# UNITED STATES ENVIRONMENTAL PROTECTION AGENCY 

NATIONAL CENTER FOR ENIRONMENTAL ASSESSMENT- RTP DIVISION
Research Triangle Park, NC 27711

OFFICE OF RESEARCH AND DEVELOPMENT

May 9, 2014

## MEMORANDUM

Subject: Identification and consideration of errors in Lanphear et al. (2005), "Low-Level Environmental Lead Exposure and Children's Intellectual Function: An International Pooled Analysis"

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To: Integrated Science Assessment for Lead Docket (EPA-HQ-ORD-2011-0051)

This memorandum documents errors in a publication cited in the 2013 Integrated Science Assessment for Lead (U.S. EPA, 2013, hereafter, 2013 Pb ISA). These errors in Lanphear et al. (2005), "Low-Level Environmental Lead Exposure and Children's Intellectual Function: An International Pooled Analysis," were identified after the completion of the 2013 Pb ISA (see Attachment 1 with Appendix). This memorandum identifies these errors and provisionally considers whether the changes to aspects of Lanphear et al. (2005) that result from correction of the errors materially affect the scientific conclusions made in the 2013 Pb ISA about the effects of Pb exposure on cognitive function or intelligence quotient (IQ).

The 2006 Air Quality Criteria Document for Lead (U.S. EPA, 2006, hereafter, 2006 Pb AQCD) and the 2013 Pb ISA in the current review conclude that the concentration-response relationship between blood Pb and cognitive function in young children is nonlinear, meaning that the IQ decrement per $\mu \mathrm{g} / \mathrm{dL}$ increase in blood Pb level is larger at lower (versus higher) blood Pb levels. This conclusion is based on the findings from several studies (TellezRojo et al., 2006; Kordas et al., 2006; Lanphear et al., 2005; Canfield et al., 2003; Bellinger and Needleman 2003; Lanphear et al., 2000). Lanphear et al. (2005) conducted a pooled analysis of seven cohorts of children and reported a log-linear relationship between IQ and concurrent blood Pb levels; and linear regression coefficients describing the concentration-response relationship for linear models that were larger for subsets of children with peak blood Pb levels less than $7.5 \mu \mathrm{~g} / \mathrm{dL}$ or $10 \mu \mathrm{~g} / \mathrm{dL}$, as compared to subsets with higher peak blood Pb levels. Lanphear et al. (2005) reported these models for concurrent blood Pb, which they state to have the strongest relationship with IQ as measured by R ${ }^{2}$. ${ }^{1}$ The quantitative modeling of Lanphear et al. (2005), focusing on the shape of the concentration-response relationship, was subsequently corroborated in a separate analysis of the same dataset by Rothenberg and Rothenberg (2005).

[^0]Since completion of the 2013 Pb ISA, a publication by Crump et al. (2013) reports findings from a re-analysis of the data for the seven cohorts studied in Lanphear et al. (2005). Crump et al. (2013) reported "some small errors" in the dataset analyzed by Lanphear et al. (2005) and presented results based on analysis of the corrected pooled dataset. ${ }^{2}$ Two of these errors were identified after the completion of the final 2013 Pb ISA (see Attachment 2), while EPA had corrected others in the last Pb NAAQS review such that presentations in the 2013 Pb ISA are not affected. ${ }^{3}$

Using a copy of the pooled dataset, we were able to correct the errors and confirm the calculations of Crump et al. (2013) for specific study results that were affected by these errors (see Attachment 1 with Appendix): (1) the nonlinear effect estimate for the association between IQ and concurrent blood Pb levels; (2) the linear coefficients for the regressions of concurrent blood Pb on IQ for four groups of children in the dataset with peak blood Pb levels below $7.5 \mu \mathrm{~g} / \mathrm{dL}$, at or above $7.5 \mu \mathrm{~g} / \mathrm{dL}$, below $10 \mu \mathrm{~g} / \mathrm{dL}$, and at or above $10 \mu \mathrm{~g} / \mathrm{dL}$; and (3) the $\mathrm{R}^{2}$ values for the models with concurrent, early childhood, peak, and lifetime average blood Pb levels. We re-calculated additional statistics that were not reported in Crump et al. (2013) using the corrected dataset (see Attachment 1 with Appendix): (1) absolute IQ decrements over various concurrent blood Pb ranges based on the log-linear model; (2) statistics on the concurrent blood Pb distribution and number of children in the subsets with peak blood Pb levels below $7.5 \mu \mathrm{~g} / \mathrm{dL}$, at or above $7.5 \mu \mathrm{~g} / \mathrm{dL}$, below $10 \mu \mathrm{~g} / \mathrm{dL}$, and at or above $10 \mu \mathrm{~g} / \mathrm{dL}$; and (3) the coefficients for the concurrent blood Pb level-IQ relationship based on the log-linear model, leaving one cohort out at a time.

