APPENDIX D1

Assumptions and Scientific Evidence to Account for the Effect of Pica for Paint

APPENDIX D1

ASSUMPTIONS AND SCIENTIFIC EVIDENCE TO ACCOUNT FOR THE EFFECT OF PICA FOR PAINT

The scientific evidence on paint chip ingestion is scant and can be contradictory. It is well known that pica for paint and plaster is associated with lead poisoning. However, survey data and blood-lead concentrations collected in the Rochester Lead-in-Dust Study (USHUD, 1995a) indicated that children whose parents responded that they have a tendency to eat paint chips had blood-lead levels only slightly more elevated, on average, than those who do not exhibit pica. The scientific evidence and assumptions required to estimate the percentage of children who exhibit pica for paint and their blood-lead levels are summarized in this section.

PERCENTAGE OF CHILDREN WHO INGEST PAINT CHIPS

In a study involving 2,402 children attending the Child Development Center of the University of Virginia, de la Burde and Reames (1973) reported that 9% of mothers of children between eight months and seven years of age responded that their child exhibited pica for paint or plaster. A similar estimate (10%) was reported for 205 children ages 1 to 2 years in the Rochester study (USHUD, 1995a). For this risk analysis, the incidence of paint pica is assumed to be 9% of children living in homes with damaged lead-based paint (defined as greater than 0 ft^2 of interior or exterior deteriorated lead-based paint). Both children with recent paint chip ingestion and those who ingested paint chips at some time are included in the 9%.

Although detailed information on the condition of homes was not available, children in the University of Virginia study were generally from low income families and lived in substandard housing, where flaking paint or falling plaster were likely to be accessible. However, it is not clear whether the homes of all children with pica contained paint chips. Of the children reported to have a history of pica for paint or plaster, 83% lived in urban neighborhoods with old and dilapidated housing and 9% lived in newer urban or suburban homes. The remaining children lived in rural areas, or the type of housing was unknown. It was reported that some children with a history of pica were known to have eaten paint chips or plaster in the home of a relative or babysitter, where they spent a large part of the day. Thus it is possible that children living in homes without damaged lead-based paint may ingest paint chips. It is also possible that children may not be observed eating paint chips, or may ingest paint chips by chewing on intact paint. Because blood-lead concentrations are adjusted only for the incidence of observed pica, only in homes with damaged lead-based paint, the effect of pica on childhood blood-lead levels may be underestimated in the risk analysis. However, it is assumed that the impact is minimal, because estimated blood-lead concentrations are adjusted for pica even in homes with small amounts of damaged lead-based paint.

For HUD National Survey homes where no damaged lead-based paint is present, the IEUBK model and the empirical model (with paint/pica = 0) predicted values are used to estimate

blood-lead concentrations for all children represented by the home. When damaged lead-based paint is present, the same predicted values are used to estimate blood-lead concentrations under each model for 91% of the children, who are assumed not to ingest paint chips. The modeling approaches differ for the remaining 9% of children, who are assumed to ingest paint chips. Because the empirical model incorporates the effect of pica for paint, the model predicted values are used to estimate blood-lead concentrations for children who ingest paint chips. The IEUBK model does not include a direct mechanism for estimating the effect of pica for paint. Thus, adjustments are made to the IEUBK model estimates after the model is applied. The assumptions utilized in this risk analysis, to account for the effect of paint pica under the IEUBK model, are described in the sections that follow.

BLOOD-LEAD CONCENTRATION FOR CHILDREN WITH RECENT PAINT CHIP INGESTION (IEUBK MODEL)

When the IEUBK model is used, the blood-lead concentration is set equal to 63 µg/dL for children who have recently ingested paint chips. The basis underlying this blood-lead concentration and the percentage of children assumed to have recently ingested paint chips are discussed in this section.

The effect of pica for paint will be applied only for HUD National Survey homes where damaged lead-based paint is present. Fifty-five of the 284 homes in the HUD National Survey have damaged lead-based paint. These homes represent 15.2% of U.S. housing, based on 1997-projected weights used in the risk analysis.

Of the 924 children ages 1-2 years in the NHANES III Survey (Brody, et al., 1994), just one child had a blood-lead level greater than 40 µg/dL. The percentage of children ages 1-2 with blood lead greater than 40 µg/dL, adjusted for sampling weights, is 0.03%.

Information on condition of housing was not available for NHANES III participants. It is assumed that blood-lead levels greater than 40 µg/dL are extremely rare in homes with no damaged lead-based paint. Thus the entire 0.03% of children nationwide with blood lead greater than 40 µg/dL are assumed to reside in the 15.2% of homes with damaged lead-based paint. Combining these figures, we estimate that 0.20% of children in homes with damaged lead-based paint have blood-lead levels greater than 40 µg/dL.

A St. Louis study (McElvaine, et al., 1992) found that 13 of 90 (14.4%) children less than age 3 years with blood-lead levels greater than 40 µg/dL, or less than age 7 years with blood lead levels greater than 50 µg/dL, had radiographic evidence of recent paint chip ingestion. This information, combined with the preceding estimate, leads us to conclude that 0.03% of children in homes with damaged lead-based paint have blood lead greater than 40 µg/dL due to recent paint chip ingestion. Table D1-1 shows step by step the methodology for computing the percentage of children living in homes with damaged lead-based paint who have blood-lead levels greater than 40 µg/dL and have recently ingested paint chips. The underlying assumptions of this approach are that 1) blood-lead concentrations are greater than equal to 40 for children who have recently ingested paint chips containing lead and 2) only children who reside in homes with damaged lead

based paint ingest paint chips containing lead. The 13 children in the St. Louis study, who were confirmed to have ingested paint chips, had a mean blood-lead level of 63 µg/dL. The blood lead levels of children with recent pica (0.03% of children in homes with damaged lead-based paint) will be mapped to 63 µg/dL.

Table D1-1. Calculation of Percentage of Children Who Have Recently Ingested Paint Chips.

Variable Name	Variable Definition	Method of Calculation	Value
PC_EAT	Percentage of children with blood lead concentration ≥ 40 µg/dL, living in homes with damaged lead-based paint, who have recently ingested paint chips containing lead.	(PbB ≥ 40 µg/dL| Damaged LBP) * (PC_EAT | PbB ≥ 40 µg/dL)	.197% x .144 = .03%
(PbB ≥ 40 µg/dL| Damaged LBP)	Percentage of children with blood-lead concentration ≥ 40 µg/dL, living in homes with damaged lead based paint.	(PbB ≥ 40 µg/dL) / (Damaged LBP)	0.03% / 0.152 = 0.197%
Damaged LBP	Percent of US housing units with damaged lead based paint.	Percentage of housing units with damaged lead-based paint, estimated in the HUD National Survey.	15.2%
PbB ≥ 40 µg/dL	Percentage of children aged 1-2 with blood-lead concentration ≥ 40 µg/dL.	Taken from NHANES III for children 1-2 years of age.	0.03%
(PC_EAT | PbB ≥ 40 µg/dL)	Percentage of children with blood-lead concentration ≥ 40 µg/dL who have recently ingested paint chips.	Taken from McElvaine's St. Louis study.	13/90 = 14.4%

BLOOD-LEAD CONCENTRATION FOR CHILDREN WHO INGESTED PAINT CHIPS AT SOME TIME (IEUBK)

For HUD National Survey homes with damaged lead-based paint, 9% of the children represented by those homes are assumed to ingest paint chips, with 0.03% of children assumed to have recent paint chip ingestion, as described above. The remaining 8.97% of children are assumed to have ingested paint chips at some time, but not recently. The geometric mean blood-lead concentration for the 8.97% of children in homes with damaged lead-based paint, who have ingested paint chips at some time, is estimated to be 3 µg/dL greater than the IEUBK predicted value for children who do not eat paint chips. The basis for this adjustment is presented in this section.

Although the University of Virginia study was used to estimate the percentage of children who ingest paint chips, children in this study would have been exposed to lead from sources, such as automobile exhaust, no longer present in the environment. Thus their blood-lead levels, if available, would not be comparable to those of present-day children. A current estimate of the effect of pica for paint may be derived from Rochester Lead-in-Dust study (USHUD, 1995a). In that study, 20 of 205 children (10%) were reported to exhibit pica for paint. The geometric mean blood lead for children who were reported to have ingested paint chips was 9.1 µg/dL, while the

geometric mean blood lead for children who were reported to have never ingested paint chips was 6.1 µg/dL. Thus, the geometric mean blood-lead concentration for children who ingested paint chips at some time is assumed to be 3.0 µg/dL greater than the IEUBK model predicted geometric mean for children who do not ingest paint chips.

APPENDIX D2

Results of Three Published Meta-Analyses on the Relationship Between IQ Point Loss and Childhood Blood-Lead Levels

APPENDIX D2

RESULTS OF THREE PUBLISHED META-ANALYSES ON THE RELATIONSHIP BETWEEN IQ POINT LOSS AND CHILDHOOD BLOOD-LEAD LEVELS

INTRODUCTION

The association between blood-lead levels and low IQ scores has been consistently reported in the scientific literature. The estimates of the dose-response relationship published in the literature have been combined via meta-analysis and reported in the three articles listed below. This appendix provides a summary of each article and a discussion of the key results, relative to this risk analysis. The studies cited in these articles are summarized in Tables D2-1 and D2-2 at the end of this appendix.

