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REPORT ON SOIL CONCENTRATION LIMIT FOR LEAD BASED ON RISK FROM ACUTE EXPOSURE FOR A SMALL CHILD NAS CECIL FIELD FL

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A Soil Concentration Limit for Lead Based on Risk from Acute Exposure for a Small Child

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INTRODUCTION

Lead is a common contaminant of soils in both industrial and residential settings. Historical use of lead in gasoline has resulted in elevated soil concentrations near roadways, and very high concentrations of lead may remain in soils and slag near smelter operations and in tailings from mining operations (Eckel et al., 2002). Improper disposal of lead-containing waste, such as incinerator ash and lead battery cores, have created hazards at numerous waste sites in the U.S. Prior to 1978, lead comprised as much as 50% of some house paints. The weathering,

chipping, and peeling of lead-based paints are an important source of lead contamination of soils in residential settings, and this remains an important source of lead exposure for children in many urban areas (CDC, 1997).

Children are particularly vulnerable to lead contamination in soil for several reasons. Small children tend to have a much higher soil incidental ingestion rate of soils than adults, due to extensive contact with soil while at play and frequent mouthing behavior (Stanek et al., 1998). Thus, intake of lead [and other contaminants] by ingestion from soil is generally higher on an absolute basis in small children than in older children or adults. On a per unit body weight basis, the differences in lead dose from soil are even larger due to the smaller body weight of young children. The gastrointestinal absorption of lead is greater in children than adults (Ziegler et al., 1978; Alexander et al., 1974), further accentuating the differences in effective lead dose resulting from exposure to soil lead contamination. Finally, the developing nervous systems of children appear to be especially sensitive to neurotoxic effects of lead (Schwartz, 1994).

To develop concentration limits for lead in soil protective for small children, the U.S. Environmental Protection Agency (EPA) uses a probabilistic model to predict blood lead concentrations in children exposed to lead in soil at a specified concentration — the Integrated Exposure Uptake Biokinetic (IEUBK) Model (EPA, 1994a). With this model, a soil lead concentration limit can be derived such that a target blood lead concentration is not exceeded. Because the model is probabilistic and accounts for variability in lead toxicokinetics among individuals, the output is a distribution of blood lead concentrations that would arise in a population of children exposed to lead in soil at a specified concentration. Currently, the target blood lead concentration is $\leq$ 10 µg/dL to prevent neurobehavioral effects, per Centers for Disease Control and Prevention (CDC) recommendation (CDC, 1991). Typically, a soil concentration limit is selected such that only a small percentage (e.g., $\leq$ 5%) of exposed children would be predicted to have a blood concentration above this value (EPA, 1994b).

The IEUBK model and soil lead concentration limits derived from it are based on chronic exposure. As a regulatory tool, limits based on chronic exposure are appropriate in that the vast majority of situations in which risks to children from soil lead contamination are contemplated involve at least the potential for repeated contact. There are some circumstances, however, where consideration of risks from acute exposure to soil is warranted. For example, an acute exposure scenario could be relevant for a park or recreational area where an individual child might play, but only on one or a few occasions.

A soil lead concentration limit based on acute exposure can also be useful for sites where chronic exposure is anticipated. Soil concentration limits based on chronic exposure are often compared with the average contaminant concentration over the exposure area, since this is thought to best offer the best representation of the concentration to which an individual is exposed over time. In this situation, soils with concentrations above the limit are allowed to remain in place in some areas as long as other areas contacted by the child have offsetting lower concentrations. An acute exposure limit, used as a not-to-exceed value for all areas of the site, would help to insure that even a single exposure event with soils above the chronic exposure limit is safe.

Developing an acute exposure limit for lead in soils is more complicated than simply adjusting the exposure frequency assumptions in the IEUBK model. First, it is important to recognize that the amount of soil ingested acutely by a small child can be substantially different from the average daily incidental soil ingestion rate used to assess chronic intake. Unfortunately, there is little documentation of the frequency of these soil pica events or the amounts of soil ingested. Using data from their soil ingestion studies in children, Stanek and Calabrese (1995) estimated that 42% of small children ingest > 5 g of soil on one or two days a year, and 33% ingest > 10 g. These occasional soil doses are up to 70-fold or more higher than the default average daily soil ingestion rate assumption currently recommended for use with the IEUBK model (135 mg soil per day; EPA, 1994a). Second, the target blood lead concentration limit for chronic exposure (10 µg/dL) may not be applicable for acute exposure because it is based on neurobehavioral effects in chronically exposed individuals. The deficits observed in studies of these individuals likely require more than transient elevations in blood lead, as would occur with an acute lead dose. An assessment of the consequences of acute exposure requires endpoints relevant specifically to acute toxicity. Third, the computer model used to predict blood concentrations resulting from exposure to lead in soils must be capable of simulating a single acute dose. Many of the models currently available, including the IEUBK, do not provide this capability.

