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TO: Lead NAAQS Review Docket (OAR-2006-0735)

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SUBJECT: Air-related IQ Loss Evidence-based Framework and Estimates from Quantitative Risk Assessment

This memo describes an evidence-based approach for considering air-related effects on neurocognitive function (using the metric of intelligence quotient, IQ) loss associated with alternative levels for the national ambient air quality standard (NAAQS) for lead (Pb), which has been considered in developing the notice of proposed rulemaking for the lead NAAQS review. Additionally, for comparison purposes, this memo provides interpolated air-related IQ loss estimates derived from the quantitative risk assessment conducted for the review.

I. Air-related IQ Loss Evidence-based Framework

In consideration of a level for the NAAQS for Pb, EPA has considered how to apply the much expanded body of evidence that is now available to an evidence-based framework that builds on a recommendation by the Clean Air Scientific Advisory Committee (CASAC) Pb Panel (i.e., air-related IQ loss framework) and which focuses on the effects of air related Pb on neurocognitive functions. In this framework, we have drawn from the entire body of evidence as a basis for concluding that there are causal associations between air-related Pb exposures and population IQ loss. We have also drawn more quantitatively from the evidence by using evidence-based C-R functions to quantify the association between air Pb concentrations and air-related population mean IQ loss.

A. Parameters

In this framework air-related population mean IQ loss for children exposed at the level of the standard is estimated from the evidence using the following inputs:

- Level of standard ($\mu g/m^3$) - Standard levels considered in these calculations range from 0.50 $\mu g/m^3$ down to 0.02 $\mu g/m^3$, consistent with the range of levels considered in the quantitative risk assessment.

- Air-to-blood ratio ($\mu g/m^3$ air Pb to $\mu g/dL$ blood Pb) - Estimates of air-to-blood ratio considered in these calculations include 1:3, 1:5 and 1:7. These values fall within the range of values indicated by the evidence and the quantitative risk assessment which general range from 1:3 to 1:5 and higher, with some on the order of 1:10 (USEPA, 1986; Henderson, 2007; WHO, 2000; Hilts, 2003; USEPA, 2007).

- Concentration-response (C-R) function (IQ points per μg/dL concurrent blood Pb) – Calculations have been performed with two sets of C-R functions (described below).

First Set of Concentration-Response Functions

These C-R functions are particular to lower blood Pb levels that are more representative of, although still somewhat higher, than the distribution of blood Pb levels in the current U.S. population of children. This set of C-R functions is bounded by linear functions recommended by CASAC as more appropriate to application at lower blood Pb levels, and inclusive of the nonlinear function also recommended by CASAC for consideration in the quantitative risk assessment.

The linear function yielding lower end IQ loss estimates is from the analysis by Tellez-Rojo and others (2006) of IQ and concurrent blood Pb levels for 24 month old children in which the dataset was restricted to children with blood Pb levels below 5 μg/dL. The slope of this linear function is -1.71 IQ points per μg/dL blood Pb (Tellez-Rojo et al., 2006). The function yielding higher end estimates is from the analysis by Lanphear and others (2005) of IQ and concurrent blood Pb levels for children of average 6.9 years in which the dataset was restricted to children for whom blood Pb levels measurements throughout their life were below 7.5 μg/dL. The slope of this linear function is -2.94 IQ points per μg/dL blood Pb (Lanphear et al., 2005).

The nonlinear function represented in this set is from the international pooled analysis by Lanphear and others (2005). The nonlinear shape explicitly recognizes a steeper slope at lower blood Pb levels. The form of this function that is used here is that given emphasis in the risk assesssment, the loglinear with low-exposure linearization, LLL (described in USEPA, 2007 , section 5.3.1.1). This C-R function yields risk estimates falling within the range of the two linear functions identified above.[1]

To avoid bias in the estimation of air-related risk, resulting from application of this nonlinear function, we derived estimates of air-related IQ loss giving equal weight to all contributions of Pb to total blood Pb. How this was done is illustrated by the following example.