PRIMARY REFERENCES

Schwartz, J., 1993, Beyond LOEL's, p Values, and Vote Counting: Methods for Looking at the Shapes and Strengths of Associations, Neuro Toxicology 14(2-3):237-246.

Schwartz, J., 1994, Low-Level Lead Exposure and Children's IQ: A Meta-analysis and Search for a Threshold, Environmental Research 65:42-55.

Pocock, S. J., Smith, M., and Baghurst, P., 1994, Environmental Lead and Children's Intelligence: A Systematic Review of the Epidemiological Evidence, BMJ 309:1189-1197.

SUMMARY OF SCHWARTZ, J., 1993

This paper uses examples from the lead literature to illustrate statistical methods for determining the shape of dose-response relationships, including the possible existence of thresholds, and for assessing the strengths of associations within a study and for the literature as a whole. Of interest to this risk analysis is a meta-analysis of the results from 7 studies that estimated a slope for the relationship between children's blood-lead levels and IQ scores. These studies used linear, or log-linear, regression models to fit the relationship between IQ scores and PbB in children. Up to 17 additional covariates were included in the models. The weighted mean regression slope over the 7 studies, weighted by the inverse of the estimated variance, was -0.245 (±0.039). That is, a 1 µg/dL increase in PbB was associated with a 0.245 decrease in IQ score.

SUMMARY OF SCHWARTZ, J., 1994

This article focuses on the relationship between blood lead and IQ scores, while the earlier paper by Schwartz used this relationship to illustrate a statistical method. The 1994 paper presents a meta-analysis of 7 studies, some of which had been cited in the earlier paper, that

estimated a slope for the relationship between children's blood-lead levels and IQ scores. Three longitudinal and four cross-sectional studies were included in the analysis. The studies used linear, or log-linear, regression models to fit the relationship between IQ scores and PbB in children. Additional covariates were included in the models. A random effects model was employed in the meta-analysis, using the method of Dersimonian and Laird (1986). The weighted mean regression slope over the 7 studies, weighted by the inverse of the estimated variance, was -0.257 (±0.041). That is, a 1 µg/dL increase in PbB was associated with a 0.257 decrease in IQ score.

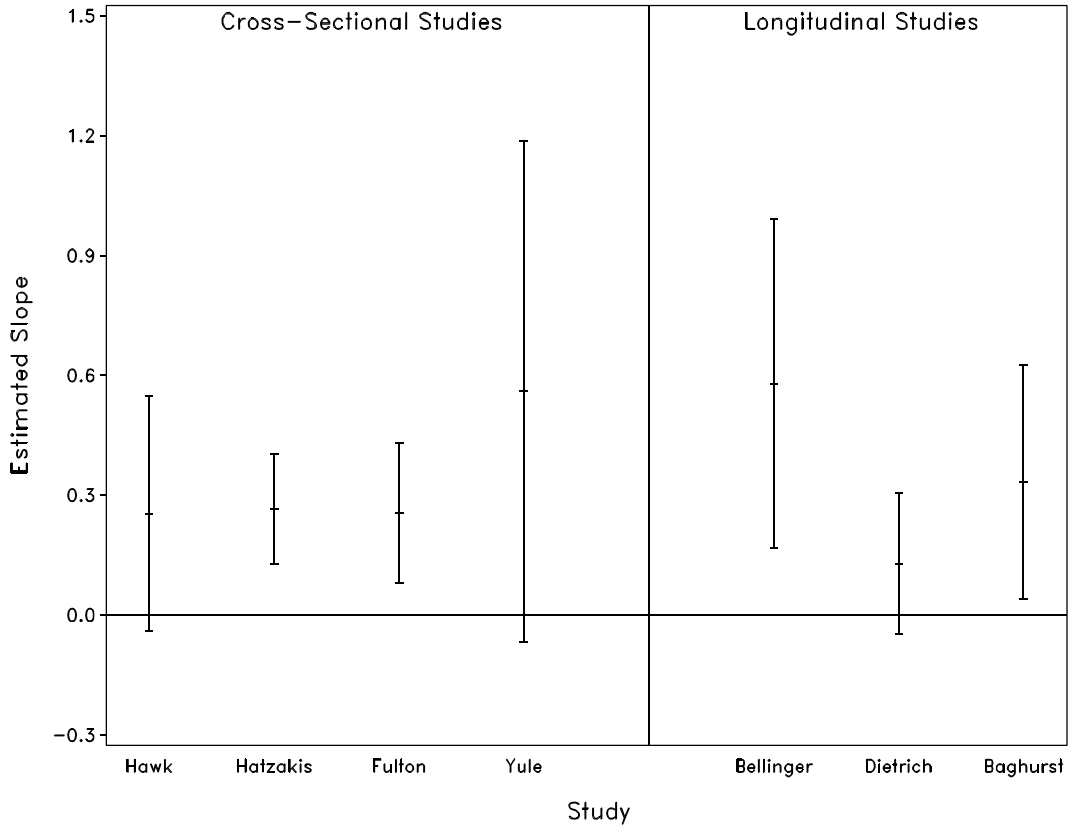

Figure D2-1. Estimated Slopes from the Seven Studies Used in the Schwartz (1994) Meta-analysis, with 95% Confidence Intervals.

SENSITIVITY ANALYSIS

Schwartz conducted a sensitivity analysis to measure the robustness of the meta-analysis and to determine the influence of differences in study design and study populations. The results of the sensitivity analysis are summarized in the following table.

Revised Analysis	Resulting Slope (± 1 standard error of the mean)
Study with Largest Effect Size Removed:	-0.243 (± 0.034)
Study with Most Significant Effect Removed:	-0.252 (± 0.058)
Add 8 Studies with No Effect (each with average weight of the 7 studies):	Association still significant, but slope reduced to about half of original estimate
Longitudinal vs. Cross-sectional:	-0.296 (± 0.125) vs. -0.269 (± 0.051)
Disadvantaged vs. Nondisadvantaged Lifestyle:	-0.185 (± 0.092) vs. -0.289 (± 0.050)
Add 2 Studies that Included Younger Children:	-0.239 (± 0.031)

Three analyses were used to examine the robustness of the meta-analysis. First, the study with the largest effect size (Bellinger et al., 1992) was removed. Next, the study with the most significant effect (Hatzakis et al., 1987) was removed. Based on these results, Schwartz concluded that the meta-analysis was not dominated by any individual study. The third analysis added eight hypothetical studies that reported no association between blood-lead levels and IQ scores. Each study was assigned the average weight of the seven original studies. In this analysis, the association between blood-lead levels and IQ scores was still highly significant ($p<0.01$), but the estimated slope was reduced.

Additional analyses were conducted to determine the effect of differences in study design (longitudinal vs. cross-sectional) and study populations (advantaged vs. disadvantaged, age of child). Schwartz concluded that there was little evidence of a difference in effect size between longitudinal and cross-sectional studies. It did appear that estimates of IQ loss were lower in studies of disadvantaged children. Schwartz suggested that this result may be due to the greater influence of confounding variables in a disadvantaged population. Finally, the addition of two studies that examine younger children did not have a great impact on the estimated slope.

THRESHOLD ANALYSIS

The question of whether a threshold exists in the relationship between IQ scores and PbBs was examined through a meta-analysis that compared studies with different mean blood lead levels. In studies with mean blood lead levels of 15 µg/dL or lower, the estimated slope was -0.323 (±0.126) compared to -0.232 (±0.040) for studies with means above 15 µg/dL. Thus, if anything, a trend toward a higher slope at lower concentrations was observed. This result suggests that the log-linear model may be more appropriate than the linear model, for this relationship.

An alternative approach to the threshold issue examined the data from the Boston study (Bellinger, 1992) more thoroughly. The Boston study was chosen because it had the lowest mean PbB. For this analysis, separate regression models for IQ score and PbB were fit using the same

set of covariates. A nonparametric smoothed curve (LOESS) was fit to the relationship between the two sets of residuals. Based on this analysis, Schwartz concluded that the relationship between blood lead and IQ continues at PbB below 5 µg/dL in this study, i.e., no threshold was evident.

SUMMARY OF POCOCK, S. J., SMITH, M., AND BAGHURST, P., 1994

This paper presents a meta-analysis of 26 epidemiological studies: 5 prospective studies, 14 cross-sectional studies of blood-lead, and 7 cross-sectional studies of tooth-lead. The three types of studies are considered in separate meta-analyses. The results are summarized as follows:

Analysis	Resulting Slope (± 1 standard error of the mean)
Prospective Studies, PbB at Birth:	0.018 (± 0.062)
Prospective Studies, PbB around 2 Years:	-0.185 (± 0.051)
Prospective Studies, Postnatal Mean PbB:	-0.088 (± 0.058)
Cross-Sectional Blood-Lead Studies:	-0.253 (± 0.041)
Cross-Sectional Blood-Lead Studies, Excluding Shanghai:	-0.174 (± 0.043)
Cross-Sectional Tooth-Lead Studies:	-0.095 (± 0.025)

Only the analysis of cross-sectional blood-lead studies had a statistically significant slope.

