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**ESTIMATION OF  
RELATIVE BIOAVAILABILITY OF LEAD  
IN SOIL AND SOIL-LIKE MATERIALS USING  
*IN VIVO* AND *IN VITRO* METHODS**

Office of Solid Waste and Emergency Response  
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Washington, DC 20460

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### IN VIVO STUDIES

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### IN VITRO STUDIES

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## **REVIEWERS**

A draft of this report was provided to three independent experts for external peer review and comment. This satisfies the Agency's requirements for peer review. These reviewers were:

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## EXECUTIVE SUMMARY

### 1.0 INTRODUCTION

Reliable analysis of the potential hazard to children from ingestion of lead in environmental media depends on accurate information on a number of key parameters, including the rate and extent of lead absorption from each medium (“bioavailability”). Bioavailability of lead in a particular medium may be expressed either in absolute terms (absolute bioavailability, ABA) or in relative terms (relative bioavailability, RBA). For example, if 100 micrograms ( $\mu\text{g}$ ) of lead dissolved in drinking water were ingested and a total of 50  $\mu\text{g}$  were absorbed into the body, the ABA would be 0.50 (50%). Likewise, if 100  $\mu\text{g}$  of lead contained in soil were ingested and 30  $\mu\text{g}$  were absorbed into the body, the ABA for soil would be 0.30 (30%). If the lead dissolved in water was used as the frame of reference for describing the relative amount of lead absorbed from soil, the RBA would be  $0.30/0.50$ , or 0.60 (60%).

When reliable data are available on the absolute or relative bioavailability of lead in soil, dust, or other soil-like waste material at a site, this information can be used to improve the accuracy of exposure and risk calculations at that site. Based on available information in the literature on lead absorption in humans, the U.S. Environmental Protection Agency (U.S. EPA) estimates that relative bioavailability of lead in soil compared to water and food is about 60%. Thus, when the measured RBA in soil or dust at a site is found to be less than 60%, it may be concluded that exposures to and hazards from lead in these media at that site are probably lower than typical default assumptions. Conversely, if the measured RBA is higher than 60%, absorption of and hazards from lead in these media may be higher than usually assumed.

This report summarizes the results of a series of studies performed by scientists in U.S. EPA Region 8 to measure the RBA of lead in a variety of soil and soil-like test materials using both *in vivo* and *in vitro* techniques.

### 2.0 *IN VIVO* STUDIES

#### Basic Approach for Measuring RBA *In Vivo*

The *in vivo* method used to estimate the RBA of lead in a particular test material compared to lead in a reference material (lead acetate) is based on the principle that equal absorbed doses of lead will produce equal increases in lead concentration in the tissues of exposed animals. Stated another way, RBA is the ratio of oral doses that produce equal increases in tissue burden of lead.

Based on this, the technique for estimating lead RBA in a test material is to administer a series of oral doses of reference material (lead acetate) and test material (site soil) to groups of experimental animals, and to measure the increase in lead concentration in one or more tissues in the animals. For each tissue, the RBA is calculated by fitting an appropriate dose-response model to the data, and then solving the equations to find the ratio of doses that produce equal responses. The final estimate of RBA for the test material then combines the RBA estimates across the different tissues.

## Animal Exposure and Sample Collection

All animals used in this program were intact male swine approximately 5 to 6 weeks of age. In general, exposure occurred twice a day for 15 days. Most groups were exposed by oral administration, with one group usually exposed to lead acetate by intravenous injection.

Lead concentrations were measured in four different tissues: blood, liver, kidney, and bone. For blood, samples were collected from each animal at multiple times during the course of the study (*e.g.*, days 0, 1, 2, 3, 4, 6, 9, 12, and 15), and the blood concentration integrated over time (commonly referred to as “area under the curve” or AUC) was used as the measure of blood lead response. For liver, kidney, and bone, the measure of response was the concentration of lead in these tissues on day 15.

## Calculation of RBA

Based on testing several different types of dose-response models to the data, it was concluded that most dose-response curves for liver, kidney, and bone lead were well described by a linear model, and that most blood lead AUC data sets were well described by an exponential model:

### Liver, Kidney, Bone

$$C_{tissue} = a + b \cdot Dose$$

### Blood AUC

$$AUC = a + b \cdot [1 - \exp(-c \cdot Dose)]$$

where  $C_{tissue}$  is the concentration of lead in a given tissue;  $a$ ,  $b$ , and  $c$  are the terms of the mathematic equation used to describe the shape of the curve; and  $Dose$  is the total daily administered dose of lead ( $\mu\text{g}/\text{kg}\cdot\text{day}$ ).

Based on these models, RBA is calculated from the best model fits as follows:

$$RBA_{liver, kidney, bone} = \frac{b_{test\ material}}{b_{reference\ material}}$$

$$RBA_{blood\ AUC} = \frac{b_{test\ material}}{b_{reference\ material}}$$

## Results and Discussion

### *RBA Values for Various Test Materials*

Table ES-1 lists the 19 different materials tested in this program and shows the RBA values estimated using each of the four alternative endpoints (blood AUC, liver, kidney, bone).

Based on an analysis that indicated that each endpoint has approximately equal reliability, the point estimate for each test material is the mean of the four endpoint-specific values.

Inspection of these RBA point estimates for the different test materials reveals that there is a wide range of values across different samples, both within and across sites. For example, at the California Gulch site in Colorado, RBA estimates for different types of material range from about 6% (Oregon Gulch tailings) to 105% (Fe/Mn lead oxide sample). This wide variability highlights the importance of obtaining and applying reliable RBA data in order help to improve risk assessments for lead exposure.

***Correlation of RBA with Mineral Phase***

Available data are not yet sufficient to establish reliable quantitative estimates of RBA for each of the different mineral phases of lead that are observed to occur in the test materials. However, multivariate regression analysis between point estimate RBA values and mineral phase content of the different test materials allows a tentative rank ordering of the phases into three semi-quantitative tiers (low, medium, or high RBA), as follows:

Low Bioavailability	Medium Bioavailability	High Bioavailability
Fe(M) Sulfate Anglesite Galena Pb(M) Oxide Fe(M) Oxide	Lead Phosphate Lead Oxide	Cerussite Mn(M) Oxide

(M) = Metal

**3.0 IN VITRO STUDIES**

Measurement of lead RBA in animals has a number of potential benefits, but is also rather slow and costly and may not be feasible in all cases. It is mainly for this reason that a number of scientists have been working to develop alternative *in vitro* procedures that may provide a faster and less costly alternative for estimating the RBA of lead in soil or soil-like samples. These methods are based on the concept that the rate and/or extent of lead solubilization in gastrointestinal fluid is likely to be an important determinant of lead bioavailability *in vivo*, and most *in vitro* tests are aimed at measuring the rate or extent of lead solubilization in an extraction solvent that resembles gastric fluid. The fraction of lead which solubilizes in an *in vitro* system is referred to as *in vitro* bioaccessibility (IVBA).

**Description of the Method**

The IVBA extraction procedure is begun by placing 1.0 g of test substrate into a bottle and adding 100 mL of extraction fluid (0.4 M glycine, pH 1.5). This pH is selected because it is similar to the pH in the stomach of a fasting human. Each bottle is placed into a water bath adjusted to 37°C, and samples are extracted by rotating the samples end-over-end for 1 hour. After 1 hour, the bottles are removed, dried, and placed upright on the bench top to allow the soil

to settle to the bottom. A sample of supernatant fluid is removed directly from the extraction bottle into a disposable syringe and is filtered to remove any particulate matter. This filtered sample of extraction fluid is then analyzed for lead.

## Results

Table ES-2 summarizes the *in vitro* bioaccessibility results for the set of 19 different test materials evaluated under the Phase II program. As seen, IVBA values span a considerable range (min of 4.5%, max of 87%), with a mean of about 55%. This variability among test materials indicates that the rate and extent of solubilization of lead from the solid test material into the extraction fluid do depend on the attributes of the test material, and that IVBA may be a useful indication of absorption *in vivo* (see below).

### Comparison of *In Vivo* and *In Vitro* Results

In order for an *in vitro* bioaccessibility test system to be useful in predicting the *in vivo* RBA of a test material, it is necessary to establish empirically that a strong correlation exists between the *in vivo* and the *in vitro* results across many different samples. Figure ES-1 shows the best fit weighted linear regression correlation between the *in vivo* lead RBA estimates and the *in vitro* lead bioaccessibility estimates for each of the 19 test materials investigated during this program. The equation of the line is:

$$\text{RBA} = 0.878 \cdot \text{IVBA} - 0.028 \quad (r^2 = 0.924)$$

These results indicate that the *in vivo* RBA of lead in soil-like materials can be estimated by measuring the IVBA and using the equation above to calculate the expected *in vivo* RBA. Actual RBA values may be either higher or lower than the expected value, as indicated by the 95% prediction interval shown in Figure ES-1.

At present, it appears that this equation is likely to be widely applicable, having been found to hold true for a wide range of different soil types and lead phases from a variety of different sites. However, most of the samples tested have been collected from mining and milling sites, and it is plausible that some forms of lead that do not occur at this type of site might not follow the observed correlation. Thus, whenever a sample that contains an unusual and/or untested lead phase is evaluated by the *in vitro* bioaccessibility protocol, this should be identified as a potential source of uncertainty. In the future, as additional samples with a variety of new and different lead forms are tested by both *in vivo* and *in vitro* methods, the applicability of the method will be more clearly defined.

## 4.0 CONCLUSIONS

The data from the investigations performed under this program support the following main conclusions:

1. Juvenile swine are believed to be a useful model for the evaluation of lead absorption in children and provide a reliable system for measuring the RBA of lead in a variety of soil and soil-like materials.

2. Each of the four different endpoints employed in these studies (blood AUC, liver, kidney, bone) to estimate RBA *in vivo* yield reasonable data, and the best estimate of the RBA value for any particular sample is the average across all four endpoint-specific RBA values.
3. There are clear differences in the *in vivo* RBA of lead between different types of test material, ranging from near zero to close to 100%. Thus, knowledge of the RBA value for different types of materials at a site can be very important in improving lead risk assessments at a site.
4. Available data support the view that certain types of lead minerals are well-absorbed (*e.g.*, cerussite, manganese lead oxide), while other forms are poorly absorbed (*e.g.*, galena, anglesite). However, the data are not yet sufficient to allow reliable quantitative calculation or prediction of the RBA for a test material based on knowledge of the lead mineral content alone.
5. *In vitro* measurements of bioaccessibility performed using the protocol described in this report correlate well with *in vivo* measurements of RBA, at least for 19 materials tested under this program. At present, the results appear to be broadly applicable, although further testing of a variety of different lead forms is required to determine if there are exceptions to the apparent correlation.

**TABLE ES-1. SUMMARY OF ESTIMATED RBA VALUES FOR TEST MATERIALS**

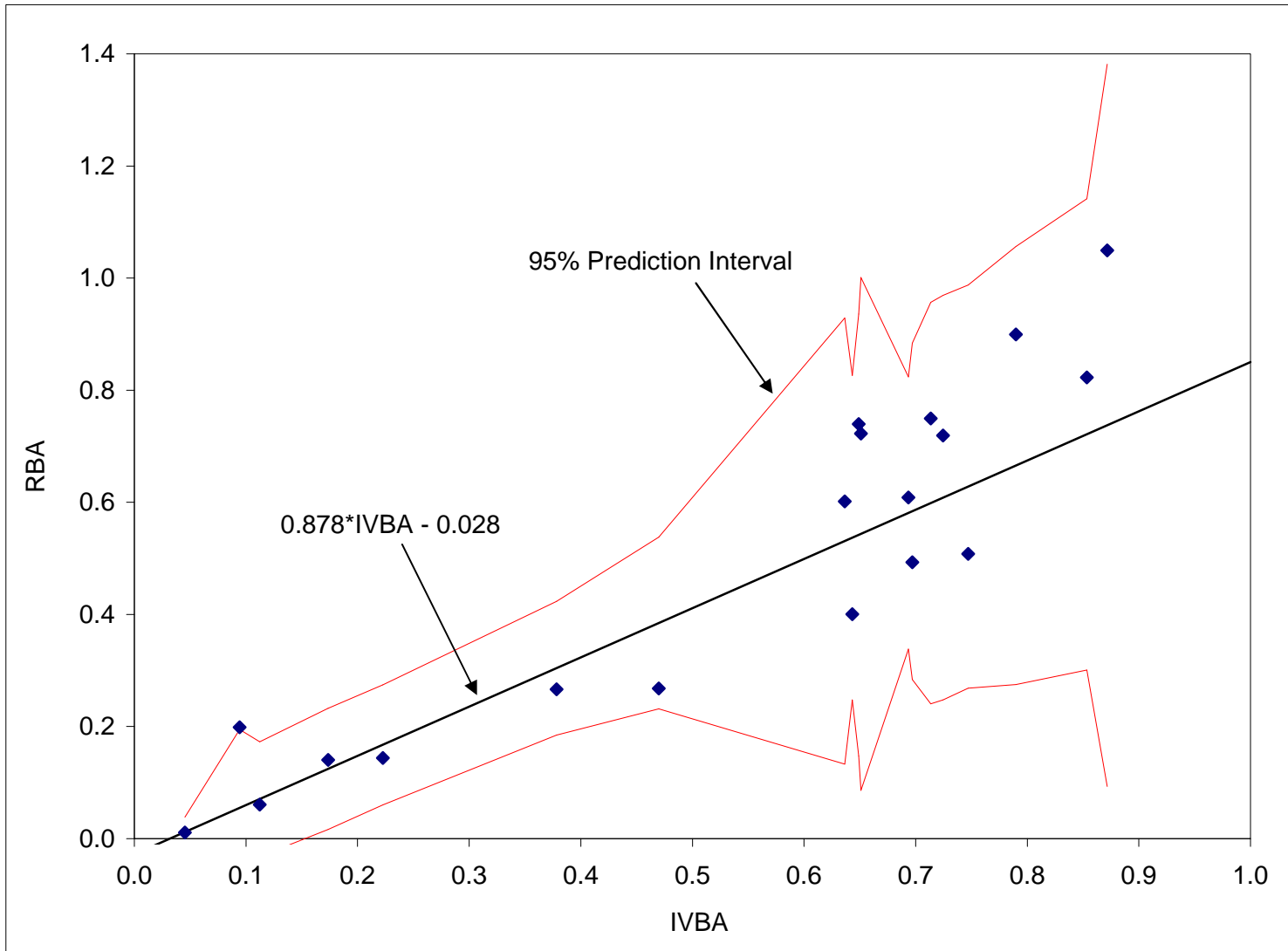
Experiment	Test Material	Blood AUC			Liver			Kidney			Femur			Point Estimate		
		RBA	LB	UB	RBA	LB	UB	RBA	LB	UB	RBA	LB	UB	RBA	LB	UB
2	Bingham Creek Residential	0.34	0.23	0.50	0.28	0.20	0.39	0.22	0.15	0.31	0.24	0.19	0.29	0.27	0.17	0.40
	Bingham Creek Channel Soil	0.30	0.20	0.45	0.24	0.17	0.34	0.27	0.19	0.37	0.26	0.21	0.31	0.27	0.19	0.36
3	Jasper County High Lead Smelter	0.65	0.47	0.89	0.56	0.42	0.75	0.58	0.43	0.79	0.65	0.52	0.82	0.61	0.43	0.79
	Jasper County Low Lead Yard	0.94	0.66	1.30	1.00	0.75	1.34	0.91	0.68	1.24	0.75	0.60	0.95	0.90	0.63	1.20
4	Murray Smelter Slag	0.47	0.33	0.67	0.51	0.33	0.88	0.31	0.22	0.46	0.31	0.23	0.41	0.40	0.23	0.64
	Jasper County High Lead Mill	0.84	0.58	1.21	0.86	0.54	1.47	0.70	0.50	1.02	0.89	0.69	1.18	0.82	0.51	1.14
5	Aspen Berm	0.69	0.54	0.87	0.87	0.58	1.39	0.73	0.46	1.26	0.67	0.51	0.89	0.74	0.48	1.08
	Aspen Residential	0.72	0.56	0.91	0.77	0.50	1.21	0.78	0.49	1.33	0.73	0.56	0.97	0.75	0.50	1.04
6	Midvale Slag	0.21	0.15	0.31	0.13	0.09	0.17	0.12	0.08	0.18	0.11	0.06	0.18	0.14	0.07	0.24
	Butte Soil	0.19	0.14	0.29	0.13	0.09	0.19	0.15	0.09	0.22	0.10	0.04	0.19	0.14	0.06	0.23
7	California Gulch Phase I Residential Soil	0.88	0.62	1.34	0.75	0.53	1.12	0.73	0.50	1.12	0.53	0.33	0.93	0.72	0.38	1.07
	California Gulch Fe/Mn PbO	1.16	0.83	1.76	0.99	0.69	1.46	1.25	0.88	1.91	0.80	0.51	1.40	1.05	0.57	1.56
8	California Gulch AV Slag	0.26	0.19	0.36	0.19	0.11	0.32	0.14	0.08	0.25	0.20	0.13	0.30	0.20	0.09	0.31
9	Palmerton Location 2	0.82	0.61	1.05	0.60	0.41	0.91	0.51	0.30	0.91	0.47	0.37	0.60	0.60	0.34	0.93
	Palmerton Location 4	0.62	0.47	0.80	0.53	0.37	0.79	0.41	0.25	0.72	0.40	0.32	0.52	0.49	0.29	0.72
11	Murray Smelter Soil	0.70	0.54	0.89	0.58	0.42	0.80	0.36	0.25	0.52	0.39	0.31	0.49	0.51	0.29	0.79
	NIST Paint	0.86	0.66	1.09	0.73	0.52	1.03	0.55	0.38	0.78	0.74	0.59	0.93	0.72	0.44	0.98
12	Galena-enriched Soil	0.01	0.00	0.02	0.02	0.00	0.04	0.01	0.00	0.02	0.01	-0.01	0.03	0.01	0.00	0.03
	California Gulch Oregon Gulch Tailings	0.07	0.04	0.13	0.11	0.04	0.21	0.05	0.02	0.09	0.01	-0.04	0.06	0.06	-0.01	0.15

LB = 5% Lower Confidence Bound  
 UB = 95% Upper Confidence Bound

**TABLE ES-2 IN VITRO BIOACCESSIBILITY VALUES**

Experiment	Test Material	Sample	In Vitro Bioaccessibility (%) (Mean ± Standard Deviation)
2	1	Bingham Creek Residential	47.0 ± 1.2
2	2	Bingham Creek Channel Soil	37.8 ± 0.7
3	1	Jasper County High Lead Smelter	69.3 ± 5.5
3	2	Jasper County Low Lead Yard	79.0 ± 5.6
4	1	Murray Smelter Slag	64.3 ± 7.3
4	2	Jasper County High Lead Mill	85.3 ± 0.2
5	1	Aspen Berm	64.9 ± 1.6
5	2	Aspen Residential	71.4 ± 2.0
6	1	Midvale Slag	17.4 ± 0.9
6	2	Butte Soil	22.3 ± 0.6
7	1	California Gulch Phase I Residential Soil	65.1 ± 1.5
7	2	California Gulch Fe/Mn PbO	87.2 ± 0.5
8	1	California Gulch AV Slag	9.4 ± 1.6
9	1	Palmerton Location 2	63.6 ± 0.4
9	2	Palmerton Location 4	69.7 ± 2.7
11	1	Murray Smelter Soil	74.7 ± 6.8
11	2	NIST Paint	72.5 ± 2.0
12	1	Galena-enriched Soil	4.5 ± 1.2
12	3	California Gulch Oregon Gulch Tailings	11.2 ± 0.9

**FIGURE ES-1. RELATION BETWEEN RBA AND IVBA**





## TABLE OF CONTENTS

1.0	INTRODUCTION .....	1
1.1	Overview.....	1
1.2	Using Bioavailability Data to Improve Exposure Calculations for Lead .....	2
1.3	Overview of U.S. EPA's Program to Study Lead Bioavailability in Animals .....	3
1.4	Overview of Methods for Estimating Lead RBA <i>In Vitro</i> .....	3
2.0	<i>IN VIVO</i> STUDIES .....	4
2.1	Basic Approach for Measuring RBA <i>In Vivo</i> .....	4
2.2	Animal Exposure and Sample Collection.....	4
2.3	Preparation of Biological Samples for Analysis.....	5
2.4	Data Reduction .....	5
2.5	Results and Discussion .....	6
2.5.1	Effect of Dosing on Animal Health and Weight.....	6
2.5.2	Time Course of Blood Lead Response .....	6
2.5.3	Dose-Response Patterns.....	7
2.5.4	Estimation of ABA for Lead Acetate.....	7
2.5.5	Estimation of RBA for Lead in Test Materials.....	8
2.5.6	Effect of Food .....	9
2.5.7	Correlation of RBA with Mineral Phase.....	10
2.5.8	Quality Assurance.....	12
3.0	<i>IN VITRO</i> STUDIES .....	14
3.1	Introduction.....	14
3.2	<i>In Vitro</i> Method .....	14
3.2.1	Sample Preparation .....	14
3.2.2	Apparatus .....	14
3.2.3	Selection of IVBA Test Conditions .....	15
3.2.4	Summary of Final Leaching Protocol .....	16
3.2.5	Analysis of Extraction Fluid for Lead .....	17
3.2.6	Quality Control/Quality Assurance .....	17
3.3	Results and Discussion .....	18
3.3.1	IVBA Values.....	18
3.3.2	Comparison with In Vivo Results.....	19
4.0	REFERENCES .....	21

## LIST OF TABLES

TABLE	TITLE
2-1	Typical Feed Composition
2-2	Typical <i>In Vivo</i> Study Design
2-3	Description of Phase II Test Materials
2-4	Relative Lead Mass of Mineral Phases Observed in Test Materials
2-5	Matrix Associations for Test Materials
2-6	Particle Size Distributions for Test Materials
2-7	Estimated RBA Values for Test Materials
2-8	Grouped Lead Phases
2-9	Curve Fitting Parameters for Oral Lead Acetate Dose-Response Curves
2-10	Reproducibility of RBA Measurements
3-1	<i>In Vitro</i> Bioaccessibility Values

## LIST OF FIGURES

FIGURE	TITLE
2-1	Average Rate of Body Weight Gain in Test Animals
2-2	Example Time Course of Blood Lead Response
2-3	Dose Response Curve for Blood Lead AUC
2-4	Dose Response Curve for Liver Lead Concentration
2-5	Dose Response Curve for Kidney Lead Concentration
2-6	Dose Response Curve for Femur Lead Concentration
2-7	Estimated Group-Specific RBA Values
2-8	Correlation of Duplicate Analyses
2-9	Results for CDC Blood Lead Check Samples
2-10	Interlaboratory Comparison of Blood Lead Results
3-1	<i>In Vitro</i> Bioaccessibility Extraction Apparatus
3-2	Effect of Temperature, Time, and pH on IVBA
3-3	Precision of <i>In Vitro</i> Bioaccessibility Measurements
3-4	Reproducibility of <i>In Vitro</i> Bioaccessibility Measurements
3-5	RBA vs. IVBA
3-6	Prediction Interval for RBA Based on Measured IVBA

## LIST OF APPENDICES

APPENDIX	TITLE
A	Evaluation of Juvenile Swine as a Model for Gastrointestinal Absorption in Young Children
B	Detailed Description of Animal Exposure
C	Detailed Methods of Sample Collection and Analysis
D	Detailed Methods for Data Reduction and Statistical Analysis
E	Detailed Dose-Response Data and Model Fitting Results
F	Detailed Lead Speciation Data for Test Materials

## ACRONYMS AND ABBREVIATIONS

°C	Degrees Celsius
µg	Microgram
µm	Micrometer
ABA	Absolute bioavailability
AF <sub>o</sub>	Oral absorption fraction
AIC	Akaike's Information Criterion
AUC	Area under the curve
cc	Cubic centimeter
CDC	Centers for Disease Control and Prevention
dL	Deciliter
g	Gram
GLP	Good Laboratory Practices
HCl	Hydrochloric acid
HDPE	High density polyethylene
ICP-AES	Inductively Coupled Plasma-Atomic Emission Spectrometry
ICP-MS	Inductively Coupled Plasma-Mass Spectrometry
IV	Intravenous
IVBA	<i>In vitro</i> bioaccessibility
kg	Kilogram
L	Liter
M	Molar
(M)	Metal
MDL	Method detection limit
mg	Milligram
mL	Milliliter
mm	Millimeter
NIST	National Institute of Standards and Testing
Pb	Lead
PbAc	Lead acetate
ppm	Parts per million
RBA	Relative bioavailability
RLM	Relative lead mass

**ACRONYMS AND ABBREVIATIONS**  
**(CONTINUED)**

rpm	Revolutions per minute
SOP	Standard operating procedure
SRM	Standard Reference Material
TAL	Target Analyte List
TCLP	Toxicity Characteristic Leaching Procedure
U.S. EPA	U.S. Environmental Protection Agency

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# ESTIMATION OF RELATIVE BIOAVAILABILITY OF LEAD IN SOIL AND SOIL-LIKE MATERIALS USING *IN VIVO* AND *IN VITRO* METHODS

## 1.0 INTRODUCTION

### 1.1 Overview

Reliable analysis of the potential hazard to children from ingestion of lead in the environment depends on accurate information on a number of key parameters, including 1) lead concentration in environmental media (*e.g.*, soil, dust, water, food, air, paint), 2) childhood intake rates of each medium, and 3) the rate and extent of lead absorption from each medium (“bioavailability”). Knowledge of lead bioavailability is important because the amount of lead which actually enters the body from an ingested medium depends on the physical-chemical properties of the lead and of the medium. For example, lead in soil may exist, at least in part, as poorly water-soluble minerals, 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 absorption (bioavailability) of lead when ingested. Thus, equal ingested doses of different forms of lead in different media may not be of equal health concern.

Bioavailability of lead in a particular medium may be expressed either in absolute terms (absolute bioavailability) or in relative terms (relative bioavailability).

Absolute Bioavailability (ABA) is the ratio of the amount of lead absorbed compared to the amount ingested:

$$ABA = \frac{\textit{Absorbed Dose}}{\textit{Ingested Dose}}$$

This ratio is also referred to as the oral absorption fraction ( $AF_o$ ).

Relative Bioavailability (RBA) is the ratio of the absolute bioavailability of lead present in some test material compared to the absolute bioavailability of lead in some appropriate reference material:

$$RBA = \frac{ABA_{\textit{test material}}}{ABA_{\textit{reference material}}}$$

Usually the form of lead used as reference material is a soluble compound such as lead acetate that is expected to completely dissolve when ingested.

For example, if 100 micrograms ( $\mu\text{g}$ ) of lead dissolved in drinking water were ingested and a total of 50  $\mu\text{g}$  entered the body, the ABA would be 50/100, or 0.50 (50%). Likewise, if

100 µg of lead contained in soil were ingested and 30 µg entered the body, the ABA for soil would be 30/100, or 0.30 (30%). If the lead dissolved in water were used as the frame of reference for describing the relative amount of lead absorbed from soil, the RBA would be 0.30/0.50, or 0.60 (60%).

For additional discussion about the concept and application of bioavailability, see Gibaldi and Perrier (1982), Goodman *et al.* (1990), Mushak (1991), and/or Klaassen *et al.* (1996).

## 1.2 Using Bioavailability Data to Improve Exposure Calculations for Lead

When reliable data are available on the bioavailability of lead in soil, dust, or other soil-like waste material at a site, this information can be used to improve the accuracy of exposure and risk calculations at that site. For example, the basic equation for estimating the site-specific ABA 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

$RBA_{soil}$  = Relative bioavailability of lead in soil

Based on available information in the literature on lead absorption in humans, the U.S. EPA estimates that the absolute bioavailability of lead from water and the diet is usually about 50% in children (U.S. EPA, 1994). Thus, when a reliable site-specific RBA value for soil is available, it may be used to estimate a site-specific absolute bioavailability in that soil, 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 U.S. EPA to be about 30% (U.S. EPA, 1994). Thus, the default RBA used by U.S. EPA for lead in soil and dust compared to lead in water is 30%/50%, or 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 exposures to and hazards from lead in these media at that site are probably lower than typical default assumptions. If the measured RBA is higher than 60%, absorption of and hazards from lead in these media may be higher than usually assumed.



### 1.3 Overview of U.S. EPA's Program to Study Lead Bioavailability in Animals

Scientists in U.S. EPA Region 8 have been engaged in a multi-year investigation of lead absorption from a variety of different environmental media, especially soils and solid wastes associated with mining, milling, and smelting sites. All studies in this program employed juvenile swine as the animal model. Juvenile swine were selected for use in these studies because they are considered to be a good physiological model for gastrointestinal absorption in children (see Appendix A).

Initial studies in the program (referred to as "Phase I") were performed by Dr. Robert Poppenga and Dr. Brad Thacker at Michigan State University (Weis *et al.*, 1995). The Phase I study designs and protocols were refined and standardized by Dr. Stan Casteel and his colleagues at the University of Missouri, Columbia, and this group has performed a large number of studies (collectively referred to as "Phase II") designed to further characterize the swine model and to quantify lead absorption from a variety of different test materials. Section 2 of this report summarizes the Phase II work performed at the University of Missouri.

### 1.4 Overview of Methods for Estimating Lead RBA *In Vitro*

Measurement of lead RBA in animals has a number of potential benefits, but is also rather slow and costly and may not be a feasible option in all cases. It is mainly for these reasons that a number of scientists have been working to develop *in vitro* procedures that may provide faster and less costly alternatives for estimating the RBA of lead in soil or soil-like samples (Miller and Schricker, 1982; Imber, 1993; Ruby *et al.*, 1993, 1996; Medlin, 1997; Rodriguez *et al.*, 1999). These methods are based on the concept that the rate and/or extent of lead solubilization in the gastrointestinal fluid are likely to be important determinants of lead bioavailability *in vivo*, and most *in vitro* tests are aimed at measuring the rate or extent of lead solubilization from soil into an extraction solvent that resembles gastric fluid. To help avoid confusion in nomenclature, the fraction of lead which solubilizes in an *in vitro* system is referred to as **bioaccessibility**, while the fraction that is absorbed *in vivo* is referred to as **bioavailability**.

More recently, development and testing of a simplified *in vitro* method for estimating lead bioaccessibility has been performed by Dr. John Drexler at the University of Colorado. Section 3 of this report describes this *in vitro* method and presents the results.

## 2.0 *IN VIVO* STUDIES

### 2.1 Basic Approach for Measuring RBA *In Vivo*

The basic approach for measuring lead absorption *in vivo* is to administer an oral dose of lead to test animals and measure the increase in lead level in one or more body compartments (blood, soft tissue, bone). In order to calculate the RBA value of a test material, the increase in lead in a body compartment is measured both for that test material and a reference material (lead acetate). Equal absorbed doses of lead (as  $\text{Pb}^{+2}$ ) are expected to produce approximately equal increases in concentration in tissues regardless of the source or nature of the ingested lead, so the RBA of a test material is calculated as the ratio of doses (test material and reference material) that produce equal increases in lead concentration in the body compartment. Note that this approach is general and yields reliable results for both non-linear and linear responses.

### 2.2 Animal Exposure and Sample Collection

All *in vivo* studies carried out during this program were performed as nearly as possible within the spirit and guidelines of Good Laboratory Practices (GLP: 40 CFR 792). Standard Operating Procedures (SOPs) for all of the methods are documented in a project notebook that is available through the administrative record.

#### Experimental Animals

All animals used in this program were intact male swine approximately 5 to 6 weeks of age. All animals were monitored to ensure they were in good health throughout the study.

#### Diet

In order to minimize lead exposure from the diet, animals were fed a special low-lead diet purchased from Zeigler Brothers, Inc. (Gardners, PA). The amount of feed provided was equal to 5% of the average body weight of animals on study. The feed was nutritionally complete and met all requirements of the National Institutes of Health–National Research Council (NRC, 1988). The typical nutritional components and chemical analysis of the feed are presented in Table 2-1. Periodic analysis of feed samples during this program indicated the mean lead level was less than 50  $\mu\text{g}/\text{kg}$ , corresponding to a daily intake of less than 2.5  $\mu\text{g}/\text{kg}$ -day.

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 was less than 2  $\mu\text{g}/\text{L}$ , corresponding to a daily intake of less than 0.2  $\mu\text{g}/\text{kg}$ -day.

## Exposure

Appendix B provides the details of animal exposure, including the design (number of dose groups, number of animals, dosing material, and dose levels) for all of the Phase II studies. A typical study design is summarized in Table 2-2. In general, groups of animals were exposed to a series of doses of either lead acetate or test material. For convenience, in this report, lead acetate is abbreviated as “PbAc.” Exposure occurred twice a day for 15 days. Most groups were exposed by oral administration, with one group usually exposed to lead acetate by intravenous (IV) injection via an indwelling venous catheter.

### **2.3 Preparation of Biological Samples for Analysis**

Samples of blood were collected from each animal at multiple times during the course of a study (*e.g.*, days 0, 1, 2, 3, 4, 6, 9, 12, and 15). On day 15, the animals were sacrificed and samples of liver, kidney, and bone (femur) were collected.

Appendix C presents details of biological sample collection, preparation, and analysis. In brief, samples of blood were diluted in “matrix modifier,” a solution recommended by the Centers for Disease Control and Prevention (CDC) for analysis of blood samples for lead (CDC, 2001). Samples of soft tissue (kidney, liver) were digested in hot acid, while samples of bone were ashed and then dissolved in acid.

Prepared samples were analyzed for lead using a Perkin Elmer Model 5100 graphite furnace atomic absorption spectrophotometer. All results from the analytical laboratory were reported in units of  $\mu\text{g Pb/L}$  of prepared sample. The detection limit was defined as three-times the standard deviation of a set of seven replicates of a low-lead sample (typically about 2 to 5  $\mu\text{g/L}$ ).

### **2.4 Data Reduction**

The basic data reduction task required to calculate an RBA for a test material is to fit mathematical equations to the dose-response data for both the test material and the reference material, and then solve the equations to find the ratio of doses that would be expected to yield equal responses. After testing a variety of different equations, it was found that nearly all blood lead AUC data sets could be well-fit using an exponential equation, while most data sets for liver, kidney, and bone lead could be well-fit using a linear equation:

$$\text{Linear:} \quad \text{Response} = a + b \cdot \text{Dose} \quad (1)$$

$$\text{Exponential:} \quad \text{Response} = a + b \cdot [1 - \exp(-c \cdot \text{Dose})] \quad (2)$$

where  $a$ ,  $b$ , and  $c$  are the parameters of the models, and  $\text{Dose}$  is the total daily administered dose of lead ( $\mu\text{g/kg-day}$ ).

Appendix D presents a detailed description of the curve-fitting methods and rationale, along with the methods used to quantify uncertainty in the RBA estimates for each test material. Detailed dose-response data and curve-fitting results are presented in Appendix E.

## **2.5 Results and Discussion**

### ***2.5.1 Effect of Dosing on Animal Health and Weight***

Lead exposure levels employed in this program are substantially below those which cause clinical symptoms in swine, and no evidence of treatment-related toxicity was observed in any dose group. All animals exposed to lead by the oral route remained in good health throughout each study, and the only clinical signs observed were characteristic of normal swine. However, animals implanted with indwelling venous catheters (used for intravenous injections) were subject to infection, and a few animals became quite ill. This was a problem mainly at the start of the program and tended to diminish as experience was gained on the best surgical and prophylactic techniques for catheter implantation. When an animal became ill, if good health could not be restored by administration of antibiotics, the animal was promptly removed from the study.

All animals were weighed every three days during the course of each study. The rate of weight gain (kg/day) averaged across all Phase II studies is illustrated in Figure 2-1. As shown, animals typically gained about 0.3 to 0.5 kg/day, and the rate of weight gain was generally comparable in all groups.

### ***2.5.2 Time Course of Blood Lead Response***

The time course of the blood lead response to oral or intravenous exposure may be thought of on two different time scales: the short-term “spike” that occurs immediately following an exposure, and the longer-term trend toward “steady-state” blood lead following repeated exposures.

Initial studies performed during Phase I of this program revealed that a single oral dose of lead acetate causes blood lead levels rise to a peak about two hours post-ingestion, and then decrease over the course of 12 to 24 hours to a near steady-state value (Weis *et al.*, 1993). Although knowledge of these rapid kinetics is important in fully understanding the toxicokinetics of lead, investigations in Phase II of this program focused mainly on quantifying the slower rise in “steady-state” blood lead following repeated exposures. To achieve this goal, all blood lead samples were collected 17 hours after lead exposure, at a time when the rate of change in blood lead due to the preceding dose is minimal.

Figure 2-2 presents an example graph of the time course of “steady-state” blood lead levels following repeated oral and intravenous exposure to lead acetate. As seen, blood lead levels begin below the detection limit (usually about 1 µg/dL) and stay very low in control animals throughout the course of the study. In animals exposed to lead acetate, blood lead values begin to rise within 1 to 2 days and tend to flatten out to a near steady-state in about 7 to 10 days.

### 2.5.3 Dose-Response Patterns

Figures 2-3 to 2-6 present the dose response patterns observed for blood, liver, kidney, and bone (femur) following repeated oral or intravenous exposure to lead acetate. For blood, the endpoint is the area under the blood lead vs time curve (AUC). For femur, kidney, and liver, the endpoint is the concentration in the tissue at the time of sacrifice. The data for intravenous exposure are based on a single study<sup>1</sup>, while the patterns for oral exposure are based on the combined results across all studies performed during Phase II.

As seen, there is substantial variability in response between individuals (both within and between studies), and this variability tends to increase as dose (and response) increases. This pattern of increasing variance in response is referred to as heteroscedasticity, and is accounted for in the model-fitting procedure through the use of weighted least squares regression (see Appendix D). Despite the variability in response, the regression analyses indicate that the dose response pattern is typically non-linear for blood lead AUC following both oral and intravenous exposure, but is approximately linear in both cases for liver, kidney, and bone lead (see Table D1). This pattern of dose-response relationships suggests that, at least over the dose range tested in this program, absorption of lead from the gastrointestinal tract of swine is linear, and that the non-linearity observed in blood lead AUC response is due to some sort of saturable binding in the blood.

### 2.5.4 Estimation of ABA for Lead Acetate

Inspection of Figures 2-3 to 2-6 reveals that each of the measured responses to ingested lead acetate is smaller than the response for intravenously injected lead acetate. These data were used to calculate the absolute bioavailability of ingested lead acetate using the data reduction approach described in Section 2.4. The results are summarized below:

Measurement Endpoint	Estimated ABA of PbAc
Blood AUC	0.10 ± 0.02
Liver	0.16 ± 0.05
Kidney	0.19 ± 0.05
Femur	0.14 ± 0.03

Although the four different measurement endpoints do not agree precisely, it seems clear that the absolute bioavailability of lead acetate in juvenile swine is about 15% ± 4%. Although data are limited, results from balance studies in infants and young children (age 2 weeks to 8 years) suggest that lead absorption is probably about 42% to 53% (Alexander *et al.*, 1974; Ziegler *et al.*, 1978). If so, lead absorption in juvenile swine is apparently lower than for young

<sup>1</sup> Most studies in Phase II utilized only one intravenous dose level (100 µg/kg-day) and, hence, do not provide dose-response data. Study 8 included three intravenous exposure levels (25, 50, and 100 µg/kg-day); the data from this study are shown in Figures 2-3 to 2-6.

humans. Although the reason for this apparent difference is not known, it is important to note that even if swine do absorb less lead than children under similar dosing conditions, this does not invalidate the swine as an animal model for estimating relative bioavailability of lead in different test materials.

### ***2.5.5 Estimation of RBA for Lead in Test Materials***

#### Characterization of Test Materials

Table 2-3 describes the Phase II test materials for which RBA was measured in this program and provides the analytical results for lead. Data on other Target Analyte List (TAL) metals, if available, are provided in Appendix F. As seen, 17 different samples from eight different sites were investigated, along with one sample of paint flakes mixed with clean soil and one sample of finely-ground native galena mixed with clean soil. Prior to analysis and dosing, all samples were dried (<40°C) and sieved, and only materials which passed through a 60-mesh screen (corresponding to particles smaller than about 250 µm) were used. This range of particle sizes was selected because the U.S. EPA considers particles less than about 250 µm to be the most likely to adhere to the hands and be ingested by hand-to-mouth contact, especially in young children (U.S. EPA, 2000).

Each sample of test material that was evaluated in the swine bioassay program was thoroughly characterized with regard to mineral phase, particle size distribution, and matrix association using electron microprobe analysis. Detailed results for each test material are presented in Appendix F, and the results are summarized in Tables 2-4 to 2-6.

Table 2-4 lists the different lead phases observed in the test materials, and gives the relative lead mass (RLM) for each phase in each test material. The RLM is the estimated percentage of the total lead in a sample that is present in a particular phase. Of the 22 different phases detected in one or more samples, 9 are very minor, with RLM values no higher than 2% in any sample. However, 13 of the phases occur at concentrations that could contribute significantly to the overall bioavailability of the sample (RLM >10%). It should be noted that a particle is classified as “slag” only if the particle is glassy or vitreous in nature. Inclusions or other non-vitreous grains of lead-bearing material are classified according to their mineral content and are not classified as slag particles (even if they are observed in bulk samples that are referred to as “slag”).

Table 2-5 summarizes information on the degree to which lead-bearing grains in each sample are partially or entirely liberated (i.e., exposed to gastric fluids when ingested) or included (i.e., fully enclosed or encased in mineral or vitreous matrices). Data are presented both on a particle frequency basis and on the basis of relative lead mass. As seen, the majority of lead-bearing particles in most samples are partially or entirely liberated, although the tailings sample from Oregon Gulch is a clear exception.

Table 2-6 summarizes data on the distribution (frequency) of particle sizes (measured as the longest dimension) in each sample. For convenience, the data presented are for liberated particles only (Appendix F contains the data for all particles). As seen, most samples contain a

range of particle sizes, often with the majority of the particles being less than 50 µm. (Remember that all samples were sieved to isolate particles less than 250 µm before analysis.)

### RBA Results for Test Materials

Detailed model fitting results and RBA calculations for each test material are presented in Appendix E and are summarized in Table 2-7.

As shown in Table 2-7, there are four independent estimates of RBA (based on blood AUC, liver, kidney, and bone) for each test material. Conceptually, each of these four values is an independent estimate of the RBA for the test material, so the estimates from all four endpoints need to be combined to yield a final point estimate for each test material. As discussed in Appendix D (Section 4.7), an analysis of the relative statistical reliability of each endpoint (as reflected in the average coefficient of variation in RBA values derived from each endpoint) suggests that the four endpoint-specific RBA values are all approximately equally reliable. Based on this, the point estimate for a test material is the simple average across the four endpoint-specific RBA values. The resulting point estimate values are presented in the far right portion of Table 2-7. Uncertainty bounds around the point estimates were derived as described in Appendix D (Section 4.7).

Inspection of these point estimates for the different test materials reveals that there is a wide range of values across different samples, both within and across sites. For example, at the California Gulch site in Colorado, RBA estimates for different types of material range from about 6% (Oregon Gulch tailings) to about 105% (Fe/Mn lead oxide sample). This wide variability highlights the importance of obtaining and applying reliable RBA data to site-specific samples in order help to improve risk assessments for lead exposure.

### **2.5.6 Effect of Food**

Studies in humans indicate that lead absorption is reduced by the presence of food in the stomach (Garber and Wei, 1974; U.S. EPA, 1996). The mechanism by which the presence of food leads to decreased absorption is not certain, but may be related to competition between lead and calcium for active and/or passive uptake sites in the gastrointestinal epithelium (Diamond, 2000). Because of the potential inhibitory effects of food, all of the studies performed during this program were designed to estimate the RBA of lead associated with a fasting state, each dose being administered to animals no less than six hours after the last feeding. In order to investigate how the presence of food in the stomach might influence absorption, a study was performed to measure the absorption of lead acetate given two hours before feeding and compare that to the absorption of lead acetate given either at the time of feeding or two hours after feeding. The results, expressed using the absorption two hours before feeding as the frame of reference, are summarized below:

Measurement Endpoint	Ratio of PbAc Absorption Given With Food Compared to PbAc Given Without Food	Ratio of PbAc Absorption Given 2 Hours After Feeding Compared to PbAc Given Without Food
Blood Lead AUC	0.39 ± 0.05	0.40 ± 0.06
Liver Lead	0.86 ± 0.24	0.58 ± 0.16
Kidney Lead	0.72 ± 0.26	0.73 ± 0.27
Bone Lead	0.35 ± 0.05	0.33 ± 0.05
Point Estimate	0.58 ± 0.28	0.51 ± 0.22

These findings indicate that uptake of lead is reduced by close to half (RBA point estimates are 51% and 58%) when the lead is administered to animals along with food compared to when it is administered on an empty stomach. This effect appears to endure for at least two hours after feeding, which is consistent with the results of a gastric emptying time study in juvenile swine that indicated that food is held in the stomach for up to four hours after eating (Casteel *et al.*, 1998).

This study, which utilized lead acetate only, does not provide information about the effect of food on the absorption of lead ingested in a solid form such as soil. However, it is suspected that the magnitude of the decrease in absorption caused by food is likely to be at least as large as that observed for lead acetate, and perhaps even larger. This is because food may influence not only the absorption of soluble lead ions, but might also tend to decrease the rate and extent of lead solubilization from soil by tending to increase the pH of gastric fluids.

### 2.5.7 Correlation of RBA with Mineral Phase

In principle, each unique combination of phase, size, and matrix association constitutes a unique mineralogical form of lead, and each unique form could be associated with a unique RBA that is the inherent value for that “type” of lead. If so, then the concentrated-weighted average RBA value for a sample containing a mixture of different types of lead is given by:

$$RBA_{sample} = \sum_{i=1}^n \sum_{j=1}^s \sum_{k=1}^m C_{i,j,k} \cdot RBA_{i,j,k} \quad (3)$$

where:

- $RBA_{sample}$  = Observed RBA of lead in a sample
- $C_{i,j,k}$  = Fraction of total lead in phase  $i$  of size  $j$  and matrix association  $k$
- $RBA_{i,j,k}$  = RBA of lead in phase  $i$  of size  $j$  and matrix association  $k$
- $n$  = Number of different lead phase categories
- $s$  = Number of different size categories
- $m$  = Number of different matrix association categories



If the number of different lead phases which can exist in the environment is on the order of 20, the number of size categories is on the order of five, and the number of matrix association categories is two (included and liberated), then the total number of different “types” of lead is on the order of 200. Because measured RBA data are available from this study for only 19 different samples, it is clearly impossible (with the present data set) to estimate type-specific RBA values for each combination of phase, size, and matrix association. Therefore, in order to simplify the analysis process, it was assumed that the measured RBA value for a sample was dominated by the liberated mineral phases present, and the effect of included materials or of particle size were not considered. That is, the data were analyzed according to the following model:

$$RBA_{sample} = \sum_{i=1}^n C_{i,liberated} \cdot RBA_{i,liberated} \quad (4)$$

Because 22 different phases were identified and only 19 different samples were analyzed, it was necessary to reduce the number of phases to a smaller number so that regression analysis could be performed. Therefore, the different phases were grouped into ten categories as shown in Table 2-8. These groups were based on professional judgment regarding the expected degree of similarity between members of a group, along with information on the relative abundance of each phase (see Table 2-4).

The total lead mass in each group was calculated by summing the relative lead mass for each individual component in the group. As noted above, only the lead mass in partially or entirely liberated particles was included in the sum.

Group-specific RBA values were estimated by fitting the grouped data to the model (equation 4) using minimization of squared errors. Two different options were employed. In the first option, each parameter (group-specific RBA) was fully constrained to be between zero and one, inclusive. In the second option, each parameter was partially constrained to be greater than or equal to zero. Because Group 10 contains only phases which are present in relatively low levels, an arbitrary coefficient of 0.5 was assumed for this group and the coefficient was not treated as a fitting parameter.

The resulting estimates of the group-specific RBA values are shown in Figure 2-7. As seen, there is a wide range of group-specific RBA values, with equal results being obtained by both methods of constraint. It is important to stress that these group-specific RBA estimates are derived from a very limited data set (nine independent parameter estimates based on only 19 different measurements), so the group-specific RBA estimates are inherently uncertain. In addition, both the measured sample RBA values and the relative lead mass in each phase are subject to additional uncertainty. Therefore, the group-specific RBA estimates should not be considered to be highly precise, and calculation of a quantitative sample-specific RBA value from these estimates is not appropriate. Rather, it is more appropriate to consider the results of this study as sufficient to support only semi-quantitative rank-order classification of phase-specific RBA values, as follows:

Low Bioavailability (RBA <0.25)	Medium Bioavailability (RBA = 0.25-0.75)	High Bioavailability (RBA >0.75)
Fe(M) Sulfate Anglesite Galena Fe(M) Oxide Pb(M) Oxide	Lead Oxide Lead Phosphate	Cerussite Mn(M) Oxide

(M) = Metal

As noted above, the estimates apply only to particles that are liberated, not those that are included.

### 2.5.8 *Quality Assurance*

A number of steps were taken throughout each of the studies in this program to assess and document the quality of the data that were collected. These steps are summarized below.

#### Duplicates

A randomly selected set of about 5% of all blood and tissue samples generated during each study were submitted to the laboratory in a blind fashion for duplicate analysis. Figure 2-8 plots the results for blood (Panel A) and for liver, kidney, and bone (Panel B). As seen, there was good intra-laboratory reproducibility between duplicate samples for both blood and tissues, with both linear regression lines having a slope near 1.0, an intercept near zero, and an R<sup>2</sup> value near 1.00.

#### Standards

The CDC provides blood lead “check samples” that may be used for use in quality assurance programs for blood lead studies. Three types of check samples (nominal concentrations of 1.7 µg/dL, 4.8 µg/dL, and 14.9 µg/dL) were used in these studies. Each day that blood samples were collected from experimental animals, several check samples of different concentrations were also prepared and submitted for analysis in random order and in a blind fashion. The results (averaged across all studies) are plotted in Figure 2-9. As seen, the analytical results obtained for the check samples were generally in good agreement with the expected value at all three concentrations, with an overall mean of 1.4 µg/L for the low standards (nominal concentration of 1.7 µg/L), 4.3 µg/L for the middle standard (nominal concentration of 4.8 µg/L), and 14.5 µg/L for the high standards (nominal concentration of 14.9 µg/L).

#### Interlaboratory Comparison

In each study, an interlaboratory comparison of blood lead analytical results was performed by sending a set of about 15 to 20 randomly selected whole blood samples to CDC for blind independent preparation and analysis. The results are plotted in Figure 2-10. As seen, the results of analyses by U.S. EPA’s laboratory are generally similar to those of CDC, with a mean inter-sample difference (U.S. EPA minus CDC) of 0.07 µg/dL. The slope of the best-fit straight line through the data is 0.84, indicating that the concentration values estimated by the U.S. EPA

laboratories tended to be about 15% lower than those estimated by CDC. The reason for this apparent discrepancy between the U.S. EPA laboratory and the CDC laboratory is not clear, but might be related to differences in sample preparation techniques. 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 material dose-response curves are biased by the same factor, then the biases cancel in the calculation of the ratio.

### Reproducibility of RBA Estimates

As with any study involving animals, there may be substantial variability between animals within each dose group, and there may also be variability in observed responses to exposure across different studies. Because each study involved administration of a standard series of doses of lead acetate, the data for lead acetate can be used to assess the stability and reproducibility of the swine model. Table 2-9 lists the best-fit parameters for the best-fit curves for oral lead acetate dose responses for blood AUC, liver, kidney, and bone in each study, and for all studies combined. As seen, the variability (expressed as the between-study coefficient of variation) is generally on the order of 25 to 50% for the  $b$  and  $c$  parameters, with somewhat higher variability in the intercept parameter ( $a$ ). This degree of between-study variability is not unexpected for a study in animals and emphasizes the need for generating the dose-response curve for the reference material within each study. The source of the between-study variation is likely to be mainly a consequence of variation in animals between different groups (different dams, different ages, different weights), although a possible contribution from other variables (time of year, laboratory personnel, etc.) cannot be excluded.

Because RBA calculations are based on the within-study ratio of responses between a test material and reference material, the variability in response between studies may be at least partly cancelled in the calculation of the RBA. The most direct way to test this hypothesis is to compare RBA estimates for the same material that has been tested in two different studies. To date, only two test materials have been tested more than once. The results are shown in Table 2-10 and are summarized below.

For the Palmerton Location 2 sample (tested twice in Phase II), agreement is moderately good between the two studies for the blood AUC and kidney endpoints and for the point estimate, although there is relatively low agreement for the liver and bone endpoints. For the Residential Soil Composite from the California Gulch Superfund site (tested once by the University of Michigan during Phase I and again by the University of Missouri during Phase II), agreement is good for all four endpoints, with between-study differences of less than 20%. These differences are generally similar to the within-study confidence bounds, which are typically in the 10% to 20% range. Taken together, these studies support the view that the *in vivo* RBA assay has acceptable inter-study and inter-laboratory reproducibility.

## 3.0 *IN VITRO* STUDIES

### 3.1 Introduction

Measurement of lead RBA in animals using the approach described above has a number of potential benefits, but is also rather slow and costly and may not be feasible in all cases. It is mainly for this reason that a number of scientists have been working to develop alternative *in vitro* procedures that may provide a faster and less costly alternative for estimating the RBA of lead in soil or soil-like samples. These methods are based on the concept that the rate and/or extent of lead solubilization in gastrointestinal fluid is likely to be an important determinant of lead bioavailability *in vivo*, and most *in vitro* tests are aimed at measurement of the rate or extent of lead solubilization in an extraction solvent that resembles gastric fluid. The fraction of lead which solubilizes in an *in vitro* system is referred to as *in vitro* bioaccessibility (IVBA), which may then be used as an indicator of *in vivo* RBA.

Background on the development and validation of *in vitro* methods for estimating lead bioaccessibility can be found in Imber (1993), Ruby *et al.* (1993, 1996), and Medlin (1997).

### 3.2 *In Vitro* Method

The method described in this report represents a simplification from most preceding approaches. The method was designed to be fast, easy, and reproducible, and some test conditions were adjusted to yield results that best correlated with *in vivo* measurements of lead bioavailability. The detailed standard operating procedure (SOP) is presented below; additional information on this procedure may be obtained from <http://www.colorado.edu/geolsci/legs>.

#### 3.2.1 *Sample Preparation*

All test materials tested in the bioaccessibility protocol were identical to the test materials administered to swine in the *in vivo* studies described above. As noted previously, soils were prepared by drying (<40°C) and sieving to <250 µm. The <250-µm size fraction was used because this particle size is representative of that which adheres to children's hands. Samples were thoroughly mixed prior to use to ensure homogenization. All samples were archived after the study completion and retained for further analysis for a period of six months.

#### 3.2.2 *Apparatus*

The main piece of equipment used for this procedure is the extraction device shown in Figure 3-1. An electric motor (the same motor as is used in the Toxicity Characteristic Leaching Procedure, or TCLP) drives a flywheel, which in turn drives a Plexiglass block situated inside a temperature-controlled water bath. The Plexiglass block contains ten 5-centimeter holes with stainless steel screw clamps, each of which is designed to hold a 125-mL wide-mouth high density polyethylene (HDPE) bottle. The water bath was filled such that the extraction bottles were completely immersed. Temperature in the water bath was maintained at 37±2 °C using an immersion circulator heater. The 125-mL HDPE bottles had air-tight screw-cap seals, and care

was taken to ensure that the bottles did not leak during the extraction procedure. All equipment was properly cleaned, acid washed, and rinsed with deionized water prior to use.

### 3.2.3 Selection of IVBA Test Conditions

The dissolution of lead from a test material into the extraction fluid depends on a number of variables including extraction fluid composition, temperature, time, agitation, solid/fluid ratio, and pH. These parameters were evaluated to determine the optimum values for maximizing sensitivity, stability, and the correlation between *in vitro* and *in vivo* values.

All reagents were free of lead and the final fluid was tested to confirm that lead concentrations were less than one-fourth the project required detection limit (PRDL) of 10 µg/L (i.e., less than 2 µg/L lead in the final fluid). Cleanliness of all materials used to prepare and/or store the extraction fluid and buffer is essential; all glassware and equipment used to prepare standards and reagents were properly cleaned, acid washed, and triple-rinsed with deionized water prior to use.

Extraction Fluid: The extraction fluid selected for this procedure was 0.4 M glycine (free base, reagent grade glycine in deionized water), adjusted to a pH of 1.50±0.05 at 37°C using trace metal grade concentrated hydrochloric acid (HCl). Most previous *in vitro* test systems have employed a more complex fluid intended to simulate gastric fluid. For example, Medlin (1997) used a fluid that contained pepsin and a mixture of citric, malic, lactic, acetic, and hydrochloric acids. When the bioaccessibility of a series of test substances were compared using 0.4 M glycine buffer (pH 1.5) with and without the inclusion of these enzymes and metabolic acids, no significant difference was observed (p=0.196). This indicates that the simplified buffer employed in the procedure is appropriate, even though it lacks some constituents known to be present in gastric fluid.

Temperature: In order to evaluate the effect of the extraction temperature, seventeen substrates were analyzed (generally in triplicate) at both 37°C and 20°C. The results are shown in Figure 3-2 (Panel A). In some cases, temperature had little effect, but in three cases the amount of lead solubilized was more than 20% greater at 37°C than at 20°C, and in two cases it was more than 20% less. Because the results appeared to depend on temperature in at least some cases, a temperature of 37°C was selected because this is approximately the temperature of gastric fluid *in vivo*.

Extraction Time: The time that ingested material is present in the stomach (i.e., stomach-emptying time) is about one hour for a child, particularly when a fasted state is assumed (see Appendix A). To investigate the effect of extraction time on lead solubilization, 11 substrates were extracted for periods of 1, 2, or 4 hours. The results are shown in Figure 3-2 (Panel B). As seen, in most cases, the amount of lead solubilized was approximately constant over time, with only one substrate (test material 6) showing a variation that exceeded the method precision. Therefore, an extraction time of one hour was selected for the final method. In a subsequent test (data not shown), it was found that allowing the bottles to stand at room temperature for up to 4 hours after rotation at 37°C caused no significant variation (<10%) in lead concentration.

**pH:** Human gastric pH values tend to range from about 1 to 4 during fasting (see Appendix A). Previous studies have used stomach phase pH values between 1.0 and 2.5 for their *in vitro* experiments (Ruby *et al.*, 1993; CBR, 1993; Gasser *et al.*, 1996; Buckley, 1997; Medlin, 1997; Rodriguez *et al.*, 1999; Mercier *et al.*, 2000). To evaluate the effect of pH on lead bioaccessibility, 24 substrates were analyzed at pH values of 1.5, 2.5, or 3.5. As shown in Figure 3-2 (Panel C), the amount of lead solubilized is strongly pH-dependent, with the highest extraction at pH 1.5. For the subset of test materials for which *in vivo* RBA had been estimated at that time (N = 13), the empiric correlation between IVBA and *in vivo* RBA was slightly better at pH 1.5 ( $\rho = 0.919$ ) than at pH 2.5 ( $\rho = 0.881$ ). Thus, a pH of 1.5 was selected for use in the final protocol.

**Agitation:** If the test material is allowed to accumulate at the bottom of the extraction apparatus, the effective surface area of contact between the extraction fluid and the test material may be reduced, and this may influence the extent of lead solubilization. Depending on which theory of dissolution is relevant (Nernst and Brunner, 1904, or Dankwerts, 1951), agitation will greatly affect either the diffusion layer thickness or the rate of production of fresh surface. Previous workers have noted problems associated with both stirring and argon bubbling methods (Medlin and Drexler, 1995; Drexler, 1997). Although no systematic comparison of agitation methods was performed, an end-over-end method of agitation was chosen to best simulate the complex peristaltic motion of the gastrointestinal system.

**Solid/Fluid Ratio and Mass of Test Material:** A solid to fluid ratio of 1/100 (mass per unit volume) was chosen to reduce the effects of metal dissolution that were noted by Sorenson *et al.* (1971) when lower ratios (1/5 and 1/25) were used. Tests using Standard Reference Materials showed no significant variation (within  $\pm 1\%$  of control means) in the fraction of lead extracted with soil masses as low as 0.2 gram (g) per 100 mL. However, use of low masses of test material could introduce variability due to small scale heterogeneity in the sample and/or to weighing errors. Therefore, the final method employs 1.0 g of test material in 100 mL of extraction fluid.

In special cases, the mass of test material may need to be less than 1.0 g to avoid the potential for saturation of the extraction solution. Tests performed using lead acetate, lead oxide, and lead carbonate indicate that if the bulk concentration of a test material containing these relatively soluble forms of lead exceeds approximately 50,000 ppm, the extraction fluid becomes saturated at 37°C and, upon cooling to room temperature and below, lead chloride crystals will precipitate. To prevent this from occurring, the concentration of lead in the test material should not exceed 50,000 ppm, or the mass of the test material should be reduced to  $0.50 \pm 0.01$  g.

### **3.2.4 Summary of Final Leaching Protocol**

The extraction procedure began by placing  $1.00 \pm 0.05$  g of sieved test material and  $100 \pm 0.5$  mL of the buffered extraction fluid (0.4 M glycine, pH 1.5) into a 125-mL wide-mouth HDPE bottle. Care was taken to ensure that static electricity did not cause soil particles to adhere to the lip or outside threads of the bottle; if necessary, an antistatic brush was used to eliminate static electricity prior to adding the test substrate. The bottle was tightly sealed and then shaken or inverted to ensure that there was no leakage and that no soil was caked on the bottom of the bottle.

Each bottle was placed into the modified TCLP extractor (water temperature  $37 \pm 2^\circ\text{C}$ ). Samples were extracted by rotating the samples end-over-end at  $30 \pm 2$  rpm for 1 hour. After 1 hour, the bottles were removed, dried, and placed upright on the bench top to allow the soil to settle to the bottom. A 15-mL sample of supernatant fluid is removed directly from the extraction bottle into a disposable 20-cc syringe. After withdrawal of the sample into the syringe, a Luer-Lok attachment fitted with a  $0.45\text{-}\mu\text{m}$  cellulose acetate disk filter (25 mm diameter) is attached, and the 15 mL aliquot of fluid is filtered through the attachment to remove any particulate matter. This filtered sample of extraction fluid is then analyzed for lead, as described below. If the total time elapsed for the extraction process exceeds 90 minutes, the test must be repeated.

As noted above, in some cases (mainly slags), the test material can increase the pH of the extraction buffer, and this could influence the results of the bioaccessibility measurement. To guard against this, the pH of the fluid was measured at the end of the extraction step (just after a sample was withdrawn for filtration and analysis). If the pH was not within 0.5 pH units of the starting pH (1.5), the sample was re-analyzed. If the second test also resulted in an increase in pH of greater than 0.5 units, it was apparent that the test material was buffering the solution. In these cases, the test was repeated using manual pH adjustment during the extraction process, stopping the extraction at 5, 10, 15, and 30 minutes and manually adjusting the pH down to pH 1.5 at each interval by drop-wise addition of HCl.

### ***3.2.5 Analysis of Extraction Fluid for Lead***

The filtered samples of extraction fluid were stored in a refrigerator at  $4^\circ\text{C}$  until they were analyzed (within 1 week of extraction). Once received by the laboratory, all media were maintained under standard chain-of-custody. The samples were analyzed for lead by ICP-AES or ICP-MS (U.S. EPA Method 6010 or 6020, U.S. EPA 1986). The method detection limit (MDL) in extraction fluid was calculated to be around  $19\ \mu\text{g/L}$  for Method 6010 and typically  $0.1\text{-}0.3\ \mu\text{g/L}$  for Method 6020.

### ***3.2.6 Quality Control/Quality Assurance***

Quality assurance for the extraction procedure consisted of the following quality control samples:

- Reagent Blank — extraction fluid analyzed once per batch.
- Bottle Blank — extraction fluid only (no test soil) run through the complete procedure at a frequency of 1 in 20 samples (minimum of 1 per batch).
- Blank Spike — extraction fluid spiked at  $10\ \text{mg/L}$  lead, and run through the complete procedure at a frequency of 1 in 20 samples (minimum of 1 per batch).
- Matrix Spikes — a subsample of each material used for duplicate analyses was used as a matrix spike. The spike was prepared at  $10\ \text{mg/L}$  lead and run through the extraction procedure at a frequency of 1 in 10 samples (minimum of 1 per batch).

- Duplicate Sample — duplicate sample extractions were performed on 1 in 10 samples (minimum of 1 per batch).
- Control Soil — National Institute of Standards and Testing (NIST) Standard Reference Material (SRM) 2711 (Montana Soil) was used as a control soil. The SRM was analyzed at a frequency of 1 in 20 samples (minimum 1 per batch).

