BIOAVAILABILITY OF LEAD IN SOIL SAMPLES FROM THE KENNECOTT NPL SITE SALT LAKE CITY, UTAH

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EXECUTIVE SUMMARY

A study using young swine as test animals was performed to measure the gastrointestinal absorption of lead from two soil samples from the Kennecott Superfund site located near Salt Lake City, Utah. Young swine were selected for use in the study primarily because the gastrointestinal physiology and overall size of young swine are similar to that of young children, who are the population of prime concern for exposure to soil lead.

The two test soils were both composites from areas located along Bingham Creek in the community of West Jordan, Utah. One sample was prepared by compositing 22 individual residential yard-soil samples, each of which contained less than 2,500 ppm lead. The concentration in the composite was 1,590 ppm lead. This was referred to as the "Residential" sample. The second sample was prepared by compositing 28 individual soil samples from the Bingham Creek channel in areas adjacent to residential yards. Each of these subsamples contained at least 3,000 ppm lead, and the concentration in the composite was 6,330 ppm. This was referred to as the "Channel" sample.

Groups of 5 swine were given oral doses of 75, 225, or 450 ug/kg/day of lead for the Residential sample or 75, 225 or 675 ug/kg-day for the Channel sample. This corresponded to doses of 11.8, 35.5, or 107 mg/kg-day of Channel soil, or 47.2, 142, or 283 mg/kg-d of Residential soil. Exposure continued for either 16 or 17 days (inclement weather delayed part of the study by one day). Other groups of animals were given a standard lead reference material (lead acetate) either orally at doses of 0, 25, 75, or 225 ug Pb/kg-day, or intravenously at a dose of 100 ug Pb/kg-day. The amount of lead absorbed by each animal was evaluated by measuring the amount of lead in the blood (measured on days -2, 0, 2, 4, 6, 8, 10, 12, 14 and 16 or 17), and the amount of lead in liver, kidney and bone (measured on day 16 or 17 at study termination). The amount of lead present in blood or tissues of animals exposed to test soils was compared to that for animals exposed to lead acetate, and the results were expressed as relative bioavailability (RBA). For example, a relative bioavailability of 50% means that 50% of the lead in soil was absorbed equally as well as lead from lead acetate, and 50% behaved as if it were not available for absorption. Thus, if lead acetate were 40% absorbed on an absolute basis, the test material would be 20% absorbed

The RBA results for the two soil samples from the Bingham Creek site are summarized below:

Measurement	Relative Bioavailability		
Endpoint	Residential Soil	Channel Soil	
Blood Lead AUC	0.325	0.289	
Liver Lead	0.333	0.265	
Kidney Lead	0.208	0.223	
Bone Lead	0.213	0.265	

Because the estimates of RBA based on blood, liver, kidney, and bone do not precisely agree in all cases, judgment must be used in interpreting the data. In general, we recommend greatest emphasis be placed on the RBA estimates derived from the blood lead data. This is because blood

lead data are more robust and less susceptible to random errors than the tissue lead data because the blood lead data are based on multiple measurements collected over time rather than a single sample at termination, so there is greater confidence in RBA estimates based on blood lead. In addition, absorption into the central compartment is an early indicator of lead exposure, is the most relevant index of central nervous system exposure, and is the standard biomedical measurement endpoint in investigations of this sort. However, data from the tissue endpoints (liver, kidney, bone) also provide valuable information on bioavailability. We consider the plausible range to extend from the RBA based on blood AUC to the mean of the other three tissues (liver, kidney, bone). The preferred range is the interval from the RBA based on blood to the mean of the blood RBA and the tissue mean RBA. Our suggested point estimate is the midpoint of the preferred range. These RBA values are presented below:

Relative Bioavailability	Test Material		
of Lead	Residential Soil	Channel Soil	
Plausible range	0.251 - 0.325	0.251 - 0.289	
Preferred range	0.288 - 0.325	0.270 - 0.289	
Suggested Point Estimate	0.307	0.280	

These RBA estimates may be used to help assess lead risk at this site by refining the estimate of absolute bioavailability (ABA) of lead in soil, as follows:

$$ABA_{soil} = ABA_{soluble} \cdot RBA_{soil}$$

Available data from the literature indicate that fully soluble forms of lead are about 50% absorbed by a child, and this value is used by EPA in the IEUBK model as the default absorption fraction for lead in water and food ingested by children. Based on this value, the estimated absolute bioavailability of lead in the test soils are as follows:

Absolute Bioavailability	Test Material		
of Lead	Residential Soil	Channel Soil	
Plausible Range	13%-16%	13%-14%	
Preferred Range	14%-16%	13%-14%	
Suggested Point Estimate	15%	14%	

Because the RBA estimates for the two test materials are nearly identical, 15% was taken to apply to both Bingham Creek soil samples.

These absolute bioavailability estimates are appropriate for use in EPA's IEUBK model for this site, although it is clear that there is both natural variability and uncertainty associated with these estimates. This variability and uncertainty arises from several sources, including: 1) the inherent variability in the responses of different individual animals to lead exposure, 2) uncertainty in the relative accuracy and applicability of the different measurement endpoints, 3) the extrapolation of

measured RBA values in swine to young children, and 4) the potential effect of food in the stomach on lead absorption. Thus, the values reported above are judged to be reasonable estimates of typical lead absorption by children at this site, but should be interpreted with the understanding that the values are not certain.

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1.0 INTRODUCTION

Absolute and Relative Bioavailability

Bioavailability is a concept that relates to the absorption of chemicals and how absorption depends upon the physical-chemical properties of the chemical and its medium (e.g., dust, soil, rock, food, water, etc.) and the physiology of the exposed receptor. Bioavailability is normally described as the fraction (or percentage) of a chemical which enters into the blood following an exposure of some specified amount, duration, and route (usually oral). In some cases, bioavailability may be measured using chemical levels in peripheral tissues such as liver, kidney, and bone, rather than blood. The fraction or percentage absorbed may be expressed either in absolute terms (absolute bioavailability, ABA) or in relative terms (relative bioavailability, RBA). Absolute bioavailability is measured by comparing the amount of chemical entering the blood (or other tissue) following oral exposure to test material with the amount entering the blood (or other tissue) following intravenous exposure to an equal amount of some dissolved form of the chemical. Similarly, relative bioavailability is measured by comparing oral absorption of test material to oral absorption of some fully soluble form of the chemical (e.g., either the chemical dissolved in water, or a solid form that is expected to fully dissolve in the stomach). For example, if 100 ug of dissolved lead were administered in drinking water and a total of 50 ug entered the blood, the ABA would be 0.50 (50%). Likewise, if 100 ug of lead in soil were administered and 30 ug entered the blood, the ABA for soil would be 0.30 (30%). If the lead dissolved in water were used as the reference substance for describing the relative amount of lead absorbed from soil, the RBA would be 0.30/0.50 = 0.60 (60%). These values (50% absolute bioavailability of dissolved lead and 30% absolute absorption of lead in soil) are the values currently employed as defaults in EPA's IEUBK model

It is important to recognize that simple <u>solubility</u> of a test material in water or some other fluid (e.g., a weak acid intended to mimic the gastric contents of a child) may not be a reliable estimator of <u>bioavailability</u> due to the non-equilibrium nature of the dissolution and transport processes that occur in the gastrointestinal tract (Mushak 1991). For example, fluid volume and pH are likely to be changing as a function of time, and transport of lead across the gut will prevent an approach to equilibrium concentrations, especially for poorly soluble lead compounds. However, information on the solubility of lead in different materials is useful in interpreting the importance of solubility as a determinant of bioavailability. To avoid confusion, the term "bioaccessability" is preferred when describing the relative amount of lead that is <u>dissolved</u> (vs the amount absorbed into the blood) under a specified set of test solution conditions.

For additional discussion about the concept and application of bioavailability see Goodman et al. (1996), Klaassen et al. (1996), and/or Gibaldi and Perrier (1982).

Using Bioavailability Data to Improve Exposure Calculations for Lead

Data on bioavailability are important for evaluating exposure and potential health effects for a variety of different types of chemicals. This investigation focused mainly on evaluating the bioavailability of lead in various samples of soil or other solid materials from mining, milling or smelting sites. This is because lead may exist, at least in part, as poorly water soluble minerals (e.g., galena), and may also exist inside particles of inert matrix such as rock or slag of variable size, shape and association. These chemical and physical properties may tend to influence (usually decrease) the solubility (bioaccessability) and the absorption (bioavailability) of lead when ingested.

When data are available on the bioavailability of lead in soil, dust, or other soil-like waste material at a site, this information can often be used to improve the accuracy of exposure and risk calculations at that site. The basic equation for estimating the site-specific RBA of a test soil is as follows:

 $ABA_{soil} = ABA_{soluble} \cdot RBA_{soil}$

where:

 ABA_{soil} = Absolute bioavailability of lead in soil ingested by a child $ABA_{soluble}$ = Absolute bioavailability in children of some dissolved or fully soluble form of lead

 RBA_{soil} = RBA for soil measured in swine

Based on available information on lead absorption in humans, the EPA estimates that the absolute bioavailability of lead from water and other fully soluble forms of lead is usually about 50% in children. Thus, when a reliable site-specific RBA value for soil is available, it may be used to estimate a site-specific absolute bioavailability as follows:

$$ABA_{soil} = 50\% \cdot RBA_{soil}$$

In the absence of site-specific data, the absolute absorption of lead from soil, dust and other similar media is estimated by EPA to be about 30%. Thus, the default RBA used by EPA for lead in soil and dust compared to lead in water is 30%/50% = 60%. When the measured RBA in soil or dust at a site is found to be less than 60% compared to some fully soluble form of lead, it may be concluded that absorption of lead from these media (and hence the toxicological hazard) is probably lower than typical default assumptions. If the measured RBA is higher than 60%, both the absorption and toxicologic hazard of lead in these media may be higher than usually assumed.

2.0 STUDY DESIGN

A standardized study protocol for measuring absolute and relative bioavailability of lead was developed based upon previous study designs and investigations that characterized the young pig model (Weis et al. 1995). The study was performed as nearly as possible within the spirit and guidelines of Good Laboratory Practices (GLP: 40 CFR 792). Standard Operating Procedures (SOPs) that included detailed methods for all aspects of the study were prepared, approved, and distributed to all study members prior to the study. The generalized study design, quality assurance project plan and all standard operating procedures are documented in a project notebook that is available through the administrative record.

2.1 Test Materials

Soil samples were collected from a residential area (Jordan View Estates) located along Bingham Creek in the community of West Jordan, Utah. The Residential sample was prepared by compositing 22 individual residential yard-soil samples, each of which contained less than 2,500 ppm lead. The Channel sample was prepared by compositing 28 individual soil samples from the Bingham Creek channel adjacent to residential yards. Each of these subsamples contained at least 3,000 ppm. Both samples were sieved with a 100-mesh stainless steel screen, and only the fine fraction (particles less than about 150 um in diameter) derived from each sample were evaluated. This is because it is believed that very fine soil particles are the most likely to adhere to the hands and be ingested by hand-to-mouth contact, especially in young children.

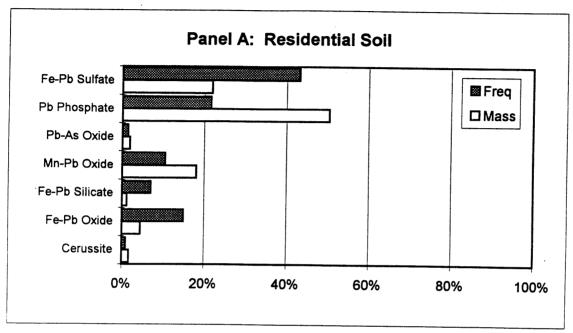
Table 2-1 lists the metal content of these samples measured using standard EPA Contract Laboratory program (CLP) methods. Inspection of the data in this table reveals that the two test materials are generally similar in most regards, although they do differ in the content of some constituents.

Each soil was well mixed and samples were analyzed by electron microprobe in order to identify a) how <u>frequently</u> particles of various lead minerals were observed, b) how frequently different types of mineral particles occur entirely inside particles of rock or slag ("<u>included</u>") and how often they occur partially or entirely outside rock or slag particles ("<u>liberated</u>"), c) the <u>size</u> distribution of particles of each mineral class, and d) approximately how much of the total amount of lead in the sample occurs in each mineral type. This is referred to as "relative lead <u>mass</u>". The results are summarized in Figure 2-1 and in Table 2-2.

As seen in Figure 2-1, there are a variety of different lead mineral forms present in each soil sample. In terms of length-weighted particle frequency (shaded bars), the most frequent particle type is iron-lead sulfate. In terms of relative lead mass (open bars), the majority of the lead is contained in particles of lead phosphate, iron-lead sulfate, and (in the Channel sample only) lead sulfate (anglesite).

¹ The Standard Operating Procedure developed for sample preparation called for sieving with a 60-mesh screen to isolate particles < 250 um. Because the samples in this study were prepared with a finer mesh screen, the measured RBA values might tend to be somewhat higher than otherwise.

FIGURE 2-1 LEAD MINERALS OBSERVED IN SITE SOILS



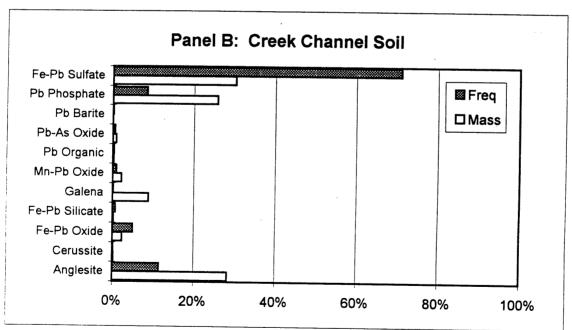


TABLE 2-1 METAL ANALYSIS OF TEST MATERIALS

Chemical	Concentration (ppm)		
	Residential Soil	Channel Soil	
Aluminum	10,600	10,100	
Antimony	< 10	18.7	
Arsenic	51.2	149	
Barium	143	152	
Beryllium	0.71	0.73	
Cadmium	4.2	8.7	
Calcium	13,600	8,500	
Chromium	16.6	17.9	
Cobalt	7.50	7.90	
Copper	691	1,720	
Iron	16,100	22,500	
Lead	1,590	6,330	
Magnesium	7,020	5,970	
Manganese	466	376	
Nickel	15.0	15.1	
Potassium	4,340	4,150	
Selenium	< 17	< 17	
Silver	4.10	17.2	
Sodium	362	314	
Thallium	< 17	< 17	
Vanadium	20.8	22.0	
Zinc	903		

TABLE 2-2 GEOCHEMICAL CHARACTERISTICS OF TEST MATERIALS FOR THE LEAD PHASE⁴

Mineral Form			Residential Soil	ial Soil					Cham	Channel Soil		
	Partick	Particle Freq.(%)	Рал	Particle Size ^d (um)	(mn)	Relative Lead Mass * (%)	Particle	Particle Freq. (%)	Par	Particle size (um)	(Wr	Relative Lead Mass (%)
	Count- Based ^b	Length- Weighted ^c	mim	тах	mean		Count- Based	Length- Weighted	min	max	mean	
Anglesite		-					11.6	6.3	1	30	4	28.4
Cerussite	1	0.28	2	5	4	1.8	0.2	0.05	2	2	2	0.3
Fe-Pb Oxide	15.1	17.9	2	75	15	4.6	5.1	10.9	4	09	17	2.4
Fe-Pb Silicate	7.0	5.5	∞	20	10	1.2	8.0	1.6	10	20	15	0.3
Galena							0.2	1.3	50	50	50	8.9
Mn-Pb Oxide	10.6	18.1	2	110	22	18.1	1.0	2.7	\$	50	21	2.3
Pb Organic							0.4	5.5	100	110	105	0.3
Pb-As Oxide	1.5	0.5	2	∞	4	1.9	9.0	0.3	-	8	4	6.0
Pb Barite							0.2	0.3	10	10	10	Trace
Pb Phosphate	21.6	21.7	1	110	13	50.4	9.8	13.0	1	100	12	25.8
Fe-Pb Sulfate	43.2	35.9	-	120	10	21.9	71.1	58.1	1	110	9	30.4

Samples were analyzed using an electron microprobe (JEOL 8600) to identify the number of particles of each lead species present in each sample and the particle size (largest dimension) of each particle.
 Percentage of all lead-bearing particles of the mineral form shown
 Percentage of total length of all lead particles consisting of mineral form shown
 Based on longest dimension of each particle
 Rough estimate of the percent of the total mass of lead present in each mineral form

As shown in Figure 2-2, most of the lead-bearing particles are **small** (less than about 50 um). As noted above, small particles are often assumed to be more likely to adhere to the hands and be ingested and/or be transported into the house. Further, small particles have larger surface area-to-volume ratios than larger particles, and so may tend to dissolve more rapidly in the acidic contents of the stomach than larger particles with relatively lower surface area to volume ratios. Thus, small particles (e.g., less than 25-50 um) are thought to be of greater potential concern to humans due to the potential for increased bioavailability than larger particles.

Essentially all of the lead-bearing particles in both soil samples are "liberated" (i.e., they have some or all of their surface lead-salts exposed to the outside). This is of potential importance because liberated grains are thought to be more likely to be solubilized by acidic fluids in the stomach than are grains that are entirely confined within a glassy or rocky matrix that could serve as a protective barrier.

2.2 Experimental Animals

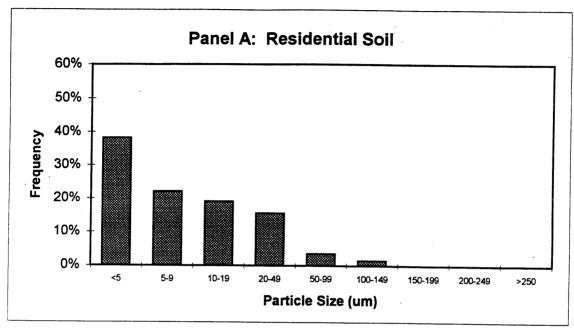
Young swine were selected for use in these studies because they are considered to be a good physiological model for gastrointestinal absorption in children (Weis and LaVelle 1991). The animals were intact males of the Pig Improvement Corporation (PIC) genetically defined Line 26, and were purchased from Chinn Farms, Clarence, MO. The animals were held under quarantine to observe their health for one week before beginning exposure to test materials. Any animals that did not appear to be healthy were excluded from the study. To minimize weight variations between animals and groups, the number of animals purchased from the supplier was six more than needed for the study, and the six animals most different in body weight on day -4 (either heavier or lighter) were excluded from further study. The remaining animals were assigned to dose groups at random. When exposure began (day zero), the animals were about 5-6 weeks old (juveniles, weaned at 3 weeks) and weighed an average of about 10-12 kg. Animals were weighed every three days during the course of the study. The group mean body weights over the course of the study are shown in Figure 2-3. On average, animals gained about 0.5 kg/day, and the rate of weight gain was comparable in all groups.

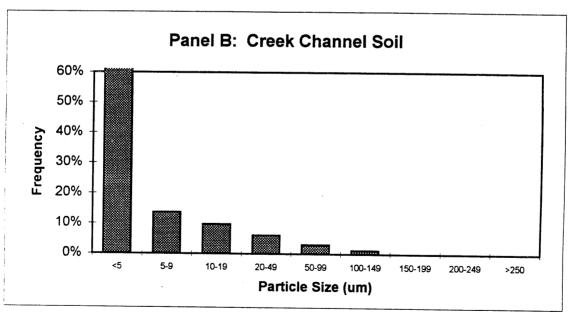
All animals were housed in individual lead-free stainless steel cages. Each animal was examined by a certified veterinary clinician (swine specialist) prior to being placed on study, and all animals were examined daily for health status by an attending veterinarian while on study. Blood samples were collected for clinical chemistry and hematological analysis on days -4, 7, and 15 to assist in clinical health assessments. In this study, there were two animals, both from the IV dose group, that were judged by the principal investigator and the veterinary clinician to be seriously ill, and these two animals were removed from the study. (Infections in the IV-catheterized animals was relatively common in other studies in this program). All other animals appeared healthy and were maintained for the duration of the study.

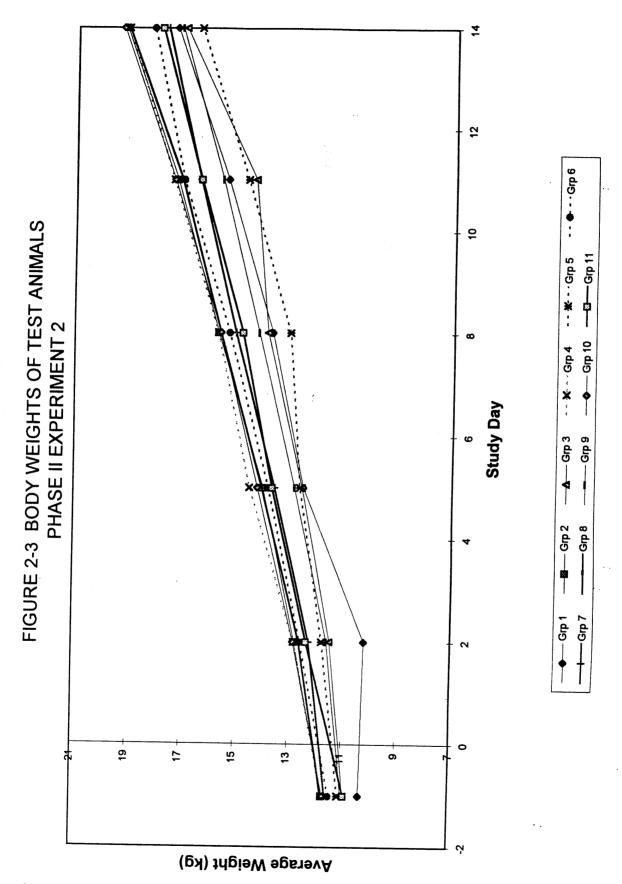
2.3 Diet

Animals provided by the supplier were weaned onto standard pig chow purchased from MFA Inc., Columbia, MO. In order to minimize lead exposure from the diet, the animals were gradually transitioned from the MFA feed to a special low-lead feed (guaranteed less than 0.2

FIGURE 2-2 PARTICLE SIZE DISTRIBUTION







ppm lead, purchased from Zeigler Brothers, Inc., Gardners, PA) over the time interval from day -7 to day -3, and this feed was then maintained for the duration of the study. The feed was nutritionally complete and met all requirements of the National Institutes of Health-National Research Council. The typical nutritional components and chemical analysis of the feed is presented in Table 2-3. Typically, the feed contained approximately 5.7% moisture, 1.7% fiber, and provided about 3.4 kcal of metabolizable energy per gram. Periodic analysis of feed samples during this program indicated the mean lead level (treating non-detects at one-half the quantitation limit of 0.05 ppm) was less than 0.05 ppm.

Each day every animal was given an amount of feed equal to 5% of the mean body weight of all animals on study. Feed was administered in two equal portions of 2.5% of the mean body weight at each feeding. Feed was provided at 11:00 AM and 5:00 PM daily. Drinking water was provided ad libitum via self-activated watering nozzles within each cage. Periodic analysis of samples from randomly selected drinking water nozzles indicated the mean lead concentration (treating values below the quantitation limit of 1 ug/L at one-half the quantitation limit) was less than 2 ug/L.

2.4 Dosing

The basic protocol for exposing animals to lead is shown in Table 2-4. The dose levels for lead acetate were based on experience from previous investigations that showed that doses of 25-75 ug Pb/kg/day or higher gave clear and measurable increases in lead levels in all endpoints measured (blood, liver, kidney, bone). The doses of test materials were selected to overlap and exceed the lead acetate doses in case the test materials were found to yield low responses.

