Calculating the Interindividual Geometric Standard Deviation for Use in the Integrated Exposure Uptake Biokinetic Model for Lead in Children

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The integrated exposure uptake biokinetic (IEUBK) model, recommended for use by the U.S. Environmental Protection Agency at residential Superfund sites to predict potential risks to children from lead exposure and to establish lead remediation levels, requires an interindividual geometric standard deviation (GSD) as an essential input parameter. The GSD quantifies the variability of blood lead concentrations for children exposed to similar environmental concentrations of lead. Estimates of potential risks are directly related to the GSDi, and therefore the GSD, directly impacts the scope of remediation at Superfund sites. Site-specific GSDs can be calculated for sites where blood lead and environmental lead have been measured. This paper uses data from the U.S. Environmental Protection Agency at residential Superfund sites conducted at the Bingham Creek and Sandy, Utah, Superfund sites to calculate GSDs using regression modeling, box modeling, and structural equation modeling. GSDs were calculated using various methods for treating values below the analytical method detection and quantitation limits. Treatment of nonquantifiable blood lead concentrations affected the GSD, more than the statistical method used to calculate the GSD. For any given treatment, the different statistical methods produced similar GSDs. Because of the uncertainties associated with data in the blood lead studies, we recommend that a range of GSDs be used when analyzing site-specific risks associated with exposure to environmental lead instead of a single estimate. Because the different statistical methods produce similar GSDs, we recommend a simple procedure to calculate site-specific GSDs from a scientifically sound blood and environmental lead study. Key words: blood lead variability, integrated exposure uptake biokinetic model, interindividual geometric standard deviation, lead exposure, risk analysis. Environ Health Perspect 107:481–487 (1999). [Online 6 May 1999] http://ehpnet1.niehs.nih.gov/docs/1999l107p481-487/griffinlabstract.html

The integrated exposure uptake biokinetic (IEUBK) model for lead is recommended for use by the U.S. Environmental Protection Agency (EPA) at residential Superfund sites to predict potential risks to children from lead exposure and to establish lead remediation levels. The IEUBK model is designed to integrate exposure from lead in air, water, soil, dust, diet, paint, and other sources with pharmacokinetic modeling to predict blood lead concentrations in children 6 months to 7 years of age. Based on the available information about children's exposure to lead, the model estimates a distribution of blood lead concentrations centered on the geometric mean blood lead concentration. This distribution is described by the interindividual geometric standard deviation (GSDi) and is intended to represent the variability in blood lead concentrations for children exposed to similar environmental concentrations of lead. This variability is a result of behavioral and physiological differences and variability introduced during laboratory analysis. From this distribution, the IEUBK model calculates the probability that children's blood lead concentrations will exceed a level of health concern. The EPA has established a blood lead concentration of 10 µg/dL as the level of health concern. The EPA Superfund program has also made a policy decision that no more than 5% of the distribution of blood lead concentrations should exceed this 10 µg/dL concentration of health concern. For example, lead-contaminated soil at Superfund sites will be remediated to a level where there is no more than a 5% probability of blood lead concentrations in children exceeding 10 µg/dL, as calculated by the IEUBK model, even when measured blood lead concentrations in the site population are below 10 µg/dL. For a given geometric mean blood lead concentration predicted by the IEUBK model, when the GSDi is large, a larger portion of the population is expected to be above the blood lead concentration of 10 µg/dL. This results in a larger estimate of risk and a greater extent of remediation at a site. When the GSDi is smaller, even though the estimated geometric mean blood lead concentration is the same, less of the population falls above 10 µg/dL, and less remediation is needed. Given that blood lead concentrations in the U.S. population have been decreasing since the 1970s and that the national average is 2.3 µg/dL, even minor changes in the GSDi can have a significant impact on the extent and costs of lead site remediation.

The recommended default GSDi for the IEUBK model for lead is 1.6 and is based on an average of GSDs, calculations from blood lead studies at three lead-contaminated sites. The GSDi for these sites ranged from 1.5 to 1.7. These GSDi were calculated using residual standard deviation estimates in a system of structural equations and used all blood lead concentrations as reported. At the majority of hazardous waste sites where lead is a contaminant, few environmental data and no blood lead concentrations are collected. At these sites it is appropriate, and generally protective, to use the default GSDi in the IEUBK model to characterize variability in blood lead distributions and calculate media-specific cleanup goals. However, given regional differences in population demographics and behaviors, the GSDi may vary from site to site. GSDi estimates for several mining and smelting sites ranging from 1.3 to 1.8 have been reported. A well-designed and representative blood lead study has been conducted for a site, this information can be useful in calculating a site-specific GSDi, which improves the accuracy of the IEUBK model predictions and the calculation of media-specific cleanup goals.

This paper presents several methodologies for calculating the GSDi, including those described in the Guidance Manual for the IEUBK Model for Lead in Children and discusses the performance advantages and limitations of each. Statistical methods used to calculate the GSDi include nonlinear regression analysis, structural equation modeling, and two variations of the box model. For the box model, three methods to derive the median were used to estimate the GSDi.

