with a <5.0% probability of exceeding 5.0 µg/dL.

At the top of the screen, press <Done> to return to the “Simulation Control” tab. Sex is changed in Cell E14 of the Simulation Control tab. Change the sex from female to male and press <Run Simulation>. From the “Output Selection” tab, press <Explore Data>. The average blood lead from the age of 1 year until the child turns 6 years is 2.327 µg/dL with a 5.2% probability of exceeding 5.0 µg/dL. Thus, the average (male and female) blood lead is 2.38 µg/dL with a 5.7% probability of exceeding 5.0 µg/dL.

If users opt to run a different soil lead concentration, then for consistency with the IEUBK model, the dust concentration should equal 0.7*(soil lead concentration)+100*(air lead concentration). That is, an equation can be entered into Cell F39 as =0.7*F12+100*F93. Press the <Done> button to return to the “Simulation Control” tab. If <Go to Lung> is selected, users can see parameters imported to mimic the IEUBK model’s respiratory compartment.

Example 1a: IEUBK Exposure Scenario

Import: LeggettInput_Ex1a.txt

Rather than averaging the results for males and females as done in Example 1, this example uses a modified growth curve and hematocrit level to approximate the average of males and females in a single simulation. This approximation is valid for the average blood lead level over the age of 1 to 6 years (i.e., 12 to 72 months in the IEUBK model version 2.0), the age range recommended for assessment of residential sites when using the IEUBK model. The approximation overestimates the average of male and female blood lead levels for 1–2 year-olds by ~1% and underestimates the blood leads of 5–6 year olds by ~1%. Thus, the approximation is best for the average over the full age range from 1 to 6 years and not any individual year of life. The approximation yields a predicted blood lead that is within ±0.01 µg/dL

of the average for males and females for soil lead concentrations between 0 and 700 µg/g with other media (air, diet, and water) remaining at IEUBK v2.0 defaults.

Example 2: Background BLL

Import: LeggettInput_Ex2.txt

This scenario models background blood lead levels. The objective of this scenario was to have a blood lead of 0.6 µg/dL in a female at age 30 using the “Other” pathway. The “Other” pathway can be used to match blood lead levels to NHANES at a particular age. For this example, intakes by the “Other” pathway replace the pathways of soil, indoor dust, water, air, and food. Using the “Other” pathway provides a simple alternative to entering intake rates and concentrations for all media pathways as a function of age to achieve a desired blood lead level.

Press the <Go To Media> button. The “Media” tab will only show a single intake source from the “Other” source. Since a constant intake is used for all ages in this scenario, it is only necessary to enter this value at the age of zero. Press the <Done> button to return to the “Simulation Control” tab and the press the <Run Simulation> button. After a few seconds, when the run completes, users will be on the “Output Summary” tab. Press the <Explore Data> button to access the data results. When viewing results, users may wish to zoom in on age ranges. To the side of each graph, the min and max value for an axis may be entered. To return to Excel defaults, a non-numeric value may be entered. Also, users should notice that some statistics are provided to the right of each graph. The age ranges can be adjusted by users.

This simulation was for a female and it took 5.59 µg/day (with an assumed relative bioavailability of 100%, RBA = 1) to achieve a blood lead concentration of 0.60 µg/dL at 30 years of age. When done viewing the data, press the <Done> button to return to the “Simulation Control” tab. What would it take to reach this same level in a male? Change the sex from Female to Male in Cell E14 and rerun the simulation. The male is found to only reach a blood lead concentration of 0.462 µg/dL at 30 years of age. The difference in the blood concentrations is due largely to the difference in compartmental volumes (in this case blood volume) between males and females. The required intake for a male may be quickly estimated as 5.59 µg/day × (0.600 / 0.462) = 7.26 µg/day. This may be check by adjusting the intake in the “Other” media from 5.59 to 7.62 µg/day and rerunning the simulation.