For technical convenience and experimental practicality, animals in even-numbered and oddnumbered groups were exposed on a schedule that was off-set by one day. That is, Day Zero of the exposure schedule was on a Monday for Groups 1, 3, 5, 7, 9, and 11, and on Tuesday for groups 2, 4, 6, 8, and 10. In all cases, the dose for each day was administered in two equal portions, given at 9:00 AM and 3:00 PM (two hours before feeding). Doses were based on measured group mean body weights, and were adjusted every three days to account for animal growth. For animals exposed by the oral route, dose material was placed in the center of a small portion (about 5 grams) of moistened feed, and this was administered to the animals by hand. Most animals consumed the dose promptly, but occasionally some animals delayed ingestion of the dose for up to two hours (the time the daily feed portion was provided). These relatively minor delays are noted in the data provided in Appendix A, but are not considered to be a significant source of error. Occasionally, some animals did not consume some or all of the dose (usually because the dose dropped from their mouth while chewing and fell through the grated floor). All missed doses were recorded and the time-weighted average dose calculation for each animal was adjusted downward accordingly. If an animal missed 5 or more oral doses during the study (out of a total of about 30 doses), the data for that animal were excluded from analysis. One animal from Group 3 was excluded on this basis.

For animals exposed by intravenous injection, doses were given via a vascular access port (VAP) attached to an indwelling venous catheter that had been surgically implanted according to

TABLE 2-3 TYPICAL FEED COMPOSITION^a

Nutrient Name	Amount	Nutrient Name	Amount
Protein	20.1021%	Chlorine	0.1911%
Arginine	1.2070%	Magnesium	0.0533%
Lysine	1.4690%	Sulfur	0.0339%
Methionine	0.8370%	Manganese	20.4719 ppm
Met+Cys	0.5876%	Zinc	118.0608 ppm
Tryptophan	0.2770%	Iron	135.3710 ppm
Histidine	0.5580%	Copper	8.1062 ppm
Leucine	1.8160%	Cobalt	0.0110 ppm
Isoleucine	1.1310%	Iodine	0.2075 ppm
Phenylalanine	1.1050%	Selenium	0.3196 ppm
Phe+Tyr	2.0500%	Nitrogen Free Extract	60.2340%
Threonine	0.8200%	Vitamin A	5.1892 kIU/kg
Valine	1.1910%	Vitamin D3	0.6486 kIU/kg
Fat	4.4440%	Vitamin E	87.2080 IU/kg
Saturated Fat	0.5590%	Vitamin K	0.9089 ppm
Unsaturated Fat	3.7410%	Thiamine	9.1681 ppm
Linoleic 18:2:6	1.9350%	Riboflavin	10.2290 ppm
Linoleic 18:3:3	0.0430%	Niacin	30.1147 ppm
Crude Fiber	3.8035%	Pantothenic Acid	19.1250 ppm
Ash	4.3347%	Choline	1019.8600 ppm
Calcium	0.8675%	Pyridoxine	8.2302 ppm
Phos Total	0.7736%	Folacin	2.0476 ppm
Available Phosphorous	0.7005%	Biotin	0.2038 ppm
Sodium	0.2448%	Vitamin B12	23.4416 ppm
Potassium	0.3733%		•

^a Nutritional values provided by Zeigler Bros., Inc.

TABLE 2-4 DOSING PROTOCOL

Group	Number of Animals	Material Administered	Exposure Route	Lead Dose ((ug Pb/kg-d)
				Target	Actual ^a
1	2	None (control)	Oral	0	0
2	5	PbAc	Oral	25	25.3
3	5	PbAc	Oral	75	73.5
4	5	PbAc	Oral	225	227
5	5	Residential Soil	Oral	75	78.0
6	5	Residential Soil	Oral	225	230
7	5	Residential Soil	Oral	450	459
. 8	5	Channel Soil	Oral	75	75.8
9	5	Channel Soil	Oral	225	230
10	5	Channel Soil	Oral	675	675
11	8	PbAc	IV	100	102

Doses were administered for 16 days (even numbered groups) or 17 days (odd numbered groups). Each daily dose was and split in two equal portions that were given at 9:00 AM and 3:00 PM each day. Doses were based on the mean weight of the animals in each group, and were adjusted every three days to account for weight gain.

^a The value shown is the average based on days 0-14. This time interval was used because all measured lead responses were adjusted to estimate the response on day 15 in order to be consistent with other studies in this program. Because administered doses were adjusted based on revised body weights every three days, the measured average dose rate would not have been significantly different had an interval of 0-16 or 0-17 been used.

standard operating procedures by a board-certified veterinary surgeon through the external jugular vein to the anterior vena cava about 3 to 5 days before exposure began.

The nominal exposure schedule called for all groups to be exposed for the final time on day 15 and then sacrificed (after collection of a blood sample) on day 16. However, because of a blizzard which occurred at the end of the study, animals in the odd-numbered groups could not be sacrificed on the planned schedule. Therefore, these animals were exposed with another set of split doses for one extra day, and were sacrificed on day 17.

Actual mean doses, calculated from the administered doses and the measured body weights, are summarized in Table 2-4.

2.5 Collection of Biological Samples

Blood

Samples of blood were collected from each animal four days before exposure began (day -4), on the first day of exposure (day 0), and on study-days 2, 4, 6, 8, 10, 12, 14, and 16 (even-numbered groups) or 17 (odd-numbered groups) following the start of exposure. All blood samples were collected by routine clinical vena-puncture of the anterior vena cava, and samples were immediately placed in purple-top Vacutainer® tubes containing EDTA as anticoagulant. Blood samples were collected each sampling day beginning at 8:00 AM, approximately one hour before the first of the two daily exposures to lead on the sampling day and 17 hours after the last lead exposure on the previous day. This blood collection time was selected because the rate of change in blood lead resulting from the preceding exposures is expected to be relatively small after this interval (LaVelle et al. 1991, Weis et al. 1993), so the exact timing of sample collection relative to last dosing is not likely to be critical as long as collection times are reasonably uniform.

Following collection of the final blood sample at 8:00 AM on day 16 or 17, all animals were humanely euthanized and samples of liver, kidney and bone (the right femur) were removed and stored in lead-free plastic bags for lead analysis. Samples of all biological samples collected were archived in order to allow for reanalysis and verification of lead levels, if needed, and possibly for future analysis for other metals (arsenic, cadmium, etc.). All animals were also subjected to detailed examination at necropsy by a certified veterinary pathologist in order to assess overall animal health

2.6 Preparation of Biological Samples for Analysis

Blood

One mL of whole blood was removed from the purple-top Vacutainer and added to 9.0 mL of "matrix modifier", a solution recommended by the Centers for Disease Control and Prevention (CDCP) for analysis of blood samples for lead. The composition of matrix modifier is 0.2% (v/v) ultrapure nitric acid, 0.5% (v/v) Triton X-100, and 0.2% (w/v) dibasic ammonium phosphate in deionized and ultrafiltered water. In general, a large batch of matrix modifier was prepared at the start of each study so that sufficient material would be available to last the entire experiment.

Samples of the matrix modifier were periodically analyzed for lead to ensure the absence of lead contamination.

Liver and Kidney

One gram of soft tissue (liver or kidney) was placed in a lead-free screw-cap teflon container with 2 mL of concentrated (70%) nitric acid and heated in an oven to 90°C overnight. After cooling, the digestate was transferred to a clean lead-free 10 mL volumetric flask and diluted to volume with deionized and ultrafiltered water.

Bone

The right femur of each animal was removed and defleshed, and dried at 100°C overnight. The dried bones were then broken in half and placed in a muffle furnace and dry-ashed at 450°C for 48 hours. Following dry ashing, the bone was ground to a fine powder using a lead-free mortar and pestle, and 200 mg was removed and dissolved in 10.0 mL of 1:1 (v:v) concentrated nitric acid/water. After the powdered bone was dissolved and mixed, 1.0 mL of the acid solution was removed and diluted to 10.0 mL by addition of 0.1% (w/v) lanthanum oxide (La₂O₃) in deionized and ultrafiltered water.

2.7 Lead Analysis

Samples of biological tissue (blood, liver, kidney, bone) and other materials (food, water, reagents and solutions, etc.) were arranged in a random sequence and provided to EPA's analytical laboratory in a blind fashion (identified to the laboratory only by a chain of custody tag number). Each sample was analyzed for lead using a Perkin Elmer Model 5100 graphite furnace atomic absorption spectrophotometer. Internal quality assurance samples were run every tenth sample, and the instrument was recalibrated every 15th sample. A blank, duplicate and spiked sample were run every 20th sample.

All results from the analytical laboratory were reported in units of ug Pb/L of prepared sample. The quantitation limit was defined by EPA as three-times the standard deviation of a set of seven replicates of a low-lead sample (typically about 2-5 ug/L) run on non-consecutive days. The standard deviation was usually about 0.3 ug/L, so the quantitation limit was usually about 0.9-1.0 ug/L (ppb). For prepared blood samples (diluted 1/10), this corresponds to a quantitation limit of 10 ppb (1 ug/dL). For soft tissues (liver and kidney, diluted 1/10), this corresponds to a quantitation limit of 10 ppb (ug/kg) wet weight, and for bone (final dilution = 1/500) the corresponding quantitation limit is 500 ppb (ug/kg) ashed weight.

3.0 DATA ANALYSIS

3.1 Overview

Studies on the absorption of lead are often complicated because the dose-response curve for blood lead is usually non-linear (i.e., tending to flatten out or plateau as dose increases). Based on intravenous dose-response studies performed as part of this program, it appears this non-linearity is probably due to non-linear lead binding in blood per unit dose absorbed, rather than non-linear absorption kinetics. In any event, when the dose-response curve for either the reference material (lead acetate) and/or the test material is <u>non-linear</u>, RBA is equal to the ratio of doses that produce equal responses (not the ratio of responses at equal doses). This is based on the simple but biologically plausible assumption that equal absorbed doses of Pb⁺⁺ yield equal biological responses². Applying this assumption leads to the following general methods for calculating RBA from a set of non-linear experimental data:

- 1. Plot the biological responses of individual animals exposed to a series of oral doses of a readily soluble "reference" form of lead (e.g., lead acetate). Fit an equation which gives a smooth curvilinear line through the observed data points.
- 2. Plot the biological responses of individual animals exposed to a series of doses of test material. Fit an equation which gives a smooth curvilinear line through the observed data.
- 3. Using the best-fit equations for reference material and test material, calculate RBA as the ratios of doses (x-axis) of test material and reference material which yield equal biological responses (y-axis). Depending on the relative shape of the best-fit lines through the lead acetate and test material dose response curves, RBA may either be constant (dose-independent) or variable (dose-dependent). In our studies, we have found that RBA is usually approximately constant over dose.

The principal advantage of this approach is that it is not necessary to understand the biological basis for a non-linear dose response curve (non-linear absorption and/or non-linear biological response) in order to derive valid RBA estimates. Also, it is important to realize that this method is very general, as it will yield correct results even if one or both of the dose-response curves are linear. In the case where both curves are linear, RBA is dose-independent and is simply equal to the ratio of the slopes of the best-fit linear equations. Generally, blood-lead responses were non-linear functions of dose, while tissue-uptakes were linear functions of dose.

3.2 Fitting the Curves

There are a number of different mathematical equations which can yield reasonable fits with the dose-response data sets obtained in this study. Conceptually, any equation which gives a smooth best-fit line through the data would be acceptable, since the main purpose is to allow for interpolation of responses between different dose levels. In selecting which equations to employ,

² Small amounts of lead may also enter the body by pinocytosis, of intact particles but this is not believed to be quantitatively significant compared to the amount absorbed as Pb⁺⁺ absorbed across the gastrointestinal tract.

the following principles were applied: 1) mathematically simple equations were preferred over mathematically complex equations, 2) the shape of the curves had to be smooth and biologically realistic, without inflection points or internal maxima or minima, and 3) the general form of the equations had to be able to fit data not only from this one study, but from all the standardized studies that are part of this bioavailability project. After testing a wide variety of different equations, it was found that all data sets could be well fitted using one of the following three forms:

<u>Linear (LIN):</u> Response = $a + b \cdot Dose$

Exponential (EXP): Response = $a + c \cdot (1-exp(-d \cdot Dose))$

<u>Combination (LIN+EXP):</u> Response = $a + b \cdot Dose + c \cdot (1-exp(-d \cdot Dose))$

Each dose-response data set was fit to each of the equations above. As noted earlier, plots of blood lead AUC versus dose were usually nonlinear, and these were generally well-fit by the EXP equation. Dose-response curves for liver, kidney and bone were typically linear, and these were well-fit by the LIN equation. If one equation yielded a fit that was clearly superior (as judged by the value of the adjusted correlation coefficient R²) to the others, that equation was selected. If two or more models fit the data approximately equally well, then the simplest model (that with the fewest parameters) was selected. In the process of finding the best-fits of these equations to the data, the values of the parameters (a, b, c, and d) were subjected to some constraints (gleaned form historical dose-responses of PbAc standards), and some data points (those that were outside the 95% prediction limits of the fit) were excluded. These constraints and outlier exclusion steps are detailed in Appendix A (Section 3).

3.3 Responses Below Quantitation Limit

In some cases, most or all of the responses in a group of animals were below the quantitation limit for the endpoint being measured. For example, this was normally the case for blood lead values in unexposed animals (both on day -4 and day 0, and in control animals), and also occurred during the early days in the study for animals given test materials with low bioavailability. In these cases, all animals which yielded responses below the quantitation limit were evaluated as if they had responded at one-half the quantitation limit. This approach will slightly under-estimate RBA compared to use of zero for non-detects, or slightly over-estimate RBA if the quantitation limit was used for non-detects.

3.4 Quality Assurance

A number of steps were taken throughout this study and the other studies in this project to ensure the quality of the results. These steps are summarized below.

Duplicates

A randomly selected set of about 5% of all samples generated during the study were submitted to the laboratory in a blind fashion for duplicate analysis. The raw data are presented in Appendix

A, and Figure 3-1 plots the results for blood (Panel A, upper) and for bone, liver and kidney (Panel B, lower). As seen, there was good intra-laboratory reproducibility between duplicate samples for both blood and tissues, with linear regression lines having a slope near 1.0, an intercept near zero, and an R² value near 1.0.

Standards

The Centers for Disease Control and Prevention (CDCP) provides a variety of blood lead "check samples" for use in quality assurance programs for blood lead studies. Each time a group of blood samples was prepared and sent to the laboratory for analysis, several CDCP check samples of different concentrations were included in random order and in a blind fashion.

The results for the samples submitted during this study are presented in Appendix A, and the values are plotted in Figure 3-2 (Panel A, upper). As seen, the analytical results obtained for the check samples were generally reasonable, although samples analyzed on days -2, 0 12 or 14 tended to be high. As discussed in greater detail below (see Section 4.1), this is believed to be due to an external source of lead contamination on these days. After excluding these check samples, the following results were obtained:

Standard	Nominal (ug/dL)	Measured (mean) ^a (ug/dL)
Low	1.7	1.7
Medium	4.8	5.7
High	14.9	15.9

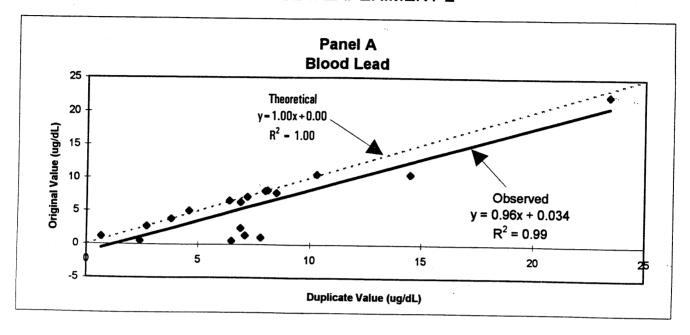
^a Excludes data from days -2, 0, 12 and 14

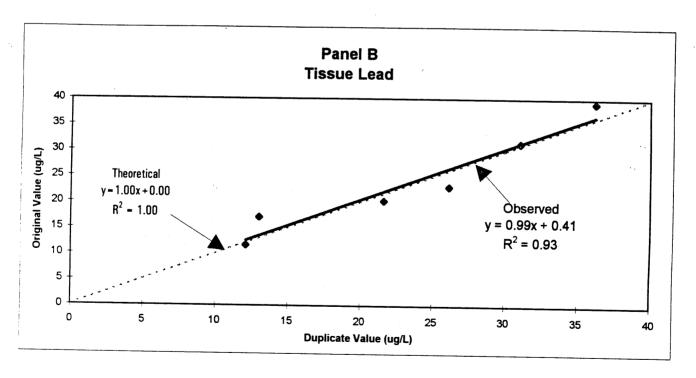
As seen, there is generally good agreement, although there was a tendency for the results to be about 1 ug/dL higher than the nominal CDCP value for the medium and high standards.

Interlaboratory Comparison

An interlaboratory comparison of blood lead analytical results was performed by sending a set of 24 randomly selected whole blood samples from this study to CDCP for blind independent preparation and analysis. The results are presented in Appendix A, and the values are plotted in Figure 3-2 (Panel B, lower). As seen, although there was good agreement for most samples, some values obtained by EPA tended to be higher than the values reported by CDCP. The reason for this apparent discrepancy between the EPA laboratory and the CDCP laboratory is not entirely clear. However, CDCP was provided with whole blood samples which they prepared independently, so the laboratories did not analyze exact aliquots of blood samples, but just variably processed blood from identical animals using similar procedures in different facilities (thus, possibly accounting for some inter-laboratory variation.

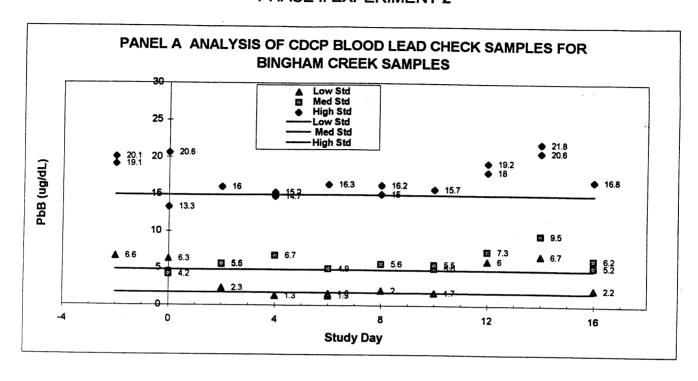
FIGURE 3-1 COMPARISION OF DUPLICATE ANALYSES
BINGHAM CREEK SAMPLES
PHASE II EXPERIMENT 2

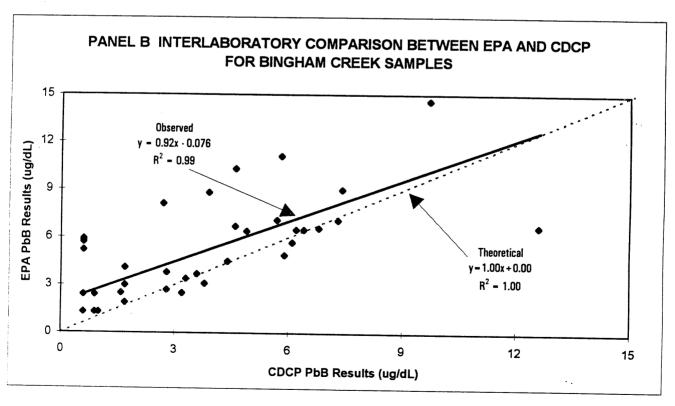




Blind random duplicates submitted at a 5% rate to EPA laboratories to provide a measure of analytical precision (reproducibility)

FIGURE 3-2 CDCP CHECK SAMPLES FOR BINGHAM CREEK SITE SAMPLES PHASE II EXPERIMENT 2





Regardless of the reason, the differences are sufficiently small that they are likely to have no significant effect on calculated RBA values. In particular, it is important to realize that if both the lead acetate and test soils dose-response curves are biased by the same factor, then the biases cancel in the calculation of the ratio.

Data Audits and Spreadsheet Validation

All analytical data generated by EPA's analytical laboratory were validated prior to being released in the form of a database file. These electronic data files were "decoded" (linking the sample tag to the correct animal and day) using Microsoft's database system ACCESS® (Version 5 for Windows). To ensure that no errors occurred in this process, original electronic files were printed out and compared to printouts of the tag assignments and the decoded data.

All spreadsheets used to manipulate the data and to perform calculations (see Appendix A) were validated by hand-checking random cells for accuracy.

4.0 RESULTS

The following sections provide results based on the group means for each dose group investigated in this study. Appendix A provides detailed data for each individual animal. Results from this study will be compared and contrasted with the results from other studies in a subsequent report.

4.1 Blood Lead vs Time

Original analyses of blood lead levels for this study suggested that some samples were contaminated with low levels of lead. This conclusion was based mainly on the finding that reported blood lead levels were about 4-6 ug/dL on days -2 and zero (i.e., before exposure to lead began), while the expected result is that pre-exposure blood lead levels should be at or below the quantitation limit of 1 ug/dL. In addition, blood lead levels in control animals were at or below the quantitation limit on days 2-10 (as expected), but then rose into the 4-6 ug/dL range on days 12-14. A similar 'bump" was also observed in other groups on days 12-14, suggesting a general problem with exogenous lead contamination. These patterns are illustrated in Figure A-17 in the Appendix.

The source of this lead contamination is not certain, but it is suspected that it may have originated in the acid bath used to prepared some glassware and/or in some batches of matrix modifier. In any event, based on the unexpected patterns in blood lead, samples from days -2, 0, 12, and 14 were reanalyzed by preparing fresh dilutions from the archived whole blood samples. These reanalyzed samples appeared to be nominal in that no observable lead was detected in pre-exposure samples or in control animals. However, lead levels in exposed animals tended to be somewhat lower than expected based on extrapolation of the blood lead levels on days 8-10.

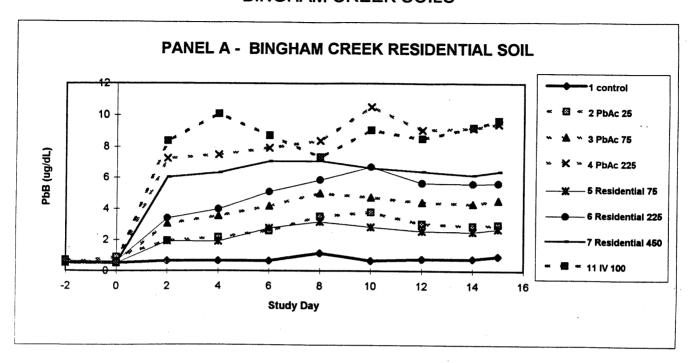
A number of alternative data reduction approaches were considered regarding the reanalyzed data from days 12-14, including a) use of the data without adjustment, b) exclusion of the data, and c) use of a "rolling average" technique to help smooth out the data. After consultation and discussion with a number of scientists, including representatives of the PRPs at this site, it was agreed that the rolling average approach was most likely to yield the strongest and best estimate of the blood lead response. In this approach, the blood lead values on days 12, 14 and 16 were recalculated as follows:

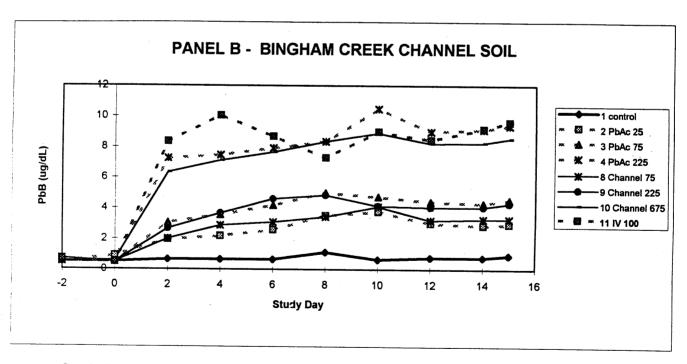
```
\begin{aligned} &PbB(12)_{adj} = \left[PbB(8)_{raw} + PbB(10)_{raw} + PbB(12)_{raw}\right] / 3 \\ &PbB(14)_{adj} = \left[PbB(10)_{raw} + PbB(12)_{adj} + PbB(14)_{raw}\right] / 3 \\ &PbB(16)_{adj} = \left[PbB(12)_{adj} + PbB(14)_{adj} + PbB(16)_{raw}\right] / 3 \end{aligned}
```

These calculations are detailed in the Appendix (see Table A-3), and all further blood lead calculations were based on the reanalyzed and adjusted data. It is important to note, however, that use of the rolling average approach did not significantly alter the results of the RBA calculations.