The guidance manual for the IEUBK model describes two methods for estimating the GSDi. The first is commonly called a box model, and the second is a direct regression method based on the assumption that blood lead concentrations are approximately linear functions of soil and dust lead.

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concentrations, with age-dependent regression coefficients (I).

Environmental, blood lead, and behavioral data used in this paper were collected by the University of Cincinnati (Cincinnati, OH). The blood lead studies were for children from Bingham Creek and Sandy, Utah. Bingham Creek is a residential community southwest of Salt Lake City. Homes in the community are located on or adjacent to tailings deposits from mining and milling operations in the Oquirrh Mountains. Sandy is also southwest of Salt Lake City in Salt Lake County and was home to four lead smelters that operated in the 1870s. One of these smelters continued to operate until 1902.

Methods

This section briefly describes the methods used by the University of Cincinnati to collect data for the two blood lead studies and the statistical analyses used for calculating the GSD, for the studies.

Blood lead studies. Investigators from the University of Cincinnati measured environmental concentrations of lead, potential exposure variables, social and demographic variables, and blood lead for both the Bingham Creek and the Sandy studies. Results of these studies are available as part of the administrative records for these Superfund sites (5,6). Measured variables included in the calculations of the GSD, were lead concentrations in residential interior surface dust; exterior surface dust at entry; exterior surface dust at street curb; soil collected from the house perimeter, garden, bare yard area, play area, or sandbox; water at the kitchen tap; and interior paint. Other variables measured and included were house age, dust loading, the Hollingshead socioeconomic status (SES), child’s age, and frequency of child’s mouthing behaviors as determined through a survey. The minimal amount of data required for an individual child to be included in the statistical analyses was blood lead, soil lead, and interior dust lead concentrations.

In the Bingham Creek study, environmental media sampling occurred during June, July, August, and September of 1993, and blood lead sampling occurred during August, September, and October of 1993. In the Sandy study, environmental media sampling occurred during April, May, and June of 1994, and blood lead sampling occurred during October and November of 1994.

Soil, exterior dust, and paint lead concentrations were analyzed using X-ray fluorescence spectroscopy. Atomic absorption spectroscopy (AA) was used as a verification technique. Handwipe, interior dust, and water samples were analyzed by AA.

Air sampling data were not collected at the Sandy smelter or Bingham Creek sites. However, lead concentrations in the air were collected from air monitoring samplers at other residential smelter sites in the Salt Lake City area. Results of that sampling showed lead concentrations in air are less than 0.11 μg/m³ (7)—below average urban air lead concentrations.

Blood lead was analyzed using anodic stripping voltometry (ASV). Each sample was analyzed twice, and the duplicate values were averaged. Method detection limits for ASV were reported by the University of Cincinnati at 1.4 ± 0.4 μg/dL. Method quantitation limits, defined as 5–10 standard deviations above the blank signal (δ), were determined from the reported standard deviation. For the statistical analyses, the method quantitation limit of 5 standard deviations above the blank signal was selected. The resulting method quantitation limit was 2 μg/dL.

Child mouthing behavior was reported in a graduated manner for 14 questions that addressed sucking behavior and mouthing behavior toward 10 objects, and whether the child took food or a pacifier while in the yard. A weighted system was used to normalize the results of the responses.

Statistical analyses. Statistical analyses used to evaluate the GSD, were nonlinear regression analysis, structural equation modeling, and box modeling. Each of these analyses is described in this section.

Initial exploratory data analysis consisted of univariate distributional fitting; Spearman rank correlations among blood, environmental, and behavioral lead data; and three-dimensional plots of log-transformed blood, soil, and dust lead data.

Both the Bingham Creek and Sandy blood lead data sets reported blood lead concentrations below the detection limit of 1.4 μg/dL and values below the lowest method quantitation limit of 2.0 μg/dL. Values reported below the method quantitation limit are considered nonquantifiable values. Several data treatments were used to address the nonquantifiable values. GSD values were calculated using the data as reported, replacing values below the detection limit with one-half the detection limit (0.7 μg/dL), values below the detection limit with the detection limit (1.4 μg/dL), values below the method quantitation limit with one-half the method quantitation limit (1.0 μg/dL), and values below the method quantitation limit with the method quantitation limit (2.0 μg/dL).

Nonlinear regression analysis. Nonlinear regression analysis consisted of two log regression model equations—the log of linear and the linear in log models (9,10). The log of linear model regresses the log of the sum of all explanatory variables on the response variable, the log of blood lead. The linear in log model regresses the sum of the log of each explanatory variable on the log of blood lead. The explanatory variables consist of combinations of age, soil lead, dust leads inside and outside the home, mouthing index, and the SES. Age was represented by a dummy variable and was stratified in 12-month intervals from 0 to 72 months.

Nonlinear regression model selection. Competitive models using various combinations of the explanatory variables were evaluated for selection of the best model on the basis of greater adjusted R², positive coefficients (except SES), and positive coefficients significantly greater than zero. Some simple regression diagnostics as residual normality, autocorrelation, and homogeneity of variance were performed to assess model validity. Nonlinear regression models were fit using the nonlinear regression program in SYSTAT (SYSTAT for Windows: Statistics, version 5 edition; Evanston, IL). Nonlinear regression was performed to accommodate small departures from linearity.