Although the model coefficients based on the corrected dataset differ slightly from those in Lanphear et al. (2005) (see Attachment 1), the conclusion drawn regarding the finding of a steeper concentration-response relationship at lower blood Pb levels is unaffected. Further, the errors in Lanphear et al. (2005) do not affect the conclusion in the 2013 Pb ISA or the 2006 Pb AQCD, which was based on findings from several studies, that multiple blood Pb metrics including blood Pb level measured concurrent to $I \mathrm{Q}$, were associated with decrements in cognitive function. After correcting and re-analyzing the Lanphear et al. (2005) dataset, Crump et al. (2013) confirmed the primary findings of Lanphear et al. (2005) stating that, "Although we found some small errors and questionable decisions by Lanphear et al. that, taken alone, could cause doubt in their conclusions, our reanalysis tended to support their conclusions." Further sensitivity analyses performed by Crump et al. (2013), including those designed to test whether findings were robust to various interim modeling decisions, do not alter conclusions drawn from the data.

After this provisional consideration of the corrected results for Lanphear et al. (2005) and the publication by Crump et al. (2013), we conclude that the conclusions drawn in the 2013 Pb ISA are not materially affected by these newly identified errors. Accordingly, EPA is not re-opening the air quality criteria for this review to further consider these studies.

[^1]
## References

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Crump KS, Van Landingham C, Bowers TS, Cahoy D, Chandalia JK. (2013). A statistical reevaluation of the data used in the Lanphear et al. ( 2005 ) pooled-analysis that related low levels of blood lead to intellectual deficits in children. Crit Rev Toxicol 43:785-799.
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ATTACHMENT 1: Errors Identified in Lanphear et al. (2005)
ATTACHMENT 2: Emails from R. Hornung (May 1, 2014) and B. Lanphear (February 24, 2014)

## ATTACHMENT 1

 Errors Identified in Lanphear et al. (2005)Two aspects to the dataset for the Boston cohort were not accurately represented in the analyses reported in Lanphear et al. 2005. ${ }^{4}$ They are as follows (see Attachment 2).

- The IQ data analyzed were for performance IQ rather than full-scale IQ.
- The blood Pb measurements at 6,12 , and 24 months were transformed incorrectly.

Selected Crump et al. (2013) calculations that were confirmed by NCEA with the Boston cohort data correctly represented ${ }^{5}$ and statistics from Lanphear et al. (2005) that were re-calculated by EPA are summarized below and presented in detail in Table 1.
a. The log-linear coefficient for concurrent blood Pb changes from -2.70 to -2.65.
b. The model with early childhood blood Pb (rather than concurrent) would have highest $\mathrm{R}^{2}$, although the values are still very similar ( 0.6433 as compared to 0.6414 for concurrent metric).
c. The linear coefficient for concurrent blood Pb with IQ for the subgroup of children with peak blood Pb levels $<7.5 \mu \mathrm{~g} / \mathrm{dL}$ changes from -2.94 to -2.53 .
d. The number of children in each of the four linear subset analyses (peak blood Pb below $7.5 \mu \mathrm{~g} / \mathrm{dL}$, at or above $7.5 \mu \mathrm{~g} / \mathrm{dL}$, below $10 \mu \mathrm{~g} / \mathrm{dL}$, and at or above $10 \mu \mathrm{~g} / \mathrm{dL}$ ) changes as do the descriptive statistics for concurrent blood in these subsets. For example for the subgroup with peak $<7.5 \mu \mathrm{~g} / \mathrm{dL}$, the sample size changes from 103 to 118 and the mean blood Pb concentrations from 3.24 to $3.3 \mu \mathrm{~g} / \mathrm{dL}$.

[^2]Table 1. Statistics associated with Lanphear et al. (2005) that were recalculated by EPA

