**TO:** Rob DeWoskin, EPA

**FROM:** Gary Diamond, SRC

**DATE:** June 17, 2014

**RE:** Revision to AALM.acsl (or other actions) based on comments received from EPA (06/15/13, 07/11/13, 09/09/13 and 11/06/13 project meetings) and other issues identified by SRC since version AALM v2 061313.

Suggested revisions to AALM-LG.acsl and actual revisions made are shown in the accompanying table. Actual revisions differ from some suggestions; however, these achieve the same objectives.

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| # | Suggested Revision or Action Item | Actual Revision/Action | Files Revised |
| 1 | Create index of output variable names that map to names in AALM-% INPUT&OUTPUT.xlsm | Index created in SUMMARY worksheets | OF INPUT&OUTPUT.xlsm/ SYSTEMIC  LG INPUT&OUTPUT.xlsm/ SYSTEMIC |
| 2 | Create a “READ ME” text file that provides instructions on how to install and run the model | READ ME text file created | README.docx |
| 3 | Convert exposure inputs to days in AALM-OF INPUT&OUTPUT.xlsm | Revised time units of exposure inputs to per day from per year | OF INPUT&OUTPUT.xlsm/ AIR, DUST, WATER, FOOD, OTHER, LUNG |
| 4 | Develop code in AALM-OF.acsl that allows the user to specify a maternal blood lead concentration and initial (day zero) values for lead in blood and tissues (similar the AALM-LG.acsl) | Revised to include parameters and equations to simulate blood and tissue Pb masses at birth based on maternal blood Pb concentration (see Attachment A) | OF.csl  OF INPUT&OUTPUT.xlsm/ SYSTEMIC  OF\_v2\_IN.m |
| 5 | Check text in acslX files and Excel files for typographic errors (e.g., references to OF in LG IN.m files) | Errors corrected | LG\_v2\_IN.m  OF\_v2.csl |
| 6 | Compare output of models for same exposure and absorption assumptions | Completed | Draft report: *Development and Evaluation of All Ages Lead Model (AALM)* |
| 7 | Conduct sensitivity analysis on blood and bone lead (or other useful output variables) | Completed | Draft report: *Development and Evaluation of All Ages Lead Model (AALM)* |
| 8 | Search for and collect data sets to be used for re-optimizing both models against the same data | Completed | Draft report: *Development and Evaluation of All Ages Lead Model (AALM)* |
| 9 | Optimize both models against same data sets | Evaluated RBC models in AALM-LG and AALM-OF. Further evaluations will be conducted in Phase 2. | Draft report: *Development and Evaluation of All Ages Lead Model (AALM)* |
| 10 | Send to Rob for his COTR signoff an updated QA Delivery Tracking Form for review and approval | Workbook was approved by Rob DeWoskin on 06/19/13 |  |
| 11 | Continue to capture notes, screen shots, videos or documentation to include in the user guide and training materials (from 05/15/13 project meeting) | TBD |  |
| 12 | Revise “Gender” tab in INPUT&OUTPUT.xlsm |  | LG IN&OUTPUT.xlsm  OF IN&OUTPUT.xlsm |
| 13 | Revise and finalize “Model Comparison” report | Delivered 11/27/13 | Draft report: *Development and Evaluation of All Ages Lead Model (AALM)* |
| 14 | Archive data collected for model evaluation | Data and references archived in Endnote library (delivered 11/27/13) | Draft report: *Development and Evaluation of All Ages Lead Model (AALM)* |
| Other Miscellaneous Revisions | | | |
| 1 |  | Revised CBLOOD, CRBC and CPLAS to include infinity trap conditional | LG.csl  OF.csl |
| 2 |  | Correct text definition of TOSWET | LG IN&OUTPUT.xlsm/ SYSTEMIC |
| 3 |  | Revised EXPORT macro to save to xlCSV rather than xlTEXT | LG INPUT&OUTPUT.xlsm/ SIMULATION CONTROL  OF INPUT&OUTPUT.xlsm/ SIMULATION CONTROL |
| 4 |  | Revised to output CBLOOD and CPLAS as ug/dL (consistent with AALM-LG) | OF INPUT&OUTPUT.xlsm/ OUTPUT  OF\_OUT.m |
| 5 |  | Revised EXPORT macro to recognize file name from SIM CONTROL | LG INPUT&OUTPUT.xlsm  OF INPUT&OUTPUT.xlsm |
| 6 |  | Revised OF output to include AOTHER (sum of AWELL and APOOR) | OF.csl  OF\_OUT.m  OF INPUT&OUTPUT.xlsm |
| 7 |  | Revised SUMMARY worksheet to include OUTPUT variables | LG INPUT&OUTPUT.xlsm  OF INPUT&OUTPUT.xlsm |
| 8 |  | Revised AALM-LG to output total bone Pb concentration (CBONE) | LG.csl  LG\_OUT.m  LG INPUT&OUTPUT.xlsm |
| 9 |  | Revised AALM-OF output variable name from CBONET to CBONE | OF\_OUT.m  OF INPUT&OUTPUT.xlsm |