The residual log blood lead is the difference between the observed log blood lead and the estimated log blood lead. The GSD, for nonlinear regression models is calculated as the exponential of the square root of the variance of the residual log blood lead. The approximate two-sided 95% confidence interval (CI) around the GSD, is given by:

\[ CI = \exp\left(\hat{r} \pm t_{0.975, df}(rv)\sqrt{2/df}\right) \]

where \(rv\) is the residual variance; \(df\) is the degrees of freedom (sample size minus number of explanatory variables minus 1) of the nonlinear regression; and \(t\) is the 97.5 percentile of the \(t\) distribution with \(df\).

Structural equation modeling. Structural equation models (SEqMs) were developed for this study in a manner analogous to the nonlinear regression models. SEqM in this comparison was performed using EQS version 4.02 (BMDP Statistical Software, Inc., Los Angeles, CA) and PROC MODEL in the SAS/ETS (Econometrics and Time Series) package (SAS Institute, Inc., Cary, NC). EQS was used to develop linear in log models, and PROC MODEL was used to develop log of linear models. Data were also analyzed using SAS PROC LIFEREG, an alternative method using censored regression modeling.

There are a number of differences in the purposes and methods between EQS and PROC MODEL, although similar results
can be obtained when comparable methods are used. The EQS estimation procedure used in the SEmA was maximum-likelihood with robust error estimates. The PROC estimation procedures evaluated in this comparison were: seemingly unrelated regressions (SUR); iterated three-stage least squares (IT3SLS); generalized method of moments (GMM); iterated generalized method of moments (ITGMM); and full information maximum likelihood (FIML). Details of differences among the methods are described in the ETS User’s Guide (11).

The EQS and SAS models were evaluated and a best model for each data treatment was selected based on goodness-of-fit statistics, and significantly positive environmental lead coefficients for those explanatory variables regressed directly on blood lead (12–15).

Box models. The box model is a simple approach to calculating a GSD, without complex statistical programs. It is based on the assumption that children of similar environmental exposure will have similar blood lead concentrations. Children with similar soil lead, dust lead, and other lead exposures can be grouped together in boxes. The geometric mean lead and the geometric standard deviation of each box (GSD) is calculated. The GSDs are ranked from smallest to largest. The GSD is then calculated from the ranked GSD. Three methods were used to calculate GSD; using the box model results: using the median value (the middle value), calculating the weighted median value (the value associated with the median number of children), and calculating the weighted variance (multiplying the intra-box variance by the number of children in the box, dividing the square root of the sum by the square root of the degrees of freedom, and exponentiating the result). The 95% confidence limits around the GSD were determined for the median and weighted median using nonparametric confidence limits for quantiles (16) and for the weighted variance using approximate confidence limits for the mean (16). Variables included in this comparison were soil, dust, child’s age, and numbers of families per box.

For the static box model, the data set is first divided into subgroups by the variable selected. Each subgroup represents a box. Boxes were defined by graduating soil and dust concentrations in increments of 200 mg/kg. The natural logarithm of each blood lead was then placed in the appropriate box and the GSD of the cell is calculated. Microsoft Excel (version 5.0; Microsoft Corp., Redmond, WA) pivot tables were used to create each model.

The sliding box model develops less arbitrary boxes. For sliding box models, data were treated identically to static box models; however, the cells overlapped. By overlapping concentrations of soil and dust, a child could be a member of more than one cell. This method adds power to the results by increasing the number of boxes that can be used and by increasing the number of children in each box. However, because the mean blood lead concentration of some, but not all, children is used more than once, it could be argued that sliding box results are biased.

Results

The results of the statistical analyses of the Bingham Creek and Sandy studies are presented separately. There were 875 children in the Bingham Creek data set with blood lead, soil lead, and interior dust lead concentrations included in the analysis. In blood lead samples from 170 of the children, at least 1 of the duplicate values was below the method detection limit. In blood lead samples from 65 children, both of the values were below the method detection limit. Samples from 377 of the children had at least 1 of the duplicate values below the method quantitation limit, and samples from 94 of the children had both values below the method quantitation limit. A large majority of the children (n = 832) lived in homes where both the soil and dust lead concentrations were below 400 mg/kg. The geometric mean lead concentration for the Bingham Creek data set was 3.1 µg/dL and the sample GSD was 1.6.

None of the environmental data for children included in the analysis fit any of the common univariate distributions. Concentrations of lead in soil, water, and interior and exterior dust were significantly correlated with blood lead concentrations at the 5% level of significance. Age and SES were negatively correlated, whereas the environmental variables were positively correlated with blood lead concentrations. Average soil concentration was significantly correlated with both interior and exterior dust. Generally, the correlations were significant but were small. The three-dimensional plot of soil, interior dust, and blood lead did not reveal any apparent outliers.

