Comments on the Updated Lead Model and Proposal for a Reduced PEL

Dale Hattis, Ph.D

Clark University

The Experience of Reviewing the OEHHA Modeling and Contributing to Its Refinement

- It is astonishing and gratifying to me to find that work started 36 years ago is still being used today.
- The researchers have shown excellent professionalism and dedication to getting the final predictions as true to the data as possible through several iterations.
- Thorough disclosure of the final model fits and the process for achieving those fits.

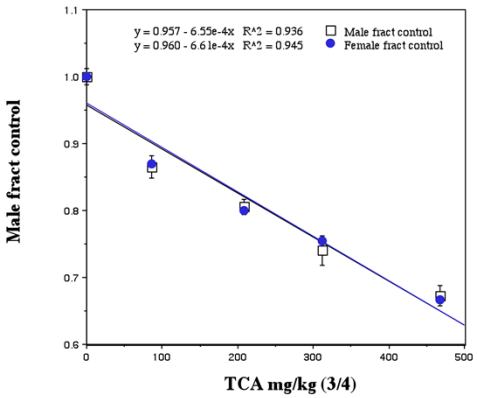
Further Tweaks of Interest for the Kinetic Modeling

- Sensitivity analysis—The parameter set derived clearly produces acceptable fits to the data. But how much would the policy-relevant conclusions change with other choices of acceptable sets of parameter values?
- What differences are likely for workers of different sexes?
- How should the model be adapted for the effects of pregnancy?
  - Likely greater fractional uptake of lead because of the use of the same transporter system involved with extra calcium needed for the baby's bones.
  - Some likely release of lead from bones in late pregnancy if calcium needs are not fully satisfied via the diet.
  - Shorter period of pre-pregnancy exposure than a full working lifetime.

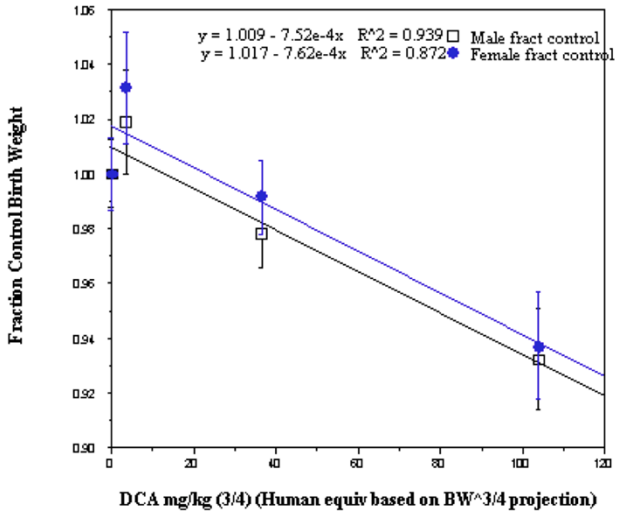
Low Level Effects of Lead Amply Justify Efforts to Further Reduce Worker Exposures into the 5-10 µg/dl Range

- Low level effects on birth weight represent an important signal for likely indirect impacts on infant mortality, neurodevelopmental impairment, and likely other effects.
- From experience with other toxicants, effects on fetal growth are often nearly linear, rather than threshold-like.

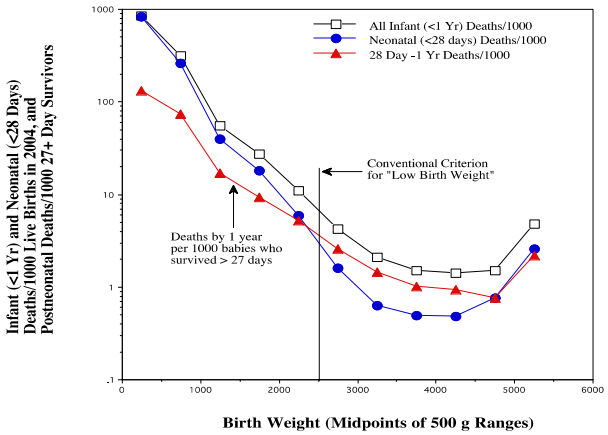
Data of Smith et al. (1989) on the Fetal Weight Response of Rats to Trichloroacetic Acid



Data of Smith et al. (1992) on the Fetal Weight Response of Rats to Dichloroacetic Acid



Continuous Relationship Between Birth Weight and Infant Mortality



Projected Effect on Infant Mortality of Exposure to a Developmental Toxicant Causing a 1% Change in Birth Weights Across the Whole Birth Weight Distribution (assuming that the change in birth weight is closely associated with the causal factors for neonatal and infant deaths)

Birth Weight Range (500g Intervals)	Excess Neonatal Death Rate/1000 Live Births from 1% Birth Weight Shift	Excess Postneonatal Death Rate/1000 Live Births from 1% Birth Weight Shift	Excess Total Infant Death Rate/1000 Live Births from 1% Birth Weight Shift
Less than 500 grams	0.0346	0.0010	0.0355
500-999 grams	0.0797	0.0174	0.0972
1000-1499 grams	0.0152	0.0062	0.0214
1500-1999 grams	0.0235	0.0119	0.0353
2000-2499 grams	0.0290	0.0257	0.0546
2500-2999 grams	0.0219	0.0347	0.0565
3000-3500 grams	0.0021	0.0047	0.0067
3500-3999 grams	-0.0071	-0.0148	-0.0219
4000-4499 grams	-0.0037	-0.0072	-0.0109
4500-4999 grams	-0.0011	-0.0011	-0.0023
5000+ grams	-0.0004	-0.0004	-0.0008
Total <2500 g	0.1819	0.0621	0.2440
Total 2500+g	0.0116	0.0158	0.0274
Total, all birth weights	0.193	0.078	0.271
% of Deaths <2500 g	94.0	79.7	89.9