> For a level of 0.20 $\mu g/m^3$, and an air-to-blood ratio of 1:5, the resultant estimate of air-related blood Pb is 1.0 μg/dL. Using estimates for nonair blood Pb levels of 1 and 1.4 μg/dL, the estimates of total blood Pb are 2 and 2.4 μg/dL. The corresponding total Pb-related IQ loss estimates based on the LLL function are 4.6 and 5.1 points IQ loss. These estimates are then multiplied by the fraction of total Pb that is air-related (i.e., 1/2 and 1/2.4) to derive the estimated range of air-related IQ loss (2.1 – 2.3 points).

[1] At blood Pb levels extending below 2 μg/dL, the average slope is -2.29 IQ points per μg/dL blood Pb (see USEPA 2007 , Table 5-8).

Second Set of C-R Functions

This set of C-R functions draws from the multiple studies that have examined the quantitative relationship between IQ and blood Pb levels in children with blood Pb concentrations below 10 µg/dL (e.g., CD[2], Table 6-1). This has been done in studies where all or the majority of study subjects had blood Pb levels below 10 µg/dL and also where an analysis was performed on a subset of children with blood Pb levels below 10 µg/dL. For studies not restricted to blood Pb levels below 10 µg/dL, EPA has estimated the average slope of change in IQ with change in blood Pb between the 10th percentile blood Pb level and 10 µg/dL. The resultant group of reported and estimated average linear slopes for IQ change with blood Pb levels no higher than 10 µg/dL range from -0.4 to -1.8 IQ points per µg/dL blood Pb (CD, Tables 6-1 and 8-7), with a median of -0.9 IQ points per µg/dL blood Pb (CD, p. 8-80). This second set of C-R functions is represented here by this median value.

B. Calculation of mean air-related IQ loss estimates

Within this evidence-based framework, estimates of mean air-related IQ loss for children exposed at the level of the standard are derived as follows:

$$I = L \times B \times S$$

Where,

I = mean air-related IQ loss for children exposed at the level of the standard
L = level of the standard ($\mu g/m^3$)
B = the air-to-blood ratio in terms of µg/dL blood Pb per $\mu g/m^3$ air concentration
S = slope for the C-R function in terms of points IQ loss per µg/dL blood Pb

For example, to derive an estimate of mean air-related IQ loss for children exposed at the level of the standard for a level of 0.10 $\mu g/m^3$, and using an air-to-blood ratio of 1:5 and the lower bound C-R function from the first set of C-R functions (-1.71 points IQ loss per µg/dL blood Pb), we multiply these three parameter values together (0.10 x 5 x -1.71) which yields a value of 0.9 points IQ loss.

Estimates associated with the inputs described above are presented in Table 1.

[2] In this memo, CD refers to the Air Quality Criteria Document for this review (USEPA, 2006).

Table 1. Estimates of air-related population mean IQ loss for children exposed at the level of the standard.

Potential Level for Standard (µg/m³)	**Air-related Population Mean IQ Loss (points)** for children exposed at level of the standard					
	Air-to-Blood Ratio of 1:3		***Air-to-Blood Ratio of 1:5***		***Air-to-Blood Ratio of 1:7***	
	1st group of C-R functions *(from lower blood Pb analyses)*	**2nd group of C-R functions** *(from higher blood Pb analyses)*	**1st group of C-R functions** *(from lower blood Pb analyses)*	**2nd group of C-R functions** *(from higher blood Pb analyses)*	**1st group of C-R functions** *(from lower blood Pb analyses)*	**2nd group of C-R functions** *(from higher blood Pb analyses)*
0.50	2.9 – 3.1*	1.4	4.1 - 4.3*	2.3	5.0 – 5.3*	3.2
0.40	2.4 - 2.6*	1.1	3.5 - 3.8*	1.8	4.4 – 4.6*	2.5
0.30	1.5 - 2.6	0.8	2.9 – 3.1*	1.4	3.6 – 3.9*	1.9
0.20	1.0 - 1.8	0.5	1.7 - 2.9	0.9	2.7 – 3.0*	1.3
0.10	0.5 - 0.9	0.3	0.9 - 1.5	0.5	1.2 – 2.1	0.6
0.05	0.3 - 0.4	0.14	0.4 - 0.7	0.2	0.6 – 1.0	0.3
0.02	0.1 - 0.2	0.05	0.2 - 0.3	0.09	0.2 – 0.4	0.1
	* These estimates were derived using only the nonlinear C-R function from the risk assessment which, given its nonlinearity, is considered to better assess risk across the range that includes extending into these higher standard levels (and the associated higher blood Pb levels).					