DISCUSSION

There was considerable overlap in the studies cited by the three meta-analysis papers. Two studies, Fulton et al. (1987) and Yule et al. (1981), were cited in all three papers, while several others were cited in two of the three papers. In addition, some studies cited by Schwartz (1993) or Pocock were used by Schwartz (1994) in the sensitivity analysis.

The three papers are directly comparable in that a common endpoint was used for all meta-analyses. For the meta-analysis endpoint, the regression coefficients and standard errors calculated by the original authors were used to estimate the change in IQ for an increase in blood-lead from 10 to 20 µg/dL. This was necessary, because some of the original authors worked with log-transformed data, while others did not transform the data. In most cases, the regression coefficients were adjusted for other covariates included in the model. The other covariates varied from study to study. For this risk analysis, we have converted the estimated change in IQ back to a slope for untransformed blood-lead concentrations.

The Schwartz (1993) paper focuses on introducing the statistical methods to a non-technical audience. The Schwartz (1994) and Pocock papers focus on the relationship between

IQ and blood-lead levels. The Schwartz (1994) paper includes a sensitivity analysis and search for threshold in the relationship. These topics are not covered in the Schwartz (1993) and Pocock papers. However, in the meta-analysis of prospective studies, the Pocock paper does include separate analyses for blood-lead measures at three ages. Also, one of the studies (Schroeder, 1985) used in the Schwartz (1993) paper included approximately 50 children under 30 months of age. This study and another (Ernhart, 1989) with younger children were included in the sensitivity analysis in Schwartz (1994).

The Pocock paper analyzes longitudinal and cross-sectional studies separately, while the Schwartz papers include both types of studies in the same meta-analysis. The Schwartz (1994) paper considers the study designs separately in the sensitivity analysis. It is important to point out that the measures of blood-lead concentration are different between longitudinal and cross-sectional studies. Cross-sectional studies generally have a single blood lead measurement, taken when the IQ test is administered to school age children. Longitudinal studies generally have several blood-lead measurements available, which may be taken years prior to the IQ testing. In some longitudinal studies (Dietrich et al, 1993; Baghurst et al, 1992), the lifetime average blood-lead concentration is related to IQ. In others (Bellinger et al, 1992; Ernhart et al, 1989), blood-lead concentration at a specified age is related to IQ. The interpretation of the modeled relationships should take into account the differing blood-lead measurements employed. While each author attempts to take this into account, by modeling longitudinal and cross-sectional studies separately, neither distinguishes between the differing measures of blood-lead concentration in longitudinal studies.

In the analysis of prospective studies, Pocock includes an analysis of how PbB at approximately age 2 affects IQ measured at school age. The slope for this analysis (-0.185) is less than the values (approximately -0.25) from Schwartz (1993 and 1994) and the Pocock cross-sectional studies analysis.

Both Schwartz (1994) and Pocock included "full scale IQ score" in school-age children as a selection criteria for studies used in the meta-analysis. Most of the studies cited used the Wechsler Intelligence Scale for Children - Revised (WISC-R) test. The 1993 Schwartz paper includes one study, Schroeder (1985), that uses the Bayley Scales of Infant Development (BSID), for children less than 30 months of age. The BSID score is not directly comparable with the IQ scores, as this test measures developmental endpoints as well as cognitive ability.

Table D2-1. Design Information for Studies that Investigate the Relationship Between Child's IQ and Blood-Lead Level.

Primary References That Cite the Study	Study	Type of Study	Year(s) of Study	Location of Study Participants	Age of Study Participants		IQ Test Instrument	Sample Size	Other Study Information
					Blood Lead Measure	IQ Measure			
Schwartz (1993) Schwartz (1994)	Hatzakis et al. (1987)	Prospective	1985	Lavrion, Greece (a lead smelter city; soil lead levels of 1,300-18,000 ppm)		Primary school age	WISC-R	509	Study participants enrolled in one of four schools in the town in 1984-85.
Pocock	Hatzakis et al. (1989)	Prospective		Lavrion, Greece (a lead smelter city)		6-12 yrs	WISC-R	509	
Schwartz (1993)	Bellinger et al. (1991)	Prospective	Mid- to late-1980s	Boston, MA		Approx. 57 mos	GCI	150	Middle and upper-middle class families, not in inner-city or housing projects. Children born at Brigham and Women's Hospital from 1979-1981
Schwartz (1994) Pocock	Bellinger et al. (1992)	Prospective	1979(Aug.) - 1981(April)	Boston, MA	24 months	School Age	WISC-R	147	Middle class, advantaged
Schwartz (1994) Pocock	Baghurst et al. (1992)	Prospective	1979-1982	Port Pirie, Australia	0 - 3 yrs	7 yrs	WISC-R	494	Smelter town and rural surroundings, middle class families
Pocock	Ernhart et al. (1989)	Prospective		Cleveland, OH	at 2yrs	5 yrs	WPPSI	212	Inner city, disadvantaged, 50% of mothers alcoholic
Pocock	Cooney et al. (1991)	Prospective	1983-1990	Sidney, Australia	1 and 2 yrs	7 yrs	WISC-R	175	Mixed urban
Schwartz (1993)	Schroeder et al. (1985)	Prospective	1977-1978	Wake County, NC		10 mos - 6.5 yrs (half < 30 mos)	BSID (< 30 mos) SBIS (≥ 30 mos)	104	Low income families
Schwartz (1993) Schwartz (1994)	Hawk et al. (1986)	Replication of Schroeder Study		Lenoir & New Hanover counties, NC		3-7 yrs	SBIS	75	Black study participants from low income and SES families, at high risk of exposure to deteriorated LBP
Schwartz (1994) Pocock	Dietrich et al. (1993)	Prospective		Cincinnati, OH	0 - 3 yrs	Approx. 6.5 yrs	WISC-R	231	Inner city, black, disadvantaged

Primary References That Cite the Study	Study	Type of Study	Year(s) of Study	Location of Study Participants	Age of Study Participants		IQ Test Instrument	Sample Size	Other Study Information
					Blood Lead Measure	IQ Measure			
Schwartz (1993) Schwartz (1994) Pocock	Yule et al. (1981)	Pilot Study	Summer 1980 (PbB taken 9-12 months earlier)	Outer London, England		6-12 yrs	WISC-R	166	Results for younger children are reported elsewhere.
Schwartz (1993) Pocock	Lansdown et al. (1986)	Replication of Yule Study		Within 1 km of a factory in London, England		6-12 yrs	WISC-R	166	Mostly middle class families with homes near a main road
Pocock	Winneke et al (1990)	Multi-Center, Cross - Sectional Study		Bucharest		9.2 yrs (mean age)	WISC-Short Form	301	General population
				Budapest		8.5 yrs (mean age)	WISC-Short Form	254	General population
				Moden		7.8 yrs (mean age)	WISC-Short Form	216	Industrial city, lead industry
				Sofia		7.3 yrs (mean age)	WISC-Short Form	142	General population
				Dusseldorf		6.5 yrs (mean age)	WISC-Short Form	109	Industrial city, near smelter
				Dusseldorf		8.3 yrs (mean age)	WISC-Short Form	109	Industrial city, near smelter
Schwartz(1994) Pocock	Silva (1988)	Cross - Sectional	1972-1973	Dunedin, New Zealand		11 yrs (mean age)	WISC-R	579	Mixed urban and rural
Pocock	Harvey et al (1988)	Cross - Sectional	Late 1979-early1981	Birmingham, England		5.5 yrs (mean age)	WPPSI	177	Mixed, inner city
Pocock	Wang et al (1989)	Cross - Sectional		Shanghai, China		6-14 yrs	WISC-R	157	Near battery plant, rural control
Pocock	Winneke et al (1985a)	Cross - Sectional		Nordenham, Germany		7 yrs	WISC-R	122	Smelter town, rural surroundings
Schwartz (1993) Schwartz (1994) Pocock	Fulton et al. (1987)	Cross - Sectional	1983-1985	Edinburgh, Scotland		6-9 yrs	BAS	501	Study participants enrolled in one of 18 primary schools Mixed urban - previously hish water lead

Table D2.2. Summary of Results from Studies that Investigate the Relationship Between Child's IQ and Blood Lead Level

Table D2-2. Summary of Results from Studies that Investigate the Relationship Between Child's IQ and Blood-Lead Level. (Continued)