Control limits for these quality control samples were as follows:

Analysis	Frequency	Control Limits
Reagent blank	once per batch	<25 µg/L lead
Bottle blank	5%*	<50 µg/L lead
Blank spike (10 mg/L)	5%*	85-115% recovery
Matrix spike (10 mg/L)	10%*	75-125% recovery
Duplicate sample	10%*	±20% RPD
Control soil (NIST 2711)	5%*	±10% RPD

RPD = Relative percent difference

\*Minimum of once per batch

To evaluate the precision of the *in vitro* bioaccessibility extraction protocol, approximately 67 replicate analyses of both NIST SRM 2710 and 2711 were conducted over a period of several months. Results are shown in Figure 3-3. As seen, both standards yield highly reproducible results, with a mean coefficient of variation of about 6%.

### 3.3 Results and Discussion

#### 3.3.1 IVBA Values

Table 3-1 summarizes the *in vitro* bioaccessibility results for the set of 19 different test materials evaluated under the Phase II program. Each value is the mean and standard deviation of three independent measurements performed at the University of Colorado at Boulder.

Figure 3-4 shows the results of an inter-laboratory comparison of results for these test materials. The participating laboratories included ACZ Laboratories Inc.; University of Colorado at Boulder; U.S. Bureau of Reclamation Environmental Research Chemistry Laboratory; and National Exposure Research Laboratory. As seen in the figure, within-laboratory variability (as shown by the error bars) is quite small (average ≤2%) and there is very good agreement between laboratories (average difference of 2 to 3%, range of difference from 1 to 9%).



### 3.3.2 Comparison with In Vivo Results

In order for an *in vitro* bioaccessibility test system to be useful in predicting the *in vivo* RBA of a test material, it is necessary to establish empirically that a strong correlation exists between the *in vivo* and the *in vitro* results across many different samples. A scatter plot of the *in vivo* RBA and *in vitro* bioaccessibility data from this program is shown in Figure 3-5. The Spearman rank order correlation coefficient between the paired RBA and IVBA point estimates is 0.896 ( $p < 0.001$ ) and the Pearson product moment correlation coefficient is 0.917 ( $p < 0.001$ ), indicating that there is a statistically significant positive correlation between IVBA and RBA.

Several different mathematical models were tested to describe the relation between RBA and IVBA, including linear, power, and exponential. All fitting was done using weighted least square regression, as detailed in Appendix D. The results are summarized below:

Model	R <sup>2</sup>	AIC
Linear: $RBA = a + b \cdot IVBA$	0.924	-30.46
Power: $RBA = a + b \cdot IVBA^c$	0.931	-29.92
2-Parameter Exponential: $RBA = a + b \cdot \exp(IVBA)$	0.936	-33.02
3-Parameter Exponential: $RBA = a + b \cdot \exp(c \cdot IVBA)$	0.936	-31.11

As seen, all of the models fit the data reasonably well, with the two exponential models fitting slightly better than the linear model. However, as discussed in Appendix D, the difference in quality of fit between linear and exponential models is not judged to be meaningful, and the linear model is selected as the preferred model at present. As more data become available in the future, the relationship between IVBA and RBA will be reassessed and the best-fit model form will be reconsidered and revised if needed.

Because there is measurement error not only in RBA but also in IVBA, linear fitting was also performed taking the error in both RBA and IVBA into account. There was nearly no difference in fit, so the results of the weighted linear regression were selected for simplicity. This decision may be revisited as more data become available. Based on this decision, the currently preferred model is:

$$RBA = 0.878 \cdot IVBA - 0.028$$

It is important to recognize that use of this equation to calculate RBA from a given IVBA measurement will yield the “typical” RBA value expected for a test material with that IVBA, and the true RBA may be somewhat different (either higher or lower). The best fit line and the 95% prediction interval for this data set are shown in Figure 3-6.

#### Applicability of the IVBA-RBA Model

At present, it appears that the equation relating IVBA to RBA should be widely applicable, having been found to hold true for a wide range of different soil types and lead

phases from a variety of different sites. However, most of the samples tested have been collected from mining and milling sites, and it is plausible that some forms of lead that do not occur at this type of site might not follow the observed correlation. Thus, whenever a sample containing an unusual and/or untested lead phase is evaluated by the IVBA protocol, this should be identified as a potential source of uncertainty. In the future, as additional samples with a variety of new and different lead forms are tested by both *in vivo* and *in vitro* methods, the applicability of the method will be more clearly defined.

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## **TABLES**

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**TABLE 2-1. TYPICAL FEED COMPOSITION**

Nutrient Name	Amount
Protein	20.1021%
Arginine	1.2070%
Lysine	1.4690%
Methionine	0.8370%
Met+Cys	0.5876%
Tryptophan	0.2770%
Histidine	0.5580%
Leucine	1.8160%
Isoleucine	1.1310%
Phenylalanine	1.1050%
Phe+Tyr	2.0500%
Threonine	0.8200%
Valine	1.1910%
Fat	4.4440%
Saturated Fat	0.5590%
Unsaturated Fat	3.7410%
Linoleic 18:2:6	1.9350%
Linoleic 18:3:3	0.0430%
Crude Fiber	3.8035%
Ash	4.3347%
Calcium	0.8675%
Phos Total	0.7736%
Available Phosphorous	0.7005%
Sodium	0.2448%
Potassium	0.3733%

Nutrient Name	Amount
Chlorine	0.1911%
Magnesium	0.0533%
Sulfur	0.0339%
Manganese	20.4719 ppm
Zinc	118.0608 ppm
Iron	135.3710 ppm
Copper	8.1062 ppm
Cobalt	0.0110 ppm
Iodine	0.2075 ppm
Selenium	0.3196 ppm
Nitrogen Free Extract	60.2340%
Vitamin A	5.1892 kIU/kg
Vitamin D3	0.6486 kIU/kg
Vitamin E	87.2080 IU/kg
Vitamin K	0.9089 ppm
Thiamine	9.1681 ppm
Riboflavin	10.2290 ppm
Niacin	30.1147 ppm
Pantothenic Acid	19.1250 ppm
Choline	1019.8600 ppm
Pyridoxine	8.2302 ppm
Folacin	2.0476 ppm
Biotin	0.2038 ppm
Vitamin B12	23.4416 ppm

Feed obtained from and nutritional values provided by Zeigler Bros., Inc

**TABLE 2-2. TYPICAL *IN VIVO* STUDY DESIGN**

Dose Group	Dose Material	Exposure Route	Target Dose $\mu\text{g Pb/kg-day}$	Number of Animals
1	None	Oral	--	2-5
2	Lead Acetate	Oral	25	5
3			75	5
4			225	5
5	Test Material 1	Oral	75	5
6			225	5
7			625	5
8	Test Material 2	Oral	75	5
9			225	5
10			625	5
11	Lead Acetate	Intravenous	100	5-8

**TABLE 2-3. DESCRIPTION OF PHASE II TEST MATERIALS**

Experiment	Sample Designation	Site	Sample Description	Lead Concentration (ppm) <sup>1</sup>
2	Bingham Creek Residential	Kennecott NPL Site, Salt Lake City, Utah	Soil composite of samples containing less than 2500 ppm lead; collected from a residential area (Jordan View Estates) located along Bingham Creek in the community of West Jordan, Utah.	1,590
	Bingham Creek Channel Soil	Kennecott NPL Site, Salt Lake City, Utah	Soil composite of samples containing 3000 ppm or greater of lead; collected from a residential area (Jordan View Estates) located along Bingham Creek in the community of West Jordan, Utah.	6,330
3	Jasper County High Lead Smelter	Jasper County, Missouri Superfund Site	Soil composite collected from an on-site location.	10,800
	Jasper County Low Lead Yard	Jasper County, Missouri Superfund Site	Soil composite collected from an on-site location.	4,050
4	Murray Smelter Slag	Murray Smelter Superfund Site, Murray City, Utah	Composite of samples collected from areas where exposed slag existed on site.	11,700
	Jasper County High Lead Mill	Jasper County, Missouri Superfund Site	Soil composite collected from an on-site location.	6,940
5	Aspen Berm	Smuggler Mountain NPL Site, Aspen, Colorado	Composite of samples collected from the Racquet Club property (including a parking lot and a vacant lot).	14,200
	Aspen Residential	Smuggler Mountain NPL Site, Aspen, Colorado	Composite of samples collected from residential properties within the study area.	3,870
6	Midvale Slag	Midvale Slag NPL Site, Midvale, Utah	Composite of samples collected from a water-quenched slag pile in Midvale Slag Operable Unit 2.	8,170
	Butte Soil	Silver Bow Creek/Butte Area NPL Site, Butte, Montana	Soil composite collected from waste rock dumps in Butte Priority Soils Operable Unit (BPSOU).	8,530
7	California Gulch Phase I Residential Soil	California Gulch NPL Site, Leadville, Colorado	Soil composite collected from residential properties within Leadville.	7,510
	California Gulch Fe/Mn PbO	California Gulch NPL Site, Leadville, Colorado	Soil composite collected from near the Lake Fork Trailer Park located southwest of Leadville near the Arkansas River.	4,320
8	California Gulch AV Slag	California Gulch NPL Site, Leadville, Colorado	Sample collected from a water-quenched slag pile on the property of the former Arkansas Valley (AV) Smelter, located just west of Leadville.	10,600
9	Palmerton Location 2	New Jersey Zinc NPL Site, Palmerton, Pennsylvania	Soil composite collected from on-site.	3,230
	Palmerton Location 4	New Jersey Zinc NPL Site, Palmerton, Pennsylvania	Soil composite collected from on-site.	2,150
11	Murray Smelter Soil	Murray Smelter Superfund Site, Murray City, Utah	Soil composite collected from on-site.	3,200
	NIST Paint	--	A mixture of approximately 5.8% NIST Standard Reference Material (SRM) 2589 and 94.2% low lead soil (< 50 ppm) collected in Leadville, Colorado. NIST SRM 2589, composed of paint collected from the interior surfaces of houses in the US, contains a nominal lead concentration of 10% (100,000 ppm); the material is powdered with more than 99% of the material being less than 100 um in size.	8,350
12	Galena-enriched Soil	--	A mixture of approximately 1.2% galena and 98.8% low lead soil (< 50 ppm) that was collected in Leadville, Colorado. The added galena consisted of a mineralogical (i.e., native) crystal of pure galena that was ground and sieved to obtain fine particles smaller than about 65 um.	11,200
	California Gulch Oregon Gulch Tailings	California Gulch NPL Site, Leadville, Colorado	A composite of tailings samples collected from the Oregon Gulch tailings impoundment.	1,270

<sup>1</sup> Samples were analyzed for lead by inductively coupled plasma-atomic emission spectrometry (ICP-AES) in accord with USEPA Method 200.7.

**TABLE 2-4. RELATIVE LEAD MASS OF MINERAL PHASES OBSERVED IN TEST MATERIALS**

Experiment:	2		3		4		5		6		7		8		9		11		12	
Phase	Bingham Creek Residential	Bingham Creek Channel Soil	Jasper County High Lead Smelter	Jasper County Low Lead Yard	Murray Smelter Slag	Jasper County High Lead Mill	Aspen Berm	Aspen Residential	Midvale Slag	Butte Soil	Cal. Gulch Phase I Residential Soil	Cal. Gulch Fe/Mn PbO	Cal. Gulch AV Slag	Palmerton Location 2	Palmerton Location 4	Murray Smelter Soil	NIST Paint	Galena-enriched Soil	Cal. Gulch Oregon Gulch Tailings	
Anglesite		28%	1%	0.5%	1.0%	2%	7%	1%		36%	10%		2%	6%	4%		1%			
As(M)O																0.003%				
Calcite			0.2%			0.1%														
Cerussite	2%	0.3%	32%	81%	1.1%	57%	62%	64%	4%	0.3%	20%		1%			14%	55%			
Clay			0.018%	0.003%		0.017%	0.1%			0.1%		0.01%		0.03%	0.13%					
Fe-Pb Oxide	6%	3%	14%	2%	2%	10%	9%	7%	0.3%	7%	6%	8%	51%	2%	2%	0.13%				
Fe-Pb Sulfate	22%	30%	3%	1%	0.3%	1%	5%	5%	0.1%	20%	6%	3%	0.3%	1%		0.6%				
Galena		9%		8%	9%	3%	12%	17%	6%	12%	2%		3%			20%		100%	100%	
Lead Barite		0.04%				0.01%	0.06%			0.007%	0.15%	0.14%		1%	0.1%					
Lead Organic		0.3%					0.03%	0.03%			0.11%	0.11%	1%							
Lead Oxide			0.09%		69%	7%										27%	44%			
Lead Phosphate	50%	26%	21%	6%		7%	1%	1%		3.6%	30%	15%		24%	1%					
Lead Silicate				0.04%		0.5%					1.9%	0.8%			1.4%					
Lead Vanadate											0.1%	0.4%			18%					
Mn-Pb Oxide	18%	2%	2%	2%	0.8%	9%	4%	5%		20.2%	22%	72%		66%	66%					
Native Lead			22%		0.7%	2%			15%											
Pb(M)O					4%				26%						7%	3%				
Pb-As Oxide	2%	1%		0.15%	6%				33%		0.1%		31%			29%				
PbO-Cerussite											1%									
Slag			4%		7%	1%			16%		1%		10%			6%				
Sulfosalts									0.4%											
Zn-Pb Silicate					0.03%										2%					

(M) = Metal

**TABLE 2-5. MATRIX ASSOCIATIONS FOR TEST MATERIALS**

Experiment	Test Material	Particle Frequency		Relative Lead Mass	
		Liberated	Included	Liberated	Included
2	Bingham Creek Residential	100%	0%	100%	0%
	Bingham Creek Channel Soil	100%	0%	100%	0%
3	Jasper County High Lead Smelter	81%	19%	76%	24%
	Jasper County Low Lead Yard	100%	0%	94%	6%
4	Murray Smelter Slag	87%	13%	77%	23%
	Jasper County High Lead Mill	96%	4%	93%	7%
5	Aspen Berm	86%	14%	93%	8%
	Aspen Residential	98%	2%	94%	6%
6	Midvale Slag	91%	9%	77%	23%
	Butte Soil	91%	9%	91%	9%
7	California Gulch Phase I Residential Soil	79%	21%	65%	35%
	California Gulch Fe/Mn PbO	98%	2%	100%	0%
8	California Gulch AV Slag	78%	22%	80%	20%
9	Palmerton Location 2	100%	0%	100%	0%
	Palmerton Location 4	79%	21%	89%	11%
11	Murray Smelter Soil	80%	20%	70%	30%
	NIST Paint	100%	0%	100%	0%
12	Galena-enriched Soil	100%	0%	100%	0%
	California Gulch Oregon Gulch Tailings	2%	98%	5%	95%

**TABLE 2-6. PARTICLE SIZE DISTRIBUTIONS FOR TEST MATERIALS**

Experiment	Test Material	Particle Size (µm)								
		<5	5-9	10-19	20-49	50-99	100-149	150-199	200-249	>250
2	Bingham Creek Residential	38%	22%	19%	16%	4%	2%	0%	0%	0%
	Bingham Creek Channel Soil	66%	13.6%	10%	6.1%	3%	1%	0%	0%	0%
3	Jasper County High Lead Smelter	44%	19%	8%	8%	9%	9%	2%	1%	1%
	Jasper County Low Lead Yard	29%	20%	21%	20%	8%	3%	0%	0%	0%
4	Murray Smelter Slag	14%	13%	15%	6%	20%	24%	4%	3%	0%
	Jasper County High Lead Mill	23%	21%	22%	19%	9%	6%	1%	1%	0%
5	Aspen Berm	27%	19%	22%	17%	8%	6%	1%	1%	0%
	Aspen Residential	38%	35%	12%	8%	4%	2%	0%	0%	0%
6	Midvale Slag	6%	1%	3%	4%	20%	29%	18%	13%	5%
	Butte Soil	23%	15%	14%	23%	14%	9%	2%	1%	0%
7	California Gulch Phase I Residential Soil	24%	9%	18%	22%	15%	9%	1%	1%	1%
	California Gulch Fe/Mn PbO	26%	19%	24%	17%	10%	4%	0%	0%	0%
8	California Gulch AV Slag	19%	8%	8%	5%	9%	19%	10%	13%	9%
9	Palmerton Location 2	26%	23%	25%	18%	6%	1%	0%	0%	0%
	Palmerton Location 4	25%	15%	21%	25%	13%	2%	0%	0%	0%
11	Murray Smelter Soil	23%	10%	29%	17%	6%	8%	3%	3%	1%
	NIST Paint	76%	4%	6%	8%	6%	0%	0%	0%	0%
12	Galena-enriched Soil	48%	2%	4%	41%	4%	0%	0%	0%	0%
	California Gulch Oregon Gulch Tailings	85%	8%	6%	0%	0%	0%	0%	0%	0%

**TABLE 2-7. ESTIMATED RBA VALUES FOR TEST MATERIALS**

Experiment	Test Material	Blood AUC			Liver			Kidney			Femur			Point Estimate		
		RBA	LB	UB	RBA	LB	UB	RBA	LB	UB	RBA	LB	UB	RBA	LB	UB
2	Bingham Creek Residential	0.34	0.23	0.50	0.28	0.20	0.39	0.22	0.15	0.31	0.24	0.19	0.29	0.27	0.17	0.40
	Bingham Creek Channel Soil	0.30	0.20	0.45	0.24	0.17	0.34	0.27	0.19	0.37	0.26	0.21	0.31	0.27	0.19	0.36
3	Jasper County High Lead Smelter	0.65	0.47	0.89	0.56	0.42	0.75	0.58	0.43	0.79	0.65	0.52	0.82	0.61	0.43	0.79
	Jasper County Low Lead Yard	0.94	0.66	1.30	1.00	0.75	1.34	0.91	0.68	1.24	0.75	0.60	0.95	0.90	0.63	1.20
4	Murray Smelter Slag	0.47	0.33	0.67	0.51	0.33	0.88	0.31	0.22	0.46	0.31	0.23	0.41	0.40	0.23	0.64
	Jasper County High Lead Mill	0.84	0.58	1.21	0.86	0.54	1.47	0.70	0.50	1.02	0.89	0.69	1.18	0.82	0.51	1.14
5	Aspen Berm	0.69	0.54	0.87	0.87	0.58	1.39	0.73	0.46	1.26	0.67	0.51	0.89	0.74	0.48	1.08
	Aspen Residential	0.72	0.56	0.91	0.77	0.50	1.21	0.78	0.49	1.33	0.73	0.56	0.97	0.75	0.50	1.04
6	Midvale Slag	0.21	0.15	0.31	0.13	0.09	0.17	0.12	0.08	0.18	0.11	0.06	0.18	0.14	0.07	0.24
	Butte Soil	0.19	0.14	0.29	0.13	0.09	0.19	0.15	0.09	0.22	0.10	0.04	0.19	0.14	0.06	0.23
7	California Gulch Phase I Residential Soil	0.88	0.62	1.34	0.75	0.53	1.12	0.73	0.50	1.12	0.53	0.33	0.93	0.72	0.38	1.07
	California Gulch Fe/Mn PbO	1.16	0.83	1.76	0.99	0.69	1.46	1.25	0.88	1.91	0.80	0.51	1.40	1.05	0.57	1.56
8	California Gulch AV Slag	0.26	0.19	0.36	0.19	0.11	0.32	0.14	0.08	0.25	0.20	0.13	0.30	0.20	0.09	0.31
9	Palmerton Location 2	0.82	0.61	1.05	0.60	0.41	0.91	0.51	0.30	0.91	0.47	0.37	0.60	0.60	0.34	0.93
	Palmerton Location 4	0.62	0.47	0.80	0.53	0.37	0.79	0.41	0.25	0.72	0.40	0.32	0.52	0.49	0.29	0.72
11	Murray Smelter Soil	0.70	0.54	0.89	0.58	0.42	0.80	0.36	0.25	0.52	0.39	0.31	0.49	0.51	0.29	0.79
	NIST Paint	0.86	0.66	1.09	0.73	0.52	1.03	0.55	0.38	0.78	0.74	0.59	0.93	0.72	0.44	0.98
12	Galena-enriched Soil	0.01	0.00	0.02	0.02	0.00	0.04	0.01	0.00	0.02	0.01	-0.01	0.03	0.01	0.00	0.03
	California Gulch Oregon Gulch Tailings	0.07	0.04	0.13	0.11	0.04	0.21	0.05	0.02	0.09	0.01	-0.04	0.06	0.06	-0.01	0.15

LB = 5% Lower Confidence Bound  
 UB = 95% Upper Confidence Bound

**TABLE 2-8. GROUPED LEAD PHASES**

Group	Group Name	Phase Constituents
1	Galena	Galena (PbS)
2	Cerussite	Cerussite
3	Mn(M) Oxide	Mn-Pb Oxide
4	Lead Oxide	Lead Oxide
5	Fe(M) Oxide	Fe-Pb Oxide (including Fe-Pb Silicate) Zn-Pb Silicate
6	Lead Phosphate	Lead Phosphate
7	Anglesite	Anglesite
8	Pb(M) Oxide	As(M)O Lead Silicate Lead Vanadate Pb(M)O Pb-As Oxide
9	Fe(M) Sulfate	Fe-Pb Sulfate Sulfosalts
10	Minor Constituents	Calcite Clay Lead Barite Lead Organic Native Lead PbO-Cerussite Slag

(M) = Metal



**TABLE 2-9. CURVE FITTING PARAMETERS FOR ORAL LEAD ACETATE DOSE-RESPONSE CURVES**

Experiment	Blood AUC			Liver Lead		Kidney Lead		Bone Lead	
	a	b	c	a	b	a	b	a	b
2	13.6	116	0.0084	63	2.0	44	2.4	0.7	0.084
3	8.3	163	0.0040	10	2.3	10	2.2	1.8	0.062
4	8.5	144	0.0064	57	1.7	68	2.8	0.5	0.076
5	8.0	163	0.0038	62	2.0	60	1.8	0.5	0.062
6	8.4	85	0.0101	23	2.0	15	2.1	0.4	0.043
7	-- <sup>a</sup>	-- <sup>a</sup>	-- <sup>a</sup>	10	1.7	10	1.4	0.8	0.059
8	8.0	159	0.0032	11	2.1	17	2.4	0.8	0.065
9	7.5	96	0.0087	11	2.3	14	2.3	0.6	0.071
11	7.2	160	0.0035	14	1.3	20	1.7	0.7	0.053
12	7.6	169	0.0040	9	0.7	8	1.1	0.6	0.032
Mean	8.6	140	0.0058	27	1.8	27	2.0	0.7	0.061
Standard Deviation	1.9	32	0.0026	24	0.5	22	0.5	0.4	0.015
Coefficient of Variation	23%	23%	46%	88%	27%	84%	26%	55%	25%

**Basic Equations:**

Blood AUC =  $a + b \cdot (1 - \exp(-c \cdot \text{Dose}))$

a = baseline blood lead value in unexposed animals

b = maximum increase in steady-state blood lead cause by exposure

c = "shape" parameter that determines how steeply the response increases as dose increases

Tissue concentration (bone, liver, kidney) =  $a + b \cdot \text{Dose}$

a = baseline blood lead value in unexposed animals

b = slope of the increase in tissue content per unit increase in dose

Coefficient of Variation = Standard Deviation / Mean

<sup>a</sup> Experiment 7 Blood AUC: No stable solution was obtained using the exponential model.

**TABLE 2-10. REPRODUCIBILITY OF RBA MEASUREMENTS**

RBA Estimate	Palmerton Location 2		California Gulch Phase I Residential Soil	
	Test 1 (Phase 2 Study 9)	Test 2 (Phase 2 Study 12)	Test 1* (Phase 1 Study 2)	Test 2 (Phase 2 Study 7)
Blood AUC	0.82 ± 0.12	0.71 ± 0.09	0.69	0.88 ± 0.19
Liver	0.60 ± 0.14	1.25 ± 0.32	0.58	0.75 ± 0.16
Kidney	0.51 ± 0.16	0.54 ± 0.13	0.62	0.73 ± 0.17
Bone	0.47 ± 0.07	0.95 ± 0.18	0.50	0.53 ± 0.15
Point Estimate	0.60 ± 0.18	0.86 ± 0.33	0.60	0.72 ± 0.21

\*Calculated using ordinary least squares.

**TABLE 3-1. IN VITRO BIOACCESSIBILITY VALUES**

Experiment	Test Material	Sample	In Vitro Bioaccessibility (%) (Mean ± Standard Deviation)
2	1	Bingham Creek Residential	47.0 ± 1.2
2	2	Bingham Creek Channel Soil	37.8 ± 0.7
3	1	Jasper County High Lead Smelter	69.3 ± 5.5
3	2	Jasper County Low Lead Yard	79.0 ± 5.6
4	1	Murray Smelter Slag	64.3 ± 7.3
4	2	Jasper County High Lead Mill	85.3 ± 0.2
5	1	Aspen Berm	64.9 ± 1.6
5	2	Aspen Residential	71.4 ± 2.0
6	1	Midvale Slag	17.4 ± 0.9
6	2	Butte Soil	22.3 ± 0.6
7	1	California Gulch Phase I Residential Soil	65.1 ± 1.5
7	2	California Gulch Fe/Mn PbO	87.2 ± 0.5
8	1	California Gulch AV Slag	9.4 ± 1.6
9	1	Palmerton Location 2	63.6 ± 0.4
9	2	Palmerton Location 4	69.7 ± 2.7
11	1	Murray Smelter Soil	74.7 ± 6.8
11	2	NIST Paint	72.5 ± 2.0
12	1	Galena-enriched Soil	4.5 ± 1.2
12	3	California Gulch Oregon Gulch Tailings	11.2 ± 0.9

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## **FIGURES**

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**FIGURE 2-1. AVERAGE RATE OF BODY WEIGHT GAIN IN TEST ANIMALS**

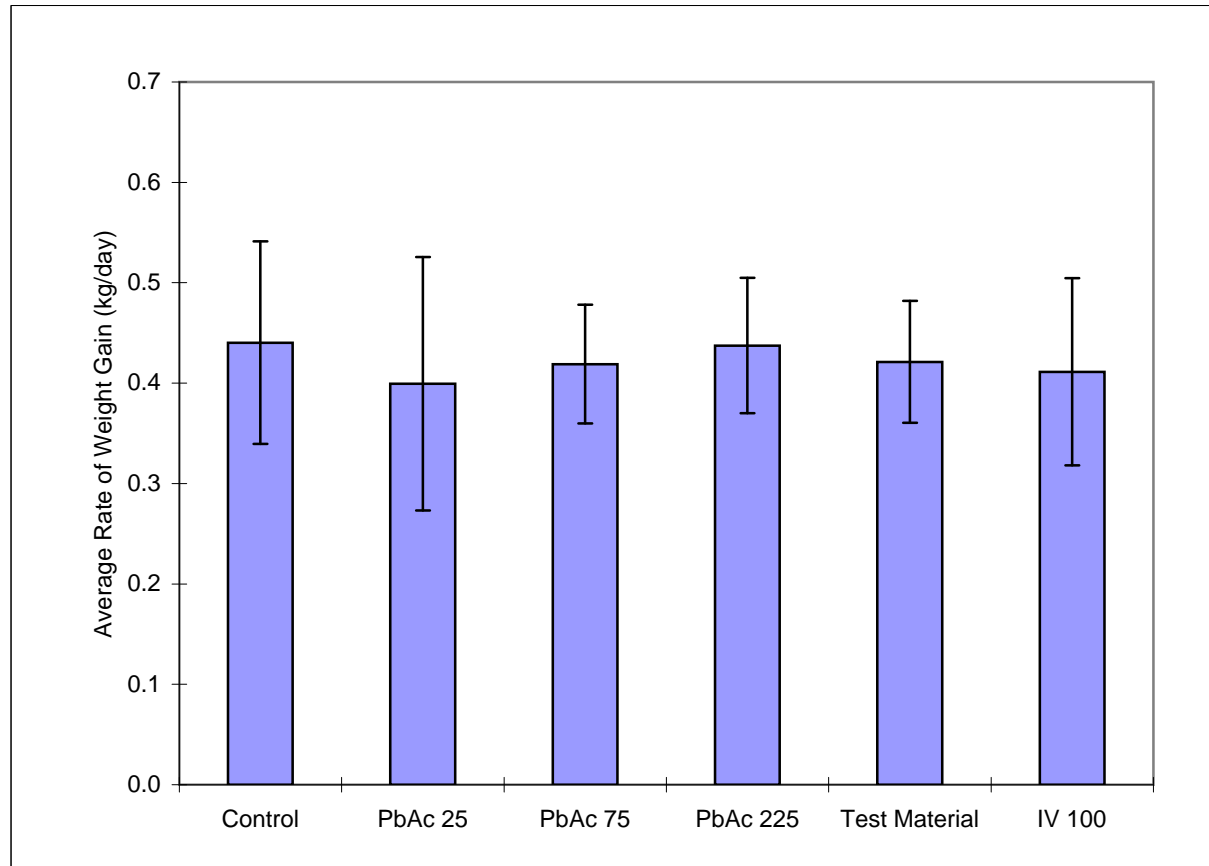
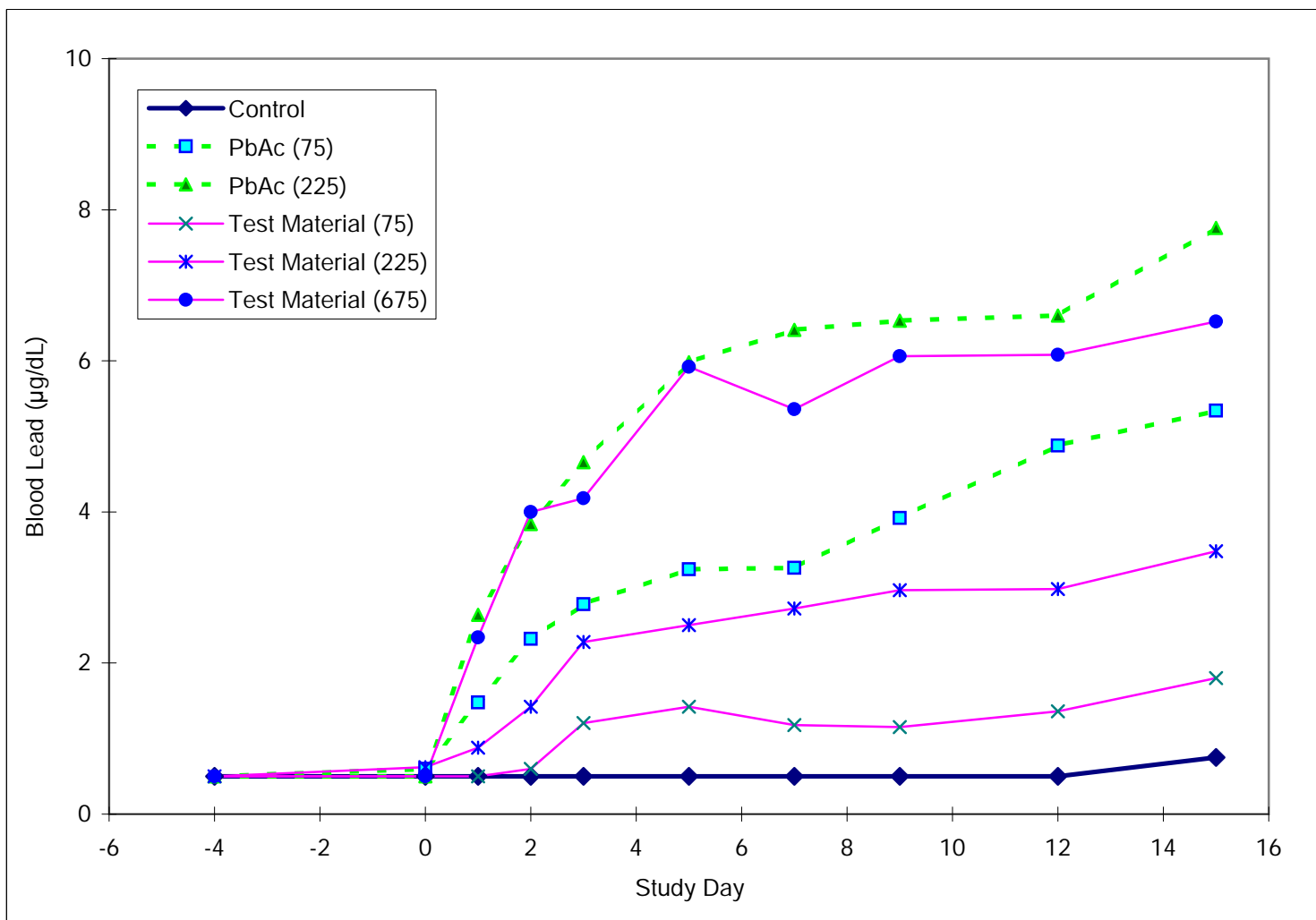
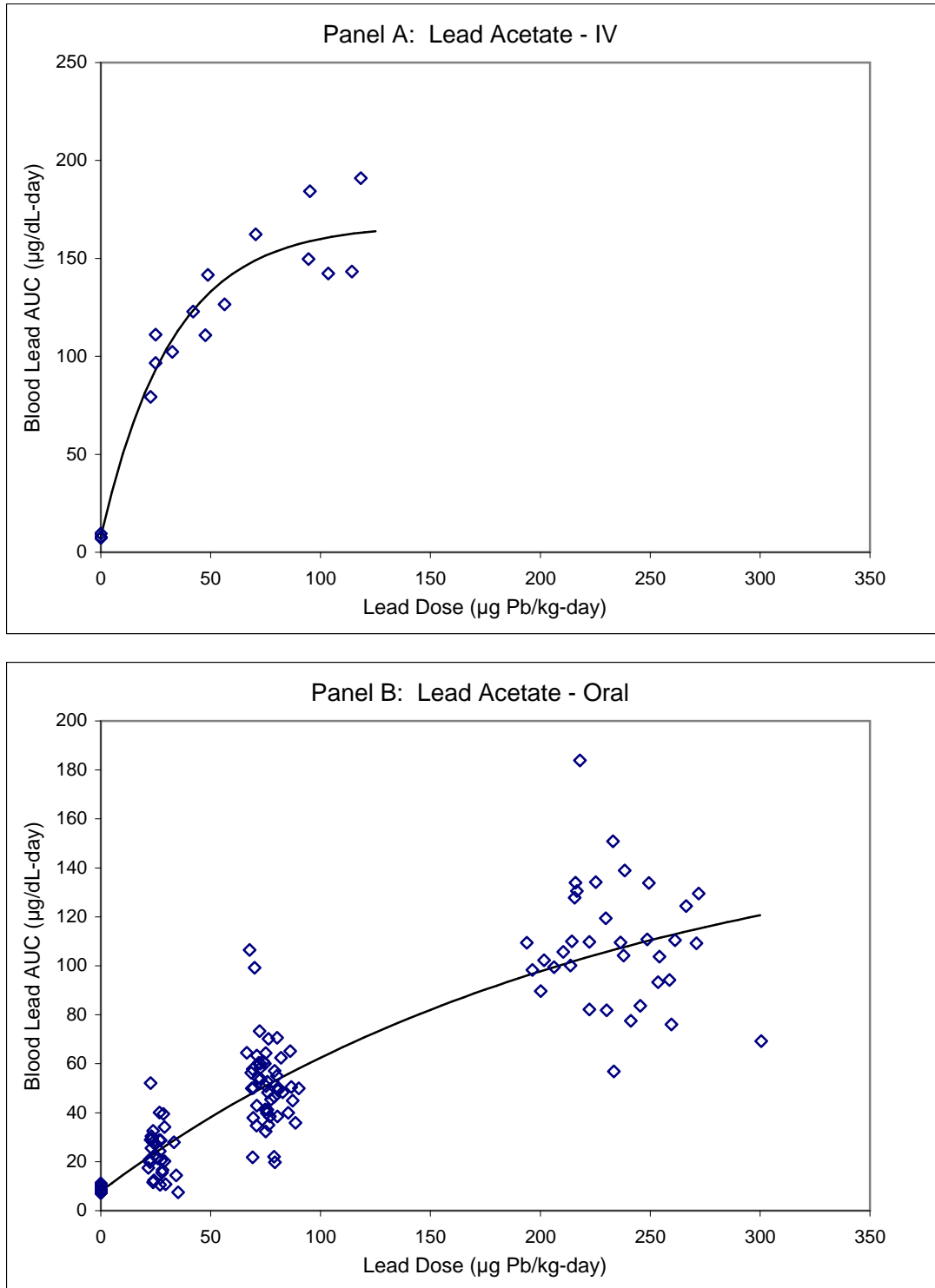


FIGURE 2-2. EXAMPLE TIME COURSE OF BLOOD LEAD RESPONSE

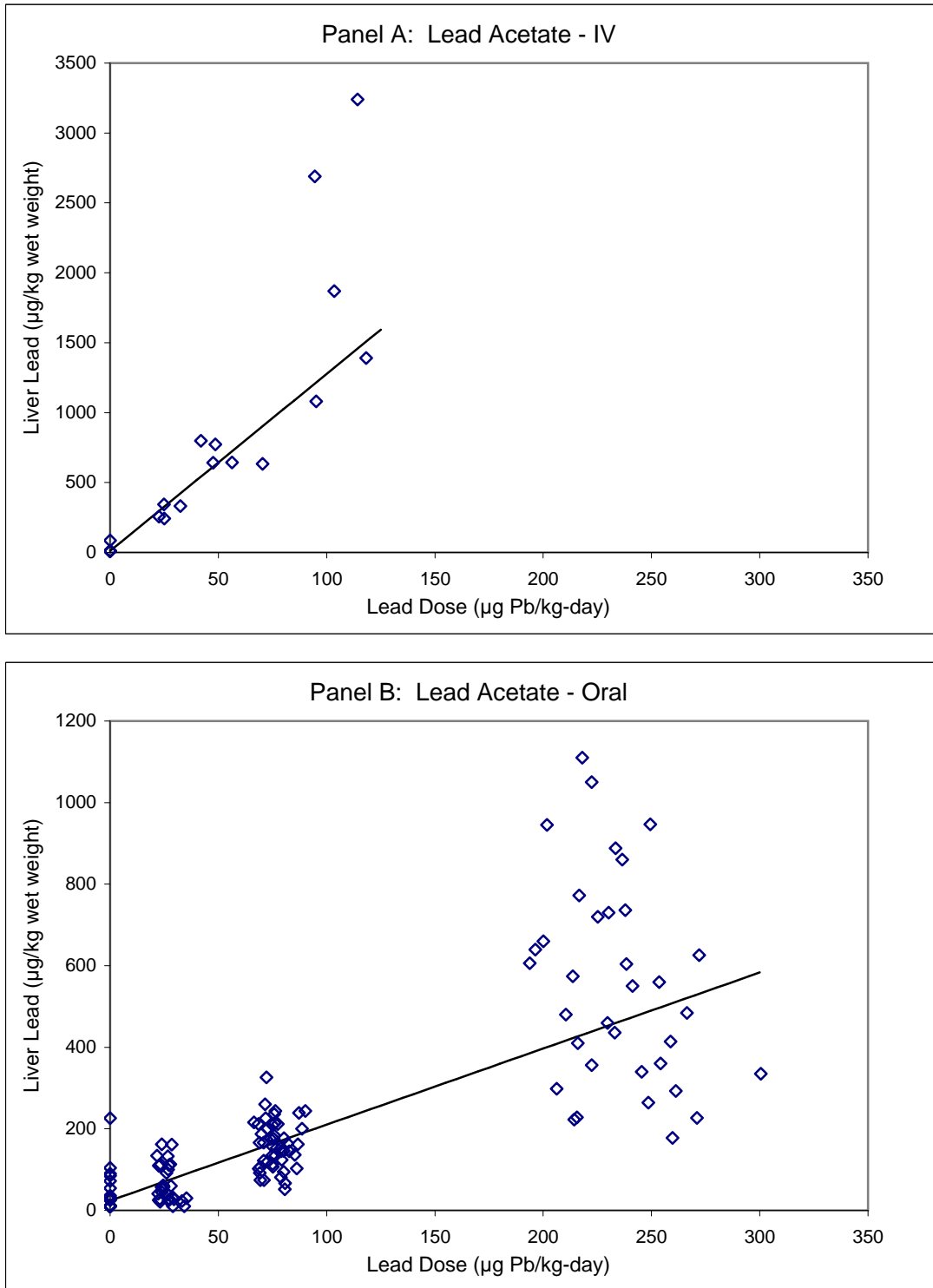




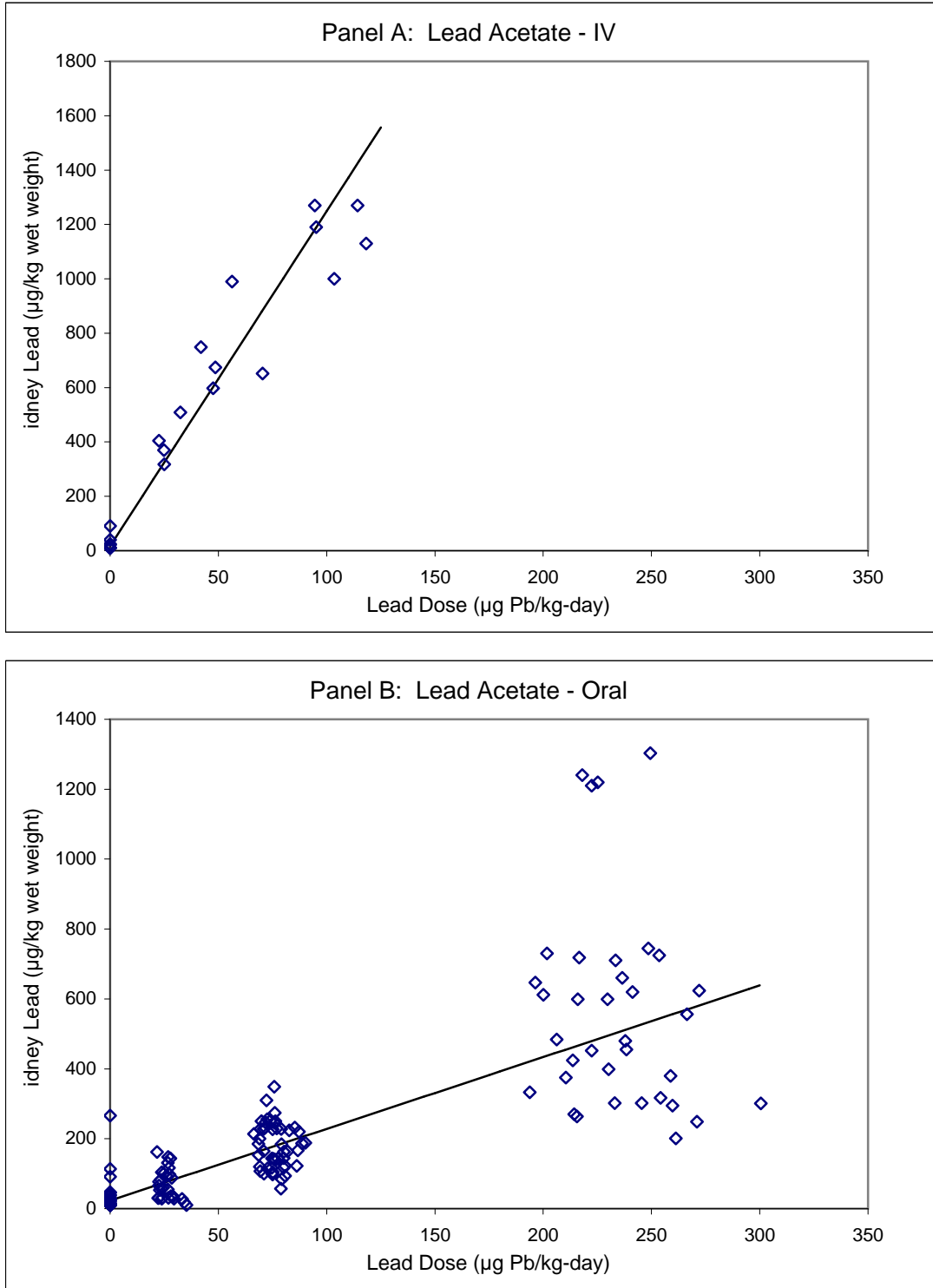
**FIGURE 2-3. DOSE RESPONSE CURVE FOR BLOOD LEAD AUC**



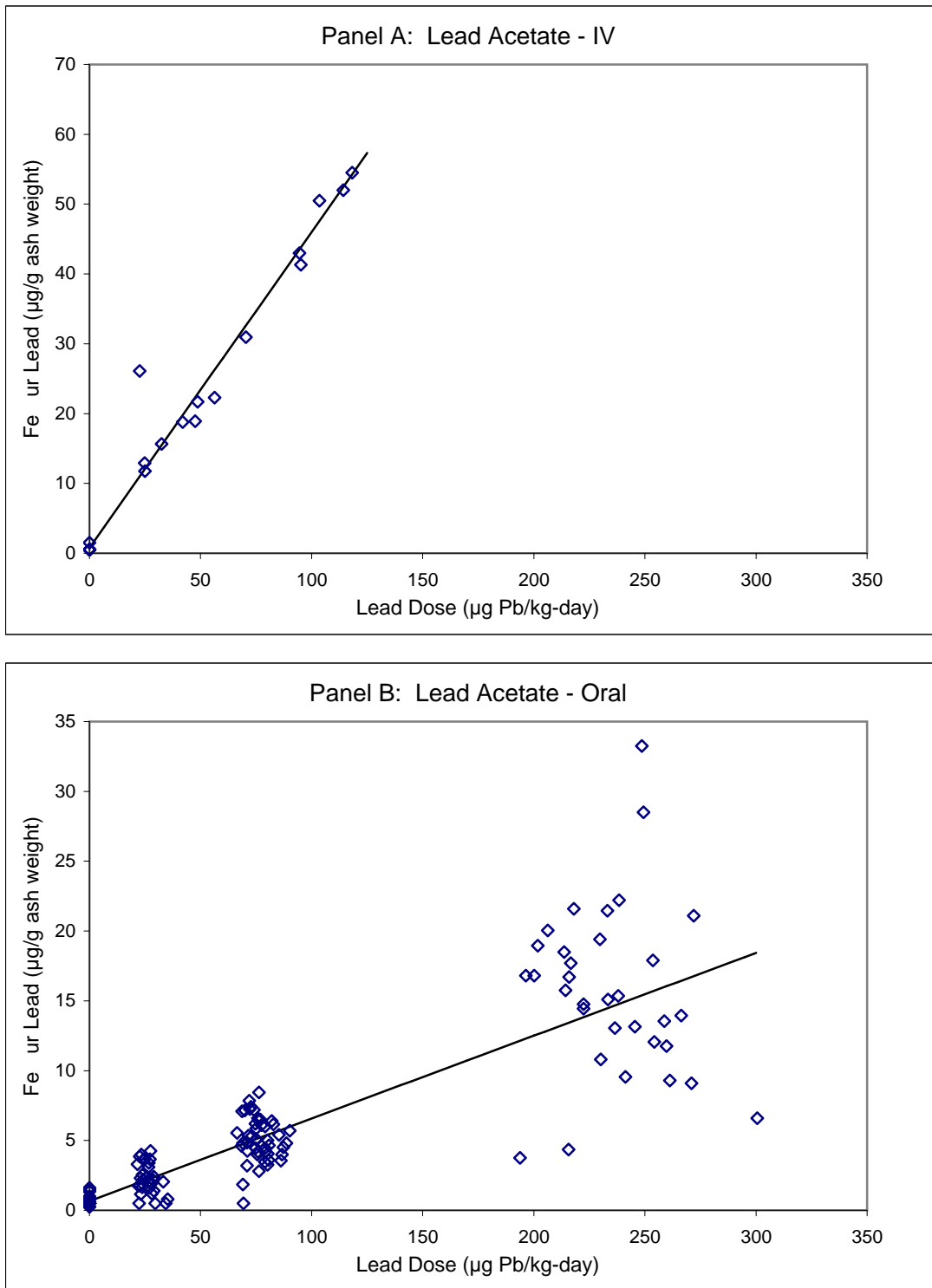
**FIGURE 2-4. DOSE RESPONSE CURVE FOR LIVER LEAD CONCENTRATION**



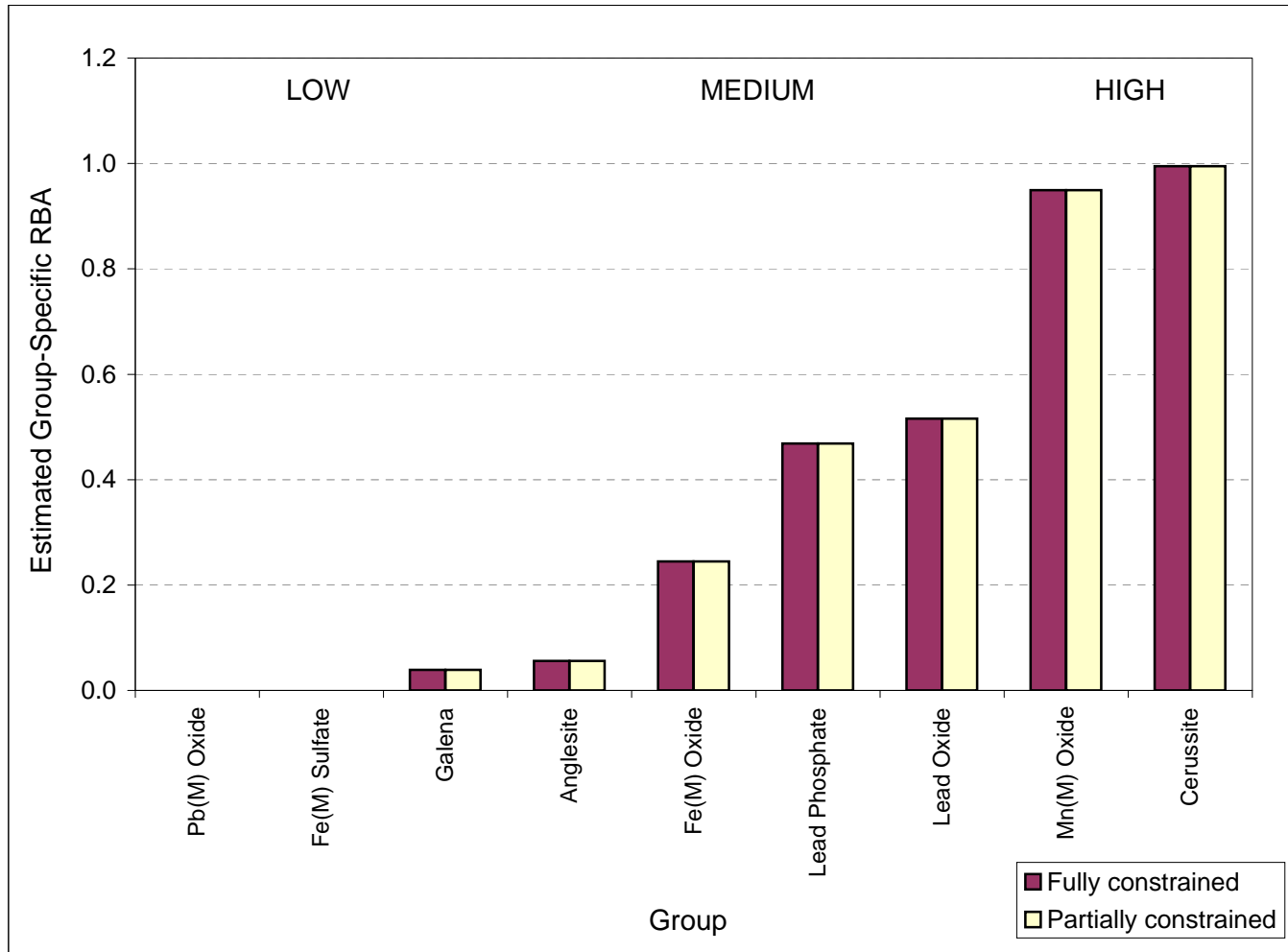
**FIGURE 2-5. DOSE RESPONSE CURVE FOR KIDNEY LEAD CONCENTRATION**



**FIGURE 2-6. DOSE RESPONSE CURVE FOR FEMUR LEAD CONCENTRATION**



**FIGURE 2-7. ESTIMATED GROUP-SPECIFIC RBA VALUES**



**FIGURE 2-8. CORRELATION OF DUPLICATE ANALYSES**

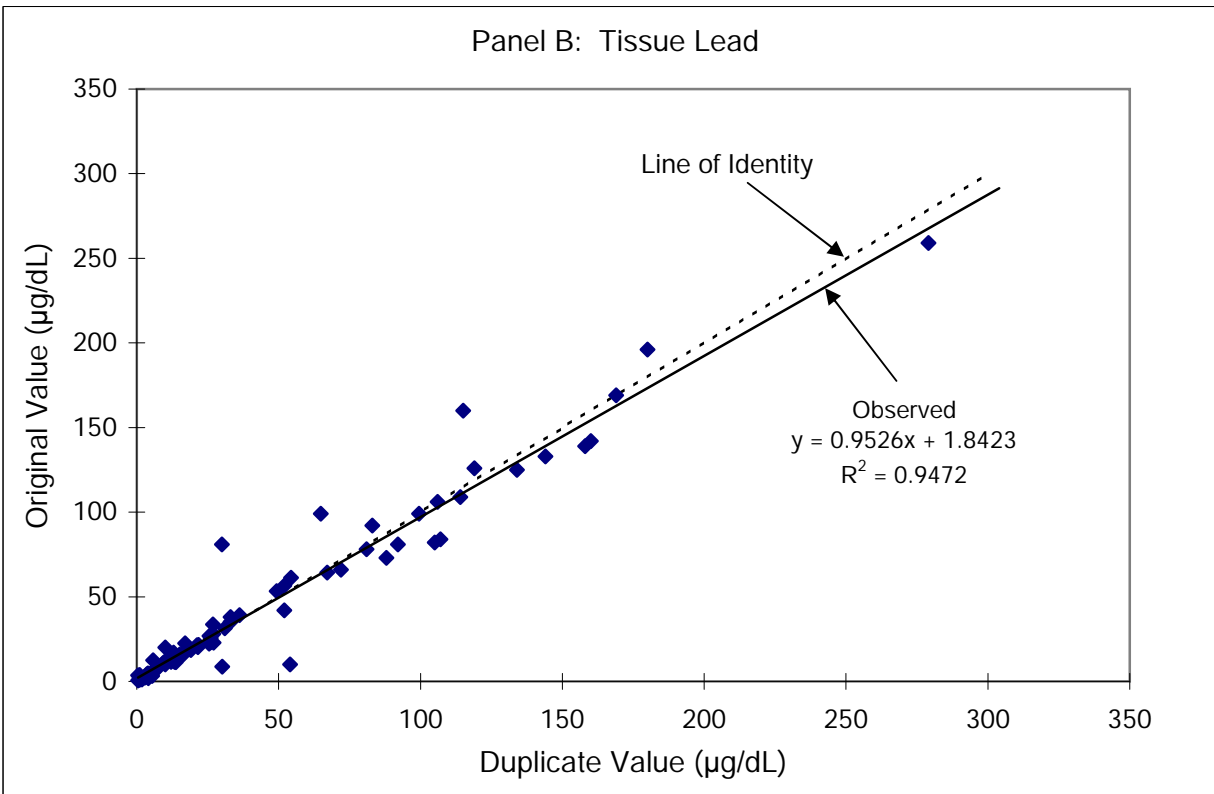
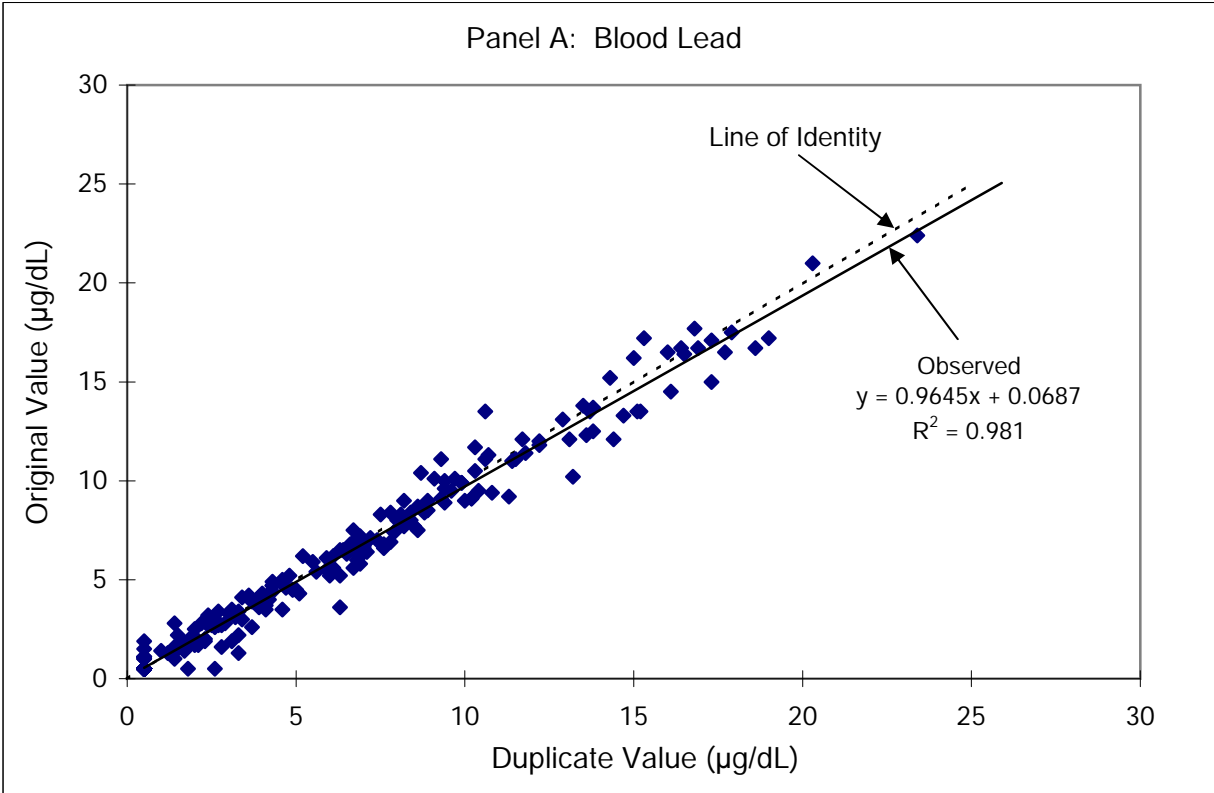
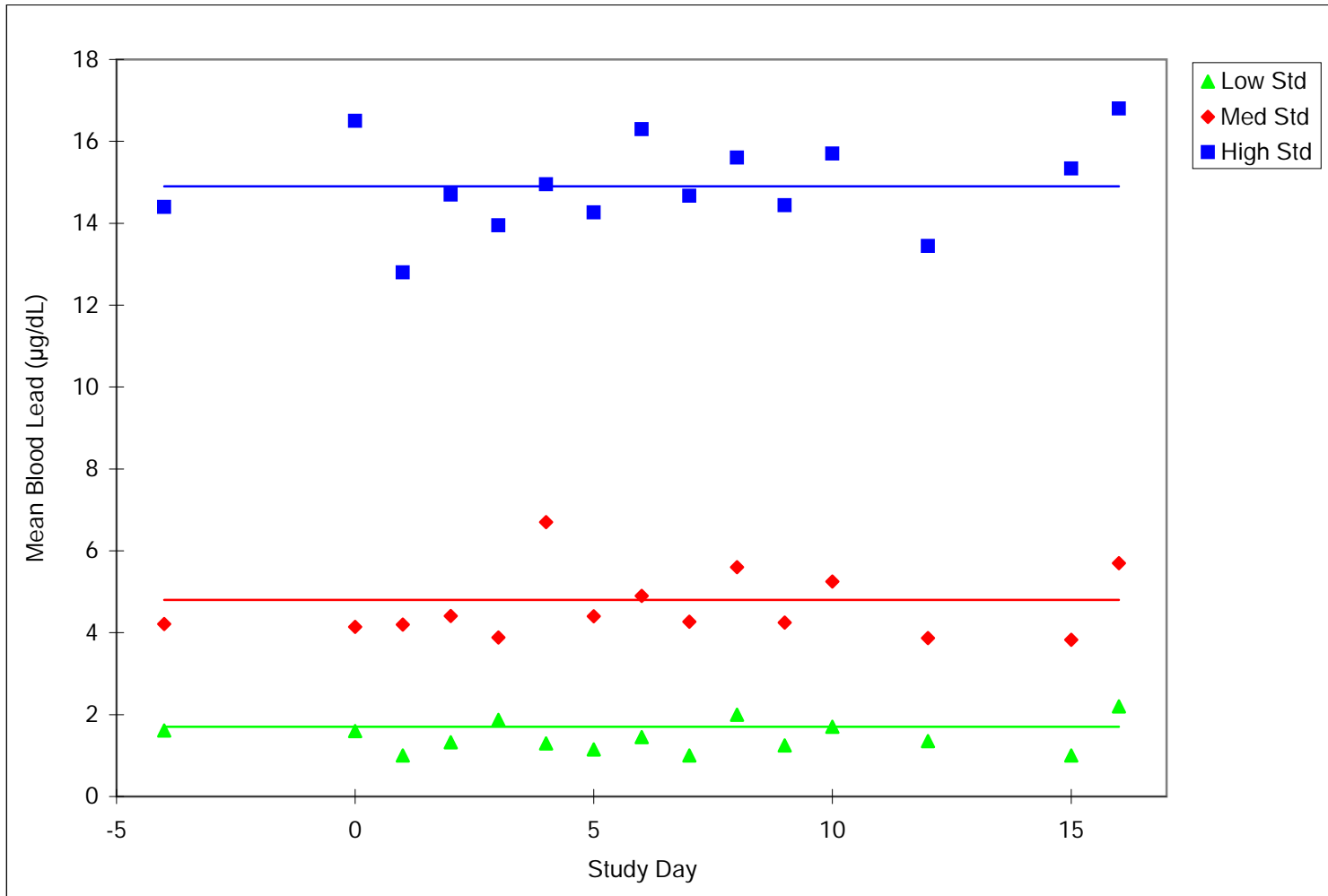
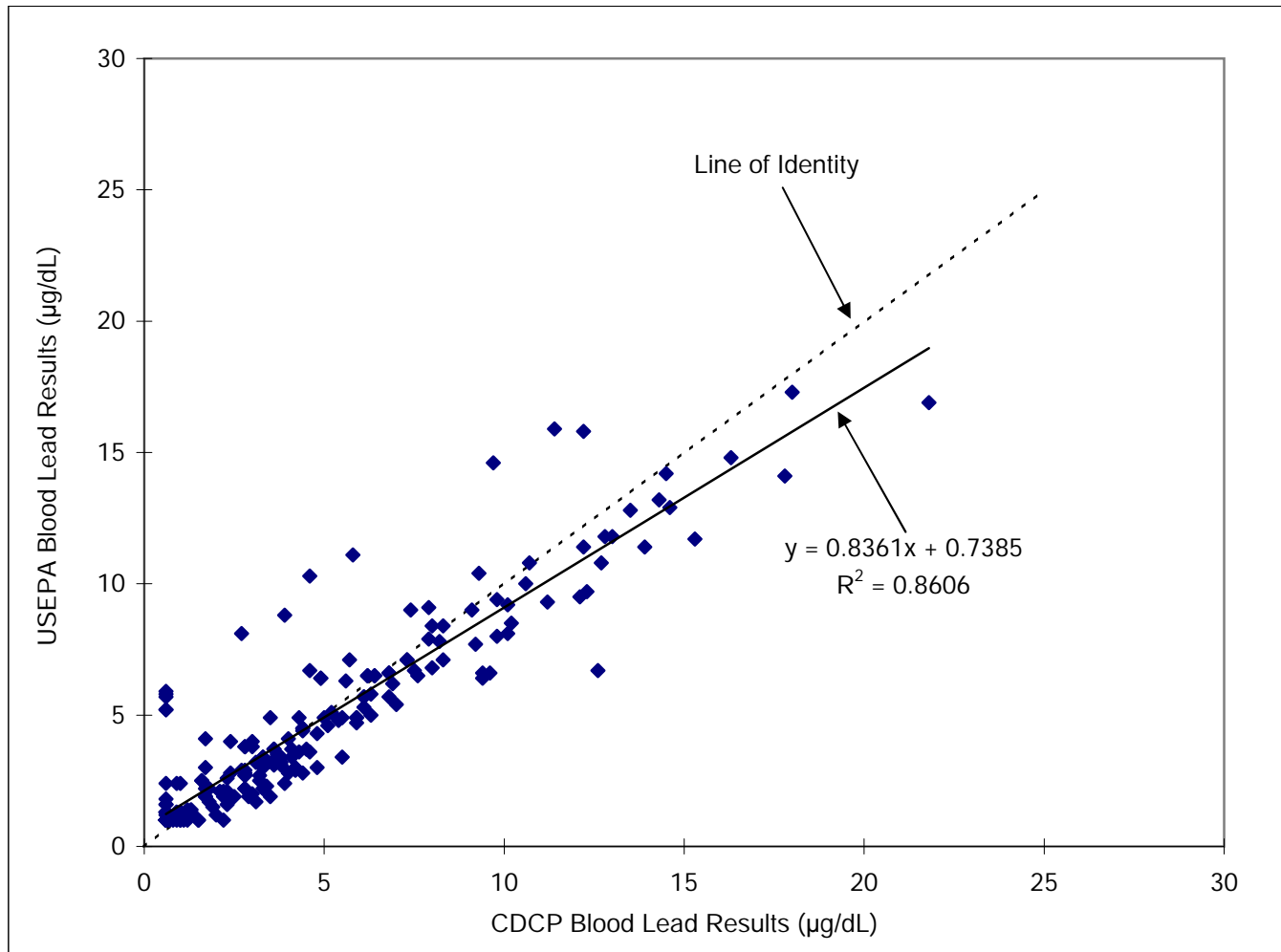