| Finding from Lanphear et al. (2005) | Corrected information | Previously reported information | Page number in 2013 Pb ISA where mentioned |
| :---: | :---: | :---: | :---: |
| Log-linear model coefficient for blood Pb metrics and IQ, adjusted for site, HOME score, birth weight, maternal IQ, and maternal education (Table 4) | Early childhood: -2.21 (-3.38, -1.04) <br> Peak: -2.86 (-4.10, -1.61) <br> Lifetime average: -3.14 (-4.39, -1.88) <br> Concurrent: - $2.65(-3.69,-1.61)^{6}$ | Early childhood: -2.04 (-3.27, -0.81) <br> Peak: -2.85 (-4.10, -1.60) <br> Lifetime average: -3.04 (-4.33, -1.75) <br> Concurrent: -2.70 (-3.74, -1.66) | 4-70, 4-254 |
| IQ decrement over different concurrent blood Pb ranges based on the log-linear model | 2.4 to $30 \mu \mathrm{~g} / \mathrm{dL}$ : 6.7 IQ pts (4.1-9.3) 2.4 to $10 \mu \mathrm{~g} / \mathrm{dL}: 3.8 \mathrm{IQ}$ pts (2.3-5.3) 10 to $20 \mu \mathrm{~g} / \mathrm{dL}: 1.8 \mathrm{IQ}$ pts (1.1-2.6) 20 to $30 \mu \mathrm{~g} / \mathrm{dL}$ : 1.1 IQ pts ( $0.7-1.5$ ) | $\begin{aligned} & 2.4-30 \mu \mathrm{~g} / \mathrm{dL}: 6.9 \mathrm{IQ} \text { pts (4.2-9.4) } \\ & 2.4-10 \mu \mathrm{~g} / \mathrm{dL}: 3.9 \mathrm{IQ} \text { pts (2.4-5.3) } \\ & 10-20 \mu \mathrm{~g} / \mathrm{dL}: 1.9 \mathrm{IQ} \text { pts }(1.2-2.6) \\ & 20-30 \mu \mathrm{~g} / \mathrm{dL}: 1.1 \mathrm{IQ} \text { pts (0.7-1.5) } \end{aligned}$ | 4-70 |
| Linear coefficient, sample size ( n ) and concurrent blood Pb level measurements (mean, minimum, $5^{\text {th }}$ and $95^{\text {th }}$ percentiles, and maximum) for subset with peak blood Pb levels $<7.5 \mu \mathrm{~g} / \mathrm{dL}$ | $\begin{aligned} & -2.53(-4.48,-0.58)^{6} \\ & \mathrm{~N}=118 \\ & (3.3,0.9,1.1,6.7,7.4 \mu \mathrm{~g} / \mathrm{dL}) \end{aligned}$ | $\begin{aligned} & -2.94(-5.16,-0.71) \\ & \mathrm{N}=103 \\ & (3.24,0.9,1.3,6.0,7.4 \mu \mathrm{~g} / \mathrm{dL})^{7} \end{aligned}$ | Figure 4-2, Table 4-3, Figure 4-15, Table 4-16 pp. 4-70, 4-124, 4-285 |
| Linear coefficient, sample size ( n ) and concurrent blood Pb measurements (mean, minimum, $5^{\text {th }}$ and $95^{\text {th }}$ percentiles, and maximum) for subset with peak blood Pb levels $\geq 7.5 \mu \mathrm{~g} / \mathrm{dL}$ | $\begin{aligned} & -0.15(-0.19,-0.11)^{6} \\ & \mathrm{~N}=1215 \\ & (13.0,0.1,3.7,34.2,71.7) \end{aligned}$ | $\begin{aligned} & -0.16(-0.24,-0.08) \\ & N=1230 \\ & (12.9,0.1,3.5,34.0,71.7)^{7} \end{aligned}$ | Figure 4-15, Table 4-16 |
| Linear coefficient, sample size ( n ) and concurrent blood Pb measurements (mean, minimum, $5^{\text {th }}$ and $95^{\text {th }}$ percentiles and maximum) for subset with peak blood $\mathrm{Pb}<10 \mu \mathrm{~g} / \mathrm{dL}$ | $\begin{aligned} & -0.77(-1.65,0.12)^{6} \\ & \mathrm{~N}=258 \\ & (4.4,0.1,1.4,8.0,9.8) \end{aligned}$ | $\begin{aligned} & -0.80(-1.74,0.14) \\ & \mathrm{N}=244 \\ & (4.3,0.1,1.4,8,0,9.8)^{7} \end{aligned}$ | Figure 4-15, Table 4-16 pp. 4-70, 4-124 |
| Linear coefficient, sample size ( n ) and concurrent blood Pb measurements (mean, minimum, $5^{\text {th }}$ and $95^{\text {th }}$ percentiles, and maximum) for subset with peak blood Pb levels $\geq 10 \mu \mathrm{~g} / \mathrm{dL}$ ) | $\begin{aligned} & -0.13(-0.22,-0.04)^{6} \\ & \mathrm{~N}=1075 \\ & (14.0,0.1,4.4,35.5,71.7) \end{aligned}$ | $\begin{aligned} & -0.13(-0.23,-0.03) \\ & N=1089 \\ & (13.9,0.1,4.3,35.4,71.7)^{7} \end{aligned}$ | Figure 4-15, Table 4-16 |
| Blood Pb metric with the largest $\mathrm{R}^{2}$ for the relationship with IQ in the log-linear models | Early childhood R2: 0.6433 = largest <br> Peak R²: 0.6401 <br> Lifetime average $\mathrm{R}^{2}$ : 0.6411 <br> Concurrent R2: 0.6414 | Concurrent (no quantitative results presented) | 4-256 |
| Sensitivity of concurrent blood $\mathrm{Pb}-\mathrm{IQ}$ association to omitting one cohort | Slopes ranged from -2.36 to -2.94 | Slopes range from -2.31 to -2.94 | 4-72, 4-76, 4-124, 4-284 |
| Number of children from Boston cohort with peak blood Pb levels $<7.5 \mu \mathrm{~g} / \mathrm{dL}$ | Boston $=28$ | Boston $=13$ | 4-62 |