We report here the results of an analysis to develop a risk-based soil concentration limit for lead protective of small children for situations of acute exposure. For the purposes of this analysis, an acute exposure was defined as ingestion of soil containing lead on a single occasion. In order to produce a soil concentration limit that is broadly protective, the circumstance regarded as most likely to result in the highest soil lead dose was addressed — a soil pica episode by a small (2-year old) child. The overall approach was as follows. Clinical information regarding acute lead poisoning in children was assessed, and a blood lead concentration limit was selected. From the blood lead concentration limit, a corresponding dose limit from soil was calculated using biokinetic modeling. The dose limit was the dose from soil producing a peak blood lead concentration equal to the blood lead concentration limit. Finally, a soil lead concentration limit was calculated from the soil dose limit with an assumption regarding the volume of soil ingested during a pica episode.

SELECTION OF A BLOOD LEAD CONCENTRATION LIMIT

The clinical literature contains numerous reports of lead poisoning in children, and from these a reasonably complete picture of the signs and symptoms of acute lead intoxication can be obtained. The most serious manifestation of acute lead toxicity in children is acute encephalopathy. Signs and symptoms of acute encephalopathy include apathy, bizarre behavior, frequent and persistent vomiting, loss of coordination, intractable seizures, and coma. Acute encephalopathy is usually associated with blood lead concentrations over 100 µg/dL, although it has been observed with blood lead concentrations as low as 70 µg/dL (Piomelli et al., 1984). Peripheral neuropathy, common in lead poisoning in adults, is rare in children. Gastrointestinal effects such as colic - characterized by abdominal pain, constipation, cramps, nausea, vomiting, anorexia, and weight loss - have been observed as one of the early symptoms in acute exposures at blood lead concentrations of ≥ 60 µg/dL in children and adults (ATSDR 1999; NAS 1972). Acute lead intoxication can also produce renal effects, including a Fanconi-like syndrome, a triad

of hypophosphatemia, aminoaciduria, and glycosuria (Chisholm, 1962). While nephropathy can occur as a consequence of acute lead toxicity in children, it is more common in adult lead poisoning, and is typically found in workers with blood lead concentrations > 60 µg/dL (Henretig, 2002).

Lead produces anemia, both through an inhibition of hemoglobin synthesis and diminished erythrocyte survival (Henretig, 2002). Lead impairs hemoglobin synthesis by interfering with the critical phases of the dehydration of aminolevulinic acid (catalyzed by the cytosolic enzyme, δ-aminolevulinic acid dehydratase, ALAD) and the incorporation of iron into the protoporphyrin molecule. Although effects on ALAD activity can be detected at low blood lead concentrations (> 10 µg/dL), the clinical manifestation of anemia in children is associated with much higher concentrations, ca. > 80 µg/dL.

The CDC has defined a blood lead concentration of > 10 µg/dL in children as an intervention level. This definition is based on evidence that blood lead concentrations above 10 µg/dL are associated with neurobehavioral effects and deficits in cognitive performance. There are no data to indicate how long a blood lead concentration must be elevated for these effects to occur, but the studies showing subtle neurological effects of lead in children used populations that likely had repeated exposures (such as to lead-containing paint chips, house dust, or soil). As a result, the 10 µg/dL blood lead concentration as a threshold for concern is based on a persistent elevation, rather than a transient spike in blood lead as would be expected from an acute lead dose. The endpoint — subtle neurological deficits — is relevant to acute exposure, and these effects may occur as sequelae to a severe, acute intoxication episode. However, the use of 10 µg/dL as a blood concentration limit to protect against this effect from a single *acute* lead exposure is arguably not appropriate.

Most cases of acute symptomatic lead poisoning in children are associated with blood lead concentrations greater than 100 µg/dL (NAS, 1972). The EPA has identified a 60-100 µg/dL lead in blood as a lowest observable adverse effect level (LOAEL) for acute toxicity in children (EPA, 1986), and from the discussion above, clinical signs and symptoms of lead poisoning are associated with concentrations at or above 60 µg/dL. For the purposes of this analysis, a concentration of 60 µg/dL was selected as the target limit for the peak blood lead concentration after an ingested soil dose.