FIGURE 2-9. RESULTS FOR CDC BLOOD LEAD CHECK SAMPLES

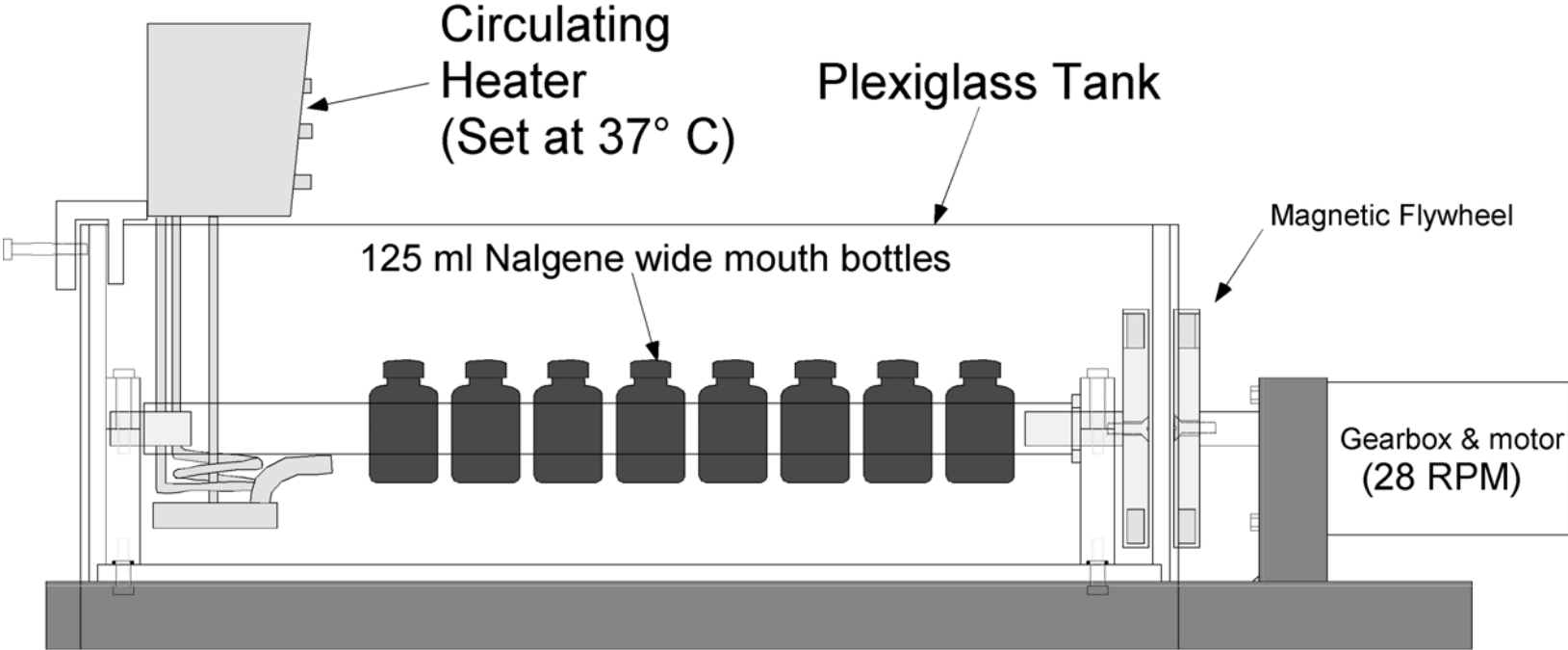


**FIGURE 2-10. INTERLABORATORY COMPARISON OF BLOOD LEAD RESULTS**

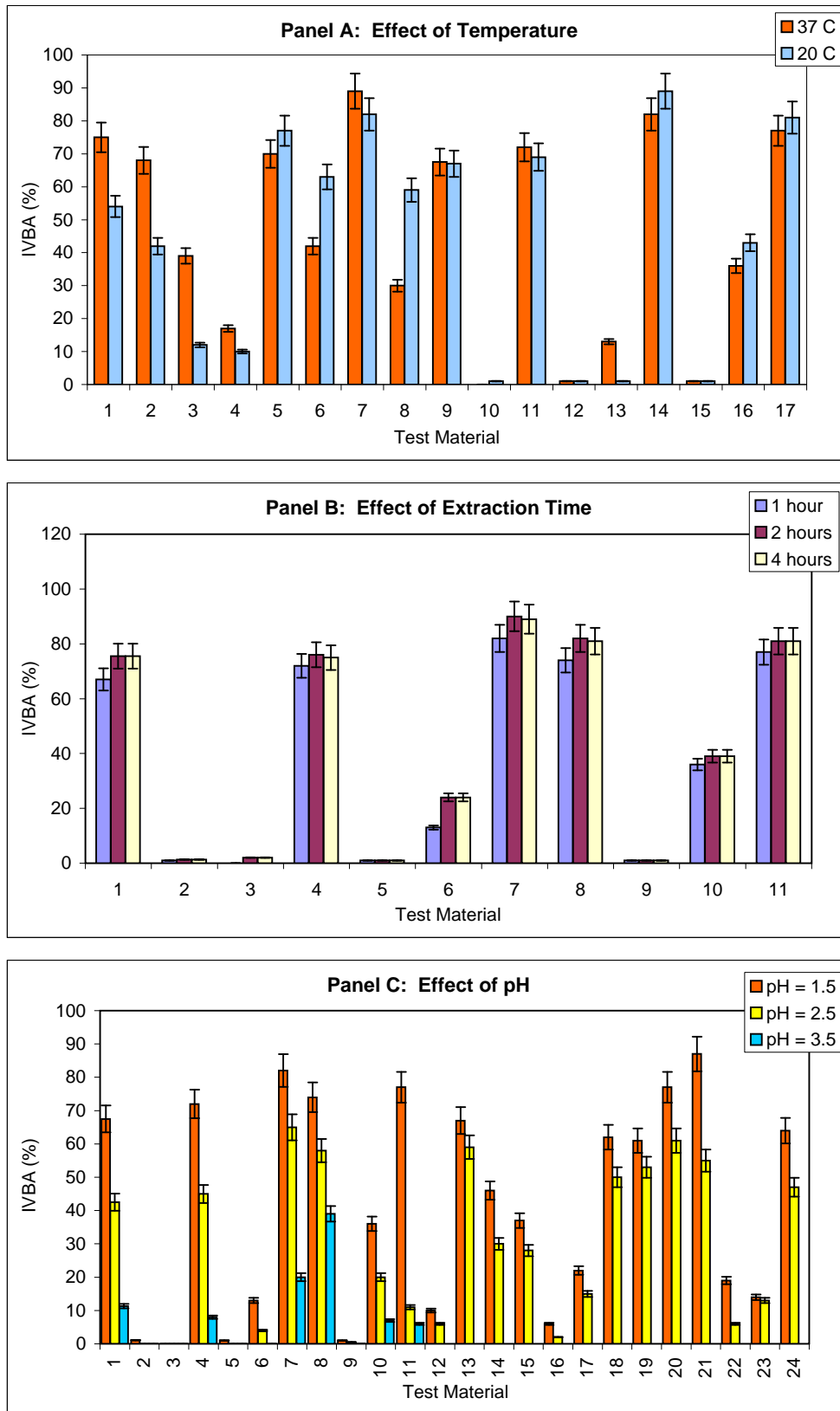




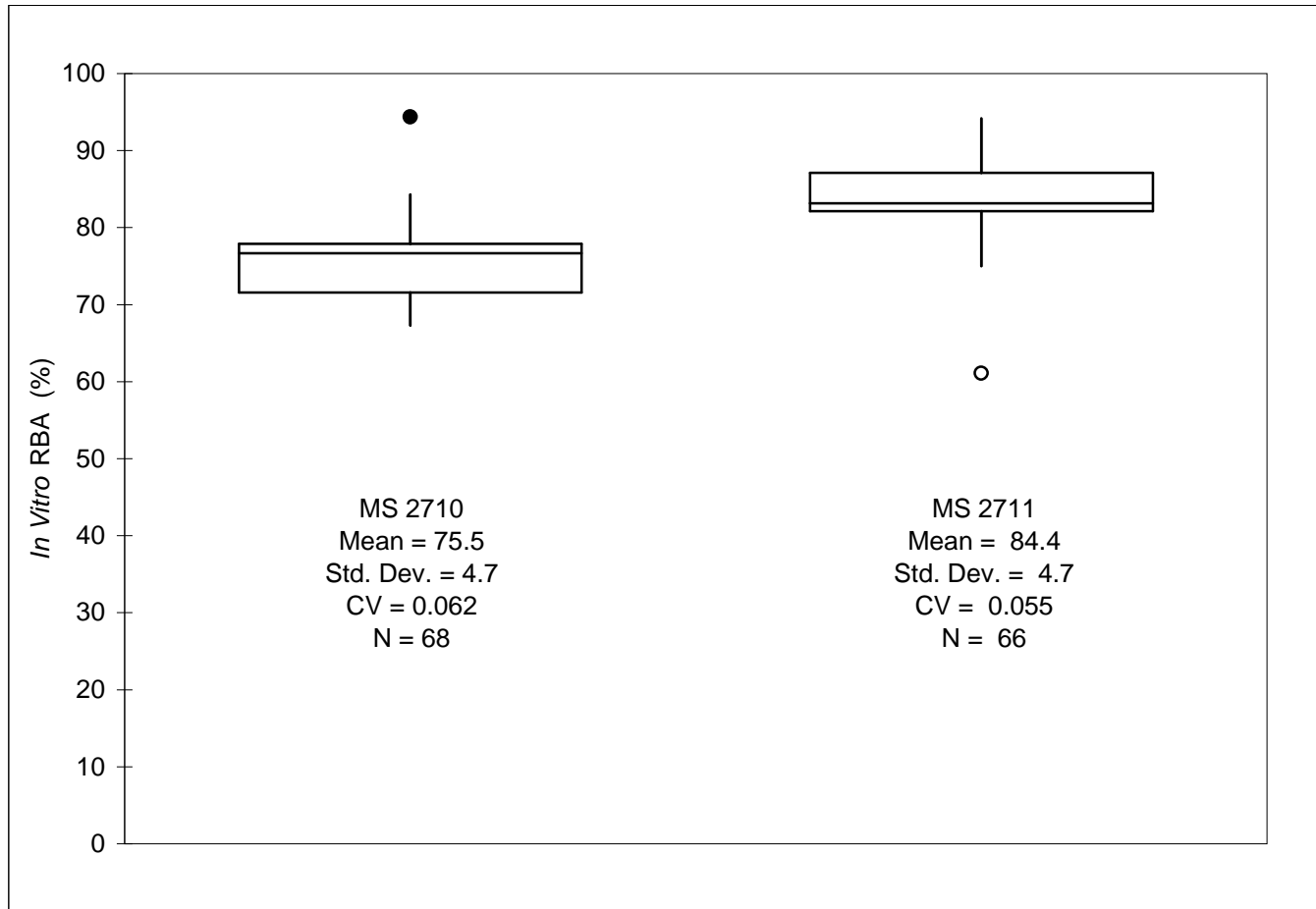
**FIGURE 3-1. *IN VITRO* BIOACCESSIBILITY EXTRACTION APPARATUS**



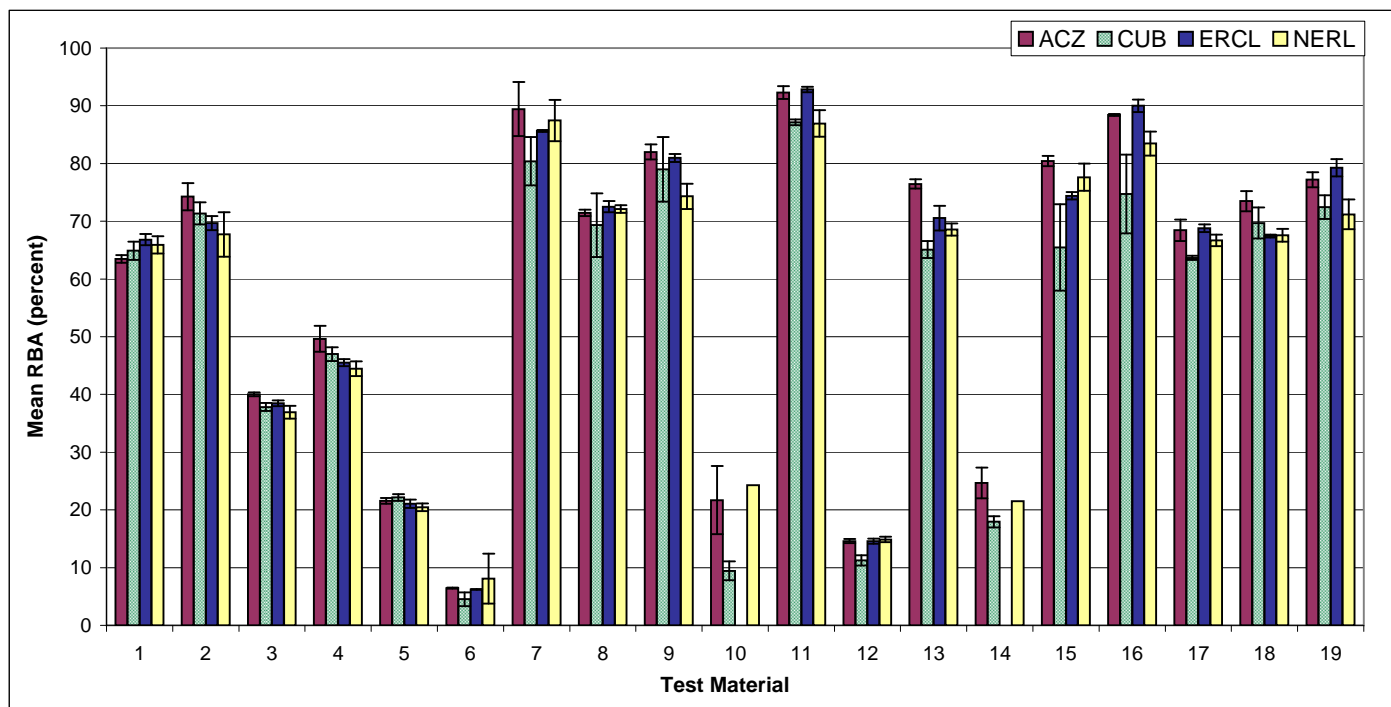
**FIGURE 3-2. EFFECT OF TEMPERATURE, TIME, AND pH ON IVBA**



**FIGURE 3-3. PRECISION OF *IN VITRO* BIOACCESSIBILITY MEASUREMENTS**



**FIGURE 3-4. REPRODUCIBILITY OF *IN VITRO* BIOACCESSIBILITY MEASUREMENTS**



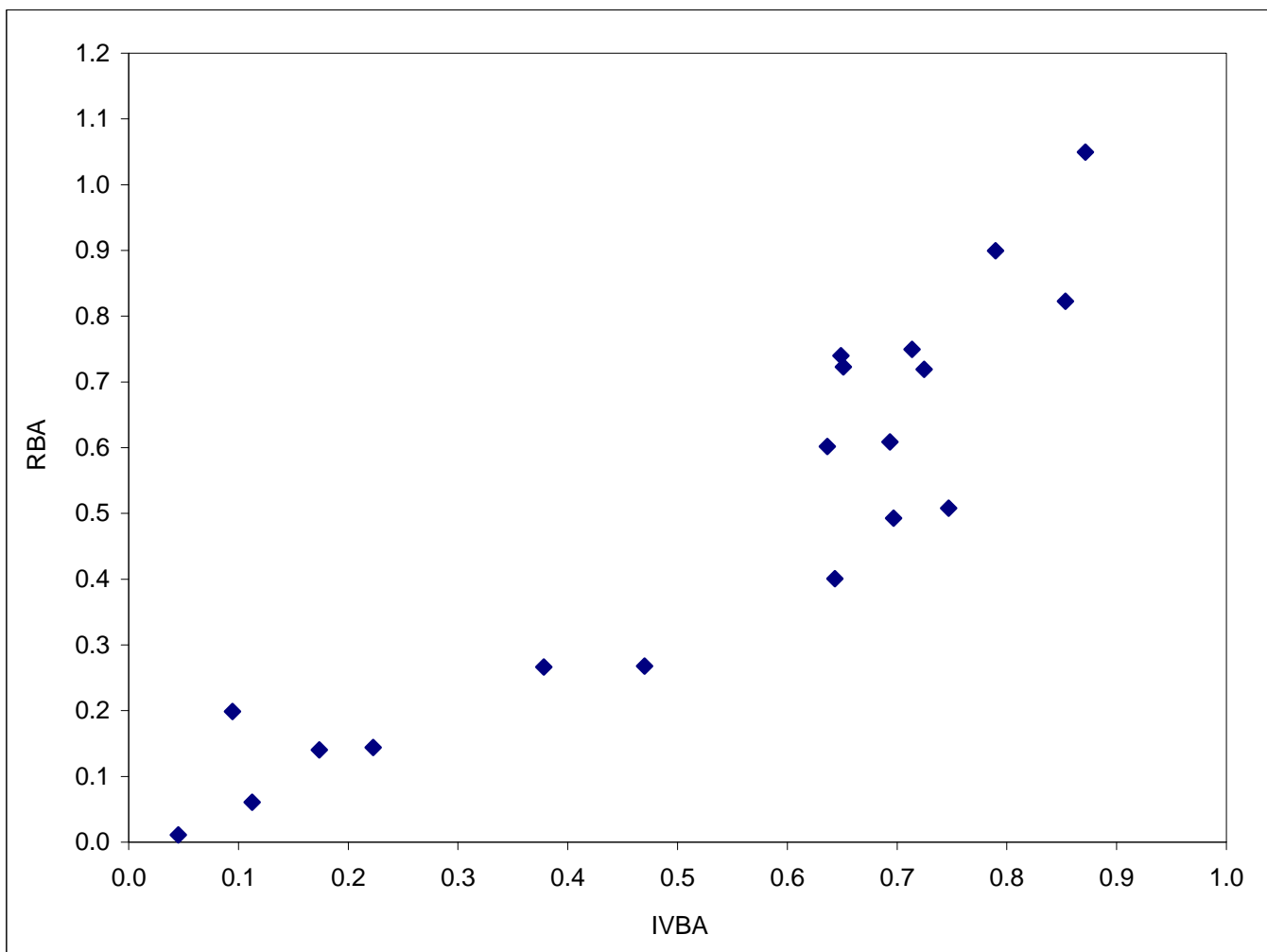
**Test Materials**

1 = Aspen Berm	8 = Jasper County High Lead Smelter	14 = Midvale Slag
2 = Aspen Residential	9 = Jasper County Low Lead Yard	15 = Murray Smelter Slag
3 = Bingham Creek Channel Soil	10 = California Gulch AV Slag	16 = Murray Smelter Soil
4 = Bingham Creek Residential	11 = California Gulch Fe/Mn PbO	17 = Palmerton Location 2
5 = Butte Soil	12 = California Gulch Oregon Gulch Tailings	18 = Palmerton Location 4
6 = Galena-enriched Soil	13 = California Gulch Phase I Residential Soil	19 = NIST Paint
7 = Jasper County High Lead Mill		

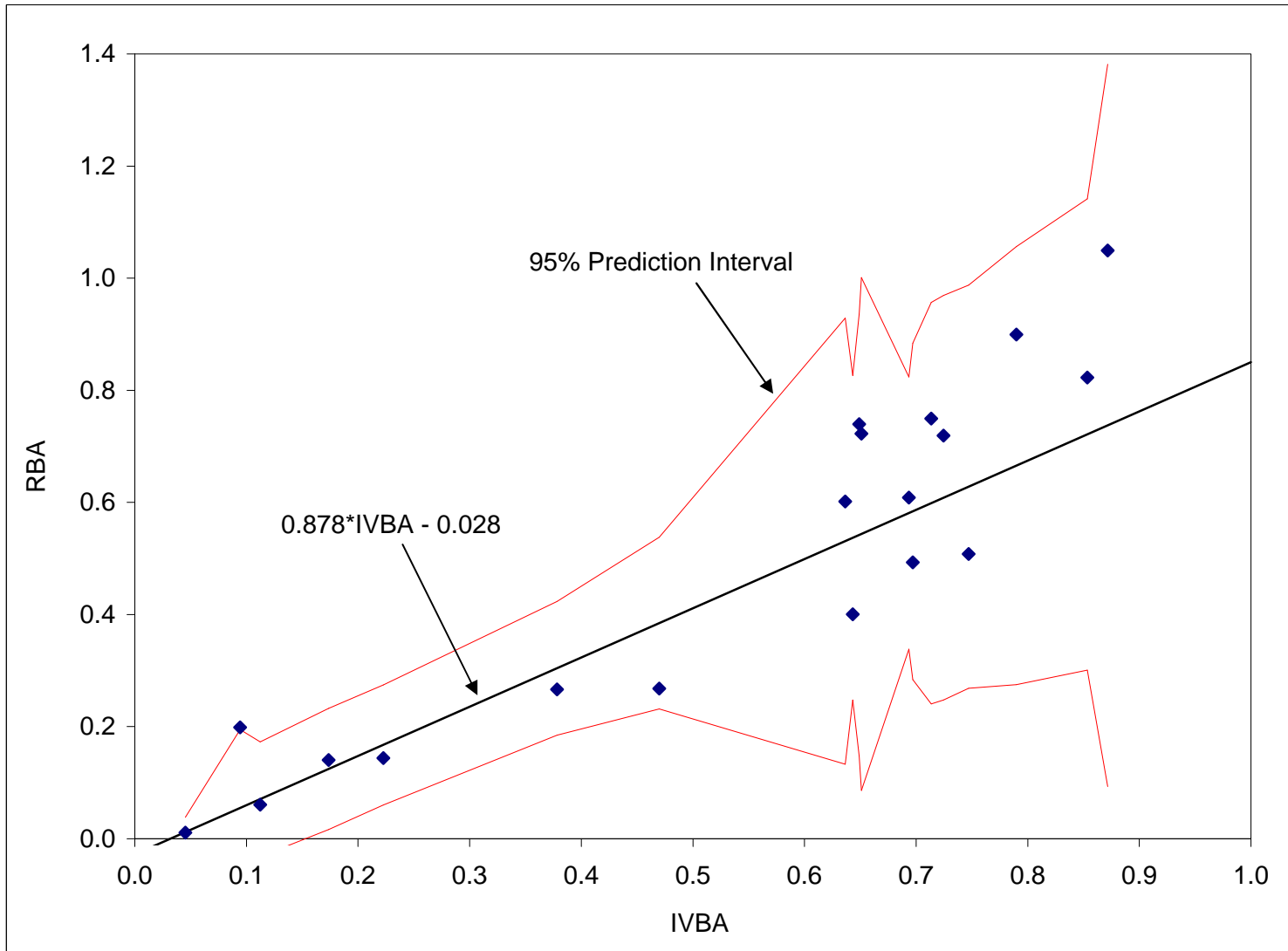
**Laboratories**

ACZ = ACZ Laboratories, Inc.  
 CUB = University of Colorado at Boulder  
 ERCL = Environmental Research Chemistry Laboratory, U.S. Bureau of Reclamation  
 NERL = National Exposure Research Laboratory

FIGURE 3-5. RBA vs. IVBA



**FIGURE 3-6. PREDICTION INTERVAL FOR RBA BASED ON MEASURED IVBA**



**APPENDIX A**

**EVALUATION OF JUVENILE SWINE AS A MODEL  
FOR GASTROINTESTINAL ABSORPTION  
IN YOUNG CHILDREN**

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# APPENDIX A

## EVALUATION OF JUVENILE SWINE AS A MODEL FOR GASTROINTESTINAL ABSORPTION IN YOUNG CHILDREN

### 1.0 INTRODUCTION

Ideally, the reliability of an animal model as a predictor for toxicokinetic responses in humans would be based on a direct comparison of results in humans and the animal species under consideration. However, because intentional dosing of children with lead is not feasible, a direct comparison of lead absorption results in swine with that for children is not possible. Nevertheless, the relevance of the swine as an animal model for lead absorption can be evaluated by comparing a number of physiological attributes of the gastrointestinal system that are likely to be important in influencing the degree to which lead in ingested soil material is released from its soil or mineral matrix to form soluble compounds that can be absorbed into the body. Factors that may affect dissolution include gastric acidity and gastric holding time, which determine the exposure of the ingested material to the acidic environment of the stomach, where dissolution initially occurs. Morphological and physiological factors in the small intestine, where absorption of lead is thought to occur, may also affect RBA; however, these are likely to be less important for those soil materials for which solubility is the limiting factor for RBA.

Weis and LaVelle (1991) and Casteel et al. (1996) determined that gastric function in juvenile swine is sufficiently similar to that of human children so that juvenile swine could serve as a model for predicting RBA of soil-borne lead in children. This view is supported by several reviews on the comparative anatomy and physiology of the human and pig gastrointestinal systems (Dodds, 1982; Miller and Ullrey, 1987; Moughan et al., 1992; Pond and Houpt, 1978) and, in particular, the following pertinent observations.

### 2.0 GASTROINTESTINAL TRACT MORPHOLOGY AND HISTOLOGY

The anatomy of the neonatal digestive system in the pig and human are very similar (Moughan et al., 1992). The body-weight adjusted ratios of intestinal length to stomach volume in the child and piglet are comparable, as shown below:

Species	Stomach Volume (cm <sup>3</sup> /kg)	Small Intestine Length (cm/kg)	Large Intestine length (cm/kg)	Small intestine length/stomach volume	Large intestine length/stomach volume
Human	9.6	95.6	19.4	9.96	4.93
Swine	28.9	229.2	59.6	7.93	3.85

Source: Moughan et al., 1992.

Birth body weights of 3.4 (human) and 1.3 (pig) kg were assumed.

The histology of the small intestine, colon, and rectum in the piglet is similar to that of the human (Moughan et al., 1992). Small anatomical differences between humans and swine would

not be expected to markedly affect digestion in the neonate (Moughan et al., 1992). The piglet is considered to be a useful model of the anatomical development of the human neonatal digestive tract (Moughan et al., 1992; Miller and Ullrey, 1987).

### **3.0 GASTRIC HOLDING TIMES**

Gastric emptying time in humans is highly variable (USEPA, 2001). The rate of emptying of stomach contents varies depending on the type of food, the volume of the meal, and its caloric content. High caloric substances such as fat empty more slowly than carbohydrates. The most important factor effecting liquid gastric emptying is the caloric content of the liquid meal. Upright positioning and ambulation have been described to speed gastric emptying. Other factors that are believed to affect gastric emptying include the osmolality, acidity, and chain length of fatty acids in the meal. Differences in emptying may also exist between males and females. These factors tend to make direct comparisons of data from different reports difficult. Nevertheless, the available data do not suggest any substantial differences in gastric holding times between children and juvenile swine.

In the 4-week old pig, gastric emptying following a meal was rapid, with 30 to 40% passing into the duodenum within 15 minutes and the remaining portion of gastric contents following about one hour later (Pond and Houpt, 1978). Gastric pH did not affect gastric emptying time in juvenile swine (Pond and Houpt, 1978). In an unpublished study by Casteel (personal communication), gastric emptying in juvenile swine was shown to be influenced by feeding intervals, both pre- and post-dosing. The investigators reported rapid clearance of the bolus (complete within 2 hours) after an overnight fast; however, feeding 4 hours prior to dosing slowed completion of gastric emptying to 4 hours. Feeding at two hours post-dosing accelerated the movement of the residual gastric contents, although most of the bolus had already cleared the stomach.

In humans, gastric emptying time in neonates and premature infants is typically about 87 minutes, but can be as long as 6 to 8 hours, with adult values (typically about 65 minutes) being reached at 6 to 8 months of age (FDA, 1998; Balis, 2000).

### **4.0 GASTRIC ACIDITY**

Direct comparisons of gastric acidity as a function of age in humans and swine are not available. However, available information on gastric acid secretion does not suggest there are any major differences that would affect extrapolation of RBA values measured in juvenile swine to humans. Agunod et al. (1969) reported that gastric acid output (corrected for body weight) reached normal adult levels in swine at 2 to 3 months post partum. In humans, gastric pH is neutral at birth, but drops to 1 to 3 within hours of birth. Gastric acid secretion then declines on days 10 to 30, and does not approach adult values until approximately 3 months of age (FDA, 1998). Nagita et al. (1996) reported that the intragastric pH of infants was <4 for only half of the day, whereas baseline pH in normal adults is <2. The development of maximal acid secretion in the pig also has some similarities to that of humans (Xu and Cranwell, 1990). In both the pig and human, maximal acid secretion correlates with age and body weight with pentagastrin,

histamine, and histalog used as secretagogues (Xu and Cranwell, 1990). A limitation of the available pig data is that all of the studies measure the maturation of gastric acid output rather than intragastric pH, which Nagita et al. (1996) asserts is a preferable measure of gastric maturity. Temporal studies of the intragastric pH of juvenile swine are not available.

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## **APPENDIX B**

### **DETAILED DESCRIPTION OF ANIMAL EXPOSURE**

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## **APPENDIX B**

### **DETAILED DESCRIPTION OF ANIMAL EXPOSURE**

#### **1.0 EXPERIMENTAL ANIMALS**

All animals used in this program were young intact males of the Pig Improvement Corporation (PIC) genetically defined Line 26, and were purchased from Chinn Farms, Clarence, MO. The number of animals purchased for each study was typically 6 to 8 more than required by the protocol. These animals were usually purchased at age 4 to 5 weeks (weaning occurs at age 3 weeks), and they were then held under quarantine for one week to observe their health before beginning exposure to test materials. Any animals that appeared to be in poor health during this quarantine period were excluded. To minimize weight variations between animals and groups, extra animals that were most different in body weight on day -4 (either heavier or lighter) were also excluded from the study. The remaining animals were assigned to dose groups at random. When exposure began (day zero), the animals were about 5 to 6 weeks old and weighed an average of about 8 to 11 kg.

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 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. Any animal that became ill and could not be promptly restored to good health by appropriate treatment was promptly removed from the study.

#### **2.0 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 ppm lead, purchased from Zeigler Brothers, Inc., Gardners, PA) over the time interval from day -7 to -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 (NRC, 1988). The typical nutritional components and chemical analysis of the feed are presented in Table 2-1 of the main text. Periodic analysis of feed samples during this program indicated the mean lead level was less than the detection limit (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 was less than 2 µg/L.

### 3.0 DOSING

The dose levels used in these studies were selected to be as low as possible in an effort to make measurements at the low end of the dose-response curve where saturation of biological systems is minimal. Based on experience from previous investigations, doses of lead acetate in the range of 25 to 675 µg Pb/kg-day were found to give clear and measurable increases in lead levels in all endpoints measured (blood, liver, kidney, bone), so doses in this range (usually 25 to 225 µg Pb/kg-day) were employed in most studies. The doses of test materials were usually set at the same level as lead acetate, except that one higher dose was often included in case the test materials were found to yield very low responses. Depending on the concentration of lead in the test material and the target dose level for lead, soil intake rates by the swine were in the range of 500 to 2500 mg/day.

Animals were exposed to lead acetate or a test material for 15 days, with the dose for each day being administered in two equal portions given at 9:00 AM and 3:00 PM (two hours before feeding). These exposure times were selected so that lead ingestion would occur at a time when the stomach was largely or entirely empty of food. This is because the presence of food in the stomach is known to reduce lead absorption (e.g., Chamberlain et al., 1978; Rabinowitz et al., 1980; Heard and Chamberlain, 1982; Blake et al., 1983; James et al., 1985). Dose calculations 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. This “doughball” 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). Random and intermittent delays of this sort 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). All missed doses were recorded and the time-weighted average dose calculation for each animal was adjusted downward accordingly.

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

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**APPENDIX B**  
**ATTACHMENT 1**  
**DETAILED STUDY DESIGNS**

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**EXPERIMENT 1A STUDY DESIGN**

Pig Number	Group	Material Administered*	Dose ( $\mu\text{g}$ Pb/kg-day)
3 20	1	Control	0
2 22 23 24 27	2	PbAc	25
1 26 29 32 35	3	PbAc	75
9 14 17 31 34	4	PbAc (-2 hr)	225
7 12 19 30 33	5	PbAc (0 hr)	225
5 18 21 25 36	6	PbAc (+2 hr)	225
4 15 16	7A	PbAc (IV)	100

\*All materials administered orally unless designated IV (intravenously)

**EXPERIMENT 2 STUDY DESIGN**

Pig Number	Group	Material Administered*	Dose ( $\mu\text{g Pb/kg-day}$ )
206 226	1	Control	0
215 220 222 229 251	2	PbAc	25
209 228 244 248 258	3	PbAc	75
204 216 247 252 260	4	PbAc	225
201 207 221 238 259	5	Bingham Creek Residential	75
236 237 240 242 249	6	Bingham Creek Residential	225
224 234 235 243 257	7	Bingham Creek Residential	450
202 217 219 253 254	8	Bingham Creek Channel Soil	75
203 225 227 232 250	9	Bingham Creek Channel Soil	225
205 210 213 218 255	10	Bingham Creek Channel Soil	675
208 214 230 231 239 241 246 256	11	PbAc (IV)	100

\*All materials administered orally unless designated IV (intravenously)

**EXPERIMENT 3 STUDY DESIGN**

Pig Number	Group	Material Administered*	Dose ( $\mu\text{g Pb/kg-day}$ )
304 339	1	Control	0
309 312 324 337 340	2	PbAc	75
313 315 342 354 356	3	PbAc	225
305 311 318 321 331	4	Jasper County High Lead Smelter	75
316 317 330 352 353	5	Jasper County High Lead Smelter	225
319 341 344 345 348	6	Jasper County High Lead Smelter	625
325 329 338 343 351	7	Jasper County Low Lead Yard	75
302 326 328 332 346	8	Jasper County Low Lead Yard	225
306 333 334 335 349	9	Jasper County Low Lead Yard	625
307 320 322 347 350	10	PbAc (IV)	100

\*All materials administered orally unless designated IV (intravenously)

**EXPERIMENT 4 STUDY DESIGN**

Pig Number	Group	Material Administered*	Dose ( $\mu\text{g Pb/kg-day}$ )
417 430	1	Control	0
409 419 429 443 444	2	PbAc	75
408 410 426 449 455	3	PbAc	225
402 407 411 423 450	4	Murray Smelter Slag	75
420 431 432 440 446	5	Murray Smelter Slag	225
412 418 427 437 442	6	Murray Smelter Slag	625
404 406 416 428 454	7	Jasper County High Lead Mill	75
401 433 434 435 441	8	Jasper County High Lead Mill	225
403 405 413 448 453	9	Jasper County High Lead Mill	625
415 421 424 425 438 439 445 451	10	PbAc (IV)	100

\*All materials administered orally unless designated IV (intravenously)



**EXPERIMENT 5 STUDY DESIGN**

Pig Number	Group	Material Administered*	Dose ( $\mu\text{g Pb/kg-day}$ )
530 536	1	Control	0
514 518 519 520 524	2	PbAc	75
501 513 529 534 547	3	PbAc	225
503 523 532 549 555	4	Aspen Berm	75
509 512 539 540 550	5	Aspen Berm	225
510 516 525 537 542	6	Aspen Berm	675
502 507 517 522 528	7	Aspen Residential	75
505 506 521 553 554	8	Aspen Residential	225
526 535 541 545 548	9	Aspen Residential	675
504 508 515 538 543 544 546 551	10	PbAc (IV)	100

\*All materials administered orally unless designated IV (intravenously)

**EXPERIMENT 6 STUDY DESIGN**

Pig Number	Group	Material Administered*	Dose ( $\mu\text{g Pb/kg-day}$ )
614 638	1	Control	0
613 624 630 639 641	2	PbAc	75
616 644 651 653 654	3	PbAc	225
619 623 626 631 647	4	Midvale Slag	75
602 605 628 640 650	5	Midvale Slag	225
603 615 629 633 645	6	Midvale Slag	675
610 611 617 637 643	7	Butte Soil	75
601 609 618 621 635	8	Butte Soil	225
620 627 634 646 655	9	Butte Soil	675
604 606 607 612 625 632 642 648	10	PbAc (IV)	100

\*All materials administered orally unless designated IV (intravenously)

**EXPERIMENT 7 STUDY DESIGN**

Pig Number	Group	Material Administered*	Dose ( $\mu\text{g Pb/kg-day}$ )
706 714 718 735 743	1	Control	0
703 709 748 750 755	2	PbAc	25
711 715 716 747 752	3	PbAc	75
704 712 736 740 753	4	California Gulch Phase I Residential Soil	25
702 708 728 739 756	5	California Gulch Phase I Residential Soil	75
717 723 725 732 737	6	California Gulch Phase I Residential Soil	225
707 713 730 738 741	7	California Gulch Fe/Mn PbO	25
733 742 746 749 751	8	California Gulch Fe/Mn PbO	75
719 721 729 744 745	9	California Gulch Fe/Mn PbO	225
722 724 727 734 754	10	PbAc (IV)	100

\*All materials administered orally unless designated IV (intravenously)

**EXPERIMENT 8 STUDY DESIGN**

Pig Number	Group	Material Administered*	Dose ( $\mu\text{g Pb/kg-day}$ )
808 810 836	1	PbAc (IV)	0
805 807 812 827 834	2	PbAc (IV)	25
813 815 825 845 853	3	PbAc (IV)	50
801 816 820 843 852	4	PbAc (IV)	100
809 830 841 848 855	5	Control	0
817 818 819 838 846	6	PbAc	25
804 840 842 844 849	7	PbAc	75
857 826 828 831 851	8	California Gulch AV Slag	25
806 814 823 847 854	9	California Gulch AV Slag	75
811 822 824 837 856	10	California Gulch AV Slag	225

\*All materials administered orally unless designated IV (intravenously)

**EXPERIMENT 9 STUDY DESIGN**

Pig Number	Group	Material Administered*	Dose ( $\mu\text{g Pb/kg-day}$ )
907 912 919 930 942 943 953	1	PbAc (IV)	100
901 902 920 925 928	2	Control	0
905 909 927 931 940	3	PbAc	25
923 933 948 950 956	4	PbAc	75
911 929 934 947 954	5	Palmerton Location 2	25
903 910 938 951 955	6	Palmerton Location 2	75
906 908 916 918 922	7	Palmerton Location 2	225
913 914 932 937 946	8	Palmerton Location 4	25
924 926 944 949 957	9	Palmerton Location 4	75
917 921 939 941 945	10	Palmerton Location 4	225

\*All materials administered orally unless designated IV (intravenously)

**EXPERIMENT 11 STUDY DESIGN**

Pig Number	Group	Material Administered*	Dose ( $\mu\text{g Pb/kg-day}$ )
1109 1124 1135 1139 1151	1	Control	0
1103 1104 1116 1117 1118	2	PbAc	25
1105 1123 1129 1130 1144	3	PbAc	75
1121 1136 1138 1146 1150	4	PbAc	225
1106 1112 1133 1142 1149	5	Murray Smelter Soil	75
1102 1122 1128 1143 1154	6	Murray Smelter Soil	225
1126 1137 1140 1141 1155	7	Murray Smelter Soil	675
1110 1115 1134 1148 1153	8	NIST Paint	75
1101 1108 1111 1132 1152	9	NIST Paint	225
1113 1119 1120 1125 1147	10	NIST Paint	675

\*All materials administered orally

**EXPERIMENT 12 STUDY DESIGN**

Pig Number	Group	Material Administered*	Dose ( $\mu\text{g Pb/kg-day}$ )
1205 1228 1236	1	Control	0
1208 1213 1215 1217 1248	2	PbAc	25
1227 1240 1243 1244 1255	3	PbAc	75
1222 1225 1226 1241 1249	4	PbAc	225
1201 1233 1250 1251 1253	5	Galena-enriched Soil	75
1203 1209 1214 1231 1247	6	Galena-enriched Soil	225
1218 1229 1235 1237 1254	7	Galena-enriched Soil	675
1207 1223 1230 1245 1252	8	Palmerton Location 2 (reproducibility)	25
1202 1210 1212 1220 1232	9	Palmerton Location 2 (reproducibility)	75
1211 1216 1221 1239 1246	10	Palmerton Location 2 (reproducibility)	225
1204 1224 1238 1242	11	California Gulch Oregon Gulch Tailings	225

\*All materials administered orally

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**APPENDIX C**

**DETAILED METHODS OF  
SAMPLE COLLECTION AND ANALYSIS**

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## **APPENDIX C**

### **DETAILED METHOD OF SAMPLE COLLECTION AND ANALYSIS**

#### **1.0 COLLECTION OF BIOLOGICAL SAMPLES**

##### Blood

Samples of blood were collected from each animal three or four days before exposure began, on the first day of exposure (day 0), and on multiple days thereafter (usually days 1, 2, 3, 5, 7, 9, 12, and 15). All blood samples were collected by vena-puncture of the anterior vena cava, and samples were immediately placed in purple-top Vacutainer<sup>®</sup> tubes containing EDTA (ethylenediaminetetra-acetic acid) 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 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.

##### Liver, Kidney, and Bone

Following collection of the final blood sample at 8:00 AM on day 15, all animals were humanely euthanized and samples of liver, kidney, and bone (the right femur) were removed and stored in 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 (e.g., arsenic, cadmium). All animals were also subjected to detailed examination at necropsy by a certified veterinary pathologist in order to assess overall animal health.

#### **2.0 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 (CDC, 2001). 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. Samples of the matrix modifier were routinely 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 screw-cap Teflon container with 2 mL of Optima grade concentrated (70%) nitric acid and heated in an oven to 90°C overnight. After cooling, the digestate was transferred to a clean 10 mL volumetric flask and diluted to volume with deionized and ultrafiltered water.

## Bone

The right femur of each animal was removed, defleshed, and dried at 100°C overnight. The dried bones were then broken in half, 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 mortar and pestle, and 200 mg was removed and dissolved in 10.0 mL of 1:1 (v:v) Optima grade 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 (La<sub>2</sub>O<sub>3</sub>) in deionized and ultrafiltered water.

### **3.0 LEAD ANALYSIS**

Samples of biological tissue (blood, liver, kidney, bone) and other materials (e.g., food, water, reagents and solutions) were arranged in a random sequence and provided to USEPA'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 15<sup>th</sup> sample. A blank, duplicate, and spiked sample were run every 20<sup>th</sup> sample. In addition, a series of quality assurance (QA) samples were prepared and submitted to the laboratory in blind fashion, including a variety of duplicates, blanks, and standards.

All results from the analytical laboratory were reported in units of µg Pb/L of prepared sample. The quantitation limit was defined as three-times the standard deviation of a set of seven replicates of a low-lead sample (typically about 2 to 5 µg/L). The standard deviation was usually about 0.3 µg/L, so the quantitation limit was usually about 0.9 to 1.0 µg/L (ppb). However, because different dilution factors were used for different sample types, the detection limit varies from sample type to sample type. For prepared blood samples (diluted 1/10), this corresponds to a quantitation limit of 10 µg/L (1 µg/dL). For soft tissues (liver and kidney, also diluted 1/10), this corresponds to a quantitation limit of 10 µg/kg (ppb) wet weight, and for bone (final dilution of 1/500) the corresponding quantitation limit is 0.5 µg/g (ppm) ashed weight.

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## **APPENDIX D**

### **DETAILED METHODS FOR DATA REDUCTION AND STATISTICAL ANALYSIS**

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## APPENDIX D

### DETAILED METHODS FOR DATA REDUCTION AND STATISTICAL ANALYSIS

#### 1.0 INTRODUCTION

The method used to estimate the RBA of lead in a particular test material compared to lead in a reference material (lead acetate) is based on the principal that equal absorbed doses of lead will produce equal biological responses. By definition:

$$Absorbed\ Dose_{ref} = Administered\ Dose_{ref} \cdot ABA_{ref}$$

$$Absorbed\ Dose_{test} = Administered\ Dose_{test} \cdot ABA_{test}$$

where *ref* and *test* indicate the reference and test material, respectively. When the responses are equal, then:

$$Administered\ Dose_{ref} \cdot ABA_{ref} = Administered\ Dose_{test} \cdot ABA_{test}$$

Thus:

$$RBA = \frac{ABA_{test}}{ABA_{ref}} = \frac{Administered\ Dose_{ref}}{Administered\ Dose_{test}}$$

That is, given the dose-response curve for some particular endpoint (e.g., the concentration of lead in blood or tissue) for both the reference material and the test material, RBA may be calculated as the ratio of administered doses that produce equal biological responses.

Note that, in this approach, the mathematical form of the dose-response model must be the same for both reference material and test material. This is because the shape of the dose-response curve is a function only of the pharmacokinetic response of the biological organism to an absorbed dose of lead, and the response per unit dose absorbed dose does not depend on whether the absorbed lead was derived from reference material or test material. Another way to envision this is to recognize that, if the unit of exposure were absorbed dose (rather than administered dose), the dose-response curves for reference material and test material would be identical. Note that, in this approach, RBA is a sample-specific constant and does not depend on administered dose.

Based on this, the general procedure for estimating the value of RBA from measured dose-response data for reference and test materials is as follows:

1. Plot the biological responses of individual animals exposed to a series of oral doses of reference material. Select an exposure-response model which can fit smoothly

through the observed data points. The model may be either linear or non-linear, depending on the response endpoint being used.

2. Plot the biological responses of individual animals exposed to a series of doses of test material. Fit the same exposure-response model as was used for the reference material. Note that the intercept term must be the same for both curves, but that other coefficients may be different.
3. To find the ratio of doses that produce equal responses, set the two exposure response curves equal to each other and solve for the ratio of doses expressed in terms of the model parameters.

For example, assume that the increase in lead in femur (*PbF*) is observed to be a linear function of administered dose. Assume that the best-fit exposure-response models derived from the experimental data for animals exposed to reference material and test material are as follows:

$$PbF_{ref} = 2 + 6 \cdot Dose_{ref}$$

$$PbF_{test} = 2 + 3 \cdot Dose_{test}$$

Setting the two equations equal yields:

$$2 + 6 \cdot Dose_{ref} = 2 + 3 \cdot Dose_{test}$$

Solving yields:

$$\frac{Dose_{ref}}{Dose_{test}} = \frac{3}{6} = 0.5$$

That is, the ratio of administered doses that produce equal responses is 0.5, so the RBA is 0.5 (50%).

An important assumption used in this approach is that administration of increasing doses of test material will cause increased biological responses. However, this may not occur in the case of a test material in which the form of lead has very low solubility. For example, the solubility of lead sulfide (galena) in water is less than 1 µg/L. Thus, if a dose of lead sulfide results in saturation of the gastric fluid, administration of more lead sulfide will not increase the concentration of bioavailable lead and, hence, little or no increase in response would be expected. An example of this is shown in Figure D-1. In this case, RBA cannot be defined as the ratio of doses that produce equal responses, since many different doses of lead sulfide all produce the same response. However, this is not a substantial difficulty, since the amount of lead that becomes bioavailable will be small (and hence the response will be close to control), and simple inspection of the data will demonstrate that the test material is not likely to be of health concern.

## 2.0 MEASUREMENT ENDPOINTS

### 2.1 Description of Measurement Endpoints

Four independent measurement endpoints were evaluated in each study, based on the concentration of lead observed in blood, liver, kidney, and bone (femur). For liver, kidney, and bone, the measurement endpoint was simply the concentration in the tissue at the time of sacrifice (day 15). For blood, the measurement endpoint used to quantify response was the area under the curve (AUC) for blood lead vs. time (days 0-15). 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 (i.e., the interval between successive blood collection days) using the trapezoidal rule:

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

where:

$d$  = day number, where  $i$  and  $j$  are successive blood sampling events

$r$  = response (blood lead value) on day  $i$  ( $r_i$ ) or day  $j$  ( $r_j$ )

The areas of the trapezoids for each time step were then summed to yield the final AUC for each animal.

### 2.2 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 was used because an assumed value of one-half the detection limit minimizes the potential bias in the assumption.

### 2.3 Assessment of Blood Lead Outliers

Occasionally blood lead values were obtained that were clearly different than expected. A value was considered to be an outlier if it was clearly different from other values within the same dose group on the same day, and/or if the value was clearly different from the time trend established by preceding and following time points in the same animal. A total of 21 such cases occurred out of a total of 4,284 blood lead data points (0.5%). These values were excluded in the calculation of AUC, and the missing value was replaced by a value interpolated from the preceding and following values from the same animal.

### 3.0 DERIVATION OF STATISTICAL DOSE-RESPONSE MODELS

The techniques used to derive statistical models of the dose-response data and to estimate RBA are based on the methods recommended by Finney (1978). All model fitting was performed using JMP™ version 3.2.2, a commercial software package developed by SAS®. Details are provided below.

#### 3.1 Use of Simultaneous Regression

As noted by Finney (1978), when the data to be analyzed consist of two dose-response curves (the reference material and the test material), it is obvious that both curves must have the same intercept, since there is no difference between the curves when the dose is zero. This requirement is achieved by combining the two dose response equations into one and solving for the parameters simultaneously. For example, if the dose response model is linear, the approach is as follows:

Separate Models:

$$\mu_r(i) = a + b_r \cdot x_r(i)$$

$$\mu_t(i) = a + b_t \cdot x_t(i)$$

Combined Model

$$\mu(i) = a + b_r \cdot x_r(i) + b_t \cdot x_t(i)$$

where  $\mu(i)$  indicates the expected mean response of animals exposed at dose  $x(i)$ , and the subscripts  $r$  and  $t$  refer to reference and test material, respectively. The coefficients of this combined model are derived using multivariate regression, with the understanding that the combined data set is restricted to cases in which one (or both) of  $x_r$  and  $x_t$  are zero (Finney, 1978). The same approach may be extended for use when there are three data sets (reference material, test material 1, test material 2) that are all derived from a single study and must therefore all have the same intercept.

#### 3.2 Use of Weighted Regression

Regression analysis based on ordinary least squares assumes that the variance of the responses is independent of the dose and/or the response (Draper and Smith, 1998). In these studies, this assumption is generally not satisfied. Figure D-2 provides two example data sets that show a clear increase in the variability of the responses as a function of increasing dose. This is referred to as heteroscedasticity. Most other data sets from this study display a similar tendency toward increasing variance in response as a function of increasing dose.

One method for dealing with heteroscedasticity is through the use of weighted least squares regression (Draper and Smith, 1998). In this approach, each observation in a group of animals is assigned a weight that is inversely proportional to the variance of the response in that group:

$$w_i = \frac{1}{\sigma_i^2}$$

where:

$w_i$  = weight assigned to all data points in dose group  $i$

$\sigma_i^2$  = variance of responses in animals in dose group  $i$

When the distributions of responses at each dose level are normal, weighted regression is equivalent to the maximum likelihood method. There are several options available for estimating the value of  $\sigma_i^2$ :

*Option 1:* Utilize the observed variance ( $s_i^2$ ) in the responses of animals in dose group  $i$ .

*Option 2:* Establish a variance model of the form  $\sigma_i^2 = \alpha\mu_i^\rho$ , where  $\mu_i$  is the predicted mean response for dose group  $i$ . Simultaneously fit the data to derive values of  $\alpha$  and  $\rho$  along with the other coefficients of the dose-response model using the data from a particular study. This approach is identical to the non-constant variance approach used by USEPA's BMDS (USEPA 1995, 2000a).

*Option 3A:* Establish an "external" variance model based on an analysis of the relationship between variance and mean response using observations combined from all studies and dose groups. Use that model to predict the expected variance in dose group  $i$  as a function of the predicted mean response for that dose group.

*Option 3B:* Establish an "external" variance model based on an analysis of the relationship between variance and mean response using observations combined from all studies and dose groups. Use that model to predict the expected variance in dose group  $i$  as a function of the observed mean response level for that dose group.

In this study, all four options were investigated for possible use. The advantages and disadvantages of each are discussed below.

Option 1 (use of group-specific sample variances) is the simplest approach, and does not require any assumptions or extrapolations. If the number of animals in each dose group was large enough to provide reliable estimates of the true variance for the dose group, this would be the preferred method. However, sample variance in a dose group is a random variable and, because the sample variance is based on only five observations (five animals per dose group), it can vary widely (especially when true variance is large). Therefore, weights assigned using this approach may occasionally be substantially higher or lower than the data actually warrant. For

example, this approach yielded poor results in cases where two adjacent groups (usually the control and the low dose group) had very low variance. In this situation, the weights for those groups were so high that the model fit was constrained to pass through them with very little deviation and other dose groups exerted very little influence. Figure D-3 shows an example of this. Because this outcome was judged to be inappropriate, Option 1 was not used.

Option 2 (using a non-constant variance model derived from the within-study data only) utilizes the entire data set from a single study to estimate expected variance as a function of dose, and so is less vulnerable to random variations in group-specific sample variances than Method 1. Despite this advantage, however, this approach requires that two additional parameters ( $\alpha$  and  $\rho$ ) be derived along with the other model parameters. This tends to over-parameterize the model and, when this option was tested (using the Solver tool in Microsoft<sup>®</sup> Excel), the fits were often not stable (i.e., different results were obtained with different starting guesses). On this basis, Option 2 was not employed.

Option 3 (both Options 3A and 3B) requires development of an external variance model based on the consolidated data from all studies. Figure D-4 shows the log-variance in response plotted as a function of the log-mean response in the group<sup>1</sup>. One panel is presented for each of the four different endpoints. As seen, log-variance increases as an approximately linear function of log-mean response for all four endpoints:

$$\ln(s^2_i) = k_1 + k_2 \cdot \ln(\bar{y}_i)$$

Values of  $k_1$  and  $k_2$  are derived from the data for each endpoint using ordinary least squares minimization, and the resulting values are shown in the figures. Note that this variance model is of the same basic form as used in Option 2:

$$s^2_i = \exp(k_1) \cdot (\bar{y}_i)^{k_2}$$

In Option 3A, the weights for each response are assigned based on the predicted mean response at each dose level within that model. For example, assuming a linear model:

$$\mu_x(i) = a + b_1 \cdot x_1(i) + b_2 \cdot x_2(i)$$

$$\sigma^2_i = \exp[k_1 + k_2 \cdot \ln(\mu_x(i))]$$

In Option 3B, the same approach is used, except that the observed mean response rather than the predicted mean response is used to estimate  $\sigma^2_i$ :

$$\sigma^2_i = \exp[k_1 + k_2 \cdot \ln(\mu_x(i))]$$

---

<sup>1</sup> In this analysis, some dose groups were excluded if the estimate of variance and/or mean response was judged to be unreliable, based on the following two criteria: a) the number of animals in the dose group was  $\leq 2$  or b) the fraction of responses below the detection limit was more than 20%. For the blood lead AUC endpoint (where the raw data consist of multiple blood lead values as a function of time), this corresponds to an AUC less than about 15  $\mu\text{g}/\text{dL}$ -days.

In testing both options, it was found that Options 3A and 3B gave similar results in most cases. However, Option 3A (in which weights are not pre-assigned but are optimized during the fitting procedure) tended to be very sensitive to starting guesses, often failing to find solutions even when the starting guesses were good, and sometimes yielding different results depending on the starting guesses. In addition, this approach uses the expected mean response rather than the observed mean response to estimate the variance, which tends to diminish the role of the measured data in defining the best fit curve. In contrast, Option 3B was less prone to unstable solutions, and is based more directly on the data.

Based on a consideration of the advantages and disadvantages of each approach, Option 3B was selected for use in this project. This is mainly because it has relatively less vulnerability than Option A to random variations in observed variances in a dose group (which results in assignment of weights that are either too high or too low), and also because it could be implemented with relatively few difficulties. It should be noted, however, that Option 3B is somewhat vulnerable to poor fits when one particular dose group in a data set lies well below the expected smooth fit through the other dose groups. In this case, the variance assigned to the group (based on the observed mean response) is lower than typical for that dose level (and hence the weights assigned to the data are higher than usual), tending to force the line through that data set at the expense of the other data sets.

### 3.3 Choice of Model Forms

As noted above, the main objective of the curve-fitting effort is to find a mathematical model that fits both the reference and test group dose-response data sets smoothly. Note that there is no requirement that the model have a mechanistic basis or that the coefficients have a biological meaning. As discussed by Finney (1978), it is generally not appropriate to choose the form of the dose-response model based on only one experiment, but to make the choice based on the weight of observations across many different studies. Because simple inspection of the data suggest that, over the range of doses tested in these studies, some dose-response curves (mainly those for liver, kidney, and bone) appear to be approximately linear, while others (mainly those for blood lead AUC) appear to be nonlinear (tending to plateau as dose increases), the linear model and three alternative non-linear models were evaluated:

$$1) \text{ Linear: } y = a + b_r \cdot x_r + b_t \cdot x_t$$

$$RBA = \frac{b_t}{b_r}$$

$$2) \text{ Exponential: } y = a + b \cdot (1 - \exp(-c_r \cdot x_r)) + b \cdot (1 - \exp(-c_t \cdot x_t)) =$$

$$RBA = \frac{c_t}{c_r}$$

$$3) \text{ Michaelis-Menton: } y = a + b \cdot \left( \frac{x_r}{c_r + x_r} + \frac{x_t}{c_t + x_t} \right)$$

$$RBA = \frac{c_r}{c_t}$$

$$4) \text{ Power: } y = a + b_r \cdot x_r^c + b_t \cdot x_t^c$$

$$RBA = \left( \frac{b_t}{b_r} \right)^{1/c}$$

Appendix E presents the detailed results for every data set fit to each of the four different models investigated. Goodness-of-fit was assessed using the  $F$  test statistic and the adjusted coefficient of multiple determination ( $Adj R^2$ ), calculated as follows (Draper and Smith, 1998):

$$F = \frac{MSE_{fit}}{MSE_{error}}$$

$$Adj R^2 = 1 - \frac{MSE_{error}}{MSE_{total}}$$

where:

$$MSE_{fit} = \sum w_i \cdot \frac{(\mu_i - \bar{y}^*)^2}{p-1}$$

$$MSE_{error} = \sum w_i \cdot \frac{(\mu_i - y_i)^2}{n-p}$$

$$MSE_{total} = \sum w_i \cdot \frac{(y_i - \bar{y}^*)^2}{n-1}$$

and:

$$\bar{y}^* = \frac{\sum (w_i \cdot y_i)}{\sum w_i}$$

$p$  = number of parameters in model

$n$  = number of observations (animals)

$F$  is distributed as an F distribution with  $(p-1)$  and  $(n-p)$  degrees of freedom. Models with  $p$  values larger than 0.05 were not considered to be acceptable. Of the models that were acceptable



( $p < 0.05$ ), the preferred model was identified based on Akaike's Information Criterion (AIC) (USEPA, 2000a and 2000b), which is calculated as:

$$AIC = -2 \cdot L + 2 \cdot p$$

where:

$L$  = Log-likelihood function

$p$  = number of parameters in the model

At the  $k$ th dose, the sample log-likelihood function is:

$$L_k = -\frac{N_k}{2} \cdot \ln(2\pi\sigma_k^2) - \frac{1}{2\sigma_k^2} \cdot \sum_{j=1}^{N_k} [y_{k,j} - f(x_k)]^2$$

(Nelson, 1982). The overall log-likelihood is the sum across all dose groups ( $g$ ):

$$L = \sum_{k=1}^g L_k$$

so that

$$L = -\sum_{k=1}^g \frac{N_k}{2} \cdot \ln(2\pi\sigma_k^2) - \sum_{k=1}^g \frac{1}{2\sigma_k^2} \cdot \sum_{j=1}^{N_k} [y_{k,j} - f(x_k)]^2$$

The detailed results are presented in Appendix E, and the findings are summarized in Table D-1. Inspection of this table reveals the following main conclusions:

- For liver, kidney, and bone, the linear model generally gave the best fit, although this varied somewhat by endpoint (7/10 for kidney, 6/10 for bone, 4/10 for liver). In cases where the linear model was not the best fit, the RBA value given by the linear model was usually close to that given by whatever other model did provide the best fit, with an average absolute difference of 12% (6% if one data set [study 9] was excluded). On this basis, the linear model was selected for application to all dose-response data sets for liver, kidney, and bone.
- For the blood lead AUC endpoint, the linear model usually gave the worst fit, and on this basis it was rejected as a candidate for the AUC endpoint. In general, each of the three nonlinear models (exponential, Michaelis-Menton, and power) all tended to give similar results in terms of RBA value (the standard deviation in RBA for a particular test material averaged across the three models was usually less than 3%), and differences in the AIC were usually small. On this basis, it was concluded that any of these three models would be acceptable. The power model was not selected because it does not tend toward a plateau, while data from early blood lead pilot

studies (using higher doses than commonly used in the Phase II studies) suggest that the blood lead endpoint does tend to do so. Of the remaining two models (exponential and Michaelis-Menton), the exponential model was selected mainly because it yielded the best fit more often than the Michaelis-Menton model (4 out of 10 vs. 2 out of 10), and because the exponential model had been used in previous analyses of the data. Thus, the exponential model was selected for application to all dose-response data sets for the blood AUC endpoint, except in one special case noted below in section 4.5.

### **3.4 Assessment of Endpoint Outliers**

In biological assays, it is not uncommon to note the occurrence of individual measured responses that appear atypical compared to the responses from other animals in the same dose group. For the purposes of this program, endpoint responses that yielded standardized weighted residuals greater than 3.5 or less than -3.5 were considered to be potential outliers (Canavos, 1984). When such data points were encountered in a data set, the RBA was calculated both with and without the potential outlier(s) excluded, and the result with the outlier excluded was used as the preferred estimate.

### **3.5 Treatment of Problematic Data Sets**

Although the data reduction approach described above works well in most cases, a few data sets yielded atypical results. In particular, fitting the blood lead data set from Experiment 7 proved difficult. In this study, the blood lead AUC data set did not yield a solution in JMP for the exponential model, even though solutions could be obtained in Excel using minimization of weighted squared errors. However, the solutions tended to be unstable. This difficulty in modeling the data appears to be due to the fact that the data have relatively less curvature than most blood lead AUC data sets. Because of this lack of curvature, it is not possible to estimate the exponential plateau value (b) with confidence, which in turns makes it difficult to estimate the other parameters of the exponential model.

Several alternative solutions were evaluated, including a) using the model fits from one of the other nonlinear models, b) using the fit for the linear model, and c) fitting the data to the exponential model using a defined value for the plateau based on results from other data sets. The results (i.e., the RBA values based on the blood lead AUC endpoint) were generally similar for all three of these approaches:

Model	RBA of TM1	RBA of TM2
Power	0.65	0.83
Linear	0.69	0.90
Michaelis-Menton	0.69 ± 0.01*	0.90 ± 0.01*
Exponential fit	0.70 ± 0.02*	0.93 ± 0.04*
Exponential fit (parameter $b = 126.4$ )**	0.75	1.04
Exponential fit (parameter $b = 169.1$ )***	0.74	1.01

\*Solution was unstable; values represent the mean and standard deviation of five different fitting results.

\*\*Parameter  $b$  set to the mean of the estimates obtained for all other blood AUC data sets using the exponential model.

\*\*\*Parameter  $b$  set to the maximum of the estimates obtained for all other blood AUC data sets using the exponential model.

All estimates are based on all data (outliers not excluded).

Based on these results, it was concluded that the results from the linear fit were representative of the range of values derived by other alternatives, so the JMP fit for the linear model was used for this data set.