[^3]
## Appendix to Attachment 1

## Computer Code for EPA Recalculations

```
libname pooled '\\AA.AD.EPA.GOV\ORD\RTP\USERS\K-Q\mpatel04\Net
MyDocuments\Lead\Pooled Dataset';
proc format;
value lgender 0='Male'
            1='Female';
value lrace 0='Non-white'
                1='White';
value YN O='NO'
    1='Yes';
data pooled.BostonPb; set pooled.tablespaper;
/*tablespaper is the uncorrected SAS dataset */
if site NE "Boston" then delete;
pbch6m2 = pbch6m-2;
pbch1y2 = pbch1y-2;
pbch2y2 = pbch2y-2;
rename pbch6m2 = pbch3 pbch1y2 = pbch1 pbch2y2 = pbch2 pbch4y = pbch4;
/*This program was first run without subtracting 2 from the blood Pb metrics.
The purpose of this first run on the original variables was to check whether
the calculations in this program could replicate the early childhood and
lifetime average blood Pb levels reported in the Lanphear paper*/
keep ID pbch6m2 pbch1y2 pbch2y2 pbch4y lead peaklead meanlead6m_concurrent
meanlead6m_24m pbch6m pbch1y pbch2y peakl10 peakl75;
run;
proc sort; by ID;
run;
data pooled.BostonPb2; set pooled.BostonPb;
array pbarray[4] pbch1-pbch4;
do I = 1 to 4;
pbch = pbarray[I];
if pbch NE . then output;
end;
keep ID pbch;
run;
proc sort; by ID;
run;
proc means noprint;
var pbch;
by ID;
output out = pooled.bostonPb3;
run;
data pooled.Bostonmax; set pooled.bostonPb3;
if _stat_ = "MAX";
peak2 = pbch;
drop _type_ _freq_ __stat_ pbch;
```

```
run;
data pooled.Bostonavg; set pooled.bostonPb3;
if _stat_ = "MEAN";
life = pbch;
drop _type_ _freq_ _stat_ pbch;
run;
data pooled.Bostonearly; set pooled.BostonPb;
array pbarray[3] pbch1-pbch3;
do M = 1 to 3;
pbch = pbarray[M];
if pbch NE . then output;
end;
keep ID pbch;
run;
proc sort; by ID; run;
proc means noprint;
var pbch;
by ID;
output out = pooled.Bostonpb4;
run;
data pooled.bostonearly2; set pooled.Bostonp.b4;
if _stat_ = "MEAN";
early = pbch;
drop _type_ _freq_ _stat_ pbch;
run;
data pooled.bostonnewPb;
merge pooled.Bostonmax pooled.BostonPb pooled.Bostonearly2 pooled.BostonPb
pooled.Bostonavg;
by ID;
if peak2 LT 10 then peakl10_2 = 1;
if peak2 GE 10 then peakl10_2 = 0;
if peak2 LT 7.5 then peakl75_2 = 1;
if peak2 GE 7.5 then peakl75_2 = 0;
keep ID peaklead peak2 peakl10 peakl10_2 peakl75 peakl75_2 early life;
run;
data pooled.Lanphearcorrected;
merge pooled.bostonnewPb (keep = ID peak2 early life peakl10_2 peakl75_2)
pooled.tablespaper;
by ID;
if Site = "Boston" then iq = wiscrl0v;
if Site = "Boston" then meanlead6m_24m = early;
if Site = "Boston" then meanlead6m_concurrent = life;
if Site = "Boston" then peaklead = peak2;
if Site = "Boston" then if peakll0 = 1 then if peakl10_2 = 1 then peakl10 =
1;
if Site = "Boston" then if peakll0 = 0 then if peakl10_2 = 0 then peakl10 =
0;
```

```
if Site = "Boston" then if peakl10 = 0 then if peakl10_2 = 1 then peakl10 =
1;
if Site = "Boston" then if peakl75 = 1 then if peakl75_2 = 1 then peakl75 =
1;
if Site = "Boston" then if peakl75 = 0 then if peakl75_2 = 0 then peakl75 =
0;
if Site = "Boston" then if peakl75 = 0 then if peakl75_2 = 1 then peakl75 =
1;
if lead=0 then lead=0.1;
loglead = log(lead);
logpeak = log(peaklead);
logearly = log(meanlead6m_24m);
loglife = log(meanlead6m_concurrent);
run;
proc freq; tables peakl10 peakl75; run;
proc glm;
            class site;
            model wiscr10t = lead/ solution ss3;
            where site = "Boston";
run;
proc glm;
    class site;
    model wiscr10p = lead/ solution ss3;
    where site = "Boston";
run;
proc glm;
    class site;
    model wiscr10t = pbch2y/ solution ss3;
    where site = "Boston";
run;
proc glm;
    class site;
    model wiscr10p = pbch2y/ solution ss3;
    where site = "Boston";
run;
proc glm;
    class site;
    model iq = loglead site birthwt HOME momiq momeduc/ solution ss3;
run;
proc glm;
    class site;
    model iq = logpeak site birthwt HOME momiq momeduc/ solution ss3;
run;
proc glm;
    class site;
    model iq = logearly site birthwt HOME momiq momeduc/ solution ss3;
```

run;

```
proc glm;
    class site;
    model iq = loglife site birthwt HOME momiq momeduc/ solution ss3;
run;
```