| 10 |  | Revised AALM-LG to include output variable for blood volume (AMTBLDT) | LG-csl |
| 11 |  | Revised AALM-LG to simulated blood volume based on OF growth algorithms (i.e., use VBL in place of AMTBLD(T)) | LG.csl |
| 12 |  | Revised AALM-OF to output tissue Pb concentrations in units of ug/g, rather than ug/ml. | OF.csl  OF INPUT&OUTPUT.xlsm |
| 13 |  | Correct bug that omitted water Pb from calculation of total Pb ingested | LG.csl  OF.csl |
| 14 |  | Revised AALM-LG to implement AALM-OF growth algorithm for hematocrit (HCT replaces ADJRBC) | LG.csl  LG\_IN.m  LG INPUT&OUTPUT.xlsm |
| 15 |  | Revised AALM-LG in allow input of parameters for tissue growth | LG INPUT&OUTPUT.xlsm  LG\_IN.m |
| 16 |  | Corrected default values for RCS2B, RCS2DF, RT2SB, RTS2DF (values for S2B and S2DF were transposed) | LG INPUT&OUTPUT.xlsm |
| 17 |  | Added parameter P0 to AALM-OF SYSTEMIC parameter list | OF INPUT&OUTPUT.xlsm  OF\_IN.m |
| 18 |  | Corrected definition of RAD1- RAD8 in AALM-OF SYSTEMIC | OF INPUT&OUTPUT.xlsm |
| 19 |  | Corrected equations for plasma-urine and blood-urine clearance to output in L/day | LG.csl  LG\_OUT.m |
| 20 |  | Added variable PCLEAR to output renal plasma clearance (RAKX/CPLASMA) | OF.csl  OF\_OUT.m |
| 21 |  | Added variables CKICCORT, CLICCORT, CWECCORT to output tissue/bone concentration ratios | OF.csl  OF INPUT&OUTPUT.xlsm  OF\_IN.m |
| 22 |  | Added parameters PKC, PKA, PLC, PLA, PWC, PWA and function using these parameters to calculate age-dependent values for PB, PL and PW. | OF.csl  OF INPUT&OUTPUT.xlsm  OF\_IN.m |
| 23 |  | Added parameters to output bone Pb in units of µg Pb/g mineral (ash) | LG.csl  LG\_OUT.m.  OF.csl  OF\_OUT.m |
| 24 |  | Revised IN…TOTAL statements to remove conditional so that BASE and PULSE intakes are always summed. | LG.csl  OF.csl |
| 19 |  | Added GI-tract state variables for each exposure medium to replace FIN…. statements (e.g. FINDUST). This allows medium-specific absorption to continue when the exposure PULSE is off. | LG.csl |
| 20 |  | Added negative value trap for trabecular bone (TAB) in AALM-OF | OF.csl |
| 21 |  | Revised fetal distribution of Pb (FABLZ, FAKX, FALZ, FABZ, FAOZ) to match AALM-LG | OF INPUT&OUTPUT.xlsm |
|  | Optimization | Revised AF1 parameters (GI absorption fraction) | LG INPUT&OUTPUT.xlsm |
|  | Optimization | Revised TOKDN1 (kidney deposition fraction) | LG INPUT&OUTPUT.xlsm |
|  | Optimization | Revised TOKDN2 kidney deposition fraction) | LG INPUT&OUTPUT.xlsm |
|  | Optimization | Revised TOURIN (urine deposition fraction) | LG INPUT&OUTPUT.xlsm |
|  | Optimization | Revised FLONG (internal bone Pb kinetics) | LG INPUT&OUTPUT.xlsm |
|  | Optimization | Revised RCORT (rate from cortical bone to plasma) | LG INPUT&OUTPUT.xlsm |
|  | Optimization | Revised RKDN2 ((rate from kidney to plasma) | LG INPUT&OUTPUT.xlsm |
|  | Optimization | Revised RLVR2 (rate from liver to plasma) | LG INPUT&OUTPUT.xlsm |
|  | Optimization | Revised RTRAB (rate from trabecular bone to plasma) | LG INPUT&OUTPUT.xlsm |
|  | Optimization | Revised AF1 parameters (GI absorption fraction) | OF INPUT&OUTPUT.xlsm |
|  | Optimization | Revised BIND and KBIND (RBC binding) | OF INPUT&OUTPUT.xlsm |
|  | Optimization | Revised C1, C2, C3 (GFR) | OF INPUT&OUTPUT.xlsm |
|  | Optimization | Added parameters PKZ, PKC and PKA and PK function to simulate age-dependent kidney/plasma partition coefficient | OF.csl  OF\_IN.m  OF INPUT&OUTPUT.xlsm |
|  | Optimization | Added parameters PLZ, PLC and PLA and PL function to simulate age-dependent liver/plasma partition coefficient | OF.csl  OF\_IN.m  OF INPUT&OUTPUT.xlsm |
|  | Optimization | Added parameters PWZ, PWC. and PLA and PW function to simulate age-dependent well-perfused/plasma partition coefficient | OF.csl  OF\_IN.m  OF INPUT&OUTPUT.xlsm |
|  | Optimization | Revised R0 (bone Pb diffusion) | OF INPUT&OUTPUT.xlsm |
|  | Harmonization with IEUBK model | Revised RRBC (rate from RBC to plasma) | LG INPUT&OUTPUT.xlsm |
|  | Harmonization with IEUBK model | Added BIND C1, BINDC2 BINDC3 and BIND function to simulate age-dependent RBC binding kinetics | OF.csl  OF\_IN.m  OF INPUT&OUTPUT.xlsm |
|  | Harmonization with IEUBK model | Added KBIND C1, KBINDC2 KBINDC3 and KBIND function to simulate age-dependent RBC binding kinetics | OF.csl  OF\_IN.m  OF INPUT&OUTPUT.xlsm |