### 3.6 Characterization of Uncertainty Bounds

Each RBA value is calculated as the ratio of a model coefficient for the reference data set and for the test data set:

$$RBA_{linear\ endpoints} = \frac{b_t}{b_r}$$

$$RBA_{blood\ AUC} = \frac{c_t}{c_r}$$

However, there is uncertainty in the estimates of the model coefficients in both the numerator and denominator and, hence, there is uncertainty in the ratio. As described by Finney (1978), the fiduciary limits (uncertainty range) about the ratio  $R$  of two model coefficients may be calculated using Fieller's Theorem:

$$LB, UB = \frac{R - g \pm \frac{covar_{r,t}}{var_r} \pm \frac{t}{b_r} \cdot \sqrt{W}}{1 - g}$$

$$W = var_t - 2 \cdot R \cdot covar_{t,r} + R^2 \cdot var_r = \left( \frac{covar_{r,t}^2}{var_r} \right)$$

$$g = \frac{t^2}{b_r^2} \cdot \text{var}_r$$

where:

$R$  = ratio ( $b_t / b_r$  for linear model,  $c_t / c_r$  for exponential model)

$\text{var}_r$  = variance in the coefficient for the reference material

$\text{covar}_{r,t}$  = covariance in the coefficients for the reference and test materials

$b_r$  = coefficient for the reference material ( $c_r$  in the case of the exponential model)

$t$  = t statistic for alpha (0.05) and  $(n-p)$  degrees of freedom

When  $g$  is small ( $<0.05$ ), the variance of the ratio is approximated as (Finney 1978):

$$\text{var}_R = \frac{\text{var}_t - 2 \cdot R \cdot \text{covar}_{r,t} + R^2 \cdot \text{var}_r}{b_r^2}$$

### 3.7 Combination of RBA Estimates Across Endpoints

As discussed above, each study of RBA utilized four different endpoints to estimate absorption of lead, including blood AUC, liver, kidney, and bone. Consequently, each study yielded four independent estimates of RBA for each test material. Thus, the final RBA estimate for a test material involves combining the four end-point specific RBA values into a single value (point estimate), and estimating the uncertainty around that point estimate. The methods used to achieve these goals are described below.

#### *Derivation of the Point Estimate*

The basic strategy for deriving a point estimate of RBA for a test material is to calculate a confidence-weighted average of the four endpoint-specific RBA values. If all four endpoints are considered to be equally reliable, the weighting factors are all equal (i.e., the point estimate is the simple average). If reliability is considered to differ from endpoint to endpoint, then weights are assigned in proportion to the reliability:

$$RBA_{\text{point estimate}} = \frac{\sum (RBA_i \cdot w_i)}{\sum w_i}$$

Because each endpoint-specific RBA value is calculated as the ratio of the parameters of the dose-response curves fitted to the experimental data for reference material and test material, the reliability of an endpoint-specific RBA is inherently related to the quality of the data that define the dose-response curve for that endpoint. For endpoints that tend to have low within-group variability and generate data that fit the dose-response model well, the uncertainty around

the model parameters will tend to be small and hence the uncertainty around the RBA value will also tend to be small. Conversely, if the underlying dose-response data for an endpoint are highly variable and the dose-response model does not fit the data well, there will tend to be high uncertainty in the model parameters and hence in the RBA estimate. Thus, a good indicator of relative reliability between the four different endpoints is the relative magnitude of the uncertainty (standard error) around RBA estimates based on each endpoint.

Figure D-5 plots the standard error in each RBA estimate as a function of the RBA value for each of the four different endpoints. As seen, uncertainty in RBA increases as a function of the estimated value of RBA in all four cases. This is expected because of the heteroscedasticity in the underlying dose-response data. Although RBA values based on blood AUC and femur tend to yield estimates with slightly lower standard errors than RBA values based on liver or kidney, the magnitude of the standard errors tends to be generally similar for all four endpoints, and the difference between the four regression lines is not statistically significant ( $p = 0.699$ ). Based on this, each endpoint-specific RBA value was judged to have approximately equal validity, and the point estimate was calculated as the simple average across all four endpoint-specific RBA values.

#### *Estimation of Uncertainty Bounds Around the Point Estimate*

The uncertainty bounds around each point estimate were estimated using Monte Carlo simulation. For each test material, values for RBA were drawn from the uncertainty distributions for each endpoint with equal frequency. Each endpoint-specific uncertainty distribution was assumed to be normal, with the mean equal to the best estimate of RBA and the standard deviation estimated from Fieller's Theorem (see Section 4.6 above). The uncertainty in the point estimate was characterized as the range from the 5<sup>th</sup> to the 95<sup>th</sup> percentile of the average across endpoints.

## 4.0 RELATION BETWEEN RBA AND IVBA

### 4.1 Choice of Model Form

As discussed in Section 3.3.2 of the main text, one of the important objectives of this program was to characterize the degree to which measures of *in vitro* bioaccessibility (IVBA) correlate with and can be used to predict *in vivo* measurements of RBA. This objective was approached by plotting the point estimate of *in vivo* RBA vs. the corresponding IVBA value for each of the 19 different test materials and fitting several different mathematical models to the data. Because the measurement error in RBA is heteroscedastic (tending to increase as RBA increases), all of the model fitting was performed by minimizing the sum of the weighted squared errors between observed and predicted RBA, as described above (Section 4.2). The weighting factor assigned to each RBA point estimate was the inverse of the variance derived from Monte Carlo simulation, as described in Section 4.7 and shown in Table D-2. Goodness of fit was assessed using the AIC, as described in Section 4.3. The fitting results are shown in Figure D-6 (Panels A to D), and are summarized below:

Model	a	b	c	R <sup>2</sup>	AIC
Linear: $RBA = a + b \cdot IVBA$	-0.028	0.878	--	0.924	-30.46
Power: $RBA = a + b \cdot IVBA^c$	-0.003	0.978	1.293	0.931	-29.92
2-Parameter Exponential: $RBA = a + b \cdot \exp(IVBA)$	-0.634	0.619	--	0.936	-33.02
3-Parameter Exponential: $RBA = a + b \cdot \exp(c \cdot IVBA)$	-0.476	0.464	1.225	0.936	-31.11

As seen, all of the models fit the data reasonably well, with the two exponential models fitting somewhat better than the linear model. However, the improved fit of the exponential models is due mainly to the fact that the two data points that occur in the central part of the x-range (IVBA = 0.378 and 0.470) lie below the best fit linear line, and these two data points tend to pull the central part of the curve down slightly when a non-linear model is used. If these two data points were absent, or if a third data point were present that were above the linear fit, the quality of the fits would be approximately equal for linear and non-linear models. Based on the judgment that two data points are not sufficient evidence to conclude that a non-linear fit is preferable to a linear model, the linear model is selected as the interim recommended model. As more data become available in the future, the relationship between IVBA and RBA will be reassessed and the model will be revised if needed.

Figure D-7 shows a graph of the best fit linear model through the data, along with the 95% prediction interval, calculated using SAS<sup>®</sup>. As noted above, the best fit equation is:

$$RBA = 0.878 \cdot IVBA - 0.028$$

## 4.2 Adjusting for Measurement Error in Both IVBA and RBA

In most cases, linear and non-linear regression techniques assume that there are no measurement errors in the independent variable (IVBA). However, as noted in Section 3 of the main text, IVBA is derived by experimental measurement and, hence, there is some degree of measurement error in each IVBA value. In this situation, use of weighted linear regression (which accounts only for the measurement errors in RBA) may yield a fit that is biased, with the magnitude of the error depending on the relative magnitude of the measurement errors in IVBA compared to RBA. In order to investigate whether this was an important adjustment, the data were fit by minimizing the chi-square merit function for a linear model (Cheng and Van Ness 1999):

$$X^2 = \sum \frac{(RBA_i - a - b \cdot IVBA_i)^2}{(Sy_i^2 + b^2 \cdot Sx_i^2)}$$

where:

$a$  = Intercept of the linear equation

$b$  = Slope of the linear equation

$Sy_i^2$  = Variance of RBA estimate  $i$

$Sx_i^2$  = Variance of IVBA estimate  $i$

As above, the value of  $Sy_i^2$  was derived from the Monte Carlo simulation used to derive the point estimate for each RBA value, and the value of  $Sx_i^2$  was the variance of the three independent measurements of IVBA (see Table D-2). Based on this approach, the best fit equation is:

$$RBA = 0.884 \cdot IVBA - 0.028$$

As seen, this fit is very similar to the weighted linear regression fit above, with the same intercept and a slightly greater slope. This relatively small effect of adjusting for measurement error in IVBA is expected, because measurement errors in IVBA tend to be substantially smaller (average coefficient of variation = 6%) than those in RBA (average coefficient of variation = 33%) (see Table D-2). Because the difference in results is so small for this data set, the fit based on weighted linear regression is selected as the preferred model at this time, because of its relative simplicity. This decision may be re-evaluated in the future as additional data become available.

## 5.0 REFERENCES

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APPENDIX D

TABLE D-1. MODEL COMPARISONS

Endpoint	Experiment	LINEAR						EXPONENTIAL						MICHAELIS-MENTON						POWER						Lowest AIC
		AIC	p	Adj R <sup>2</sup>	RBA1	RBA2	RBA3	AIC	p	Adj R <sup>2</sup>	RBA1	RBA2	RBA3	AIC	p	Adj R <sup>2</sup>	RBA1	RBA2	RBA3	AIC	p	Adj R <sup>2</sup>	RBA1	RBA2	RBA3	
Blood AUC	2	412.4014	< 0.001	0.779	0.38	0.31	--	393.6549	< 0.001	0.827	0.34	0.30	--	391.8262	< 0.001	0.831	0.33	0.30	--	386.1163	< 0.001	0.846	0.34	0.30	--	POWER
Blood AUC	3	428.5143	< 0.001	0.818	0.53	0.63	--	377.8492	< 0.001	0.896	0.65	0.94	--	376.0574	< 0.001	0.899	0.65	0.94	--	374.4287	< 0.001	0.902	0.62	0.85	--	POWER
Blood AUC	4	455.6739	< 0.001	0.787	0.34	0.48	--	382.9415	< 0.001	0.896	0.47	0.84	--	379.6654	< 0.001	0.901	0.47	0.84	--	374.2627	< 0.001	0.909	0.40	0.73	--	POWER
Blood AUC	5	385.03	< 0.001	0.864	0.50	0.55	--	345.1702	< 0.001	0.933	0.69	0.72	--	344.7351	< 0.001	0.934	0.68	0.73	--	344.9323	< 0.001	0.934	0.61	0.68	--	MM
Blood AUC	6	333.5853	< 0.001	0.820	0.28	0.30	--	311.8304	< 0.001	0.888	0.21	0.19	--	312.3221	< 0.001	0.886	0.21	0.19	--	316.066	< 0.001	0.875	0.24	0.23	--	EXP
Blood AUC	7	394.3537	< 0.001	0.692	0.69	0.90	--	NS	NS	NS	NS	NS	--	NS	NS	NS	NS	NS	--	394.2826	< 0.001	0.689	0.65	0.83	--	POWER
Blood AUC	8	377.1965	< 0.001	0.822	0.26	--	--	337.9125	< 0.001	0.898	0.26	--	--	336.9394	< 0.001	0.900	0.26	--	--	344.3656	< 0.001	0.885	0.20	--	--	MM
Blood AUC	9	328.7634	< 0.001	0.862	0.62	0.54	--	312.2198	< 0.001	0.909	0.82	0.62	--	312.6794	< 0.001	0.908	0.80	0.62	--	316.1967	< 0.001	0.899	0.73	0.60	--	EXP
Blood AUC	11	436.4331	< 0.001	0.857	0.49	0.60	--	390.4143	< 0.001	0.922	0.70	0.86	--	391.3314	< 0.001	0.921	0.70	0.86	--	402.3932	< 0.001	0.905	0.66	0.83	--	EXP
Blood AUC	12	375.1354	< 0.001	0.906	0.01	0.78	0.09	370.3802	< 0.001	0.910	0.01	0.71	0.07	370.7599	< 0.001	0.910	0.01	0.72	0.07	374.8385	< 0.001	0.905	0.01	0.74	0.07	EXP
Liver	2	543.2988	< 0.001	0.567	0.35	0.25	--	NS	NS	NS	NS	NS	--	NS	NS	NS	NS	NS	--	543.0502	< 0.001	0.574	0.39	0.26	--	POWER
Liver	3	562.2981	< 0.001	0.782	0.56	1.20	--	NS	NS	NS	NS	NS	--	NS	NS	NS	NS	NS	--	561.4696	< 0.001	0.786	0.60	1.08	--	POWER
Liver	4	558.5529	< 0.001	0.564	0.51	0.86	--	NS	NS	NS	NS	NS	--	NS	NS	NS	NS	NS	--	555.8161	< 0.001	0.586	0.39	0.74	--	POWER
Liver	5	674.4086	0.003	0.268	0.93	1.13	--	NS	NS	NS	NS	NS	--	NS	NS	NS	NS	NS	--	675.8198	0.007	0.249	0.87	1.02	--	LIN
Liver	6	468.3743	< 0.001	0.622	0.13	0.14	--	470.3592	< 0.001	0.612	0.13	0.14	--	470.3592	< 0.001	0.612	0.13	0.14	--	470.2987	< 0.001	0.613	0.13	0.13	--	LIN
Liver	7	503.4618	< 0.001	0.679	0.54	0.71	--	505.44	< 0.001	0.671	0.54	0.72	--	NS	NS	NS	NS	NS	--	505.3976	< 0.001	0.672	0.54	0.72	--	LIN
Liver	8	629.6988	< 0.001	0.452	0.18	--	--	NS	NS	NS	NS	--	--	NS	NS	NS	NS	--	--	630.6132	< 0.001	0.441	0.18	--	--	LIN
Liver	9	484.9237	< 0.001	0.727	0.60	0.53	--	470.6533	< 0.001	0.777	1.11	0.65	--	471.6336	< 0.001	0.774	1.07	0.65	--	475.7101	< 0.001	0.760	0.89	0.62	--	EXP
Liver	11	561.4438	< 0.001	0.757	0.58	0.73	--	561.5909	< 0.001	0.757	0.66	0.71	--	561.5427	< 0.001	0.757	0.65	0.71	--	560.9762	< 0.001	0.759	0.63	0.73	--	POWER
Liver	12	506.975	< 0.001	0.716	0.02	1.25	0.11	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	493.7966	< 0.001	0.746	0.02	0.98	0.12	POWER
Kidney	2	530.2226	< 0.001	0.687	0.22	0.27	--	NS	NS	NS	NS	NS	--	NS	NS	NS	NS	NS	--	532.2104	< 0.001	0.679	0.22	0.27	--	LIN
Kidney	3	533.5968	< 0.001	0.834	0.58	0.91	--	534.2703	< 0.001	0.833	0.58	0.97	--	534.219	< 0.001	0.834	0.58	0.97	--	534.0045	< 0.001	0.834	0.56	0.95	--	LIN
Kidney	4	550.1067	< 0.001	0.715	0.31	0.70	--	NS	NS	NS	NS	NS	--	NS	NS	NS	NS	NS	--	551.8207	< 0.001	0.709	0.30	0.68	--	LIN
Kidney	5	547.8196	< 0.001	0.529	0.73	0.78	--	NS	NS	NS	NS	NS	--	NS	NS	NS	NS	NS	--	548.0081	< 0.001	0.527	0.64	0.74	--	LIN
Kidney	6	500.2596	< 0.001	0.552	0.12	0.16	--	501.6143	< 0.001	0.543	0.11	0.14	--	501.6373	< 0.001	0.543	0.11	0.14	--	501.9909	< 0.001	0.541	0.12	0.14	--	LIN
Kidney	7	501.5953	< 0.001	0.657	0.51	0.86	--	NS	NS	NS	NS	NS	--	NS	NS	NS	NS	NS	--	503.5096	< 0.001	0.649	0.51	0.85	--	LIN
Kidney	8	586.5547	< 0.001	0.573	0.14	--	--	585.9632	< 0.001	0.571	0.14	--	--	585.9527	< 0.001	0.571	0.14	--	--	581.2902	< 0.001	0.587	0.13	--	--	POWER
Kidney	9	535.8631	< 0.001	0.579	0.51	0.41	--	511.6407	< 0.001	0.661	1.62	0.52	--	513.5473	< 0.001	0.655	1.63	0.55	--	518.7502	< 0.001	0.636	1.36	0.56	--	EXP
Kidney	11	576.6481	< 0.001	0.725	0.36	0.55	--	578.6496	< 0.001	0.718	0.53	0.47	--	578.7016	< 0.001	0.717	0.48	0.48	--	578.2471	< 0.001	0.720	0.39	0.52	--	LIN
Kidney	12	868.9066	< 0.001	0.329	0.01	0.47	0.04	870.0698	< 0.001	0.315	0.01	0.34	0.03	870.32	< 0.001	0.315	0.01	0.36	0.03	864.5181	< 0.001	0.326	0.01	0.73	0.08	POWER
Femur	2	180.5215	< 0.001	0.863	0.24	0.26	--	NS	NS	NS	NS	NS	--	NS	NS	NS	NS	NS	--	182.5211	< 0.001	0.859	0.24	0.26	--	LIN
Femur	3	187.2204	< 0.001	0.863	0.65	0.75	--	186.1918	< 0.001	0.870	0.70	0.81	--	186.1445	< 0.001	0.870	0.70	0.81	--	186.099	< 0.001	0.870	0.68	0.79	--	POWER
Femur	4	196.1178	< 0.001	0.886	0.31	0.89	--	NS	NS	NS	NS	NS	--	NS	NS	NS	NS	NS	--	195.6032	< 0.001	0.888	0.32	0.96	--	POWER
Femur	5	221.1807	< 0.001	0.856	0.67	0.73	--	NS	NS	NS	NS	NS	--	NS	NS	NS	NS	NS	--	222.5578	< 0.001	0.854	0.65	0.72	--	LIN
Femur	6	227.7994	< 0.001	0.465	0.11	0.10	--	229.7051	< 0.001	0.451	0.11	0.10	--	229.7112	< 0.001	0.451	0.11	0.10	--	229.612	< 0.001	0.451	0.11	0.11	--	LIN
Femur	7	216.3481	< 0.001	0.615	0.53	0.80	--	216.5913	< 0.001	0.611	0.56	0.95	--	NS	NS	NS	NS	NS	--	216.3737	< 0.001	0.612	0.56	0.93	--	LIN
Femur	8	193.9091	< 0.001	0.830	0.20	--	--	195.1797	< 0.001	0.828	0.20	--	--	195.1037	< 0.001	0.828	0.20	--	--	185.5952	< 0.001	0.850	0.18	--	--	POWER
Femur	9	118.6208	< 0.001	0.855	0.47	0.40	--	112.175	< 0.001	0.884	0.50	0.43	--	111.9654	< 0.001	0.885	0.50	0.43	--	111.1541	< 0.001	0.888	0.48	0.41	--	POWER
Femur	11	198.2084	< 0.001	0.871	0.39	0.74	--	NS	NS	NS	NS	NS	--	NS	NS	NS	NS	NS	--	200.0238	< 0.001	0.869	0.38	0.73	--	LIN
Femur	12	137.1663	< 0.001	0.865	0.01	0.95	0.01	139.1501	< 0.001	0.856	0.01	0.95	0.01	139.1506	< 0.001	0.856	0.01	0.95	0.01	139.1826	< 0.001	0.861	0.01	0.95	0.01	LIN

-- = The respective test material does not exist for this study.  
NS = No solution; the software could not find a solution, or the solution was unstable and/or had unrealistic parameter estimates.  
NA = Not applicable; the preferred model has the best fit, or no solution was found for the preferred model.

## APPENDIX D

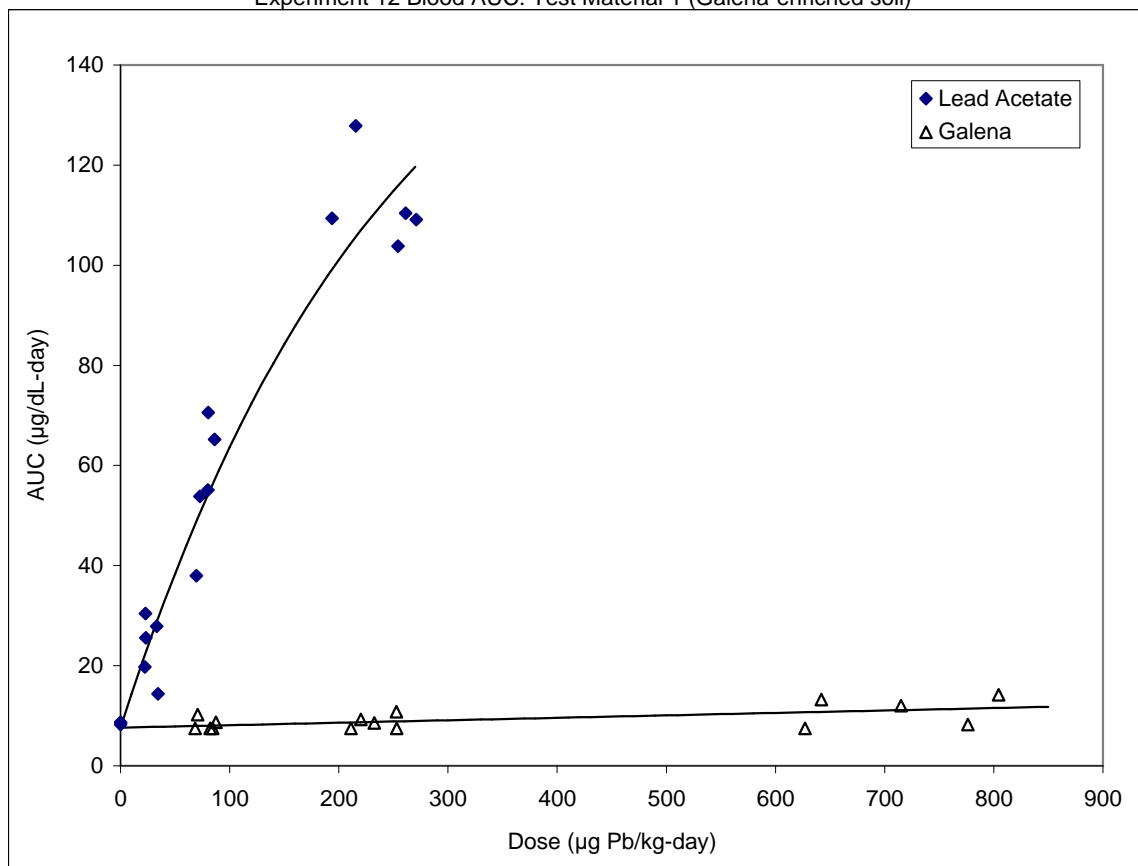
**TABLE D-2. DATA FOR WEIGHTED REGRESSION OF RBA vs. IVBA**

Sample	RBA				IVBA			
	Best Estimate	Standard Deviation	Variance		Best Estimate	Standard Deviation	Variance	
Galena-enriched Soil	0.011	0.009	82%	8.12E-05	0.045	0.012	26%	1.40E-04
California Gulch AV Slag	0.199	0.065	33%	4.26E-03	0.094	0.016	17%	2.64E-04
California Gulch Oregon Gulch Tailings	0.061	0.047	78%	2.24E-03	0.112	0.009	8%	7.73E-05
Midvale Slag	0.141	0.050	35%	2.49E-03	0.174	0.009	5%	8.93E-05
Butte Soil	0.144	0.049	34%	2.39E-03	0.223	0.006	2%	3.03E-05
Bingham Creek Channel Soil	0.266	0.053	20%	2.78E-03	0.378	0.007	2%	5.01E-05
Bingham Creek Residential	0.268	0.068	25%	4.58E-03	0.470	0.012	3%	1.45E-04
Palmerton Location 2	0.602	0.184	31%	3.38E-02	0.636	0.004	1%	1.29E-05
Murray Smelter Slag	0.401	0.132	33%	1.73E-02	0.643	0.073	11%	5.39E-03
Aspen Berm	0.740	0.182	25%	3.31E-02	0.649	0.016	2%	2.45E-04
California Gulch Phase I Residential Soil	0.723	0.212	29%	4.50E-02	0.651	0.015	2%	2.20E-04
Jasper County High Lead Smelter	0.609	0.108	18%	1.16E-02	0.693	0.055	8%	3.04E-03
Palmerton Location 4	0.493	0.136	28%	1.85E-02	0.697	0.027	4%	7.51E-04
Aspen Residential	0.749	0.164	22%	2.68E-02	0.714	0.020	3%	3.83E-04
NIST Paint (SRM 2589)	0.719	0.165	23%	2.72E-02	0.725	0.020	3%	4.12E-04
Murray Smelter Soil	0.508	0.164	32%	2.69E-02	0.747	0.068	9%	4.64E-03
Jasper County Low Lead Yard	0.900	0.178	20%	3.18E-02	0.790	0.056	7%	3.13E-03
Jasper County High Lead Mill	0.823	0.192	23%	3.68E-02	0.853	0.002	0%	2.97E-06
California Gulch Fe/Mn PbO	1.049	0.299	28%	8.93E-02	0.872	0.005	1%	2.37E-05

APPENDIX D

FIGURE D-1. DOSE-RESPONSE CURVE FOR GALENA

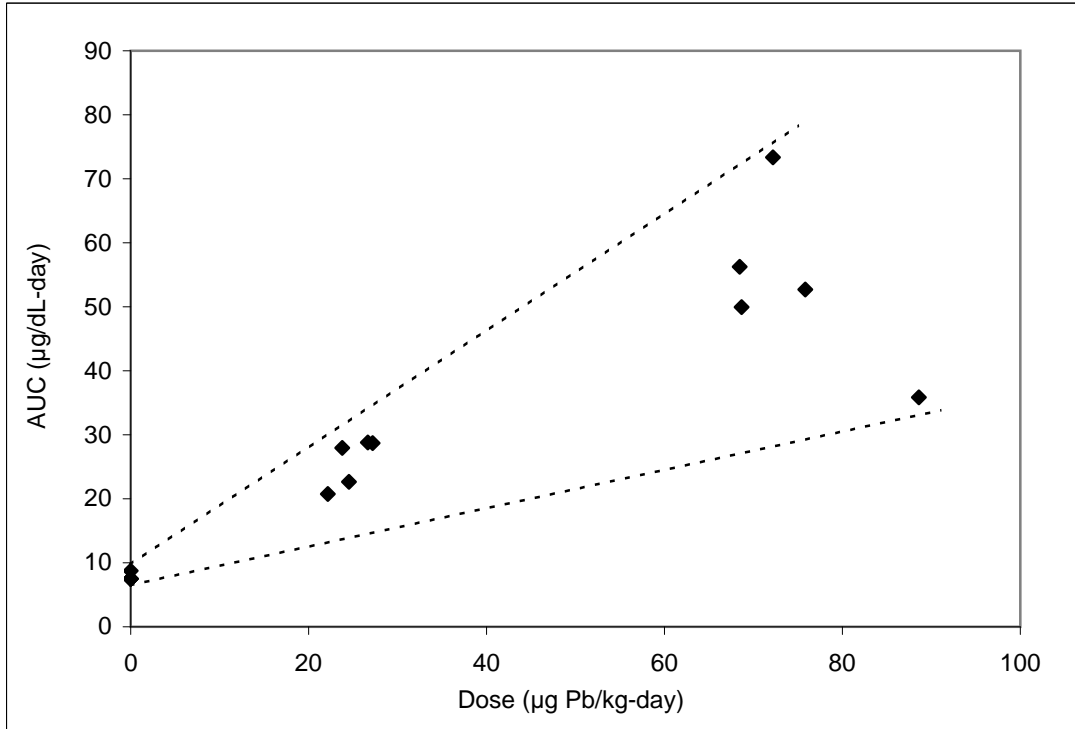
Experiment 12 Blood AUC: Test Material 1 (Galena-enriched soil)



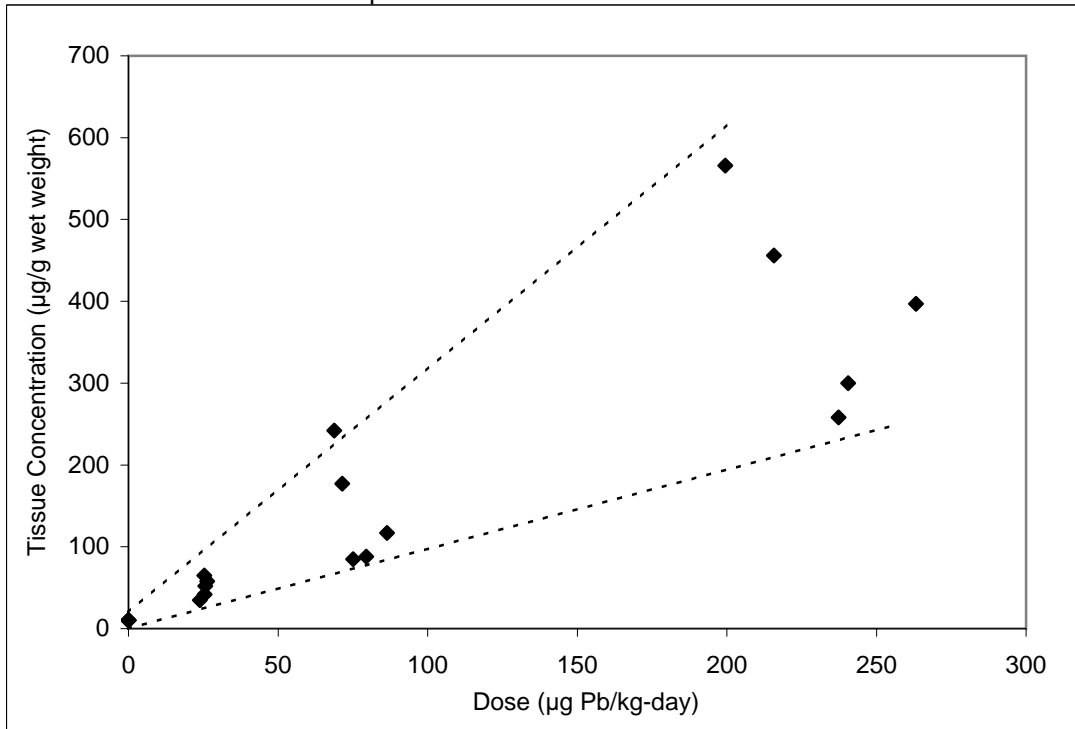
APPENDIX D

FIGURE D-2. EXAMPLES OF HETEROSCEDASTICITY

Experiment 9 Blood AUC: Lead Acetate



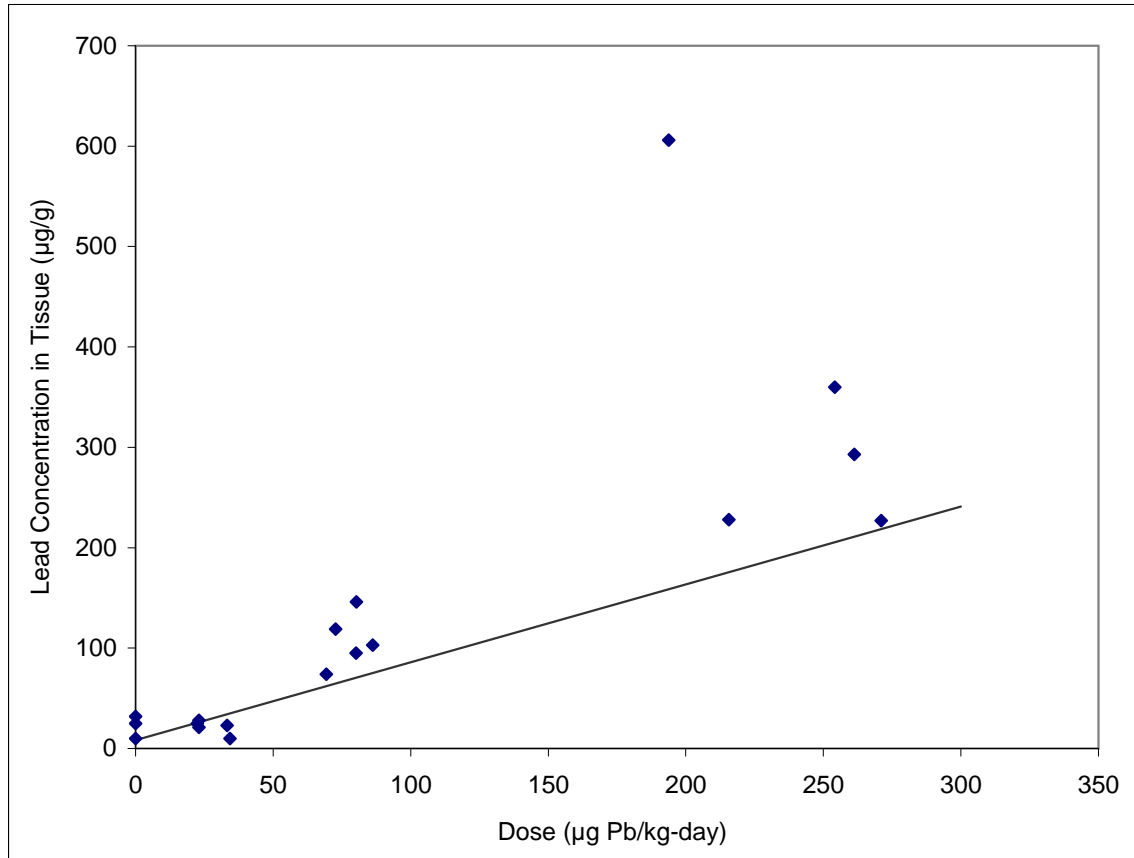
Experiment 7 Liver: Test Material 2



APPENDIX D

**FIGURE D-3. EXAMPLE OF POOR FIT DUE TO LOW VARIANCE  
IN SOME DOSE GROUPS**

Option 1, Linear Fit: Experiment 12 Liver, Lead Acetate



**FIGURE D-4. VARIANCE MODELS**

All Phase II Lead Studies. Data Quality Exclusion Rules Enforced.

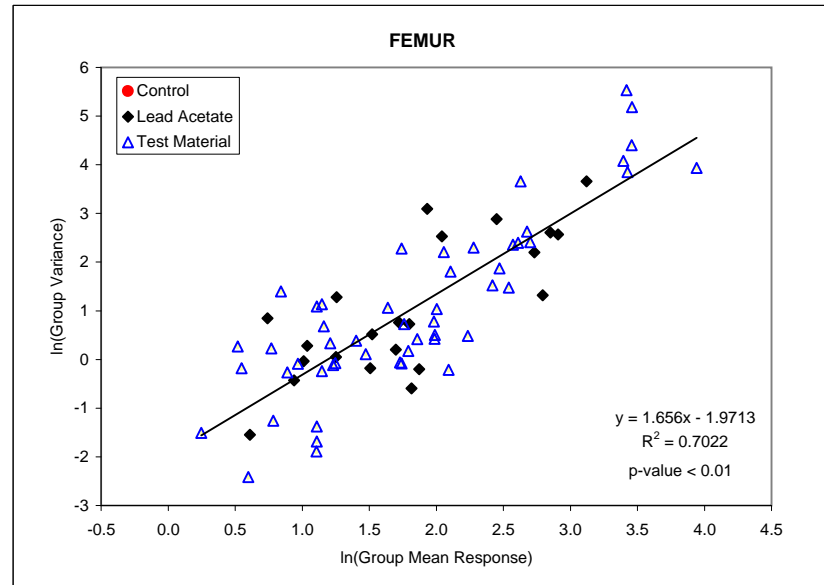
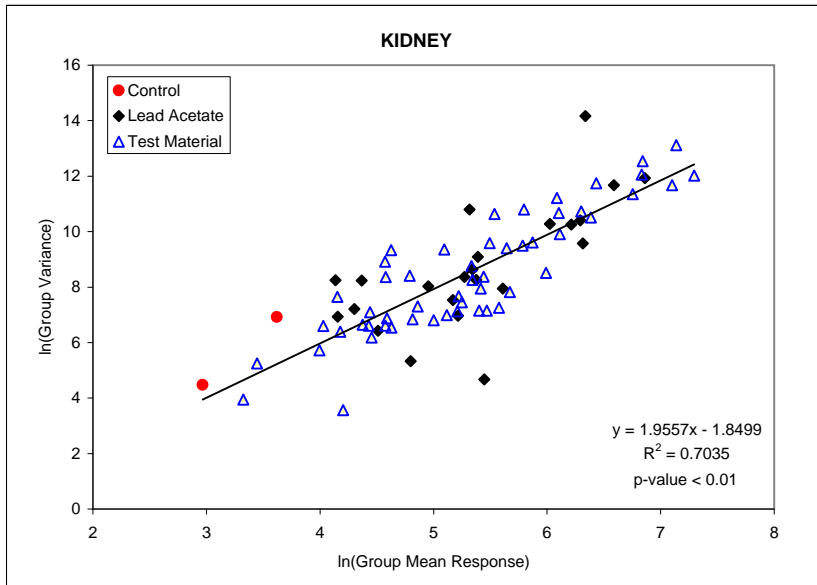
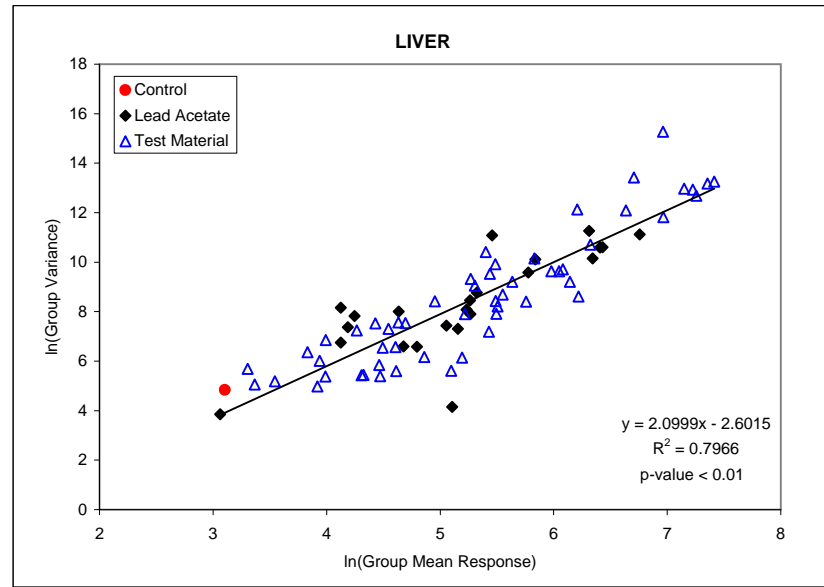
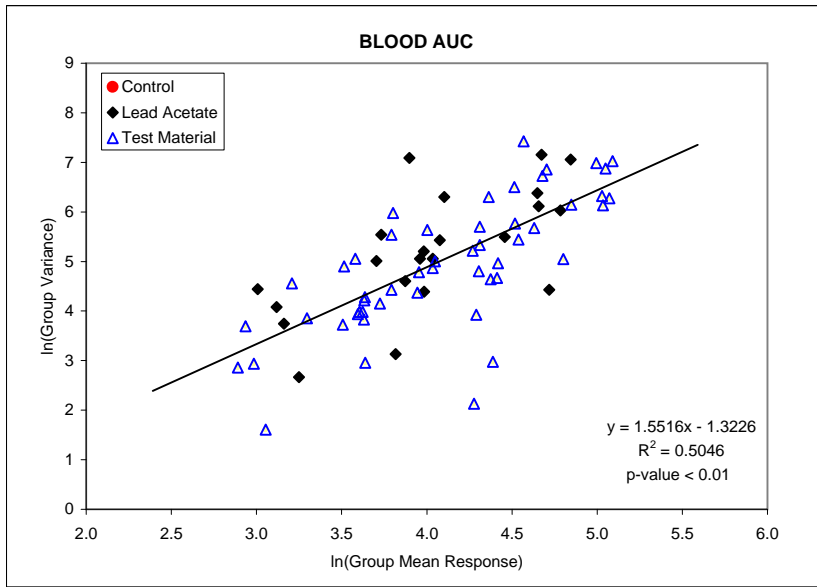
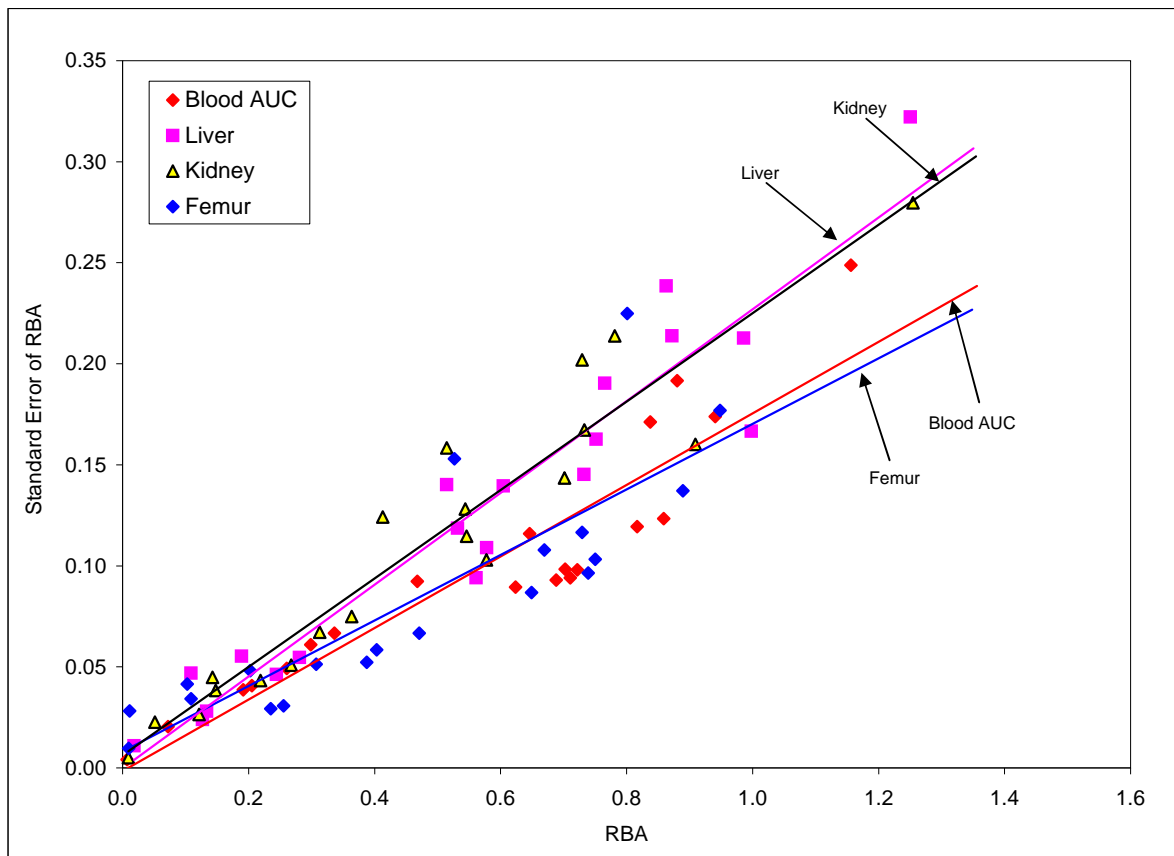


FIGURE D-5. EVALUATION OF RELATIVE PRECISION OF MEASUREMENT ENDPOINTS

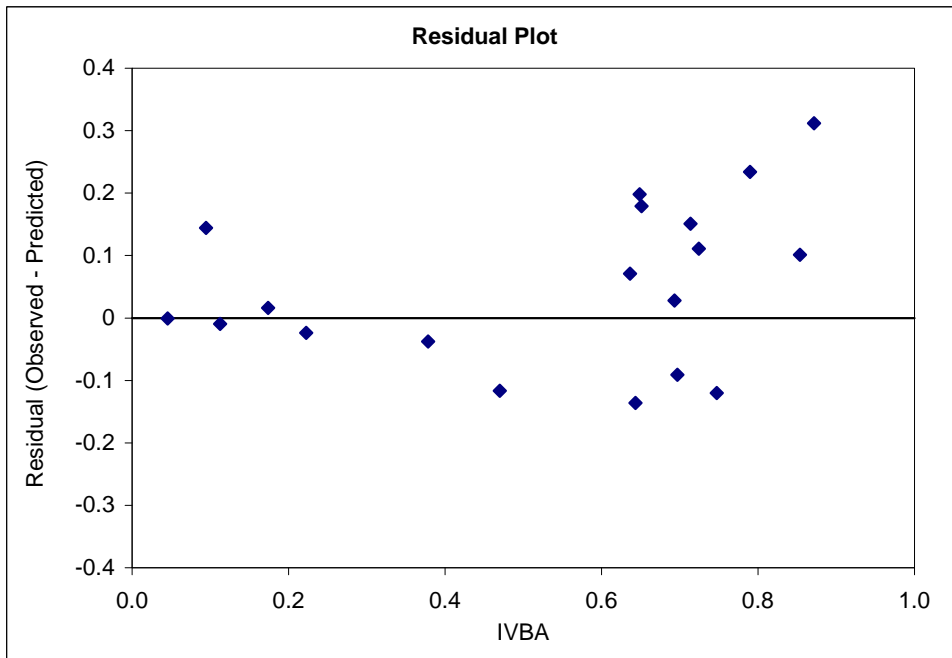
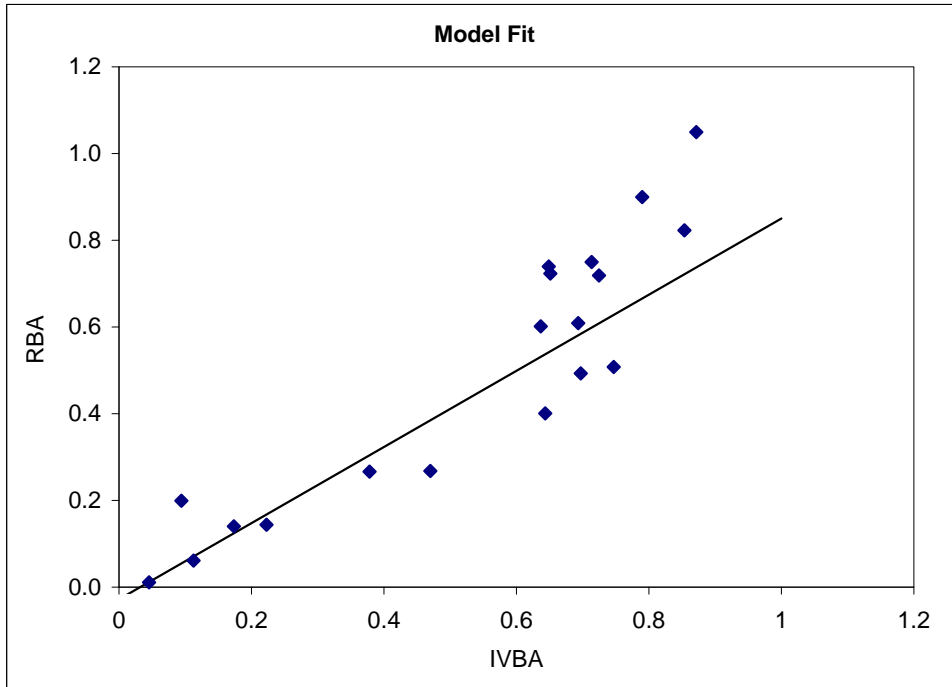


Endpoint	Slope	Intercept	R <sup>2</sup>
Blood AUC	0.177	-0.002	0.867
Liver	0.227	0.000	0.916
Kidney	0.219	0.006	0.914
Femur	0.162	0.008	0.732

Comparison of Regression Lines	
F	0.638
Fcrit(0.05)	2.227
p	0.699



**FIGURE D-6. FIT OF DIFFERENT MODELS TO IVBA-RBA DATA**  
**Panel A: Linear Model ( $y = a + b \cdot x$ )**



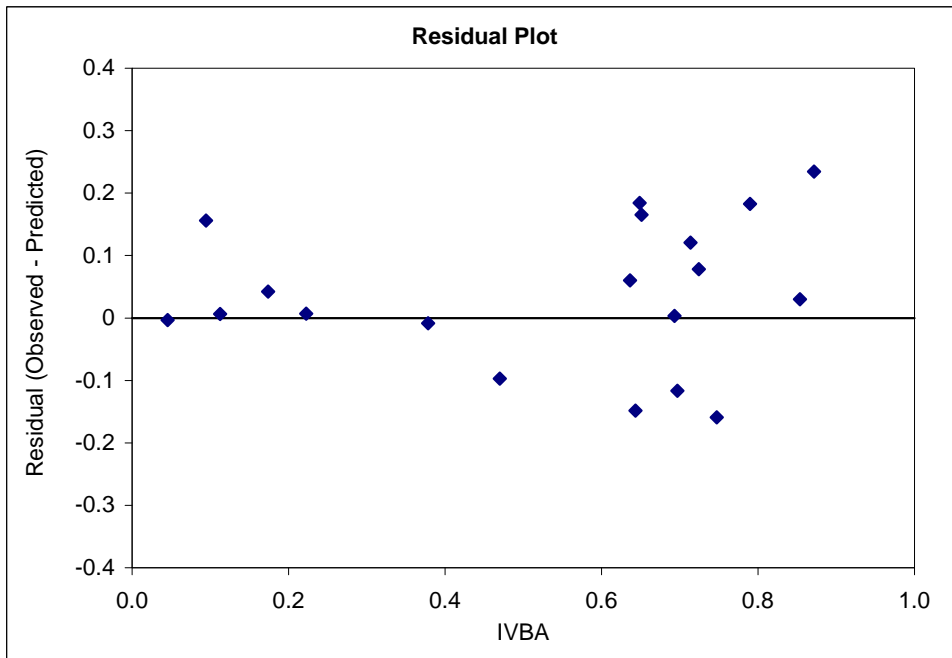
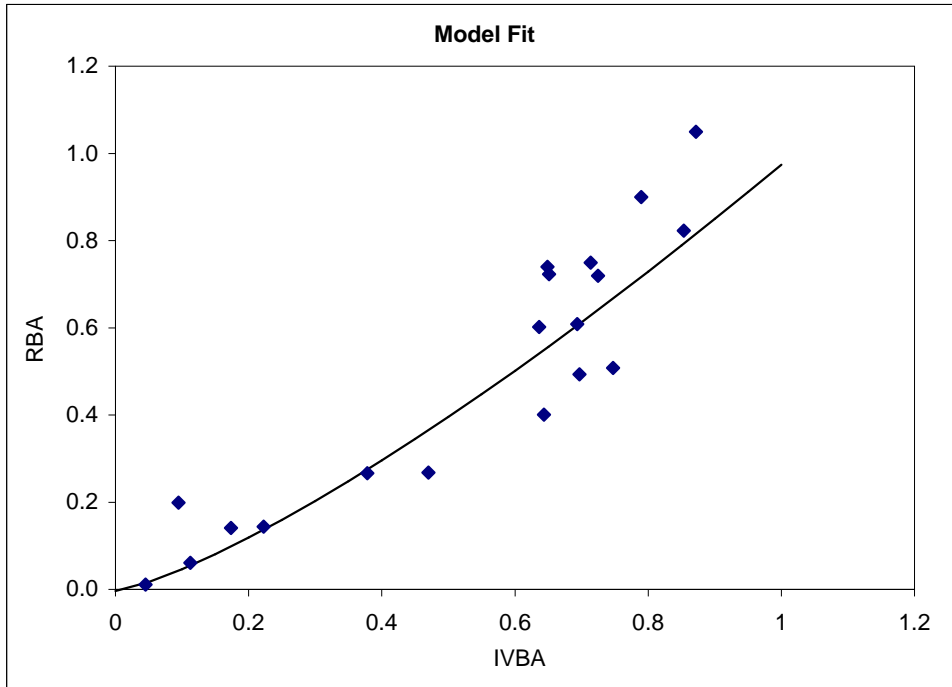
**Parameter Estimates**

a	-0.0281
b	0.8782

**Fit Statistics**

$r^2$	0.9243
Adj $r^2$	0.9199
AIC	-30.46

**FIGURE D-6, Continued. FIT OF DIFFERENT MODELS TO IVBA-RBA DATA**  
**Panel B: Power Model ( $y = a + b \cdot x^c$ )**



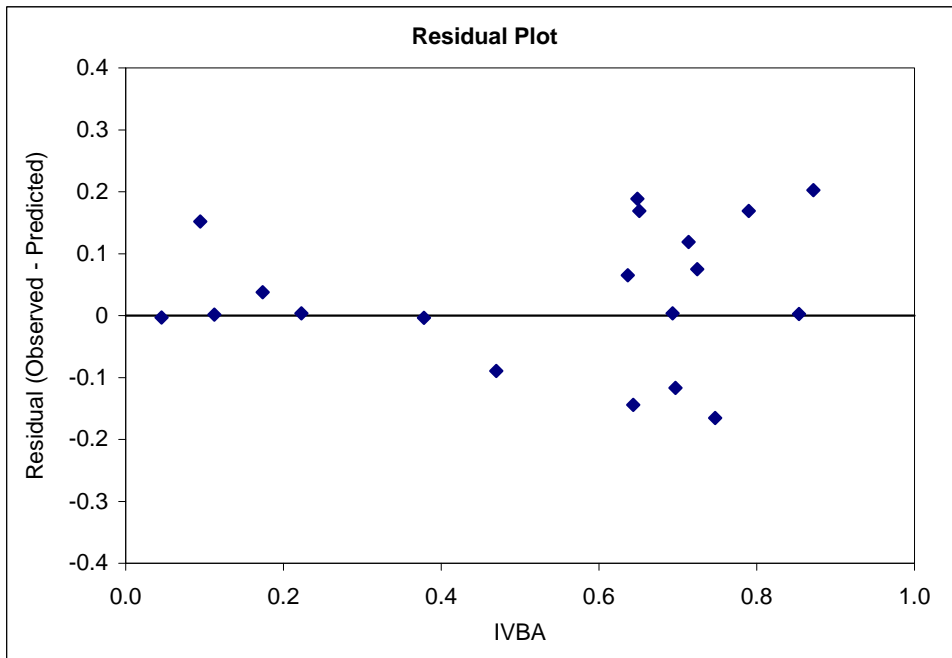
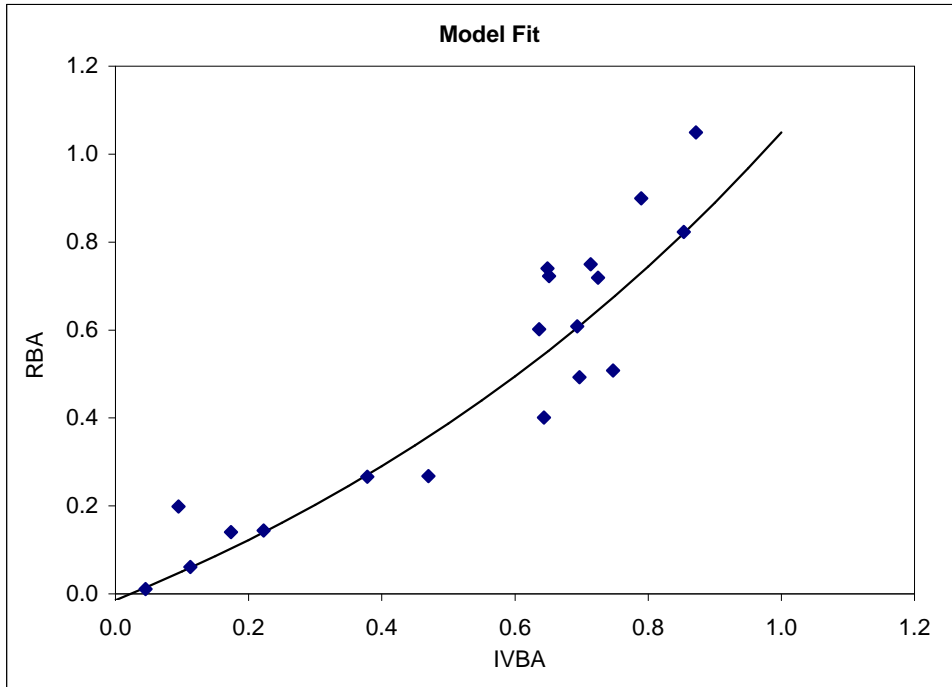
**Parameter Estimates**

a	-0.0033
b	0.9775
c	1.2933

**Fit Statistics**

R <sup>2</sup>	0.9307
Adj R <sup>2</sup>	0.9220
AIC	-29.92

**FIGURE D-6, Continued. FIT OF DIFFERENT MODELS TO IVBA-RBA DATA**  
**Panel C: 2-Parameter Exponential Model ( $y = a + b \cdot \exp(x)$ )**



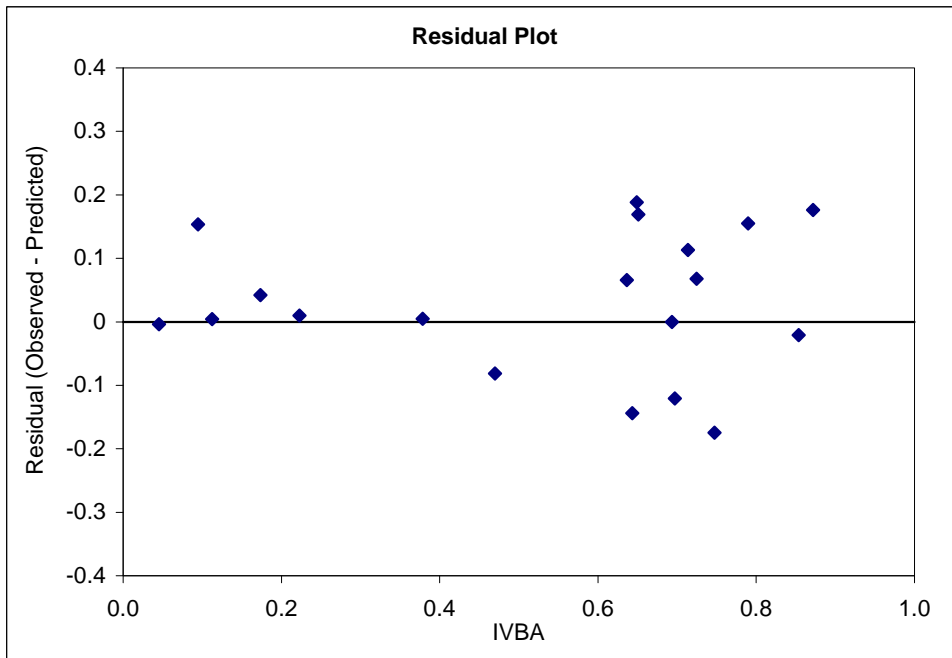
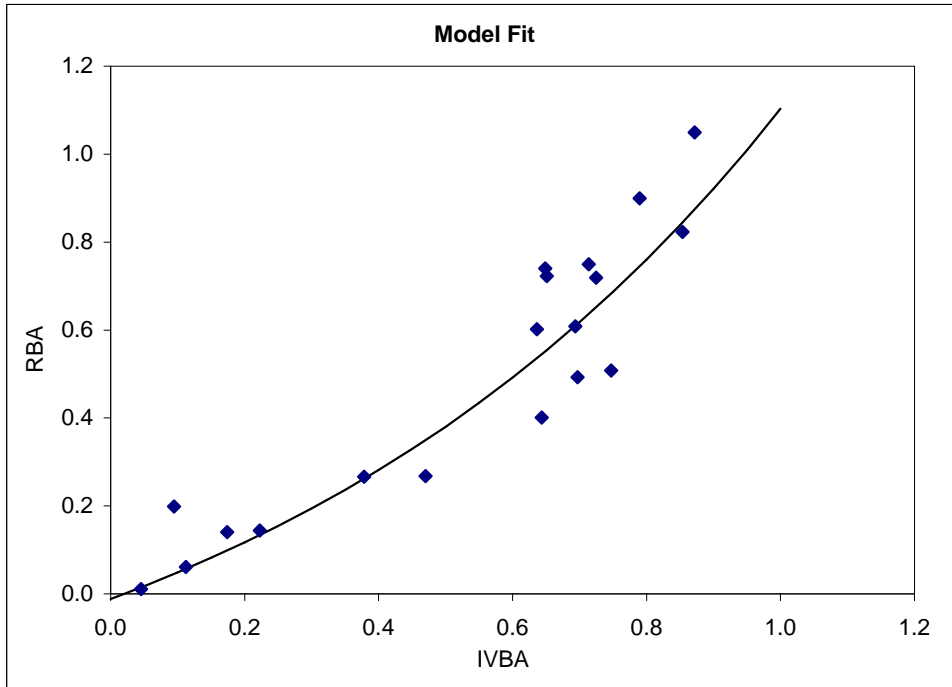
**Parameter Estimates**

a	-0.6339
b	0.6193

**Fit Statistics**

R <sup>2</sup>	0.9355
Adj R <sup>2</sup>	0.9317
AIC	-33.02

**FIGURE D-6, Continued. FIT OF DIFFERENT MODELS TO IVBA-RBA DATA**  
**Panel D: 3-Parameter Exponential Model ( $y = a + b \cdot \exp(c \cdot x)$ )**



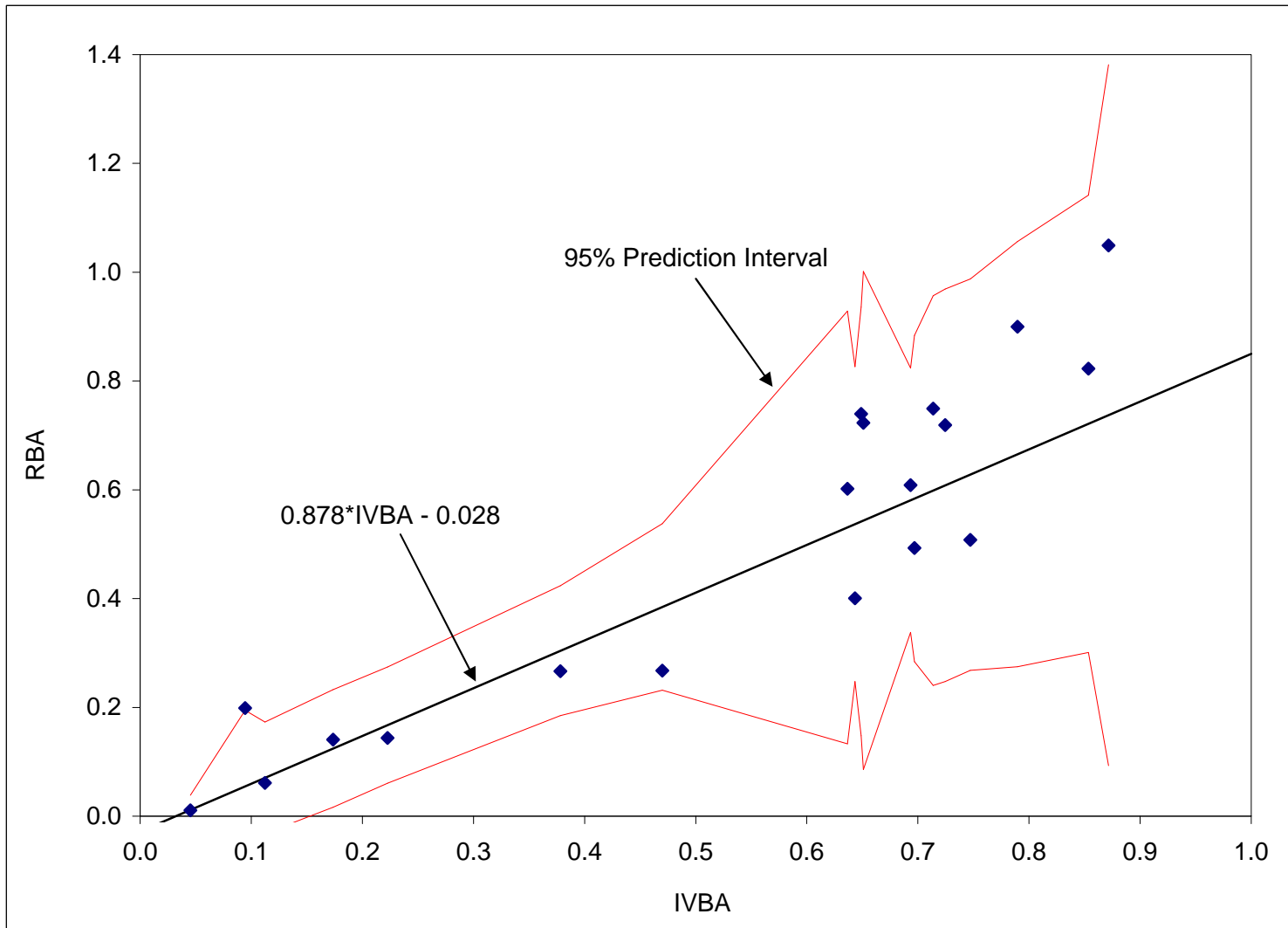
**Parameter Estimates**

a	-0.4756
b	0.4639
c	1.2245

**Fit Statistics**

R <sup>2</sup>	0.9359
Adj R <sup>2</sup>	0.9279
AIC	-31.11

FIGURE D-7. PREDICTION INTERVAL FOR RBA BASED ON MEASURED IVBA



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**APPENDIX E**

**DETAILED DOSE-RESPONSE DATA AND  
MODEL FITTING RESULTS**

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## APPENDIX E

### **EXPERIMENT 1a** **Effects of Food**

Test Material 1: Lead Acetate, simultaneous with feeding

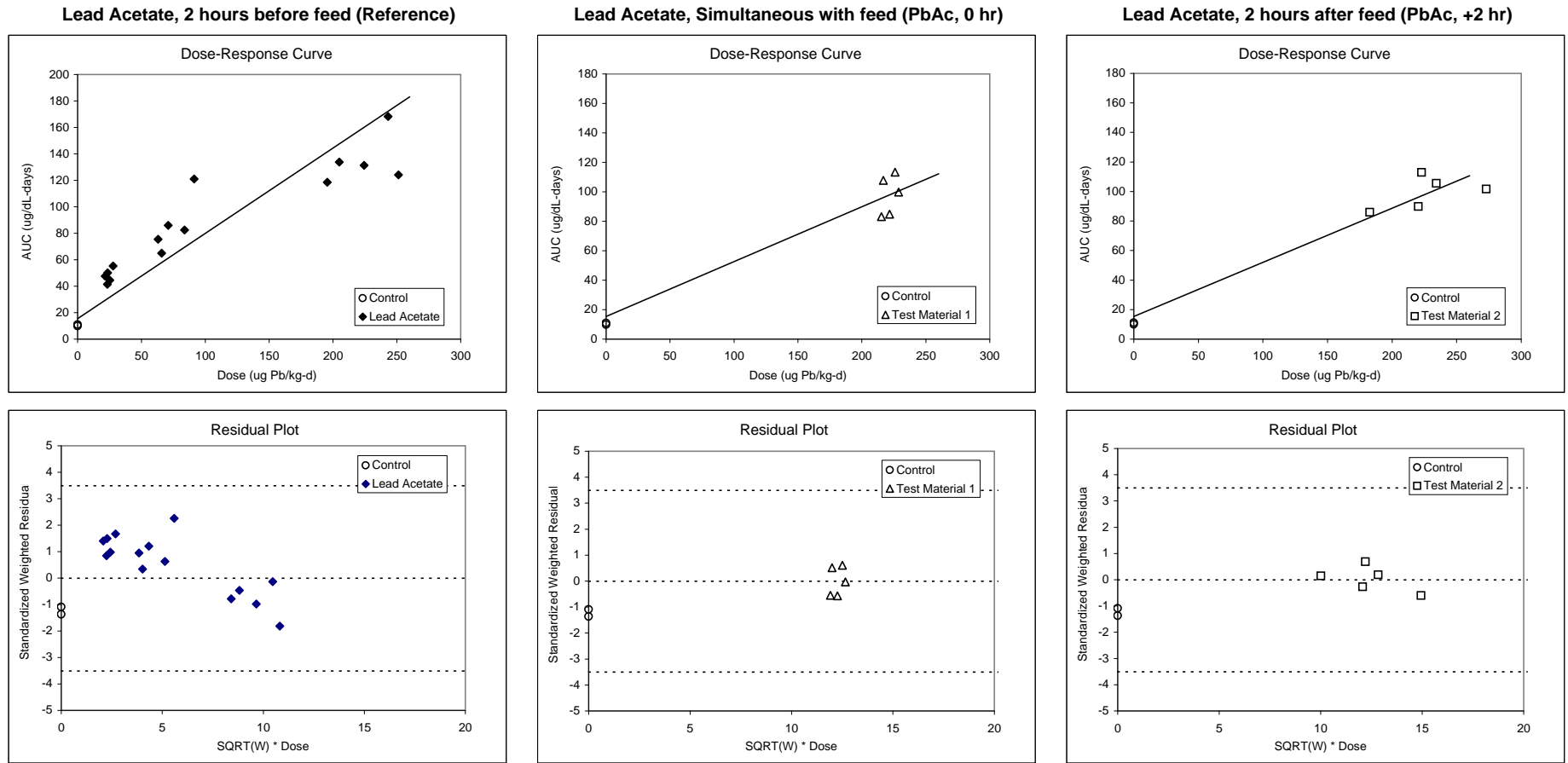
Test Material 2: Lead Acetate, 2 hours after feeding