proc glm;
class site;
model iq = lead site birthwt HOME momiq momeduc/ solution ss3;
where peakl10 = 1;
run;
proc glm;
class site;
model iq = lead site birthwt HOME momiq momeduc/ solution ss3;
where peakl10 = 0;
run;
proc glm;
class site;
model iq = lead site birthwt HOME momiq momeduc/ solution ss3;
where peakl75 = 1;
run;
proc glm;
class site;
model iq = lead site birthwt HOME momiq momeduc/ solution ss3;
where peakl75 = 0;
run;
proc sort; by peakl10; run;
proc univariate; var lead; by peakl10; run;
proc sort; by peakl75; run;
proc univariate; var lead; by peakl75; run;
/*The data steps and models below estimate the concurrent blood Pb-IQ
association for a log linear model, excluding one of the seven cohorts*/
data pooled.noBos; set pooled.Lanphearcorrected;
if site EQ "Boston" then delete;
run;
proc glm;
class site;
model iq = loglead site birthwt HOME momiq momeduc/ solution ss3;
run;
data pooled.noRoc; set pooled.Lanphearcorrected;
if site EQ "Rochester" then delete;
run;

```
proc glm;
        class site;
    model iq = loglead site birthwt HOME momiq momeduc/ solution ss3;
run;
data pooled.noCle; set pooled.Lanphearcorrected;
if site EQ "Cleveland" then delete;
run;
proc glm;
        class site;
    model iq = loglead site birthwt HOME momiq momeduc/ solution ss3;
run;
data pooled.noCin; set pooled.Lanphearcorrected;
if site EQ "Cincinnati" then delete;
run;
proc glm;
        class site;
        model iq = loglead site birthwt HOME momiq momeduc/ solution ss3;
run;
data pooled.noMC; set pooled.Lanphearcorrected;
if site EQ "Mexico" then delete;
run;
proc glm;
        class site;
        model iq = loglead site birthwt HOME momiq momeduc/ solution ss3;
run;
data pooled.noPir; set pooled.Lanphearcorrected;
if site EQ "PortPirie" then delete;
run;
proc glm;
        class site;
    model iq = loglead site birthwt HOME momiq momeduc/ solution ss3;
run;
data pooled.noYug; set pooled.Lanphearcorrected;
if site EQ "Yugoslavia" then delete;
run;
proc glm;
    class site;
    model iq = loglead site birthwt HOME momiq momeduc/ solution ss3;
run;
```

Output from Statistical Program

| The SAS System |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: |
| The FREQ Procedure |  |  |  |  |
| peakl10 | Frequency | Percent | Cumulative Frequency | Cumulative Percent |
| 0 | 1075 | 80.65 | 1075 | 80.65 |
| 1 | 258 | 19.35 | 1333 | 100.00 |
| peakl75 | Frequency | Percent | Cumulative Frequency | Cumulative Percent |
| 0 | 1215 | 91.15 | 1215 | 91.15 |
| 1 | 118 | 8.85 | 1333 | 100.00 |







| Parameter | Estimate | Standard Error | t Value | $\operatorname{Pr}>\|\mathrm{t}\|$ |
| :--- | ---: | ---: | ---: | ---: |
| momiq | 0.28757382 | 0.02995124 | 9.60 | $<.0001$ |
| momeduc | 0.42930586 | 0.16258963 | 2.64 | 0.0084 |

Note: The $X^{\prime} X$ matrix has been found to be singular, and a generalized inverse was used to solve the normal equations. Terms whose estimates are followed by the letter ' $B$ ' are not uniquely estimable.


| Parameter | Estimate | Standard Error | t Value | $\operatorname{Pr}>\|t\|$ |
| :--- | ---: | ---: | ---: | ---: |
| momiq | 0.29342850 | 0.02994677 | 9.80 | $<.0001$ |
| momeduc | 0.43788970 | 0.16283718 | 2.69 | 0.0073 |

Note: The $X^{\prime} X$ matrix has been found to be singular, and a generalized inverse was used to solve the normal equations. Terms whose estimates are followed by the letter ' $B$ ' are not uniquely estimable.


| Parameter | Estimate | Standard Error | t Value | $\operatorname{Pr}>\|t\|$ |
| :--- | ---: | ---: | ---: | ---: |
| momiq | 0.29979643 | 0.03008290 | 9.97 | $<.0001$ |
| momeduc | 0.45768747 | 0.16355034 | 2.80 | 0.0052 |

Note: The $X^{\prime} X$ matrix has been found to be singular, and a generalized inverse was used to solve the normal equations. Terms whose estimates are followed by the letter ' $B$ ' are not uniquely estimable.


| Parameter | Estimate | Standard Error | t Value | $\operatorname{Pr}>\|\mathrm{t}\|$ |
| :--- | ---: | ---: | ---: | ---: |
| momiq | 0.29347023 | 0.02990008 | 9.82 | $<.0001$ |
| momeduc | 0.42795513 | 0.16267152 | 2.63 | 0.0086 |

Note: The $X^{\prime} X$ matrix has been found to be singular, and a generalized inverse was used to solve the normal equations. Terms whose estimates are followed by the letter ' $B$ ' are not uniquely estimable.


| Parameter | Estimate | Standard Error | t Value | $\mathrm{Pr}>\|\mathrm{t}\|$ |
| :--- | ---: | ---: | ---: | ---: |
| momeduc | 0.55327718 | 0.42961372 | 1.29 | 0.1990 |

Note: The X'X matrix has been found to be singular, and a generalized inverse was used to solve the normal equations. Terms whose estimates are followed by the letter ' $B$ ' are not uniquely estimable.