Example 2a: Background BLL

Import: LeggettInput_Ex2a.txt

Users may notice for Example 2 that using a constant rate of intake from birth to 30 years of age results in rather high blood leads during the first 10 years of life. The file LeggettInput_Ex2a.txt achieves a blood lead of 0.60 µg/dL at 30 years of age while maintaining an average blood lead level of 0.60 µg/dL from 1 to 50 years. After loading LeggettInput_Ex2a.txt, notice that cell E34 on the “Simulation Control” tab has changed from Stepwise to Interpolated. Run the simulation and view results to see that the blood lead is relatively constant across all ages. After returning to the “Simulation Control” tab, users my select <Go to Media> to view the intake array that produced the rather constant blood leads. If the LeggettInput_Ex2.txt is reload, in the “Media” tab, notice that the number of ages in Cell D141 says 1, but more than one age is displayed. This may be corrected by entering 20 into Cell D141 and subsequently entering 1 into Cell D141.

Example 3: Background BLL and Short-term Soil Exposure
Import: LeggettInput_Ex3.txt

This scenario builds on Example 2, with an additional short-term, intermittent soil exposure of 5 days per week to 1000 µg-Pb/g-soil (also, mg/kg or ppm) for 3 months beginning at age 30.

After importing the file, press the <Go to Media> button. Then, notice how the soil exposure is set up and making any desired changes to the scenario. Subsequently, press <Done> to return to the "Simulation Control" tab and press the <Run Simulation> button. After a few seconds, when the run completes, users will be on the "Output Summary" tab. Press the <Explore Data> button to access the data results. When viewing results, users may wish to zoom in on the age range when the intermittent exposure to soil occurred. This may be accomplished by entering 30 in Cell E32 and 30.5 in Cell J32. The y-axis can also be zoomed into by changing Cells C16 and C27 to 0.5 and 1, respectively. After zooming in on the intermittent exposure period, the weekly changes in the estimated blood lead levels are apparent.

Users should notice that some statistics are provided to the right of each graph. The age ranges can be adjusted by users. During this intermittent exposure, the blood lead rises from 0.60 µg/dL at 30 years and is 0.93 µg/dL at 30.25 years. At 30.5 years, the blood lead has decrease back to 0.63 µg/dL.

Example 3b: Background BLL and Short-term Soil Exposure
Import: LeggettInput_Ex3b.txt

This scenario builds on Example 2a, with an additional short-term, intermittent soil exposure of 5 days per week to 1000 µg-Pb/g-soil (also, mg/kg or ppm) for 3 months beginning at age 30. After loading LeggettImput_Ex3a.txt, E34 on the "Simulation Control" tab has changed from Stepwise to Interpolated. This requires that soil exposure be zero until 1 day before 30 years, with an increase at 30 years to 1000 mg/kg. Similarly, the soil exposure goes back to zero at 1 day after 30.25 years.

After running the simulation, on the "Explore Data" tab the results appear nearly identical to Example 2a. The blood lead rises from 0.60 µg/dL at 30 years and is 0.93 µg/dL at 30.25 years. At 30.5 years, the blood lead has decrease back to 0.63 µg/dL. Thus, the increased complexity of keeping the blood lead at approximately 0.60 µg/dL using the "Other" media did not change the results of this adult exposure scenario.

Example 4: Occupational Air Exposure
Import: LeggettInput_Ex4.txt

This scenario models only exposures from air but could also accommodate background blood lead levels using the "Other" media as illustrated in Example 2 and 2a. The objective of this scenario was to model the effect of an occupational air lead exposure on blood lead of a male from birth to 60 years of age. The occupational exposure is assumed to occur for 20 years beginning at the age of 20 years.

After importing the file, users can see and adjust imported values from the "Simulation Control" tab by going down the screen to item "3. Set Active Media" and pressing the <Go to Media> button. The aerosol concentration at the workplace was 50 µg-Pb/m^3 with a daily intake of 3.09 m^3/day. This ventilation rate is from an hourly rate of 0.54 m^3/hour times an 8-hour daily

exposure period times a time-weighting factor of 5/7 for a five day per week exposure. Press the <Done> button to return to the “Simulation Control” tab.