Primary References That Cite the Study	Study	PbB of Study Participants[1] (µg/dL)		IQ of Study Participants[2]		Measure of Association Between IQ and Blood-Lead Levels[3]			
		Range	Summary Statistics	Endpoint Type	Range/Summary Statistics	Measure	P-Value	Covariates	Other Information
Schwartz (1993) Schwartz (1994)	Hatzakis et al. (1987)	7.4 - 63.9	AM = 23.7 STD = 9.2 10%ile = 13.9 50%ile = 21.5 90%ile = 36.0	WISC-R		-0.270 change in IQ per unit increase in PbB (-0.403, -0.137)	< 0.001	17 potential confounders or IQ correlates[4] (called the "optimal" model)	Dose-response investigation showed no PbB effect on IQ when PbB < 25 µg/dL.
Pocock	Hatzakis et al. (1989)	7.4-63.9	AM = 23.7 STD = 9.2		AM = 87.7 STD = 14.8	-2.7 change in IQ for increase from 10-20 µg/dL in PbB	< 0.001	Up to 24, including mother's IQ	Dose-reponse curve showed evidence of a threshold at the level of about 25 µg/dL PbB
Schwartz (1993)	Bellinger et al. (1991)	0.0 - 23.3	AM = 6.4 STD = 4.1 19% were > 10µg/dL 4% were > 15µg/dL	GCI	80-150 AM = 115.5 STD = 14.5	-2.28 change in IQ per unit increase in Log(PbB) (-6.0, 1.4) --- -0.250 change in IQ per unit increase in PbB from 5-15 µg/dL PbB	0.23	13 covariates[5]	Regression diagnostics were used to check the robustness of estimates. These results reflect only PbB data at age 57 months.
Schwartz (1994) Pocock	Bellinger et al (1992)		AM = 6.5 STD = 4.9	WISC-R	71-147 AM = 119.1 STD = 14.8	-5.8 change in IQ for increase from 10 to 20 µg/dL in PbB	0.007	HOME mother's IQ, 8 other covariates[8]	Slightly elevated blood lead levels around the age of 24 months are associated with intellectual and academic performance deficits at age 10 years.
Schwartz (1994) Pocock	Baghurst et al (1992)		AM = 20	WISC-R	AM = 104.7	-3.3 change in IQ for an increase from 10-20 µg/dL in PbB	0.04	HOME, mother's IQ, 11 others [9]	Found low-level exposure to lead during early childhood is inversely associated with neuropsychological development through first seven years of life.
Pocock	Ernhart et al (1989)		AM = 16.7 STD = 6.45	WPPSI	AM = 87.5 STD = 16.6	-1.1 change in IQ for an increase from 10-20 µg/dL in PbB	< 0.01	HOME , mothers IQ, and 11 others[11]	
Pocock	Cooney et al (1991)		AM = 14.2	WISC-R		0.39 change in IQ for an increase from 10-20 µg/dL in PbB		HOME ,mothers IQ, and 4 others [12]	

Table D2-2. Summary of Results from Studies that Investigate the Relationship Between Child's IQ and Blood-Lead Level. (Continued)

Primary References That Cite the Study	Study	PbB of Study Participants[1] (µg/dL)		IQ of Study Participants[2]		Measure of Association Between IQ and Blood-Lead Levels[3]			
		Range	Summary Statistics	Endpoint Type	Range/Summary Statistics	Measure	P-Value	Covariates	Other Information
Schwartz (1993)	Schroeder et al. (1985)	6 - 58		BSID (< 30 mo.) SBIS (≥30 mo.)	45-140	-0.199 change in IQ per unit increase in PbB	< 0.01	7 covariates[6] plus interaction with PbB. Quadratic and cubic components of PbB also considered.	Unforced stepwise regression. SES was only other significant covariate.
Schwartz (1993) Schwartz (1994)	Hawk et al. (1986)	6.2 - 47.4	AM = 20.9 STD = 9.7	SBIS	59-118	-0.255 change in IQ per unit increase in PbB (-0.554, 0.043)	< 0.05	Gender, HOME score, maternal IQ	
Schwartz (1994) Pocock	Dietrich et al (1993)		AM = 15.2 STD = 11.3	WISC-R	AM = 86.9 STD = 11.3	1.3 esimated loss in IQ for an increase from 10 to 20 µg/dL in PbB	< 0.10	HOME score, maternal IQ, birth weight, birth length, child sex, cigarette consumption during pregnancy	Postnatal PbB concentrations were inversely associated with Full Scale IQ.
Schwartz (1993) Schwartz (1994) Pocock	Yule et al. (1981)	7 - 33	AM = 13.52 STD = 4.13 80% were > 10µg/dL 4.8% were > 20µg/dL	WISC-R	AM = 98.21 STD = 13.44	-8.08 change in IQ per unit increase in Log(PbB) (4.63) -0.560 change in IQ per unit increase in PbB from 10-20 µg/dL	0.084	Age, social class	Social class was considered a crude measure.
Schwartz (1993) Pocock	Lansdown et al. (1986)	7 - 24	AM = 12.75 STD = 3.07 77% were > 10µg/dL 1.5% were > 20µg/dL	WISC-R WISC-R	AM = 105.24 STD = 14.20	2.15 change in IQ per unit increase in Log(PbB) 0.149 change in IQ per unit increase in PbB from 10-20 µg/dL	0.63	Age, social class	N = 86 for regression analysis. Social class was also a significant factor.

Table D2-2. Summary of Results from Studies that Investigate the Relationship Between Child's IQ and Blood-Lead Level. (Continued)

Primary References That Cite the Study	Study	PbB of Study Participants[1] (µg/dL)		IQ of Study Participants[2]		Measure of Association Between IQ and Blood-Lead Levels[3]			
		Range	Summary Statistics	Endpoint Type	Range/Summary Statistics	Measure	P-Value	Covariates	Other Information
Pocock	Winneke et al (1990) Bucharest		GM = 18.9 STD = 1.3	WISC-Short Form			<0.1	Gender, age, social class, mother's education	
	Winneke et al (1990) Budapest		GM = 18.2 STD = 1.7	WISC-Short Form			< 0.1	Gender, age, social class	
	Winneke et al (1990) Moden		GM = 11.0 STD = 1.3	WISC-Short Form			< 0.1	Gender, age, social class, mother's education	
	Winneke et al (1990) Sofia		GM = 18.2 STD = 1.6	WISC-Short Form			< 0.1	Gender, age, social class, mother's education	
	Winneke et al (1990) Dusseldorf		GM = 8.3 STD = 1.4	WISC-Short Form	AM = 116		< 0.1	Gender, age, social class, mother's education	
	Winneke et al (1990) Dusseldorf		AM = 7.4 STD = 1.3	WISC-Short Form			< 0.1	Gender, age, social class, mother's education	
Schwartz (1994) Pocock	Silva (1988)	4 - 50 µg/dL	AM = 11.1 STD = 4.91	WISC-R	AM = 108.9 STD = 15.12	Loss of 1.51 in IQ for an increase in PbB of 10-20µg/dL		None	
Pocock	Harvey et al (1988)	0.2-1.4 mol/L	AM = 12.3 STD = 0.2	WPPSI	AM = 105.9 STD = 10.6			None	No significant relationship was found between overall IQ and PbB

Table D2-2. Summary of Results from Studies that Investigate the Relationship Between Child's IQ and Blood-Lead Level. (Continued)

Primary References That Cite the Study	Study	PbB of Study Participants[1] (µg/dL)		IQ of Study Participants[2]		Measure of Association Between IQ and Blood-Lead Levels[3]			
		Range	Summary Statistics	Endpoint Type	Range/Summary Statistics	Measure	P-Value	Covariates	Other Information
Pocock	Wang et al (1989)	4.5 - 52.8 µg/dL	AM = 21.1 STD = 10.11	WISC	AM = 89	A decrease of IQ of 9 per 10µg/dL increase in PbB		Mother's education and 4 others [10]	Found a dose - effect relation between PbB and IQ even after confounding variables were controlled for by stepwise regression analysis
Pocock	Winneke et al (1985a)	4.4 - 23.8 µg/dL	AM = 8.2 STD = 1.4	WISC-R	AM = 120.2 STD = 10.3		< 0.1	Age, sex and hereditary background	
Schwartz (1993) Schwartz (1994) Pocock	Fulton et al. (1987)	3.3 - 34	GM = 11.5 1.2% were > 25µg/dL	BASC	AM = 112 STD = 13.4	-3.70 change in IQ per unit increase in Log(PbB) (1.31) --- -0.256 change in IQ per unit increase in PbB from 10-20 µg/dL	0.003	13 covariates[7] + school attended ("optimal" regression model)	Adjusted R^2 = 45.5%

Notes for Table D2-2:

(1) "Range" indicates the observed range of PbB levels among the study participants. Among the summary statistics, AM = arithmetic mean; GM = geometric mean; STD = standard deviation; x%ile = x percentile of observed distribution.

(2) "Type" indicates the type of IQ endpoint measured in the study. WISC-R = Wechsler Intelligence Scale for Children - Revised (full-scale IQ measurement); GCI = McCarthy Scales of Children's Abilities: General Cognitive Index; BSID = Bayley Scales of Infant Development; SBIS = Stanford-Binet Intelligence Scale; BASC = British Ability Scales: Combined Score. Among the summary statistics, AM = arithmetic mean; STD = standard deviation.