| Parameter | Estimate | Standard Error | t Value | Pr $>\|t\|$ |
| :--- | ---: | ---: | ---: | ---: |
| momiq | 0.28269110 | 0.03355449 | 8.42 | $<.0001$ |
| momeduc | 0.42897703 | 0.17660106 | 2.43 | 0.0153 |

Note: The $X^{\prime} X$ matrix has been found to be singular, and a generalized inverse was used to solve the normal equations. Terms whose estimates are followed by the letter ' $B$ ' are not uniquely estimable.


| Parameter | Estimate | Standard Error | t Value | $\mathrm{Pr}>\|\mathrm{t}\|$ |
| :--- | ---: | ---: | ---: | ---: |
| momeduc | 1.04376665 | 0.74059265 | 1.41 | 0.1616 |

Note: The X'X matrix has been found to be singular, and a generalized inverse was used to solve the normal equations. Terms whose estimates are followed by the letter ' $B$ ' are not uniquely estimable.


| Parameter | Estimate | Standard Error | t Value | $\operatorname{Pr}>\|\mathrm{t}\|$ |
| :--- | ---: | ---: | ---: | ---: |
| momiq | 0.30003407 | 0.03106150 | 9.66 | $<.0001$ |
| momeduc | 0.42343226 | 0.16570453 | 2.56 | 0.0107 |

Note: The $X^{\prime} X$ matrix has been found to be singular, and a generalized inverse was used to solve the normal equations. Terms whose estimates are followed by the letter ' $B$ ' are not uniquely estimable.


| Value | Obs | Value | Obs |
| ---: | ---: | ---: | ---: |
| 0.1 | 691 | 56.3 | 476 |
| 0.8 | 699 | 60.3 | 564 |
| 0.9 | 725 | 63.6 | 546 |
| 1.1 | 721 | 68.3 | 481 |
| 1.4 | 694 | 71.7 | 553 |



| Value | Obs | Value | Obs |
| ---: | ---: | ---: | ---: |
| 0.1 | 1290 | 9.0 | 1271 |
| 0.1 | 1288 | 9.0 | 1328 |
| 0.1 | 1266 | 9.5 | 1284 |
| 0.5 | 1257 | 9.7 | 1182 |
| 0.9 | 1296 | 9.8 | 1259 |



| Value | Obs | Value | Obs |
| ---: | ---: | ---: | ---: |
| 0.1 | 1181 | 56.3 | 476 |
| 0.1 | 1168 | 60.3 | 564 |
| 0.1 | 691 | 63.6 | 546 |
| 0.5 | 1165 | 68.3 | 481 |
| 0.8 | 699 | 71.7 | 553 |



| Extreme Observations |  |  |  |
| ---: | :---: | ---: | :---: |
| Lowest |  | Highest |  |
| Value | Obs | Value | Obs |
| 0.1 | 1323 | 6.8 | 1244 |
| 0.9 | 1328 | 7.0 | 1227 |
| 1.0 | 1305 | 7.0 | 1249 |
| 1.1 | 1302 | 7.1 | 1317 |
| 1.1 | 1279 | 7.4 | 1325 |


| The SAS System |  |
| :---: | :---: |
|  | The GLM Procedure Class Level Information |
| Class Levels site 6 | Values <br> Cincinnati Cleveland Mexico PortPirie Rochester Yugoslavia |
|  | $\begin{array}{ll}\text { Number of Observations Read } & 1217 \\ \text { Number of Observations Used } & 1217\end{array}$ |
|  | The SAS System |
|  | The GLM Procedure |

Dependent Variable: iq

| Source | DF | Sum of Squares | Mean Square | F Value | Pr $>$ F |
| :--- | ---: | ---: | ---: | ---: | ---: |
| Model | 10 | 236289.1250 | 23628.9125 | 173.27 | $<.0001$ |
| Error | 1206 | 164459.3614 | 136.3676 |  |  |
| Corrected Total | 1216 | 400748.4864 |  |  |  |
|  |  |  |  |  |  |

R-Square Coeff Var Root MSE iq Mean

| Source | DF | Type III SS |  | Mean Square | F Value | $\mathrm{Pr}>\mathrm{F}$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| loglead | 1 | 3316.01053 |  | 3316.01053 | 24.32 | <. 0001 |
| site | 5 | 64980.50802 |  | 12996.10160 | 95.30 | <. 0001 |
| birthwt | 1 | 2064.61424 |  | 2064.61424 | 15.14 | 0.0001 |
| home | 1 | 9235.3146 |  | 9235.31461 | 67.72 | <. 0001 |
| momiq | 1 | 12385.71930 |  | 12385.71930 | 90.83 | <. 0001 |
| momeduc | 1 | 613.66271 |  | 613.66271 | 4.50 | 0.0341 |
| Parameter |  | Estimate |  | Standard Error | r t Value | Pr $>\|t\|$ |
| Intercept |  | 28.31031692 | B | 4.05184024 | $4 \quad 6.99$ | <. 0001 |
| loglead |  | -2.94149749 |  | 0.59650787 | $7 \quad-4.93$ | < 00001 |
| site Cincinnati |  | 13.04475988 | B | 1.33636189 | 99.76 | < 00001 |
| site Cleveland |  | 12.27990700 | B | 1.44363380 | $0 \quad 8.51$ | < 00001 |
| site Mexico |  | 25.62621387 | B | 1.51767586 | $6 \quad 16.89$ | <. 0001 |
| site PortPirie |  | 22.18590267 | B | 1.20511010 | $0 \quad 18.41$ | < 00001 |
| site Rochester |  | 7.11859842 | B | 1.52466887 | $7 \quad 4.67$ | <. 0001 |
| site Yugoslavia |  | 0.00000000 | B |  | . . | . |
| birthwt |  | 0.00266431 |  | 0.00068473 | $3 \quad 3.89$ | 0.0001 |
| home |  | 0.50824816 |  | 0.06175976 | $6 \quad 8.23$ | < 30001 |
| momiq |  | 0.30374683 |  | 0.03187181 | 19.53 | < 30001 |