BIOKINETIC MODELING

Assessment of the hazards associated with lead in environmental media is unusual in that assessment is based on blood lead concentration as the toxicological endpoint. In some situations, empirical measurements of blood lead concentration are available for the exposed population, and the assessment of hazard is relatively straightforward. More often, however, blood lead concentrations must be modeled for exposed populations, as well as for populations that might become exposed in the future. Several PBPK or biokinetic models have been developed to predict blood lead concentrations resulting from environmental lead exposures (see EPA, 2001 for a review). Some of these models have the ability to evaluate intake of lead from a variety of sources, including ingestion of lead in food, water, and soil, and inhalation of lead in

particulates. The distribution of lead to various compartments in the body over time is considered with varying degrees of complexity among the models, but all have the ability to predict the blood concentration achieved with chronic exposure to lead under defined exposure circumstances.

Model selection

The IEUBK model used by the EPA has undergone extensive calibration and use and is judged to perform well in predicting blood lead concentration distributions for children 0 to 7 years of age. Although the model performs well in assessing chronic exposure, it is not capable, in its current configuration, of simulating blood lead concentrations arising from a single dose. This limitation makes the IEUBK model unsuitable for developing a soil lead concentration limit for acute exposure.

Other biokinetic models were evaluated as candidates for use in this analysis. The Rabinowitz model (Rabinowitz et al., 1976) is relatively simple and was developed to predict blood lead concentrations associated with long-term lead intake in adults. The Rabinowitz model is not scaled for children, which greatly limits its utility for this analysis. The same limitation applies to the Bert model (Bert et al., 1989), which is a more complex version of the Rabinowitz model. The California model (EPA, 2001) has been developed to predict blood lead concentrations from environmental exposure in both children and adults. However, like the IEUBK model, it is not capable of predicting the blood lead concentration profile resulting from a single dose. The Stern model (Stern, 1994) was developed to predict incremental changes in the steady-state blood lead concentration resulting from exposures to lead in soil, and therefore is useful only for situations of chronic lead exposure. The O'Flaherty model (O'Flaherty et al., 1995) is a true physiologically-based pharmacokinetic model. It is capable of simulating blood lead concentrations for ages 0 through adulthood, and for both short- and long-term exposures. There are indications that the model does not perform well when lead is ingested at very high concentrations (ATSDR, 1999), which could represent a problem when assessing acute exposures. Moreover, the C++ version does not allow the user to change the bioavailability from the default value.

The Leggett model (Leggett, 1993), developed by the Oak Ridge National Laboratories, is scaled for children and is capable of generating a blood concentration versus time profile for a single lead dose. Additionally, the Leggett model gives the user the option of simulating lead uptake by red blood cells as either a linear or non-linear process. These are features that many of the other models do not have. The model has been shown to perform well for a wide variety of exposure situations (EPA, 2001) and is the biokinetic core for the EPA's All-Ages Lead Model (AALM). From the comparison of model capabilities and attributes, the Leggett model was considered to be the most suitable for this acute exposure analysis.

Model inputs

Age-specific inputs for the Leggett model were chosen based on a 2-year old. This was considered to be the approximate age when a soil pica event while at play is most likely. The baseline blood lead concentration was assumed to be 4.1 μg/dL, which is the arithmetic mean

concentration for 1-2 year olds reported in the Third National Health and Nutritional Examination Survey, Phase 2 (NHANES III) (Pirkle et al., 1998). The default bioavailability assumptions for the Leggett model are age-specific, with 45 percent for birth to 1 year, and 30 percent for ages 1 to 5 years. Consequently, for a 2-year old, the default bioavailability factor would be 0.30. The EPA currently recommends a value of 0.30 (30%) for the absolute bioavailability of lead from soil for the IEUBK model (EPA, 1994a) when assessing chronic lead exposure. This assumption is derived in part from dietary absorption studies indicating that the absolute bioavailability of soluble lead from food and water in children is about 0.50 (50%; Alexander et al., 1974; Ziegler et al., 1978). Based on studies of the relative bioavailability of lead from soil versus water, an additional reduction factor of 0.6 is applied, leading to the combined absorption factor of 0.30 (i.e., 0.5 x 0.6 = 0.3). The potential applicability of this bioavailability factor (0.30) to an acute exposure scenario was evaluated as part of this analysis.

The gastrointestinal absorption of ingested lead is well documented to decrease with increasing lead dose. Aungst and Fung (1981) investigated lead absorption across the gut lumen *in vitro* in everted rat intestines and demonstrated that lead uptake involves two distinct processes: a passive diffusion process that is independent of gut concentration, and a capacity-limited active or facilitated diffusion process. At low lead concentrations, lead transport is effected almost exclusively through the active route. At higher concentrations, the lead transport mechanism becomes saturated, and the relative contribution of passive diffusion is increased. Passive diffusion of lead in the gut is poor, and as the contribution of passive diffusion increases, the fraction of ingested lead absorbed is diminished. This concentration-dependent uptake of lead from the gut may explain at least in part the non-linear relationship between lead intake and blood lead concentrations observed in children (Sherlock and Quinn, 1986; see below). It also indicates strongly the need to incorporate dose-dependent absorption when modeling blood lead concentrations from acute lead exposure.