(3) Results are the outcome of a regression analysis to predict IQ endpoint based on PbB level and other covariates. "Measure" is the estimated slope parameter indicating the change in IQ measurement associated with a unit change in the (possibly transformed) PbB level. If the PbB level is transformed, the change in IQ measurement over a given range of the untransformed PbB level is also given. When available, a 95% confidence interval associated with the slope estimate is given, or a standard error associated with the estimate. "P-value" is for the test that the slope parameter is equal to zero versus an alternative that it is not zero. "Adjusted covariates" indicates the number of covariates included in the regression model; these covariates are named if the number is small. "Other information" indicates specifics associated with the regression fit (e.g., method used, whether a log-transformation was taken on the PbB level prior to analysis, information on the covariates).

(4) Covariates include parental IQ, birth order, family size, father's age, parental education, alcoholic mother, age, bilingualism, birth weight, length of child's hospital stay after birth, walking age, history of CNS disease, history of head trauma, illness affecting sensory function, parent's divorce.

(5) Covariates include family social class, material IQ, preschool attendance, HOME total score, # hours per week of "out-of-home" care, # changes in family residence since birth, medication use in preceding month, # adults in household, gender, race, birth weight, material marital status, birth order.

(6) HOME score, maternal IQ, child's age, child's sex, SES of parents, type of IQ test, presence of father in home, number of siblings.

(7) Parent's vocabulary and matrices tests, child's interest score, age, father's qualifications, length of gestation, parental involvement with school score, class year, # days absent from school, sex, standardized height, car/telephone ownership, employment status of father.

(8) Child stress, maternal age, race, SES, sex, birth order, martial status, number of residence changes prior to age 57 months

(9) Sex, parents' level of education, maternal age at delivery, parents' smoking status, socio-economic status, quality of the home environment, birth weight, birth order, feeding method (breast feeding, bottle, or both), duration of breast - feeding, and whether the child's natural parents were living together

(10) Age, sex, father's education, father's occupation, father's daily smoking quantity

(11) Sex, race, birth weight, birth order, gestational age at birth, parental education, maternal variables like PPVT-R, AFI, MAST SCORE, AA/day in pregnancy, cigarettes per day, and use of marijuana and other drugs in pregnancy, medical problems and psychosocial problems.

(12) Gestational age, education of the mother, education and occupational status of the father.

APPENDIX E1

Methodology for Estimating Health Effects From Blood-Lead Distribution

APPENDIX E1

METHODOLOGY FOR ESTIMATING HEALTH EFFECTS FROM BLOOD-LEAD DISTRIBUTION

This appendix describes the procedure used in this report for calculating health and blood-lead endpoints for the nation's children aged 1-2 years, based on a distribution of blood-lead concentrations assumed to be lognormal. In this section, GM represents the geometric mean and GSD represents the geometric standard deviation of the blood-lead concentrations.

a. P[PbB > X], where X=10 µg/dL or 20 µg/dL

Because it is assumed that the blood-lead concentration distribution is lognormally distributed, the probability of observing a blood-lead concentration greater than X is expressed as

$$P[PbB > X] = 1 - \Phi\left(\frac{\ln(X) - \ln(GM)}{\ln(GSD)}\right) \quad (1)$$

where $\Phi(z)$ is the probability of observing a value less than z under the standard normal distribution. Therefore, setting X=10 and X=20 in equation (1) will provide estimates of the probability of observing a blood-lead level exceeding 10 µg/dL and 20 µg/dL, respectively.

b. P[IQ < 70]

As indicated in Table E1-1, the estimated probability that a child will have an IQ score less than 70 given the child's blood-lead concentration (PbB) is expressed as a piecewise linear function of PbB. To estimate the probability that a child in the national population has an IQ score less than 70, the blood-lead distribution is used with the information in Table E1-1. Using the notation x_i, α_i, and β_i (i=1,...,10) introduced in the column headings in Table E1-1, and letting LGM = ln(GM) and LGSD = ln(GSD), the expected value of the probability of observing an IQ score less than 70 is

$$P[IQ < 70] = \sum_{i=1}^{10} \alpha_i \cdot \left[\Phi\left(\frac{\ln(x_i) - LGM}{LGSD}\right) - \Phi\left(\frac{\ln(x_{i-1}) - LGM}{LGSD}\right)\right] + K \cdot \sum_{i=1}^{10} \beta_i \cdot \left[\Phi\left(\frac{\ln(x_i) - LGM - (LGSD^2)}{LGSD}\right) - \Phi\left(\frac{\ln(x_{i-1}) - LGM - (LGSD^2)}{LGSD}\right)\right] \quad (2)$$

Table E1-1. Formulas for Estimating the Probability of Observing IQ Score Less Than 70, Given a Child's Blood-Lead Concentration (PbB).

Interval # (i)	Range of PbB (µg/dL) (x_{i-1} < PbB x_i)	Function for Estimating Increased Percentage of Children Having IQ Scores less than 70 (IQ < 70 = α_i + β_i * PbB)
1	0 < PbB 5	IQ < 70 = 0.080 + 0.0036 * PbB
2	5 < PbB 7.5	IQ < 70 = 0.022 + 0.0152 * PbB
3	7.5 < PbB 10	IQ < 70 = -0.152 + 0.0384 * PbB
4	10 < PbB 12.5	IQ < 70 = -0.084 + 0.0316 * PbB
5	12.5 < PbB 15	IQ < 70 = 0.016 + 0.0236 * PbB
6	15 < PbB 17.5	IQ < 70 = -0.260 + 0.0420 * PbB
7	17.5 < PbB 20	IQ < 70 = -0.281 + 0.0432 * PbB
9	20 < PbB 22.5	IQ < 70 = -0.145 + 0.0364 * PbB
9	22.5 < PbB 25	IQ < 70 = -0.532 + 0.0536 * PbB
10	25 < PbB	IQ < 70 = -0.162 + 0.0388 * PbB

Derived From: Wallsten, T.S., and Whitfield, R.G. "Assessing the Risks to Young Children of Three Effects Associated with Elevated Blood-lead Levels." *Report by Argonne National Laboratory*. Report No. ANL/AA-32. Sponsored by the U.S. EPA Office of Air Quality Planning and Standards. 1986.

where K = exp(LGM + (LGSD)^2 /2) and Φ(z) is the probability of observing a value less than z under the standard normal distribution. In calculating (2) use the following [1] conventions: ln (0)=- , ln( )= , Φ(-)=0, and Φ( )=1.

c. P[IQ decrement > x] for x=1, 2, 3

It is assumed that each µg of lead per dL of blood corresponds to a 0.257 decline in IQ score (see Section 4.4 of the §403 Risk Assessment report). Therefore, an IQ decrement exceeding 1 is associated with blood-lead concentrations exceeding 1/0.257 = 3.9 µg/dL. Similarly, blood-lead concentrations exceeding 2/0.257 = 7.8 µg/dL are associated with an IQ decrement exceeding 2, and concentrations exceeding 3/0.257 = 11.7 µg/dL are associated with an IQ decrement exceeding 3. Therefore,

P[IQ decrement > 1] = P[PbB > 3.9 µg/dL]
P[IQ decrement > 2] = P[PbB > 7.8 µg/dL]
P[IQ decrement > 3] = P[PbB > 11.7 µg/dL]

[1] Equation (2) is equivalent to $\sum_{i=1}^{10} \int_{x_{i-1}}^{x_i} (\alpha_i + \beta_i x)\, \phi(x)\, dx$ where $\phi(x)$ is the probability density function of the lognormal distribution with parameters LGM and LGSD.

where the right-hand side of each of these equations is calculated using equation (1) with X=3.9, 7.8, or 11.7.

d. Average IQ points lost (and associated standard deviation)

The (arithmetic) average IQ points lost in the population of children aged 1-2 years is calculated using the properties of the lognormal distribution. If X corresponds to a child's blood-lead concentration and Y is the associated decline in IQ for the child due to the presence of the blood-lead, then it is assumed in this risk assessment that Y = 0.257*X. As X is assumed to be lognormally distributed, it can be shown that Y is also lognormally distributed. Furthermore, an estimate of the expected value of Y (average # IQ points lost) is as follows:

$$\text{Avg. \# IQ points lost} = 0.257 * GM * \exp(\ln(GSD)^2/2) \quad (4)$$

Note that if 0.257 is excluded from the formula in equation (4), the result would be the arithmetic average associated with the distribution of blood-lead concentrations.

APPENDIX E2

Generating Distribution of Blood-Lead Concentrations Based on Model-Predicted Geometric Mean and Geometric Standard Deviation

APPENDIX E2

GENERATING DISTRIBUTION OF BLOOD-LEAD CONCENTRATIONS BASED ON MODEL-PREDICTED GEOMETRIC MEAN AND GEOMETRIC STANDARD DEVIATION

This section discusses how the geometric mean blood-lead concentrations predicted by either model at each housing condition were combined to characterize the national distribution of children's blood-lead concentrations for children aged 1-2. This approach was used for characterizing both pre- and post-intervention distributions predicted with the models.