Next, press the <Go to Lung> button [if this button is not visible, turn the air pathway off and back on to view the deposition fractions and transfer rates for this simulation]. As described in Section 2.3.3.1 of the Technical Support Document for the AALM v3.0, parameters for lung deposition, absorption, and elimination kinetics are based largely on a study of human subjects inhaling clean (not excessively carbonaceous due to a fuel rich mixture) automotive exhaust from combustion of fuel containing ^{203}Pb-labeled tetraethyllead. The aerosol particles were reported to be 0.1 μm and below. As such, the lung kinetics (used in AALM v2.0 and v3.0) are most appropriate for near-ultrafine (around 0.1 μm in diameter) combustion aerosols prior to the phase-out of leaded gasoline, in part, because the size of airborne Pb has shifted from <2.5 μm prior to the phase-out of leaded gasoline to somewhere between 2.5 μm and 10 μm after the phase-out. It is anticipated that a future version of the AALM will offer lung kinetics based on the form and size of inhaled Pb particulates.

Press <Done> to return to the “Simulation Control” tab, then press the <Run Simulation> button. When the run completes, users will be on the “Output Summary” tab. Press the <Explore Data> button to access the data results. Adjusting the statistics to the right of the blood lead versus time plot to start at 20 and end at 40 years of age, the average blood lead is observed to be 26.1 μg/dL with a maximum of 28.8 μg/dL, which occurs at 40 years of age.

Example 5: Occupational Air Exposure

Import: LeggettInput_Ex5.txt

This scenario is nearly identical to Example 4, except that the 20-year occupational exposure occurs 5 days per week and not occur 2 days per week.

After importing the file, users can see and adjust imported values from the Simulation Control tab by going down the screen to item “3. Set Active Media”. Compared to Example 4, for Air, the number of sources is now 2 (rather than 1) and the number of “Time Masks” is 1 (rather than 0). Press the <Go to Media> button.

In Example 4, the aerosol concentration was 50 μg-Pb/m^3 with a daily intake of 3.09 m^3/day. That ventilation rate is from an hourly rate of 0.54 m^3/hour times an 8-hour daily exposure period times a time-weighting factor of 5/7 for a five day per week exposure. As in Example 4, the aerosol concentration is 50 μg-Pb/m^3, but it is listed now as a second exposure source. The daily intake is now 4.32 m^3/day rather than 3.09 m^3/day in Example 2 because it is not necessarily to time-weight the intake. In this case, the time-weighting of the intake is accomplished by applying a “Time Mask” that zeros out the exposure by Source 2 on days 6 and 7 of the week. Press the <Done> button to return to the “Simulation Control” tab.

If <Go to Lung> is selected, the deposition fractions and transfer rates for this simulation may be seen. If Source 2 does not appear, press <Done> to return to the “Simulation Control” tab, then chance the number of sources from 2 to 0 and back to 2, then select the <Go to Lung> button. The parameters for Source 1 and Source 2 can differ, but for this example are the same because the exposure outside of the occupational period is minimal. As described in Example 4, the lung kinetics (used in AALM v2.0 and v3.0) are most appropriate for near-ultrafine (around 0.1 μm in diameter) combustion aerosols prior to the phase-out of leaded gasoline.

After importing the file and making any desired changes to the scenario, press the <Run Simulation> button. After a few seconds, when the run completes, users will be on the “Output Summary” tab. Press the <Explore Data> button to access the data results.

Adjusting the statistics to the right of the blood lead versus time plot to start at 20 and end at 40 years of age, the average blood lead is observed to be 26.1 µg/dL with a maximum of 29.3 µg/dL, which occurs at 40 years of age. The maximum was 28.8 µg/dL in Example 4. This difference is due to a 5-day work week that results in slightly greater daily intakes and uptakes of lead. The average blood lead and the average area under the curve are nearly identical. Thus, other than the visualization of the weekly pattern, there is little benefit from the added complexity of this scenario versus that in Example 4. However, the differences in maximal blood leads would be larger in magnitude for scenarios where vacation periods caused a more intermittent exposure pattern.

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