- Figure 1a Blood AUC - Linear Model
- Figure 1b Blood AUC - Exponential Model
- Figure 1c Blood AUC - Michaelis-Menton Model
- Figure 1d Blood AUC - Power Model
  
- Figure 2a Liver - Linear Model (All Data)
- Figure 2a Liver - Linear Model (Outlier Excluded)
- Figure 2b Liver - Exponential Model
- Figure 2c Liver - Michaelis-Menton Model
- Figure 2d Liver - Power Model
  
- Figure 3a Kidney - Linear Model
- Figure 3b Kidney - Exponential Model
- Figure 3c Kidney - Michaelis-Menton Model
- Figure 3d Kidney - Power Model
  
- Figure 4a Femur - Linear Model
- Figure 4b Femur - Exponential Model
- Figure 4c Femur - Michaelis-Menton Model
- Figure 4d Femur - Power Model

APPENDIX E

Figure 1a - All Data

Phase II Experiment 1a: Blood AUC  
 Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.54E+01	2.81E+00
b1	6.45E-01	5.97E-02
b2	3.72E-01	5.15E-02
b3	3.66E-01	5.04E-02
Covariance (c1,c2)	0.0887	--
Covariance (c1,c3)	0.0872	--
Degrees of Freedom	23	--

Goodness of Fit

Statistic	Estimate
F	64.226
p	< 0.001
Adjusted R <sup>2</sup>	0.8795
AIC	246.105

RBA and Uncertainty

	PbAc, 0 hr	PbAc, +2 hr
RBA	0.58	0.57
Lower bound	0.43	0.42
Upper bound	0.75	0.74
Standard Error	0.092	0.090

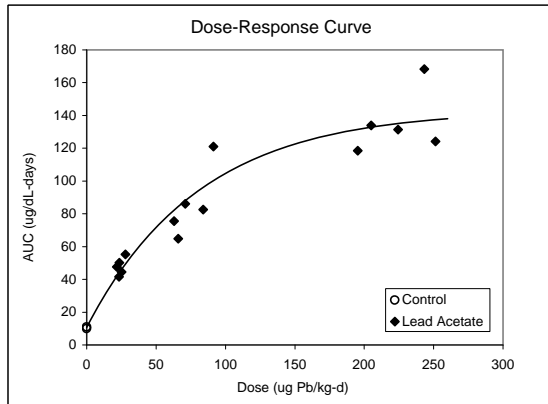
APPENDIX E

Figure 1b - All Data

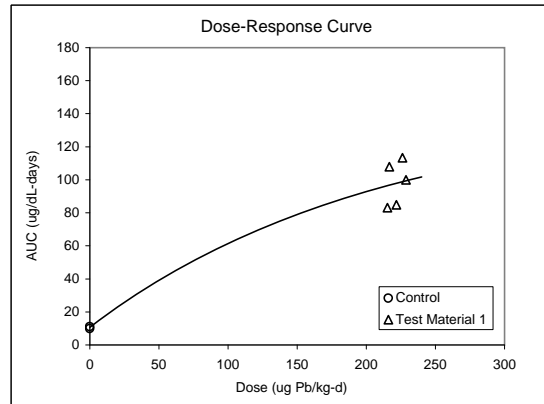
Phase II Experiment 1a: Blood AUC

Exponential Model:  $y = a + b*(1-\exp(-c1*x1)) + b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$

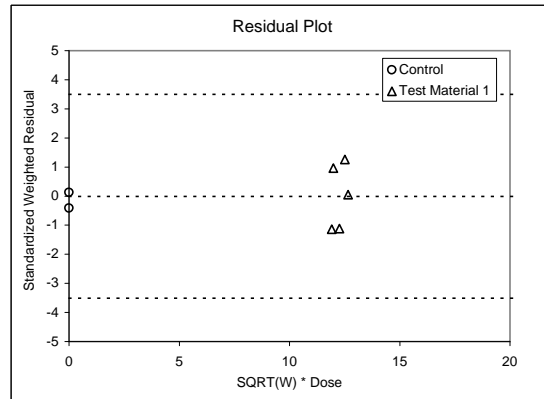
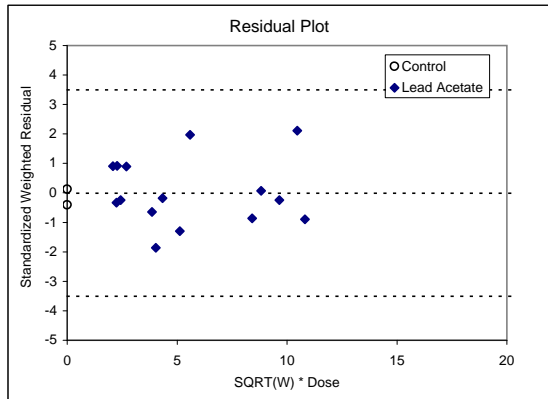
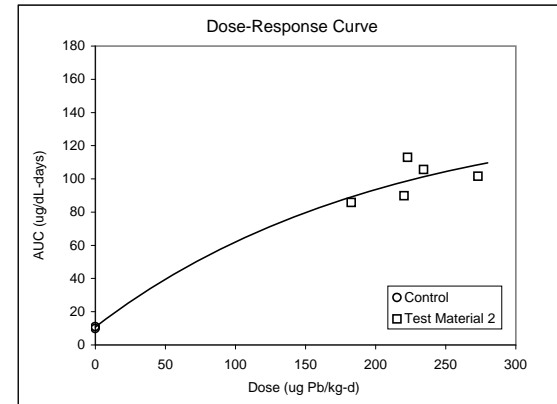
Lead Acetate, 2 hours before feed (Reference)



Lead Acetate, Simultaneous with feed (PbAc, 0 hr)



Lead Acetate, 2 hours after feed (PbAc, +2 hr)



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.07E+01	1.55E+00
b	1.33E+02	1.04E+01
c1	1.23E-02	1.88E-03
c2	4.81E-03	8.84E-04
c3	4.88E-03	9.19E-04
Covariance (c1,c2)	0.6771	--
Covariance (c1,c3)	0.6779	--
Degrees of Freedom	22	--

Goodness of Fit

Statistic	Estimate
F	202.312
p	< 0.001
Adjusted R <sup>2</sup>	0.9687
AIC	215.723

RBA and Uncertainty

	PbAc, 0 hr	PbAc, +2 hr
RBA	0.39	0.40
Lower bound	0.30	0.30
Upper bound	0.49	0.50
Standard Error	0.054*	0.056*

\*  $g \geq 0.05$ , estimate is uncertain

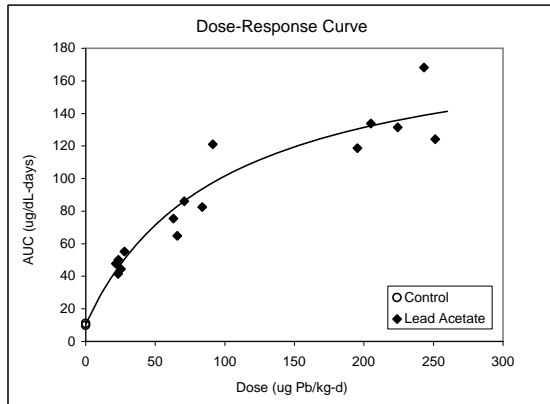
APPENDIX E

Figure 1c - All Data

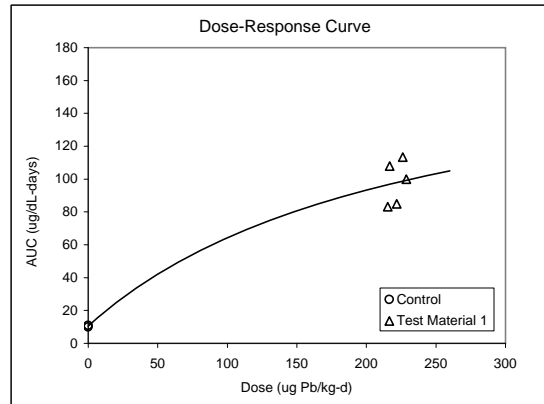
Phase II Experiment 1a: Blood AUC

Michaelis-Menton Model:  $y = a + b \cdot x1 / (c1 + x1) + b \cdot x2 / (c2 + x2) + b \cdot x3 / (c3 + x3)$

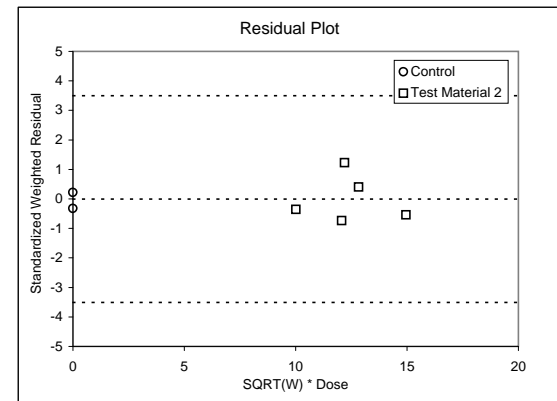
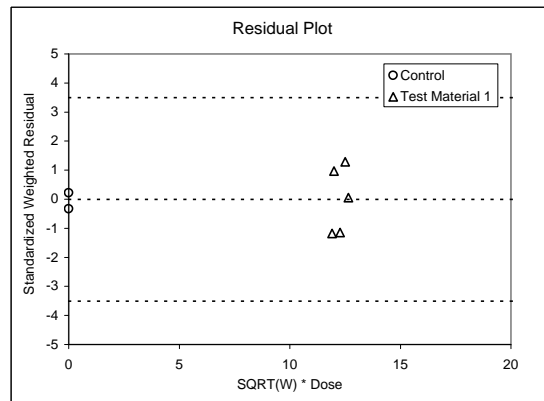
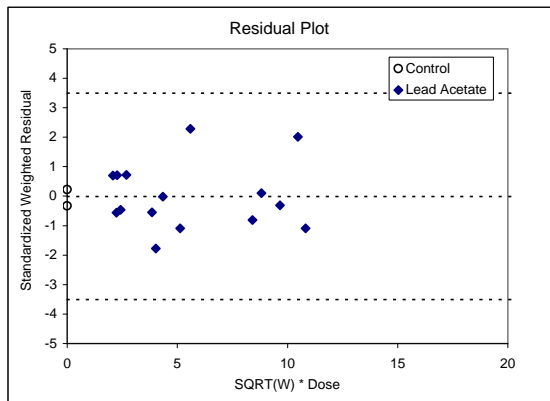
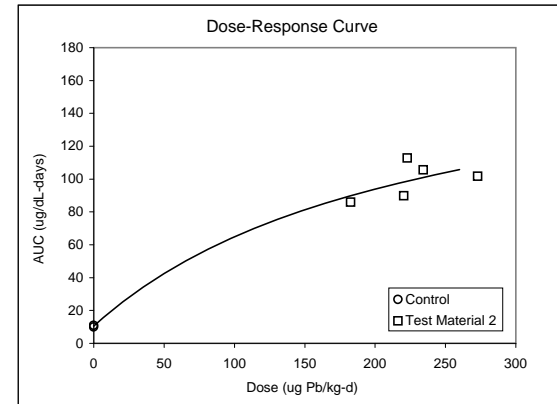
Lead Acetate, 2 hours before feed (Reference)



Lead Acetate, Simultaneous with feed (PbAc, 0 hr)



Lead Acetate, 2 hours after feed (PbAc, +2 hr)



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.06E+01	1.53E+00
b	1.80E+02	1.89E+01
c1	9.75E+01	2.02E+01
c2	2.35E+02	5.70E+01
c3	2.31E+02	5.70E+01
Covariance (c1,c2)	0.8053	--
Covariance (c1,c3)	0.8061	--
Degrees of Freedom	22	--

Goodness of Fit

Statistic	Estimate
F	211.024
p	< 0.001
Adjusted R <sup>2</sup>	0.9700
AIC	215.293

RBA and Uncertainty

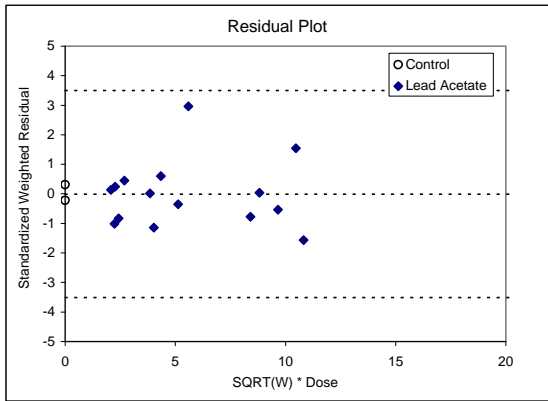
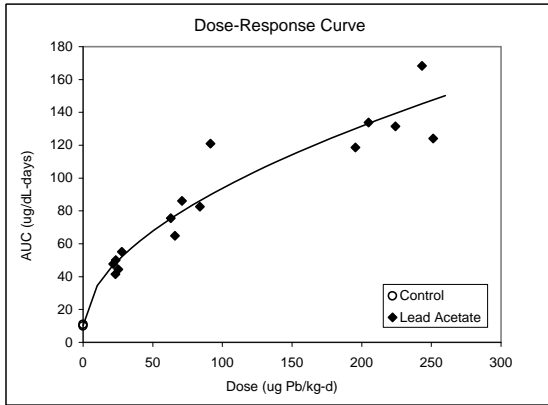
	PbAc, 0 hr	PbAc, +2 hr
RBA	0.42	0.42
Lower bound	0.33	0.33
Upper bound	0.56	0.57
Standard Error	0.060*	0.062*

\*  $g \geq 0.05$ , estimate is uncertain

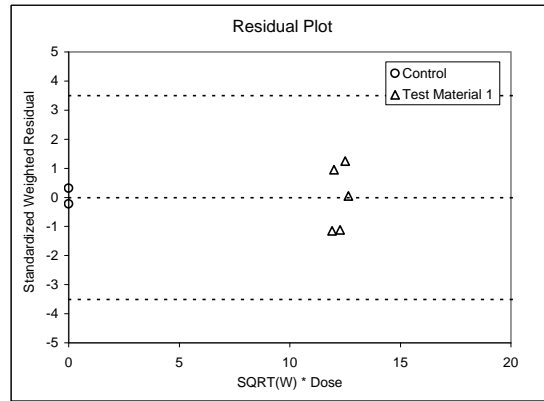
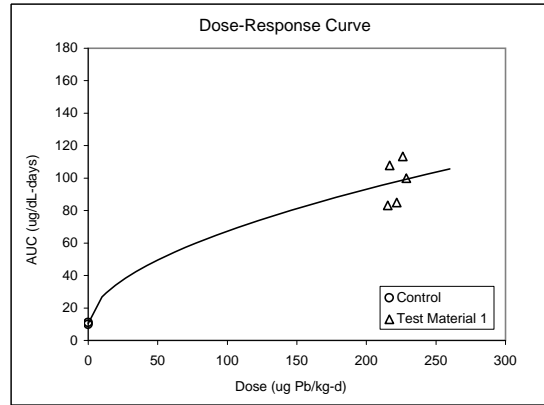
APPENDIX E

**Figure 1d - All Data**  
**Phase II Experiment 1a: Blood AUC**  
**Power Model:  $y = a + b_1 \cdot x_1^c + b_2 \cdot x_2^c + b_3 \cdot x_3^c$**

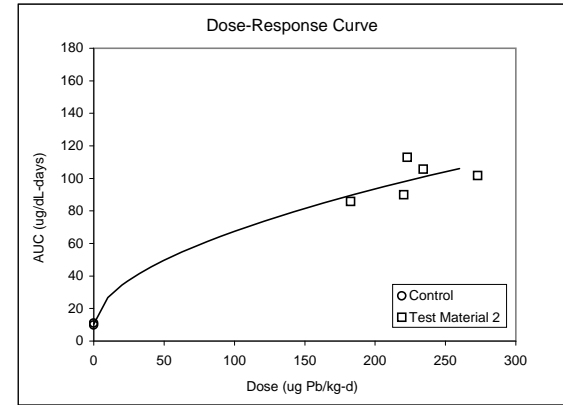
**Lead Acetate, 2 hours before feed (Reference)**



**Lead Acetate, Simultaneous with feed (PbAc, 0 hr)**



**Lead Acetate, 2 hours after feed (PbAc, +2 hr)**



**Summary of Fitting**

Parameter	Estimate	Standard Error
a	1.04E+01	1.58E+00
b1	6.94E+00	1.53E+00
b2	4.74E+00	1.23E+00
b3	4.75E+00	1.24E+00
c	5.40E-01	4.57E-02
Covariance (b1,b2)	0.9528	--
Covariance (b1,b3)	0.9534	--
Degrees of Freedom	22	--

**Goodness of Fit**

Statistic	Estimate
F	199.941
p	< 0.001
Adjusted R <sup>2</sup>	0.9684
AIC	215.846

**RBA and Uncertainty**

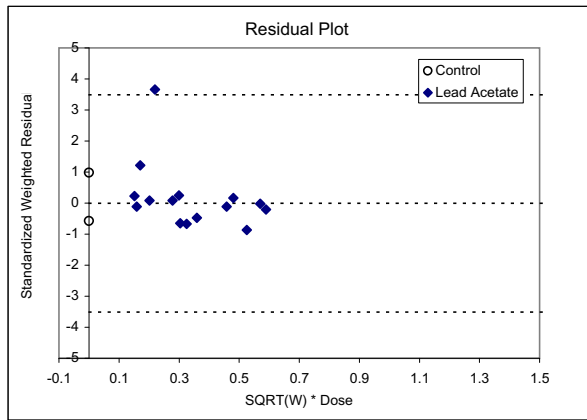
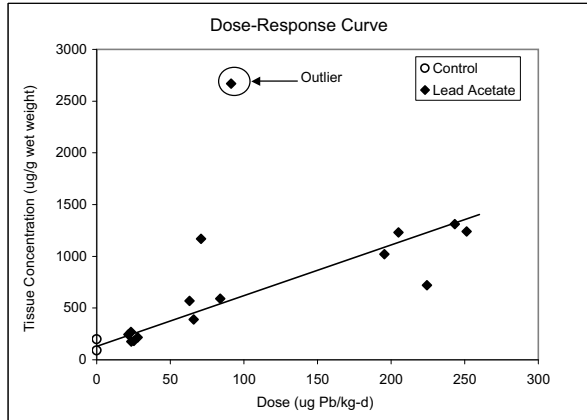
	PbAc, 0 hr	PbAc, +2 hr
RBA	0.49	0.50
Lower bound	0.34	0.34
Upper bound	0.62	0.63
Standard Error	--	--

APPENDIX E

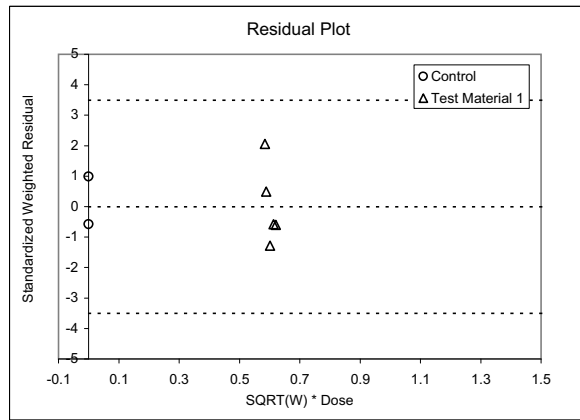
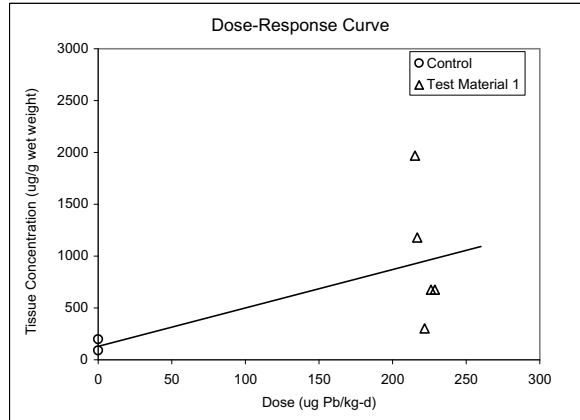
Figure 2a - All Data

Phase II Experiment 1a: Liver  
 Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$

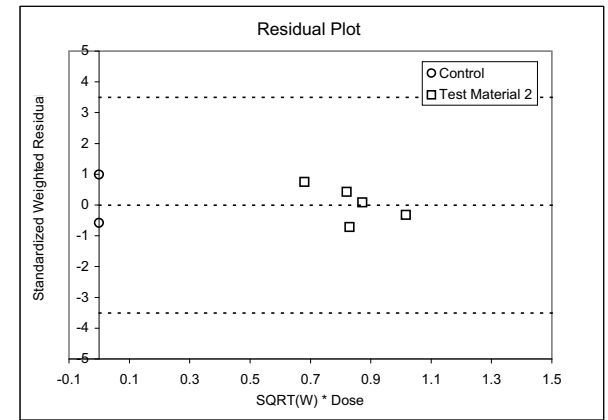
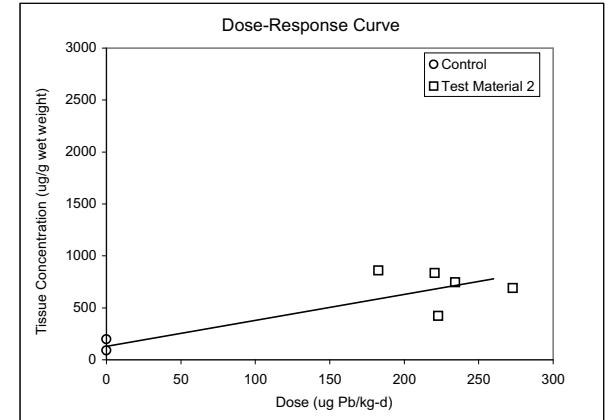
Lead Acetate, 2 hours before feed (Reference)



Lead Acetate, Simultaneous with feed (PbAc, 0 hr)



Lead Acetate, 2 hours after feed (PbAc, +2 hr)



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.30E+02	4.11E+01
b1	4.89E+00	1.18E+00
b2	3.70E+00	1.11E+00
b3	2.49E+00	7.94E-01
Covariance (c1,c2)	0.0810	--
Covariance (c1,c3)	0.1091	--
Degrees of Freedom	23	--

Goodness of Fit

Statistic	Estimate
F	11.055
p	< 0.001
Adjusted R <sup>2</sup>	0.5371
AIC	402.563

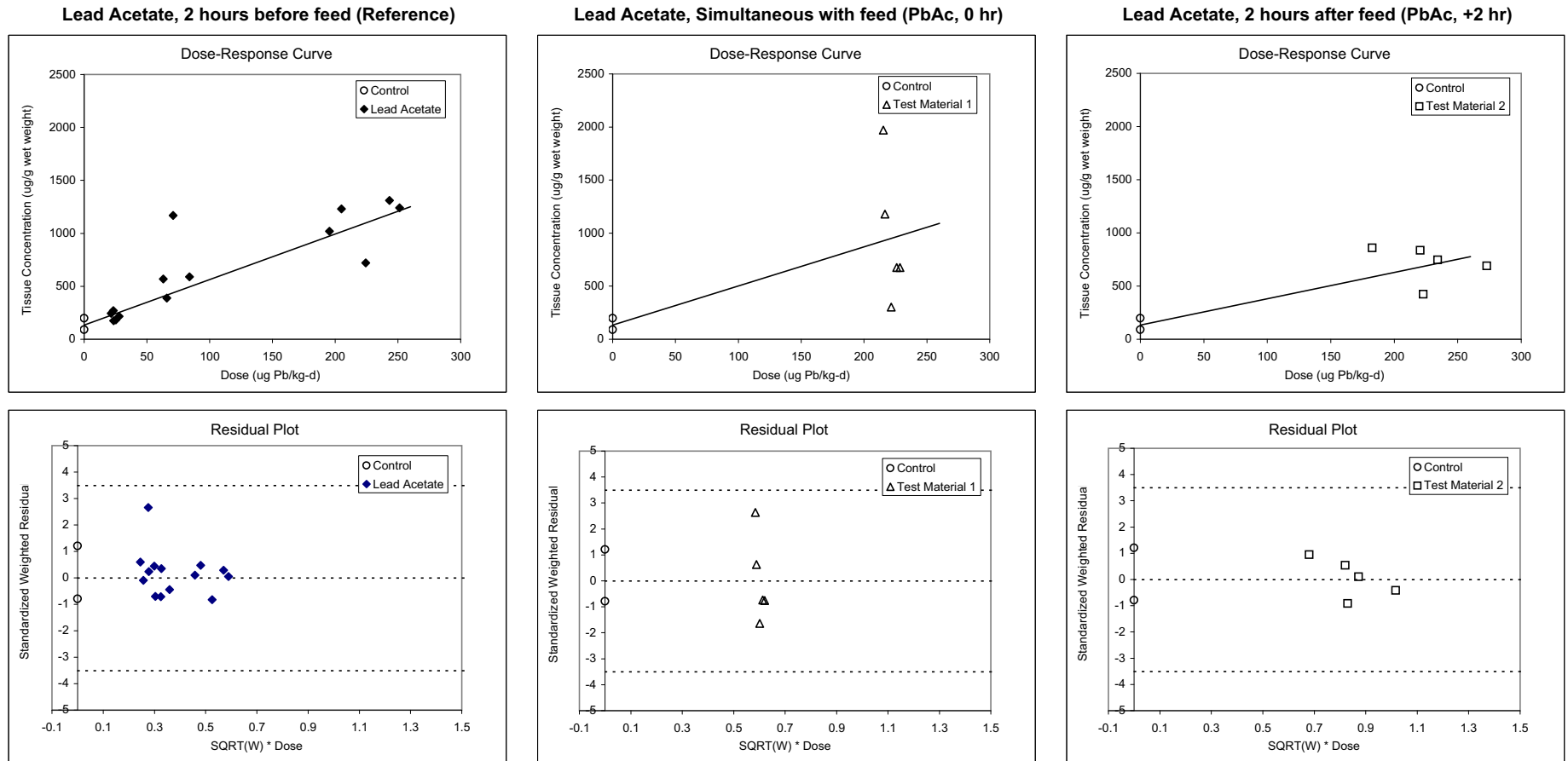
RBA and Uncertainty

	PbAc, 0 hr	PbAc, +2 hr
RBA	0.76	0.51
Lower bound	0.35	0.23
Upper bound	1.44	0.97
Standard Error	0.279*	0.192*

\*  $g \geq 0.05$ , estimate is uncertain

APPENDIX E

**Figure 2a - Outlier Excluded**  
**Phase II Experiment 1a: Liver**  
**Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$**



**Summary of Fitting**

Parameter	Estimate	Standard Error
a	1.33E+02	2.91E+01
b1	4.31E+00	8.43E-01
b2	3.69E+00	7.86E-01
b3	2.48E+00	5.63E-01
Covariance (c1,c2)	0.0807	--
Covariance (c1,c3)	0.1085	--
Degrees of Freedom	22	--

**Goodness of Fit**

Statistic	Estimate
F	16.332
p	< 0.001
Adjusted R <sup>2</sup>	0.6479
AIC	364.272

**RBA and Uncertainty**

	PbAc, 0 hr	PbAc, +2 hr
RBA	0.86	0.58
Lower bound	0.51	0.34
Upper bound	1.40	0.94
Standard Error	0.238*	0.163*

\*  $g \geq 0.05$ , estimate is uncertain

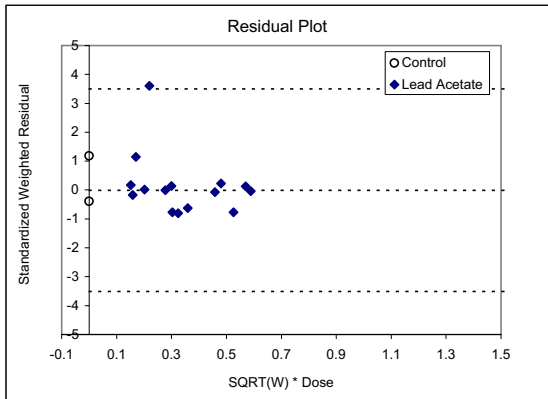
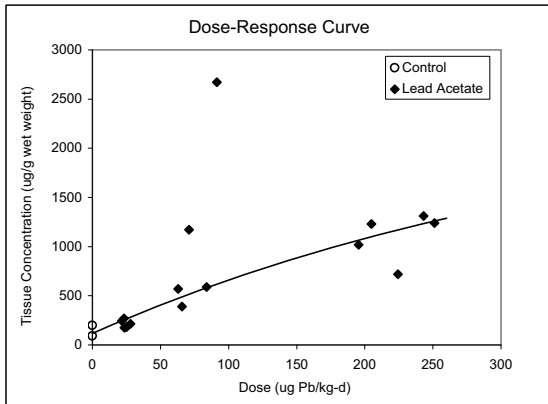
APPENDIX E

Figure 2b - All Data

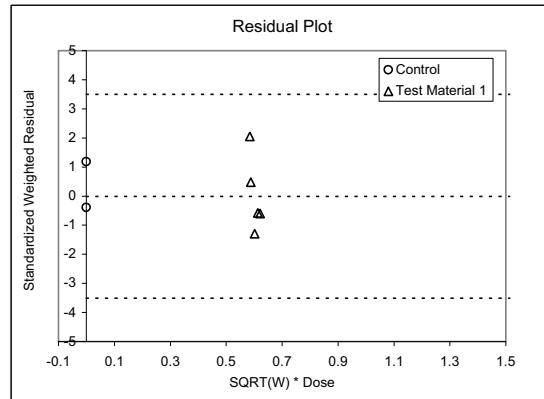
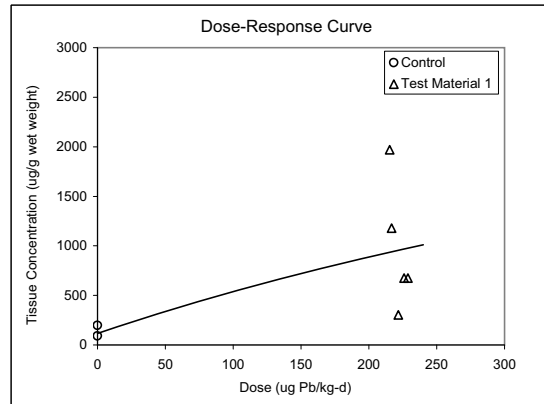
Phase II Experiment 1a: Liver

Exponential Model:  $y = a + b*(1-\exp(-c1*x1))+b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$

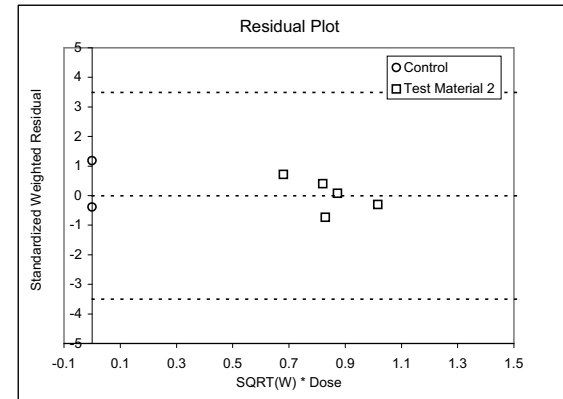
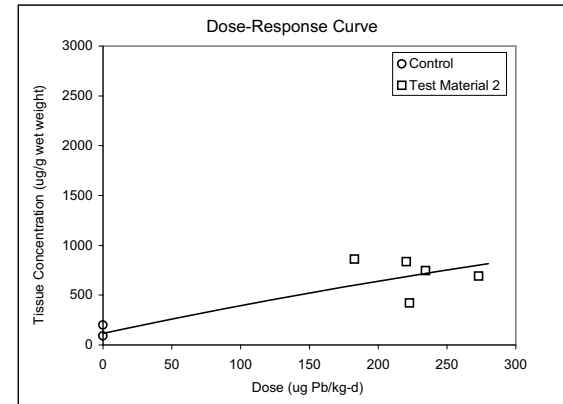
Lead Acetate, 2 hours before feed (Reference)



Lead Acetate, Simultaneous with feed (PbAc, 0 hr)



Lead Acetate, 2 hours after feed (PbAc, +2 hr)



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.17E+02	5.17E+01
b	2.45E+03	4.45E+03
c1	2.50E-03	5.67E-03
c2	1.88E-03	4.39E-03
c3	1.20E-03	2.61E-03
Covariance (c1,c2)	0.9805	--
Covariance (c1,c3)	0.9802	--
Degrees of Freedom	22	--

Goodness of Fit

Statistic	Estimate
F	8.087
p	< 0.001
Adjusted R <sup>2</sup>	0.5216
AIC	403.989

RBA and Uncertainty

	PbAc, 0 hr	PbAc, +2 hr
RBA	0.75	0.48
Lower bound	?	?
Upper bound	?	?
Standard Error	0.345*	0.216*

\*  $g \geq 0.05$ , estimate is uncertain



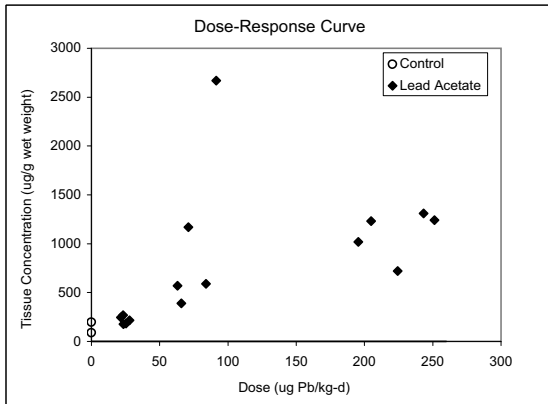
APPENDIX E

Figure 2c - All Data

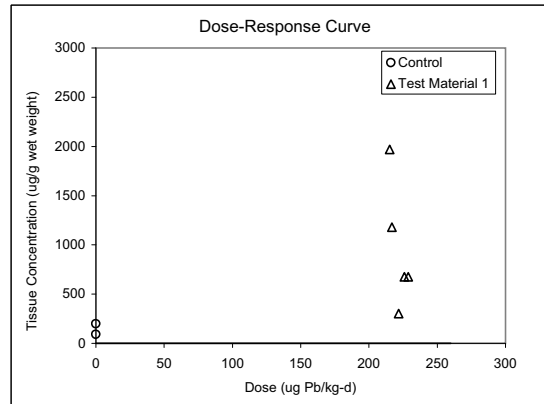
Phase II Experiment 1a: Liver

Michaelis-Menton Model:  $y = a + b \cdot x1 / (c1 + x1) + b \cdot x2 / (c2 + x2) + b \cdot x3 / (c3 + x3)$

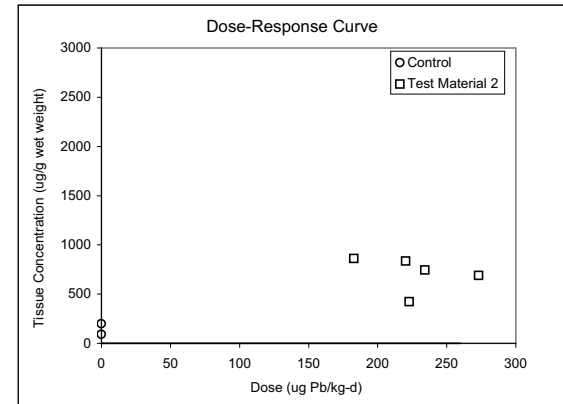
Lead Acetate, 2 hours before feed (Reference)



Lead Acetate, Simultaneous with feed (PbAc, 0 hr)



Lead Acetate, 2 hours after feed (PbAc, +2 hr)



**NO SOLUTION**

The software could not find a solution,  
or the solution was unstable and/or had unrealistic parameter estimates.

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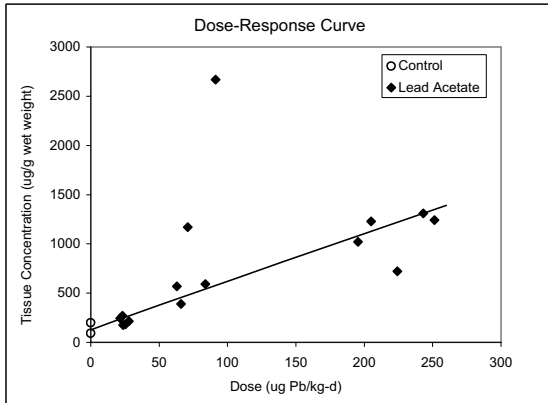
APPENDIX E

Figure 2d - All Data

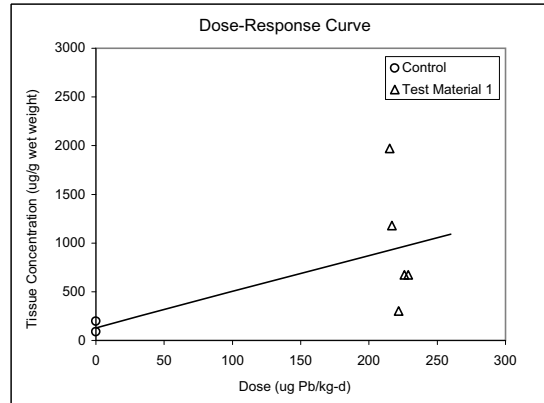
Phase II Experiment 1a: Liver

Power Model:  $y = a + b1*x1^c + b2*x2^c + b3*x3^c$

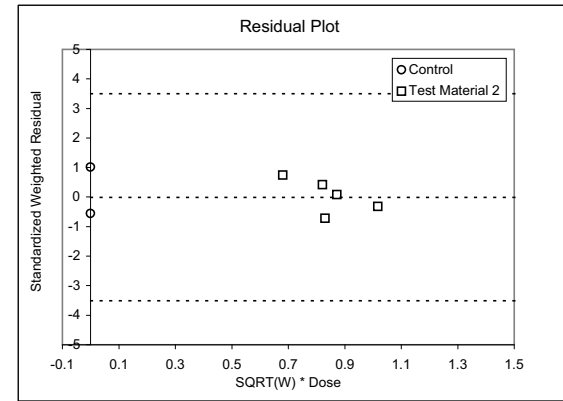
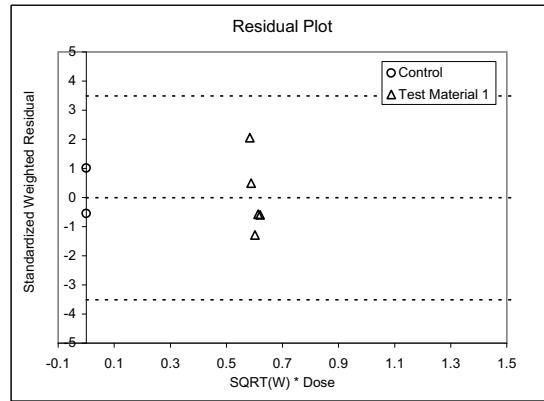
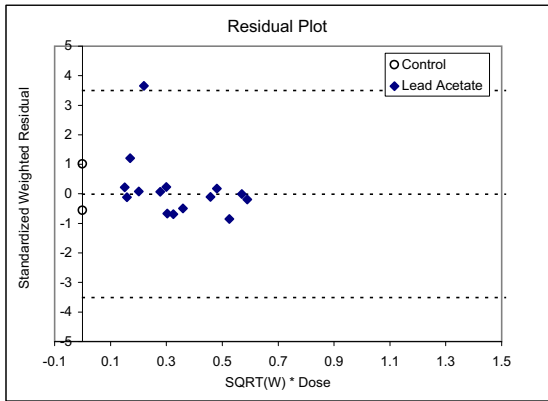
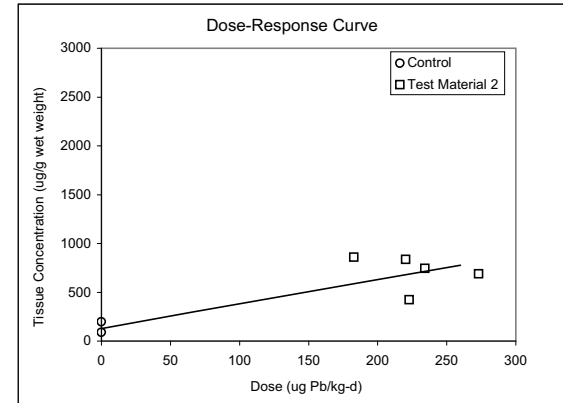
Lead Acetate, 2 hours before feed (Reference)



Lead Acetate, Simultaneous with feed (PbAc, 0 hr)



Lead Acetate, 2 hours after feed (PbAc, +2 hr)



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.28E+02	5.30E+01
b1	5.34E+00	7.63E+00
b2	4.06E+00	6.34E+00
b3	2.74E+00	4.37E+00
c	9.83E-01	2.76E-01
Covariance (b1,b2)	0.9689	--
Covariance (b1,b3)	0.9684	--
Degrees of Freedom	22	--

Goodness of Fit

Statistic	Estimate
F	7.934
p	< 0.001
Adjusted R <sup>2</sup>	0.5162
AIC	404.552

RBA and Uncertainty

	PbAc, 0 hr	PbAc, +2 hr
RBA	0.76	0.51
Lower bound	?	?
Upper bound	?	?
Standard Error	--	--

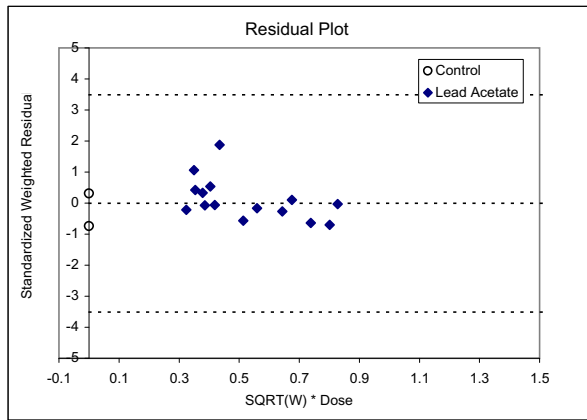
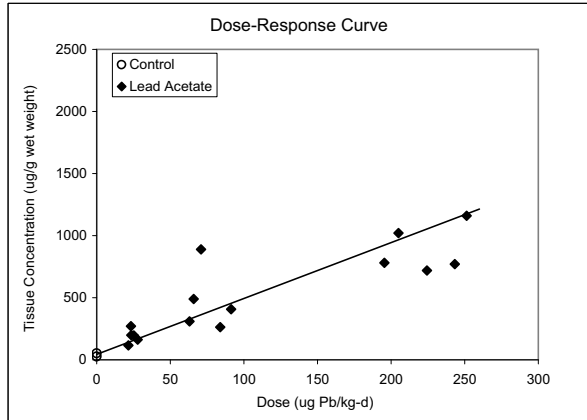
APPENDIX E

Figure 3a - All Data

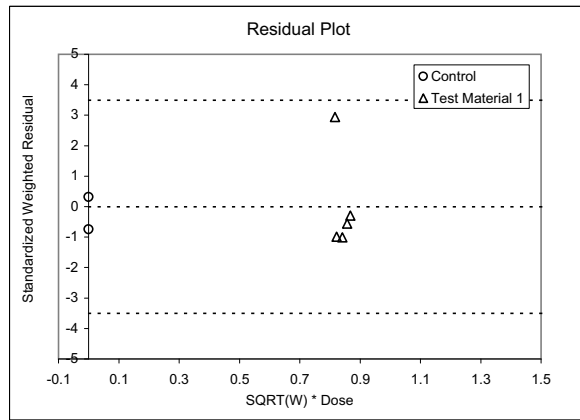
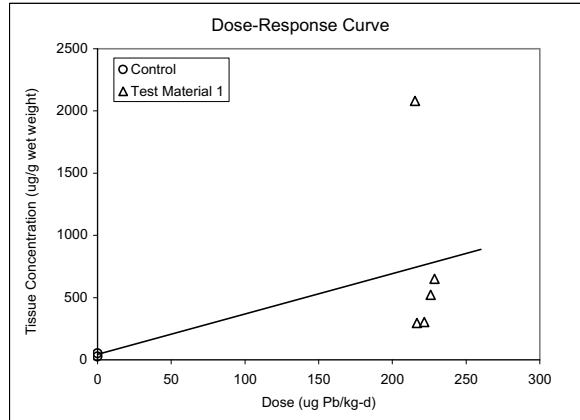
Phase II Experiment 1a: Kidney

Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$

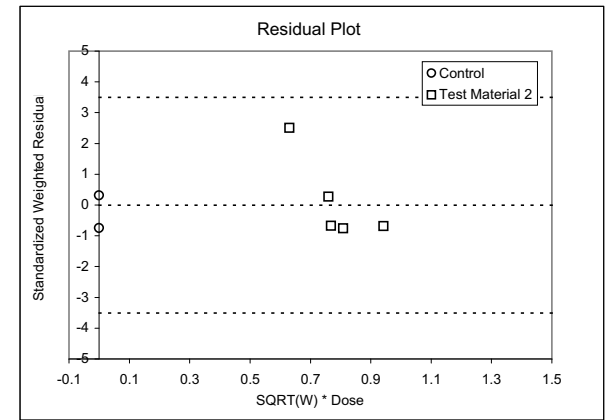
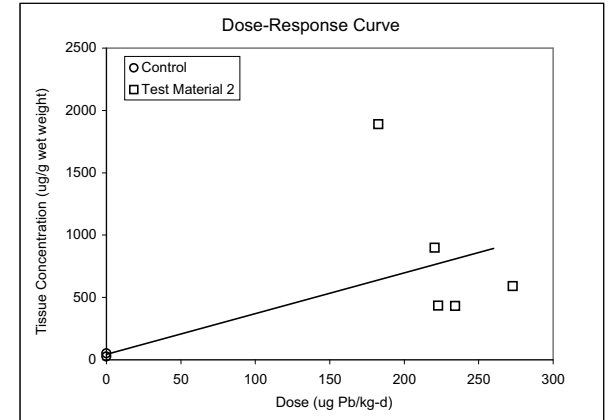
Lead Acetate, 2 hours before feed (Reference)



Lead Acetate, Simultaneous with feed (PbAc, 0 hr)



Lead Acetate, 2 hours after feed (PbAc, +2 hr)



Summary of Fitting

Parameter	Estimate	Standard Error
a	4.43E+01	1.79E+01
b1	4.50E+00	8.93E-01
b2	3.24E+00	9.81E-01
b3	3.26E+00	1.05E+00
Covariance (c1,c2)	0.0197	--
Covariance (c1,c3)	0.0178	--
Degrees of Freedom	23	--

Goodness of Fit

Statistic	Estimate
F	14.903
p	< 0.001
Adjusted R <sup>2</sup>	0.6160
AIC	408.462

RBA and Uncertainty

	PbAc, 0 hr	PbAc, +2 hr
RBA	0.72	0.73
Lower bound	0.33	0.31
Upper bound	1.29	1.32
Standard Error	0.259*	0.271*

\*  $g \geq 0.05$ , estimate is uncertain

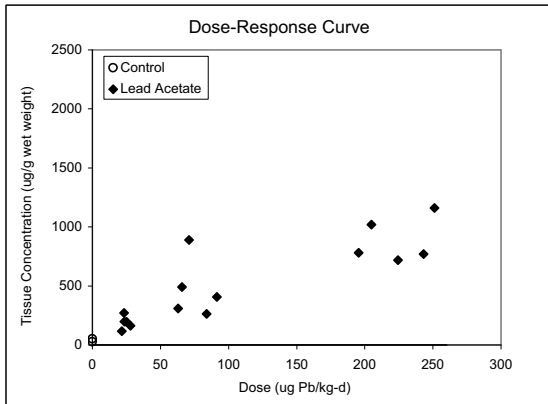
APPENDIX E

Figure 3b - All Data

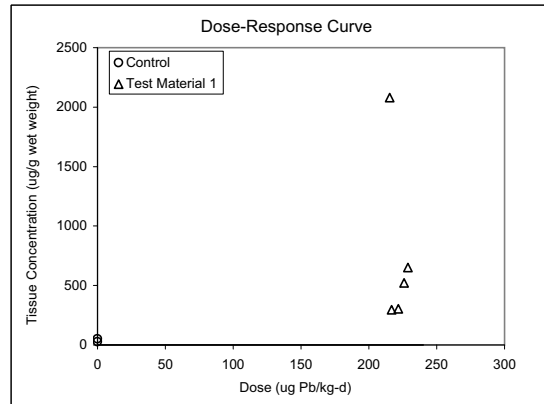
Phase II Experiment 1a: Kidney

Exponential Model:  $y = a + b*(1-\exp(-c1*x1))+b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$

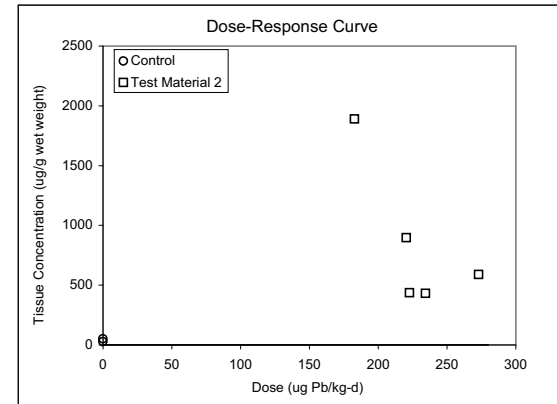
Lead Acetate, 2 hours before feed (Reference)



Lead Acetate, Simultaneous with feed (PbAc, 0 hr)



Lead Acetate, 2 hours after feed (PbAc, +2 hr)



**NO SOLUTION**

The software could not find a solution,  
or the solution was unstable and/or had unrealistic parameter estimates.

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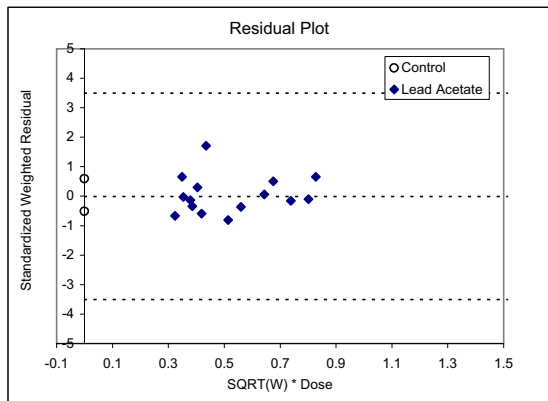
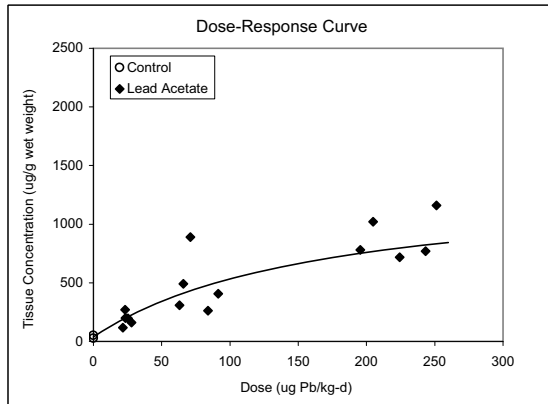
APPENDIX E

Figure 3c - All Data

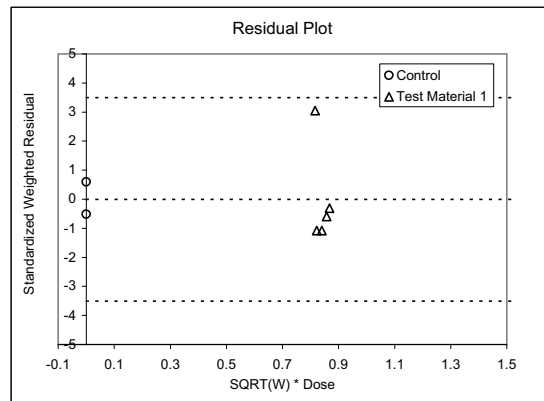
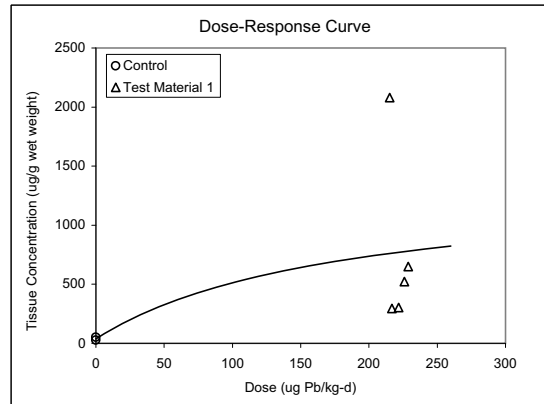
Phase II Experiment 1a: Kidney

Michaelis-Menton Model:  $y = a + b \cdot x_1 / (c_1 + x_1) + b \cdot x_2 / (c_2 + x_2) + b \cdot x_3 / (c_3 + x_3)$

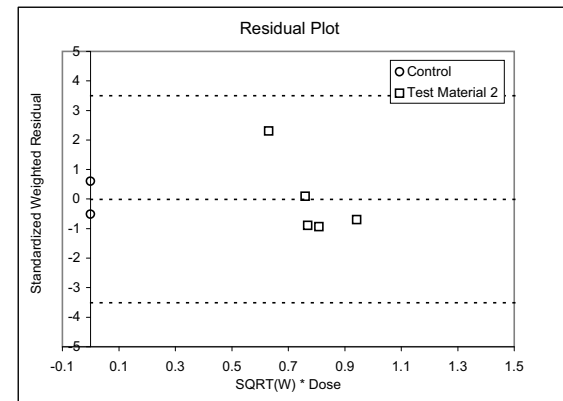
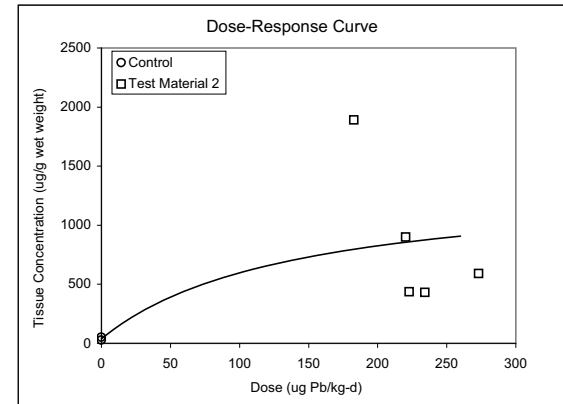
Lead Acetate, 2 hours before feed (Reference)



Lead Acetate, Simultaneous with feed (PbAc, 0 hr)



Lead Acetate, 2 hours after feed (PbAc, +2 hr)



Summary of Fitting

Parameter	Estimate	Standard Error
a	3.80E+01	1.79E+01
b	1.33E+03	9.08E+02
c1	1.69E+02	1.69E+02
c2	1.81E+02	2.99E+02
c3	1.38E+02	2.69E+02
Covariance (c1,c2)	0.8873	--
Covariance (c1,c3)	0.8896	--
Degrees of Freedom	22	--

Goodness of Fit

Statistic	Estimate
F	12.449
p	< 0.001
Adjusted R <sup>2</sup>	0.6379
AIC	402.853

RBA and Uncertainty

	PbAc, 0 hr	PbAc, +2 hr
RBA	0.94	1.22
Lower bound	?	?
Upper bound	?	?
Standard Error	0.835*	1.405*

\* g ≥ 0.05, estimate is uncertain

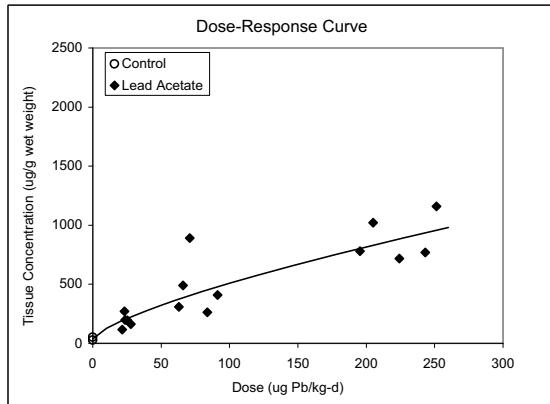
APPENDIX E

Figure 3d - All Data

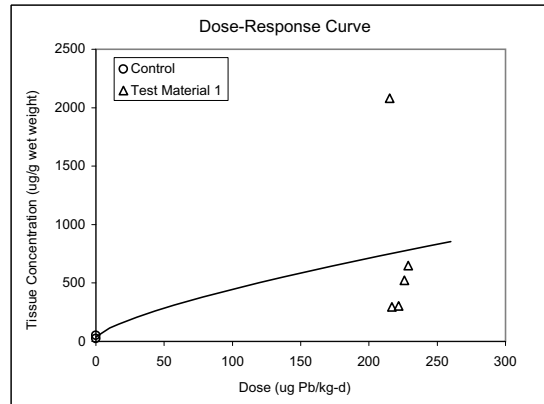
Phase II Experiment 1a: Kidney

Power Model:  $y = a + b1*x1^c + b2*x2^c + b3*x3^c$

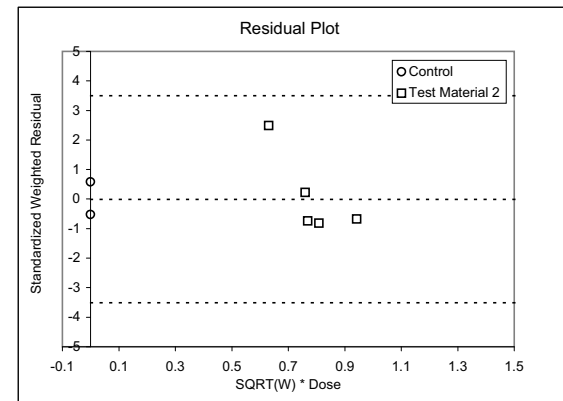
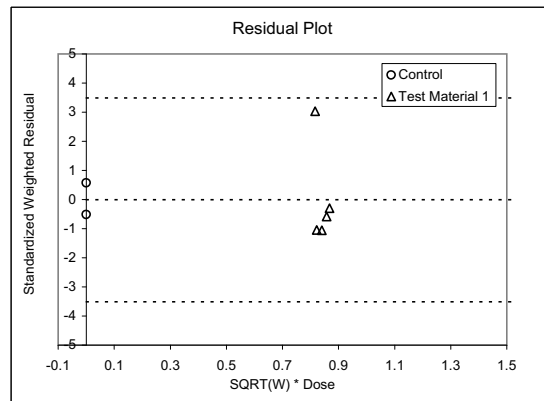
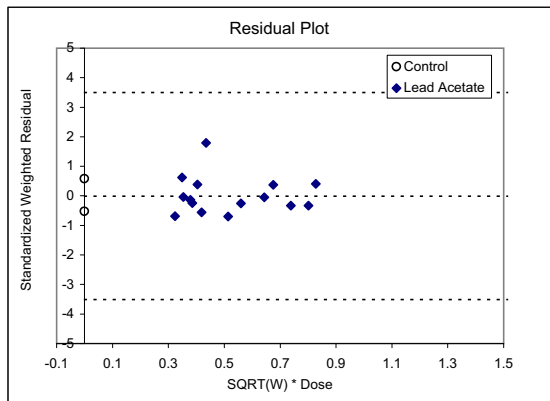
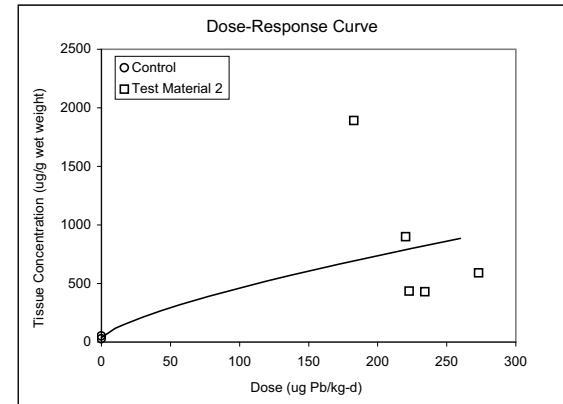
Lead Acetate, 2 hours before feed (Reference)



Lead Acetate, Simultaneous with feed (PbAc, 0 hr)



Lead Acetate, 2 hours after feed (PbAc, +2 hr)



Summary of Fitting

Parameter	Estimate	Standard Error
a	3.83E+01	1.82E+01
b1	1.65E+01	1.48E+01
b2	1.43E+01	1.58E+01
b3	1.48E+01	1.65E+01
c	7.27E-01	1.96E-01
Covariance (b1,b2)	0.9430	--
Covariance (b1,b3)	0.9407	--
Degrees of Freedom	22	--