Historical data suggest that blood-lead concentrations usually follow a lognormal distribution. A lognormal distribution can be characterized using two parameters, the geometric mean which is a measure of the "center" of the distribution, and the geometric standard deviation (GSD) which is a measure of the spread of the distribution. The empirical and IEUBK models both predict a geometric mean blood-lead concentration for a population of children exposed to specific levels of environmental lead. However, a population of children exposed to the same levels of environmental lead would not all have the same blood-lead concentration represented by the predicted geometric mean. Their blood-lead concentrations will vary about the predicted geometric mean because of the many other factors that contribute to children's blood-lead concentrations. These factors include differences in children's activity patterns, tendency to ingest dust or soil, parental supervision, dietary lead, other lead exposures, and amount of lead absorbed due to various biological factors.

Extant data from various studies indicate that the inherent variability in blood-lead concentration among children exposed to similar environmental-lead levels corresponds to a GSD of 1.6, the default GSD recommended in the IEUBK guidance manual (USEPA, 1994a). Under the assumption that blood-lead concentrations have a lognormal distribution with a geometric mean, GM, and GSD of 1.6, the logarithms of the blood-lead concentrations have a normal distribution with mean $\mu = \ln(GM)$ and standard deviation $s = \ln(1.6)=0.47$.

The predicted national distribution of children's blood-lead concentrations was also assumed to follow a lognormal distribution. The predicted geometric mean of the national distribution of children's blood-lead concentrations is calculated by taking a weighted geometric mean of the empirical or IEUBK model-predicted blood-lead concentrations associated with each home in the HUD National Survey, using the HUD National Survey weights adjusted for 1997 population totals.

The predicted national GSD is calculated by taking the square root of the sum of the predicted between-house variability and the assumed within-house variability. Between-house variability represents the variability among the predicted blood-lead concentrations for homes in the HUD National Survey and is computed as the weighted geometric variance of the model predicted blood-lead concentrations for each home in the HUD National Survey, using the adjusted weights for 1997. Within-house variability, variability in blood-lead concentrations of

children exposed to the same levels of environmental lead, is calculated as the weighted mean of the log variances assigned to each HUD National Survey home. This variability is assumed to be characterized by a GSD of 1.6 (log variance = $\ln (1.6)^2$) for all HUD National Survey homes. There is one exception where the child is assumed to have a blood-lead level of 63 µg/dL in which case the GSD is assumed to be 1.

The methodology for characterizing the national blood-lead distribution is slightly different for the IEUBK and empirical models because of the different ways the two models incorporate paint pica. For the empirical model, the national distribution of blood-lead concentrations is characterized as follows. For each house in the HUD National Survey, let N_i be the number of children aged 1-2 years associated with the housing unit, $GM1_i$ denote the model-predicted geometric mean blood-lead concentration for children without pica tendencies, and $GM2_i$ denote the model-predicted geometric mean blood-lead concentration for children with pica tendencies. Recall that $GM2_i$ is calculated only for units containing deteriorated or damaged lead-based paint.

The distribution of children's blood-lead concentrations in homes with no deteriorated lead-based paint was assumed to have a lognormal distribution with geometric mean $GM1_i$ and a GSD of 1.6. Children in housing units with damaged or deteriorated lead-based paint in either the interior or exterior, were partitioned into two groups:

Group #1: Assumed to contain 91% of the children, representing children who show no tendency toward paint pica. The blood-lead concentration distribution of this group is assumed to be lognormal with geometric mean $GM1_i$ and a GSD of 1.6.

Group #2: Assumed to contain 9% of the children representing children who have exhibited some tendency towards paint pica. The distribution of blood-lead concentrations for this group is assumed to be lognormal with geometric mean $GM2_i$ and a GSD of 1.6.

Let N be the sum of N_i across all homes represented in the HUD National survey (i.e., the total number of children aged 1-2 years in the 1997 housing stock). Furthermore, let A denote all housing units in the section containing no deteriorated lead-based paint, and let B denote the housing units that have some deteriorated lead-based paint. Then the aggregated log-transformed geometric mean blood-lead concentration, denoted by µ, is calculated as:

$$\mu = \frac{\left(\sum_{i\ A} N_i * \ln(GM1_i)\right) + \left(\sum_{i\ B} N_i * (0.91 * \ln(GM1_i) + 0.09 * \ln(GM2_i))\right)}{N}$$

The aggregated log-transformed GSD, denoted by s, is calculated as:

$$s = \sqrt{\frac{\left(\sum_{i\ A} K1_i\right) + \left(\sum_{i\ B} (0.91 * K1_i + 0.09 * K2_i)\right)}{N-1} + (\ln(1.6))^2}$$

where $K1_i = N_i*(\mu - \ln(GM1_i))^2$ and $K2_i = N_i*(\mu - \ln(GM2_i))^2$. The resulting national distribution of blood-lead concentrations is assumed to be lognormally distributed with geometric mean equal to e^{μ} and GSD equal to e^{s} .

For the IEUBK model, let GM_i be the model-predicted geometric mean blood-lead concentration for the i^{th} housing unit. For units without any damaged or deteriorated lead-based paint then the distribution of blood-lead concentrations is assumed to be lognormal with geometric mean GM_i and a GSD of 1.6. Children in housing units with damaged or deteriorated lead-based paint in either the interior or exterior, were partitioned into three groups:

Group #1: Assumed to contain 91% of the children, representing those children who show no tendency toward paint pica. The blood-lead concentration distribution of this group is assumed to be lognormal with geometric mean GM_i and a GSD of 1.6.

Group #2: Assumed to contain 8.97% of the children, representing those children who exhibit paint pica, but have not recently ingested Lead-based paint. The distribution of blood-lead concentrations for this group is assumed to be lognormal with geometric mean $GM_i + 3$ and a GSD of 1.6.

Group #3: Assumed to contain 0.03% of the children, representing those children who have recently ingested lead-based paint. The distribution of blood-lead concentrations for this group is assumed to be lognormal with geometric mean 63 µg/dL and a GSD of 1.

The national log-transformed geometric mean blood-lead concentration is:

$$\mu = \frac{\left(\sum_{i\ A} N_i * \ln(GM_i)\right)}{N} + \frac{\left(\sum_{i\ B} N_i * (0.91 * \ln(GM_i) + 0.0897 * \ln(GM_i + 3) + 0.0003 * \ln(63))\right)}{N}$$

The national log-transformed GSD is:

$$s = \sqrt{\frac{\left(\sum_{i\ A} K1_i\right) + \left(\sum_{i\ B} (0.91 * K1_i + 0.0897 * K2_i + 0.0003 * K3_i)\right)}{N - 1}} + V$$

where

$$V = \frac{\left(\sum_{i\ A} N_i * \ln(1.6)^2\right) + \left(\sum_{i\ B} N_i * 0.9997 * \ln(1.6)^2\right)}{N},$$

where $K1_i = N_i*(\mu - \ln(GM_i))^2$, $K2_i = N_i*(\mu - \ln(GM_i + 3))^2$ and $K3_i = N_i*(\mu - \ln(63))^2$. The resulting national distribution of blood-lead concentrations predicted by the IEUBK model is assumed to be lognormally distributed with geometric mean equal to e^{μ} and GSD equal to e^{s}.

APPENDIX F1

Methodology for Estimating Post-Intervention Distribution of Children's Blood-Lead Concentrations Resulting from Proposed §403 Rules

APPENDIX F1

METHODOLOGY FOR ESTIMATING POST-INTERVENTION DISTRIBUTION OF CHILDREN'S BLOOD-LEAD CONCENTRATIONS RESULTING FROM PROPOSED §403 RULES

This appendix details the procedures used to estimate the national distribution of blood-lead (PbB) concentrations in children aged 1-2 years in 1997 immediately after performing the relevant intervention strategies on the nation's housing stock under the proposed §403 rules.

Outline of the Methodology

This methodology characterizes the pre-§403 blood-lead distribution for children aged 1-2 years using reported information from NHANES III. A model-based procedure (either the empirical or IEUBK model) is used to characterize the distribution of blood-lead concentrations at both pre-§403 and post-§403, and the observed differences between the two distributions are identified. Then, a post-§403 distribution that is comparable to the pre-§403 NHANES III distribution is derived based on the differences between the two model-based estimates and the pre-§403 NHANES III distribution.

The methodology consists of the following four steps:

#1. Use blood-lead concentration data reported in the NHANES III to estimate the geometric mean (GM) and the geometric standard deviation (GSD) associated with the baseline (i.e., pre-§403) distribution of blood-lead concentration for children aged 1-2 years.

#2. Use the environmental-lead levels for HUD National Survey units as input to either the IEUBK or Empirical model to obtain a model-based estimate of the geometric mean and the geometric standard deviation (GSD) associated with the baseline distribution of blood-lead concentration for children aged 1-2 years.

#3. Use adjusted (post-§403) environmental-lead levels for HUD National Survey units as input to the model used in Step #2 to estimate the geometric mean and the geometric standard deviation (GSD) associated with the post-§403 distribution of blood-lead concentration for children aged 1-2 years.