Three studies were identified that provide information of potential value on the dose-dependent uptake of lead from the gut. Sherlock and Quinn (1986) conducted a duplicate diet study in which bottle-fed infants were exposed to lead in water and in formula mixed with contaminated water for one week in the 13th week after the infant's birth. Dietary lead intakes, believed to constitute almost all ingested lead, ranged from 0.04 to 3.4 mg/week. The authors observed a curvilinear relationship between the blood lead concentration and lead intake, with higher lead doses producing less-than-proportional increases in blood lead concentration. Reichlmayr-Lais et al (1988) investigated the effect of dietary lead intake on lead retention in adult rats. Rats were exposed to lead concentrations ranging from 0.02 to 800 µg lead per kg diet for 29 days. Absorption of lead, as inferred from lead retention, was similar for lead concentrations in diet up to 1 µg lead per kg feed, but was nearly 10-fold lower at higher dietary lead concentrations. In a study by Mallon (1983), lead absorption was examined in infant and juvenile baboons. Infant (6-7 months of age; 3 kg average body weight) baboons were administered lead acetate in gelatin capsules at doses of 100, 200, or 1000 µg lead per kg body weight per day for 4.6 – 6 months. Juvenile baboons (22-23 months of age; 5 kg body weight) received doses of 100 or 500 µg per kg body weight per day for 3.5 – 6 months. Controls received no lead acetate, and their only lead intake was 12 µg lead per kg body weight per day from standard diet. As the daily lead dose increased from 12 to 1000 µg/kg for the infant

baboons, and from 12 to 500 µg/kg for the juvenile animals, the fraction of the lead dose absorbed decreased from 0.24 to 0.02 in infants and from 0.12 to 0.01 in juvenile animals.

For the IEUBK model, the EPA used data from the Sherlock and Quinn study to address the dose-related bioavailability of lead (see EPA, 1994a). Total lead uptake from the gut was treated as the sum of saturable and non-saturable components. The data were fit to a nonlinear regression model in a form comparable to the Michaelis-Menten equation used to describe the *in vitro* results observed by Aungst and Fung (1981):

$$PbB = \frac{B + A \times Pb_{intake} + P \times Pb_{intake}}{\left(1 + Pb_{intake}/M\right)}$$

where:

B is the baseline blood lead concentration (10.85 µg/dL was used)

A and P are coefficients describing, respectively, nonlinear (active) and linear (passive) lead intake, between PbB and dietary lead intake; and

M is the Michaelis-Menten type (nonlinearity) parameter — the daily dietary intake rate at which the facilitated component of lead uptake is half saturated (Gary Diamond, personal communication).

Intake data from infant and juvenile baboons in the Mallon study were also fit to a similar model. Based on a goodness-of-fit comparison for these data sets, the EPA selected the Sherlock and Quinn data to represent the nonlinear absorption of lead in children, with the Mallon study cited as providing supporting data. From the Sherlock and Quinn data, the lead intake at which absorption is greatly reduced was estimated to be 90 µg/day.

We also evaluated the Sherlock and Quinn data to determine their suitability for use in defining the bioavailability of ingested lead. Lead uptake curves from this study were approximated by extracting the blood lead concentration versus weekly lead intake rate for the grouped data [from Figure 2 of Sherlock and Quinn, 1986] to SlideWrite v.5, and converting the dose to µg/day. The blood lead concentration versus lead intake data were then fit to the nonlinear regression model used by the EPA (see equation above). The data fit the Michaelis-Menten type equation well (Figure 1; r^2=0.98), as observed by the EPA, although the fit statistics revealed large standard errors for the estimated parameters A and P. The large errors for the parameter estimates are due to the availability of only seven data points to estimate three parameters (A, P, and M). Although this equation was a good fit to the observed data (Fig. 2), extrapolation to much higher doses (up to 5000 µg/day) did not produce plausible increases in blood lead concentration. Because the dose-blood concentration relationship produced implausible results at lead doses relevant to acute lead exposure, the use of these data and this equation was rejected. This data set was also fit to several empirical nonlinear equations with similar poor extrapolation to high doses (not shown).