| Parameter | Estimate | Standard Error | t Value | $\mathrm{Pr}>\|\mathrm{t}\|$ |
| :--- | ---: | ---: | ---: | ---: |
| momeduc | 0.34980816 | 0.16490002 | 2.12 | 0.0341 |

Note: The X'X matrix has been found to be singular, and a generalized inverse was used to solve the normal equations. Terms whose estimates are followed by the letter ' $B$ ' are not uniquely estimable.


| Parameter | Estimate | Standard Error | $\mathbf{t}$ Value | $\operatorname{Pr}>\|\mathrm{t}\|$ |
| :--- | ---: | ---: | ---: | ---: |
| momeduc | 0.39387949 | 0.16985313 | 2.32 | 0.0206 |

Note: The $X^{\prime} X$ matrix has been found to be singular, and a generalized inverse was used to solve the normal equations. Terms whose estimates are followed by the letter 'B' are not uniquely estimable.


| Parameter | Estimate | Standard Error | t Value | $\mathrm{Pr}>\|\mathrm{t}\|$ |
| :--- | ---: | ---: | ---: | ---: |
| momeduc | 0.40255200 | 0.16630391 | 2.42 | 0.0156 |

Note: The X'X matrix has been found to be singular, and a generalized inverse was used to solve the normal equations. Terms whose estimates are followed by the letter ' $B$ ' are not uniquely estimable.


| Parameter | Estimate | Standard Error | t Value | $\mathrm{Pr}>\|\mathrm{t}\|$ |
| :--- | ---: | ---: | ---: | ---: |
| momeduc | 0.47313581 | 0.17261689 | 2.74 | 0.0062 |

Note: The $X^{\prime} \mathrm{X}$ matrix has been found to be singular, and a generalized inverse was used to solve the normal equations. Terms whose estimates are followed by the letter 'B' are not uniquely estimable.


| Parameter | Estimate | Standard Error | t Value | Pr $>\|t\|$ |
| :--- | ---: | ---: | ---: | ---: |
| momeduc | 0.59716095 | 0.17751548 | 3.36 | 0.0008 |

Note: The X'X matrix has been found to be singular, and a generalized inverse was used to solve the normal equations. Terms whose estimates are followed by the letter ' $B$ ' are not uniquely estimable.


| Parameter | Estimate | Standard Error | t Value | $\mathrm{Pr}>\|\mathrm{t}\|$ |
| :--- | ---: | ---: | ---: | ---: |
| momeduc | 0.48953177 | 0.16642243 | 2.94 | 0.0033 |

Note: The X'X matrix has been found to be singular, and a generalized inverse was used to solve the normal equations. Terms whose estimates are followed by the letter ' $B$ ' are not uniquely estimable.


| Parameter | Estimate | Standard Error | t Value | $\mathrm{Pr}>\|\mathrm{t}\|$ |
| :--- | ---: | ---: | ---: | ---: |
| momeduc | 0.22179064 | 0.23465774 | 0.95 | 0.3448 |

Note: The X'X matrix has been found to be singular, and a generalized inverse was used to solve the normal equations. Terms whose estimates are followed by the letter ' $B$ ' are not uniquely estimable.

## Derivation of IQ Decrements over Various Blood Pb Ranges

| A | B | C | D | E | F | G | H | 1 | J | K | L | M | N | 0 |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Model coefficient for concurrent blood Pb | lower confidence limit | upper confidence limit | minimum <br> blood Pb <br> in range of <br> interest | maximum <br> blood Pb <br> in range of interest | In of minimum blood Pb | In of maximum blood Pb | difference in In of blood Pb | difference <br> in <br> maximum <br> and <br> minimum <br> blood Pb <br> of interest | slope over the blood Pb range of interest | lower confidence limit for slope over the blood Pb range of interest | upper confidence limit for slope over the blood Pb range of interest | IQ decrement over the blood Pb range of interest | lower <br> bound of <br> absolute <br> IQ <br> decrement | Upper bound of IQ decrement |
| -2.65 | -3.69 | -1.61 | 2.4 | 30 | 0.88 | 3.40 | 2.53 | 27.6 | -0.24 | -0.34 | -0.15 | 6.7 | 4.1 | 9.3 |
| -2.65 | -3.69 | -1.61 | 2.4 | 10 | 0.88 | 2.30 | 1.43 | 7.6 | -0.50 | -0.69 | -0.30 | 3.8 | 2.3 | 5.3 |
| -2.65 | -3.69 | -1.61 | 10 | 20 | 2.30 | 3.00 | 0.69 | 10 | -0.18 | -0.26 | -0.11 | 1.8 | 1.1 | 2.6 |
| -2.65 | -3.69 | -1.61 | 20 | 30 | 3.00 | 3.40 | 0.41 | 10 | -0.11 | -0.15 | -0.07 | 1.1 | 0.7 | 1.5 |
| Formula for cell |  |  |  |  | = LN(D) | = LN(E) | =G-F | =E-D | =A*H/I | =B*H/I | $=C^{*} \mathrm{H} / \mathrm{l}$ | $=-\left({ }^{*} \mid\right)$ | $=-\left(\right.$ L* $\left.^{*}\right)$ | $=-\left(K^{*}\right)$ |