Figure 4-1 shows the group mean blood lead values as a function of time during the study. As seen, blood lead values began at or below quantitation limits (about 1 ug/dL) in all groups, and remained low in control animals (Group 1) throughout the study. In animals given repeated oral

FIGURE 4-1 GROUP MEAN BLOOD LEAD BY DAY FOR BINGHAM CREEK SOILS





Graphs incorporate rolling averages for Days 12 and 14, and use an interpolated value for Day 15

doses of lead acetate (Groups 2-4), Residential Soil (Groups 5-7, upper panel), or Channel Soil (Groups 8-10, lower panel), blood levels began to rise within 1-2 days, and tended to plateau by the middle of the study. A similar pattern was observed in animals exposed to lead acetate by intravenous injection (Group 11).

4.2 Dose-Response Patterns

Blood Lead

The measurement endpoint used to quantify the blood lead response was the area under the curve (AUC) for blood lead vs time. AUC was selected because it is the standard pharmacokinetic index of chemical uptake into the blood compartment, and is relatively insensitive to small variations in blood lead level by day. The AUC was calculated using the trapezoidal rule to estimate the AUC between each time point that a blood lead value was measured (days 0, 2, 4, 6, 8, 10, 12, 14, and 16 or 17), and summing the areas across time. In order to be consistent with and allow comparison to other studies in this project, the AUC was calculated only through day 15, because all subsequent studies involved exposure of animals on days 0-14 with sacrifice on day 15. The detailed data and calculations are presented in Appendix A, and the results are shown graphically in Figure 4-2. Each data point reflects the group mean exposure and group mean response, with the variability in dose and response shown by standard error bars. The figure also shows the best-fit equation through each data set.

As seen, the dose response pattern is non-linear for the soluble reference material (lead acetate, abbreviated "PbAc") and for each of the two test soils. Dose response curves for the Residential and Channel soils are similar to each other, and both are clearly lower than for lead acetate.

Tissue Lead

The dose-response data for lead levels in bone, liver and kidney (measured at sacrifice on day 15) are detailed in Appendix A. In order to be consistent with and allow comparison to other studies that were part of this project (in which exposure occurred on days 0-14 with sacrifice on day 15), the tissue results (liver, kidney and bone) for each animal were adjusted by multiplying by a factor of 15/16 (even-numbered groups) or 15/17 (odd-numbered groups). The results are shown graphically in Figures 4-3 through 4-5, respectively.

As seen, all of these dose response curves for tissues are fit by linear equations. As above, the responses of the two test soils tend to be generally similar to each other, and the responses for each of the three tissues (liver, bone and kidney) are lower than for lead acetate.

Measured Data Points Avg BC Residential ▲ Avg BC Channel FIGURE 4-2 BLOOD LEAD DOSE-RESPONSE, GROUP MEANS ± SEM FOR 8 Avg PbAc ♦ Avg IV 8 Best Fit Eqn for Residential y=11.8+121.5*(1-exp(-0.0027X)) 8 **BINGHAM CREEK SITE SOILS** y=11.8+121.5*(1-exp(-0.0024X)) Lead Dose (ug Pb/kg-d) Best Fit Eqn for Channel **BLOOD AUC** y=11.8+121.5*(1-exp(-0.0083X)) Best Fit Eqn for PbAc 8 8 8 ≥ 150 125 8 75 33 Blood Lead AUC (ug/dL-days)

8 Measured Data Points Avg BC Residential ▲ Avg BC Channel 8 Avg PbAc FIGURE 4-3 BONE LEAD DOSE-RESPONSE, GROUP MEANS ± SEM FOR ♦ Avg IV 8 Best Fit Eqn for Residential y=0.812+0.019X Best Fit Eqn for Channel y=0.812+0.021X 8 **BINGHAM CREEK SITE SOILS** Lead Dose (ug/kg-d) 200 BONE 8 Best Fit Eqn for PbAc y=0.812+0.087X 200 ≥ 8 22 \$ ဓ 8 5 Bone Lead (ug/g ash wt.)

FIGURE 4-4 LIVER LEAD DOSE-RESPONSE, GROUP MEANS <u>+</u> SEM FOR BINGHAM CREEK SITE SOILS

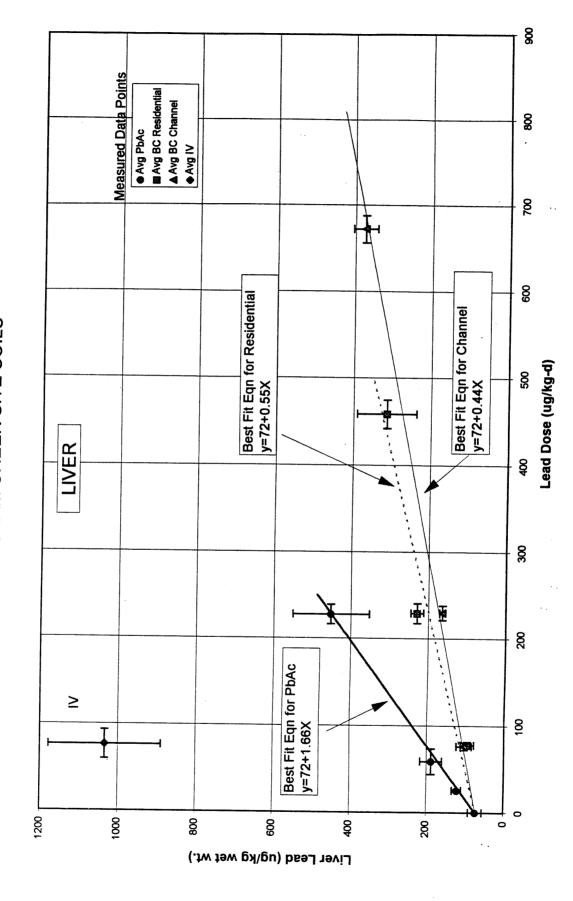
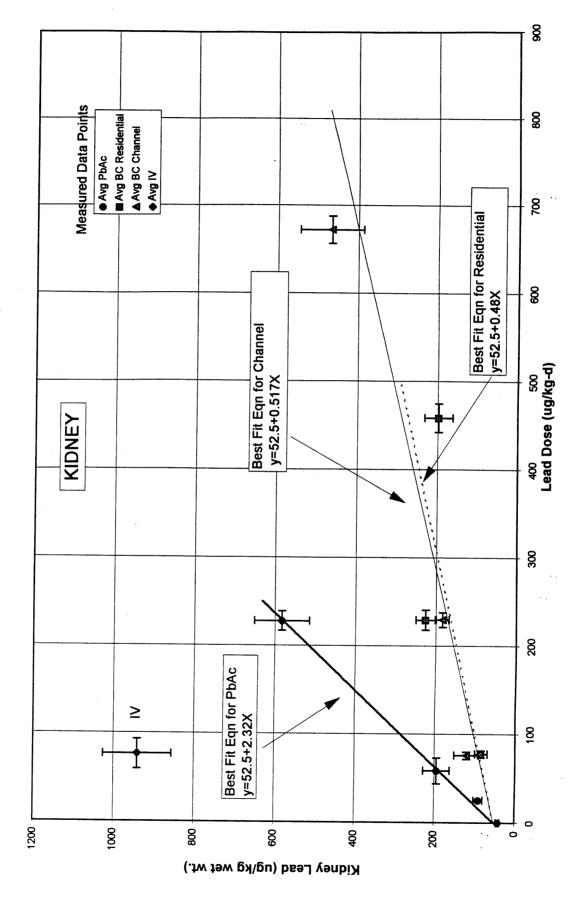


FIGURE 4-5 KIDNEY LEAD DOSE-RESPONSE, GROUP MEANS <u>+</u> SEM FOR BINGHAM CREEK SITE SOILS



4.3 Calculated RBA Values

Relative bioavailability values were calculated for each test material for each measurement endpoint (blood, bone, liver, kidney) using the method described in Section 3.0. The results are shown below:

Measurement Endpoint	Test Material		
_	Residential Soil	Channel Soil	
Blood Lead AUC	0.325	0.289	
Liver Lead	0.333	0.265	
Kidney Lead	0.208	0.223	
Bone Lead	0.213	0.265	

Recommended RBA Values

As shown above, for each test material, there are four independent estimates of RBA (based on blood, liver, kidney, and bone), and the values do not precisely agree in all cases. In general, we recommend greatest emphasis be placed on the RBA estimates derived from the blood lead data. There are several reasons for this recommendation, including the following:

- Blood lead calculations are based on multiple measurements over time, and so are statistically more robust than the single measurements available for tissue concentrations. Further, blood is a homogeneous medium, and is easier to sample than complex tissues such as liver, kidney and bone. Consequently, the AUC endpoint is less susceptible to random measurement errors, and RBA values calculated from AUC data are less uncertain.
- 2. Blood is the central compartment and one of the first compartments to be affected by absorbed lead. In contrast, uptake of lead into peripheral compartments (liver, kidney, bone) depend on transfer from blood to the tissue, and may be subject to a variety of toxicokinetic factors that could make bioavailability determinations more complicated.
- The dose-response curve for blood lead is non-linear, similar to the non-linear dose-response curve observed in children (e.g., see Sherlock and Quinn 1986). Thus, the response of this endpoint is known to behave similarly in swine as in children, and it is not known if the same is true for the tissue endpoints.
- 4. Blood lead is the classical measurement endpoint for evaluating exposure and health effects in humans, and the health effects of lead are believed to be proportional to blood lead levels.

However, data from the tissue endpoints (liver, kidney, bone) also provide valuable information. We consider the <u>plausible range</u> to extend from the RBA based on blood AUC to the mean of the other three tissues (liver, kidney, bone). The <u>preferred range</u> is the interval from the RBA based on blood to the mean of the blood RBA and the tissue mean RBA. Our <u>suggested point estimate</u> is the mid-point of the preferred range. These values are presented below:

Relative Bioavailability of Lead	Test Material	
	Residential Soil	Channel Soil
Plausible Range	0.251 - 0.325	0.251 - 0.289
Preferred Range	0.288 - 0.325	0.270 - 0.289
Suggested Point Estimate	0.307	0.280

4.4 Estimated Absolute Bioavailability in Children

These RBA estimates may be used to help assess lead risk at this site by refining the estimate of absolute bioavailability (ABA) of lead in soil, as follows:

$$ABA_{soil} = ABA_{soluble} \cdot RBA_{soil}$$

Available data indicate that fully soluble forms of lead are about 50% absorbed by a child (USEPA 1991, 1994). Thus, the estimated absolute bioavailability of lead in site soils are calculated as follows:

Based on the RBA values shown above, the estimated absolute bioavailabilities in children are as follows:

Absolute Bioavailability	Test Material	
of Lead	Residential Soil	Channel Soil
Plausible Range	13% - 16%	13% - 14%
Preferred Range	14% - 16%	13% - 14%
Suggested Point Estimate	15%	14%

Because the ABA estimates for the two soils are nearly identical, a value of 15% is recommended for the point estimate for average ABA in Bingham Creek area soils.

4.5 Uncertainty

These absolute bioavailability estimates are appropriate for use in EPA's IEUBK model for this site, although it is clear that there is both variability and uncertainty associated with these estimates. This variability and uncertainty arises from several sources. First, differences in physiological and pharmacokinetic parameters between individual animals leads to variability in response even when exposure is the same. Because of this inter-animal variability in the responses of different animals to lead exposure, there is mathematical uncertainty in the best fit doseresponse curves for both lead acetate and test material. This in turn leads to uncertainty in the calculated values of RBA, because these are derived from the two best-fit equations. Second. there is uncertainty in how to weight the RBA values based on the different endpoints, and how to select a point estimate for RBA that is applicable to typical site-specific exposure levels. Third, there is uncertainty in the extrapolation of measured RBA values in swine to young children. Even though the immature swine is believed to be a useful and meaningful animal model for gastrointestinal absorption in children, it is possible that differences in stomach pH, stomach emptying time, and other physiological parameters may exist and that RBA values in swine may not be precisely equal to values in children. Finally, studies in humans reveal that lead absorption is not constant even within an individual, but varies as a function of many factors (mineral intake, health status, etc.). One factor that may be of special importance is time after the last meal, with the presence of food tending to reduce lead absorption. The values of RBA measured in this study are intended to estimate the maximum uptake that occurs when lead is ingested in the absence of food. Thus, these values may be somewhat conservative for children who ingest lead along with food. The magnitude of this bias is not known, although preliminary studies in swine suggest the factor may be relatively minor.

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APPENDIX A

DETAILED DATA SUMMARY

1.0 OVERVIEW

Performance of this study involved collection and reduction of a large number of data items. All of these data items and all of the data reduction steps are contained in a Microsoft Excel spreadsheet named "BINGHAM.XLS" that is available upon request from the administrative record. This file is intended to allow detailed review and evaluation by outside parties of all aspects of the study.

The following sections of this Appendix present printouts of selected tables and graphs from the XLS file. These tables and graphs provide a more detailed documentation of the individual animal data and the data reduction steps performed in this study than was presented in the main text. Any additional details of interest to a reader can be found in the XLS spreadsheet.

2.0 RAW DATA AND DATA REDUCTION STEPS

2.1 Body Weights and Dose Calculations

Animals were weighed on day -1 (one day before exposure) and every three days thereafter during the course of the study. Doses of lead for the three days following each weighing were based on the group mean body weight, adjusted by addition of 1 kg to account for the expected weight gain over the interval. After completion of the experiment, body weights were estimated by interpolation for those days when measurements were not collected, and the actual administered doses (ug Pb/kg) were calculated for each day and then averaged across all days. If an animal missed a dose or was given an incorrect dose, the calculation of average dose corrected for these factors. If an animal missed a dose on more than 5 occasions (out of a total of 32), that animal was excluded from data analysis.

These data and data reduction steps are shown in Tables A-1 and A-2. Doses which required adjustment are shown by a heavy black box outlining the value in Table A-1. As seen, one dose adjustment was required (animal 257 on day 9) and one animal (animal number 248) was excluded because of multiple missed doses.

2.2 Blood Lead vs Time

Blood lead values were measured in each animal on days -4, 0, 2, 4, 6, 8, 10, 12, 14, and 16 (even-numbered groups) or 17 (odd-numbered groups). The raw laboratory data, including both the original analyses and the reanalyzed samples from days -2, 0, 12 and 14 (reported as ug/L of diluted blood) are shown in Table A-3. These data were adjusted as follows: a) non-detects were evaluated by assuming a value equal to one-half the quantitation limit, and b) the concentrations in diluted blood were converted to units of ug/dL in whole blood by dividing by a factor of 1 dL of blood per L of diluted sample. The results are shown in the right-hand column of Table A-3.

Table A-3A presents the calculation of blood lead values on days 12, 14, 16 and 17 using the rolling average method, as described in the text (see Section 4.1). Figures A-1 to A-3 plot the final results for individual animals organized by group and by day. Figure A-4 plots the mean for each dosing group by day.

After adjustment as above, values that were more than a factor of 1.5 above or below the group mean for any given day were "flagged" by computer as potential outliers. These values are shown in Table A-4 by cells that are shaded gray. Each data point identified in this way was reviewed and professional judgment was used to decide if the value should be retained or excluded. In order to avoid inappropriate biases, blood lead outlier designations were restricted to values that were clearly aberrant from a time-course and/or dose-response perspective. In this study, two of the flagged values were excluded, as shown in Table A-4 and discussed in Table A-5.

2.3 Blood Lead AUC

The area under the blood lead vs time curve for each animal was calculated by finding the area under the curve for each time step using the trapezoidal rule:

$$AUC(d_i \text{ to } d_j) = 0.5*(r_i+r_j)*(d_j-d_i)$$

where:

```
d = day number

r = response (blood lead value) on day i (r<sub>i</sub>) or day j (r<sub>i</sub>)
```

The areas were then summed for each of the time intervals to yield the final AUC for each animal. In order to be consistent with other studies in this project, the AUC was calculated only up to day 15. These calculations are shown in Table A-6. If a blood lead value was missing (either because of problems with sample preparation, or because the measured value was excluded as an outlier), the blood lead value for that day was estimated by linear interpolation.

2.4 Liver, Kidney and Bone Lead Data

At sacrifice (day 16 or 17), samples of liver, kidney and bone (femur) were removed and analyzed for lead. The raw data (expressed as ug Pb/L of prepared sample) are summarized in Table A-7. These data were adjusted as follows: a) non-detects were evaluated by assuming a value equal to one-half the quantitation limit, and b) the concentrations in prepared sample were converted to units of concentration in the original biological sample by dividing by the following factors:

Liver:

0.1 kg wet weight/L prepared sample

Kidney:

0.1 kg wet weight/L prepared sample

Bone:

2 gm ashed weight/L prepared sample

In order to be consistent with other studies in this project, all tissue results were adjusted to correspond to a 15-day exposure. Thus, the values for all animals in even-numbered groups were multiplied by a factor of 15/16, and the data for all animals in odd-numbered groups were

multiplied by a factor of 15/17. The resulting values are shown in the right-hand column of Table A-7.

3.0 CURVE FITTING

Basic Equations

A commercial curve-fitting program (Table Curve-2DTM Version 2.0 for Windows, available from Jandel Scientific) was used to derive best fit equations for each of the individual dose-response data sets derived above. A least squares regression method was used for both linear and non-linear equations. As discussed in the text, three different user-defined equations were fit to each data set:

<u>Linear (LIN):</u> Response = a + b·Dose

Exponential (EXP): Response = $a + c \cdot (1-exp(-d \cdot Dose))$

<u>Combination (LIN+EXP):</u> Response = $a + b \cdot Dose + c \cdot (1-exp(-d \cdot Dose))$

Constraints

In the process of finding the best-fits of these equations to the data, the values of the parameters (a, b, c, and d) were constrained as follows:

- Parameter "a" (the intercept, equal to the baseline or control value of the measurement endpoint) was constrained to be non-negative and was forced in all cases to be the same for the reference material (lead acetate) and the test materials. This is because, by definition, all dose-response curves for groups of animals exposed to different materials must arise from the same value at zero dose. In addition, for blood lead data, "a" was constrained to be equal to the mean of the control group ± 20% (typically 7.5 ± 1.5 AUC units).
- Parameter "b" (the slope of the linear dose-response line) was constrained to nonnegative values, since all of the measurement endpoints evaluated are observed to increase, not decrease, as a function of lead exposure.
- Parameter "c" (the plateau value of the exponential curve) was constrained to be non-negative, and was forced to be the same for the reference material (lead acetate) and the test material. This is because: 1) it is expected on theoretical grounds that the plateau (saturation level) should be the same regardless of the source of lead, and 2) curve-fitting of individual curves tended to yield values of "c" that were close to each other and were not statistically different.
- Parameter "d" (which determines where the "bend" in the exponential equation occurs) was constrained to be greater than 0.0045 for the lead acetate blood lead

(AUC) dose-response curve. This constraint was judged to be necessary because the weight of evidence from all studies clearly showed the lead acetate blood lead dose response curve was non-linear and was best fit by an exponential equation, but in some studies there were only two low doses of lead acetate used to define the dose-response curve, and this narrow range data set could sometimes be fit nearly as well by a linear as an exponential curve. The choice of the constraint on "d" was selected to be slightly lower than the observed best-fit value of "d" (0.006) when data from all lead acetate AUC dose-response curves from all of the different studies in this program were used. This approach may tend to underestimate relative bioavailability slightly in some studies (especially at low dose), but use of the information gained from all studies is judged to be more robust than basing fits solely on the data from one study.

In general, one of these models (the linear, the exponential, or the combination) usually yielded a fit (as judged by the value of the adjusted correlation coefficient R² and by visual inspection of the fit of the line through the measured data points) that was clearly superior to the others. If two or more models fit the data approximately equally well, then the simplest model (that with the fewest parameters) was selected.

Outlier Identification

During the dose-response curve fitting process, all data were carefully reviewed to identify any anomalous values. Typically, the process used to identify outliers was as follows:

- Step 1 Any data points judged to be outliers based on information derived from analysis of data across multiple studies (as opposed to conclusions drawn from within the study) were excluded.
- Step 2 The remaining raw data points were fit to the equation judged to be the most likely to be the best fit (linear, exponential, or mixed). Table Curve 2-D was then used to plot the 95% prediction limits around the best fit line. All data points that fell outside the 95% prediction limits were considered to be outliers and were excluded.
- Step 3 After excluding these points (if any), a new best-fit was obtained. In some cases, data points originally inside the 95% prediction limits were now outside the limits. However, further iterative cycles of data point exclusion were not performed, and the fit was considered final.

It should be noted that professional judgment can be imposed during any stage of the above outlier identification process.

Curve Fit Results

Table A-8 lists the data used to fit these curves, indicating which endpoints were excluded as outliers and why. Table A-9 shows the type of equation selected to fit each data set, and the best

fit parameters. The resulting best-fit equations for the data sets are shown in Figures A-5 to A-16. Values excluded as outliers are represented in the figures by the symbol "+".

4.0 RESULTS -- CALCULATED RBA VALUES

The value of RBA for a test substance was calculated for a series of doses using the following procedure:

- 1. For each dose, calculate the expected response to test material, using the best fit equation through the dose-response data for that material.
- 2. For each expected response to test material, calculate the dose of lead acetate that is expected to yield an equivalent response. This is done by "inverting" the dose-response curve for lead acetate, solving for the dose that corresponds to a specified response.
- Calculate RBA at that dose as the ratio of the dose of lead acetate to the dose of test material. For the situation where both curves are linear, the value of RBA is the ratio of the slopes (the "b" parameters). In the case where both curves are exponential and where both curves have the same values for parameters "a" and "c", the value of RBA is equal to the ratio of the "d" parameters.

The results are summarized in Table A-10.

5.0 QUALITY ASSURANCE DATA

A number of steps were taken throughout this study and the other studies in this project to ensure the quality of the results, including 5% duplicates, 5% standards, a program of interlaboratory comparison. These steps are detailed below.

Duplicates

Duplicate samples were prepared and analyzed for about 5% of all samples generated during the study. Table A-11 lists the first and second values for blood, liver, kidney, and bone. The results are shown in Figure 3-1 in the main text.

Standards

The Centers for Disease Control and Prevention (CDCP) provides a variety of blood lead "check samples" for use in quality assurance programs for blood lead studies. Each time a group of blood samples was prepared and sent to the laboratory for analysis, several CDCP check samples of different concentrations were included. Table A-12 lists the concentrations reported by the laboratory compared to the nominal concentrations indicated by CDCP for the samples submitted during this study, and the results are plotted in Figure 3-2 in the main text.

Interlaboratory Comparison

An interlaboratory comparison of blood lead analytical results was performed by sending a set of 15 randomly selected whole blood samples from this study to CDCP for independent analysis. The data are presented in Table A-13, and the results are plotted in Figure 3-3 in the main text.

TABLE A-1 BODY WEIGHTS AND ADMINISTERED DOSES, BY DAY
Body weights were measured on dept -1, 2, 5, 8, 11, 14. Weights for other days astomated, based on lever interpolation between measured values.

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Shaded boxes show days in which administered dozes were ingested late
Animal removed from study
Animal removed from study
Days which required adjustment due to deviations in dozing (a. Missed dozes)
Day 9
Pig 257 - lost one-half of one doughtait out of four doughtaits. Doze adjusted to 87.5%.