The best nonlinear regression model for the Bingham Creek data set was

\[ \log(\text{observed blood lead}) = \log(BD \times \text{interior dust lead} + BE \times \text{entryway dust lead} + B_{9-12} \times [\text{age 0–12 months}] + \ldots + B_{60-72} \times [\text{age 60–72 months}] + BM \times [\text{mouthing index}] + BM \times BS \times [\text{mouthing index}] \times \text{soil lead} + BSES \times SES) \]

where \(BD = \) parameter estimate for dust lead; \(BE = \) parameter estimate for entryway dust; \(B_{9-12} = \) parameter estimate for children between 0 and 12 months of age; \(B_{60-72} = \) parameter estimate for children between 60 and 72 months of age; \(BM = \) parameter estimate for mouthing behavior; \(BS = \) parameter estimate for soil lead; \(BSES = \) parameter estimate for socioeconomic status.

The results of different detection and quantitation limit treatments on the log of linear and linear in log model types are presented in Table 1. Depending on the treatment of values below the detection and quantitation limits, GSD, ranged from 1.4 to 1.7.

Regression residual diagnostics were problematic. The residual average was close to zero (<0.0001 for all models and below detection limit treatments), and the residual variance was typically approximately 0.2. The residuals were not normally distributed, as evidenced by normality plots and the Shapiro-Francia extension of the Shapiro-Wilk test (as implemented in the IMSL FORTRAN subroutine included in Microsoft FORTRAN Powerstation Professional Edition version 4.0). The

Table 1. Nonlinear regression analysis results for the Bingham Creek data set.

| Treatment                          | Model type   | Lower 95% CL | Interindividual GSD | Upper 95% CL |
|------------------------------------|--------------|--------------|----------------------|--------------|
| All children, blood lead           | Log of linear| 1.5          | 1.6                  | 1.6          |
| as reported                        | Linear log   | 1.5          | 1.6                  | 1.6          |
| Replacement of blood lead values   | Log of linear| 1.4          | 1.5                  | 1.5          |
| below detection limit              | Linear log   | 1.4          | 1.5                  | 1.5          |
| Replacement of blood lead values   | Log of linear| 1.6          | 1.6                  | 1.6          |
| below detection limit              | Linear log   | 1.6          | 1.6                  | 1.6          |
| Replacement of blood lead values   | Log of linear| 1.4          | 1.4                  | 1.4          |
| below quantitation limit           | Linear log   | 1.4          | 1.4                  | 1.4          |
| Replacement of blood lead values   | Log of linear| 1.6          | 1.7                  | 1.7          |
| below quantitation limit           | Linear log   | 1.6          | 1.7                  | 1.7          |

Abbreviations: CL, confidence limits; GSD, geometric standard deviation.
Spearman rank measure of heteroscedasticity (17) typically indicated the residuals exhibited homogeneity of variance, whereas the score test (18,19) indicated the residuals did not exhibit homogeneity of variance. Results of these two homogeneity of variance tests usually agree. Residual plots failed to show marked evidence of heteroscedasticity. The residuals were never serially correlated.

An SEqM diagram for the Bingham Creek data set is presented in Figure 1.

![Figure 1. Structural equation model for lead in Bingham Creek children. All paths are significant unless indicated otherwise.](image)

**Table 2. Structural equation model results for the Bingham Creek data set.**

| Treatment                                                                 | Model type          | Lower 95% CL | Interindividual GSD | Upper 95% CL |
|---------------------------------------------------------------------------|---------------------|--------------|----------------------|--------------|
| All children, blood lead as reported                                      | Log of linear       | 1.6          | 1.6                  | 1.6          |
| Replacement of blood lead values below detection limit with detection limit | Linear in log       | 1.5          | 1.5                  | 1.5          |
| Replacement of blood lead values below detection limit with 1/2 detection limit | Linear in log       | 1.6          | 1.6                  | 1.7          |
| Replacement of blood lead values below quantitation limit with quantitation limit | Linear in log       | 1.4          | 1.4                  | 1.4          |
| Replacement of blood lead values below quantitation limit with 1/2 quantitation limit | Linear in log       | 1.5          | 1.6                  | 1.7          |

Abbreviations: CL, confidence limit; GSD, geometric standard deviation.