Goodness of Fit

Statistic	Estimate
F	11.992
p	< 0.001
Adjusted R <sup>2</sup>	0.6284
AIC	404.685

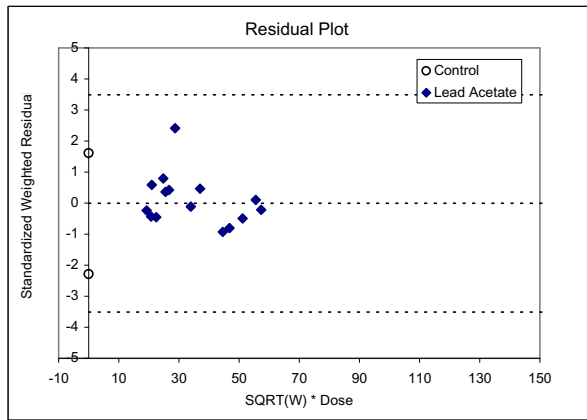
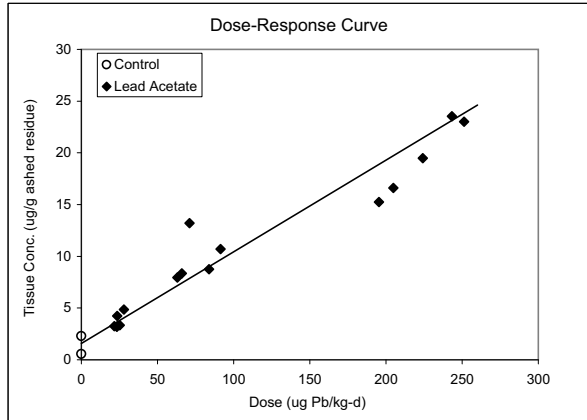
RBA and Uncertainty

	PbAc, 0 hr	PbAc, +2 hr
RBA	0.82	0.86
Lower bound	?	?
Upper bound	?	?
Standard Error	--	--

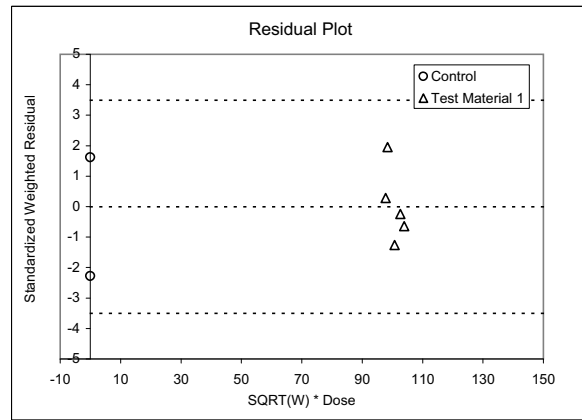
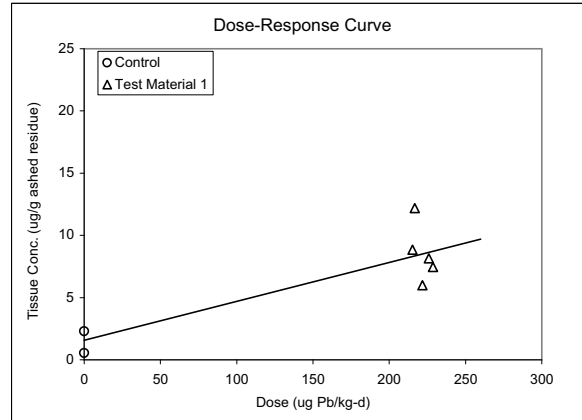
APPENDIX E

**Figure 4a - All Data**  
**Phase II Experiment 1a: Femur**  
**Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$**

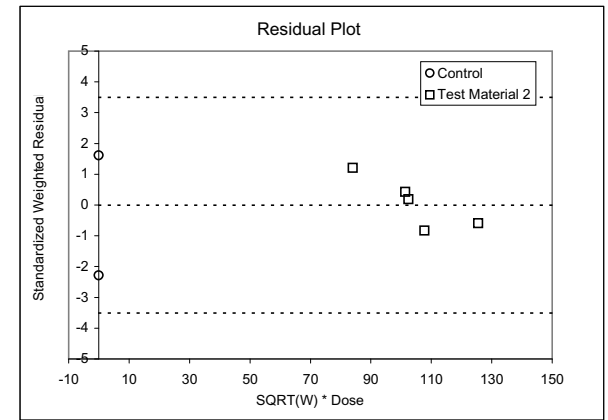
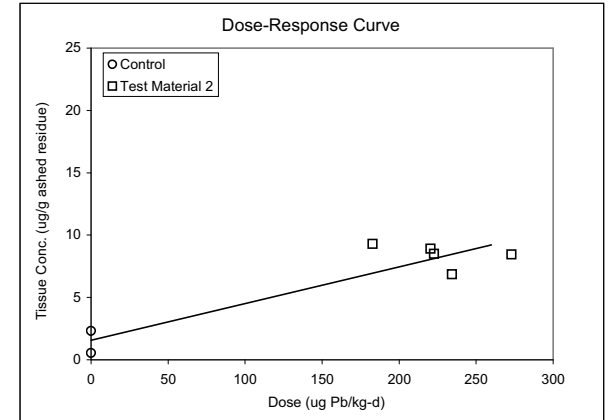
**Lead Acetate, 2 hours before feed (Reference)**



**Lead Acetate, Simultaneous with feed (PbAc, 0 hr)**



**Lead Acetate, 2 hours after feed (PbAc, +2 hr)**



**Summary of Fitting**

Parameter	Estimate	Standard Error
a	1.58E+00	2.91E-01
b1	8.87E-02	7.40E-03
b2	3.12E-02	4.44E-03
b3	2.94E-02	4.26E-03
Covariance (c1,c2)	0.1245	--
Covariance (c1,c3)	0.1250	--
Degrees of Freedom	23	--

**Goodness of Fit**

Statistic	Estimate
F	66.771
p	< 0.001
Adjusted R <sup>2</sup>	0.8836
AIC	116.460

**RBA and Uncertainty**

	PbAc, 0 hr	PbAc, +2 hr
RBA	0.35	0.33
Lower bound	0.26	0.25
Upper bound	0.45	0.43
Standard Error	0.055	0.052

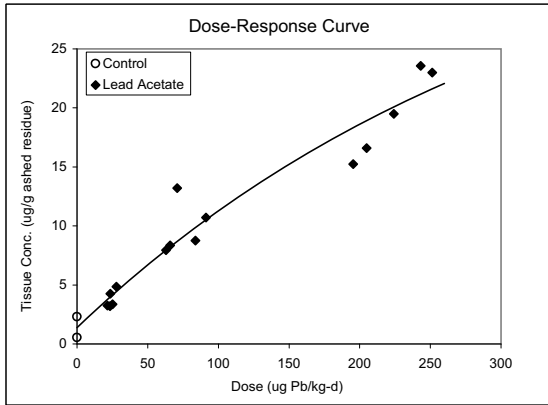
APPENDIX E

Figure 4b - All Data

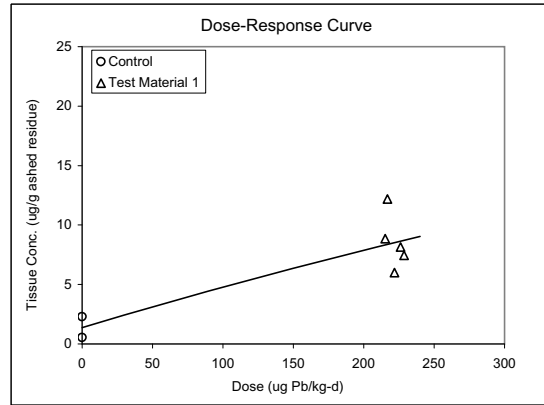
Phase II Experiment 1a: Femur

Exponential Model:  $y = a + b*(1-\exp(-c1*x1))+b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$

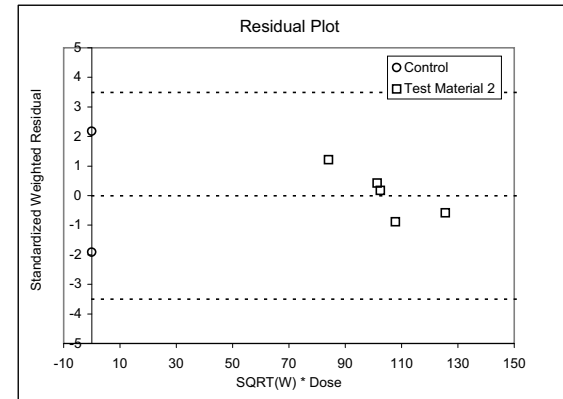
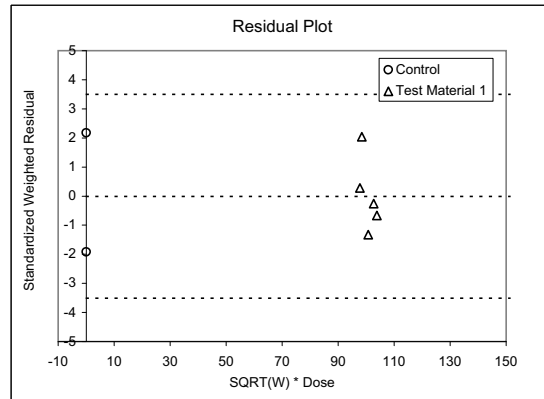
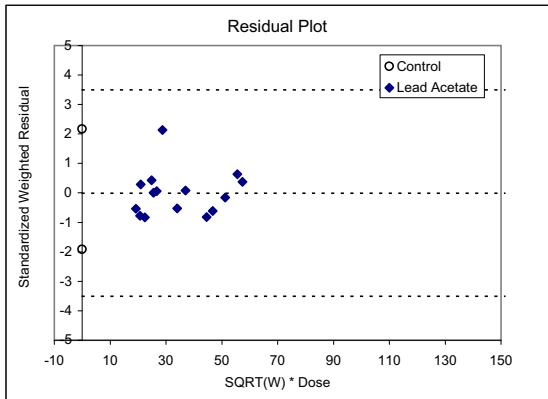
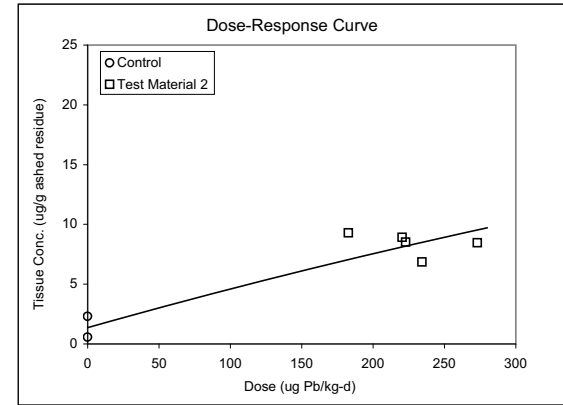
Lead Acetate, 2 hours before feed (Reference)



Lead Acetate, Simultaneous with feed (PbAc, 0 hr)



Lead Acetate, 2 hours after feed (PbAc, +2 hr)



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.37E+00	3.17E-01
b	3.83E+01	2.07E+01
c1	2.99E-03	2.07E-03
c2	9.31E-04	5.92E-04
c3	8.80E-04	5.60E-04
Covariance (c1,c2)	0.9665	--
Covariance (c1,c3)	0.9659	--
Degrees of Freedom	22	--

Goodness of Fit

Statistic	Estimate
F	53.359
p	< 0.001
Adjusted R <sup>2</sup>	0.8896
AIC	116.514

RBA and Uncertainty

	PbAc, 0 hr	PbAc, +2 hr
RBA	0.31	0.29
Lower bound	?	?
Upper bound	?	?
Standard Error	0.056*	0.053*

\*  $g \geq 0.05$ , estimate is uncertain



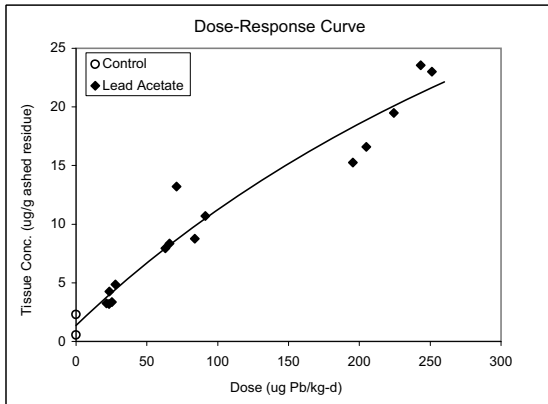
APPENDIX E

Figure 4c - All Data

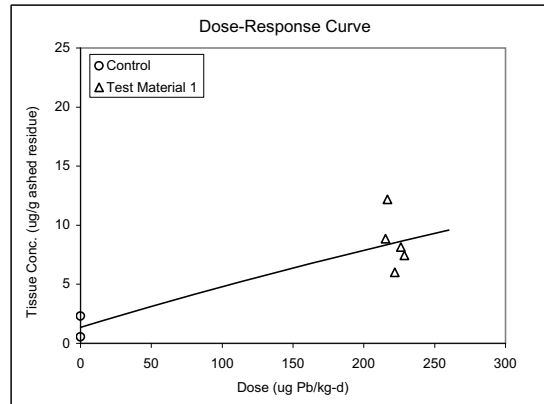
Phase II Experiment 1a: Femur

Michaelis-Menton Model:  $y = a + b \cdot x_1 / (c_1 + x_1) + b \cdot x_2 / (c_2 + x_2) + b \cdot x_3 / (c_3 + x_3)$

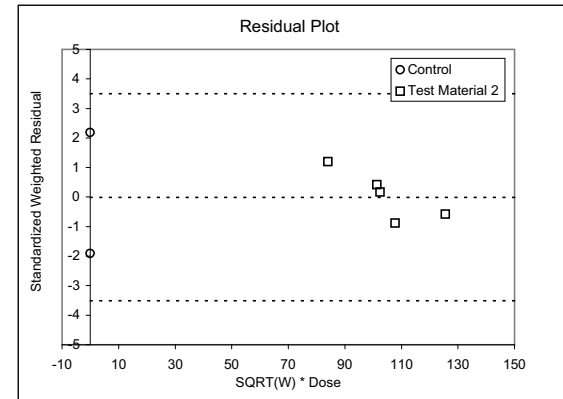
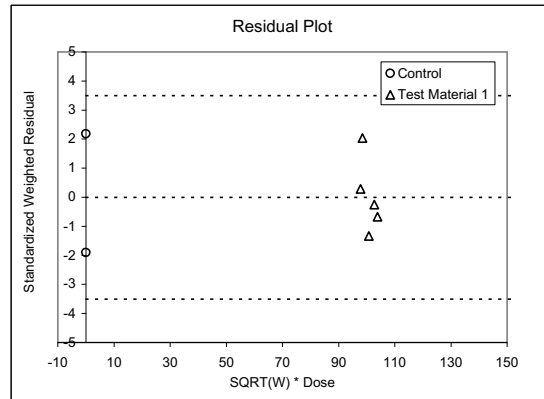
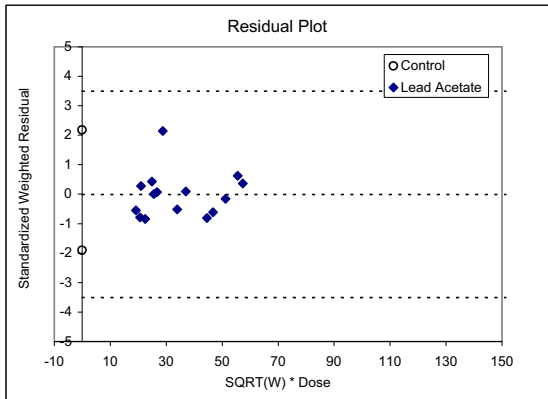
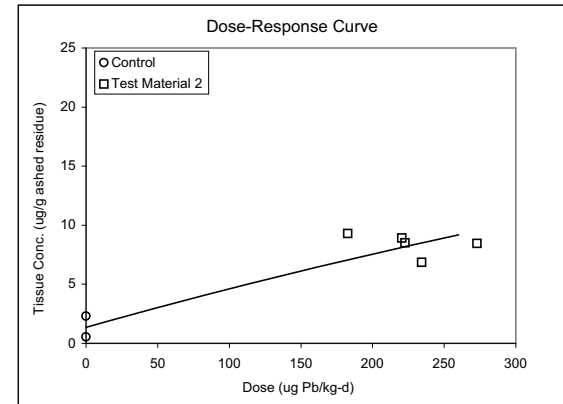
Lead Acetate, 2 hours before feed (Reference)



Lead Acetate, Simultaneous with feed (PbAc, 0 hr)



Lead Acetate, 2 hours after feed (PbAc, +2 hr)



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.37E+00	3.18E-01
b	6.71E+01	4.16E+01
c1	5.80E+02	4.53E+02
c2	1.86E+03	1.35E+03
c3	1.97E+03	1.43E+03
Covariance (c1,c2)	0.9741	--
Covariance (c1,c3)	0.9736	--
Degrees of Freedom	22	--

Goodness of Fit

Statistic	Estimate
F	53.403
p	< 0.001
Adjusted R <sup>2</sup>	0.8896
AIC	116.500

RBA and Uncertainty

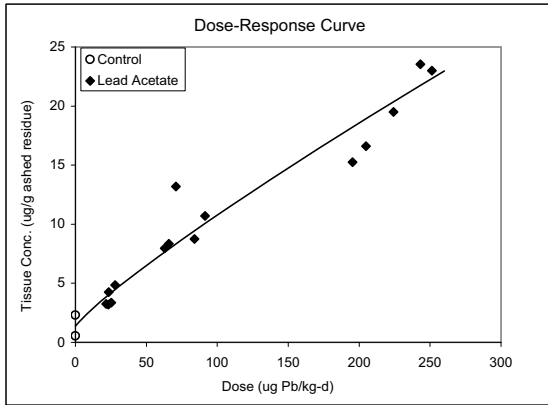
	PbAc, 0 hr	PbAc, +2 hr
RBA	0.31	0.29
Lower bound	?	?
Upper bound	?	?
Standard Error	0.056*	0.053*

\*  $g \geq 0.05$ , estimate is uncertain

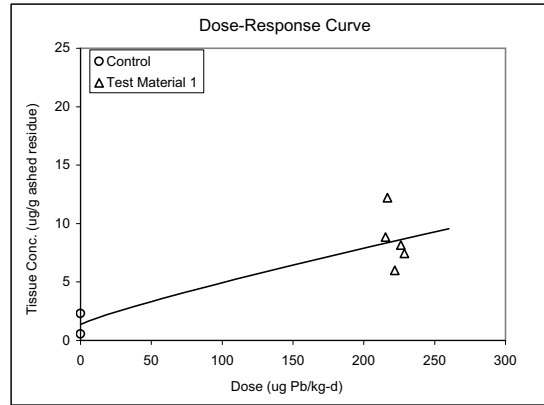
APPENDIX E

**Figure 4d - All Data**  
**Phase II Experiment 1a: Femur**  
**Power Model:  $y = a + b1*x1^c + b2*x2^c + b3*x3^c$**

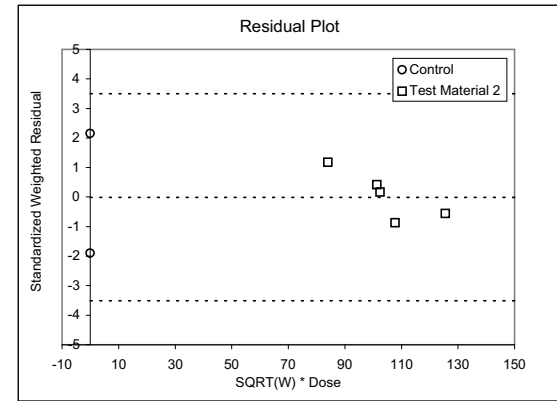
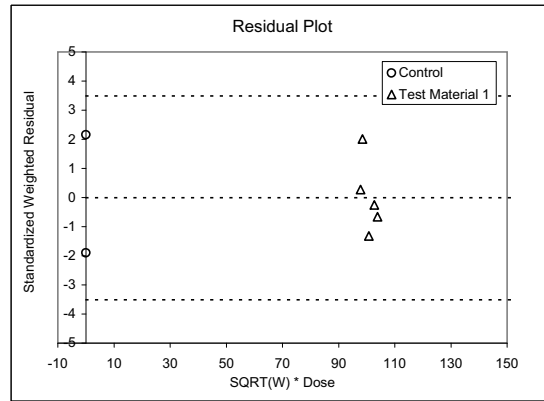
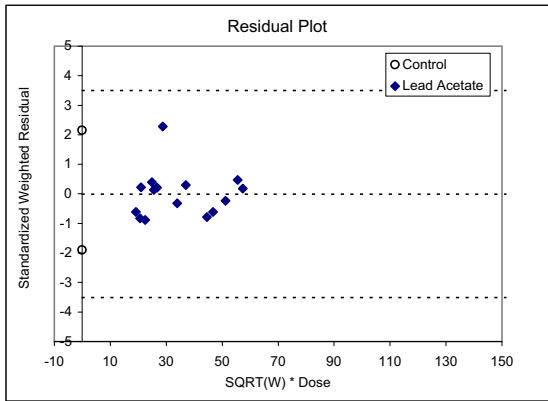
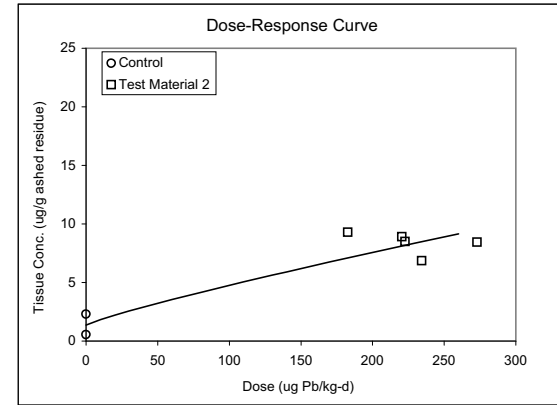
**Lead Acetate, 2 hours before feed (Reference)**



**Lead Acetate, Simultaneous with feed (PbAc, 0 hr)**



**Lead Acetate, 2 hours after feed (PbAc, +2 hr)**



**Summary of Fitting**

Parameter	Estimate	Standard Error
a	1.37E+00	3.29E-01
b1	1.71E-01	8.08E-02
b2	6.47E-02	3.54E-02
b3	6.15E-02	3.39E-02
c	8.71E-01	9.43E-02
Covariance (b1,b2)	0.9601	--
Covariance (b1,b3)	0.9598	--
Degrees of Freedom	22	--

**Goodness of Fit**

Statistic	Estimate
F	52.175
p	< 0.001
Adjusted R <sup>2</sup>	0.8873
AIC	116.905

**RBA and Uncertainty**

	PbAc, 0 hr	PbAc, +2 hr
RBA	0.33	0.31
Lower bound	0.07	0.06
Upper bound	0.45	0.42
Standard Error	--	--

## APPENDIX E

### EXPERIMENT 2

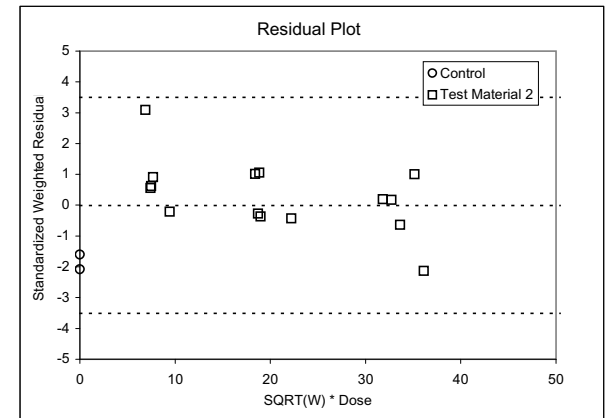
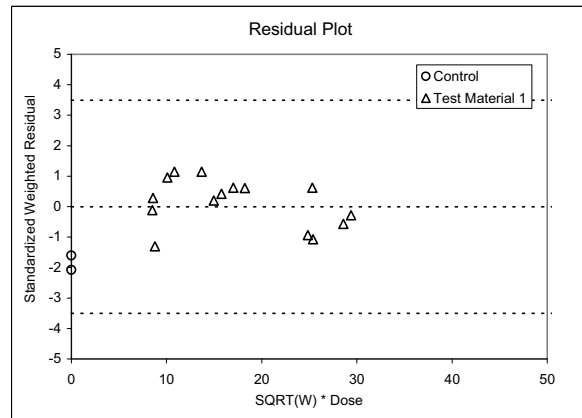
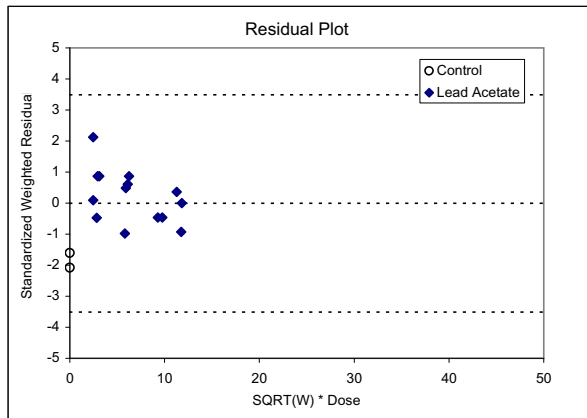
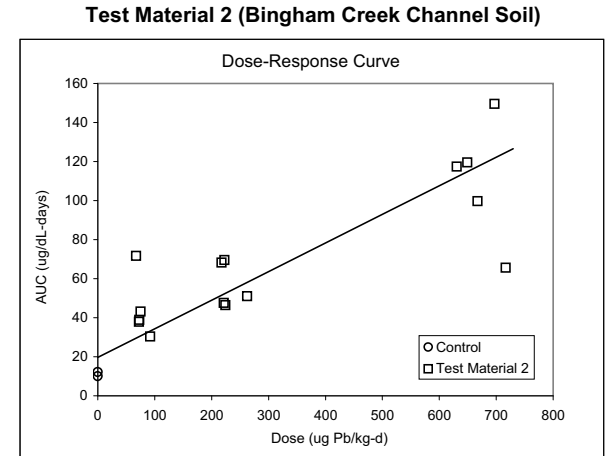
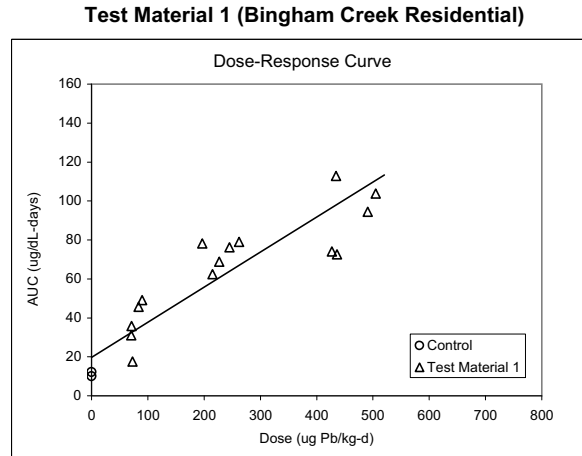
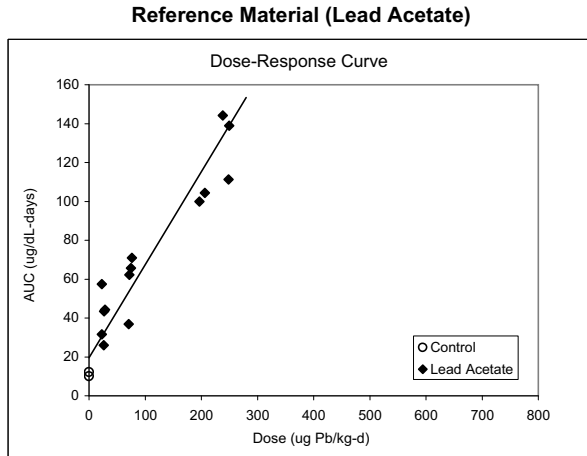
Test Material 1: Bingham Creek Residential  
Test Material 2: Bingham Creek Channel Soil

- Figure 1a Blood AUC - Linear Model
- Figure 1b Blood AUC - Exponential Model
- Figure 1c Blood AUC - Michaelis-Menton Model
- Figure 1d Blood AUC - Power Model
  
- Figure 2a Liver - Linear Model (All Data)
- Figure 2a Liver - Linear Model (Outlier Excluded)
- Figure 2b Liver - Exponential Model
- Figure 2c Liver - Michaelis-Menton Model
- Figure 2d Liver - Power Model
  
- Figure 3a Kidney - Linear Model
- Figure 3b Kidney - Exponential Model
- Figure 3c Kidney - Michaelis-Menton Model
- Figure 3d Kidney - Power Model
  
- Figure 4a Femur - Linear Model
- Figure 4b Femur - Exponential Model
- Figure 4c Femur - Michaelis-Menton Model
- Figure 4d Femur - Power Model

APPENDIX E

Figure 1a - All Data

Phase II Experiment 2: Blood AUC  
 Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.97E+01	2.56E+00
b1	4.78E-01	5.61E-02
b2	1.80E-01	2.19E-02
b3	1.46E-01	1.76E-02
Covariance (c1,c2)	0.1488	--
Covariance (c1,c3)	0.1354	--
Degrees of Freedom	42	--

Goodness of Fit

Statistic	Estimate
F	53.890
p	< 0.001
Adjusted R <sup>2</sup>	0.7791
AIC	412.401

RBA and Uncertainty

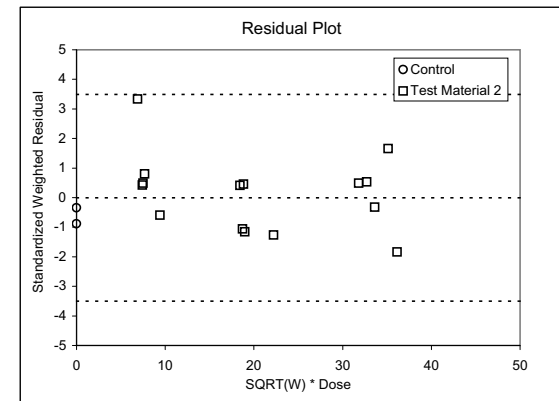
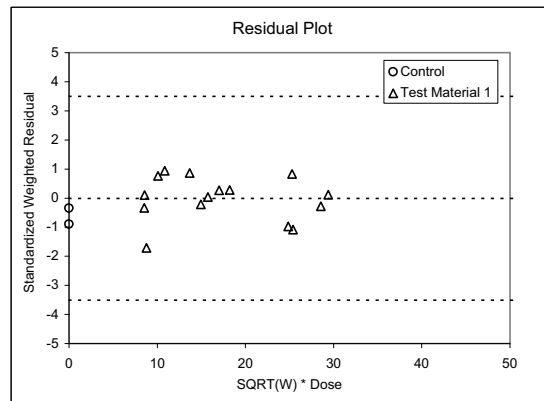
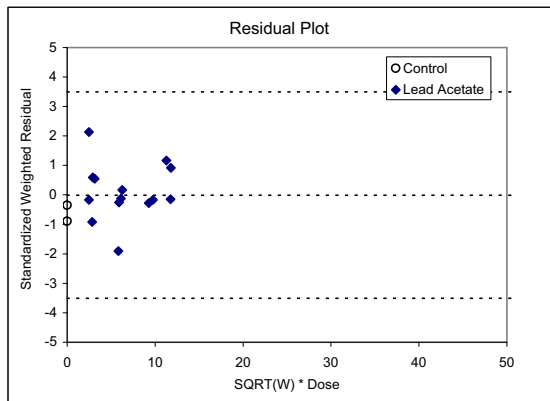
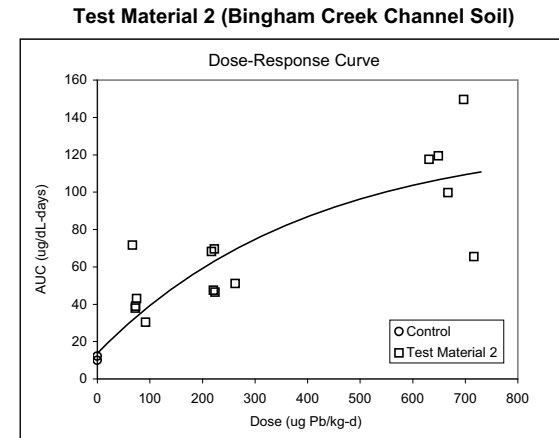
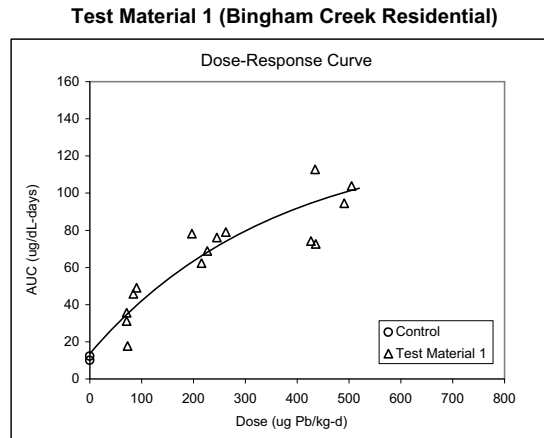
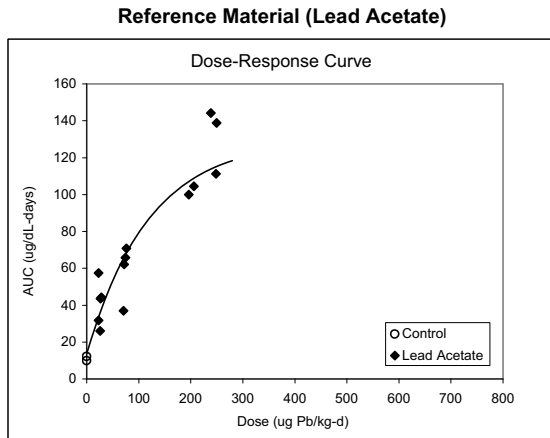
	Test Material 1	Test Material 2
RBA	0.38	0.31
Lower bound	0.29	0.23
Upper bound	0.49	0.40
Standard Error	0.059	0.048

APPENDIX E

Figure 1b - All Data

Phase II Experiment 2: Blood AUC

Exponential Model:  $y = a + b*(1-\exp(-c1*x1)) + b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.36E+01	2.84E+00
b	1.16E+02	1.83E+01
c1	8.36E-03	2.64E-03
c2	2.81E-03	8.42E-04
c3	2.50E-03	7.72E-04
Covariance (c1,c2)	0.7931	--
Covariance (c1,c3)	0.7868	--
Degrees of Freedom	41	--

Goodness of Fit

Statistic	Estimate
F	54.613
p	< 0.001
Adjusted R <sup>2</sup>	0.8266
AIC	393.655

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.34	0.30
Lower bound	0.23	0.20
Upper bound	0.50	0.45
Standard Error	0.067*	0.061*

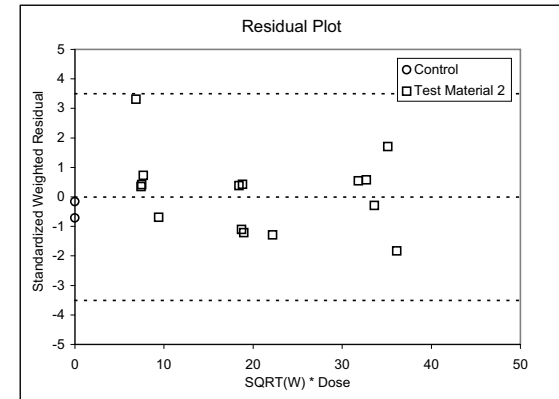
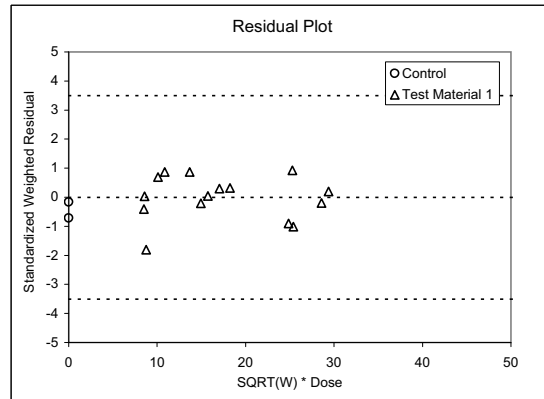
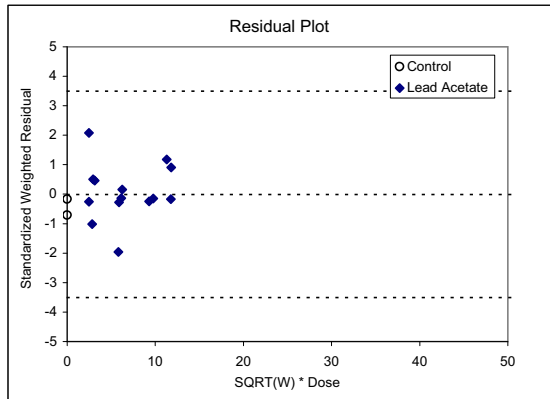
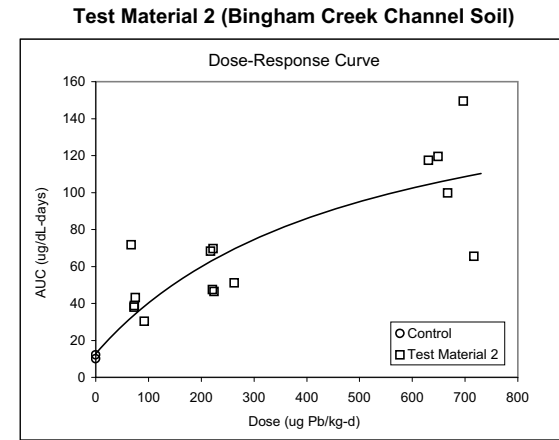
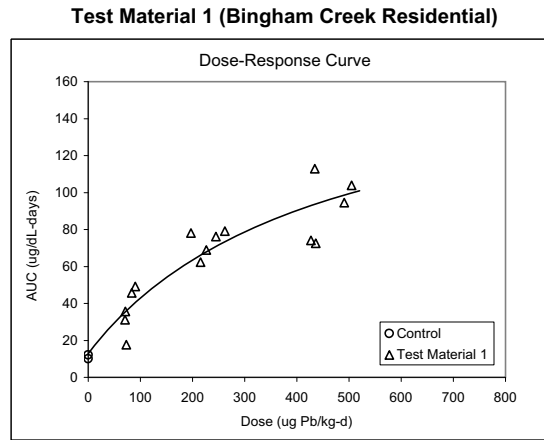
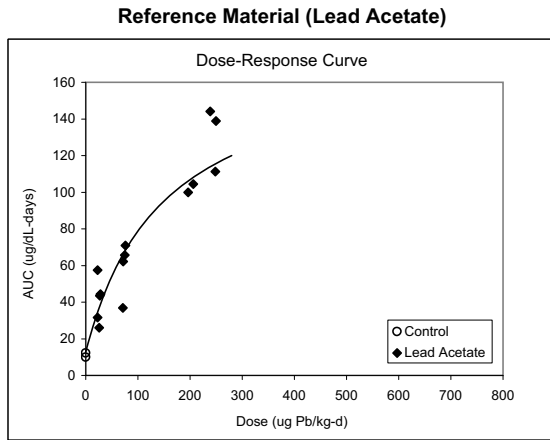
\*  $g \geq 0.05$ , estimate is uncertain

APPENDIX E

Figure 1c - All Data

Phase II Experiment 2: Blood AUC

Michaelis-Menton Model:  $y = a + b*x1/(c1+x1) + b*x2/(c2+x2) + b*x3/(c3+x3)$



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.29E+01	2.88E+00
b	1.64E+02	3.13E+01
c1	1.48E+02	5.60E+01
c2	4.46E+02	1.62E+02
c3	4.97E+02	1.85E+02
Covariance (c1,c2)	0.8595	--
Covariance (c1,c3)	0.8572	--
Degrees of Freedom	41	--

Goodness of Fit

Statistic	Estimate
F	56.405
p	< 0.001
Adjusted R <sup>2</sup>	0.8312
AIC	391.826

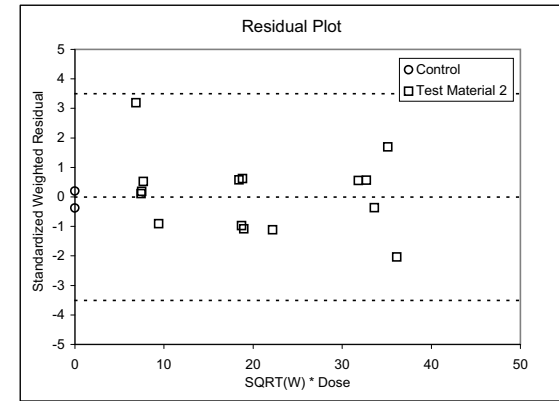
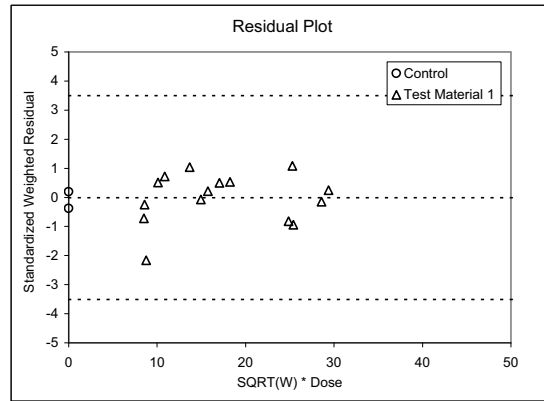
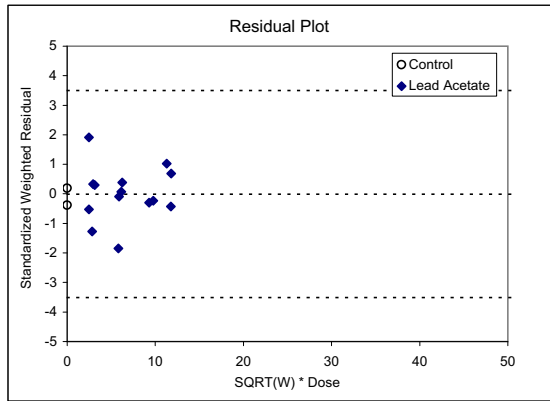
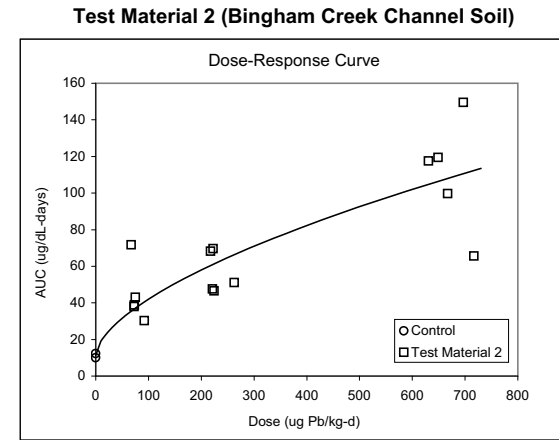
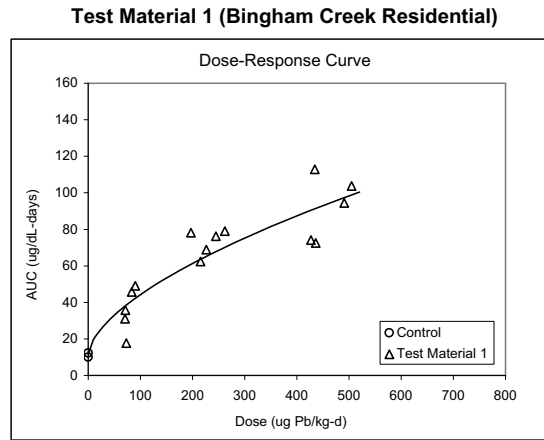
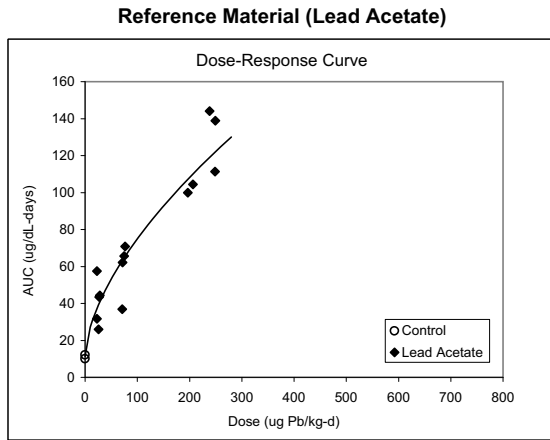
RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.33	0.30
Lower bound	0.21	0.19
Upper bound	0.49	0.46
Standard Error	0.065*	0.060*

\*  $g \geq 0.05$ , estimate is uncertain

APPENDIX E

**Figure 1d - All Data**  
**Phase II Experiment 2: Blood AUC**  
**Power Model:  $y = a + b_1 \cdot x_1^c + b_2 \cdot x_2^c + b_3 \cdot x_3^c$**



**Summary of Fitting**

Parameter	Estimate	Standard Error
a	1.14E+01	2.84E+00
b1	3.90E+00	1.36E+00
b2	2.01E+00	8.18E-01
b3	1.88E+00	7.93E-01
c	6.06E-01	6.68E-02
Covariance (b1,b2)	0.9568	--
Covariance (b1,b3)	0.9581	--
Degrees of Freedom	41	--

**Goodness of Fit**

Statistic	Estimate
F	62.696
p	< 0.001
Adjusted R <sup>2</sup>	0.8458
AIC	386.116

**RBA and Uncertainty**

	Test Material 1	Test Material 2
RBA	0.34	0.30
Lower bound	0.17	0.14
Upper bound	0.46	0.41
Standard Error	--	--

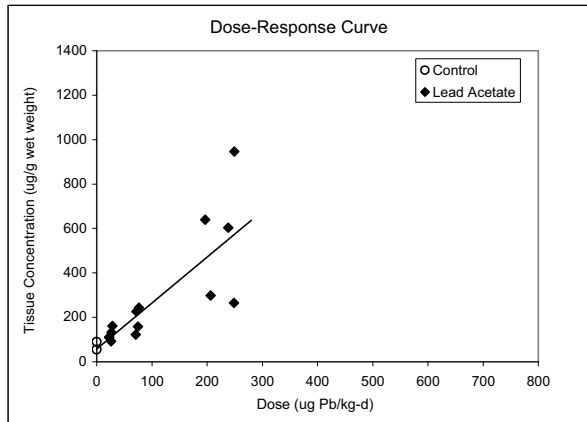
APPENDIX E

Figure 2a - All Data

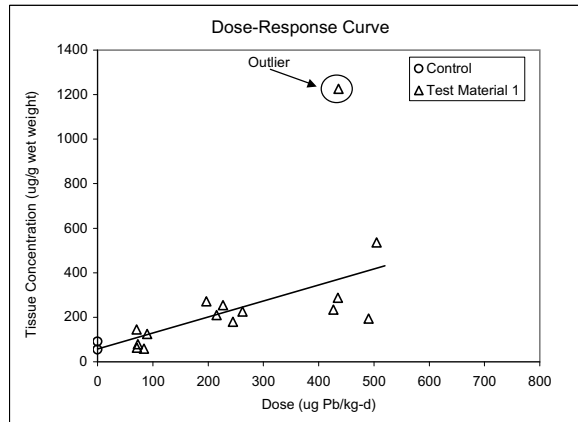
Phase II Experiment 2: Liver

Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$

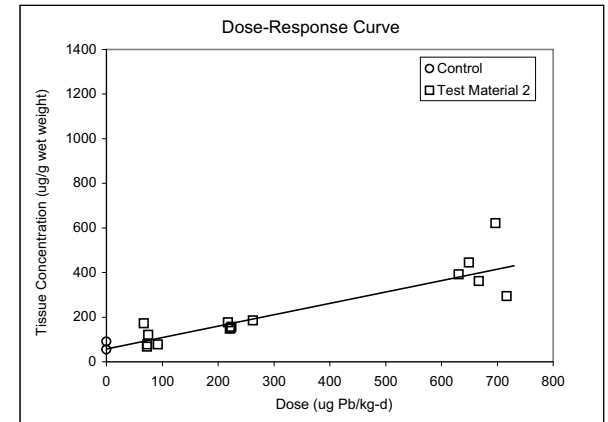
Reference Material (Lead Acetate)



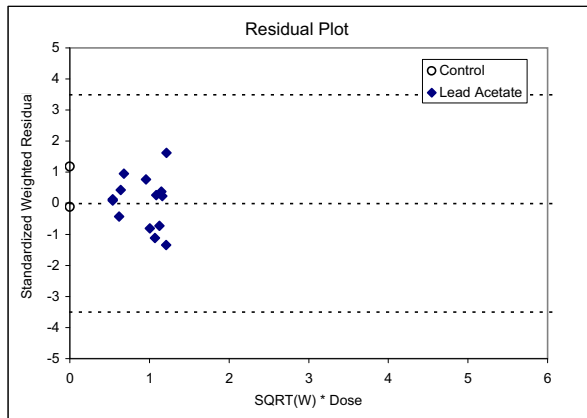
Test Material 1 (Bingham Creek Residential)



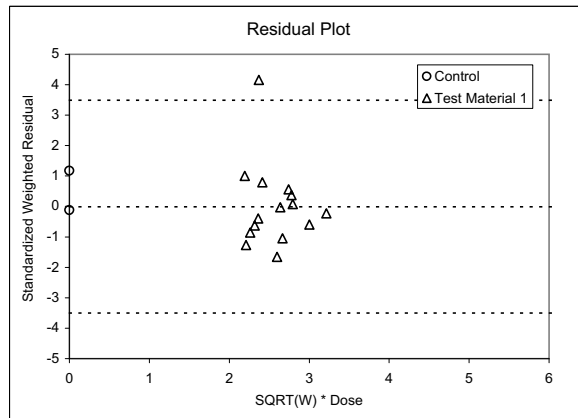
Test Material 2 (Bingham Creek Channel Soil)



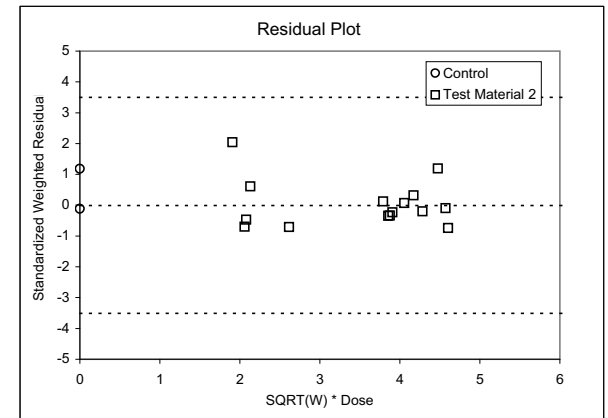
Residual Plot



Residual Plot



Residual Plot



Summary of Fitting

Parameter	Estimate	Standard Error
a	5.79E+01	1.18E+01
b1	2.07E+00	3.55E-01
b2	7.17E-01	1.36E-01
b3	5.10E-01	9.51E-02
Covariance (c1,c2)	0.2250	--
Covariance (c1,c3)	0.2118	--
Degrees of Freedom	42	--

Goodness of Fit

Statistic	Estimate
F	20.611
p	< 0.001
Adjusted R <sup>2</sup>	0.5666
AIC	543.299

RBA and Uncertainty

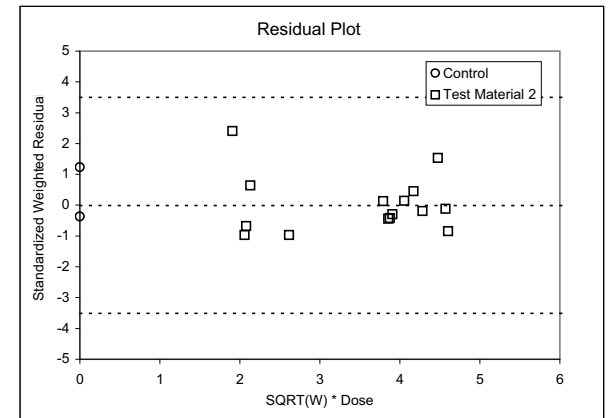
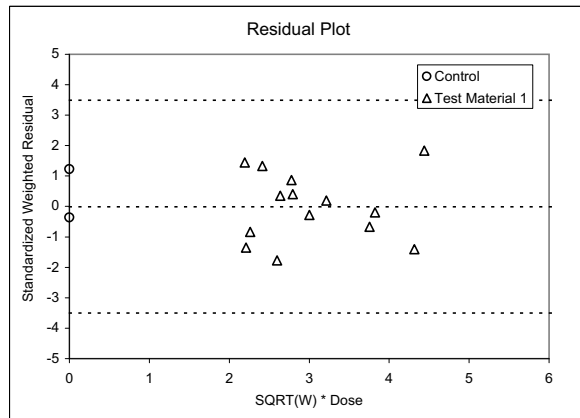
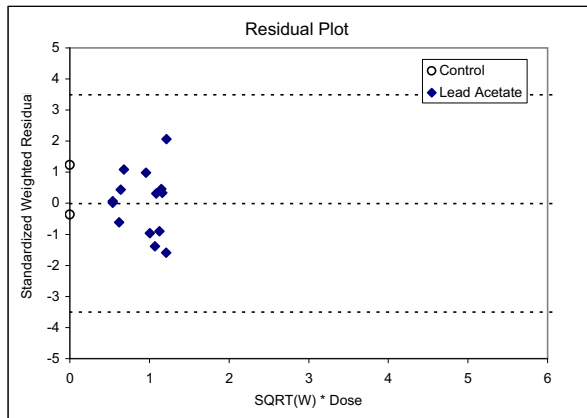
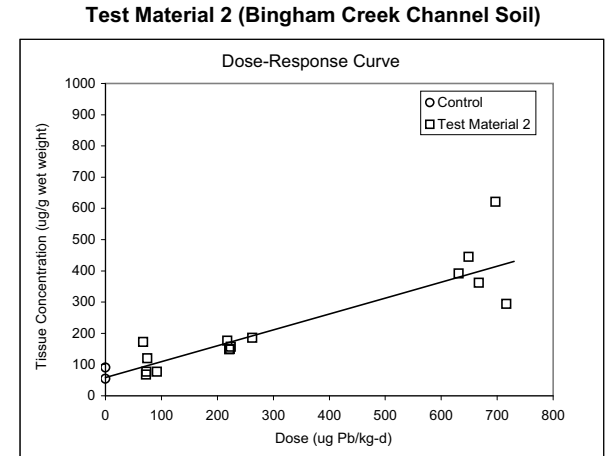
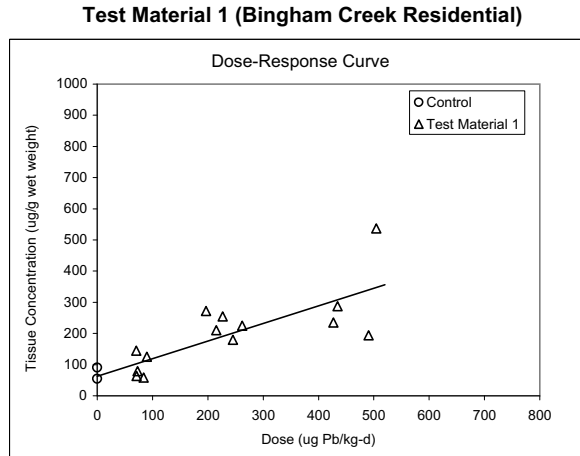
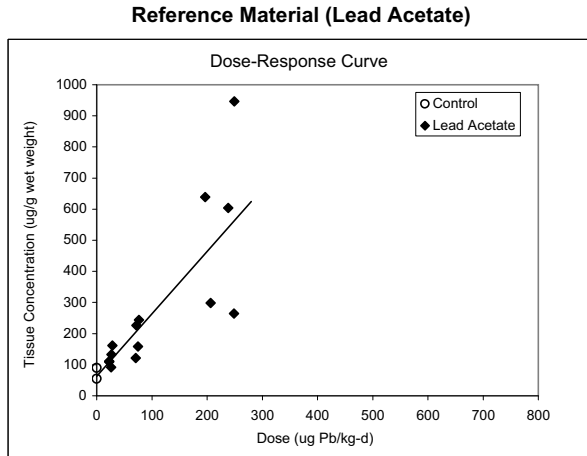
	Test Material 1	Test Material 2
RBA	0.35	0.25
Lower bound	0.23	0.16
Upper bound	0.51	0.36
Standard Error	0.078*	0.055*

\*  $g \geq 0.05$ , estimate is uncertain



APPENDIX E

**Figure 2a - Outlier Excluded**  
**Phase II Experiment 2: Liver**  
**Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$**



**Summary of Fitting**

Parameter	Estimate	Standard Error
a	6.28E+01	9.37E+00
b1	2.01E+00	2.87E-01
b2	5.63E-01	9.34E-02
b3	4.90E-01	7.67E-02
Covariance (c1,c2)	0.2120	--
Covariance (c1,c3)	0.2047	--
Degrees of Freedom	41	--

**Goodness of Fit**

Statistic	Estimate
F	29.241
p	< 0.001
Adjusted R <sup>2</sup>	0.6582
AIC	507.050

**RBA and Uncertainty**

	Test Material 1	Test Material 2
RBA	0.28	0.24
Lower bound	0.20	0.17
Upper bound	0.39	0.34
Standard Error	0.055*	0.046*

\*  $g \geq 0.05$ , estimate is uncertain

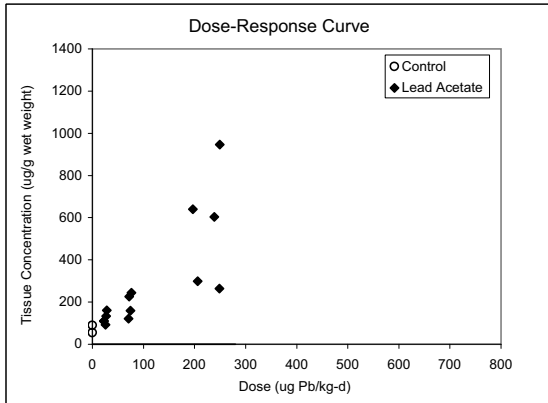
APPENDIX E

Figure 2b - All Data

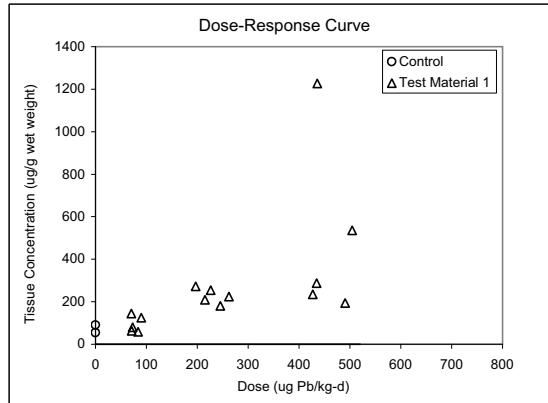
Phase II Experiment 2: Liver

Exponential Model:  $y = a + b*(1-\exp(-c1*x1)) + b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$

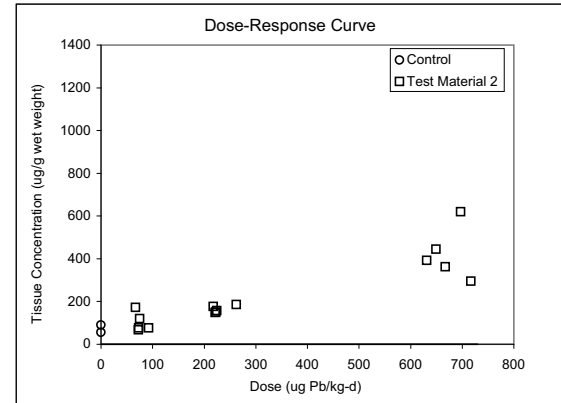
Reference Material (Lead Acetate)



Test Material 1 (Bingham Creek Residential)



Test Material 2 (Bingham Creek Channel Soil)



**NO SOLUTION**

The software could not find a solution,  
or the solution was unstable and/or had unrealistic parameter estimates.

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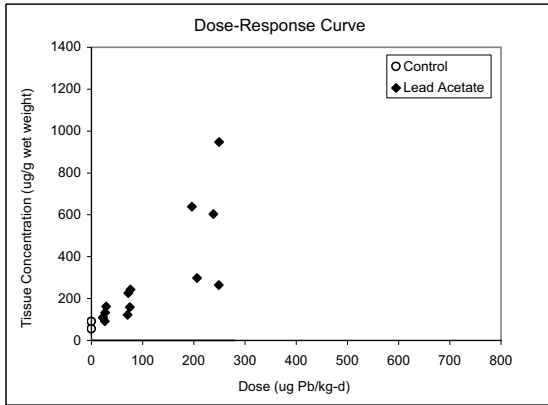
APPENDIX E

Figure 2c - All Data

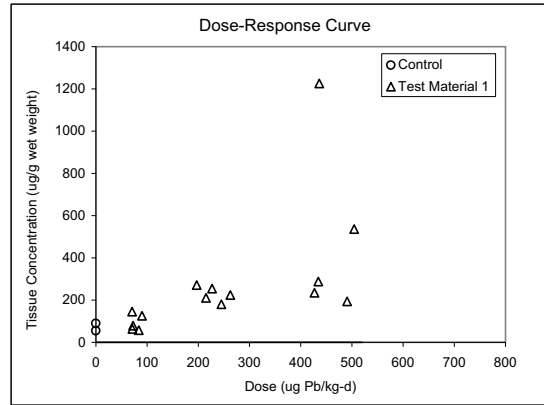
Phase II Experiment 2: Liver

Michaelis-Menton Model:  $y = a + b \cdot x_1 / (c_1 + x_1) + b \cdot x_2 / (c_2 + x_2) + b \cdot x_3 / (c_3 + x_3)$

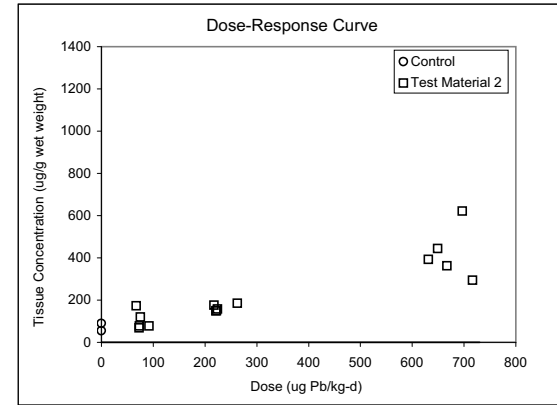
Reference Material (Lead Acetate)



Test Material 1 (Bingham Creek Residential)



Test Material 2 (Bingham Creek Channel Soil)



**NO SOLUTION**

The software could not find a solution,  
or the solution was unstable and/or had unrealistic parameter estimates.