ATTACHMENT A

Fetal model:

CONSTANT MATBLD=1. !Maternal blood Pb ug/dL (SYSTEMIC INPUT)

MBL=MATBLD/100 !Maternal blood Pb (mg/L)

CONSTANT VBLZ=0.225 !Blood volume at birth (L)

CONSTANT FEMATBL=0.85 !Fetal/maternal blood Pb ratio

CONSTANT FABLZ=0.05a !Blood/total body burden Pb mass ratio at birth

CONSTANT FAKZ=0.003a !Kidney/total body burden Pb mass ratio at birth

CONSTANT FALZ=0.009a !Liver/total body burden Pb mass ratio at birth

CONSTANT FABZ=0.90a !Bone /total body burden Pb mass ratio at birth

CONSTANT FAOZ=0.04a !Other tissues/total body burden Pb mass ratio at birth

FAWZ=FAOZ\*0.8a !Well-perfused/total body burden Pb mass ratio at birth

FAPZ=1-(FABLZ+FAKZ+FALZ+FAWZ+FABZ)

ABLZ=MBL\*FEMATBL\*VBLZ !Amount of Pb in blood at birth

BURDENZ=ABLZ/FABLZ ! Amount of Pb in blood at birth

AKZ=BURDENZ\*FAKZ ! Amount of Pb in kidney at birth

ALZ=BURDENZ\*FALZ ! Amount of Pb in liver at birth

AWZ=BURDENZ\*FAWZ ! Amount of Pb in well-perfused tissues at birth

APZ=BURDENZ\*FAPZ ! Amount of Pb in poorly-perfused tissues at birth

CAMCZ=BURDENZ\*FABZ\*0.8 ! Amount of Pb in metabolically active cortical bone at birth

TAMCZ=BURDENZ\*FABZ \*0.2 ! Amount of Pb in metabolically active trabecular bone at birth

aValues based on AALM-OF output at age 90 days (i.e., representing last trimester during which fetal skeleton becomes fully developed.