The data from infant and juvenile baboons by Mallon (1983) were also evaluated. Although not obtained in humans, these data were derived in a primate at a relevant age. There is a close resemblance between hematological, blood lead responses, and patterns of lead

distribution and retention in baboons and humans (Mallon, 1983). This data set has the advantage of direct measurement of lead absorption, rather than indirect measurements, e.g. blood lead concentration, from which absorption must be inferred, as with the Sherlock and Quinn study. Additionally, the Mallon study utilized higher doses, extending the range over which dose-dependent absorption information is provided. Lead uptake data from the Mallon study were fit to nonlinear, exponential, and power function equations (Figure 3). The three equations fit the observed data reasonably well, with $r^2>0.98$. However, the extrapolated bioavailability at higher lead doses were markedly different (Figure 4). The power function model predicted negligible uptake of lead above doses of approximately 15,000 µg/day. The nonlinear and exponential models predicted a fairly constant uptake of approximately 1 and 3 percent, respectively, for lead doses up to 80,000 µg/day.

While all treatments of the Sherlock and Quinn and Mallon data predicted low uptake of lead at high doses, there is considerable uncertainty in establishing the precise value at intakes well beyond the observed data. From the two data sets, uptakes ranging from essentially zero to 3% were obtained for lead doses greater than about 10,000 µg/day. While these differences are small, it is important to recognize that blood lead concentrations are a function of [1- uptake]. As a consequence, the difference between choosing 0.5% and 3% uptake is a 6-fold difference in the predicted blood lead concentration. That difference is a considerable margin of uncertainty. As a practical measure, we chose not to extrapolate beyond the observation range, and selected for modeling the uptake value from the highest dose tested in the Mallon study — 0.02 (2%). This uptake represents a conservative choice in that the actual uptake of lead is likely to be lower at lead doses of interest for acute exposure.

A second issue regarding bioavailability is the extent to which absorption of ingested lead is diminished when it is present in soil rather than in the form of soluble lead as in the Sherlock and Quinn and Mallon studies. The relative bioavailability of lead from soil as compared with water has been measured for several soil samples from hazardous waste sites using the swine model (Ruby et al. 1999). Among these samples, the relative bioavailability was found to vary from less than 0.10 to 0.90). The EPA has chosen a value near the middle of this range, 0.60 (60%) as the default for the IEUBK model (EPA, 1994a). For the purpose of setting a soil concentration limit for acute exposure, an argument can be made for choosing a relative bioavailability value from the upper end of the range of observed values. For example, if a relative bioavailability of 0.60 is assumed, but the actual relative bioavailability of lead in a soil sample is 1.0, a soil lead concentration predicted to yield a peak blood lead concentration of 60 µg/dL (the blood lead limit chosen for this analysis) might actually result in a peak concentration of 100 µg/dL. As discussed in "Selection of a Blood Concentration Limit," the latter concentration is capable of producing clinical acute lead poisoning. In view of this small margin for error, a relative bioavailability of 1.0 was selected for the analysis; i.e., the bioavailability of lead in soil is the same as in water. It is acknowledged that other relative bioavailability values might be used to derive a soil concentration limit for acute exposure on a site-specific basis, provided that this information can be obtained with high confidence.

ESTIMATING THE SOIL CONCENTRATION LIMIT

Soil dose corresponding to the blood concentration limit

With the input assumptions described above, the soil dose producing a peak blood concentration at the specified limit (60 µg/dL) was determined through an iterative process. Simulations were performed assuming either linear or nonlinear partitioning of lead into erythrocytes. As shown in Figure 5, the 60 µg/dL blood concentration limit is reached with a soil dose of 74,500 µg of lead if non-linear partitioning to erythrocytes is assumed, and with a soil dose of 65,000 µg lead assuming linear partitioning.

Soil concentration limit

The amount of Pb ingested depends on the soil lead concentration and the amount of soil ingested. Data on the soil mass ingested during pica episodes are extremely limited. Vermeer and Frate (1979) found that the incidence of soil pica among children in a rural black community was 16 percent, and estimated the average amount of soil ingested to be 50 g/day. In a study by Calabrese et al. (1991), one child (among 64 examined) repeatedly ingested soil at rates ranging from 74 mg to 13.6 g/day over a two-week period. Wong (1988) found that six of 52 children studied exhibited soil pica behavior. Five of these children had normal mental capacity, and the amounts of soil ingested ranged from 0 to 10.3 g/day. One mentally retarded child ingested up to 60 g of soil per day. The EPA Child-Specific Exposure Factors Handbook (EPA, 2000) recommends a value of 10 g for soil pica. Using this value, the soil concentration corresponding to soil dose limit of 74,500 µg lead under conditions of nonlinear partitioning would be 7,450 mg/kg. The dose limit of 65,000 µg assuming linear partitioning would result from ingestion of 10 g of soil at a concentration of 6,500 mg/kg.