**Table 3. Box model results for the Bingham Creek data set.**

| Treatment                                                                 | Lower 95% CL | Median | Upper 95% CL | Lower 95% CL | Weighted median | Upper 95% CL | Lower 95% CL | Weighted variance | Upper 95% CL |
|---------------------------------------------------------------------------|--------------|--------|--------------|--------------|-----------------|--------------|--------------|-------------------|--------------|
| Static box                                                                |              |        |              |              |                 |              |              |                   |              |
| All children, blood lead as reported                                      | 1.4          | 1.6    | 1.9          | 1.5          | 1.5             | 1.5          | 1.6          | 1.7               |              |
| Replacement of blood lead values below detection limit with detection limit | 1.2          | 1.6    | 1.9          | 1.6          | 1.6             | 1.6          | 1.6          | 1.7               |              |
| Replacement of blood lead values below detection limit with 1/2 detection limit | 1.4          | 1.5    | 1.7          | 1.5          | 1.5             | 1.5          | 1.4          | 1.5               |              |
| Replacement of blood lead values below quantitation limit with quantitation limit | 1.3          | 1.3    | 1.6          | 1.3          | 1.3             | 1.3          | 1.3          | 1.4               |              |
| Replacement of blood lead values below quantitation limit with 1/2 quantitation limit | 1.4          | 1.7    | 1.9          | 1.7          | 1.7             | 1.7          | 1.5          | 1.8               |              |
| Sliding box                                                               |              |        |              |              |                 |              |              |                   |              |
| All children, blood lead as reported                                      | 1.5          | 1.6    | 1.8          | 1.5          | 1.5             | 1.5          | 1.6          | 1.6               |              |
| Replacement of blood lead values below detection limit with detection limit | 1.6          | 1.6    | 1.7          | 1.6          | 1.6             | 1.6          | 1.6          | 1.7               |              |
| Replacement of blood lead values below detection limit with 1/2 detection limit | 1.5          | 1.5    | 1.6          | 1.5          | 1.5             | 1.5          | 1.5          | 1.6               |              |
| Replacement of blood lead values below quantitation limit with quantitation limit | 1.3          | 1.4    | 1.5          | 1.4          | 1.4             | 1.3          | 1.4          | 1.5               |              |
| Replacement of blood lead values below quantitation limit with 1/2 quantitation limit | 1.7          | 1.7    | 1.9          | 1.7          | 1.7             | 1.7          | 1.6          | 1.7               |              |

CL, confidence limit.

SEQM GSDs are presented in Table 2. Depending on the treatment of values below the detection and quantitation limits, GSD, ranged from 1.4 to 1.7. The SAS PROC LIFEREG model resulted in GSD, ranging from 1.7 to 1.8.

Results of the box models are presented in Table 3. Depending on treatment of values below the detection and quantitation limits, GSD, ranged from 1.3 to 1.7.

There were 105 children in the Sandy data set with blood lead, soil lead, and interior dust lead concentrations included in the analysis. In blood lead samples from 14 of the children, at least 1 of the duplicate values was below the method detection limit. In blood lead samples from six children, both of the values were below the method detection limit. Samples from 23 of the children had at least 1 of the duplicate values below the method quantitation limit, and samples from 10 of the children had both values below the method quantitation limit. The geometric mean blood lead concentration for the Sandy data set was 3.1 pg/dL. The sample GSD was 1.6.

All data for children included in the analysis of the Sandy data set fit log-normal distributions. Concentrations of lead in soil, entry dust, and mouthing index were significantly correlated with blood lead, but the correlations were small. Interior dust, curb dust, age, and SES were not significantly correlated with blood lead concentrations.

The best nonlinear regression model for the Sandy data set was

\[
\log (\text{observed blood lead}) = \log \left( BS \times \text{soil lead} + BM \times \text{mouthing index} + BSSE \times SES + B_{0-12} \times \text{(age 0–12 months)} + \ldots + B_{60-72} \times \text{(age 60–72 months)} \right).
\]

| Treatment | Lower 95% CL | Median | Upper 95% CL | Lower 95% CL | Weighted median | Upper 95% CL | Lower 95% CL | Weighted variance | Upper 95% CL |
|-----------|--------------|--------|--------------|--------------|-----------------|--------------|--------------|-------------------|--------------|
| Static box |              |        |              |              |                 |              |              |                   |              |
| All children, blood lead as reported | 1.4       | 1.6    | 1.8          | 1.5          | 1.5             | 1.5          | 1.6          | 1.6               |              |
| Replacement of blood lead values below detection limit with detection limit | 1.5       | 1.5    | 1.6          | 1.5          | 1.5             | 1.5          | 1.5          | 1.6               |              |
| Replacement of blood lead values below detection limit with 1/2 detection limit | 1.6       | 1.6    | 1.7          | 1.6          | 1.6             | 1.6          | 1.6          | 1.7               |              |
| Replacement of blood lead values below quantitation limit with quantitation limit | 1.5       | 1.6    | 1.7          | 1.5          | 1.5             | 1.5          | 1.5          | 1.6               |              |
| Replacement of blood lead values below quantitation limit with 1/2 quantitation limit | 1.6       | 1.6    | 1.7          | 1.6          | 1.6             | 1.6          | 1.6          | 1.7               |              |
| Sliding box |              |        |              |              |                 |              |              |                   |              |
| All children, blood lead as reported | 1.5       | 1.6    | 1.8          | 1.5          | 1.5             | 1.5          | 1.5          | 1.6               |              |
| Replacement of blood lead values below detection limit with detection limit | 1.5       | 1.6    | 1.7          | 1.6          | 1.6             | 1.6          | 1.6          | 1.7               |              |
| Replacement of blood lead values below detection limit with 1/2 detection limit | 1.4       | 1.5    | 1.6          | 1.5          | 1.5             | 1.5          | 1.5          | 1.6               |              |
| Replacement of blood lead values below quantitation limit with quantitation limit | 1.3       | 1.4    | 1.5          | 1.4          | 1.4             | 1.4          | 1.4          | 1.5               |              |
| Replacement of blood lead values below quantitation limit with 1/2 quantitation limit | 1.5       | 1.7    | 1.9          | 1.7          | 1.7             | 1.7          | 1.6          | 1.8               |              |
where \( SES \) = socioeconomic status. The results of different detection limit treatments on the log of linear and log in log model types with respect to the GSD, are presented in Table 4. Depending on the treatment of values below the detection and quantitation limits, GSD\(_1\) ranged from 1.3 to 1.6.