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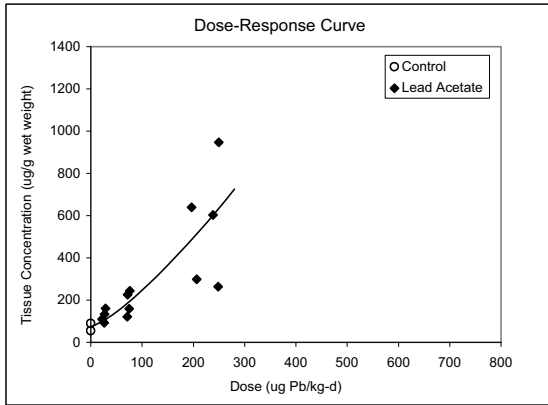
APPENDIX E

Figure 2d - All Data

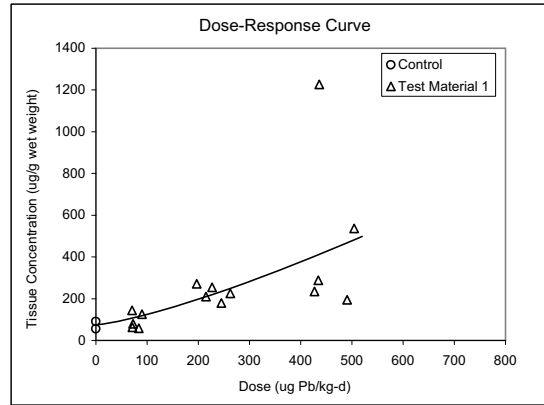
Phase II Experiment 2: Liver

Power Model:  $y = a + b_1 \cdot x_1^c + b_2 \cdot x_2^c + b_3 \cdot x_3^c$

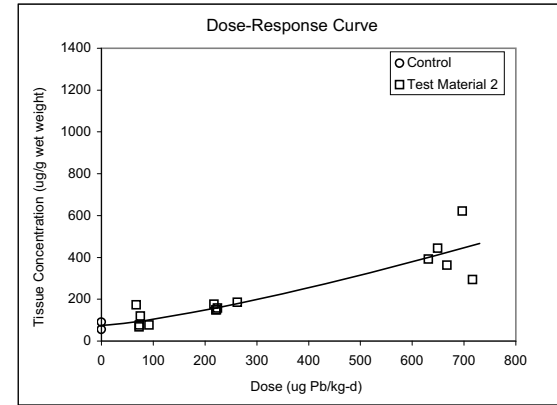
Reference Material (Lead Acetate)



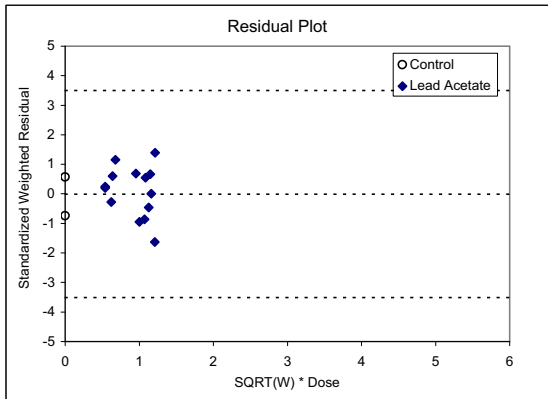
Test Material 1 (Bingham Creek Residential)



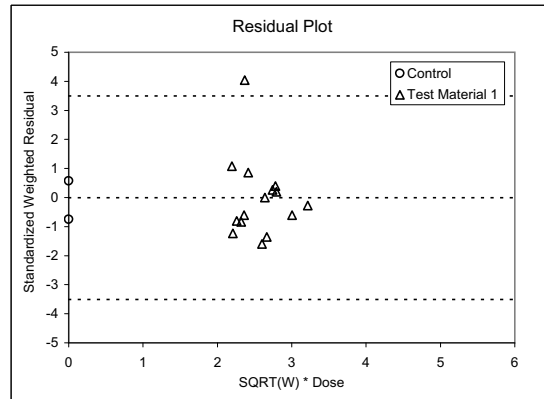
Test Material 2 (Bingham Creek Channel Soil)



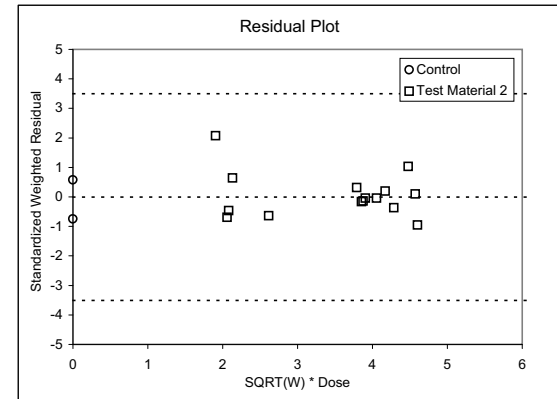
Residual Plot



Residual Plot



Residual Plot



Summary of Fitting

Parameter	Estimate	Standard Error
a	7.47E+01	1.60E+01
b1	4.40E-01	5.88E-01
b2	1.29E-01	1.95E-01
b3	7.68E-02	1.25E-01
c	1.30E+00	2.51E-01
Covariance (b1,b2)	0.9848	--
Covariance (b1,b3)	0.9854	--
Degrees of Freedom	41	--

Goodness of Fit

Statistic	Estimate
F	16.144
p	< 0.001
Adjusted R <sup>2</sup>	0.5738
AIC	543.050

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.39	0.26
Lower bound	?	?
Upper bound	?	?
Standard Error	--	--

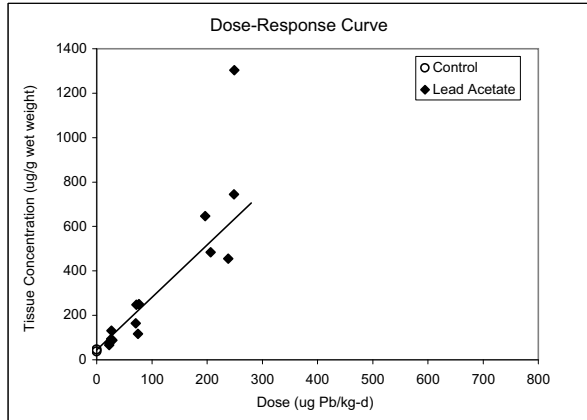
APPENDIX E

Figure 3a - All Data

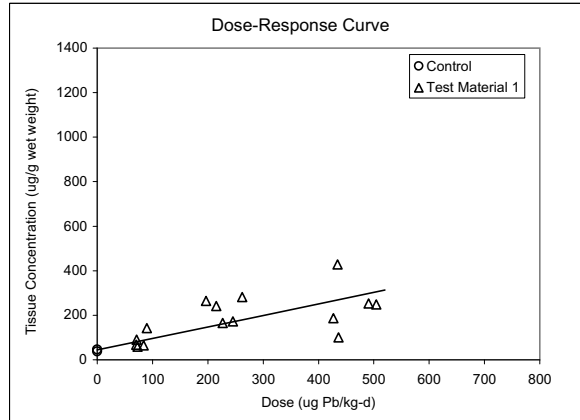
Phase II Experiment 2: Kidney

Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$

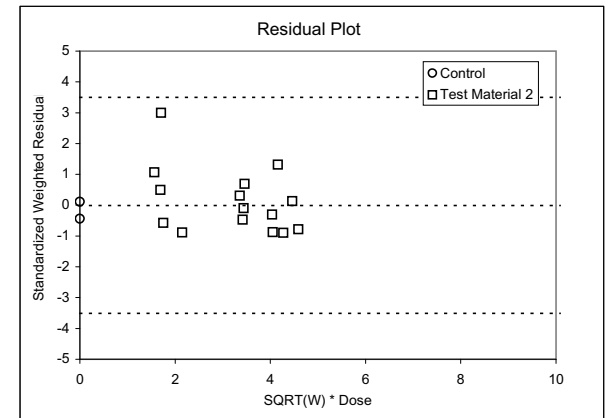
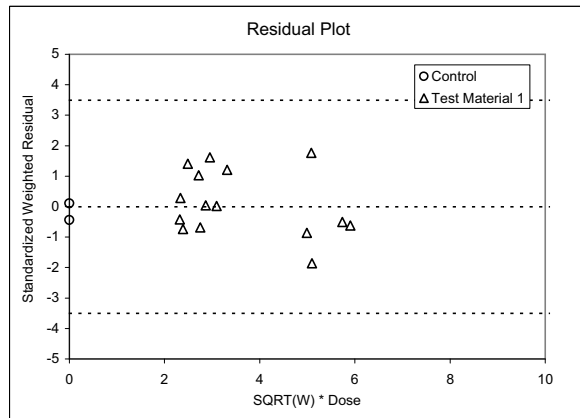
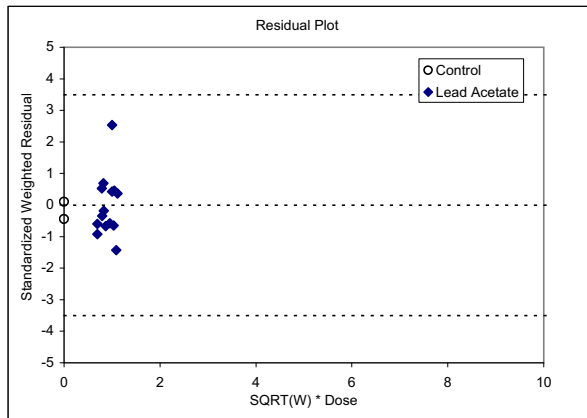
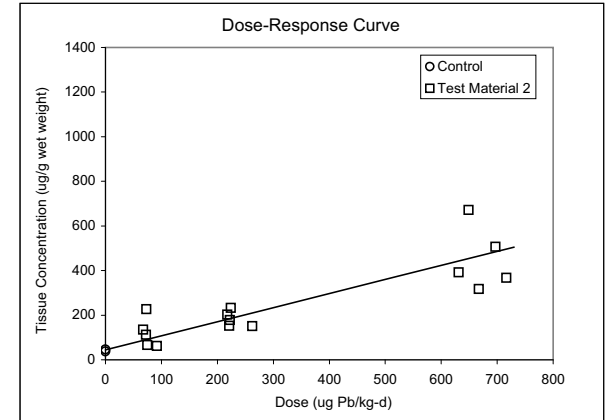
Reference Material (Lead Acetate)



Test Material 1 (Bingham Creek Residential)



Test Material 2 (Bingham Creek Channel Soil)



Summary of Fitting

Parameter	Estimate	Standard Error
a	4.42E+01	8.71E+00
b1	2.36E+00	3.52E-01
b2	5.17E-01	8.26E-02
b3	6.32E-01	8.95E-02
Covariance (c1,c2)	0.1831	--
Covariance (c1,c3)	0.1458	--
Degrees of Freedom	42	--

Goodness of Fit

Statistic	Estimate
F	33.908
p	< 0.001
Adjusted R <sup>2</sup>	0.6869
AIC	530.223

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.22	0.27
Lower bound	0.15	0.19
Upper bound	0.31	0.37
Standard Error	0.043*	0.051*

\*  $g \geq 0.05$ , estimate is uncertain

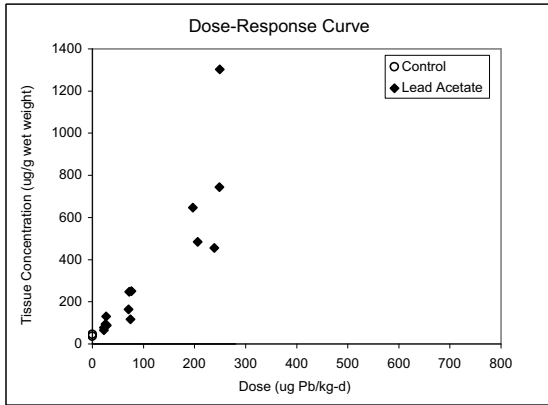
APPENDIX E

Figure 3b - All Data

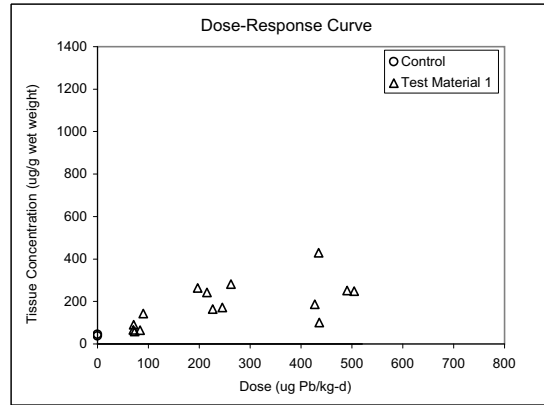
Phase II Experiment 2: Kidney

Exponential Model:  $y = a + b*(1-\exp(-c1*x1)) + b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$

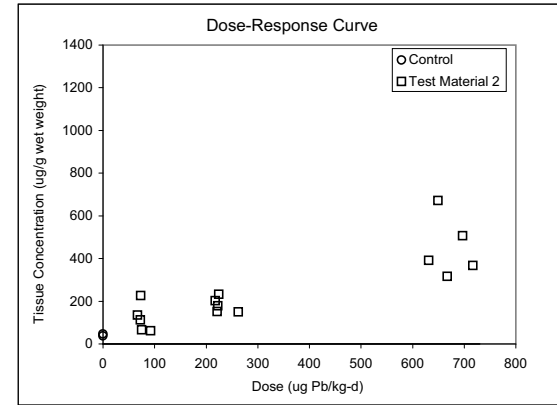
Reference Material (Lead Acetate)



Test Material 1 (Bingham Creek Residential)



Test Material 2 (Bingham Creek Channel Soil)



**NO SOLUTION**

The software could not find a solution,  
or the solution was unstable and/or had unrealistic parameter estimates.

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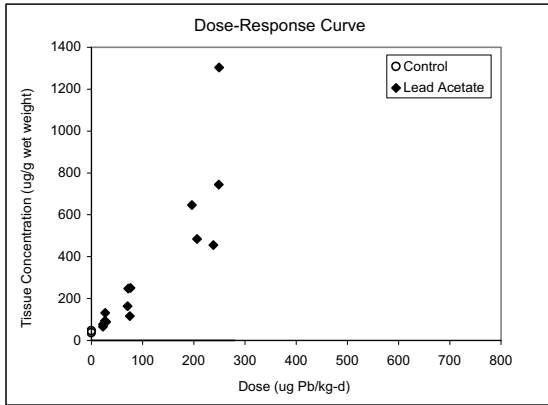
APPENDIX E

Figure 3c - All Data

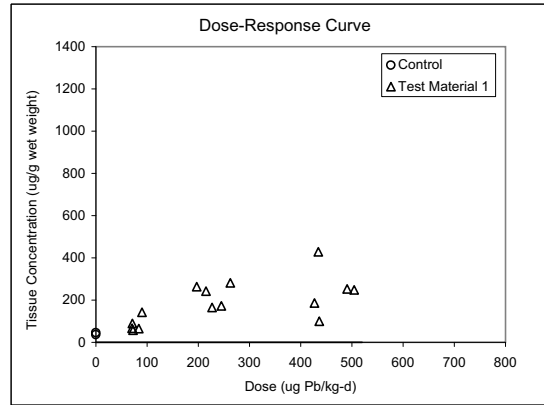
Phase II Experiment 2: Kidney

Michaelis-Menton Model:  $y = a + b \cdot x_1 / (c_1 + x_1) + b \cdot x_2 / (c_2 + x_2) + b \cdot x_3 / (c_3 + x_3)$

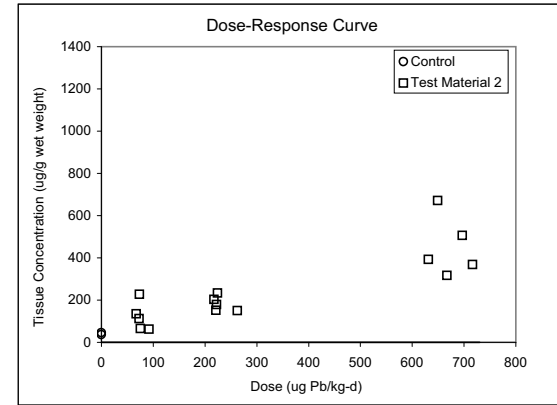
Reference Material (Lead Acetate)



Test Material 1 (Bingham Creek Residential)



Test Material 2 (Bingham Creek Channel Soil)



**NO SOLUTION**

The software could not find a solution,  
or the solution was unstable and/or had unrealistic parameter estimates.

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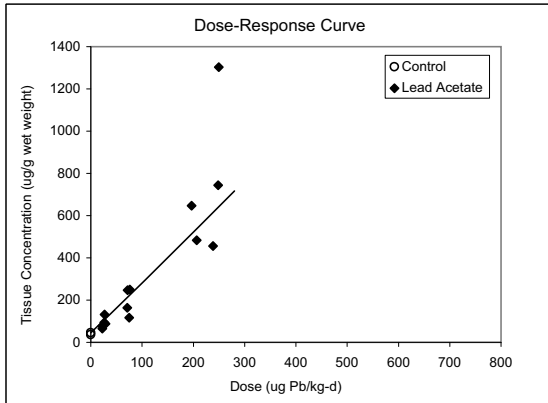
APPENDIX E

Figure 3d - All Data

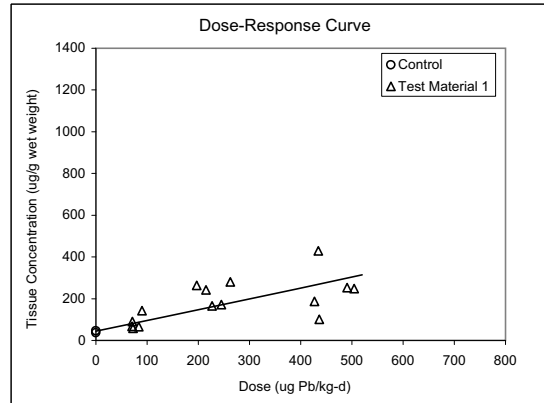
Phase II Experiment 2: Kidney

Power Model:  $y = a + b_1 \cdot x_1^c + b_2 \cdot x_2^c + b_3 \cdot x_3^c$

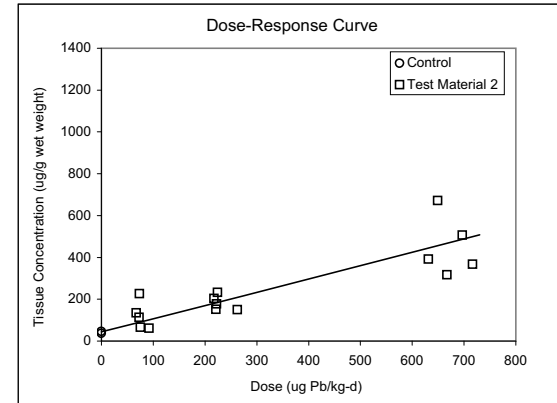
Reference Material (Lead Acetate)



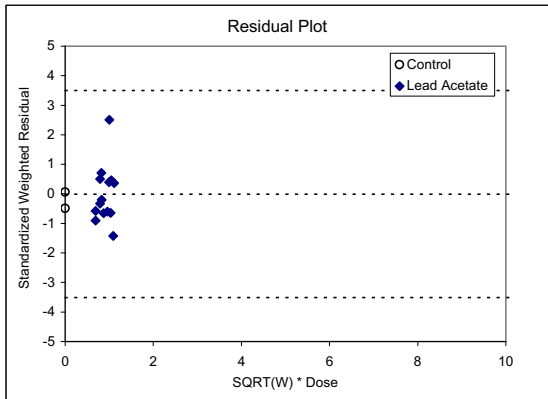
Test Material 1 (Bingham Creek Residential)



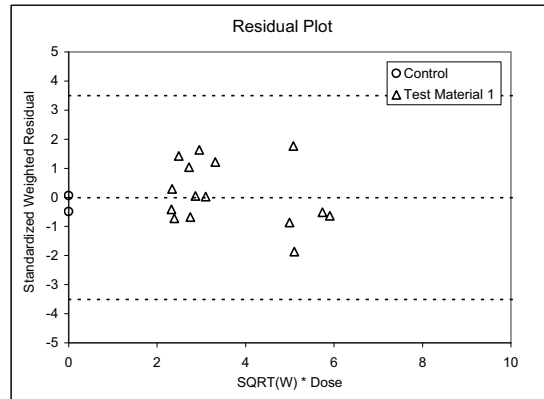
Test Material 2 (Bingham Creek Channel Soil)



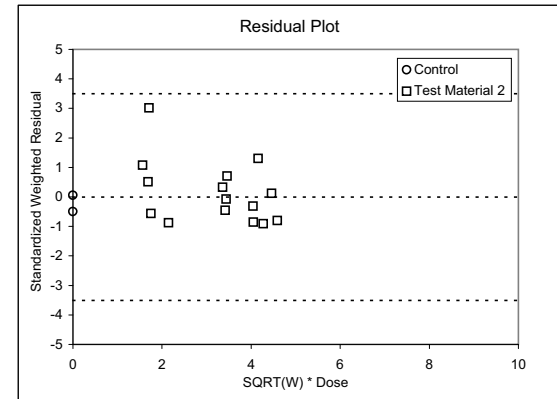
Residual Plot



Residual Plot



Residual Plot



Summary of Fitting

Parameter	Estimate	Standard Error
a	4.50E+01	1.12E+01
b1	2.20E+00	1.51E+00
b2	4.69E-01	4.10E-01
b3	5.73E-01	5.04E-01
c	1.02E+00	1.39E-01
Covariance (b1,b2)	0.9660	--
Covariance (b1,b3)	0.9676	--
Degrees of Freedom	41	--

Goodness of Fit

Statistic	Estimate
F	24.834
p	< 0.001
Adjusted R <sup>2</sup>	0.6793
AIC	532.210

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.22	0.27
Lower bound	0.50	0.63
Upper bound	0.32	0.38
Standard Error	--	--



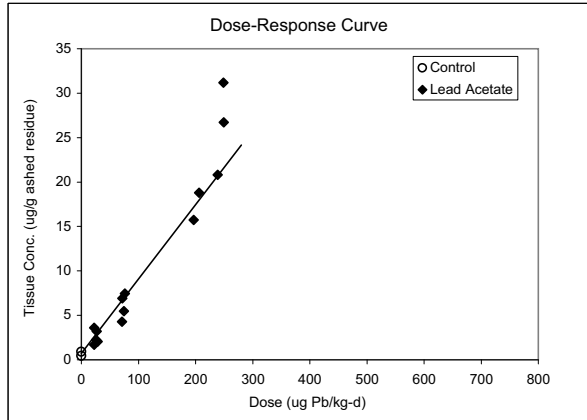
APPENDIX E

Figure 4a - All Data

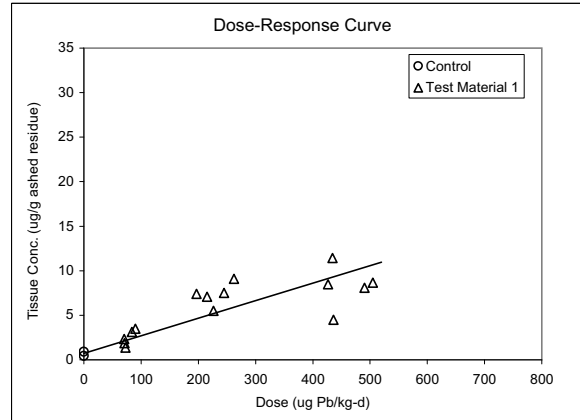
Phase II Experiment 2: Femur

Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$

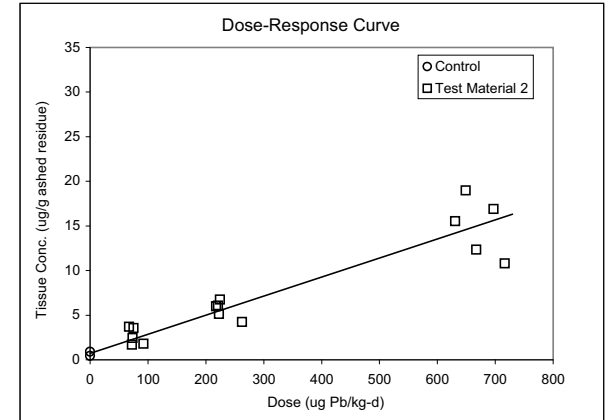
Reference Material (Lead Acetate)



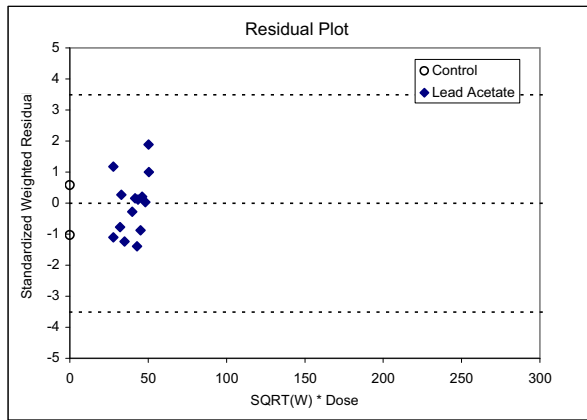
Test Material 1 (Bingham Creek Residential)



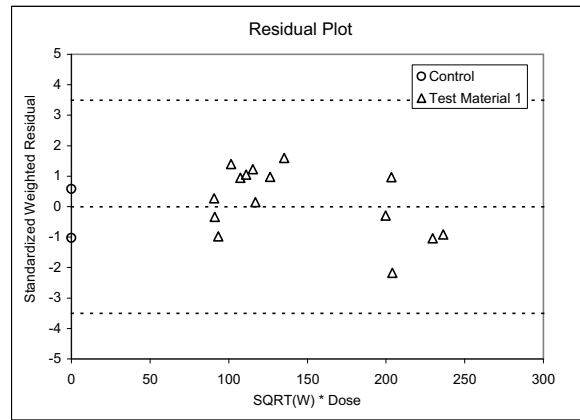
Test Material 2 (Bingham Creek Channel Soil)



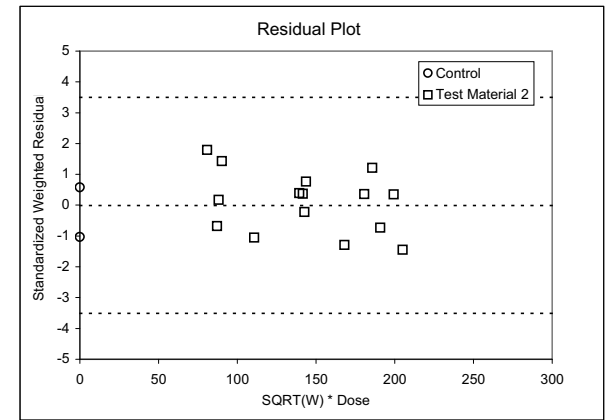
Residual Plot



Residual Plot



Residual Plot



Summary of Fitting

Parameter	Estimate	Standard Error
a	7.25E-01	1.66E-01
b1	8.37E-02	7.42E-03
b2	1.97E-02	1.94E-03
b3	2.14E-02	1.96E-03
Covariance (c1,c2)	0.1156	--
Covariance (c1,c3)	0.1070	--
Degrees of Freedom	42	--

Goodness of Fit

Statistic	Estimate
F	95.226
p	< 0.001
Adjusted R <sup>2</sup>	0.8627
AIC	180.521

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.24	0.26
Lower bound	0.19	0.21
Upper bound	0.29	0.31
Standard Error	0.029	0.031

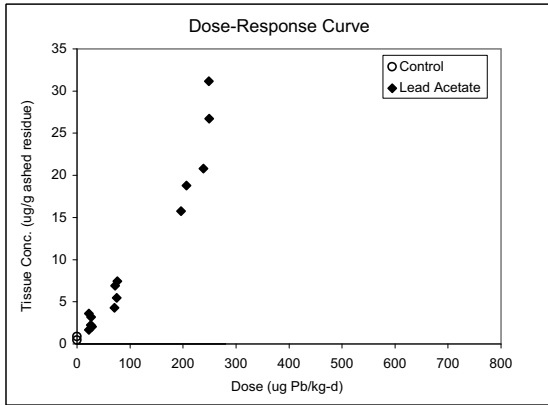
APPENDIX E

Figure 4b - All Data

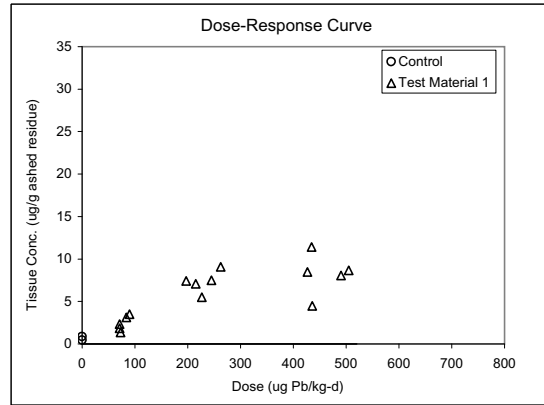
Phase II Experiment 2: Femur

Exponential Model:  $y = a + b*(1-\exp(-c1*x1)) + b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$

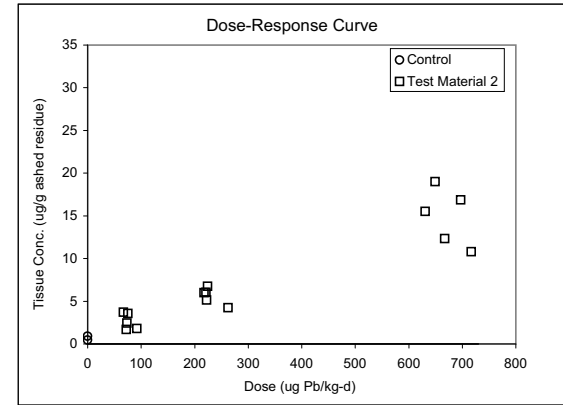
Reference Material (Lead Acetate)



Test Material 1 (Bingham Creek Residential)



Test Material 2 (Bingham Creek Channel Soil)



**NO SOLUTION**

The software could not find a solution,  
or the solution was unstable and/or had unrealistic parameter estimates.

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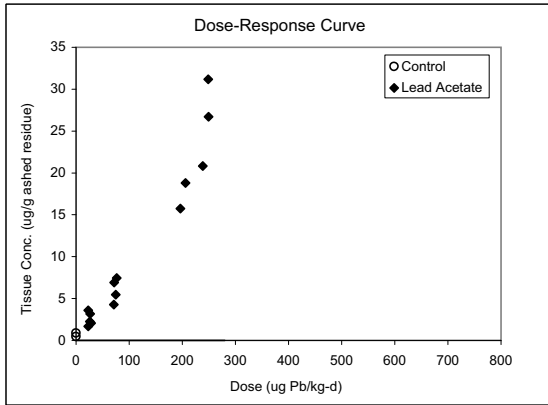
APPENDIX E

Figure 4c - All Data

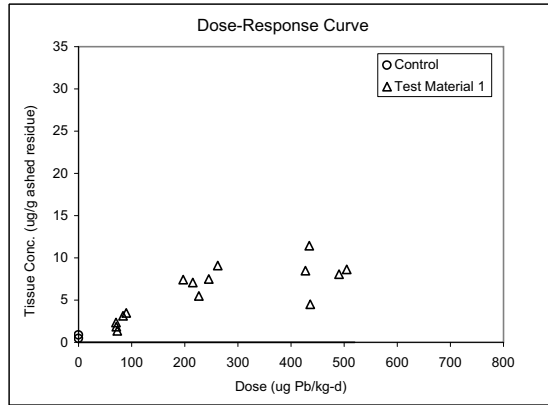
Phase II Experiment 2: Femur

Michaelis-Menton Model:  $y = a + b \cdot x_1 / (c_1 + x_1) + b \cdot x_2 / (c_2 + x_2) + b \cdot x_3 / (c_3 + x_3)$

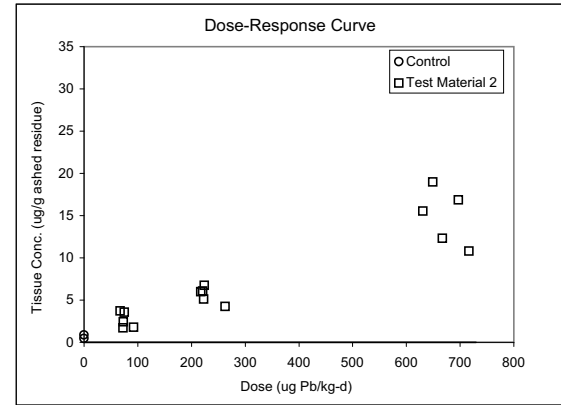
Reference Material (Lead Acetate)



Test Material 1 (Bingham Creek Residential)



Test Material 2 (Bingham Creek Channel Soil)



**NO SOLUTION**

The software could not find a solution,  
or the solution was unstable and/or had unrealistic parameter estimates.

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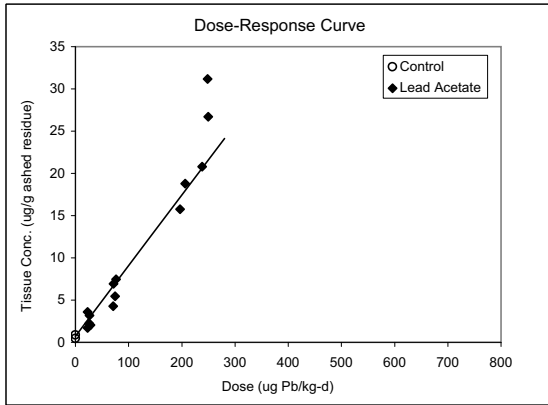
APPENDIX E

Figure 4d - All Data

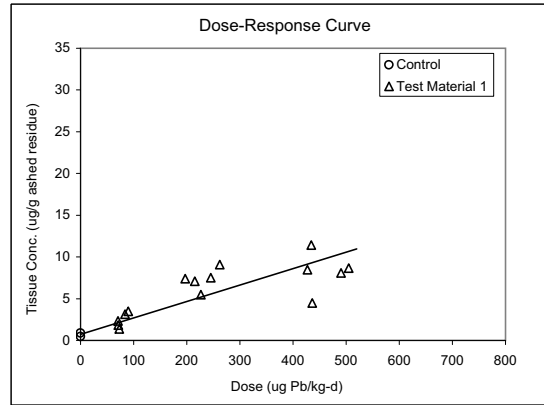
Phase II Experiment 2: Femur

Power Model:  $y = a + b1*x1^c + b2*x2^c + b3*x3^c$

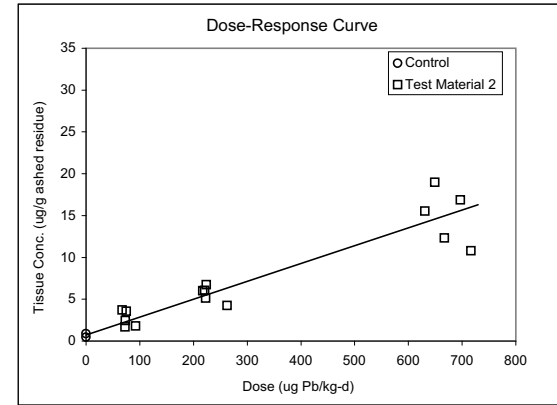
Reference Material (Lead Acetate)



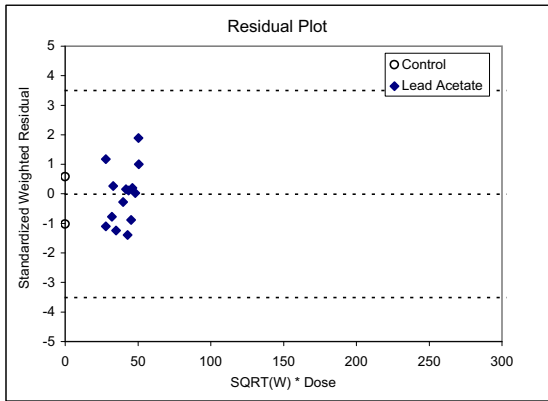
Test Material 1 (Bingham Creek Residential)



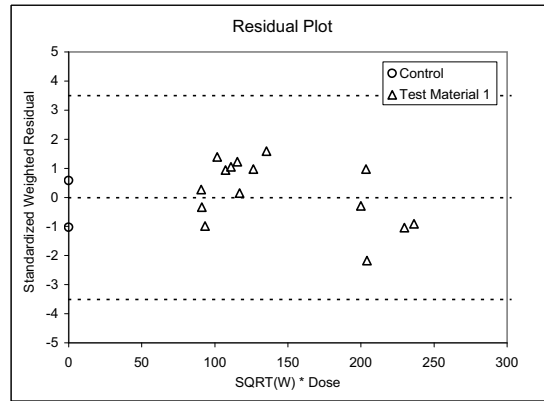
Test Material 2 (Bingham Creek Channel Soil)



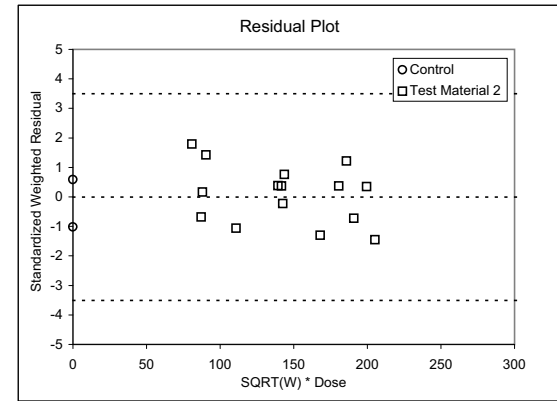
Residual Plot



Residual Plot



Residual Plot



Summary of Fitting

Parameter	Estimate	Standard Error
a	7.23E-01	1.98E-01
b1	8.43E-02	3.29E-02
b2	1.99E-02	9.63E-03
b3	2.16E-02	1.06E-02
c	9.99E-01	7.87E-02
Covariance (b1,b2)	0.9581	--
Covariance (b1,b3)	0.9605	--
Degrees of Freedom	41	--

Goodness of Fit

Statistic	Estimate
F	69.720
p	< 0.001
Adjusted R <sup>2</sup>	0.8593
AIC	182.521

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.24	0.26
Lower bound	0.11	0.12
Upper bound	0.29	0.31
Standard Error	--	--

## APPENDIX E

### EXPERIMENT 3

Test Material 1: Jasper County High Lead Smelter

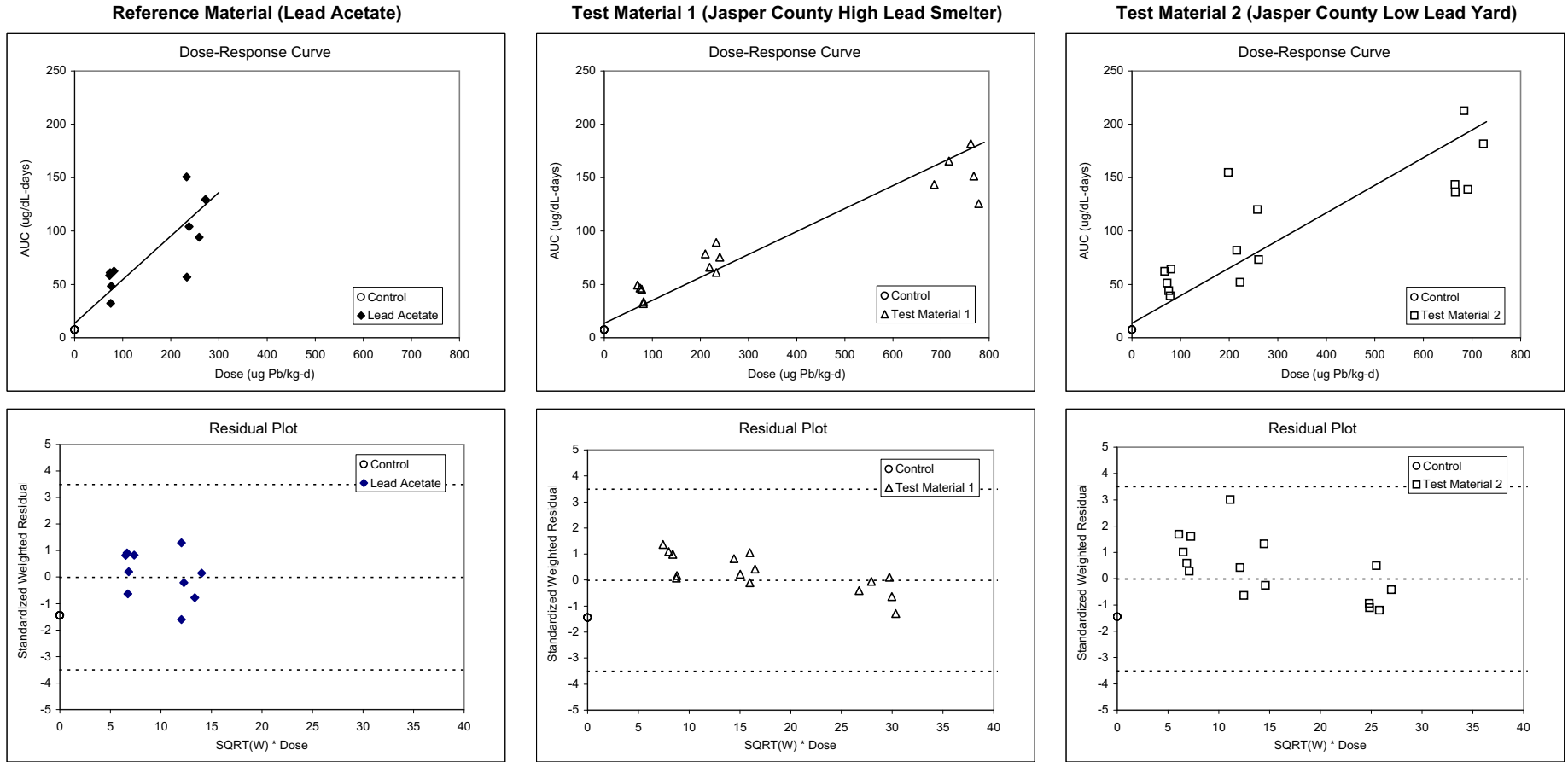
Test Material 2: Jasper County Low Lead Yard

- Figure 1a Blood AUC - Linear Model
- Figure 1b Blood AUC - Exponential Model
- Figure 1c Blood AUC - Michaelis-Menton Model
- Figure 1d Blood AUC - Power Model
  
- Figure 2a Liver - Linear Model (All Data)
- Figure 2a Liver - Linear Model (Outlier Excluded)
- Figure 2b Liver - Exponential Model
- Figure 2c Liver - Michaelis-Menton Model
- Figure 2d Liver - Power Model
  
- Figure 3a Kidney - Linear Model
- Figure 3b Kidney - Exponential Model
- Figure 3c Kidney - Michaelis-Menton Model
- Figure 3d Kidney - Power Model
  
- Figure 4a Femur - Linear Model
- Figure 4b Femur - Exponential Model
- Figure 4c Femur - Michaelis-Menton Model
- Figure 4d Femur - Power Model

APPENDIX E

Figure 1a - All Data

Phase II Experiment 3: Blood AUC  
 Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.35E+01	2.71E+00
b1	4.09E-01	5.70E-02
b2	2.15E-01	2.44E-02
b3	2.59E-01	2.77E-02
Covariance (c1,c2)	0.0086	--
Covariance (c1,c3)	0.0740	--
Degrees of Freedom	38	--

Goodness of Fit

Statistic	Estimate
F	62.590
p	< 0.001
Adjusted R <sup>2</sup>	0.8184
AIC	428.514

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.53	0.63
Lower bound	0.39	0.48
Upper bound	0.72	0.86
Standard Error	0.094*	0.107*

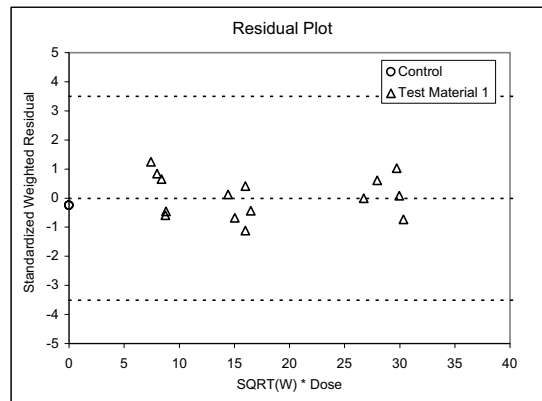
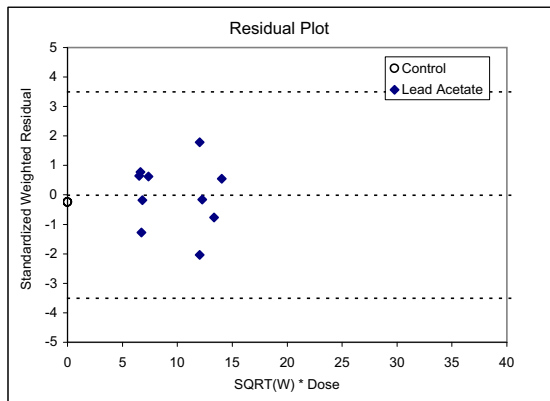
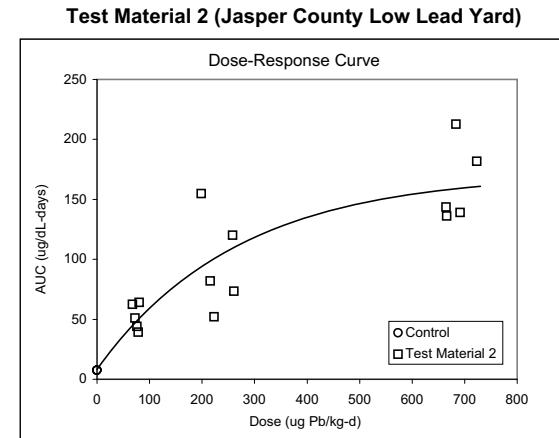
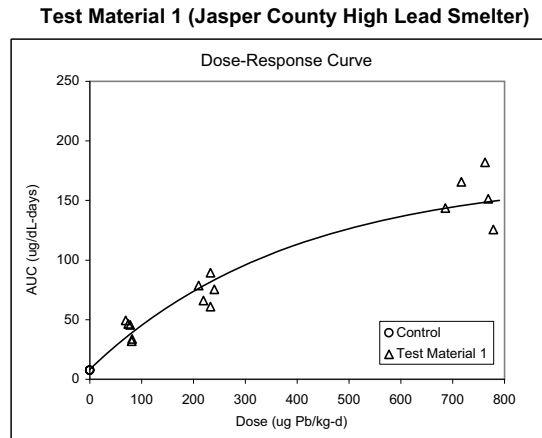
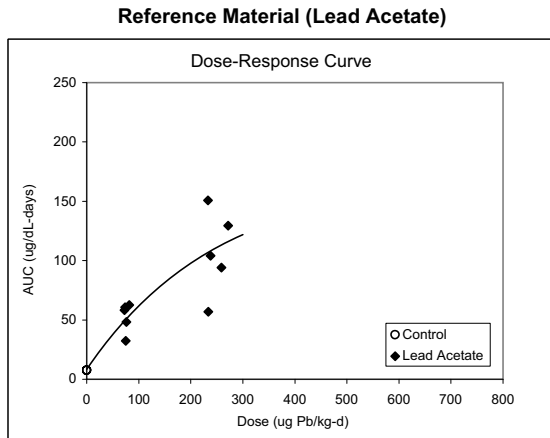
\*  $g \geq 0.05$ , estimate is uncertain

APPENDIX E

Figure 1b - All Data

Phase II Experiment 3: Blood AUC

Exponential Model:  $y = a + b*(1-\exp(-c1*x1)) + b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$



Summary of Fitting

Parameter	Estimate	Standard Error
a	8.27E+00	2.27E+00
b	1.63E+02	1.92E+01
c1	3.97E-03	8.75E-04
c2	2.56E-03	5.70E-04
c3	3.73E-03	8.76E-04
Covariance (c1,c2)	0.6715	--
Covariance (c1,c3)	0.6719	--
Degrees of Freedom	37	--

Goodness of Fit

Statistic	Estimate
F	89.559
p	< 0.001
Adjusted R <sup>2</sup>	0.8963
AIC	377.849

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.65	0.94
Lower bound	0.47	0.66
Upper bound	0.89	1.30
Standard Error	0.116*	0.174*

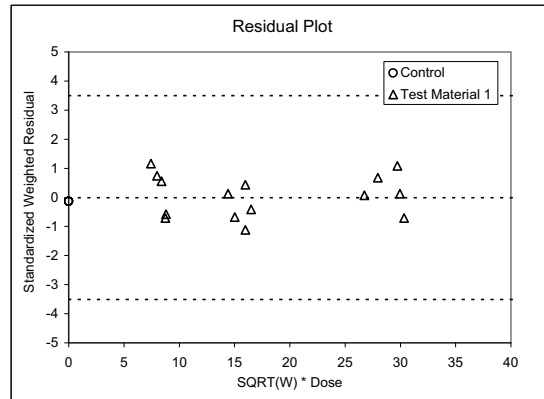
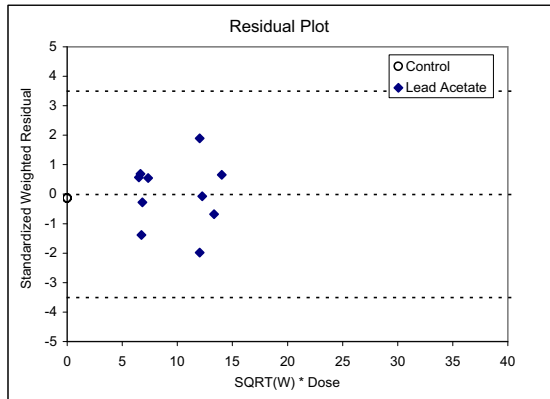
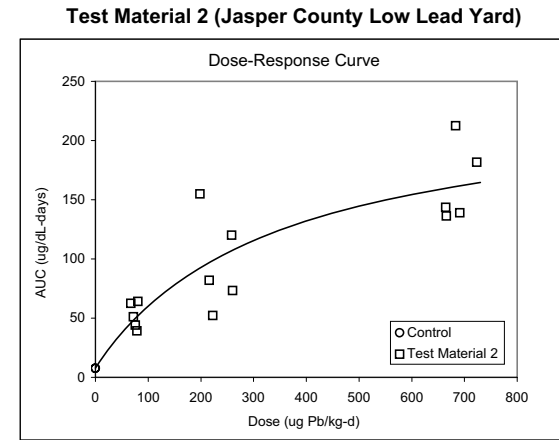
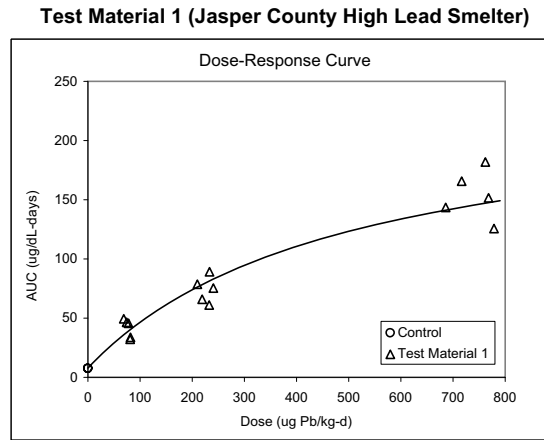
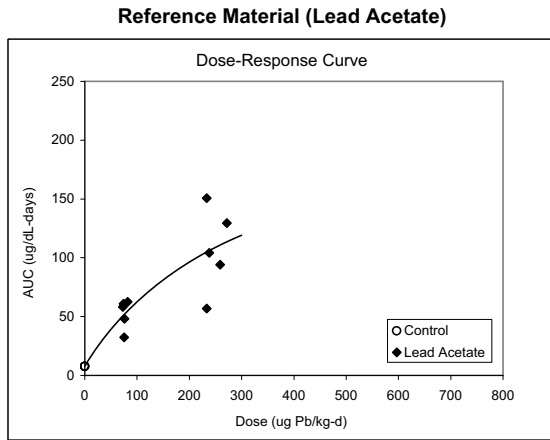
\*  $g \geq 0.05$ , estimate is uncertain

APPENDIX E

Figure 1c - All Data

Phase II Experiment 3: Blood AUC

Michaelis-Menton Model:  $y = a + b \cdot x_1 / (c_1 + x_1) + b \cdot x_2 / (c_2 + x_2) + b \cdot x_3 / (c_3 + x_3)$



Summary of Fitting

Parameter	Estimate	Standard Error
a	7.92E+00	2.27E+00
b	2.29E+02	3.48E+01
c1	3.19E+02	8.73E+01
c2	4.94E+02	1.37E+02
c3	3.40E+02	1.01E+02
Covariance (c1,c2)	0.7827	--
Covariance (c1,c3)	0.7877	--
Degrees of Freedom	37	--

Goodness of Fit

Statistic	Estimate
F	92.316
p	< 0.001
Adjusted R <sup>2</sup>	0.8991
AIC	376.057

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.65	0.94
Lower bound	0.46	0.67
Upper bound	0.91	1.38
Standard Error	0.117*	0.176*

\*  $g \geq 0.05$ , estimate is uncertain



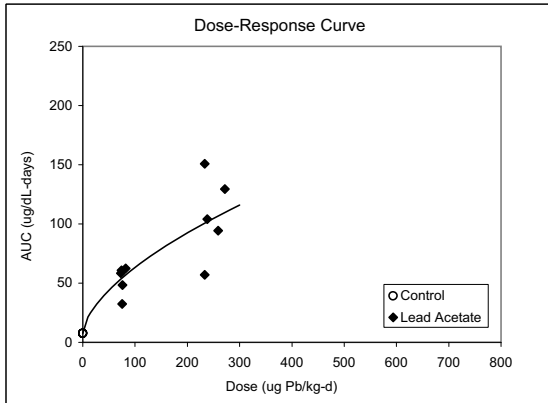
APPENDIX E

Figure 1d - All Data

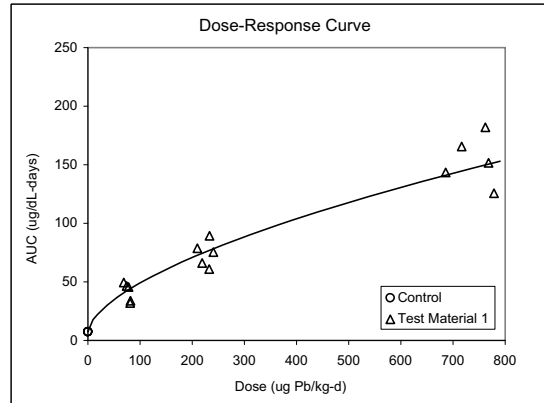
Phase II Experiment 3: Blood AUC

Power Model:  $y = a + b_1 \cdot x_1^c + b_2 \cdot x_2^c + b_3 \cdot x_3^c$

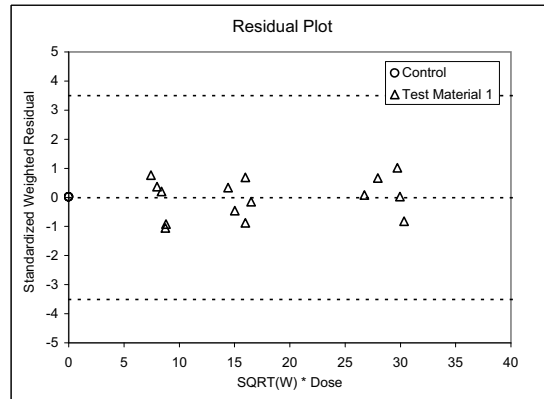
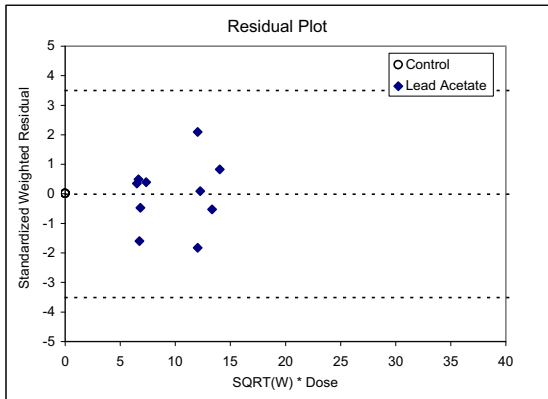
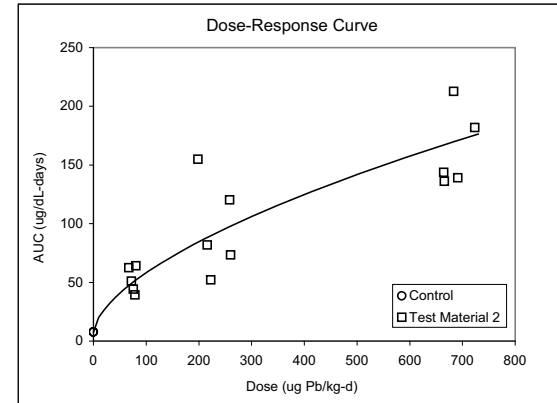
Reference Material (Lead Acetate)



Test Material 1 (Jasper County High Lead Smelter)



Test Material 2 (Jasper County Low Lead Yard)



Summary of Fitting

Parameter	Estimate	Standard Error
a	7.46E+00	2.26E+00
b1	3.43E+00	1.05E+00
b2	2.56E+00	8.65E-01
b3	3.11E+00	1.05E+00
c	6.06E-01	5.57E-02
Covariance (b1,b2)	0.9351	--
Covariance (b1,b3)	0.9366	--
Degrees of Freedom	37	--

Goodness of Fit

Statistic	Estimate
F	94.960
p	< 0.001
Adjusted R <sup>2</sup>	0.9016
AIC	374.429

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.62	0.85
Lower bound	0.38	0.53
Upper bound	0.86	1.19
Standard Error	--	--

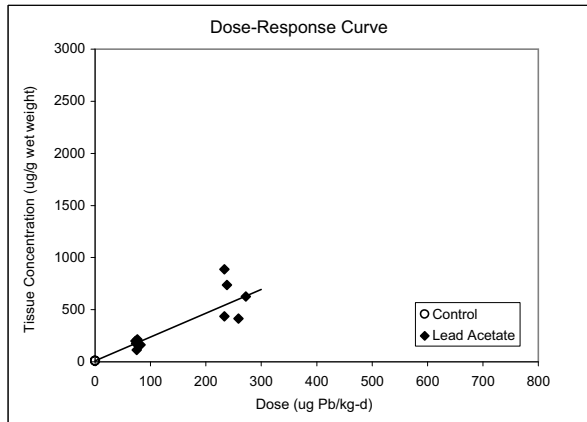
APPENDIX E

Figure 2a - All Data

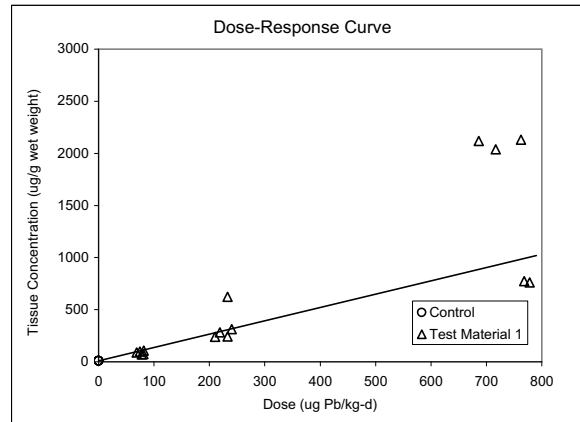
Phase II Experiment 3: Liver

Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$

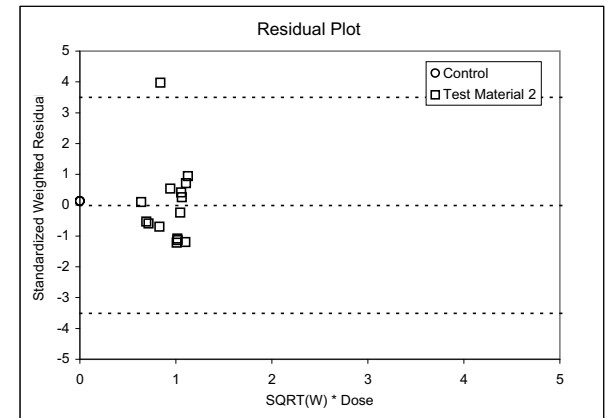
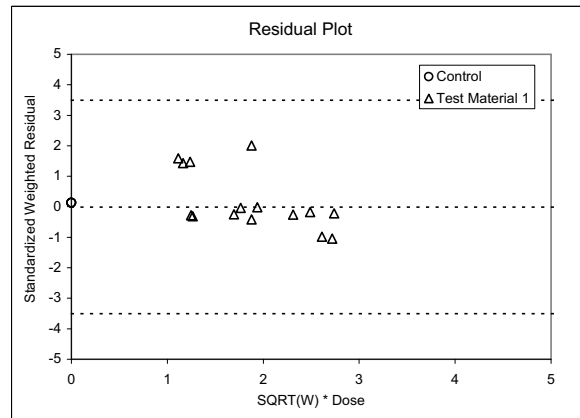
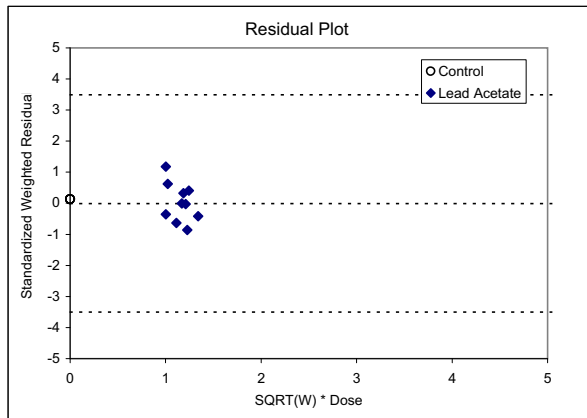
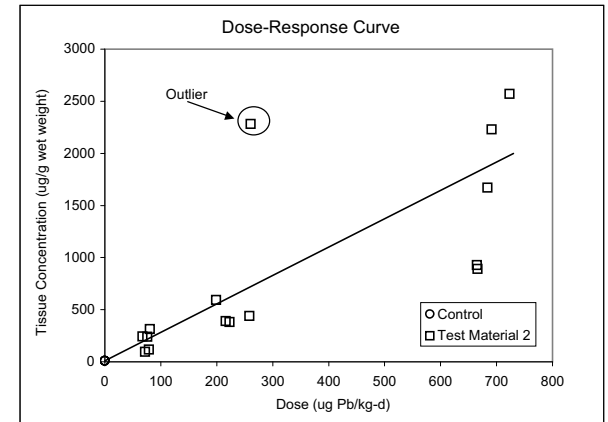
Reference Material (Lead Acetate)



Test Material 1 (Jasper County High Lead Smelter)



Test Material 2 (Jasper County Low Lead Yard)



Summary of Fitting

Parameter	Estimate	Standard Error
a	9.51E+00	2.83E+00
b1	2.28E+00	3.60E-01
b2	1.28E+00	1.76E-01
b3	2.73E+00	3.54E-01
Covariance (c1,c2)	0.0105	--
Covariance (c1,c3)	0.0039	--
Degrees of Freedom	38	--

Goodness of Fit

Statistic	Estimate
F	50.038
p	< 0.001
Adjusted R <sup>2</sup>	0.7820
AIC	562.298

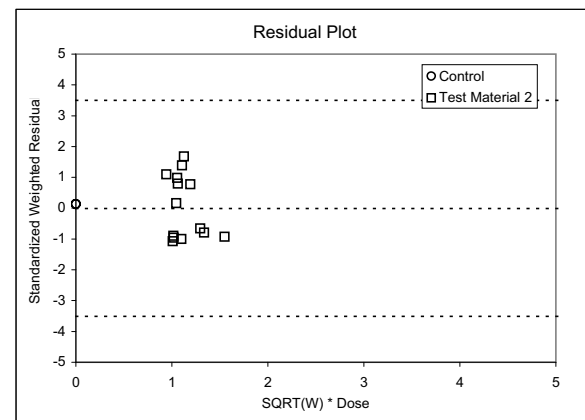
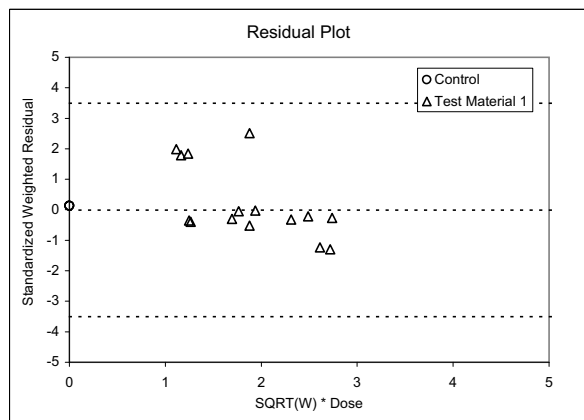
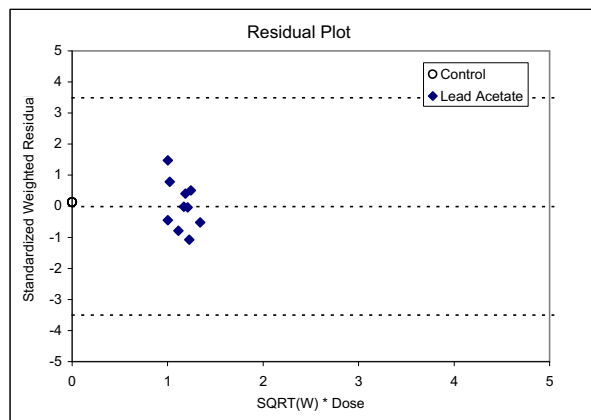
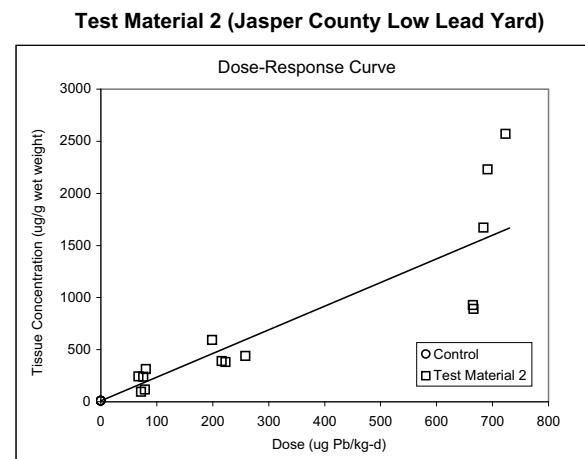
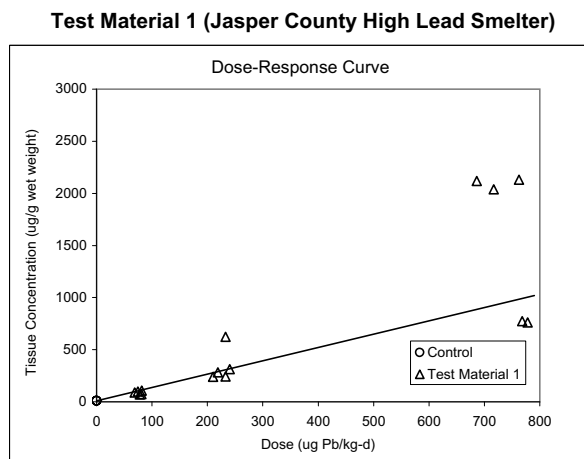
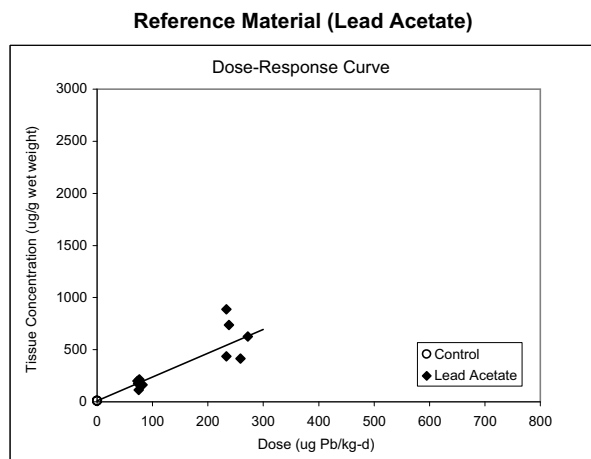
RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.56	1.20
Lower bound	0.40	0.85
Upper bound	0.81	1.73
Standard Error	0.117*	0.245*

\*  $g \geq 0.05$ , estimate is uncertain

APPENDIX E

**Figure 2a - Outlier Excluded**  
**Phase II Experiment 3: Liver**  
**Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$**



**Summary of Fitting**

Parameter	Estimate	Standard Error
a	9.59E+00	2.27E+00
b1	2.28E+00	2.90E-01
b2	1.28E+00	1.41E-01
b3	2.27E+00	2.47E-01
Covariance (c1,c2)	0.0105	--
Covariance (c1,c3)	0.0041	--
Degrees of Freedom	37	--

**Goodness of Fit**

Statistic	Estimate
F	75.057
p	< 0.001
Adjusted R <sup>2</sup>	0.8474
AIC	519.560

**RBA and Uncertainty**

	Test Material 1	Test Material 2
RBA	0.56	1.00
Lower bound	0.42	0.75
Upper bound	0.75	1.34
Standard Error	0.094	0.167

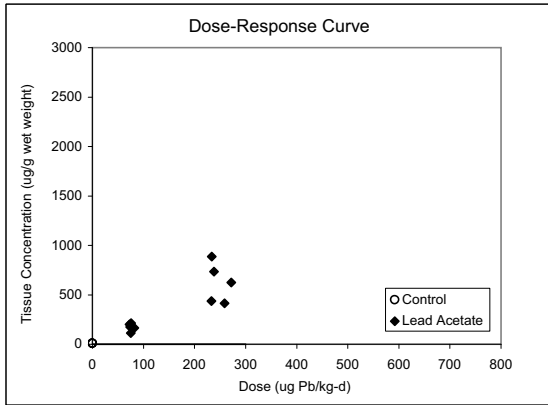
APPENDIX E

Figure 2b - All Data

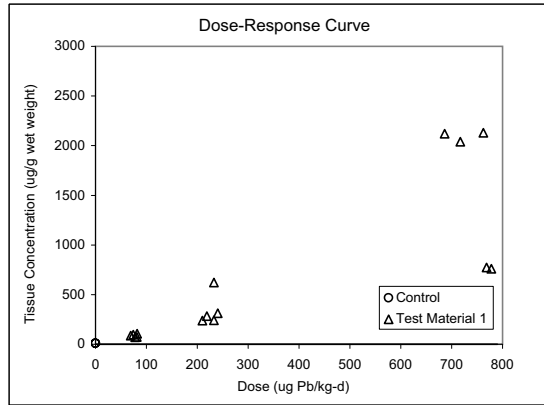
Phase II Experiment 3: Liver

Exponential Model:  $y = a + b*(1-\exp(-c1*x1)) + b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$

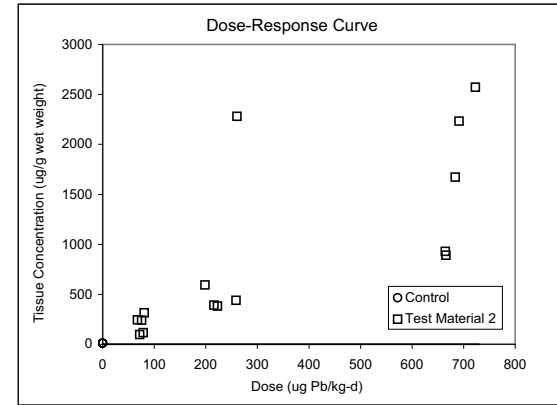
Reference Material (Lead Acetate)



Test Material 1 (Jasper County High Lead Smelter)



Test Material 2 (Jasper County Low Lead Yard)



**NO SOLUTION**

The software could not find a solution,  
or the solution was unstable and/or had unrealistic parameter estimates.