The biological mechanisms or processes underlying the nonlinear accumulation of lead in blood or red blood cells with increasing dose are not clear. While nonlinear partitioning is often assumed when predicting PbB concentrations from chronic exposure, its applicability to a single acute dose is uncertain. Given the choice between two soil lead concentration limits (7,500 mg/kg, assuming nonlinear partitioning, and 6,500 mg/kg assuming linear partitioning), and uncertainty as to which is more correct, the regulatory approach is usually to choose the more conservative of the values. On this basis, a soil concentration limit for lead based on acute toxicity in children of 6,500 mg/kg would be recommended.

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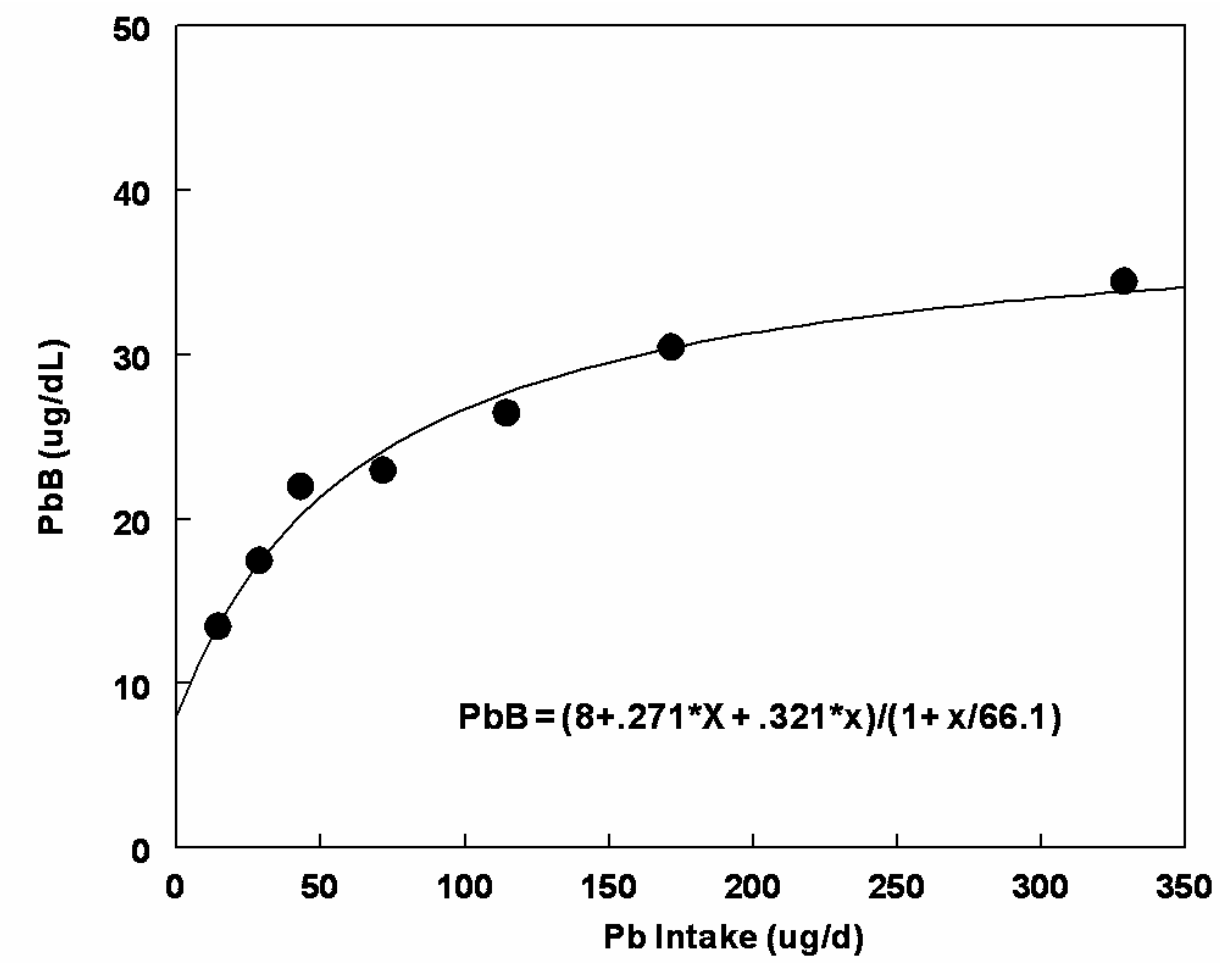

Figure 1. Nonlinear Regression of Lead Intake versus Blood Lead Concentration Data from Sherlock and Quinn

Lead intake and blood lead concentration data from Sherlock and Quinn (1986) were fit to a Michaelis-Menton-type equation as described in the section on "Model Inputs." A baseline blood lead concentration (B) was fixed at 8 µg/dL, based on the y-intercept of data presented in Figure 2 of the Sherlock and Quinn report. Parameters A, P, and M were optimized to provide the best fit of the data.