The Sandy data regression residual diagnostics were better than regression diagnostics for Bingham Creek data. The residual average was close to zero (< 0.02 for all models), and the residual variance was typically approximately 0.2. The residuals were normally distributed, as evidenced by the Shapiro-Francia test. The Spearman rank measure of heteroscedasticity and the score test typically indicated the residuals exhibited homogeneity of variance. The residuals were not serially correlated.

The most appropriate linear in log SEQM model for the Sandy data set was similar in form across different treatments of blood lead values. Soil lead, mouthing index, and SES were significant at the 95% level of confidence. SEQM GSDs are presented in Table 5. Depending on the treatment of values below the detection and quantitation limits, GSD, ranged from 1.4 to 1.6. The SAS PROC LIFEREG model resulted in GSD\(_1\) in the range of 1.8.

An example of a static box model for the Sandy data set is presented in Table 6. Results of the box models for the Sandy data set are presented in Table 7. Depending on treatment of values below the detection and quantitation limits, GSD\(_1\) ranged from 1.3 to 1.7.

**Discussion**

By definition, the GSD\(_1\) is assumed to be independent of exposure to environmental lead concentrations. The sample GSDs for both sites fell within the range of the calculated GSD. These results suggest that at Bingham Creek and Sandy environmental lead exposure contributes little to the variability in blood lead concentrations. Analysis of the box models revealed no correlation between the GSD\(_b\) and soil and interior dust lead concentration. By using the GSD\(_b\) of the individual boxes in the box models, we determined that for the Bingham Creek and Sandy data sets, the GSD\(_1\) are independent of environmental lead exposure. The GSD\(_b\) in the individual boxes ranged from 1.0 to 2.8, but the individual box location could not be predicted by environmental lead concentrations in either soil or dust. As shown in Table 6, the GSD\(_b\) for all children used in the Sandy analysis ranged from 1.0 to 1.9. The highest GSD\(_b\) was in the 0–200 mg/kg soil and dust lead box, whereas the lowest GSD\(_b\) was in the 400–600 mg/kg soil lead, 800–1,000 mg/kg dust lead box.

The GSD can be calculated using several methods. Each method has advantages and limitations. The box models do not require any model-fitting procedures, and the results are probably most representative of the strictest definition of GSD, because the results are based only on environmental variables. However, some judgment is required about the important environmental determinants of the variability in blood lead. Although soil and dust lead were valuable in defining the boxes for the Bingham Creek data set, they were less adequate for the Sandy data set. Even when the variables are chosen appropriately, the sizes of the box intervals are subjective. Regression models allow the GSD\(_1\) to be estimated from the standard deviation of the residuals for the log of blood lead.

The underlying assumption of regression models is that the residuals have the same standard deviation regardless of the values of the predictors and that the regression model is correctly specified. SEQM allows adjustment of blood lead regression models for certain measurement errors in precursor variables such as dust lead. However, when the precursor variables are not actually predictors of blood lead, complexity of the computations increases with no improvement in the fit of blood lead in the model. Many SEQM results are sensitive to the computational method chosen for fitting the model.

Variability in calculating the GSD\(_b\) is more dependent on the treatment of blood lead concentrations below the method

**Table 4. Nonlinear regression analysis results for the Sandy data set.**

| Treatment                         | Model type                  | Lower 95% CL | Interindividual GSD | Upper 95% CL |
|----------------------------------|-----------------------------|--------------|---------------------|--------------|
| All children, blood lead         | Log of linear               | 1.5          | 1.6                 | 1.7          |
| as reported                      | Linear in log               | 1.5          | 1.6                 | 1.7          |
| Replacement of blood lead        | Log of linear               | 1.4          | 1.5                 | 1.6          |
| values below detection limit     | Linear in log               | 1.4          | 1.5                 | 1.5          |
| with detection limit             |                             |              |                     |              |
| Replacement of blood lead        | Log of linear               | 1.5          | 1.6                 | 1.7          |
| values below detection limit     | Linear in log               | 1.5          | 1.6                 | 1.7          |
| with 1/2 detection limit         |                             |              |                     |              |
| Replacement of blood lead        | Log of linear               | 1.3          | 1.4                 | 1.5          |
| values below quantitation limit  | Linear in log               | 1.3          | 1.4                 | 1.4          |
| with quantitation limit          |                             |              |                     |              |
| Replacement of blood lead        | Linear in log               | 1.5          | 1.6                 | 1.7          |
| values below quantitation limit  | Linear in log               | 1.5          | 1.6                 | 1.7          |
| with 1/2 quantitation limit      |                             |              |                     |              |