TABLE A-2
Body Weight Adjusted Doses
(Dose for Day/BW for Day)

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Avg	ı		1				- 1					1				- 1					T				· I · · ·		• • • • •						····I				~~	•••••			-		>>>>	108.8	000000		***
Day 14	ľ	0 0	2 8	220	26.7	25.5	220	63.7	6.6	6		734.2	240.7	197.1	195.3	225.0	9 6	2 6	86.4	67.1	220.6	252.1	2230	210.3	440.4	414.8	423.7	453.1	493.0	82	62.6	70.7	99.6	2 2	214.7	218.4	6640	9.799	639.7	593.1	9 9	20.00		100.6	88	98.9	91.6
Day 13	,	-	2 8	22.6	27.6	797	22.7	62.6	- 5	8		239.3	247.4	202.6	202.0	232.1	5	3 2	87.2	69.5	225.1	259.6	232.8	215.1	458.4	433.9	437.9	473.2	22.5	87.6	65.2	13.4	2.5	209.8	221.0	224.1	686.4	691.6	658.0	618.1	974.4	26.7		104.4	400.8	101.4	2
Day 12	,	- c	22.0	26.3	28.5	27.3	23.5	20 6	5. 5 5. 5			247.9	254.5	208.4	209.1	239.8	9.5	69	88.1	72.1	229.8	267.6	243.5	220.2	478.0	454.9	453.1	495.1	75.6	91.7	68.0	76.3	377.6	215.9	227.7	230.1	710.3	717.3	677.5	645.3	145.0	9		108.5	103.4	104.0	7.96
Day 11	6		22.0	24.7	56.9	25.8	22.2	0 6	9.0		1 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5	233.7	238.1	194.9	197.0	225.3	4.2	65.4	79.8	67.1	212.0	249.5	230	203.8	460.3	440.7	432.8	478.6	716	88	. 65.3	72.9	261.1	203.6	215.1	276.5	675.8	684.1	641.1	619.8	407.5	940		102.6	963	96.9	90.3
Day 10	c	0	22.7	25.6	28.0	26.4	777	5 5			11111111111111111111111111111111111111	244.3	245.3	200.1	203.7	232.2	5 5	1 89	83.1	669	221.4	257.7	105.1	211.2	477.6	447.0	442.5	495.0	740	91.0	67.4	74.5	263.8	212.9	223.0	245.1	702.6	707.0	662.5	642.3 632.6	1120	97.3		106.3	99.2	100.9	92.9
Day 8	0	0	23.5	26.5	29.2	27.1	22.3	5 4	75.6		79.0	255.9	253.0	205.6	211.0	239.6	5 5	71.0	86.8	73.0	231.6	997	200.4	219.2	496.1	453.6	452.6	372.6	76.6	93.7	9.69	76.2	266.5	223.0	231.6	222.1	731.6	731.6	685.4	653.5	118.8	100.9		110.2	102.2	105.1	95.8
Day 8	c	0	21.9	24.7	27.4	52.0	F0 1	2 2	. 6		74.7	249.1	242.2	195.9	202.8	76.24	83.7	71.9	1.88	74.0	220.5	2007	187.1	206.8	468.0	417.3	420.0	300.0	71.8	87.4	65.2	502	244.8	213.0	219.0	208.7	9.069	685.9	642.5	611.6	116.3	97.0		106.2	7.78	101.7	91.6
, de	0	0	22.5	25.8	28.4	2 26.1	710	74.5	66.2		76.2	255.2	250.9	197.0	209.3	75.0	6.6	73.3	91.2	73.7	229.7	242.5	192.5	213.5	485.3	430.1	433.9	412.9	73.9	91.0	67.5	72.6	253.5	221.1	226.4	214.4	713.3	695.3	667.9	630.6	117.2	100.6		109.9	100.6	103.4	93.9
04 y a	0	0	23.2	27.0	29.5	27.0	74.9	77.7	683		7.77	261.6	260.3	198.2	216.2	75.5	86.1	7.4.7	94.6	73.3	239.6	25.0	198.2	220.5	504.0	443.7	448.8	427.3	76.0	94.8	5.5	4 7 6 5 6 5	262.8	229.8	234.4	220.5	737.4	705.0	695.3	650.8	118.1	104.4	90,,	113.9	103.7	105.1	4.96
Cay o	0	0	219	26.1	282	20.5	219	74.8	64.9		73.0	238.8	240.7	177.4	230.0	70.4	81.8	71.4	92.0	68.4	25.9.4	238.4	187.2	209.0	476.6	416.6	422.6	402.6	70.8	89.5	89.08	7.5	248.3	217.7	221.1	206.6	690.2	646.5	637.6	6.709	108.3	98.7	9 207	107.5	97.3	97.3	0.06
(1)	0	٥	22 7	26.7	28.9	22.5	74.2	77.0	67.4		76.4	248.4	248.4	1863	239.5	71.2	84.4	73.1	93.8	9 5	252.3	248 7	192.3	215.9	496.5	427.6	430.7	418.6	74.6	93.9	7.79	72.7	258.1	224.6	220.8	216.1	719.1	673.3	657.3	6229	108.0	102.0	444.7	/ 11.	100.4	6.66	93.2
í	0	0	23 5	27.3	67.	23.3	76.6	79.4	70.1		80.1	258.8	256.6	344.5	249.7	72.1	87.3	74.8	95.7	07/	275.7	260.0	197.7	223.2	518.1	439.2	439.2 536.8	436.0	78.9	98.7	69.7	74.1	268.7	232.0	227.0	226.4	750.4	702.6	678.3	645.0	107.7	105.5	116.2	7.01	103.8	102.8	Š
	0	0	22.5	25.8	- 97 26.1	22.2	75.5	78.2	9.69		80.3	248.1	243.8	305.2	239.7	69.2	85.5	72.5	92.4	248.0	263.6	249.5	186.3	211.7	513.0	6773	5324	430.8	78.1	97.2	7.76	902	266.4	228.1	222.4	226.1	732.7	6.00.0	654.4	621.2	92.6	97.1	107.7		95.6	94.0	١.
	0	0	23.1	2 62	27.62	22.8	76.4	80.5	71.7		81.7	254.7	254.0	200.	248.8	71.0	88.5	72.9	94.0	224.2	269.6	260.4	191.4	219.5	532.4	438.4	539.1	437.4	79.8	97.2	7.80	73.6	274.6	236.7	225.5	228.7	758.6	673.2	675.0	639.7	92.6	99.9	1111		101.9	96.6	od from stuc
	0	0	23.8	9 9	28.6	23.5	77.3	83.0	73.8		83.3	261.7	200.0	213.4	258.6	72.9	91.8	73.3	25.5	2303	275.8	272.2	196.8	227.8	353.Z	432.0	546 1	444.3	81.6	97.2	76.6	77.0	283.3	246.1	228.7	231.3	746.5	687.6	697.0	659.4	92.6	102.7	1147		109.0	m 0	Animal removed from study
	506	226	215	222	229	251	209	228	244	248	258	\$ 5	247	252	260	201	202	224	250	236	237	240	242	249	27.6	235	243	257	202	21/	253	254	203	225	232	250	502	213	218	255	8	214	231	239	241	256	An
	_	-	7 (۰ ۲	2 2	2	3	က	e0 -	en .	e .	• •	7 4	•	4	5	ıcı	en u	טי ט	9	9	9	9	9		- 1	. ~	7	€ 6	:o a	o e o	80	o	o	. 6	6	₽ \$	5 5	2	9	= :	= :	==	Ξ	= ;	= =	

TABLE A - 3 RAW AND ADJUSTED BLOOD LEAD DATA

PHASE II EXPERIMENT 2

pig numbe	r sample	group	material administered	docana	gualifier	reanqualifier	rennesult.			MATRIY	Adinated Maine founds 3 \$
206	8-902180	1	control	0	quanne	NAME OF TAXABLE PARTY.	reanresult	result	qay	MATRIX	Adjusted Value (ug/dL) *
226	8-902166	i	control	ŏ		<	1	5.7	-2	BLOOD	0.5
215	8-902209	2	PbAc			, <	1	5.1	-2	BLOOD	0.5
220		2		25		<	1	5.8	-2	BLOOD	0.5
222	8-902205		PbAc	25		<	1	6	-2	BLOOD	0.5
	8-902199	2	PbAc	25		<	1	4.9	-2	BLOOD	0.5
229	8-902201	2	PbAc	25		<	1	5.2	-2	BLOOD	0.5
251	8-902207	2	, PbAc	25		. <	1	5.9	-2	BLOOD	0.5
209	8-902173	3	PbAc	75		· <	. 1	5.3	-2	BLOOD	0.5
228	8-902153	3	PbAc	75		<	1 -	5.5	-2	BLOOD	0.5
244	8-902181	3	PbAc	75			1.1	5	-2	BLOOD	1.1
248	8-902162	3	PbAc	75		<	1	4.9	-2	BLOOD	0.5
258	8-902178	3	PbAc	75		<	1	5.9	-2	BLOOD	0.5
204	8-902192	4	PbAc	225		<	1	4.8	-2	BLOOD	0.5
216	8-902191	4	PbAc	225		<	i	5.3	-2	BLOOD	0.5
247	8-902188	4	PbAc	225		<	i	6.2	-2	BLOOD	0.5
252	8-902195	4	PbAc	225		<	i	5.3	-2	BLOOD	
260	8-902189	4	PbAc	225		<	i				0.5
201	8-902161	5	Residential	75				5.1	-2	BLOOD	0.5
207	8-902163	5	Residential	75 75		<	1	5.1	-2	BLOOD	0.5
221	8-902170	5				<	1	5.3	-2	BLOOD	0.5
238			Residential	75		<	1	5.8	-2	BLOOD	0.5
	8-902164	5	Residential	75		<	1	5.3	-2	Brood	0.5
259	8-902184	5	Residential	75		<	1	5.9	-2	BLOOD	0.5
236	8-902187	6	Residential	225			1.2	5.5	-2	BLOOD	1.2
237	8-902185	6	Residential	225		<	1	5.7	-2	BLOOD	0.5
240	8-902206	6	Residential	225		<	1	6.7	-2	BLOOD	0.5
242	8-902212	6	Residential	225		<	1	6	-2	BLOOD	0.5
249	8-902208	6	Residential	225		<	1	5.6	-2	BLOOD	0.5
224	8-902154	7	Residential	450		<	1	4.9	-2	BLOOD	0.5
234	8-902168	7	Residential	450		<	1	5.5	-2	BLOOD	0.5
235	8-902167	7	Residential	450		<	i	5.6	-2	BLOOD	
243	8-902158	7	Residential	450		<	i	5.5			0.5
257	8-902179	7	Residential	450		<	i		-2	BLOOD	0.5
202	8-902193	8	Channel	75				4.5	-2	BLOOD	0.5
217	8-902198	8	Channel			<	1	4.8	-2	BFOOD	0.5
219	8-902196	8		75		<	1	6.1	-2	BLOOD	0.5
			Channel	75			1 .	5	-2	BLOOD	1
253	8-902197	8	Channel	75		<	1	5	-2	BLOOD	0.5
254	8-902194	8	Channel	75			1	5.2	-2	BLOOD	1
203	8-902172	9	Channel	225		<	1	5.2	-2	BLOOD	0.5
225	8-902165	9	Channel	225		<	1	5.2	-2	BLOOD	0.5
227	8-902155	9	Channel	225		<	1	5.3	-2	BLOOD	0.5
232	8-902175	9	Channel	225		<	1	5.1	-2	BLOOD	0.5
250	8-902152	9	Channel	225		<	i	5.6	-2	BLOOD	0.5
205	8-902190	10	Channel	675		<	i	4.8	-2	BLOOD	
210	8-902210	10	Channel	675		<	i	5.4	-2 -2		0.5
213	8-902211	10	Channel	675		<u>`</u>	i	5. 4 5.7		BLOOD	0.5
218	8-902202	10	Channel	675		<	1		-2	BLOOD	0.5
255	8-902213	10	Channel	675			•	5.8	-2	BLOOD	0.5
208	8-902174	11	IV			<	1	5.8	-2	BLOOD	0.5
214	8-902156	11	iv	100		_		4.9	-2	BLOOD	4.9
230	8-902159	11		100		<	1	5.4	-2	BLOOD	0.5
231			IV D	100		<	1	5.2	-2	BLOOD	0.5
	8-902171	11	IV.	100		<	1	5.1	-2	BLOOD	0.5
239	8-902160	11	IV	100		<	1	5.6	-2	BLOOD	0.5
241	8-902151	11	IV	100		<	1	5.6	-2	BLOOD	0.5
246	8-902177	11	IV.	100			1.6	5.1	-2	BLOOD	1.6
256	8-902182	11	IV.	100		<	1	5	-2	BLOOD	0.5
206	8-902222	1	control	0		<	1	6.1	ō	BLOOD	0.5
226	8-902236	1	control	0		<	1	5.7	ō	BLOOD	0.5
215	8-902271	2	PbAc	25	<		1.2	1.3	ō	BLOOD	1.2
220	8-902252	2	PbAc	25	<	<	1	1.3	Ö	BLOOD	0.5
222	8-902270	2	PbAc	25		<	1	1.3	0		
229	8-902272	2	PbAc	25	<	-	1			BLOOD	0.5
251	8-902273	2	PbAc	25	•			1.3	0	BLOOD	1
209	8-902220	3	PbAc	75			1.3	1.7	0	BLOOD	1.3
228	8-902216	3	PbAc			<	1	5.7	0	BLOOD	0.5
244	8-902217	3	PbAc	75 75		<	1	5.9	0	BLOOD	0.5
248				75 75		<	1	5.7	0	BLOOD	0.5
	8-902237	3	PbAc	75		<	1	5.5	0	BLOOD	0.5
258	8-902246	3	PbAc	75		<	1	5.7	0	BLOOD	0.5
204	8-902259	4	PbAc	225	<	<	1	1.3	0	BLOOD	0.5
216	8-902260	4	PbAc	225	<	<	1	1.3	0	BLOOD	0.5
247	8-902276	4	PbAc	225	<	<	1	1.3	ō	BLOOD	0.5
252	8-902261	4	PbAc	225	<	<	1	1.3	ō	BLOOD	0.5
260	8-902257	4	PbAc	225	<	<	1	1.3	ō	BLOOD	0.5
201	8-902214	5	Residential	75		<	i	5.4	ŏ	BLOOD	
207	8-902240	5	Residential	75		<	i	5.7	0		0.5
221	8-902235	5	Residential	75		<	1	5.7 5.7	0	BLOOD	0.5
238	8-902239	5	Residential	75		<	1			BLOOD	0.5
259	8-902226	5	Residential	75 75		<		5.7	0	BLOOD	0.5
		-	(Condellual	75		`	1	5.4	0	Brood	0.5

pig number	sample	group	material administered	dosage	qualifier	reanqualifier	reanresult	result	day	MATRIX	Adjusted Value (ug/dL) *
236	8-902249	6	Residential	225	<	<		1.3	0	BLOOD	0.5
237	8-902256	6	Residential	225	<	<	1	1.3	ō	BLOOD	0.5
240	8-902275	6	Residential	225	• <	<	1	1.3	ŏ	BLOOD	0.5
242	8-902274	6	Residential	225	<	<	i	1.3	ŏ	BLOOD	0.5
249	8-902262	6	Residential	225	<		1.1	1.3	ŏ	BLOOD	1.1
224	8-902245	7	Residential	450		< .	1	5.8	ŏ	BLOOD	0.5
234	8-902229	7	Residential	450		<	i	5.5	ō	BLOOD	0.5
235	8-902224	7	Residential	450		<	1	5.4	ŏ	BLOOD	0.5
243	8-902231	7	Residential	450		<	1	6.4	ō	BLOOD	0.5
257	8-902221	7	Residential	450		<	i	5.3	ŏ	BLOOD	0.5
202	8-902254	8	Channel	75	<	<	i	1.3	ŏ	BLOOD	0.5
217	8-902248	8	Channel	75	<	<	i	1.3	ŏ	BLOOD	0.5
219	8-902265	8	Channel	75	<	. <	1	1.3	ŏ	BLOOD	0.5
253	8-902269	8	Channel	75	<	<	i	1.3	ŏ	BLOOD	0.5
254	8-902264	8	Channel	75	<	<	1	1.3	ŏ	BLOOD	0.5
203	8-902223	9	Channel	225		<	i	5.8	ŏ.	BLOOD	
225	8-902230	9	Channel	225		<	i	5.9	0		0.5
227	8-902242	9	Channel	225		ζ.	i	6.1	Ö	BLOOD	0.5
232	8-902219	9	Channel	225		<	i			BLOOD	0.5
250	8-902234	9	Channel	225	<	~	1	5.7	0	BLCCD	0.5
205	8-902266	10	Channel	675	2	<		1.3	0	BLOOD	0.5
210	8-902263	10	Channel	675	~	<		1.3	0	BLOOD	0.5
213	8-902255	10	Channel	675	` `		!	1.3	0	BLOOD	0.5
218	8-902253	10				<	1	1.3	0	BLOOD	0.5
255	8-902268	10	Channel Channel	675 675	<	<	. 1	1.3	0	BLOOD	0.5
208	8-902268 8-902241	11		675	<	_	1	1.3	0	BLOOD	1
208 214	8-902241 8-902238		IV N	100		<	1	2.4	0	BLCCC	0.5
214 230	8-902238 8-902225	11	IV N	100		<	1	1.3	0	BLOOD	0.5
230 231		11	IV N	100		<	1	1.3	0	BLOOD	0.5
	8-902247	11	IV N	100		<	1	1.9	0	BLOOD	0.5
239	8-902232	11	IV N	100		<	1	1.3	0	BLOOD	0.5
241	8-902227	11	IV.	100		<	1	1.3	0	BLOOD	0.5
246	8-902215	11	IV To	100		<	1	1.5	0	BLOOD	0.5
256	8-902244	11	N N	100		<	1	2.2	0	BLOOD	0.5
206	8-902309	1	control	0	<			1.3	2	BLOOD	0.65
226	8-902281	1	control	0	<			1.3	2	BLOOD	0.65
215	8-902323	2	PbAc	25				3.3	2	BLOOD	3.3
220	8-902328	2	PbAc	25	<			1.3	2	BLOOD	0.65
222	8-902330	2	PbAc	25				1.7	2	BLOOD	1.7
229	8-902326	2	PbAc	25				2.1	2	BLOOD	2.1
251	8-902325	2	PbAc	25				2	2	BLOOD	2
209	8-902302	3	PbAc	75				3.5	2	BLOOD	3.5
228	8-902291	3	PbAc	75				3.4	2	BLOOD	3.4
244	8-902282	3	PbAc	75				1.7	2	BLOOD	1.7
248	8-902305	3	PbAc	75				3.3	2	BLOOD	
258	8-902279	3	PbAc	75				3.6	2	BLOOD	3.3
204	8-902337	4	PbAc	225				6.3	2		3.6
216	8-902332	4	PbAc	225				8.6	2	BLOOD	6.3
247	8-902312	4	PbAc	225				7.2		BLOOD	8.6
252	8-902327	4	PbAc	225					2	BLOOD	7.2
260	8-902320	4	PbAc	225				7.8	2	BLOOD	7.8
201	8-902290	5	Residential	75	<			6.3	2	BLOOD	6.3
207	8-902283	5	Residential	75 75	•			1.3	2	BLOOD	0.65
221	8-902292	5	Residential	75 75				3	2	BLOOD	3
238	8-902284	5	Residential	75 75				1.6	2	Brood	1.6
259	8-902298	5	Residential					2.2	2	BLOOD	2.2
236	8-902329	6	Residential	75 225				2.2	2	BLOOD	2.2
237	8-902329	6	Residential	225 225				3.1	2	BLOOD	3.1
240								3.6	2	BLOOD	3.6
242	8-902313 8-902336	6 6	Residential Posidential	225				3.7	2	BLOOD	3.7
249	8-902335	6	Residential	225				3.1	2	BLOOD	3.1
224	8-902301	7	Residential	225				3.5	2	BLOOD	3.5
234	8-902300	7	Residential	450 450				5.8	2	BLOOD	5.8
235			Residential	450				5	2	BLOOD	5
	8-902308	7	Residential	450				8.5	2	BLOOD	8.5
243	8-902289	7	Residential	450				5.6	2	BLOOD	5.6
257	8-902297	7	Residential	450				5.3	2	BLOOD	5.3
202	8-902315	8	Channel	75				2.2	2	BLOOD	2.2
217	8-902331	8	Channel	75				1.4	2	BLOOD	1.4
219	8-902333	8	Channel	75				2.3	2	BLOOD	2.3
253	8-902338	8	Channel	75				1.4	2	BLOOD	1.4
254	8-902314	8	Channel	75				2.7	2	BLOOD	2.7
203	8-902295	9	Channel	225				2.5	2	BLOOD	2.5
225	8-902278	9	Channel	225				2.5	2	BLOOD	2.5
227	8-902310	9	Channel	225				2.1	2	BLOOD	2.1
232	8-902288	9	Channel	225				3.7	2	BLOOD	3.7
250	8-902285	9	Channel	225				2.5	2	BLOOD	3.7 . 2.5
205	8-902339	10	Channel	675					2	BLOOD	2.0
210	8-902324	10	Channel	675				9.3	2	BLOOD	0.3
213	8-902311	10	Channel	675				5.8	2		9.3
218	8-902318	10	Channel	675				5.6 7.7	2	BLOOD	5.8
255	8-902316	10	Channel	675						BLOOD	7.7
208	8-902304	11	IV	100				6.7	2	BLOOD	6.7
214	8-902286	11	IV	100				13.3	2	BLOOD	13.3
230	8-902294	11	IV	100				9.8	2	BLOOD	9.8
			• •	. 55					2	BLOOD	