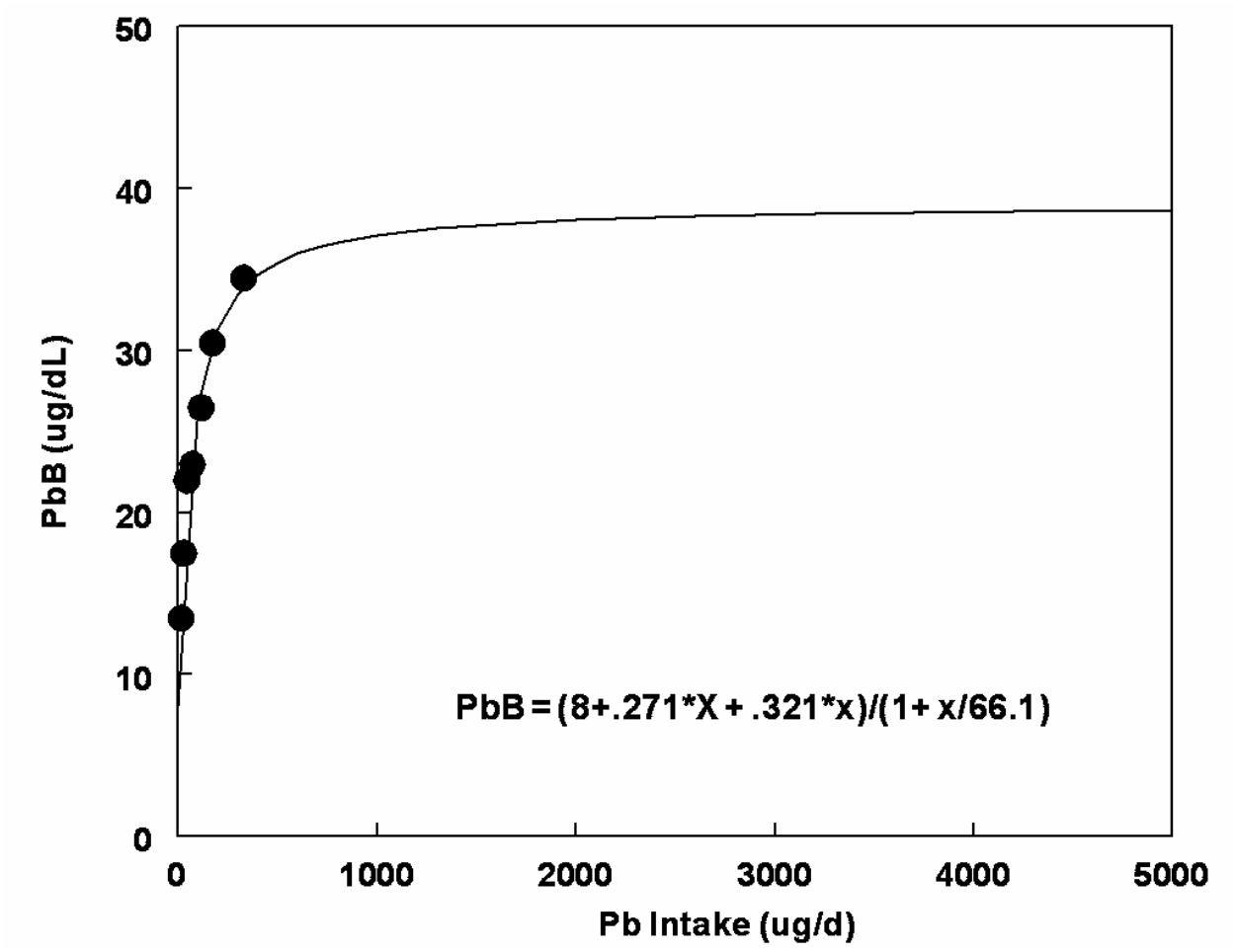

Figure 2. Extrapolation of Nonlinear Regression of Sherlock and Quinn Data to Higher Lead Intakes

Lead intake and blood lead concentration data from Sherlock and Quinn (1986) were fit to a Michaelis-Menton-type equation as in Figure 1. Using parameters (A, P, and M) providing the best fit of the data, the prediction of PbB was extrapolation to an intake of 5,000 µg Pb/day.

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Figure 3. Regression of Lead Uptake versus Lead Intake from the Mallon Study Using Nonlinear, Power, and Exponential Models.

Lead uptake and lead intake data were obtained from Mallon (1983). The data set was fit separately to a non-linear, an exponential, and a power function. All fits had r^2 values $\geq$ 0.98.

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TIFF (PackBits) decompressor
are needed to see this picture.