**Table 5. Structural equation model results for the Sandy data set.**

| Treatment                         | Model type                  | Lower 95% CL | Interindividual GSD | Upper 95% CL |
|----------------------------------|-----------------------------|--------------|---------------------|--------------|
| All children blood lead          | Log of linear               | 1.5          | 1.6                 | 1.7          |
| as reported                      | Linear in log               | 1.5          | 1.6                 | 1.7          |
| Replacement of blood lead        | Log of linear               | 1.4          | 1.5                 | 1.6          |
| values below detection limit     | Linear in log               | 1.4          | 1.5                 | 1.5          |
| with detection limit             |                             |              |                     |              |
| Replacement of blood lead        | Linear in log               | 1.5          | 1.6                 | 1.7          |
| values below detection limit     | Log of linear               | 1.5          | 1.6                 | 1.7          |
| with 1/2 detection limit         |                             |              |                     |              |
| Replacement of blood lead        | Linear in log               | 1.4          | 1.4                 | 1.4          |
| values below quantitation limit  | Linear in log               | 1.5          | 1.6                 | 1.7          |
| with quantitation limit          |                             |              |                     |              |

**Abbreviations:** CL, confidence limit; GSD, geometric standard deviation.
Article: Griffin et al.

**Table 6.** Static box model for the Sandy data set.

| Dust lead conc (mg/kg) | Soil lead concentration (mg/kg) |
|------------------------|---------------------------------|
|                        | 0–200  | 200–400 | 400–600 | 600–800 | 800–1000 | 1,000–1,200 | 1,600–1,800 | 1,800–2,000 | 2,000–2,200 | 4,200–4,400 |
| Count of LBL          | 17     | 21      | 3       | 3       | 3        | 3           | 3           | 3           | 3           | 3           |
| Avg of LBL            | 0.826257 | 1.2303045 | 1.642563 | 1.227033 | –        | –           | –           | –           | 1.02961942  | –           |
| SD of LBL             | 0.643582 | 0.470375 | 0.316902 | 0.472756 | –        | –           | –           | –           | –           | –           |
| Count of LBL          | 10     | 10      | 10      | 4       | 4        | 3           | 2           | –           | –           | –           |
| Avg of LBL            | 1.029309 | 1.084086 | 1.127876 | 1.390070 | 1.2945183 | –           | 1.62602115  | –           | 1.27040714  | –           |
| SD of LBL             | 0.457716 | 0.404658 | 0.434581 | 0.443858 | 0.3516118 | 0.25600139  | 0.39159888  | –           | –           | –           |
| Count of LBL          | –      | 2       | –       | 1       | 1        | 3           | –           | –           | –           | –           |
| Avg of LBL            | –      | 0.829114 | –       | 0.182322 | 1.2809338 | 1.17150869  | –           | –           | –           | –           |
| SD of LBL             | –      | 0.123286 | –       | –       | 0.18918157 | –           | –           | –           | –           | –           |
| Count of LBL          | –      | 1       | –       | 1       | –        | –           | –           | –           | –           | –           |
| Avg of LBL            | –      | 0.336472 | –       | 1.589235 | –        | –           | –           | –           | –           | –           |
| SD of LBL             | –      | –       | –       | –       | 1.18652178 | –           | –           | –           | –           | 1.48160454  |
| Count of LBL          | –      | –       | 2       | –       | –        | –           | –           | –           | –           | –           |
| Avg of LBL            | –      | –       | 1.062327 | –       | –        | –           | –           | –           | –           | –           |
| SD of LBL             | –      | –       | 0.097687 | –       | –        | –           | –           | –           | –           | –           |
| Count of LBL          | –      | –       | –       | 1       | –        | –           | –           | –           | –           | –           |
| Avg of LBL            | –      | –       | –       | 1.840550 | –        | –           | –           | –           | –           | –           |
| SD of LBL             | –      | –       | –       | –       | 0.78045736 | –           | –           | –           | –           | –           |

Abbreviations: Avg, average; conc, concentration; LBL, log blood level; SD, standard deviation.