pig number	sample	group	material administered	dosage	gualifier	reanqualifier	reanresult	result	day	MATRIX	Adjusted Value (ug/dL) *
231	8-902280	11	N	100				8.7	2	BLOOD	8.7
239	8-902296	11	IV	100				9.8	2	BLOOD	9.8
241	8-902287	11	IV.	100				4	2	BLOOD	4
246	8-902299	11	IV.	100				8.3	2	BLOOD	8.3
256 206	8-902277 8-902693	<u>11</u> 1	N earted	100				6	2	BLOOD	6
226	8-902471	i	control control	0	< <			1.3 1.3	4	BLOOD	0.65 0.65
215	8-902567	2	PbAc	25	•			3.1	4	BLOOD	3.1
220	8-902615	2	PbAc	25	<			1.3	4	BLOOD	0.65
222	8-902438	2	PbAc	25		•.		2.8	4	BLOOD	2.8
229	8-902402	2	PbAc	25				2.5	4	BLOOD	2.5
251	8-902469	2	PbAc	25				1.8	4	BLOOD	1.8
209	8-902412	3	PbAc	75				4.7	4	BLOOD	4.7
228 244	8-902450	3	PbAc	75				3.1	4	BLOOD	3.1
248	8-902405 8-902358	3 3	PbAc PbAc	75 75		и,		1.5	4	BLOOD	1.5
258	8-902707	3	PbAc	75 75				1.8	4	BLOOD	1.8
204	8-902516	4	PbAc	225				4.9 7.9	4	BLOOD	4.9
216	8-902419	4	PbAc	225				8.3	4	BLOOD	7.9
247	8-902386	4	PbAc	225				7.1	4	BLOOD	8.3 7.1
252	8-902354	4	PbAc	225		•		5.9	4	BLOOD	5.9
260	8-902631	4	PbAc	225				8.1	À	BLOOD	8.1
201	8-902433	5	Residential	75	<			1.3	4	BLOOD	0.65
207	8-902417	5	Residential	75				2.7	4	BLOOD	2.7
221	8-902635	5	Residential	75				2	4	BLOOD	2
238	8-902539	5	Residential	75				2	4	BLOOD	2
259 236	8-902628	5	Residential	75				2.2	4	BLOOD	2.2
237 .	8-902772 8-902557	6 6	Residential Residential	225 225				3.5	4	BLOOD	3.5
240	8-902587	6	Residential	225				3.6 5.4	4	BLOOD	3.6
242	8-902487	6	Residential	225				4.2	4	BLOOD	5.4 4.2
249	8-902652	6	Residential	225				3.2	4	BLOOD	4.2 3.2
224	8-902571	7	Residential	450				6.1	4	BLOOD	6.1
234	8-902732	7	Residential	450				6.1	4	BLOOD	6.1
235	8-902424	7	Residential	450				7.9	4	BLOOD	7.9
243	8-902467	7	Residential	450				6.4	4	BLOOD	6.4
257	8-902584	7	Residential	450				5.1	4	BLOOD	5.1
202	8-902411	8	Channel	75				2.8	4	BLOOD	2.8
217	8-902421	8	Channel	75				2.3	4	BLOOD	2.3
219 253	8-902529 8-902480	8 8	Channel Channel	75 75				4.5	4	BLOOD	4.5
254	8-902663	8	Channel	75 75				2.4	4	BLOOD	2.4
203	8-902598	9	Channel	225				2.3	4	BLOOD	2.3
225	8-902512	9	Channel	225				4 3.1	4	BLOOD	4
227	8-902518	9	Channel	225				2.2	4	BLOOD	3.1 2.2
232	8-902637	9	Channel	225				4.3	4	BLOOD	4.3
250	8-902367	9	Channel	225				4.7	4	BLOOD	4.7
205	8-902501	10	Channel	675				3.9	4	BLOOD	3.9
210	8-902425	10	Channel	675				8.4	4	BLOOD	8.4
213	8-902749	10	Channel	675				6.5	4	BLOOD	6.5
218	8-902673	10	Channel	675				8	4	BLOOD	8
255 208	8-902762	10	Channel	675				8.7	4	BLOOD	8.7
214	8-902650 8-902452	11 11	IV IV	100 100				16.3	4	BLCOD	16.3
230	8-902656	11	IV IV	100				11.1	4	BLOOD	11.1
231	8-902605	11	IV :	100				10.3	4	BLOOD	
239	8-902380	11	iv	100				10.5	4	BLOOD	10.3
241	8-902513	11	IV.	100					4	BLOOD	
246	8-902537	11	IV	100				22.4	4	BLOOD	22.4
256	8-902472	11	IV .	100				8.2	4	BLOOD	8.2
206	8-902434	1	control	0	<	-		1.3	6	BLOOD	0.65
226	8-902629	1	control	0	<			1.3	6	BLOOD	0.65
215	8-902432	2	PbAc	25		•		3.8	6	BLOOD	3.8
220	8-902445	2	PbAc	25 25	<			1.3	6	BLOOD	0.65
222 229	8-902397 8-902523	2 2	PbAc PbAc	25				3.4	6	BLOOD	3.4
251	8-902323	2	PbAc PbAc	25 25				3.1	6	BLOOD	3.1
209	8-902646	3	PbAc	25 75				1.9	6	BLOOD	1.9
228	8-902396	3	PbAc	75 75				4.7 5.3	6	BLOOD	4.7
244	8-902551	3	PbAc	75 75				2.7	6	BLOOD	5.3 2.7
248	8-902583	3	PbAc	75.				2.5	6	BLOOD	2.7 2.5
258	8-902670	3	PbAc	75				4	6	BLOOD	2.5 4
204	8-902591	4	PbAc	225				6	6	BLOOD	6
216	8-902406	4	PbAc	225				9.8	6	BLOOD	9.8
247	8-902647	4	PbAc	225				6.4	6	BLOOD	6.4
252 260	8-902527	4	PbAc	225				7.4	6	BLOOD	7.4
260 201	8-902672	4	PbAc	225				9.9	6	BLOOD	9.9
201 207	8-902676 8-902375	5 5	Residential	75 75				1.5	6	BLOOD	1.5
207	8-902375 8-902668	5 5	Residential	75 75				2.9	6	BLOOD	2.9
238	8-902538	5 5	Residential Residential	75 75				2.4	6	BLOOD	2.4
259	8-902477	5	Residential	75 75				4.4	6	BLOOD	4.4
236	8-902633	6	Residential	225				2.6 5.2	6	BLOOD	2.6
-		-						3.∠	6	BLOOD	5.2

pig number 237	sample 8-902560	group 6	material administered Residential	dosage 225	qualifier reanqualifier	reanresult	result 5.5	day	MATRIX	Adjusted Value (ug/dL) * 5.5
240	8-902550	6	Residential	225 225			5.5 5.1	6 6	BLOOD	5.5 5.1
242	8-902568	6	Residential	225 225					BLOOD	
249	8-902515	6	Residential	225			5.8 3.8	6 6	BLOOD	5. 8 3.8
224	8-902626	7	Residential	450			5.6 6.6	6	BLOOD	5.6 6.6
234	8-902470	7	Residential	450			6.4	6	BLOOD	6.4
235	8-902725	7	Residential	450			8.6	6	BLOOD	8.6
243	8-902418	7	Residential	450			7.4	6	BLOOD	7.4
257	8-902613	7	Residential	450			6.1	6	BLOOD	7. 4 6.1
202	8-902720	8	Channel	75	•,		3.1	6	BLOOD	3.1
217	8-902600	8	Channel	75			2.3	6	BLOOD	2.3
219	8-902573	8	Channel	75			5	6	BLOOD	5
253	8-902675	8	Channel	75			3.5	6	BLOOD	3.5
254	8-902620	8	Channel	75			1.5	6	BLOOD	1.5
203	8-902556	9	Channel	225	-		4.7	6	BLOOD	4.7
225	8-902504	9	Channel	225			4	6	BLOOD	4
227	8-902481	9	Channel	225			3.8	6	BLOOD	3.8
232	8-902642	9	Channel	225			4.9	6	BLOOD	4.9
250	8-902607	9	Channel	225			5.5	6	BLOOD	5.5
205	8-902495	10	Channel	675			3.6	6	BLOOD	3.6
210	8-902552	10	Channel	675			9.6	6	BLOOD	9.6
213	8-902589	10	Channel	675			7.1	6	BLOOD	7.1
218	8-902775	10	Channel	675			10.3	6	BLOOD	10.3
255	8-902488	10	Channel	675			7.6	6	BLOOD	10.3 7.6
208	8-902731	11	IV	100			11.5	6	BLOOD	
214	8-902574	11	Ň	100			9	6	BLOOD	11.5
230	8-902649	11	Ň	100			9	6	BLOOD	9
231	8-902621	11	ïV	100			8.6	6		0.6
239	8-902691	11	iv V	100			3.0	6	BLOOD	8.6
241	8-902590	11	IV	100			7.9	6	BLOOD	7.9
246	8-902374	11	 IV	100			8.7	6	BLOOD	7. 9 8.7
256	8-902708	11	IV	100			6.4	6	BLOOD	6.4
206	8-902698	1	control	0	<		1.3	8	BLOOD	0.65
226	8-902474	1	control	ŏ	•		1.6	8	BLOOD	1.6
215	8-902441	2	PbAc	25			4.2	8	BLOOD	
220	8-902753	2	PbAc	²⁵			3.1	8	BLOOD	4.2
222	8-902382	2	PbAc	25			3.8	8		3.1
229	8-902634	2	PbAc	25			3.8	8	BLOOD	3.8
251	8-902447	2	PbAc	25			2.6	8	BLOOD	3.8
209	8-902643	3	PbAc	75			5.4		BLOOD	2.6
228	8-902345	3	PbAc	75 75				8	BLOOD	5.4
244	8-902624	3	PbAc	75 75			5.6	8	BLOOD	5.6
248	8-902541	3	PbAc	75 75			3.8	8	BLOOD	3.8
258	8-902521	3	PbAc	75 75			3.2	8	BLOOD	3.2
204	8-902655	4	PbAc	225			5.1	8	BLOOD	5.1
216	8-902493	4	PbAc	225			6.3	8	BLOOD	6.3
247	8-902681	4	PbAc	225			9.7	8	BLOOD	9.7
252	8-902484	4	PbAc	225			6.5	8	BLOOD	6.5
260	8-902597	4	PbAc	225			7.4	8	BLOOD	7.4
201	8-902468	5	Residential	75			11.8	8	BLOOD	11.8
207	8-902391	5	Residential	75 75			2.1	8	BLOOD	2.1
221	8-902742	5	Residential	75			4.3	8	BLOOD	4.3
238	8-902746	5	Residential	75 75			2.3	8	BLOOD	2.3
259	8-902695	5	Residential	75 75			4.3	8	BLOOD	4.3
236	8-902506	6	Residential	75 225			2.8	8	BLOOD	2.8
237	8-902757	6	Residential	225 225			5.7	8	BLOOD	5.7
240	8-902483	6	Residential	225			6.4 5.3	8	BLOOD	6.4
242	8-902619	6	Residential	225				8	BLOOD	5.3
249	8-902728	6	Residential	225			6.3	8	BLOOD	6.3
224	8-902459	7	Residential	450			5.4	8	BLOOD	5.4
234	8-902564	7	Residential	450 450			7.4	8	BLOOD	7.4
235	8-902669	7	Residential	450 450			6.4	8	BLOOD	6.4
243	8-902416	7	Residential	450 450			6.8	8	BLOOD	6.8
257	8-902703	7	Residential	450 450			8.4	8	BLOOD	8.4
202	8-902659	8	Channel	75			6.2	8	BLOOD	6.2
217	8-902420	8	Channel	75 75			2.9	8	BLOOD	2.9
219	8-902415	8	Channel	75 75			2.5	8	BLOOD	2.5
253	8-902683	8	Channel	75 75			5.1	8	BLOOD	5.1
254	8-902463	8	Channel	75 75			3.3	8	BLOOD	3.3
203	8-902339	9	Channel	225			3.3	8	BLOOD	3.3
225	8-902778	9	Channel	225 225			2.2	8	BLOOD	
227	8-902492	9	Channel	225 225			3.3	8	BLOOD	3.3
232	8-902582	9	Channel	225			3.8	8	BLOOD	3.8
250	8-902530	9	Channel	225 225			7.1	8	BLOOD	7.1
205	8-902581	10	Channel	225 675			5.9	8	BLOOD	5.9
210	8-902430	10	Channel	675			6.7	8	BLOOD	6.7
213	8-902344	10	Channel				10.5	8	BLOOD	10.5
218	8-902531	10	Channel	675 675			8.3	8	BLOOD	8.3
255	8-902662	10	Channel	675 675			8.4	8	BLOOD	8.4
208	8-902609	11					7.8	8	BLOOD	7.8
214	8-902595	11	IV IV	100			9.4	8	BLOOD	9.4
230	8-902366	11		100			7.9	8	BLOOD	7.9
231	8-902428	11	IV IV	100				8	BLOOD	
		1.1	IV	100			7.4	8	BLOOD	7.4

pig number		group	material administered		qualifier reanqualifier	reanresult	result	day	MATRIX	Adjusted Value (ug/dL) *
239	8-902475	11	V	100				8	BLOOD	
241 246	8-902763 8-902586	11 11	IV N	100			6.5	8	BLOOD	6.5
256	8-902685	11	IV IV	100 100			7.8	8	BLOOD	7.8
206	8-902700	1	control	0	<		1.3	<u>8</u>	BLOOD	4.7 0.65
226	8-902745	i	control	ŏ	`		1.3	10	BLOOD	0.65
215	8-902617	2	PbAc	25			5.5	10	BLOOD	5.5
220	8-902407	2	PbAc	25			3.1	10	BLCCC	3.1
222	8-902502	2	PbAc	25			4	10	BLOOD	4
229	8-902739	2	PbAc	25	٠.		3.6	10	BLOOD	3.6
251 209	8-902448 8-902509	2	PbAc	25			2.6	10	BLOOD	2.6
209	8-902368	3 3	PbAc PbAc	75 75			4.1	10	BLOOD	4.1
244	8-902653	3	PbAc	75 75			5.7	10	BLOOD	5.7
248	8-902743	3	PbAc	75 75			2.9	10	BLOOD	2.9
258	8-902689	3	PbAc	75 75	*±		2.6	10	BLOOD	2.6
204	8-902765	4	PbAc	225			6.2 10.7	10 10	BLOOD	6.2
216	8-902694	4	PbAc	225			12.1	10	BLOOD	10.7 · · · · · · · · · · · · · · · · · · ·
247	8-902426	4	PbAc	225			8.1	10	BLOOD	8.1
252	8-902690	4	PbAc	225			8.7	10	BLOOD	8.7
260	8-902449	4	PbAc	225			12.8	10	BLOOD	12.8
201	8-902751	5	Residential	75			1.3	10	BLOOD	1.3
207	8-902413	5	Residential	75			3.3	10	BLOOD	3.3
221	8-902526	5	Residential	75			2.8	10	BLOOD	2.8
238	8-902464	5	Residential	75			3.9	10	BLOOD	3.9
259	8-902611	5	Residential	75			2.8	10	BLOOD	2.8
236 237	8-902616 8-902466	6 6	Residential Residential	225			6.7	10	BLOOD	6.7
240	8-902678	6	Residential	225			7.3	10	BLOOD	7.3
242	8-902764	6	Residential	225 225			6.8	10	BLCCC	6.8
249	8-902724	6	Residential	225			7	10	BLOOD	7
224	8-902593	7	Residential	450			5.5 7.5	10 10	BLOOD	5.5
234	8-902383	7	Residential	450			7.5 3.7	10	BLOOD	7.5 3.7
235	8-902606	7	Residential	450			8.8	10	BLOOD	3.7 8.8
243	8-902343	7	Residential	450			8.3	10	BLOOD	8.3
257	8-902555	7	Residential	450			4.6	10	BLOOD	4.6
202	8-902674	8	Channel	75			3.9	10	BLOOD	3.9
217	8-902510	8	Channel	75			2.6	10	BLOOD	2.6
219	8-902519	8	Channel	75			7.1	10	BLOOD	7.1
253 254	8-902686	8	Channel	75			3.2	10	BLOOD	3.2
254 203	8-902713 8-902436	8 9	Channel	75			3.6	10	BLOOD	3.6
203	8-902342	9	Channel	225			3.4	10	BLOOD	3.4
227	8-902548	9	Channel Channel	225 225			3.7	10	BLOOD	3.7
232	8-902351	9	Channel	225			3.7	10	BLOOD	3.7
250	8-902596	9	Channel	225			5 4.9	10	BLOOD	5
205	8-902755	10	Channel	675			4.9 5.9	10 10	BLOOD BLOOD	4.9
210	8-902547	10	Channel	675			13.7	10	BLOOD	5.9 13.7
213	8-902365	10	Channel	675			7.5	10	BLOOD	13.7 7.5
218	8-902360	10	Channel	675			8.3	10	BLOOD	8.3
255	8-902651	10	Channel	675			9	10	BLOOD	9
208	8-902580	11	IV.	100			10.9	10	BLOOD	10.9
214	8-902701	11	IV	100			8.1	10	BLOOD	8.1
230 231	8-902384 8-902544	11	. IV	100				10	BLOOD	
239	8-902608	11 11	IV N	100			10.5	10	BLOOD	10.5
241	8-902585	11	IV IV	100 100				10	BLOOD	
246	8-902431	11	IV	100			7.5	10	BLOOD	7.5
256	8-902741	11	N.	100			9.7 7.3	10 10	BLOOD BLOOD	9.7
206	8-902774	1	control	0	< ;	1	3	12	BLOOD	7.3 0.5
226	8-902679	1	contro!	ō	<	i	4.1	12	BLOOD	0.5
215	8-902453	2	PbAc	25		2.9	8.6	12	BLOOD	2.9
220	8-902490	2	PbAc	25		1	6.5	12	BLOOD	1
222	8-902756	2	PbAc	25		1.7	7.4	12	BLOOD	1.7
229	8-902377	2	PbAc	25		1.8	7.7	12	BLOOD	1.8
251 209	8-902388	2	PbAc	25		1.5	6.9	12	BLOOD	1.5
209	8-902748 8-902766	3 3	PbAc	75 75		3.1	7.5	12	BLOOD	3.1
244	8-902766 8-902361	3	PbAc PbAc	75 75		3.5	7.2	12	BLOOD	3.5
248	8-902442	3	PbAc	75 75		1.5	6.4	12	BLOOD	1.5
258	8-902636	3	PbAc	75 75		1.7 5.0	5.3	12	BLOOD	1.7
204	8-902601	4	PbAc	225		5.8 10.5	9.9 14.1	12	BLOOD	5.8
216	8-902704	4	PbAc	225		9	15.9	12 12	BLOOD	10.5
247	8-902577	4	PbAc	225		6.3	12.3	12	BLOOD	9
252	8-902553	4	PbAc	225		6.1	12.3	12	BLOOD	6.3 6.1
260	8-902524	4	PbAc	225		9	15.3	12	BLOOD	0.1 9
201	8-902508	5	Residential	75	<	1	3.4	12	BLOOD	0.5
207	8-902348	5	Residential	75		2.2	6.4	12	BLOOD	2.2
221	8-902723	5	Residential	75		1.7	5.5	12	BLOOD	1.7
238 259	8-902409 8-902389	5	Residential	75 75		2.7	7.8	12	BLOOD	2.7
239	8-902389 8-902761	5 6	Residential	75 225		1.2	6.3	12	BLOOD	· 1.2
237	8-902758	6	Residential Residential	225		2.3	8.6	12	BLOOD	2.3
		•	resideridal	225		6.5	13.2	12	BLOOD	6.5

pig number		group	material administered	dosage	qualifier	reanqualifier	reanresult	result	day	MATRIX	Adjusted Value (ug/dL) *
240	8-902576	6	Residential	225			5.3	10.9	12	BLOOD	5.3
242	8-902575	6	Residential	225			5.5	11.5	12	BLOOD	5.5
249 224	8-902491	6	Residential	225			2.4	8.8	12	BLOOD	2.4
234	8-902408 8-902440	7 7	Residential	450			5.6	10.9	12	BLOOD	5.6
235	8-902465	7	Residential	450			3.1	7.8	12	BLOOD	3.1
243	8-902534	7	Residential Residential	450 450			7.4	12.6	12	BLOOD	7.4
257	8-902726	7	Residential	450 450			7 4.1	10.9	12	BLOOD	7
202	8-902456	8	Channel	75			2.6	7.8 8	12 12	BLOOD	4.1
217	8-902729	8	Channel	75		< .	1	6.8	12	BLOOD	2.6
219	8-902349	8	Channel	75		•	4.5	10.4	12	BLOOD	0.5
253	8-902736	8	Channel	75			1.9	7.6	12	BLOOD	4.5 1.9
254	8-902712	8	Channel	75	-		1	7.2	12	BLOOD	1.5
203	8-902511	9	Channel	225			2.4	6.4	12	BLOOD	2.4
225	8-902499	9	Channel	225		4	2.5	6.3	12	BLOOD	2.5
227	8-902688	9	Channel	225			3.3	7.5	12	BLOOD	3.3
232	8-902353	9	Channel	225			2.7	8.8	12	BLOOD	2.7
250	8-902604	9	Channel	225			4.9	8.8	12	BLOOD	4.9
205	8-902422	10	Channel	675			2.7	9.5	12	BLOOD	2.7
210	8-902543	10	Channel	675			10.2	16.3	12	BLOOD	10.2
213	8-902641	10	Channel	675			5.4	11.7	12	BLOOD	5.4
218	8-902558	10	Channel	675			8.2	14.7	12	BLOOD	8.2
255	8-902373	10	Channel	675					12	BLOOD	0.2
208	8-902460	11	IV.	100			10.5	15.8	12	BLOOD	10.5
214	8-902528	11	N	100			10.3	15.1	12	BLOOD	10.3
230	8-902532	11	IV	100					12	BLOOD	10.0
231	8-902702	11	V	100			10.5	16	12	BLOOD	10.5
239	8-902362	11	· •	100			•		12	BLOOD	10.0
241	8-902622	11	N	100			6.8	10.9	12	BLCCD	6.8
246	8-902357	11	N	100			9	15.8	12	BLOOD	9
256	8-902716	11	V	100			7.4	11.7	12	BLOOD	7.4
206	8-902540	1	control	0			1.3	7.7	14	BLOOD	1.3
226	8-902545	1	control	0		<	1	6.3	14	BLOOD	0.5
215	8-902705	2	PbAc	25			2.5	8.8	14	BLOOD	2.5
220	8-902667	2	PbAc	25			1.1	7.9	14	BLOOD	1.1
222	8-902711	2	PbAc	25			1.9	8.1	14	BLOOD	1.9
229	8-902451	2	PbAc	25			2.4	8.6	14	BLOOD	2.4
251	8-902572	2	PbAc	25			1.2	7.2	14	BLOOD	1.2
209	8-902485	3	PbAc	75			4.3	10.8	14	BLOOD	4.3
228	8-902664	3	PbAc	75			2.9	10.2	14	BLOOD	2.9
244	8-902718	3	PbAc	75			2.9	8.6	14	BLOOD	2.9
248	8-902632	3	PbAc	75			1	8	14	BLOOD	1
258	8-902454	3	PbAc	75			4.9	11.5	14	BLOOD	4.9
204	8-902352	4	PbAc	225			6.8	14.5	14	BLOOD	6.8
216	8-902393	4	PbAc	225			8.5	16.4	14	BLOOD	8.5
247	8-902455	4	PbAc	225			7.1	14.6	14	BLOOD	7.1
252	8-902427	4	PbAc	225			5.9	12.6	14	BLOOD	5.9
260	8-902482	4	PbAc	225			11.2	17.7	14	BLOOD	11.2
201	8-902437	5	Residential	75		<	1	6.5	14	BLOOD	0.5
207	8-902733	5	Residential	75			2.8	9.1	14	BLOOD	2.8
221	8-902630	5	Residential	75		<	1	8.1	14	BLOOD	0.5
238	8-902489	5	Residential	75			3.9	10.5	14	BLOOD	3.9
259	8-902522	5	Residential	75			3.1	8.8	14	BLOOD	3.1
236	8-902446	6	Residential	225			3.7	9.5	14	BLOOD	3.7
237	8-902542	6	Residential	225			4.3	11.7	14	BLOOD	4.3
240	8-902371	6	Residential	225			4.6	11.8	14	BLOOD	4.6
242	8-902505	6	Residential	225			5.1	11.3	14	BLOOD	5.1
249	8-902738	6	Residential	225			4.6	10.5	14	BLOOD	4.6
224 234	8-902387	7	Residential	450			5.9	12.6	14	BLOOD	5.9
234 235	8-902381	7	Residential	450			3.9	10.5	14	BLOOD	3.9
235 243	8-902717	7	Residential	450			7.2	14.6	14	BLOOD	7.2
243 257	8-902535 8-902496	7	Residential	450			6.6	12.9	14	BLOOD	6.6
202	8-902666	7 g	Residential	450 75			3.8	10.3	14	BLOOD	3.8
202	8-902403	8 8	Channel	75 75			2.7	9.7	14	BLOOD	2.7
219	8-902610	8	Channel	75 75			1.3	7.9	14	BLOOD	1.3
253	8-902687	8	Channel	75 75			5.4	12.4	14	BLOOD	5.4
253 254	8-902696	8	Channel	75 75			1.6	7.8	14	BLOOD	1.6
203	8-902602	9	Channel	75 225			1.7	8.1	14	BLOOD	1.7
203	8-902400	9	Channel Channel	225			3.2	9.5	14	BLOOD	3.2
227	8-902400	9	Channel	225			4.2	10.6	14	BLOOD	4.2
232	8-902340	9	Channel	225			3.8	9.5	14	BLOOD	3.8
250	8-902473	9	Channel	225			3.7	10.7	14	BLOOD	3.7
205	8-902350	10		225			5.1	11.1	14	BLOOD	5.1
210	8-902648	10	Channel Channel	675 675			4.1	10.9	14	BLOOD	4.1
213	8-902759	10	Channel	675 675			9.4	17.2	14	BLOOD	9.4
218	8-902699	10	Channel				7.1	14.2	14	BLOOD	7.1
255	8-902363	10		675 675			8.5	16.2	14	BLOOD	8.5
208	8-902363 8-902677	11	Channel IV	675			9.3	15.7	14	BLOOD	9.3
214	8-902439	11	IV IV	100 100			12.5	21	14	BLOOD	12.5
230	8-902710	11	IV	100			11.2	18.3	14	BLOOD	11.2
231	8-902715	11	IV	100			40.4	40.0	14	BLOOD	
239	8-902536	11	IV				12.1	18.9	14	BLOOD	12.1
200	0 002000		IV	100					14	BLOOD	