Figure 4. Extrapolation of Curve Fits for Mallon Data to Higher Lead Intakes

Lead intake and blood lead concentration data from Mallon (1983) were fit to a nonlinear, exponential, and power functions as in Figure 3. Using parameters providing the best fit of the data, the prediction of PbB was extrapolated to an uptake of 80,000 µg Pb/d.

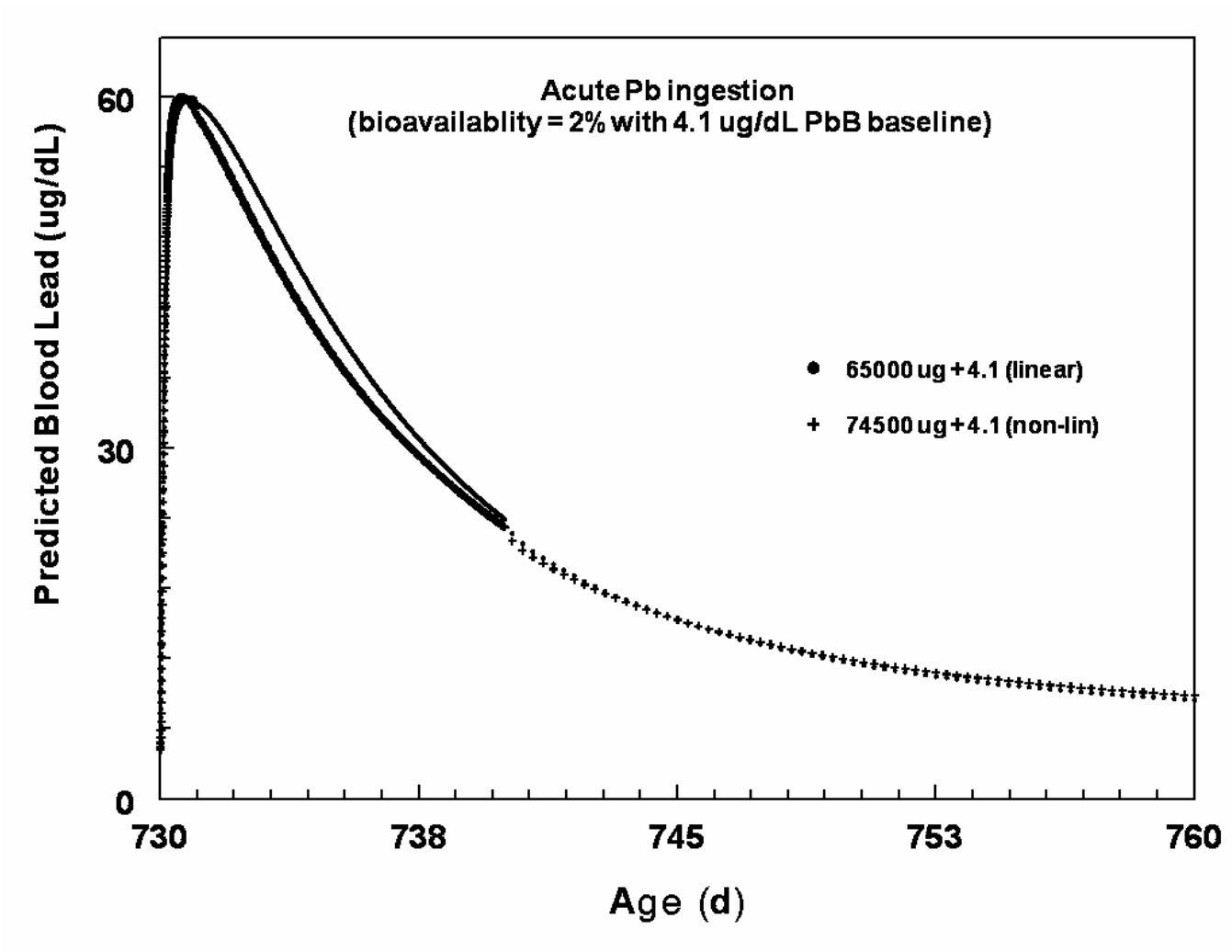

Figure 5. Predicted Blood Lead Concentrations from Ingestion of a Single Dose of Lead from Soil

Blood lead concentrations were predicted using the Leggett model scaled for a 2-year old child. The baseline blood lead concentration was assumed to be 4.1 µg/dL, and the absolute bioavailability of the lead dose from soil was assumed to be 0.02. The blood concentration versus time profiles shown are for a lead dose of 65,000 µg assuming linear partitioning of lead to erythrocytes, and 74,500 µg assuming non-linear partitioning. Both produce a peak blood lead concentration equal to the target limit of 60 µg/dL.