**Table 7.** Box model results for the Sandy data set.

| Treatment                              | Lower 95% CL | Median | Upper 95% CL | Lower 95% CL | Weighted median | Upper 95% CL | Lower 95% CL | Weighted variance | Upper 95% CL |
|----------------------------------------|--------------|--------|--------------|--------------|-----------------|--------------|--------------|-------------------|--------------|
| Static box                             |              |        |              |              |                 |              |              |                   |              |
| All children, blood lead as reported   | 1.2          | 1.5    | 1.6          | 1.5          | 1.5             | 1.6          | 1.5          | 1.6               | 1.7          |
| Replacement of blood lead values below detection limit with detection limit | 1.2          | 1.5    | 1.6          | 1.5          | 1.5             | 1.6          | 1.5          | 1.6               | 1.8          |
| Replacement of blood lead values below detection limit with 1/2 detection limit | 1.2          | 1.4    | 1.5          | 1.5          | 1.5             | 1.4          | 1.5          | 1.6               | 1.6          |
| Replacement of blood lead values below quantitation limit with quantitation limit | 1.2          | 1.4    | 1.4          | 1.4          | 1.4             | 1.3          | 1.4          | 1.5               | 1.5          |
| Replacement of blood lead values below quantitation limit with 1/2 quantitation limit | 1.3          | 1.6    | 1.6          | 1.6          | 1.6             | 1.7          | 1.5          | 1.6               | 1.8          |
| Sliding box                            |              |        |              |              |                 |              |              |                   |              |
| All children, blood lead as reported   | 1.4          | 1.5    | 1.5          | 1.5          | 1.5             | 1.6          | 1.6          | 1.6               | 1.7          |
| Replacement of blood lead values below detection limit with detection limit | 1.4          | 1.5    | 1.6          | 1.6          | 1.6             | 1.7          | 1.6          | 1.7               | 1.7          |
| Replacement of blood lead values below detection limit with 1/2 detection limit | 1.4          | 1.5    | 1.5          | 1.5          | 1.5             | 1.5          | 1.5          | 1.6               | 1.6          |
| Replacement of blood lead values below quantitation limit with quantitation limit | 1.3          | 1.4    | 1.4          | 1.4          | 1.4             | 1.4          | 1.4          | 1.5               | 1.5          |
| Replacement of blood lead values below quantitation limit with 1/2 quantitation limit | 1.4          | 1.5    | 1.6          | 1.6          | 1.6             | 1.7          | 1.6          | 1.6               | 1.7          |

CL, confidence limit.
The detection limit for isotope dilution mass spectroscopy is approximately 0.15 pg/dL, 10 times less than ASV. Because all individuals have a background blood lead concentration (20), lowering the detection limit should greatly increase the number of individuals with detectable values. This method is more expensive than ASV. However, if it were used only for blood lead samples below the method quantitation limit, costs would be minimized and the calculated GSD would be more accurate.

Some may question the necessity of more accurately measuring blood lead concentrations below concentrations of current health concern. As mentioned previously, the EPA Superfund program policy is to remediate hazardous waste sites where the IEUBK model predicts a more than 5% probability of exceeding a 10 pg/dL blood lead concentration. This remediation is recommended even when measured blood lead concentrations in the site population are all below 10 pg/dL. The value or values used to represent the GSD in the IEUBK model have a major impact on the predicted risks to lead at a site and on the extent of remediation required. For example, at the Sandy site, the use of a site-specific GSD of 1.4 resulted in removing soil from 67 residential yards at an estimated cost of $6 million. If the IEUBK default GSD of 1.6 had been used, contaminated soil would have been removed from 175 residential yards at a cost of approximately $15 million. No child in the Sandy study had measured blood lead concentrations > 10 pg/dL (5). The Sandy site is considered small in comparison with most smelting and mining sites being investigated by the Superfund program. We believe more accurate measurements of blood lead concentrations below typical detection limits, or at the very least, examinations of the impact of nondetectable values on the calculation of a site-specific GSD, has merit.

Most risk assessors will not have the computer software and/or the statistical background to perform nonlinear regression and/or SEqM. Because the different methods for calculating GSD, values yield similar results, the following simple procedure is recommended to calculate a site-specific GSD. First, log transform blood, soil, and interior dust concentrations. Using multiple linear regression, regress the log-transformed soil and dust lead concentrations on the log-transformed blood lead concentrations. Use the box model to calculate the GSD for environmental variables having positive lead concentration coefficients. We recommend the use of the median as the GSD, because, at least for data sets where many children have low concentrations of environmental exposure, the median value is least affected by the treatment of nonquantifiable values.

Although we have presented a critical evaluation of calculating a site-specific GSD for a site where a well-designed and representative blood lead study has been conducted, risk assessors must continue to use professional judgment when advising risk managers on future potential risks at the site. The site-specific GSD defines the variability in the current population. Population demographics and behavior of the community could shift in the future and should be considered during risk management decisions.

### Table 8. Summary of the interindividual geometric standard deviations as calculated with different models for each data treatment.

| Treatment | Bingham Creek | Sandy |
|-----------|---------------|-------|
|            | NL reg | SEqM | Static box | Sliding box | NL reg | SEqM | Static box | Sliding box |
| All children, blood lead as reported | 1.6 | 1.6 | 1.6 | 1.6 | 1.6 | 1.6 | 1.5 | 1.5 |
| Replacement of blood lead values below detection limit with detection limit | 1.5 | 1.5 | 1.6 | 1.6 | 1.5 | 1.5 | 1.5 | 1.5 |
| Replacement of blood lead values below detection limit with 1/2 detection limit | 1.6 | 1.6 | 1.5 | 1.5 | 1.6 | 1.6 | 1.4 | 1.5 |
| Replacement of blood lead values below quantitation limit with quantitation limit | 1.4 | 1.4 | 1.3 | 1.4 | 1.4 | 1.4 | 1.4 | 1.4 |
| Replacement of blood lead values below quantitation limit with 1/2 quantitation limit | 1.7 | 1.7 | 1.7 | 1.7 | 1.6 | 1.6 | 1.6 | 1.5 |

Abbreviations: NL, nonlinear; reg, regression; SEqM, structural equation model.