pig number	sample	group	material administered		qualifier	reanqualifier	reanresult	result	day	MATRIX	Adjusted Value (ug/dL) *
241	8-902570	11	N N	100			6.7	12.5	14	BLOOD	6.7
246	8-902594	11	N	100			11.1	17	14	BLOOD	11.1
256	8-902770	11	IV.	100			6.7	14.4	14	BLOOD	6.7
206	8-902500	1	control	0		······		2.4	17	BLOOD	2.4
226	8-902390	1	control	O				1.9	17	BLOOD	1.9
215	8-902395	2	PbAc	25				3.5	16	BLOOD	3.5
220	8-902443	2	PbAc	25				2.5	16	BLOOD	2.5
222	8-902644	2	PbAc	25				3.4	16	BLOOD	3.4
229	8-902498	2	PbAc	25				4.1	16	BLOOD	4.1
251	8-902654	2	PbAc	25				2.8	16	BLOOD	2.8
209	8-902569	3	PbAc	75				6.1	17	BLOOD	6.1
228	8-902682	3	PbAc	75				5.9	17	BLOOD	5.9
244	8-902750	3	PbAc	75				4.3	17	BLOOD	4.3
248	8-902625	3	PbAc	75				3.6	17	BLOOD	3.6
258	8-902376	3	PbAc	75				8.8	17	BLOOD	8.8
204	8-902561	4	PbAc	225		**	11.9	11.8	16		
216	8-902520	4	PbAc	225			11.8	13.6		BLOOD	11.9
247	8-902525	4	PbAc	225					16	BLOOD	13.6 .
252	8-902692	4	PbAc				0.4	8.7	16	BLOOD	8.7
260				225			8.1	8.1	16	BLOOD	8.1
	8-902769	4	PbAc	225				12	16	BLOOD	12
201	8-902735	5	Residential	\ 75				2.4	17	BLOOD	2.4
207	8-902706	5	Residential	75				4	17	BLOOD	4
221	8-902714	5	Residential	75			41	4.2	17	BLOOD	4.2
238	8-902461	5	Residential	75				6.2	17	BLOOD	6.2
259	8-902549	5	Residential	75				4.2	17	BLOOD	4.2
236	8-902623	6	Residential	225			5.1	5.7	16	BLOOD	5.1
237	8-902497	6	Residential	225				6.5	16	BLOOD	6.5
240	8-902398	6	Residential	225				5.5	16	BLOOD	5.5
242	8-902734	6	Residential	225				6.7	16	BLOOD	6.7
249	8-902657	6	Residential	225				4.6	16	BLOOD	4.6
224	8-902347	7	Residential	450				7.5	17	BLOOD	7.5
234	8-902603	7	Residential	450				6	17	BLOOD	6
235	8-902414	7	Residential	450				8.3	17	BLOOD	8.3
243	8-902773	7	Residential	450				9.5	17	BLOOD	9.5
257	8-902494	7	Residential	450				7.6	17	BLOOD	7.6
202	8-902579	8	Channel	75				3.4	16	BLOOD	3.4
217	8-902658	8	Channel	75				2	16		
219	8-902476	8	Channel	75				5.9		BLOOD	2
253	8-902754	8	Channel	75 75					16	BLOOD	5.9
254	8-902514	8	Channel	75 75				2.9	16	BLOOD	2.9
203	8-902612	9						2.9	16	BLOOD	2.9
205	8-902697	9	Channel	225				5.2	17	BLOOD	5.2
225 227			Channel	225				6.1	17	BLOOD	6.1
	8-902588	9	Channel	225				6.5	17	BLOOD	6.5
232	8-902392	9	Channel	225			ē	6.3	17	BLOOD	6.3
250	8-902722	9	Channel	225				6.7	17	BLOOD	6.7
205	8-902429	10	Channel	675			,	6.5	16	BLOOD	6.5
210	8-902776	10	Channel	675				12.1	16	BLOOD	12.1
213	8-902341	10	Channel	675				9.5	16	BLOOD	9.5
218	8-902721	10	Channel	675				11.1	16	BLOOD	11.1
255	8-902503	10	Channel	675				10.3	16	BLOOD	10.3
208	8-902661	11	ľV	100				17.4	17	BLOOD	17.4
214	8-902640	11	IV	100				13.6	17	BLOOD	13.6
230	8-902771	11	N	100			,		17	BLOOD	15.5
231	8-902671	11	N	100				16.9	17	BLOOD	16.9
239	8-902578	11	Ň	100				10.0	17	BLOOD	10.5
241	8-902744	11	iv	100			5.	7.7	17	BLOOD	77
	8-902752	11	iv	100			**	7.7 16.4	17	BLOOD	7.7 16.4
246											

a Non-detects evaluated using 1/2 the quantitation limit, laboratory results (ug/L) converted to concentration in blood (ug/dL) by dividing by dilution factor of 1 dL/L

			w 10 + Dev 123	-		V 12. + Day 143	-			ay 14 + Day 16.				my 14 + Day 17)																												٠								
	Colonidation of Bullion B		Day 12.m = (Day 8 + Day 10 + Day 12)			Day 14.s. (Day 10 + Day 12.s + Day 14)				Day 16.4 - (Day 12.4 + Day 14.4 + Day 16)				Day 17.4 * (Day 12.4 + Day 14.4 + Day 17)																																				
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	8	0.5	0.5	2.8	-	1.7	=	1.5	<u>.</u>	3.5	5,1		.	10.5	• ;	2 :	•	• ;	6.0	7 :		3 :	! 2	5	5.3	5.5	7.7			. ~	\$	2.6	9.5	2	-	. 2	2.5	 	;		10.2	20	1.2		5.0	10.3	÷	10.5		
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	control	control	² bAc	PbAc	PbAc	PbAc	PbAc	PbAc	PbAc PbAc	PbAc	² bAc	PAc.	å ¥¢	φ¢	¥ķ	ž	Ž.	Residential	Residential	Residential	Residential	Tesidential	Residential	Residential	Residential	Residential	Residential	Residential	Residential	esidential	Chamel	Charmel	Channel	Channel	Charmel	Charmet	Channel	Charmel	Channel	Chermel	Charmel	Channel		2			_	2 2		

TABLE A-4 BLOOD LEAD OUTLIERS

Flagged Data Points Outliers

test	target	Actual							BLOOD	LEAD (ug/d	IL) BY DAY			
material	dosage	Dose*	group	pig#	-2	0	2	. 4	6	8	10	12 (RA)	14 (RA)	15 (int)
control	0	0.00	1	206	0.5	0.5	0.65	0.65	0.65	0.65	0.65	0.60	0.85	0.99
control	0	0.00		226	0.5	0.5	0.65		0.65			0.9	0.7	0.8
PbAc PbAc	25 25	22.60 26.00	2 2	215	0.5	1.2	3.3		3.8			4.2	4.1	4.0
PbAc	25 25	28.45	2	220 222	0.5 0.5	0.5 0.5	0.65		0.65			2.4	2.2	2.3
PbAc	25	26.74	2	229	0.5	1	2.1		3.4 3.1			3.2	3.0	3.1
PbAc	25	22.59	2	251	0.5	1.3	2.1		1.9			3.1 ° 2.2	3.0 2.0	3.2 2.2
PbAc	75	71.87	3	209	0.5	0.5	3.5		4.7			4.2	4.2	4.4
PbAc	75	74.71	3	228	0.5	0.5	3.4	3.1	5.3			4.9	4.5	4.7
PbAc	75	70.90	3	244	1.1	0.5	1.7		2.7			2.7	2.8	3.0
PbAc	75	0.00	3	248										
PbAc	75	76.31	3	258	0.5	0.5	3.6		4			5.7	5.6	6.0
PbAc PbAc	225 225	248.59	4	204	0.5	0.5	6.3		6			9.2	8.9	9.4
PbAc	225	249.40 196.41	4	216 247	0.5	0.5	8.6		9.8			10.3	10.3	10.8
PbAc	225	206.29	4	252	0.5 0.5	0.5 0.5	7.2 7.8		6.4			7.0	7.4	7.5
PbAc	225	238.40	4	260	0.5	0.5	6.3	5.9 8.1	7.4 9.9	7.4 11.8	8.7	7.4	7.3	7.5
BC1600	75	72.77	5	201	0.5	0.5	0.65	0.65	1.5		12.8 1.3	11.2 1.3	11.7	11.7
BC1600	75	83.68	5	207	0.5	0.5	3		2.9			3.3	1.0 3.1	1.2 3.2
BC1600	75	70.68	5	221	0.5	0.5	1.6	2	2.4	2.3	2.8	2.3	1.9	2.2
BC1600	75	89.93	5	238	0.5	0.5	2.2		4.4	4.3		3.6	3.8	4.1
BC1600	75	71.10	5	259	0.5	0.5	2.2	2.2	2.6	2.8	2.8	2.3	2.7	2.8
BC1600	225	226.67	6	236	1.2	0.5	3.1	3.5	5.2	5.7	6.7	4.9	5.1	5.1
BC1600	225	262.23	6	237	0.5	0.5	3.6	3.6	5.5	6.4	7.3	6.7	6.1	6.3
BC1600	225	244.98	6	240	0.5	0.5	3.7	5.4	5.1	5.3	6.8	5.8	5.7	5.7
BC1600	225	196.83	6	242	0.5	0.5	3.1	4.2	5.8	6.3	7	6.3	6.1	6.2
BC1600 BC1600	225 450	215.18	<u>6</u> 7	249	0.5	1.1	3.5	3.2	3.8	5.4	5.5	4.4	4.8	4.7
BC1600	450 450	490.53 435.95	7	224 234	0.5	0.5	5.8	6.1	6.6	7.4	7.5	6.8	6.7	6.8
BC1600	450	433,83	7	235	0.5 0.5	0.5 0.5	5 8.5	6.1	6.4	6.4	3.7	4.4	4.0	4.3
BC1600	450	504.66	7	243	0.5	0.5	5.6	7.9 6.4	8.6 7.4	6.8	8.8	7.7	7.9	7.9
BC1600	450	426.81	7	257	0.5	0.5	5.3	5.1	6.1	8.4 6.2	8.3	7.9 5.0	7.6	7.8
BC6300	75	75.19	8	202	0.5	0.5	2.2	2.8	3.1	2.9	4.6 3.9	5.0 3.1	4.5 3.2	4.9 3.3
BC6300	75	92.20	8	217	0.5	0.5	1.4	2.3	2.3	2.5	2.6	1.9	3.2 1.9	1.9
BC6300	75	67.24	8	219	1	0.5	2.3	4.5	5	5.1	7.1	5.6	6.0	5.9
BC 6300	75	73.35	8	253	0.5	0.5	1.4	2.4	3.5	3.3	3.2	2.8	2.5	2.6
BC6300	75	72.59	8	254	1	0.5	2.7	2.3	1.5	3.3	3.6	2.6	2.6	2.7
BC6300	225	262.42	9	203	0.5	0.5	2.5	4	4.7	Missing	3.4	3.3	3.3	3.5
3C6300	225	221.23	9	225	0.5	0.5	2.5	3.1	4	33	3.7	3.2	3.7	3.9
3C6300	225	224.23	9	227	0.5	0.5	2.1	2.2	3.8	3.8	3.7	3.6	3.7	4.0
3C6300	225	222.55	9	232	0.5	0.5	3.7	4.3	4.9	7.1	5	4.9	4.5	4.8
3C6300 3C6300	225 675	217.61	9 10	250	0.5	0.5	2.5	4.7	5.5	5.9	4.9	5.2	5.1	5.3
3C6300	675 675	716.64 696.90	10	205 210	0.5	0.5	Missing	3.9	3.6		5.9	5.1	5.0	5.3
3C6300	675	667.08	10	210	0.5 0.5	0.5 0.5	9.3	8.4	9.6	10.5	13.7	11.5	11.5	11.6
3C6300	675	649.24	10	218	0.5	0.5	5.8 7.7	6.5 8	7.1	8.3	7.5	7.1	7.2	7.6
3C6300	675	631.05	10	255	0.5	1	6.7	8.7	10.3 7.6	8.4	8.3	8.3	8.4	8.8
v 100	100	109.14	11	208	49	0.5	13.3	16.3	11.5	7.8	9	9.2	9.2	9.4
100	100	99.35	11	214	0.5	0.5	9.8	11.1	9	9.4 7.9	10.9	10.3	11.2	11.8
100	100	0.00	11	230	0.5	0.5	9.0		8	7.8	8.1	8.8	9.4	9.8
/ 100	100	108.76	11	231	0.5	0.5	8.7	10.3	8.6	7.4	10.5	9.5	10.7	14.2
/ 100	100	0.00	11	239	0.5	0.5	9.8		0.0		10.5	9.5	10.7	11.2
100	100	100.67	11	241	0.5	0.5	•	Missing	7.9	6.5	7.5	6.9	7.0	7.1
100	100	100.49	11	246	1.6	0.5	8.3	22.4	8.7	7.8	9.7	8.8	9.9	10.5
100	100	93.45	11	256	0.5	0.5	6		6.4	4.7	7.3	6.5	6.8	7.3

* Average Time and Weight-Adjusted Dose for Each Pig

Animal removed during course of study due to illness

Removed due to dosing problems

Rolling Average

int interpolated value

TABLE A-5 RATIONALE FOR PbB OUTLIER DECISIONS

Pig 208 Group 11 Day -2	The measured blood lead for this sample (4.9 ug/dL) is clearly higher than all other values measured in unexposed animals or control anmals. The value was replaced with an estimated value of 0.5 ug/dL.
Pig 246 Group 11 Day 4	The measured blood lead for this sample (22.4 ug/dL) is clearly higher than the values measured in the same animal on the preceeding and following days, and in other animals in the same group on the same day. The value was replaced with a value of 8.5 ug/dL

TABLE A-6 Area Under Curve Determinations

Calculated using interpolated values for missing or excluded data and Day 15 data

		test	target	 		7001	agroc-days)	For Time S	pan Shown			AUC Tota
group	pig#	material	dosage	0-2	2-4	4-6	6-8	8-10	10-12	12-14	14-15	(ug/dL-day
1	206	control	0	1.15	1.30	1.30	1.30	1.30	1.25	1.45	0.92	9.97
1	226	control	0	1.15	1.30	1.30	2.25	2.25	1.57	1.61	0.77	12.19
2	215	PbAc	25	4.50	6.40	6.90	8.00	9.70	9.70	8.27	4.03	57.50
2	220	PbAc	25	1.15	1.30	1.30	3.75	6.20	5.50	4.60	2.24	26.04
2	222	PbAc	25	2.20	4.50	6.20	7.20	7.80	7.17	6.19	3.07	44.32
2	229	PbAc	25	3.10	4.60	5.60	6.90	7.40	6.67	6.09	3.12	43.47
2	251	PbAc	25	3.30	3.80	3.70	4.50	5.20	4.83	4.24	2.10	31.67
3	209	PbAc	75	4.00	8.20	9.40	10.10	9.50	8.30	8.40	4.31	62.21
3	228	PbAc	75	3.90	6.50	8.40	10.90	11.30	10.63	9.44	4.61	65.69
3	244	PbAc	75	2.20	3.20	4.20	6.50	6.70	5.63	5.58	2.92	36.93
3	248	PbAc	75									
3	258	PbAc	75	4.10	8.50	8.90	9.10	11.30	11.90	11.30	5.78	70.88
4	204	PbAc	225	6.80	14.20	13.90	12.30	17.00	19.87	18.06	9.16	111.29
4	216	PbAc	225	9.10	16.90	18.10	19.50	21.80	22.37	20.56	10.56	138.89
4	247	PbAc	225	7.70	14.30	13.50	12.90	14.60	15.07	14.36	7.46	99.89
4	252	PbAc	225	8.30	13.70	13.30	14.80	16.10	16.10	14.73	7.40	104.44
4	260	PbAc	225	6.80	14.40	18.00	21.70	24.60	24.00	22.93	11.71	144.14
5	201	Resid	75	1.15	1.30	2.15	3.60	3.40	2.60	2.33	1.12	17.66
5	207	Resid	75	3.50	5.70	5.60	7.20	7.60	6.57	6.39	3.18	45.73
5	221	Resid	75	2.10	3.60	4.40	4.70	5.10	5.07	4.12	2.01	31.10
5	238	Resid	75	2.70	4.20	6.40	8.70	8.20	7.53	7.44	3.93	49.11
5	259	Resid	75	2.70	4.40	4.80	5.40	5.60	5.07	4.99	2.78	35.73
6	236	Resid	225	3.60	6.60	8.70	10.90	12.40	11.60	10.00	5.08	68.88
6	237	Resid	225	4.10	7.20	9.10	11.90	13.70	14.03	12.84		
6	240		225	4.20	9.10	10.50	10.40	12.10			6.20	79.07
6	242	Resid		3.60	7.30	10.00	12.10	13.30	12.60 13.27	11.53	5.72	76.15
6	249	Resid	225	1						12.39	6.18	78.14
7	224	Resid	225	4.60	6.70	7.00	9.20	10.90	9.93	9.28	4.79	62.40
7		Resid	450	6.30	11.90	12.70	14.00	14.90	14.33	13.58	6.79	94.50
7	234	Resid	450	5.50	11.10	12.50	12.80	10.10	8.10	8.40	4.13	72.63
	235	Resid	450	9.00	16.40	16.50	15.40	15.60	16.47	15.56	7.90	112.82
7	243	Resid	450	6.10	12.00	13.80	15.80	16.70	16.20	15.50	7.72	103.82
7	257	Resid	450	5.80	10.40	11.20	12.30	10.80	9.57	9.42	4.66	74.15
8	202	Channel	75	2.70	5.00	5.90	6.00	6.80	7.03	6.38	3.25	43.06
8	217	Channel	75	1.90	3.70	4.60	4.80	5.10	4.47	3.79	1.92	30.28
8	219	Channel	75	2.80	6.80	9.50	10.10	12.20	12.67	11.59	5.97	71.63
8	253	Channel	75	1.90	3.80	5.90	6.80	6.50	6.00	5.33	2.59	38.82
8	254	Channel	75	3.20	5.00	3.80	4.80	6.90	6.23	5.28	2.66	37.88
9	203	Channel	225	3.00	6.50	8.70	8.75	7.45	6.68	6.58	3.40	51.06
9	225	Channel	225	3.00	5.60	7.10	7.30	7.00	6.87	6.86	3.79	47.52
9	227	Channel	225	2.60	4.30	6.00	7.60	7.50	7.30	7.30	3.85	46.45
9	232	Channel	225	4.20	8.00	9.20	12.00	12.10	9.93	9.48	4.66	69.57
9	250	Channel	225	3.00	7.20	10.20	11.40	10.80	10.13	10.31	5.18	68.22
10	205	Channel	675	2.70	6.10	7.50	10.30	12.60	11.00	10.13	5.16	65.49
10	210	Channel	675	9.80	17.70	18.00	20.10	24.20	25.17	22.99	11.57	149.52
10	213	Channel	675	6.30	12.30	13.60	15.40	15.80	14.57	14.29	7.40	99.65
10	218	Channel	675	8.20	15.70	18.30	18.70	16.70	16.60	16.67	8.59	119.46
10	255	Channel	675	7.70	15.40	16.30	15.40	16.80	18.20	18.37	9.26	117.43
11	208	IV	100	13.80	29.60	27.80	20.90	20.30	21.17	21.49	11.51	166.57
11	214	IV	100	10.30	20.90	20.10	16.90	16.00	16.87	18.12	9.56	128.75
11	230	IV	100			متنوال	1387	10.00	10.07	10.12		126.75
11	231	IV	100	9.20	19.00	18.90	16.00	17.90	19.97	20.16	10.97	132.09
11	239	IV	100	5.10		10.30	* 44 42			20.16	10.57	132.09
11	241	IV	100	4.50	9.95	13.85	14.40	14.00	14.43	13. 9 8	7.07	00.40
11	246	IV	100	8.80	16.80	17.20	16.50	17.50	18.53	18.71	7.07	92.19
11	256	IV	100	6.50	14.20	14.60	11.10	12.00	13.77	13.29	10.18 7.07	124.23