#4. Combine the parameters of the three distributions described in #1, 2, and 3 to estimate the geometric mean and GSD of a post-§403 blood-lead distribution that is consistent with the pre-§403 NHANES III distribution determined in Step #1 and the changes in the blood-lead distributions estimated in Steps #2 and #3.

Details of the Methodology

A key assumption in this methodology is that blood-lead concentrations are assumed to be lognormally distributed, regardless of whether they represent pre- or post-§403 concentrations or whether the distribution is based on NHANES III data or is model-based. With this assumption and by estimating the geometric mean and GSD of the distribution, the entire distribution is characterized.

All four steps of the methodology are now discussed in detail.

#1. Use NHANES III to characterize the pre-§403 distribution.

A weighted geometric mean and weighted geometric standard deviation of the blood-lead concentrations are calculated for 1-2 year old children based on NHANES III. The weights are those discussed in Section 3.4.1. Call these variables GM_1 and GSD_1, respectively. These values were calculated as geometric mean (GM_1) = 3.14 µg/dL and geometric standard deviation (GSD_1) = 2.09.

#2. Derive a model-based characterization of the pre-§403 distribution.

Because interventions under §403 have not yet occurred, precluding post-§403 blood-lead concentrations from being directly measured, the blood-lead distribution resulting from the proposed §403 rules must be estimated. For this reason, this methodology characterizes pre- and post-§403 blood-lead distributions that are model-based (i.e., predicted blood-lead concentrations as a function of environmental-lead levels are obtained using either the IEUBK or empirical model).

Environmental-lead levels in the HUD National Survey database are used as input to the model to characterize the pre-§403 distribution of blood-lead in children aged 1-2 years. The model-based pre-§403 blood-lead distribution is assumed to be lognormally distributed. A weighted geometric mean and weighted geometric standard deviation of these concentrations are calculated, where the weights correspond to the number of children associated with each concentration. Call these variables GM_2 and GSD_2, respectively.

#3. Derive a model-based characterization of the post-§403 distribution.

The same method used in Step #2 is used to characterize a model-based post-§403 distribution (Step #3). Step #3 differs from Step #2 in that the environmental-lead levels from the HUD National Survey are adjusted to reflect the effects of intervention. This adjustment is documented in Table 6-2 of Volume I. Let GM_3 and GSD_3 be the weighted geometric mean and geometric standard deviation, respectively, of the predicted post-§403 blood-lead concentrations. Thus, the model-based post-§403 blood-lead distribution is characterized as lognormally distributed with geometric mean GM_3 and geometric standard deviation GSD_3.

#4. Derive a post-§403 distribution from NHANES III and Steps #2 and #3.

The three distributions calculated in Steps #1 through #3 are used to characterize a post-§403 blood-lead distribution that is directly comparable with the pre-§403 distribution determined in Step #1. This distribution is assumed to be lognormal with geometric mean GM_4 and geometric standard deviation GSD_4 calculated by the following formulas:

$$GM_4 = GM_1 * (GM_3 / GM_2) \quad (1)$$

$$GSD_4 = GSD_1 * (GSD_3 / GSD_2) \quad (2)$$

APPENDIX F2

Estimation of Primary Prevention Efficacy Using Model of Bone-Lead Mobilization

APPENDIX F2

ESTIMATION OF PRIMARY PREVENTION EFFICACY USING MODEL OF BONE-LEAD MOBILIZATION

Though the scientific literature documents the effectiveness of a range of behavioral and environmental intervention strategies on their ability to reduce childhood lead exposure, efficacy is measured only among already exposed children (USEPA, 1995b). Specifically, declines in children's blood-lead concentration on the order of 25% as measured 6 to 12 months following a variety of intervention strategies were reported (Copley, 1983; Charney, et al., 1983; Amitai, et al., 1991; Weitzman, et al., 1993; Staes, et al., 1994; Kimbrough, et al., 1994). This secondary prevention intervention effectiveness is likely not representative of the effectiveness being sought from the promulgation of §403. The §403 standards for lead in dust, soil, and paint are mostly intended to prevent childhood lead exposure before it occurs and, therefore, their effectiveness will be assessed by measures of primary prevention efficacy.

Secondary prevention efficacy results are not necessarily representative of those expected from primary prevention because lead present in blood is a combination of current environmental exposure and internal sources of lead. A significant internal source of lead is bone tissue. After prolonged exposure to lead, bone tissue retains much more lead than the other body tissues (Schroeder and Tipton, 1968; Barry and Mossman, 1970; Barry, 1975; Barry, 1981; Leggett, et al., 1982). Nordberg, et al. suggest that bone can become an internal source of lead during periods of reduced external exposure to lead; see also (Rabinowitz, et al., 1976; Barry, 1981; Hyrhorczuk, et al., 1985; Rabinowitz, 1991). The reported declines in blood-lead concentration, therefore, may underestimate the primary prevention effectiveness of the associated intervention strategy.

Unfortunately, there is limited empirical evidence regarding the extent to which bone-lead stores are able to keep blood-lead levels elevated following an intervention, especially concerning children. One study (Markowitz, et al., 1993) measured bone-lead levels in children before and after an intervention, but found no significant decline in the levels over a period of six weeks. Despite the lack of studies concerning children, Nordberg, et al. claim that "skeletal turnover is highest among children under 10 years of age." Several studies have been conducted to study bone-lead mobilization in adults (Rabinowitz, et al., 1976; Hyrhorczuk, et al., 1985; Wrenn, et al., 1972; Cohen, et al., 1973; Rabinowitz, et al., 1973; Batschelet, et al., 1979; Heard, et al., 1984; Marcus, 1985; Christofferson, et al., 1986; Cristy, et al., 1986; Schutz, et al., 1987; Bert, et al., 1989; Nilsson, et al. 1991; Gulson, et al., 1995). For example, Gulson, et al. show that 45% to 70% of lead in the blood of adult women comes from long-term tissue stores, primarily the bone tissue. A similar result was observed in another study on five adult subjects undergoing knee and hip replacement (Smith, et al., 1996).

If the contribution of mobilized bone-lead stores can be characterized, however, it would be possible to translate the documented secondary prevention results into estimated primary prevention results. An approach is presented here for estimating the efficacy of a primary prevention intervention given an observed effectiveness for a secondary prevention intervention.

The approach is based on a bone-lead mobilization model developed to estimate the degree to which bone-lead stores could mask the full effectiveness of an intervention by mobilizing into the child's blood. This model is extensively discussed and its basis documented elsewhere (Rust, et al., 1996), though a summary is provided below.

A Model for Bone-Lead Mobilization

To evaluate the potential for continuing elevated blood-lead levels due to bone-lead mobilization, a two-compartment model (see Figure F2-1) was adopted for the transfer of lead between the blood and bone tissues within the body and elimination of lead from the body.

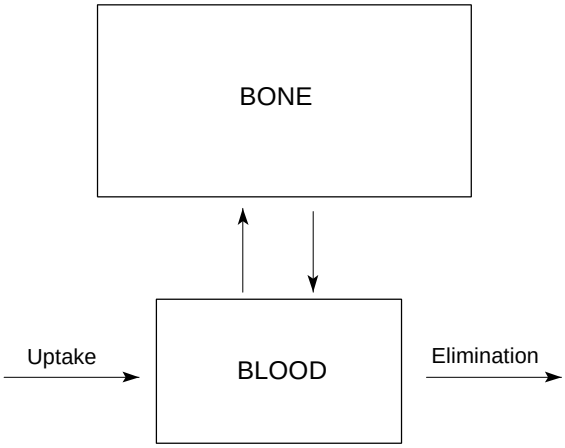

Figure F2-1. Two Compartment Model of Bone-Lead Mobilization.

In this model, lead is taken into the body (from the gastrointestinal tract and lungs) via the blood, transfers between the blood and bone tissue, and is eliminated from the body via the blood. It is assumed that the transfer of lead between the blood and bone tissues, and elimination of lead from the blood follows a first-order kinetic relationship.

While the adopted model is most certainly an oversimplification, model results will approximate those of other more complicated models involving additional tissue compartments for two reasons:

- While lead does mobilize from non-bone tissues following a decrease in environmental lead uptake, the effects are believed to be limited to a period of days or weeks due to the lower concentrations of lead amassed in these tissues, and
- While all lead elimination from the body does not occur via a direct pathway from the blood, the kinetic parameters used in the model properly include these other pathways (endogenous fecal and via other soft tissues) as if they were directly from the blood.

Based on the model illustrated in Figure F2-1, blood-lead concentrations (PbB) after intervention would follow the relationship illustrated in Figure F2-2. More specifically, immediately after intervention there would be an initial drop from the pre-intervention PbB level (PbB_{Pre}) to achieve an immediate post-intervention PbB level ($PbB_{ImmPost}$). $PbB_{ImmPost}$ represents the blood-lead concentration that can be supported by the amount of lead being transferred from the bone. After this initial drop, blood-lead concentrations would follow an exponential decline toward the long-term post-intervention PbB level ($PbB_{LongTerm}$). $PbB_{LongTerm}$ is the blood-lead level that can be supported by the post-intervention exposure level, with no additional lead from the bone. At any a particular length of time following the intervention, illustrated by the symbol "T" on the horizontal axis in Figure F2-2, a target post-intervention PbB level ($PbB_{Observed}$) will be observed. The original analysis using this model (Rust, et al., 1996) estimated the maximum length of time (T) the bone-lead stores would be capable of keeping the blood-lead concentration above the targeted observed level ($PbB_{Observed}$) for a given value of $PbB_{LongTerm}$. For the purposes of the sensitivity analysis for §403, the maximum long-term effectiveness is estimated instead. As the long-term percent decline reflects the post-intervention PbB that can be support by the post-intervention exposure level, it is assumed this decline is equal to the primary prevention effectiveness of the intervention.