## ATTACHMENT 2

Emails from R. Hornung (May 1, 2014) and B. Lanphear (February 24, 2014)

Kirrane, Ellen
From: Hornung, Richard (Rick) [Richard.Hornung@cchmc.org]
Sent: Thursday, May 01, 2014 10:03 AM
To:
Cc:
Subject:
Kirrane, Ellen
Bruce Lanphear; Patel, Molini
RE: Lanphear et al. 2005

Hi Ellen
I was able to contact Bruce and also Jane Khoury who assembled the pooled data set. We were able to check older data files and we did find that the blood Pb values for Boston for children at $6,12,18$, and 24 months had a minimum of 2.0 . Dr. Khoury did not recall adding 1.0 to the antilog of the log-transformed data, but we agree that it appears that the correction of subtracting 2.0 from these values for the Boston cohort was appropriate.

Regards,
Rick

| From: | Bruce Lanphear [bpl3@sfu.ca] |
| :--- | :--- |
| Sent: | Monday, February 24, 2014 5:27 PM |
| To: | Kirrane, Ellen |
| Cc: | Richard Hornung (Rick); Patel, Molini |
| Subject: | Re: Conference call and follow-up |

Ellen and others:
I am available on March 4th from 7:00 am to 9:00 am PT (I am assuming you meant 10:00 am to 12:00 pm ET, right?).

We did verify that we inadvertently switched full-scale IQ with performance IQ. We also verified that it didn't change the primary results.

Rick can make sure we use the correct data.
Best regards,
Bruce


[^0]:    ${ }^{1}$ The 2006 Pb AQCD and 2013 Pb ISA also evaluated scientific information regarding critical lifestages and time periods of Pb exposure and concluded that decrements in cognitive function were found with several different blood Pb metrics that represent blood Pb during lifestages or time periods from the prenatal period through adolescence (e.g., 2013 Pb ISA, pp. xciv, 4-57, 4-76, 4-248; 4-256, Table 4-14).

[^1]:    ${ }^{2}$ Errors in the Lanphear et al. (2005) pooled dataset identified by Crump et al. (2013) also apply to Rothenberg and Rothenberg (2005) who relied on the same original dataset.
    ${ }^{3}$ We have contacted the primary authors and have received confirmation of the two recently identified errors in the dataset analyzed by Lanphear et al. (2005) (see Attachment 2).

[^2]:    ${ }^{4}$ During the 2008 Pb NAAQS review, three typographical errors were identified in Lanphear et al. (2005) and corrections considered. One set of errors pertained to the two numbers associated with the confidence intervals reported at the top of the first column on page 897 (corrections reported in docket number EPA-HQ-OAR-2006-0735-5905). The two numbers were the lower bound on the confidence interval for the linear coefficient for the relationship of IQ with concurrent blood Pb levels for the subgroup of children with peak blood Pb levels $\geq 7.5$ $\mu \mathrm{g} / \mathrm{dL}$ and the lower bound on the confidence interval for linear coefficient for the relationship of IQ with concurrent blood Pb for the subgroup of children with peak blood $\mathrm{Pb} \geq 10 \mu \mathrm{~g} / \mathrm{dL}$. These errors were recognized during development of the 2006 Pb AQCD and corrected in the 2006 Pb AQCD (p. 6-70). The other errors were in the values of the two rightmost columns of Table 4 (corrections reported in docket number EPA-HQ-OAR-2006-0735-5512). These errors were recognized after the final 2006 Pb AQCD was released but prior to the conclusion of the review.
    ${ }^{5}$ Full-scale IQ was miscoded as verbal IQ. Boston IQ data were corrected by substituting the variable coded as verbal IQ. Boston blood Pb level data for age 6, 12, and 24 months were corrected by subtracting $2 \mu \mathrm{~g} / \mathrm{dL}$ from the blood Pb level. Investigators had incorrectly un-transformed data from log form by adding $1 \mu \mathrm{~g} / \mathrm{dL}$ to the anti-log of blood Pb instead of subtracting 1.

[^3]:    ${ }^{6}$ Results reported in Crump et al. (2013) and confirmed by NCEA calculations using the corrected dataset (see Appendix). Other results in this column are based only on NCEA calculations using the corrected dataset.
    ${ }^{7}$ 8/19/2008 and 2/11/2008 emails from Richard Hornung to Jee-Young Kim (docket number EPA-HQ-OAR-2006-0735-5814).