Removed due to dosing problems
Died during course of study

TABLE A - 7 TISSUE LEAD DATA

PHASE II EXPERIMENT 2

pig number	sample	group	material administered	dosage qualifier	result	day	MATRIX	Adjusted Value (ug/dL) *
206	8-902904	1	control	0	2	17	FEMUR	0.88
226	8-902967	1	control	0	1	17	FEMUR	0.44
215	8-903015	2	PbAc	25	7.7	16	FEMUR	3.61
220	8-902953	2	PbAc	25	4.8	16	FEMUR	2.25
222	8-902999	2	PbAc	25	4.4	16	FEMUR	2.06
229	8-903002	2	PbAc	25	6.8	16	FEMUR	3.19
251	8-902901	2	PbAc	25	3.6	16	FEMUR	1.69
209	8-902992	3	PbAc	75	15.7	17	FEMUR	6.93
228	8-903053	3	PbAc	75	12.4	17	FEMUR	5.47
244	8-902975	3	PbAc	75	9.7	17	FEMUR	4.28
248	8-902943	3	PbAc	75	6.4	17	FEMUR	2.82
258	8-903069	3	PbAc	75	16.9	17	FEMUR	7.46
204	8-903017	4	PbAc	225	66.5	16	FEMUR	31.17
216	8-903049	4	PbAc	225	57	16	FEMUR	26.72
247	8-903046	Ā	PbAc	225	33.6	16	FEMUR	15.75
252	8-902946	4	PbAc	225	40.1	16	FEMUR	
260 .	8-902956	4	PbAc	225			60600666666666666666	18.80
201		5			44.4	16	FEMUR	20.81
	8-903007		Residential	75	3.1	17	FEMUR	1.37
207	8-902983	5	Residential	75 	7.1	17	FEMUR	3.13
221	8-902937	5	Residential	75	5.3	17	FEMUR	2.34
238	8-903070	5	Residential	75	7.9	17	FEMUR	3.49
259	8-902908	5	Residential	75	4.2	17	FEMUR	1.85
236	8-902932	6	Residential	225	11.7	16	FEMUR	5.48
237	8-902945	6	Residential	225	19.4	16	FEMUR	9.09
240	8-902926	6	Residential	225	16	16	FEMUR	7.50
242	8-902954	6	Residential	225	15.8	16	FEMUR	7.41
249	8-902931	6	Residential	225	15.1	16	FEMUR	7.08
224	8-903039	7	Residential	450	18.3	17	FEMUR	8.07
234	8-902950	7	Residential	450	10.2	17	FEMUR	4.50
235	8-903060	7	Residential	450	25.9	17	FEMUR	11.43
243	8-902933	7	Residential	450	19.6	17	FEMUR	8.65
257	8-903063	7	Residential	450	19.2	17	FEMUR	
202	8-902963	8	Channel	75				8.47
217	8-903043	8	Channel		7.6	16	FEMUR	3.56
219		8		75 75	3.8	16	FEMUR	1.78
	8-903008		Channel	75	7.9	16	FEMUR	3.70
253	8-903059	8	Channel	75	5.2	16	FEMUR	2.44
254	8-903028	8	Channel	75	3.6	16	FEMUR	1.69
203	8-903012	9	Channel	225	9.6	17	FEMUR	4.24
225	8-902942	9	Channel	225	13.7	17	FEMUR	6.04
227	8-903042	9	Channel	225	15.3	17	FEMUR	6.75
232	8-902982	9	Channel	225	11.6	17	FEMUR	5.12
250	8-902936	9	Channel	225	13.6	17	FEMUR	6.00
205	8-902984	10	Channel	675	23	16	FEMUR	10.78
210	8-903062	10	Channel	675	36	16	FEMUR	16.88
213	8-903031	10	Channel	675	26.3	16	FEMUR	12.33
218	8-903054	10	Channel	675	40.5	16	FEMUR	18.98
255	8-902941	10	Channel	675	33.1	16	FEMUR	
208	8-902988	11	IV	100			SASSONANDAN SANANAN MARKA	15.52 31.76
214	8-902938	11	IV IV		72 68 5	17	FEMUR	31.76
230	8-903034	11		100	68.5	17	FEMUR	30.22
			IV	100		17	FEMUR	
231	8-902923	11	IV	100	79	17	FEMUR	34.85
239	8-903021	11	IV .	100		17	FEMUR	
241	8-902998	11	· IV	100	19.5	17	FEMUR	8.60
246	8-902903	11	IV	100	91	17	FEMUR	40.15
256	8-902900	11	IV	100	64	17	FEMUR	28.24
206	8-902981	1	control	0	5.2	17	KIDNEY	45.88
226	8-902990	1 .	control	0	4.2	17	KIDNEY	37.06
215	8-902915	2	PbAc	25	8.2	16	KIDNEY	76.88
220	8-902947	2	PbAc	25	10	16	KIDNEY	93.75
222	8-902994	2	PbAc	25	9.4	16	KIDNEY	· 88.13
								SS. 13
229	8-902995	2	PbAc	25	14	16	KIDNEY	131.25

pig number 209	sample 8-902930	group	material administered PbAc	dosage 75	qualifier	result	day	MATRIX	Adjusted Value (ug/dL) *
		3		75		28	17	KIDNEY	247.06
228	8-902977	3	PbAc	75		13.2	17	KIDNEY	116.47
244	8-902993	3	PbAc	75		18.6	17	KIDNEY	164.12
248	8-902965	3	PbAc	75		10.6	17	KIDNEY	93.53
258	8-902916	3	PbAc	75		28.4	17	KIDNEY	250.59
204	8-902980	4	PbAc	225		79.4	16	KIDNEY	744.38
216	8-903068	4	PbAc	225		139	16	KIDNEY	1303.13
247	8-903050	4	PbAc	225		69	16	KIDNEY	646.88
252	8-903018	4	PbAc	225		51.6	16	KIDNEY	483.75
260	8-902910	4	PbAc	225		48.6	16	KIDNEY	455.63
201	8-902979	5	Residential	75			17	000000000000000000000000000000000000000	
207	8-903013	5	Residential	75 75		6.6		KIDNEY	58.24
						7.4	17	KIDNEY	65.29
221	8-903005	5	Residential	75		7.6	17	KIDNEY	67.06
238	8-902934	5	Residential	75		16.2	17	KIDNEY	142.94
259	8-903030	5	Residential	75		10.2	17	KIDNEY	90.00
236	8-903004	6	Residential	225		17.6	16	KIDNEY	165.00
237	8-902909	6	Residential	225		30	16	KIDNEY	281.25
240	8-902962	6	Residential	225		18.4	16	KIDNEY	172.50
242	8-902919	6	Residential	225		28.2	16	KIDNEY	264.38
249	8-902912	6	Residential	225		25.8	16	KIDNEY	
224	8-902902	7	Residential	450				200000000000000000000000000000000000000	241.88
						28.6	17	KIDNEY	252.35
234	8-903056	7	Residential	450		11.4	17	KIDNEY	100.59
235	8-902918	7	Residential	450		48.6	17	KIDNEY	428.82
243	8-903032	7	Residential	450		28.2	17	KIDNEY	248.82
257	8-902978	7	Residential	450		21.2	17	KIDNEY	187.06
202	8-902976	8	Channel	75		7	16	KIDNEY	65.63
217	8-902969	8	Channel	75		6.6	16	KIDNEY	61.88
219	8-902940	8	Channei	75		14.4	16	KIDNEY	135.00
253	8-903025	8	Channel	75		24.2	16	KIDNEY	226.88
254	8-903058	8	Channel	75				22/20/20/20/20/20/20/20/20/20/20/20/20/2	
203	8-902991					12	16	KIDNEY	112.50
		9	Channel	225		17	17	KIDNEY	150.00
225	8-903026	9	Channel	225		17.2	17	KIDNEY	151.76
227	8-902935	9	Channel	225		26.4	17	KIDNEY	232.94
232	8-903065	9	Channel	225		20.2	17	KIDNEY	178.24
250	8-902948	9	Channel	225		23	17	KIDNEY	202.94
205	8-903055	10	Channel	675		39.2	16	KIDNEY	367.50
210	8-902997	10	Channel	675		54	16	KIDNEY	506.25
213	8-902944	10	Channel	675		33.8	16	200000000000000000000000000000000000000	
218	8-902939	10	Channel					KIDNEY	316.88
255				675		71.6	16	KIDNEY	671.25
	8-902911	10	Channel	675		41.8	16	KIDNEY	391.88
208	8-902985	11	. IV	100		125	17	KIDNEY	1102.94
214	8-903000	11	IV	100		125	17	KIDNEY	1102.94
230	8-902987	11	IV	100			17	KIDNEY	
231	8-903057	11	IV	100		116	17	KIDNEY	1023.53
239	8-903044	11	IV	100			17	KIDNEY	
241	8-903047	11	IV	100		29.8	17	300000000000000000000000000000000000000	202.04
246	8-903052	11	iv	100				KIDNEY	262.94
256						80.2	17	KIDNEY	707.65
	8-902914	11	IV	100		87	17	KIDNEY	767.65
206	8-902973	1	control	0		6.2	17	LIVER	54.71
226	8-903003	1	control	0		10.2	17	LIVER	90.00
215	8-903064	2	PbAc	25		11.6	16	LIVER	108.75
220	8-903037	2	PbAc	25		9.8	16	LIVER	91.88
222	8-902959	2	PbAc	25		17.2	16	LIVER	161.25
229	8-903009	2	PbAc	25		14.2	16	LIVER	133.13
251	8-902951	2	PbAc	25		11.8	16		
209	8-902906	3	PbAc	75				LIVER	110.63
228	8-903033	3				25.6	17	LIVER	225.88
			PbAc	75 		18	17	LIVER	158.82
244	8-903035	3	PbAc	75		13.8	17	LIVER	121.76
248	8-902957	3	PbAc	75		11.2	17	LIVER	98.82
258	8-903066	3	PbAc	75		27.6	17	LIVER	243.53
204	8-903038	4	PbAc	225		28.2	16	LIVER	264.38
216	8-902966	4	PbAc	225		101	16	LIVER	946.88
247	8-902961	4	PbAc	225		68.2	16	LIVER	
252	8-903022	4	PbAc	225		31.8			639.38
260	8-902929	4	PbAc				16	LIVER	298.13
201	8-903067			225		64.4	16	LIVER	. 603.75
		5	Residential	75		9	17	LIVER	79.41
207	8-903010	5	Residential	75		6.6	17	LIVER	58.24
221	8-902917	5	Residential	75		16.4	17	LIVER	144.71
									•

pig number	sample	group	material administered	dosage o	ualifier	result	day	MATRIX	Adjusted Value (ug/dL) a
238	8-902922	5	Residential	75		14.2	17	LIVER	125.29
259	8-903006	5	Residential	75		7.2	17	LIVER	63.53
236	8-903023	6	Residential	225		27.2	16	LIVER	255.00
237	8-903001	6	Residential	225		24	16	LIVER	225.00
240	8-903045	6	Residential	225		19.2	16	LIVER	180.00
242	8-902913	6	Residential	225		29	16	LIVER	271.88
249	8-902989	6	Residential	225		22.4	16	LIVER	210.00
224	8-903014	7	Residential	450	4.	22	17	LIVER	194.12
234	8-903016	7	Residential	450		139	17	LIVER	1226.47
235	8-902958	7	Residential	450		32.6	17	LIVER	287.65
243	8-903036	7	Residential	450		60.8	17	LIVER	536.47
257	8-902964	7	Residential	450		26.6	17	LIVER	234.71
202	8-902996	8	Channel	75		12.8	16	LIVER	120.00
217	8-903020	8	Channel	75		8.2	16	LIVER	76.88
219	8-902925	8	Channel	75		18.4	16	LIVER	172.50
253	8-902920	8	Channel	75		8.2	16	LIVER	76.88
254	8-902974	8	Channel	75		7.2	16	LIVER	67.50
203	8-903024	9	Channel	225		21	17	LIVER	185,29
225	8-902972	9	Channel	225		16.8	17	LIVER	148.24
227	8-902928	9	Channel	225		17.8	17	LIVER	157.06
232	8-902907	9	Channel	225		17	17	LIVER	150.00
250	8-902971	9	Channel	225		20	17	LIVER	176.47
205	8-902970	10	Channel	675		31.4	16	LIVER	294.38
210	8-902968	10	Channel	675		66.2	16	LIVER	620.63
213	8-903048	10	Channel	675		38.6	16	LIVER	361.88
218	8-903041	10	Channel	675		47.4	16	LIVER	444.38
255	8-902924	10	Channel	675		41.8	16	LIVER	391.88
208	8-903011	11	IV	100		175	17	LIVER	1544.12
214	8-902905	11	IV	100		86.4	17	LIVER	762.35
230	8-902921	11	IV	100		00 .¬	17	LIVER	. 702.33
231	8-902986	11	IV	100		86	17	LIVER	758.82
239	8-903019	11	IV	100		30	17	LIVER	130.02
241	8-903051	11	IV	100		26.4	17	LIVER	222.04
246	8-902960	11	IV	100		112	17	LIVER	232.94
256	8-902955	11	IV	100		126	17	LIVER	988.24 1111.76

Non-detects evaluated using 1/2 the quantitation limit. Laboratory results (ug/L) converted to tissue concentrations by dividing by sample dil 0.1 kg/L (liver, kidney) or 2 g/L (ashed bone). Final units are ug Pb/kg wet weight (liver, kidney) or ug Pb/g ashed bone (femur) Values were multiplied by 15/16 or 15/17 depending on duration in order to convert to 15 day values

TABLE A-8 SUMMARY OF ENDPOINT OUTLIERS

Selected Outliers
Animal died during course of study

test	target	Actual				MEASUREM	ENT ENDPOINT	,
material	dosage	Dose*	group	pig#	Blood	Femur	Liver	Kidney
control	C	0.00	1	206	10.0	0.88	54.7	45.9
control	C	0.00	1	226	12.2	0.44	90.0	37.1
PbAc	25	22.60	2	215	57.5	3.61	108.8	76.9
PbAc	25		2	220	26.0	2.25	91.9	93.8
PbAc	25		2	222	44.3	2.06	161.3	88.1
PbAc	25		2	229	43.5	3.19	133.1	131.3
PbAc	25			251	31.7	1.69	110.6	65.6
PbAc	75		3	209	62.2	6.93	225.9	247.1
PbAc	75		3	228	65.7	5.47	158.8	116.5
PbAc	75	70.90	3	244	36.9	4.28	121.8	164.1
PbAc	75		3	248		1		
PbAc	75	76.31	3	258	70.9	7.46	243.5	250.6
PbAc	225	248.59	4	204	111.3	31.17 b	264.4	744.4
PbAc	225	249.40	4	216	138.9	26.72	946.9 b	1303.1 b
PbAc	225	196.41	4	247	99.9	15.75	639.4	646.9
PbAc	225	206.29	4	252	104.4	18.80	298.1	483.8
PbAc	225	238.40	4	260	144.1	20.81	603.8	455.6
BC1600	75	72.77	5	201	17.7	1.37	79.4	58.2
BC1600	75	83.68	5	207	45.7	3.13	58.2	65.3
BC1600	75	70.68	5	221	31.1	2.34	144.7	67.1
BC1600	75	89.93	5	238	49.1	3.49	125.3	142.9
BC1600	75	71.10	5	259	35.7	1.85	63.5	90.0
BC1600	225	226.67	6	236	68.9	5.48	255.0	165.0
BC1600	225	262.23	6	237	79.1	9.09	225.0	281.3
BC1600	225	244.98	6	240	76.2	7.50	180.0	172.5
BC1600	225	196.83	6	242	78.1	7.41	271.9	264.4
BC1600	225	215.18	6	249	62.4	7.08	210.0	241.9
BC1600	450	490.53	7	224	94.5	8.07	194.1	252.4
BC1600	450	435.95	7	234	72.6	4.50	1226.5 b	100.6
BC1600	450	434.47	7	235	112.8	11.43	287.6	428.8
BC1600	450	504.66	7	243	103.8	8.65	536.5	248.8
BC1600	450	426.81	7	257	74.1	8.47	234.7	187.1
BC6300	75	75.19	8	202	43.1	3.56	120.0	65.6
BC6300	75	92.20	8	217	30.3	1.78	76.9	61.9
BC6300	75	67.24	8	219	71.6	3.70	172.5	135.0
BC6300	75 ~~	73.35	8	253	38.8	2.44	76.9	226.9
BC6300	75	72.59	8	254	37.9	1.69	67.5	112.5
BC6300	225	262.42	9	203	51.1	4.24	185.3	150.0
3C6300	225	221.23	9	225	47.5	6.04	148.2	151.8
3C6300	225	224.23	9	227	46.5	6.75	157.1	232.9
3C6300 3C6300	225	222.55	9	232	69.6	5.12	150.0	178.2
3C6300	225	217.61	9	250	68.2	6.00	176.5	202.9
	675	716.64	10	205	65.5	10.78 b	294.4	367.5
3C6300	675	696.90	10	210	149.5	16.88	620.6 b	506.3
3C6300	675	667.08	10	213	99.7	12.33	361.9	316.9
3C6300	675	649.24	10	218	119.5	18.98 b	444.4	671.3 b
3C6300	675	631.05	10	255	117.4	15.52	391.9	391.9
v 100	100	109.14	11	208	166.6	31.76	1544.1	1102.9
/ 100	100	99.35	11	214	128.7	30.22	762.4	1102.9
/ 100	100		11	230	1.7			
/ 100	100	108.76	11	231	132.1	34.85	758.8	1023.5
/ 100	100		11	239				
/ 100	100	100.67	11	241	92.2	8.60 a	232.9 a	262.9 a
100	100	100.49	11	246	124.2	40.15	988.2	707.6
/ 100	100	93.44641	11	256	92.52901	28.24	1111.8	767.6

Removed due to dosing problems

a *a priori* outlier determinations b Outside 95% Prediction Intervals

TABLE A-9 Best Curve Fit Parameters

BLOOD		BONE		LIVER		KIDNEY	
PbAc Curve -	Exp	PbAc Curve -	Linear	PbAc Curve -	Linear	Dh&c Circa	-
æ	11.8	æ	0.812	a.	3		Lillear
، م		۵	0.0873		1.662	m _c	52.5
סר ט	121.5	UT		v ·			6.318
R2	0.905	. Z2	0.963	R2	0.67	P 6	
						2	0.635
BC Residential Curve -	Ехр	BC Residential Curve -	Linear	BC Residential Curve -	Linear	BC Residential Curve -	Linear
æ	11.8		0.812				
•			0.0186	n 1	72	a	52.5
v	121.5			2 (0.354	۵	0.481
•	0.0027	ים		, τ		o •	
R2	968.0	R2	0.71	R2	0.648	- Z	0.533
BC Channel Curve -	Ехр	BC Channel Curve -	Linear	BC Channel Curve -	Linear	BC Channel Curve -	Linear
æ	11.8	æ		7	F		
، م	1	۵	0.0211	<u>م</u> .	4.	m .c	52.5
טיט	121.5	o ·		U		. 0	
. 22	0.0024	0		•			
!		2	0.949	R2	0.878	2 2	0.629
	Carretone I need		-				
	EXP Y=a+c*(1-exp(-d*dose))	se))					
	LiN Y=a+b*dose						

TABLE A-10 Relative Bioavailability of Lead in Test Materials

	Binghar Test M	n Creek laterial
Endpoint	Residential	Channel
Blood	0.325	0.289
Kidney	0.208	0.223
Liver	0.333	0.265
Bone	0.213	0.265

Definitions

Plausible Range:

RBA(Blood) to mean RBA for Tissues

Preferred Range:

RBA(Blood) to (RBA(Blood) + RBA(Tissues))/2

Suggested Point Est:

1/2(RBA(Blood) + (RBA(Blood)+RBA(Tissues))/2)

Relative Bioavailability

	Binghan Resid		_	n Creek nnel
Plausible Range	0.325	0.251	0.289	0.251
Preferred Range	0.325	0.288	0.289	0.270
Point Estimate	0.3	07	0.2	280

Absolute Bioavailability

	Binghan Resid		_	n Creek nnel
Plausible Range	16%	13%	14%	13%
Preferred Range	16%	14%	14%	13%
Point Estimate	15	%	14	%

TABLE A-11 INTRALABORATORY DUPLICATES

RPD = Relative Percent Difference RPD = 100*[Orig-Dup]/((Orig+Dup)/2

* Non detects evaluated at 1/2 DL

rig number	group	material administered	dosage	Ø	matrix	Dublicate Value*	Original Value*	Assessed			
217	8	BC6300	75	,	1000	30mm 30mm 3	Ongillar Value	Average	טאַצ	AVG KPD	
240	ď	004000	2 8	۷,	PLOOD	6.0	6.0	3.5	-171%		
643	o ;	000100	22	0	BLOOD	0.65	+ :+	0.875	21%		
214	-	iv 100	5	0	BLOOD	2.4	30	4 45	2 6 6		
218	9	BC6300	675	7	BLOOD	: v:	2.7	? •	<u> </u>		
234	7	BC1600	450	0	RI OOD	9 9	: u	- 6	? 2.		
218	10	BC6300	675			P «	n (4. 20	88		
246	; 7	1,100	5 5		BLOOD BLOOD	x o ;	∞	œ	8		
7	<u> </u>	3 .	3	4	BLOOD	23.4	22.4	22.9	48		
744	n	PbAc	75	ဖ	BLOOD	2.7	2.7	27	ğ		
213	9	BC6300	675	9	BLOOD	7.2		- 4	R 2		
229	7	PbAc	7.	α		- c	-	7.13 0.0	?		
247	4	PhAc	ָ בַּ	, 5		0 ,	χ. Σ		%		
22	. ;		C77	2	BLOOD	20	8. 1.	8 0	%0		
73		iv 100	6	9	BLOOD	10.3	10.5	10.4	36.		
204	4	PbAc	225	12	BLOOD	7 77	4 0	j (R 3		
203	o	BC6300	225	5		2 (2.0	0.7	-32%		
248	,	DP # -	3 1	<u>.</u>	פרססה	Đ.	2.4	4.65	-97%		
0170) (PDAC	ઈ	4	BLOOD	7.8	-	4.4	-155%		
/17	æ	BC6300	75	14	BLOOD	7.1	13	4.2	120%		
232	တ	BC6300	225	17	BLOOD	ď) (C	N 0	R 26		
202	5	BC6300	675	16	BLOOD	9 4		o (R p		1
232	O	BC6300	225	1	EEMID	5 5	C.D.	0.40	% 7	-38%	BLOOD
205	Ç	00000	3 5	- (12.1	9.11	11.85	4 %		
000	2 (00000	0/0	9	FEMOR	26.1	8	24.55	-13%	8	FFMIR
727	. מ	BC6300	225	17	KIDNEY	21.6	202	000	707	?	
202	9	BC6300	675	9	KIDNEY	36.2	30.2	37.7	? 6	707	
232	o	BC6300	225	17	INFR	5			R G	R -	NUNEY
205	9	BC6300	R75	. 4		2 6	<u> </u>	5	%/X		
			Sign	2	רוגע	31	31.4	31.2	%	14%	LIVER

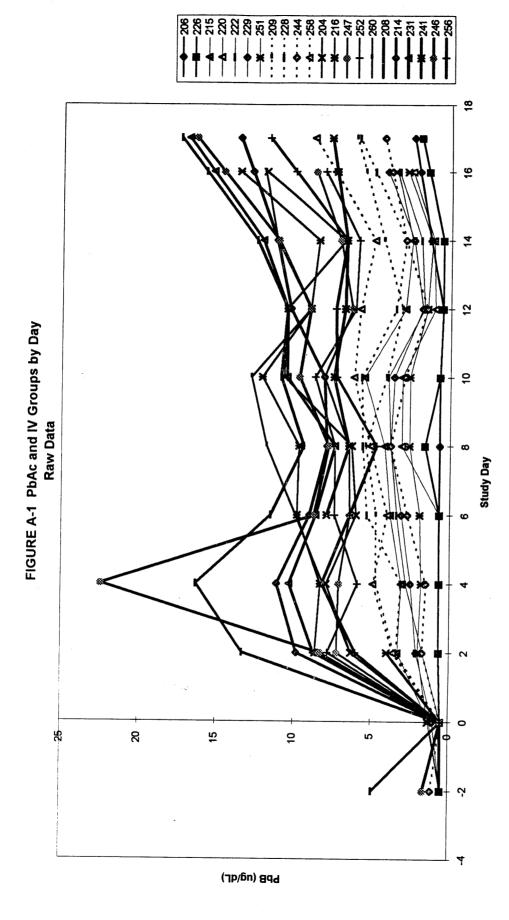
TABLE A-12 CDC STANDARDS

			M	easured*			Nominal	
Sample ID	Day	Q	Low Std	Med Std	High Std	Low Std	Med Std	High Std
1	-2		6.6		1	1.7	4.8	14.9
1	0		6.3			1.7	4.8	14.9
1	2	ļ	2.3			1.7	4.8	14.9
1	4		1.3			1.7	4.8	14.9
1	6	I	1.3	a a	·	1.7	4.8	14.9
1	6		1.6			1.7	4.8	14.9
1	8		2			1.7	4.8	14.9
1	10		1.7	1		1.7	4.8	14.9
1	12	ı	6			1.7	4.8	14.9
. 1	14	l	6.7			1.7	4.8	14.9
1	16		2.2			1.7	4.8	14.9
2	0			4.2		1.7	4.8	14.9
2 2	2			5.5		1.7	4.8	14.9
2 .	2 2			5.6		1.7	4.8	14.9
2	4			6.7		1.7	4.8	14.9
2 2 2	6	1		4.9		1.7	4.8	14.9
2	8			5.6		1.7	4.8	14.9
2	10	Ī		5.0		1.7	4.8	14.9
2 [*] 2	10			5.5		1.7	4.8	14.9
2	12	1		7.3		1.7	4.8	14.9
2	14	·		9.5		1.7	4.8	14.9
2	16	[5.2		1.7	4.8	14.9
2,	16	.		6.2		1.7	4.8	14.9
3	-2				19.1	1.7	4.8	14.9
3	-2				20.1	1.7	4.8	14.9
3	0				13.3	1.7	4.8	14.9
3	0				20.6	1.7	4.8	14.9
- 3	2			İ	16	1.7	4.8	14.9
3	4	Ī			14.7	1.7	4.8	14.9
3	4	. [15.2	1.7	4.8	14.9
3	6				16.3	1.7	4.8	14.9
3	8	[15	1.7	4.8	14.9
3	8	İ			16.2	1.7	4.8	14.9
3	10				15.7	1.7	4.8	14.9
3	12				18	1.7	4.8	14.9
3	12	l			19.2	1.7	4.8	14.9
3	14				20.6	1.7	4.8	14.9
3	14				21.8	1.7	4.8	14.9
3	16				16.8	1.7	4.8	14.9
Averages			3.45	5.93	17.41			