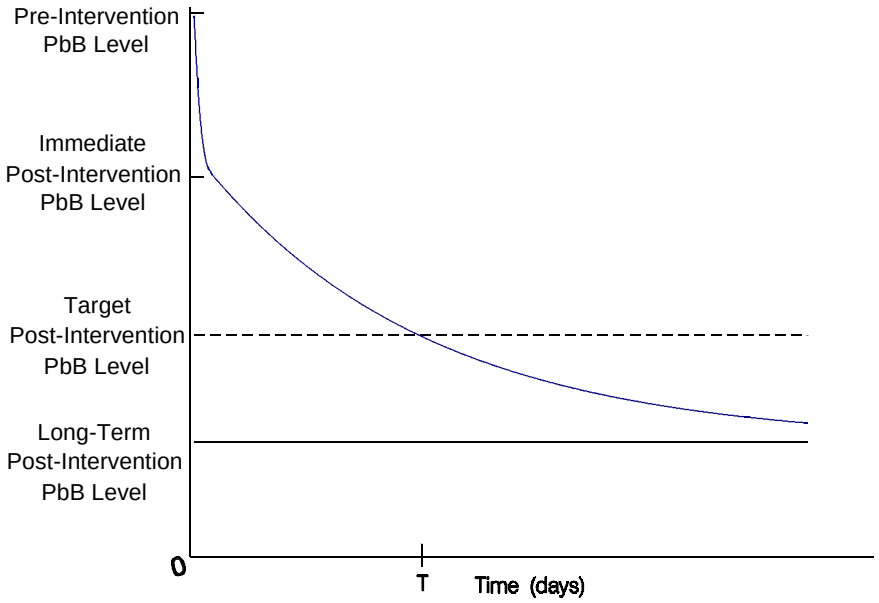

Figure F2-2. Blood-Lead Concentration Versus Time Following a Reduction in Lead Uptake.

The child's blood-lead concentration at t days post-intervention is given by the equation

$$PbB = PbB_{LongTerm} + (PbB_{ImmPost} - PbB_{LongTerm}) \cdot \exp(-t \cdot KBONEBL_{Net}) \quad (1)$$

where $KBONEBL_{Net}$ is the net rate of lead flow from bone to blood to elimination. This rate is a function of the blood-lead level following the initial drop ($PbB_{ImmPost}$) as well as other kinetic parameters (e.g., the lead mass ratio of bone to blood and the elimination rate of lead from the blood) which can be estimated from existing scientific literature (Rust, et al., 1996). As portrayed in Figure F2-2, the blood-lead concentration follows an exponential decline toward $PbB_{LongTerm}$. Setting PbB in Equation (1) equal to $PbB_{Observed}$ and solving for the long-term percent decline in blood-lead concentration ($R_{LongTerm}$) results in the following equation:

$$R_{LongTerm} = \frac{PbB_{LongTerm}}{PbB_{Pre}} = \frac{R_{Observed} - R_{ImmPost} \cdot \exp(-t \cdot KBONEBL_{Net})}{1 - \exp(-t \cdot KBONEBL_{Net})} \qquad (2)$$

where

$$R_{Observed} = \frac{PbB_{Observed}}{PbB_{Pre}} \quad \text{and} \quad R_{ImmPost} = \frac{PbB_{ImmPost}}{PbB_{Pre}} .$$

The maximum efficacy of an intervention, then, may be calculated given two parameters:

1. the observed percent decline ($R_{Observed}$) in an exposed child's blood-lead concentration following an intervention (i.e., the observed secondary prevention efficacy); and

2. the length of time (t) following the intervention when the decline was observed.

Note that this process estimates the maximum value of $R_{LongTerm}$ that might have yielded the inputted values of $PbB_{Observed}$ and t based on Equation (1). The specific value may lie between $R_{Observed}$ and $R_{LongTerm}$. The estimated primary prevention efficacy is a maximum in that $R_{ImmPost}$, and therefore $KBONEBL_{Net}$, cannot be estimated from available data (Rust, et al., 1996). It is necessary to estimate the maximum efficacy over a range of possible values for $R_{ImmPost}$.

Results of Modeling Bone-Lead Mobilization

To illustrate the efficacy of primary prevention, values of 25%, 50%, and 75% are considered for the observed secondary prevention efficacy and values of 6, 12, 18, and 24 months are considered for the lengths of time. Table F2-1 presents the maximum primary prevention efficacy for these scenarios for children 1 to 7 years of age. The standard error of the estimated efficacy—calculated by propagating, through the model, the standard errors of the underlying model parameters—is enclosed in parentheses.

As an example of the results in Table F2-1, note that if the observed effectiveness of a secondary intervention is assumed to be 25% (i.e., PbB decline to 75% percent of the pre-intervention level) at 6 months post-intervention for a 2 year old, then the implied effectiveness of primary prevention will be at most 47%. The scientific literature reports secondary prevention efficacy of approximately 25% declines in blood-lead concentration 12 months following dust

abatements, lead-based paint abatements, elevated soil lead abatements, and intensive educational efforts (USEPA, 1995b). Depending upon the age of the child benefitting from the intervention, the results in Table F2-1 would suggest these interventions would prompt primary prevention efficacy of between 30% and 59% (column: “Length of Time, 12 Months”; row: “Observed Efficacy of Secondary Prevention, 25%”).

Empty cells in Table F2-1 indicate that those scenarios cannot possibly occur based on Equation (1). For example, for a 7 year old, the impact of mobilized bone-lead stores would result in less than a 25% decline in blood-lead concentration at 6 months, even for a 100% effective intervention. Estimates of primary prevention efficacy under these “impossible” scenarios are not meaningful and are therefore not shown.

Consistent with the limited data available on bone-lead mobilization, the standard errors in Table F2-1 are quite large. By incorporating the 95% upper confidence bounds on the maximum primary prevention efficacy, the resulting bounded estimates are 1.2 to 1.9 times larger than the mean estimates reported in the table.

As described above, this analysis estimates the maximum efficacy of primary prevention interventions. Consideration was also given to obtaining the minimum efficacy. It was determined that the present model can provide a meaningful solution for the maximum case only, and that additional empirical data and extensive model enhancement are required to solve the minimum case. Only the maximum efficacy, therefore, is reported.

Table F2-1. Maximum Efficacy of Primary Prevention For Blood-Lead Levels (PbB) Observed at 25%, 50%, and 75% of Pre-Intervention Levels at 6, 12, 18, and 24 Months.

Observed Efficacy of Secondary Prevention[a]	Child's Age (years)	Length of Time[b] (months)			
		6	12	18	24
25%	1	0.39 (0.16)	0.30 (0.05)	0.28 (0.03)	0.27 (0.02)
	2	0.47 (0.18)	0.33 (0.08)	0.30 (0.04)	0.28 (0.03)
	3	0.56 (0.21)	0.36 (0.14)	0.31 (0.07)	0.29 (0.04)
	4	0.67 (0.25)	0.41 (0.19)	0.34 (0.10)	0.31 (0.06)
	5	0.79 (0.27)	0.47 (0.19)	0.37 (0.14)	0.33 (0.08)
	6	0.91 (0.32)	0.53 (0.21)	0.40 (0.19)	0.35 (0.12)
	7		0.59 (0.22)	0.44 (0.19)	0.37 (0.15)
50%	1	0.78 (0.32)	0.60 (0.09)	0.56 (0.05)	0.55 (0.04)
	2	0.94 (0.36)	0.65 (0.16)	0.59 (0.08)	0.56 (0.06)
	3		0.73 (0.27)	0.63 (0.13)	0.59 (0.08)
	4		0.83 (0.37)	0.68 (0.21)	0.62 (0.13)
	5		0.93 (0.38)	0.73 (0.29)	0.66 (0.17)
	6			0.81 (0.37)	0.70 (0.24)
	7			0.89 (0.37)	0.75 (0.31)
75%	1		0.90 (0.14)	0.84 (0.08)	0.82 (0.05)
	2		0.98 (0.25)	0.89 (0.13)	0.85 (0.09)
	3			0.94 (0.20)	0.88 (0.13)
	4				0.93 (0.19)
	5				0.98 (0.25)
	6				
	7				

Note: An empty cell means that the scenario is not possible according to model predictions.

[a] This is equivalent to the observed percent decline in an exposed child's blood-lead levels at a specified time point following the intervention.

[b] This is equivalent to the length of time following the intervention when the decline was observed.