II. Air-related IQ Loss Estimates from Quantitative Risk Assessment

A broad array of risk results are presented in the Risk Assessment Report (USEPA, 2007), including risk estimates for multiple case studies across a range of standard levels. To more specifically consider the risk assessment results with regard to the standard levels considered in the evidence-based framework above, we have interpolated within the risk estimates reported in the Risk Assessment Report (Table 5-9) thus deriving estimates of IQ loss for the median of the exposed population for additional standard levels. This has been done for those two case studies, among the various case studies in the assessment, that relate most closely to the evidence-based framework described above with regard to estimates of air-related IQ loss: the primary Pb smelter case study subarea and the general urban case study.[3]

The interpolated estimates are provided in Table 2 for alternative NAAQS levels of 0.40, 0.30, and 0.10 $\mu g/m^3$, along with the risk-assessment-derived estimates for the standard levels of 0.50, 0.20, 0.05 and 0.02, from which they were interpolated. The calculations underlying the risk-assessment-derived estimates, including all of the assessment design characteristics, assumptions, modeling steps, inputs, limitations and uncertainties, are completely described in the Risk Assessment Report (USEPA, 2007).

We note that estimates derived using the evidence-based framework and from the risk assessment will necessarily be different. These two approaches incorporate different types of information into different frameworks to generate risk estimates for children exposed to air-related Pb under particular NAAQS scenarios. In comparing the resultant estimates, however, we conclude that they are roughly consistent with and generally supportive of the evidence-based air-related IQ loss estimates described above.

[3] These two case studies provide estimates of risk for more highly air-pathway exposed children residing in neighborhoods or local residential areas with air concentrations somewhat near the standard level being evaluated, with consideration of temporal variability in air concentrations. By contrast, the three location-specific urban case studies (see USEPA 2007) provide risk estimates for an urban population with a broader range of air-related exposures. For the location-specific urban case studies, the majority of the modeled populations experience ambient air Pb levels significantly lower than the standard level being evaluated, with a relatively small population experiencing ambient air Pb levels at or near the standard.

Table 2. Estimates of air-related IQ loss for the median of the Pb-exposed population of children.

NAAQS Level Simulated (µg/m³, maximum monthly mean)	Median air-related IQ loss[A]	
	General urban case study	**Primary Pb smelter (subarea) case study[B]**
0.50	**1.9 – 3.6** (0.7 – 4.8)	**< 4.5** <(2.1 – 7.7)
0.40[C]	**1.7 - 3.5**	**< 4.2**
0.30[C]	**1.4 - 3.3**	**< 4.0**
0.20	**1.2 – 3.2** (0.4 – 4.0)	**< 3.7** <(1.2 – 5.1)
0.10[D]	**0.8 - 3.0**	**<3.4**
0.05	**0.5 – 2.8** (0.2 – 3.3)	**< 2.8** <(0.9 - 3.4)
0.02	**0.3 – 2.6** (0.1 – 3.1)	**< 2.9** <(0.9 - 3.3)

A - Air-related risk is bracketed by "recent air" (lower bound of presented range) and "recent" plus "past air" (upper bound of presented range). While differences between standard levels are better distinguished by differences in the "recent" plus "past air" estimates (upper bounds shown here), these differences are inherently underestimates. Boldface values are estimates generated using the log-linear with low-exposure linearization function. Values in parentheses reflect the range of estimates associated with all four concentration-response functions. See USEPA 2007 for details.
B – In the case of the primary Pb smelter case study, only recent plus past air estimates are available.
C – Estimates for these standard levels are interpolated from 0.50 and 0.20 level estimates based on the log-linear with low-exposure linearization function.
D – Estimates for this standard level are interpolated from 0.20 and 0.05 level estimates based on the log-linear with low-exposure linearization function.

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