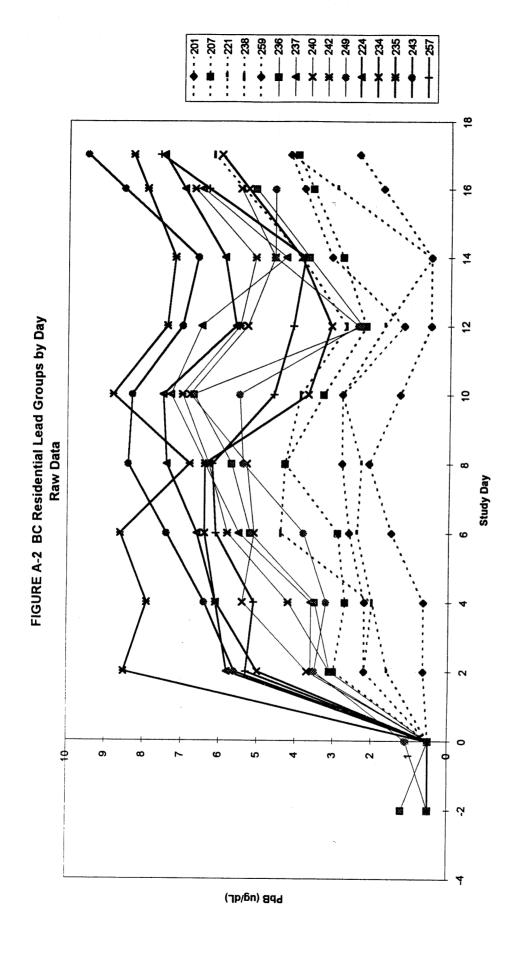
^{*} Non-detects evaluated at the detection limit

TABLE A-13 INTERLABORATORY COMPARISON

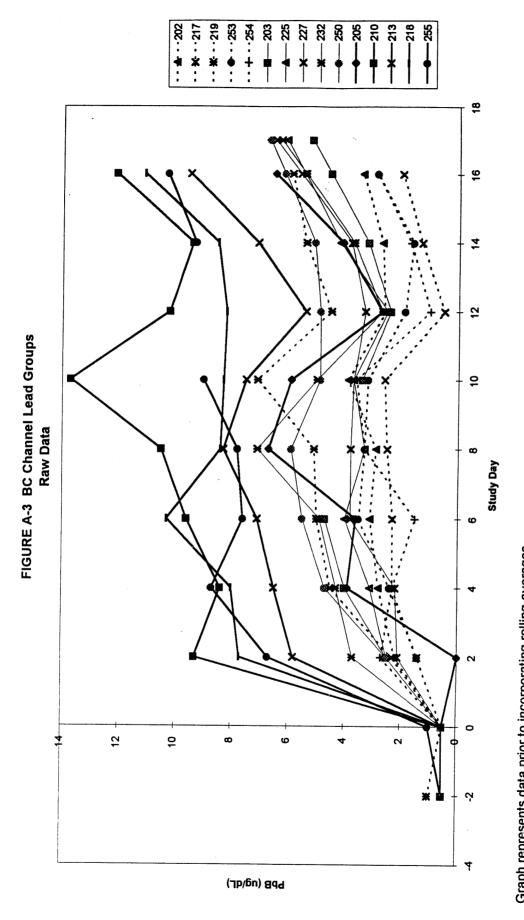
Г			_	_	_	_	_			_												_						_		_	_				-			_	-	_	_			_					_			
L	RPD	159	56	55	162	2 3	3 :	7.7		3 6	3 4	5 8	Ş	3 8	3 ო		7	?	Ξ	Ξ	7	7	8	8	\$	8	8 1	= 1	٠ :	N C	۵ ۲	, ,	7	2	7	~	5 5	, r	9 (4	4	ņ	ń	8	8	g;	7	<u> </u>	3 %	98	36	KO K
	Average	2.9	3.25	2.9	3.15	ر د د	3.6	0.95	23.5	286	20.0	345	} e:	33	3.65	3.65	7.2	7.2	6.	6.	2.75	2.75	1.15	1.15	12.15	= ;		6 4	0.4		5 5	6.5	5.9	4.9	4.45	2.45	0.60	0.00	33.5	202	2.05	6.7	6.7	8.2	2.9	25.50	, t	, rc	5,65	Ξ	Ξ	6.35 35
Result	EPA	5.2	5.9	5.2	6	7.7	, ,	, L		2.5	2.9		3.0	80	3.7	3.7	7.1	7.1	6.1	6.	2.7	2.7	. .	E	9.4	8.61	=	Ç.0		9 60	2.4	5.7	5.7	7.1	Æ.	0.4			4	2.5	2.5	9.9	9.9	o n ;	÷ ;	E 6		, ec	6.7	1.3	<u>6.</u>	6 65
	ပ္ပ	9.0	9.0	9.0	9 4	9 4	90	90	1.	3.2	12.6	80	2.8	2.8	3.6	3.6	7.3	7.3	1.7	7.7	2.8	2.8	- ,	- ;	5.5	77	0 0	97	9	4	60	6.1	£.9	5.7	:	•		333	3.3	9.	9:	6.8	89	7:	-:	t o	9 60	2.7	9.4	6.0	6.0	6.2
			•										-	:										,	•																											
fler	EPA						~	v					-										٠,	,																										-		
Qualifier	3	> =	> :	> =)		_	>													-		-					-								_															•	
Dosage	305	C 27	5 K	575	8	450	225	22	55	525	675	525	52	52	5	450	525	S 2	8 8	8 %	2 %	. K	3 %	3 5	9	225	225	450	225	225	0	522	62 1	٤ ۽	2 12	450	450	75	5	21	e (8 6	25	3	22,	22	22	52	225	5 12	e §	3 2
Material	RC6300	BC1500	PhA	BC6300	iv 100	BC1600	BC1600	PbAc	BC1600	BC6300	BC6300	BC1600	¥	PbAc	BC1600	909	9 2		2 2	00100	25.00	A d	¥	PbA	4 100	BC6300	BC1600	BC1600	BC1600	BC1600	control	BC1600	00000	BC6300	BC6300	BC1600	BC1600	BC6300	BC6300	o de	2000	90190	BC630	control	PPA	PbAc	PA	PP	BC6300	90190	2 5	v 100
Group	o	, rc	~	9	=	7	9	7	ıo ı	on :	ę ,	10	~ 0	N 1	<u> </u>		* *	• •	۷ ر	7 LC	- LC	. ~	1 00	4	=	6	9	^	9	6	- (- a	- «	. ~		7	~		, c	· ·	- ^	- =		•	6	က	7	о .	o v	· =	=
Pig	225	529	229	213	208	224	236	523	202	00 10	522	242	3 8	7 7	234	267	24.7	25.	3,5	202	202	220	220	247	508	250	249	257	237	237	9 8	236	2 5	219	219	234	234	202	505	240	226	22	255	526	216	258	258	222	200	- F	241	241
Tag Number	8-902165	8-902184	8-902201	8-902211	8-902241	8-902245	8-902249	8-9022/2	8-902283	9-902283	6-902316	0-902330	0-302382	8 002202	8-002383	8-002386	8-902386	8-902404	8-902404	8-902417	8-902417	8-902445	8-902445	8-902455	8-902460	8-902473	8-902491	8-902496	8-902497	8-902497	9-902200	8-902506	8-902519	8-902529	8-902529	8-902564	8-902564	8-902579	6/0706-0	8-902583	8-902626	8-902626	8-902651	8-902679	8-902704	8-902707	8-902707	8-902/11	8-902/22	8-902751	8-902763	8-902763



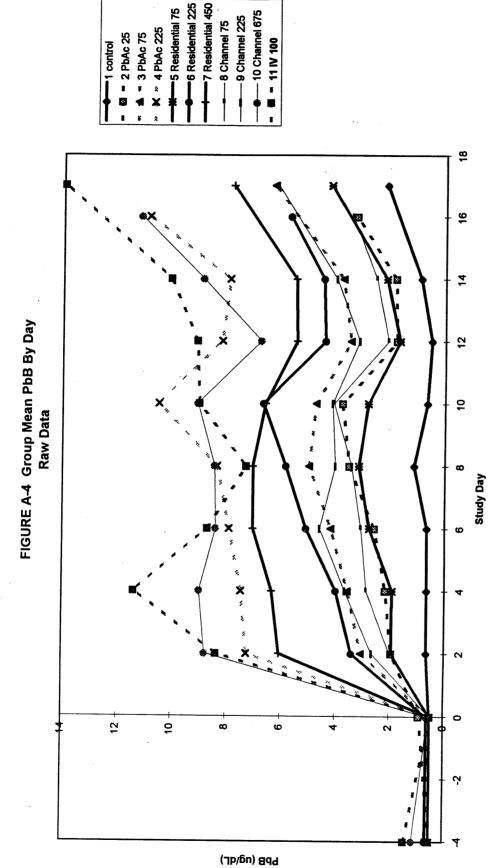
Graph represents data prior to incorporating rolling averages. Days 0, 2, 12, 14, 16, & 17 are reanalyzed values.



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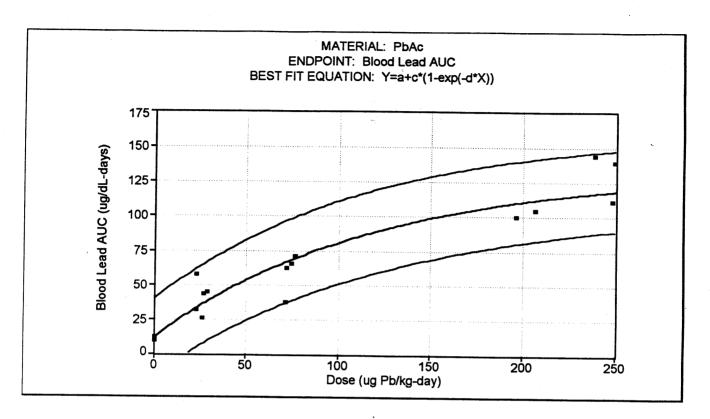


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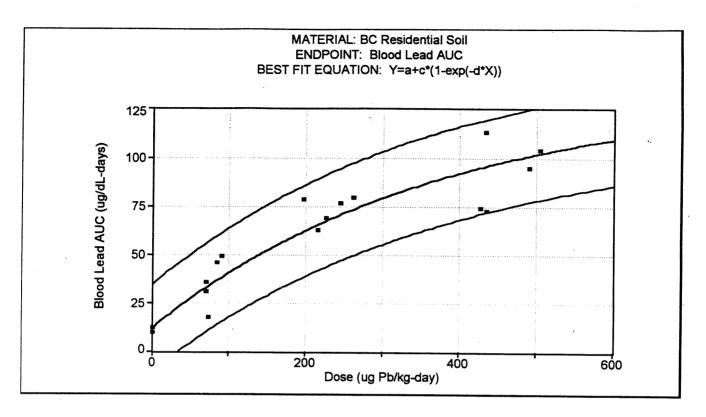
FIGURE A-5 BEST FIT CURVE WITH 95% PREDICTION INTERVALS*



Parameters	Value	Std. Error	95% Confid	dence Limits
а	11.8	fixed value	_	_
С	121.5	fixed value	_	
d	0.0083	0.0010	0.0062	0.0104

Adj	R^2	0.90)5

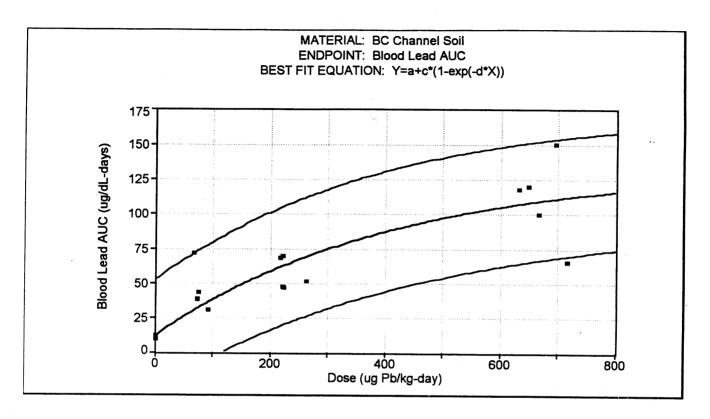
FIGURE A-6 BEST FIT CURVE WITH 95% PREDICTION INTERVALS*



Parameters	Value	Std. Error	95% Confid	lence Limits
а	11.8	fixed value		-
С	121.5	fixed value		
d	0.0027	0.0002	0.0022	0.0031

Adj	R^2	0.896

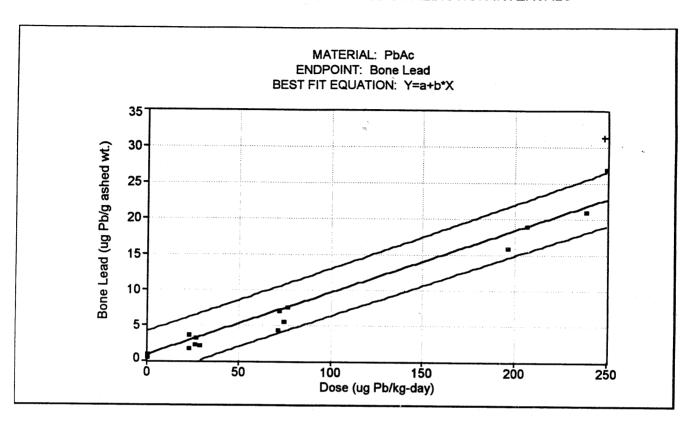
FIGURE A-7 BEST FIT CURVE WITH 95% PREDICTION INTERVALS*



Parameters	Value	Std. Error	95% Confid	lence Limits
а	11.8	fixed value	-	-
С	121.5	fixed value		
d	0.0024	0.0004	- 0.0016	0.0032

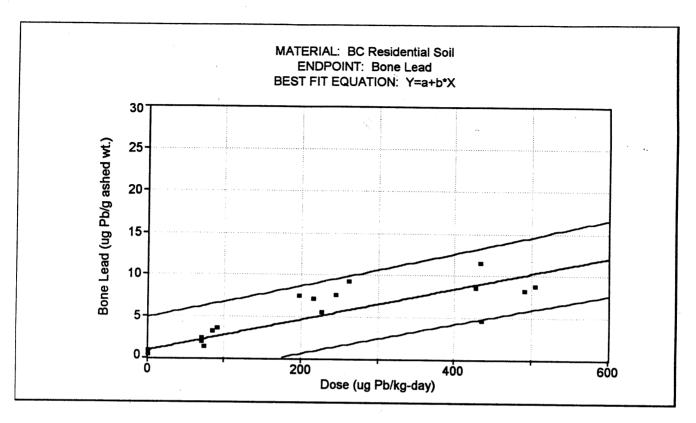
Adj R² 0.763

FIGURE A-8 BEST FIT CURVE WITH 95% PREDICTION INTERVALS*



Parameters	Value	Std. Error	95% Confid	lence Limits
а	0.812	fixed value	-	_
b	0.087	0.0035	0.080	0.095

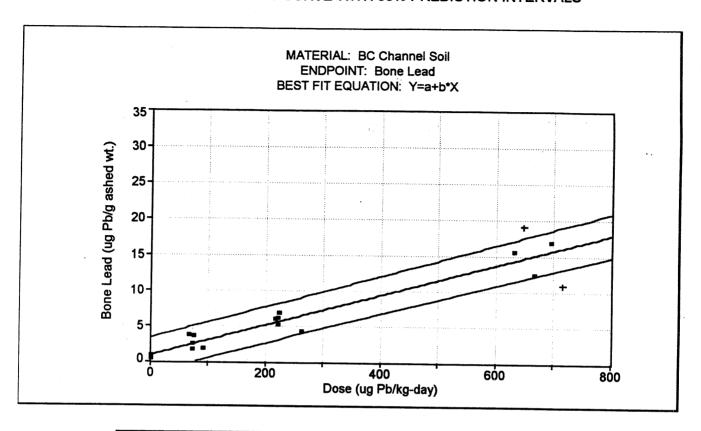
FIGURE A-9 BEST FIT CURVE WITH 95% PREDICTION INTERVALS*



Parameters	Value	Std. Error	95% Confi	dence Limits
а	0.812	fixed value	_	
b	0.019	0.0017	0.015	0.022

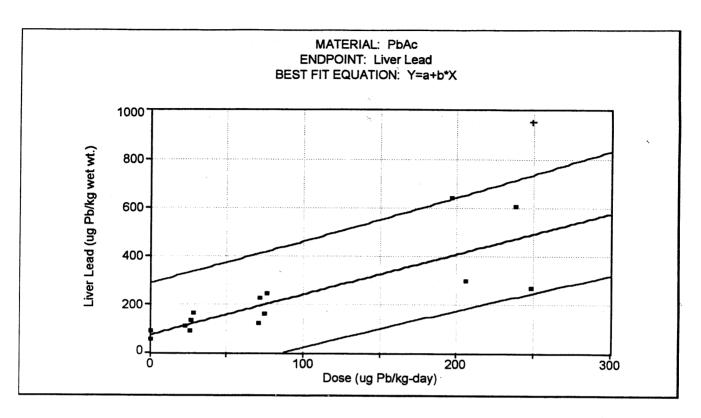
^{*}Generated using Table Curve 2D v. 3.0. Outliers represented by "+".

FIGURE A-10 BEST FIT CURVE WITH 95% PREDICTION INTERVALS*



Parameters	Value	Std. Error	95% Confid	ence Limits
а	0.812	fixed value		
b	0.021	0.0010	0.019	0.023

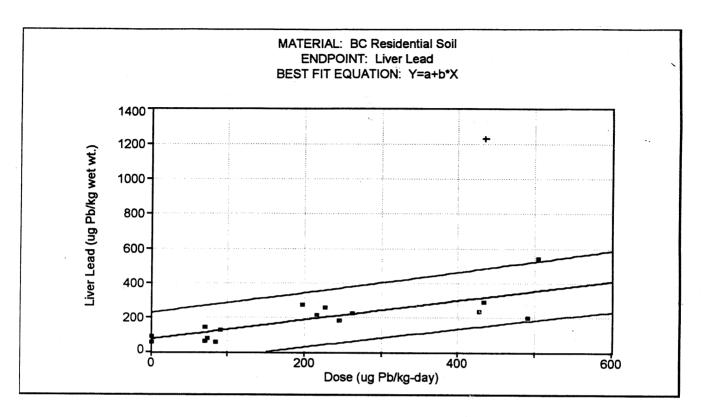
FIGURE A-11 BEST FIT CURVE WITH 95% PREDICTION INTERVALS*



Parameters	Value	Std. Error	95% Confid	dence Limits
а	72.0	fixed value	-	-
b	1.66	0.220	1.19	2.13

Adj R ²	0.670

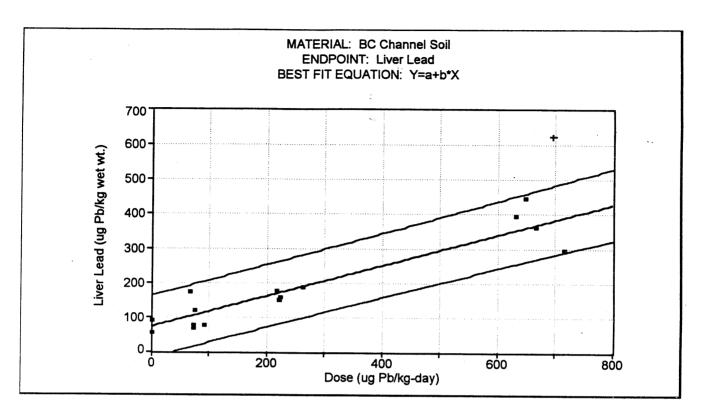
FIGURE A-12 BEST FIT CURVE WITH 95% PREDICTION INTERVALS*



Parameters	Value	Std. Error	95% Confid	lence Limits
а	72.0	fixed value	- 1	
b	0.550	0.0699	0.405	0.702

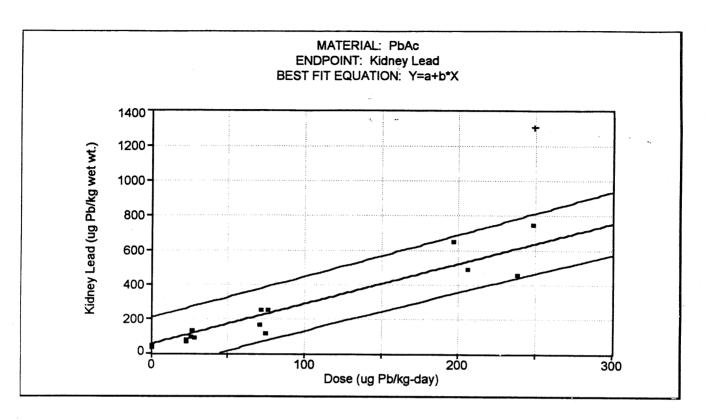
Adj	R^2	0.648

FIGURE A-13 BEST FIT CURVE WITH 95% PREDICTION INTERVALS*



Parameters	Value	Std. Error	95% Confidence Limits	
а	72.0	fixed value	· -	
b	0.440	0.0307	0.375	0.506

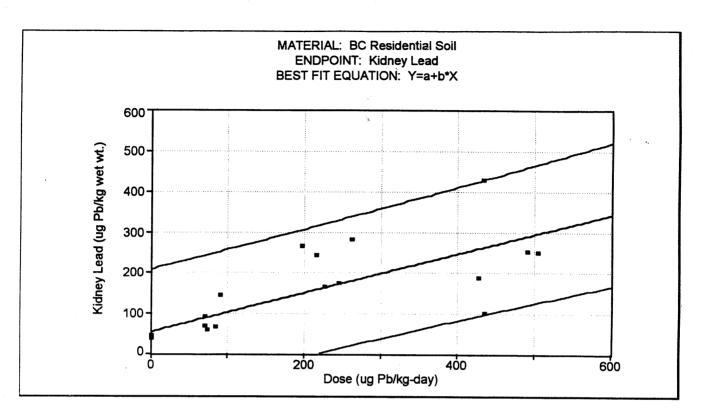
FIGURE A-14 BEST FIT CURVE WITH 95% PREDICTION INTERVALS*



Parameters	Value	Std. Error	95% Confidence Limits	
а	52.5	fixed value		
b	2.32	0.157	1.98	2.66

Adj	R^2	0.895

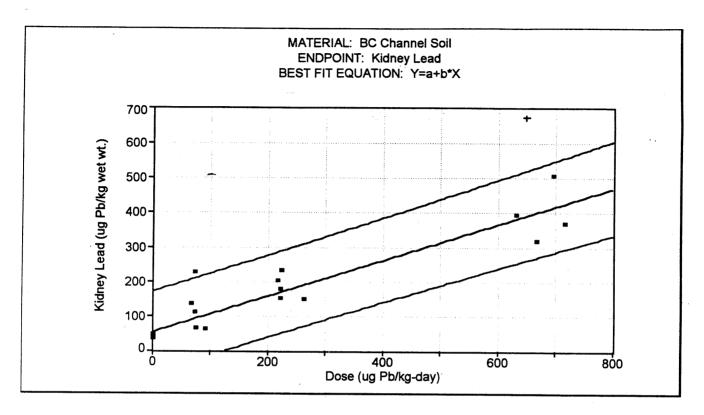
FIGURE A-15 BEST FIT CURVE WITH 95% PREDICTION INTERVALS*



Parameters	Value	Std. Error	or 95% Confidence Lir	
а	52.5	fixed value	_	-
b	0.481	0.0677	0.337	0.624

Ad	j R²	0.533

FIGURE A-16 BEST FIT CURVE WITH 95% PREDICTION INTERVALS*



Parameters	Value	Std. Error	95% Confidence Limit	
а	52.5	fixed value	_	
b	0.517	0.0394	0.434	0.601
	· Ł			
Adi R ²	0.829	**		

^{*}Generated using Table Curve 2D v. 3.0. Outliers represented by "+".

FIGURE A-17 Blood Lead Levels by Day - Phase II Experiment 2