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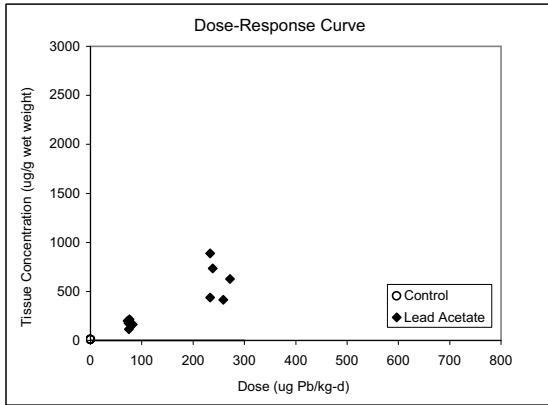
APPENDIX E

Figure 2c - All Data

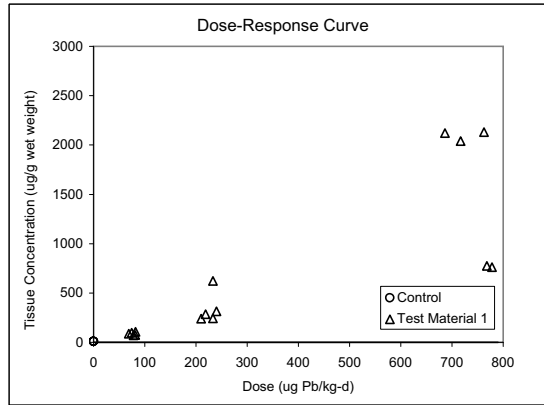
Phase II Experiment 3: Liver

Michaelis-Menton Model:  $y = a + b \cdot x_1 / (c_1 + x_1) + b \cdot x_2 / (c_2 + x_2) + b \cdot x_3 / (c_3 + x_3)$

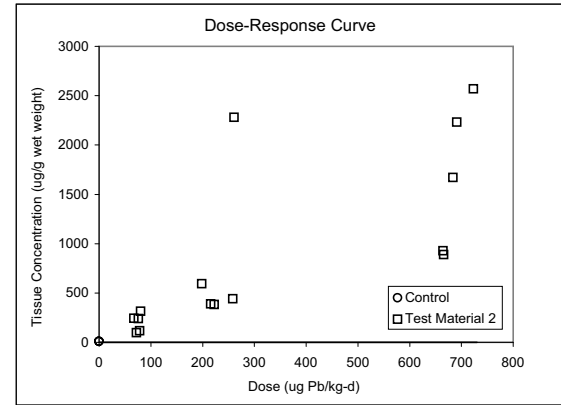
Reference Material (Lead Acetate)



Test Material 1 (Jasper County High Lead Smelter)



Test Material 2 (Jasper County Low Lead Yard)



**NO SOLUTION**

The software could not find a solution,  
or the solution was unstable and/or had unrealistic parameter estimates.

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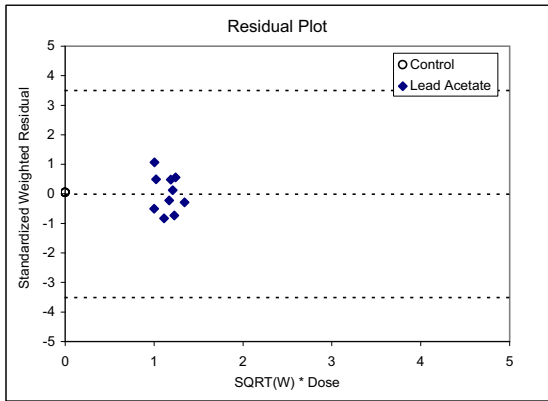
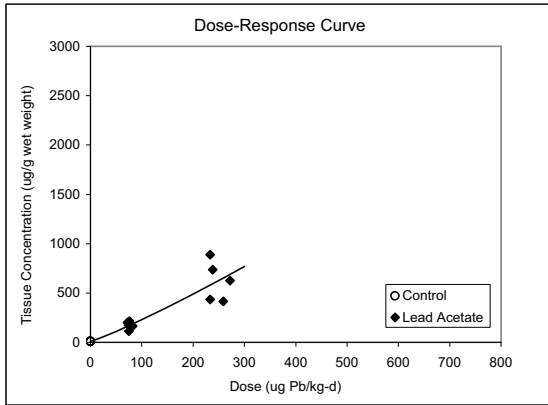
APPENDIX E

Figure 2d - All Data

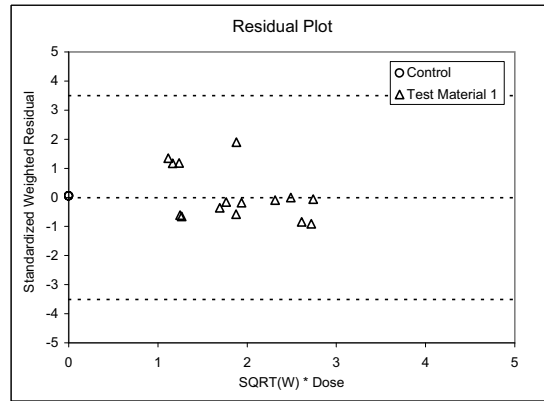
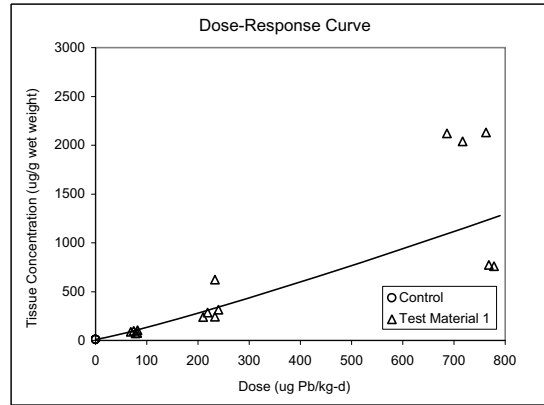
Phase II Experiment 3: Liver

Power Model:  $y = a + b1*x1^c + b2*x2^c + b3*x3^c$

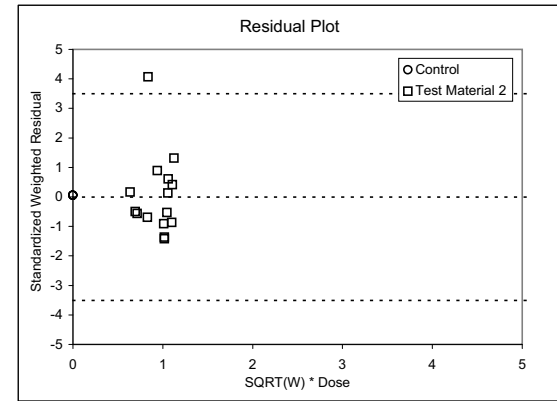
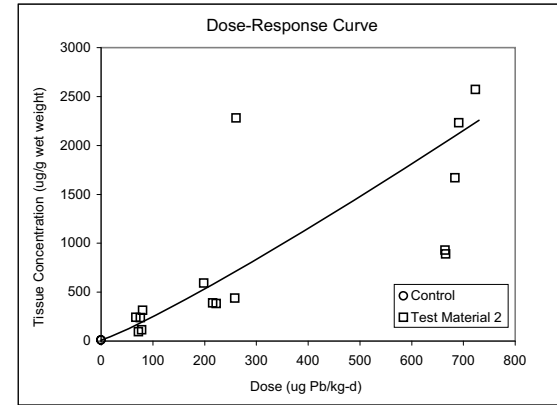
Reference Material (Lead Acetate)



Test Material 1 (Jasper County High Lead Smelter)



Test Material 2 (Jasper County Low Lead Yard)



Summary of Fitting

Parameter	Estimate	Standard Error
a	9.80E+00	2.81E+00
b1	1.23E+00	6.09E-01
b2	6.94E-01	3.51E-01
b3	1.34E+00	7.45E-01
c	1.13E+00	9.49E-02
Covariance (b1,b2)	0.9157	--
Covariance (b1,b3)	0.9221	--
Degrees of Freedom	37	--

Goodness of Fit

Statistic	Estimate
F	38.601
p	< 0.001
Adjusted R <sup>2</sup>	0.7858
AIC	561.470

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.60	1.08
Lower bound	0.32	0.32
Upper bound	1.00	1.62
Standard Error	--	--

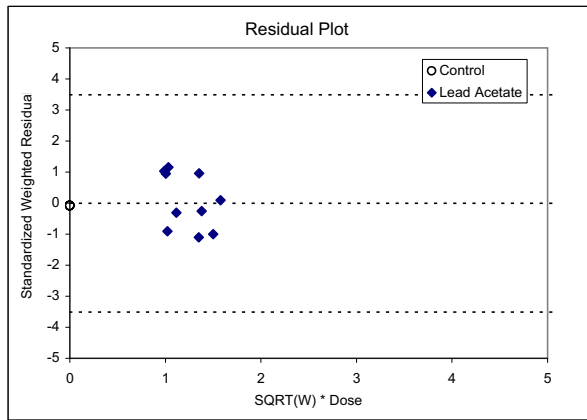
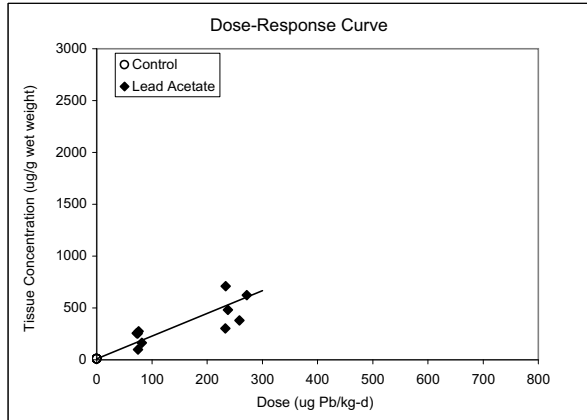
APPENDIX E

Figure 3a - All Data

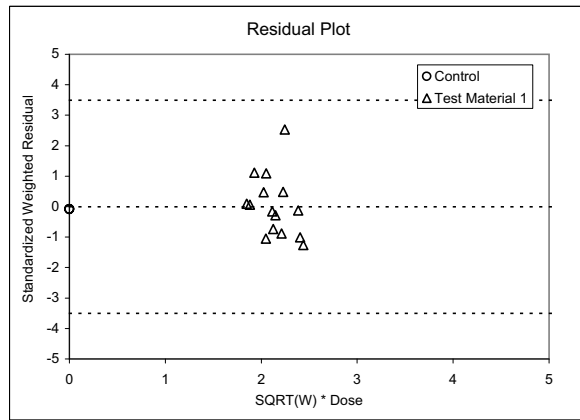
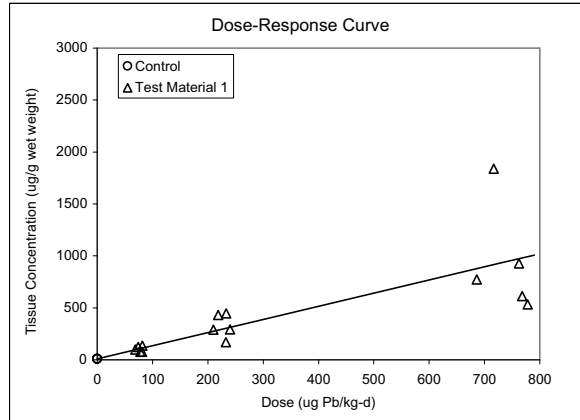
Phase II Experiment 3: Kidney

Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$

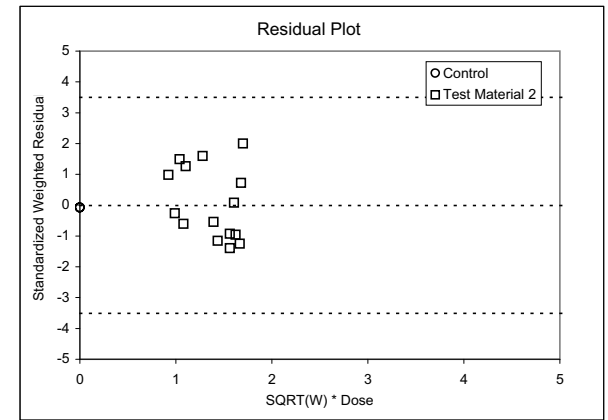
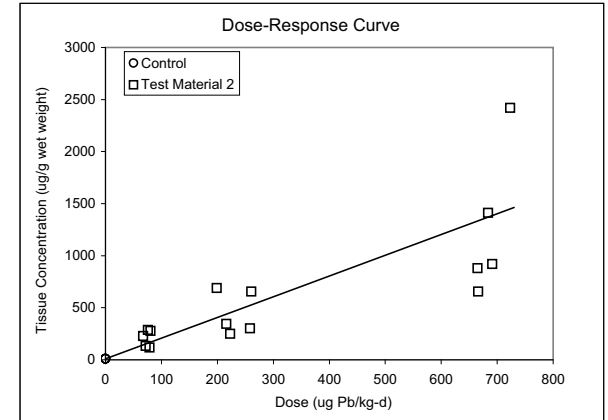
Reference Material (Lead Acetate)



Test Material 1 (Jasper County High Lead Smelter)



Test Material 2 (Jasper County Low Lead Yard)



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.04E+01	3.14E+00
b1	2.19E+00	3.02E-01
b2	1.26E+00	1.44E-01
b3	1.99E+00	2.19E-01
Covariance (c1,c2)	0.0096	--
Covariance (c1,c3)	0.0050	--
Degrees of Freedom	38	--

Goodness of Fit

Statistic	Estimate
F	69.473
p	< 0.001
Adjusted R <sup>2</sup>	0.8336
AIC	533.597

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.58	0.91
Lower bound	0.43	0.68
Upper bound	0.79	1.24
Standard Error	0.103*	0.160*

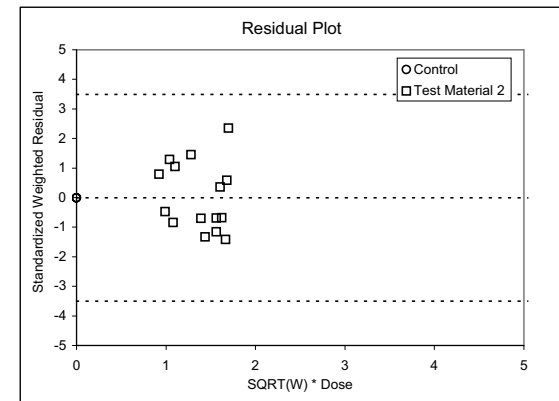
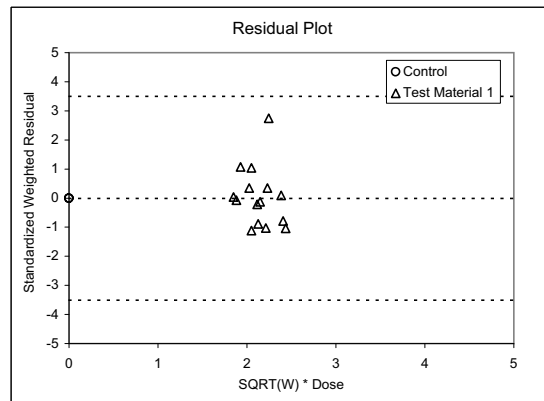
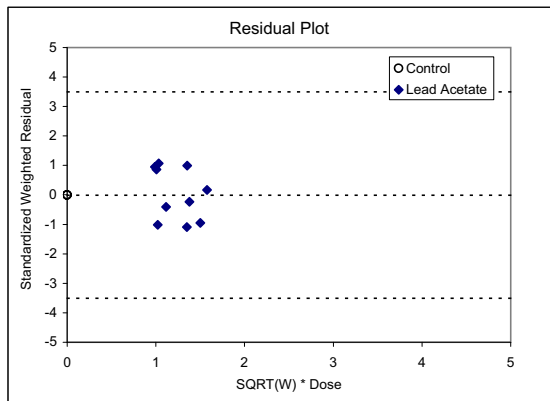
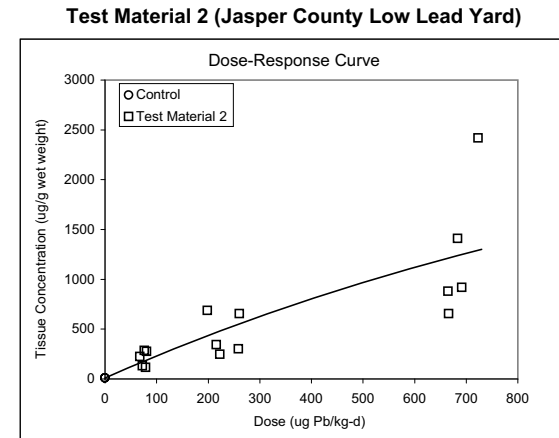
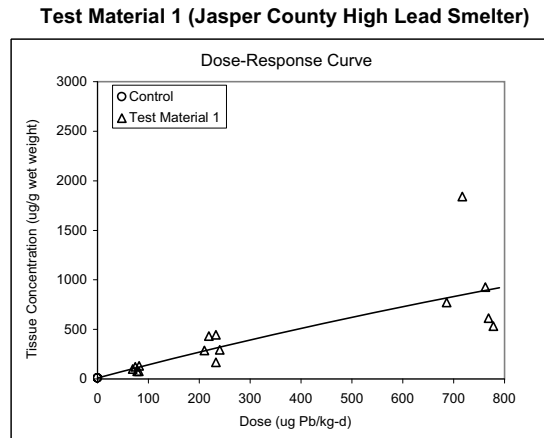
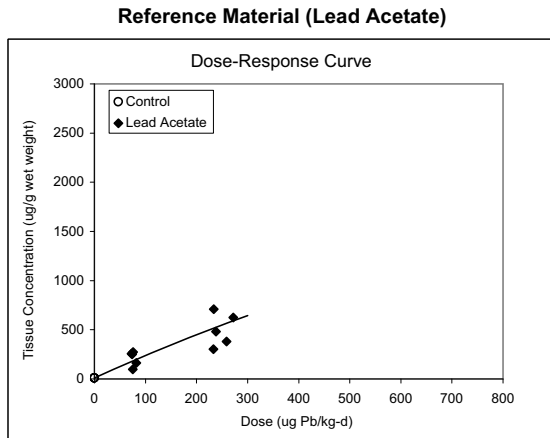
\*  $g \geq 0.05$ , estimate is uncertain

APPENDIX E

Figure 3b - All Data

Phase II Experiment 3: Kidney

Exponential Model:  $y = a + b*(1-\exp(-c1*x1)) + b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.00E+01	3.16E+00
b	3.08E+03	2.88E+03
c1	7.70E-04	7.83E-04
c2	4.44E-04	4.51E-04
c3	7.46E-04	7.98E-04
Covariance (c1,c2)	0.9824	--
Covariance (c1,c3)	0.9828	--
Degrees of Freedom	37	--

Goodness of Fit

Statistic	Estimate
F	52.252
p	< 0.001
Adjusted R <sup>2</sup>	0.8333
AIC	534.270

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.58	0.97
Lower bound	?	?
Upper bound	?	?
Standard Error	0.110*	0.194*

\*  $g \geq 0.05$ , estimate is uncertain

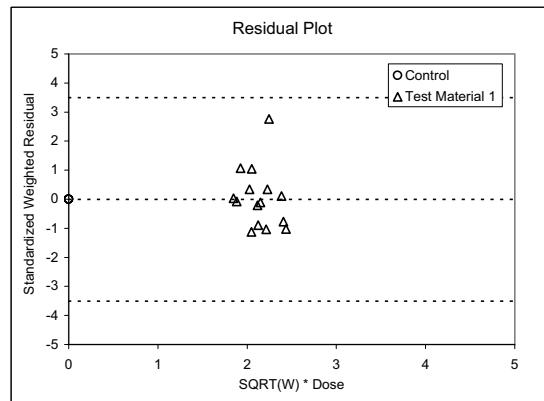
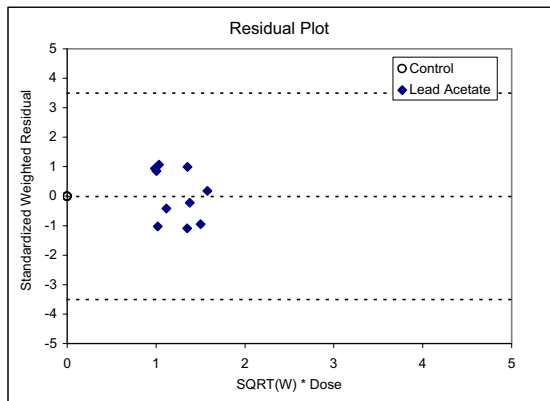
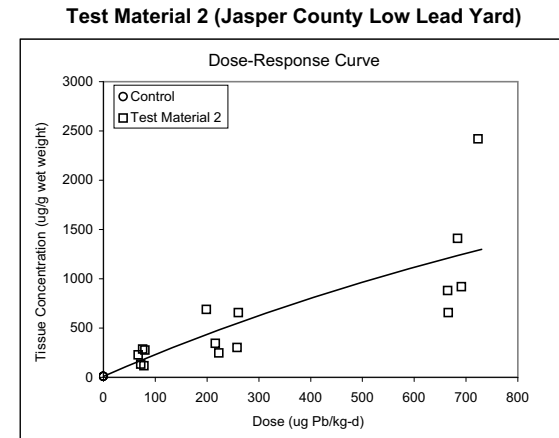
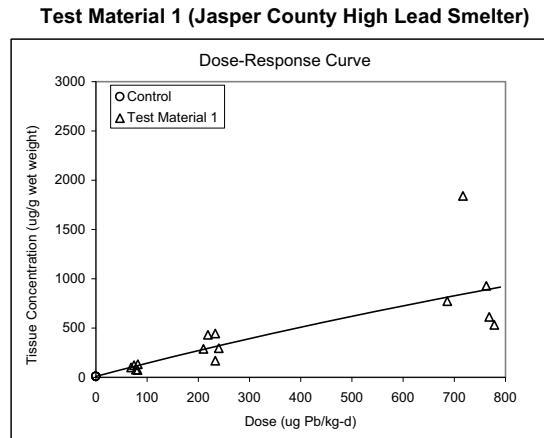
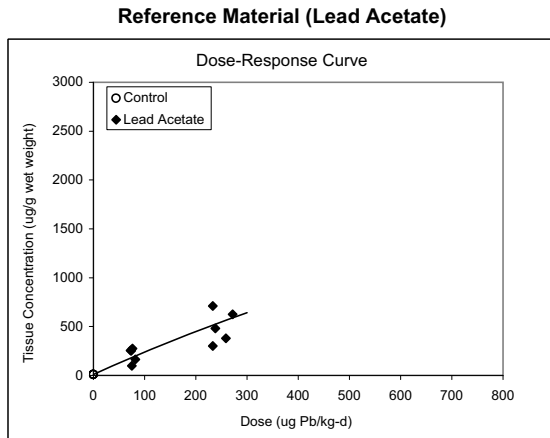


APPENDIX E

Figure 3c - All Data

Phase II Experiment 3: Kidney

Michaelis-Menton Model:  $y = a + b \cdot x_1 / (c_1 + x_1) + b \cdot x_2 / (c_2 + x_2) + b \cdot x_3 / (c_3 + x_3)$



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.00E+01	3.16E+00
b	5.45E+03	5.36E+03
c1	2.29E+03	2.45E+03
c2	3.98E+03	4.24E+03
c3	2.36E+03	2.64E+03
Covariance (c1,c2)	0.9839	--
Covariance (c1,c3)	0.9844	--
Degrees of Freedom	37	--

Goodness of Fit

Statistic	Estimate
F	52.312
p	< 0.001
Adjusted R <sup>2</sup>	0.8335
AIC	534.219

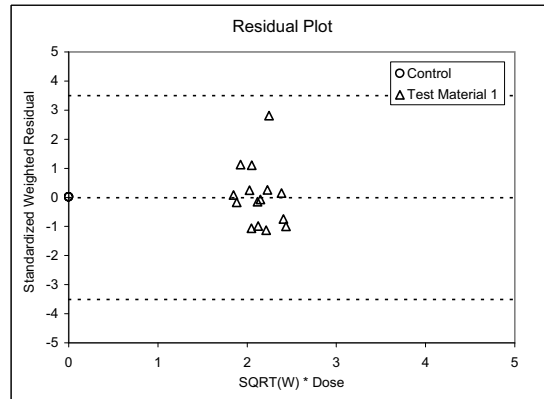
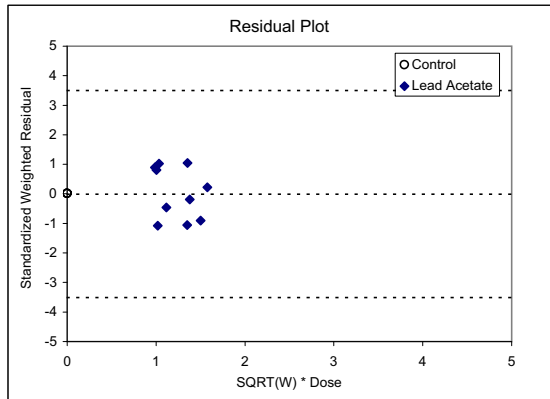
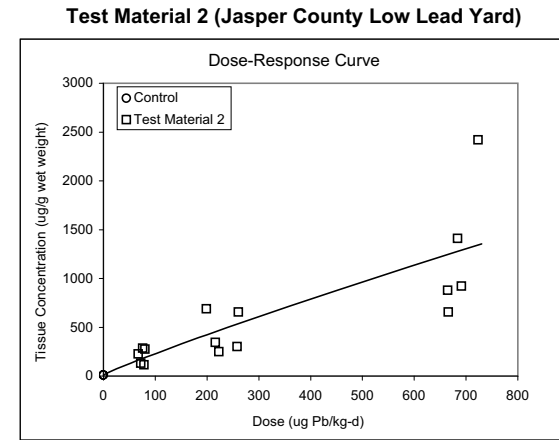
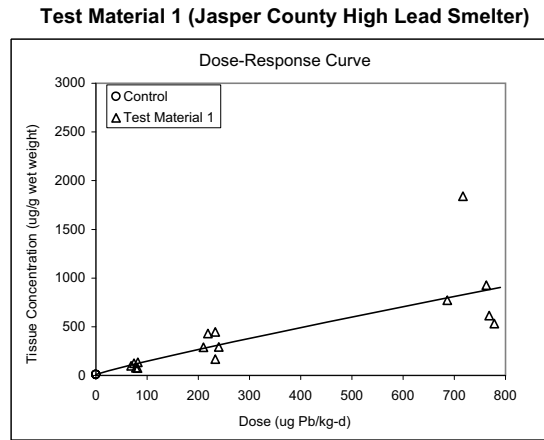
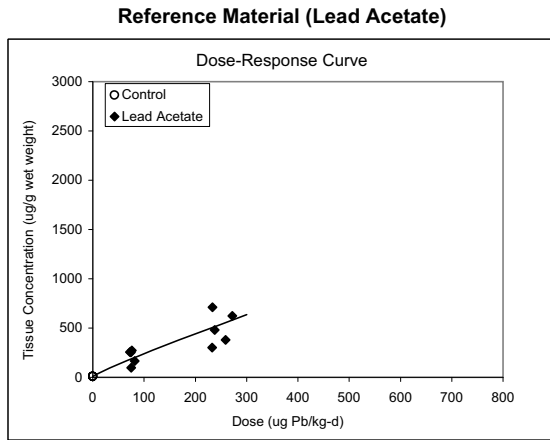
RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.58	0.97
Lower bound	?	?
Upper bound	?	?
Standard Error	0.110*	0.194*

\*  $g \geq 0.05$ , estimate is uncertain

APPENDIX E

**Figure 3d - All Data**  
**Phase II Experiment 3: Kidney**  
**Power Model:  $y = a + b_1 \cdot x_1^c + b_2 \cdot x_2^c + b_3 \cdot x_3^c$**



**Summary of Fitting**

Parameter	Estimate	Standard Error
a	9.94E+00	3.16E+00
b1	3.48E+00	1.53E+00
b2	2.06E+00	9.50E-01
b3	3.34E+00	1.59E+00
c	9.10E-01	8.26E-02
Covariance (b1,b2)	0.9216	--
Covariance (b1,b3)	0.9256	--
Degrees of Freedom	37	--

**Goodness of Fit**

Statistic	Estimate
F	52.565
p	< 0.001
Adjusted R <sup>2</sup>	0.8342
AIC	534.005

**RBA and Uncertainty**

	Test Material 1	Test Material 2
RBA	0.56	0.95
Lower bound	0.31	0.49
Upper bound	0.88	1.44
Standard Error	--	--

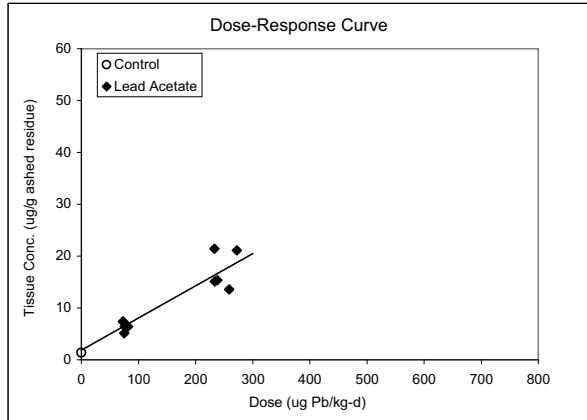
APPENDIX E

Figure 4a - All Data

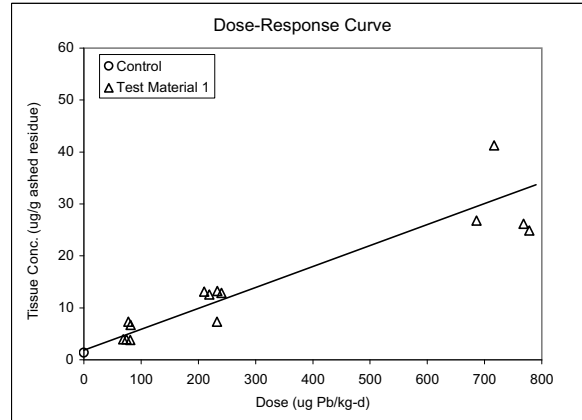
Phase II Experiment 3: Femur

Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$

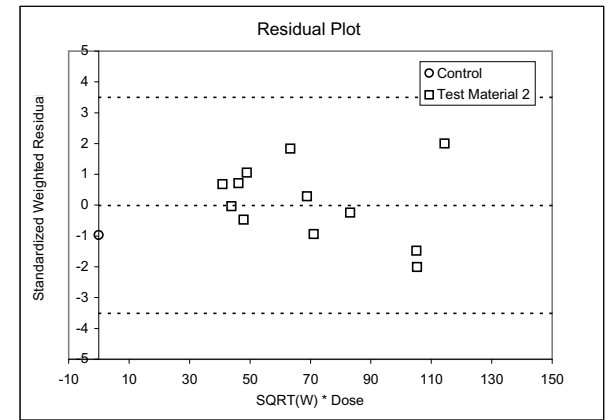
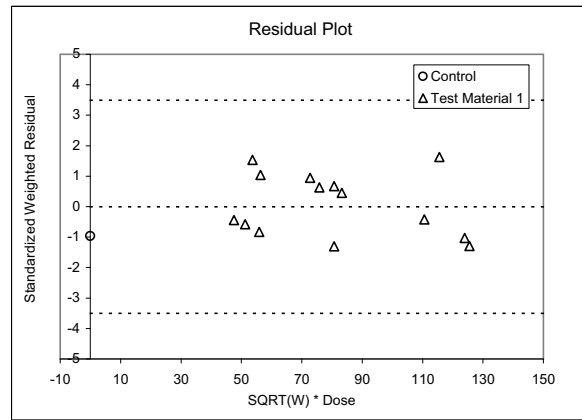
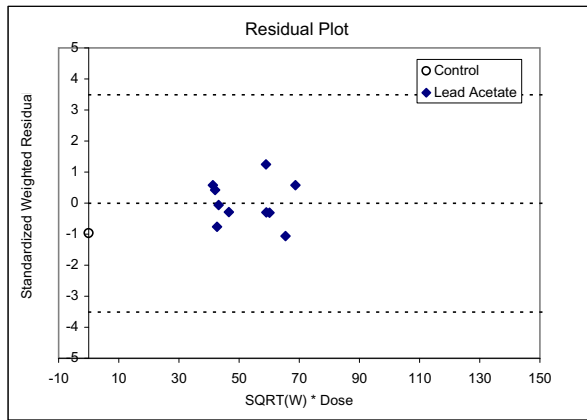
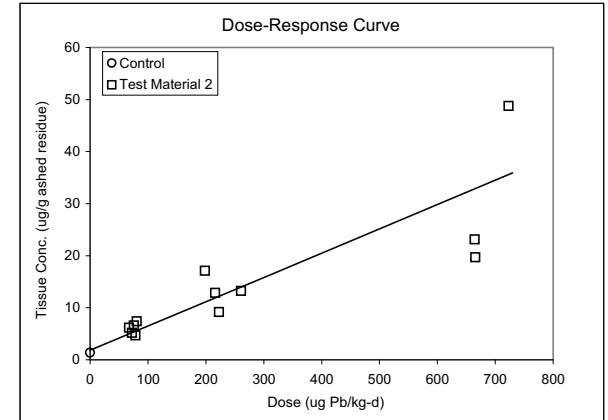
Reference Material (Lead Acetate)



Test Material 1 (Jasper County High Lead Smelter)



Test Material 2 (Jasper County Low Lead Yard)



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.83E+00	3.96E-01
b1	6.21E-02	6.98E-03
b2	4.03E-02	3.75E-03
b3	4.66E-02	4.55E-03
Covariance (c1,c2)	0.1624	--
Covariance (c1,c3)	0.1457	--
Degrees of Freedom	33	--

Goodness of Fit

Statistic	Estimate
F	76.883
p	< 0.001
Adjusted R <sup>2</sup>	0.8635
AIC	187.220

RBA and Uncertainty

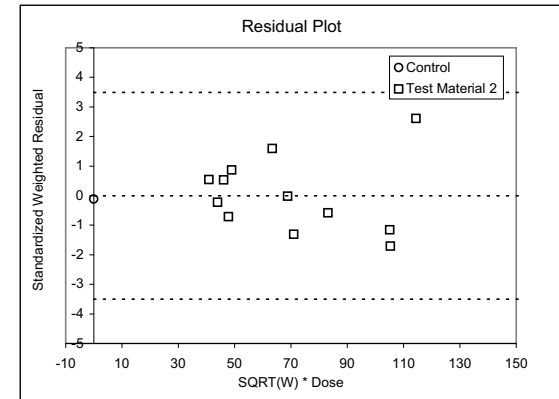
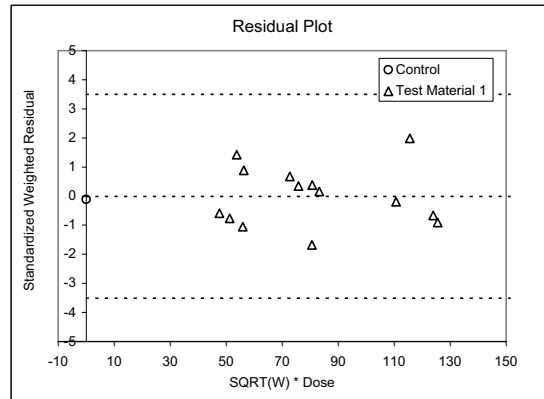
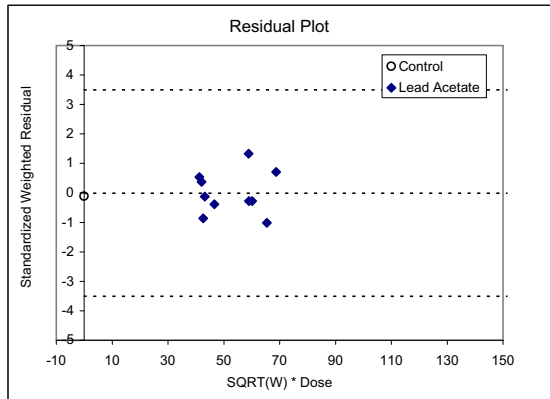
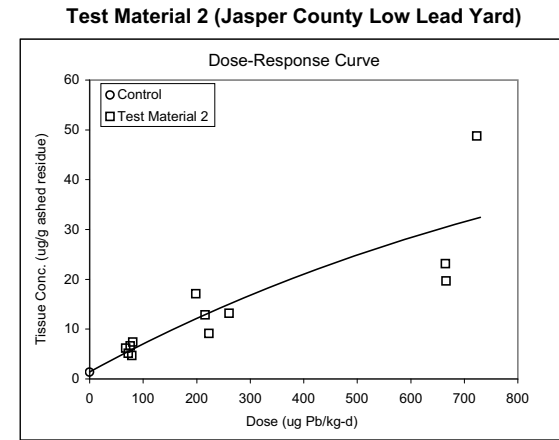
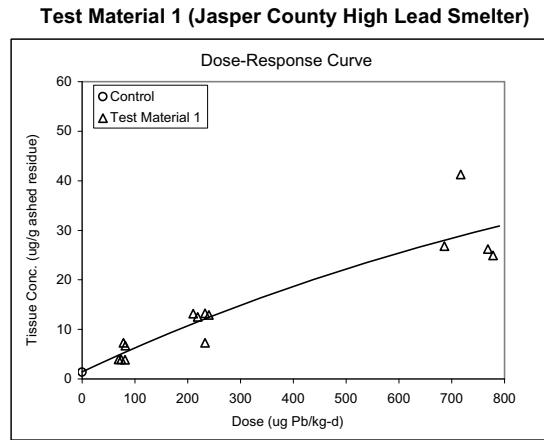
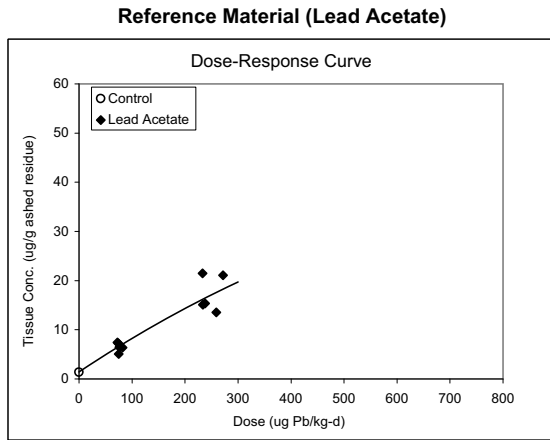
	Test Material 1	Test Material 2
RBA	0.65	0.75
Lower bound	0.52	0.60
Upper bound	0.82	0.95
Standard Error	0.087	0.103

APPENDIX E

Figure 4b - All Data

Phase II Experiment 3: Femur

Exponential Model:  $y = a + b*(1-\exp(-c1*x1))+b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.41E+00	4.67E-01
b	6.20E+01	3.08E+01
c1	1.17E-03	6.92E-04
c2	8.17E-04	5.06E-04
c3	9.52E-04	5.93E-04
Covariance (c1,c2)	0.9723	--
Covariance (c1,c3)	0.9705	--
Degrees of Freedom	32	--

Goodness of Fit

Statistic	Estimate
F	61.268
p	< 0.001
Adjusted R <sup>2</sup>	0.8701
AIC	186.192

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.70	0.81
Lower bound	4.82	7.47
Upper bound	2.28	2.25
Standard Error	0.101*	0.123*

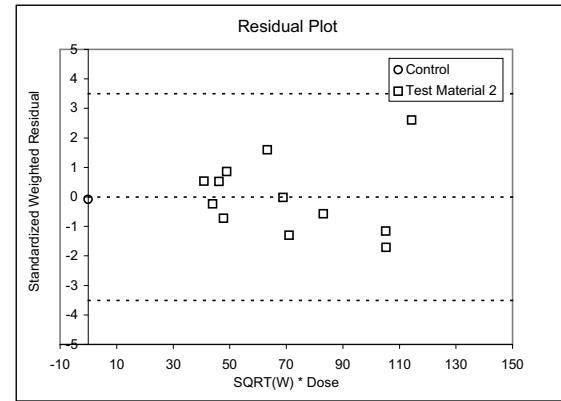
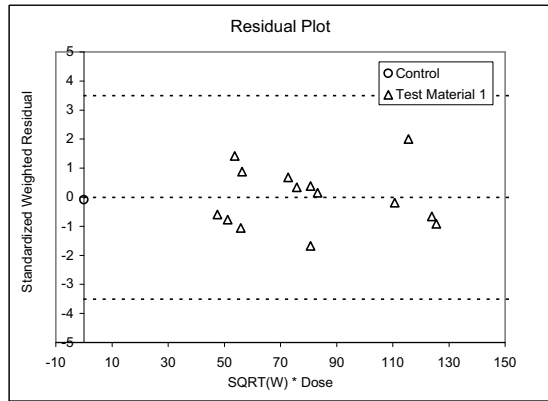
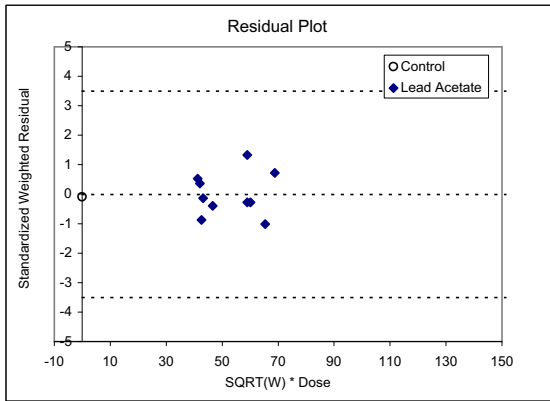
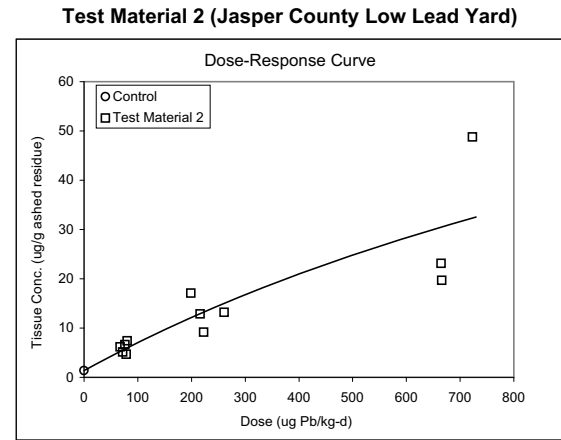
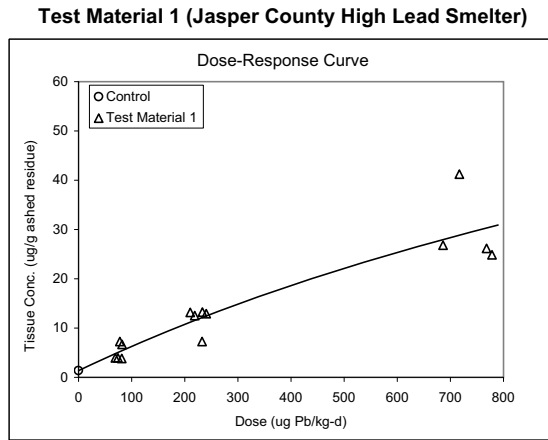
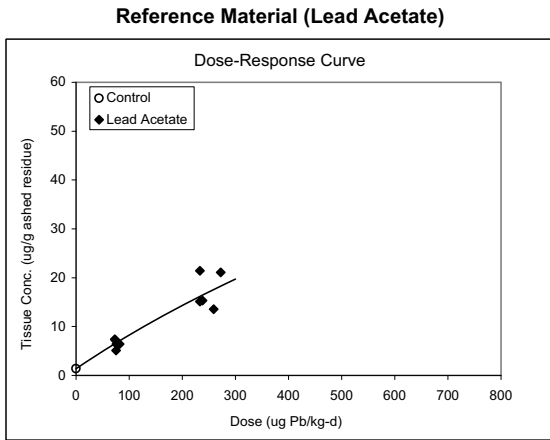
\* g ≥ 0.05, estimate is uncertain

APPENDIX E

Figure 4c - All Data

Phase II Experiment 3: Femur

Michaelis-Menton Model:  $y = a + b \cdot x_1 / (c_1 + x_1) + b \cdot x_2 / (c_2 + x_2) + b \cdot x_3 / (c_3 + x_3)$



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.39E+00	4.72E-01
b	1.09E+02	6.03E+01
c1	1.48E+03	9.77E+02
c2	2.13E+03	1.46E+03
c3	1.82E+03	1.26E+03
Covariance (c1,c2)	0.9775	--
Covariance (c1,c3)	0.9761	--
Degrees of Freedom	32	--

Goodness of Fit

Statistic	Estimate
F	61.359
p	< 0.001
Adjusted R <sup>2</sup>	0.8702
AIC	186.145

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.70	0.81
Lower bound	?	?
Upper bound	?	?
Standard Error	0.101*	0.122*

\* g ≥ 0.05, estimate is uncertain

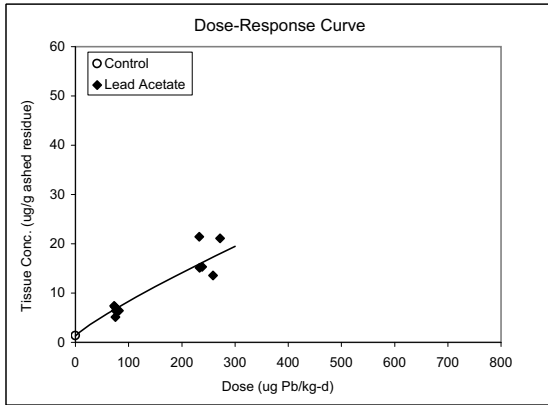
APPENDIX E

Figure 4d - All Data

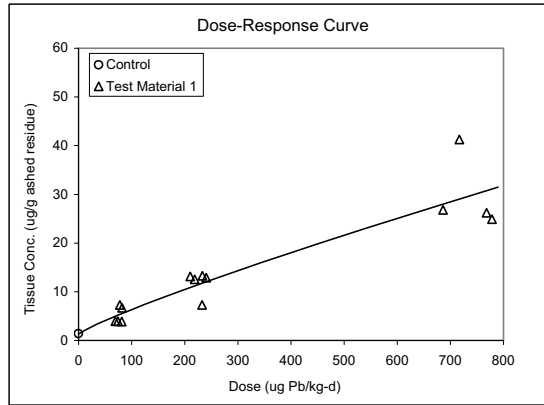
Phase II Experiment 3: Femur

Power Model:  $y = a + b1*x1^c + b2*x2^c + b3*x3^c$

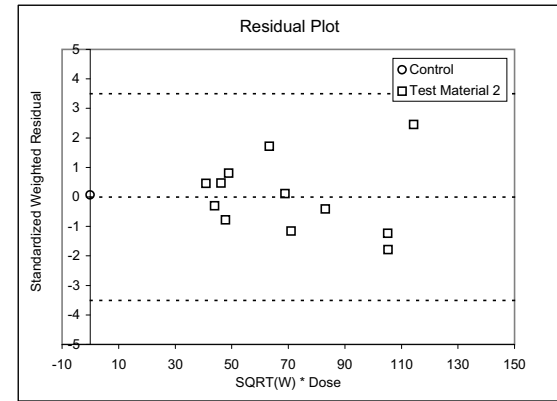
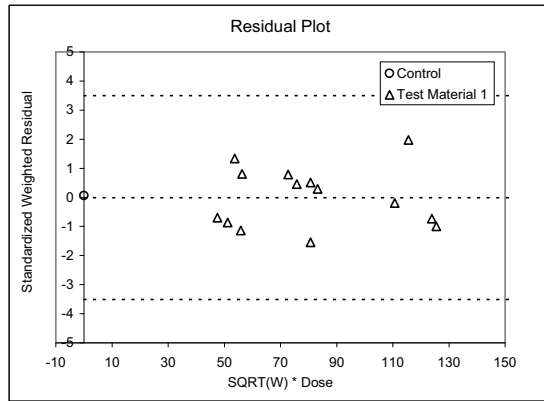
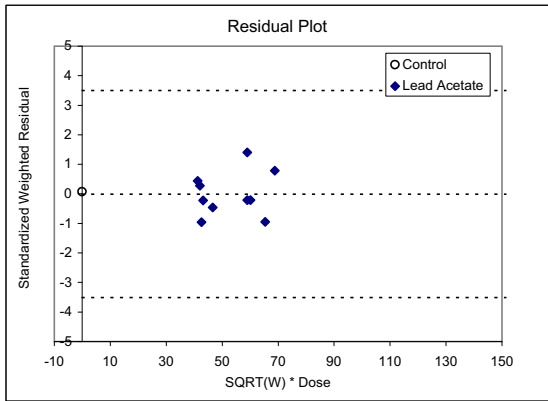
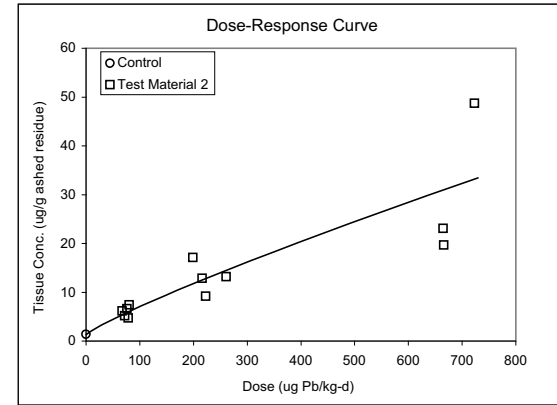
Reference Material (Lead Acetate)



Test Material 1 (Jasper County High Lead Smelter)



Test Material 2 (Jasper County Low Lead Yard)



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.32E+00	4.98E-01
b1	1.29E-01	5.45E-02
b2	9.26E-02	4.31E-02
b3	1.06E-01	4.84E-02
c	8.67E-01	7.44E-02
Covariance (b1,b2)	0.9601	--
Covariance (b1,b3)	0.9575	--
Degrees of Freedom	32	--

Goodness of Fit

Statistic	Estimate
F	61.446
p	< 0.001
Adjusted R <sup>2</sup>	0.8704
AIC	186.099

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.68	0.79
Lower bound	0.39	0.47
Upper bound	0.89	1.06
Standard Error	--	--

## APPENDIX E

### EXPERIMENT 4

Test Material 1: Murray Smelter Slag  
Test Material 2: Jasper County High Lead Mill

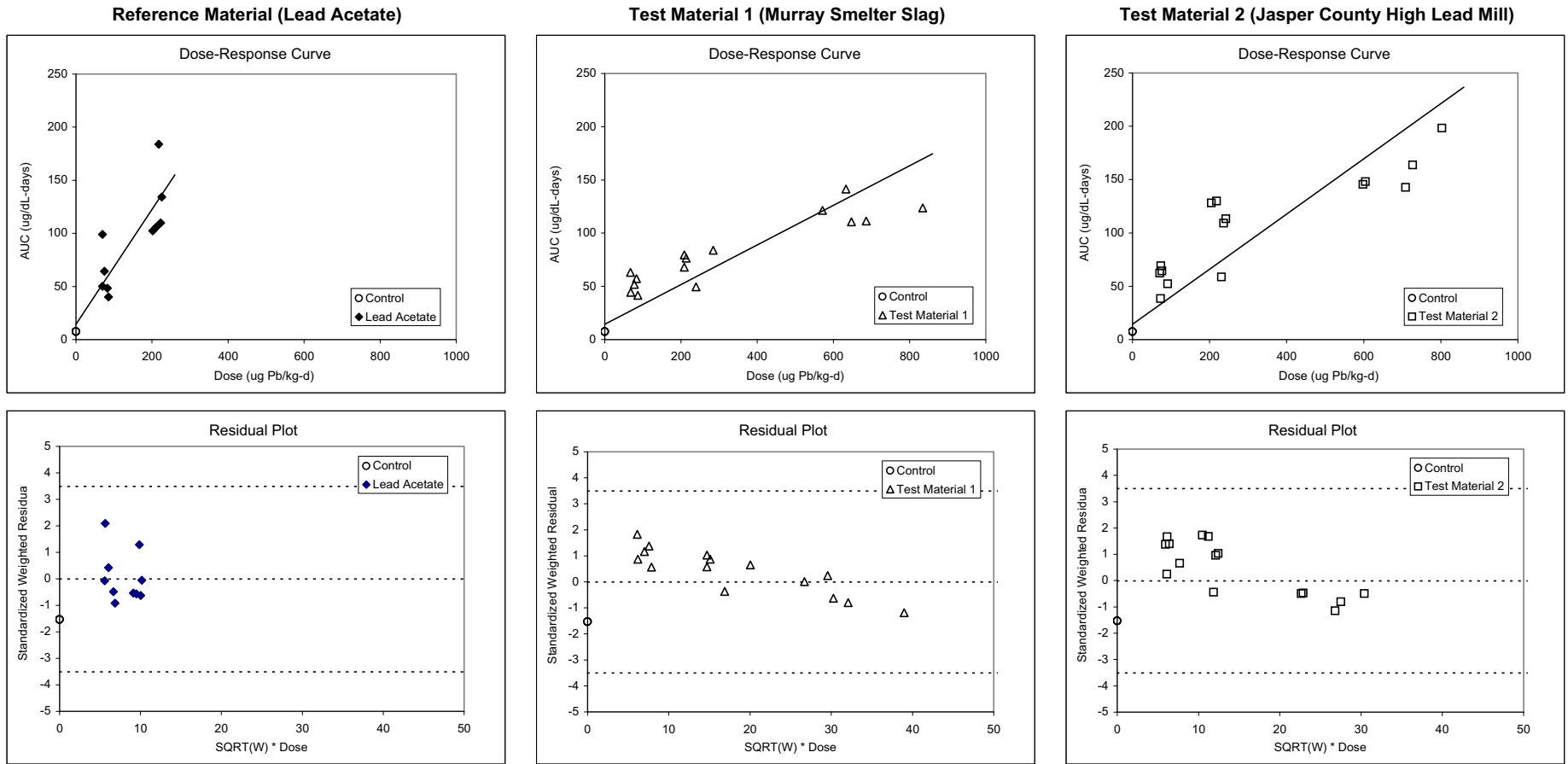
- Figure 1a Blood AUC - Linear Model
- Figure 1b Blood AUC - Exponential Model
- Figure 1c Blood AUC - Michaelis-Menton Model
- Figure 1d Blood AUC - Power Model
  
- Figure 2a Liver - Linear Model
- Figure 2b Liver - Exponential Model
- Figure 2c Liver - Michaelis-Menton Model
- Figure 2d Liver - Power Model
  
- Figure 3a Kidney - Linear Model
- Figure 3b Kidney - Exponential Model
- Figure 3c Kidney - Michaelis-Menton Model
- Figure 3d Kidney - Power Model
  
- Figure 4a Femur - Linear Model
- Figure 4b Femur - Exponential Model
- Figure 4c Femur - Michaelis-Menton Model
- Figure 4d Femur - Power Model

APPENDIX E

Figure 1a - All Data

Phase II Experiment 4: Blood AUC

Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.43E+01	3.04E+00
b1	5.42E-01	7.80E-02
b2	1.86E-01	2.49E-02
b3	2.58E-01	3.04E-02
Covariance (c1,c2)	0.0818	--
Covariance (c1,c3)	0.0672	--
Degrees of Freedom	38	--

Goodness of Fit

Statistic	Estimate
F	51.413
p	< 0.001
Adjusted R <sup>2</sup>	0.7867
AIC	455.674

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.34	0.48
Lower bound	0.25	0.35
Upper bound	0.48	0.66
Standard Error	0.065*	0.086*

\*  $g \geq 0.05$ , estimate is uncertain

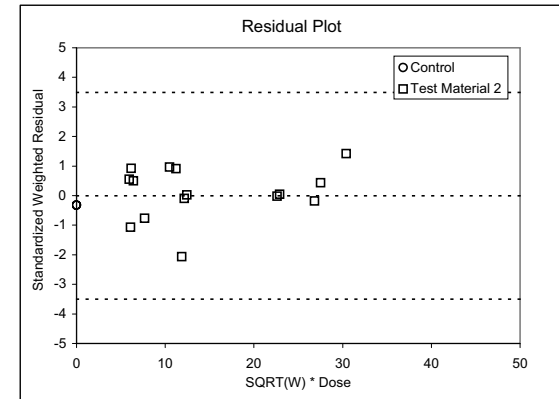
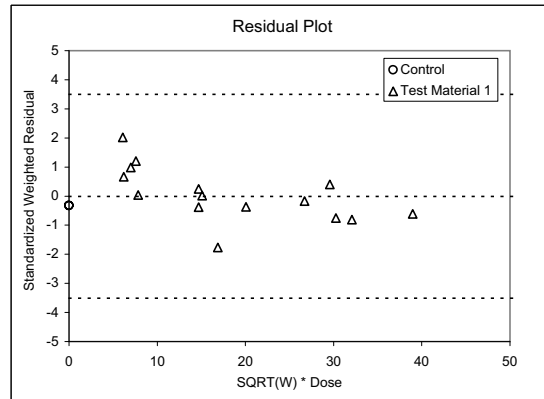
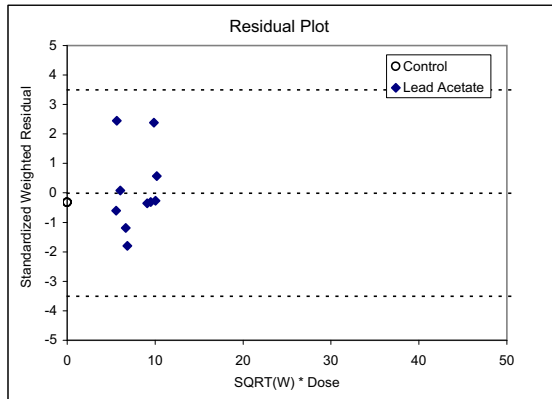
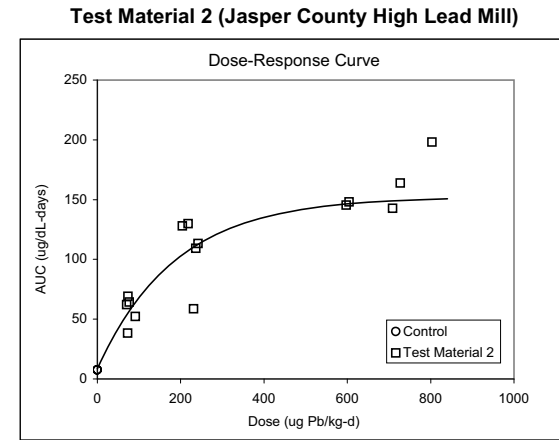
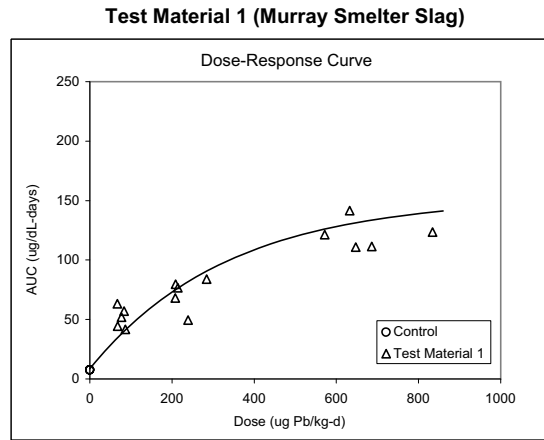
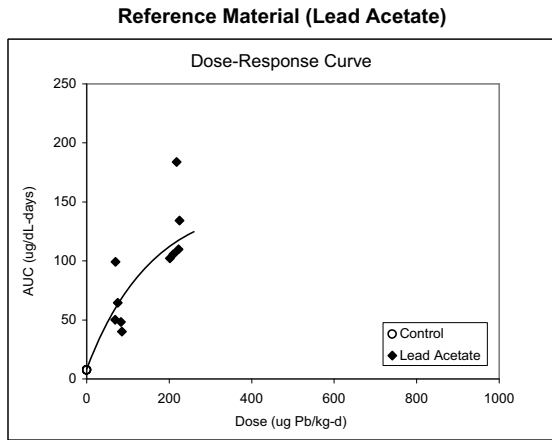


APPENDIX E

Figure 1b - All Data

Phase II Experiment 4: Blood AUC

Exponential Model:  $y = a + b*(1-\exp(-c1*x1)) + b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$



Summary of Fitting

Parameter	Estimate	Standard Error
a	8.52E+00	2.32E+00
b	1.44E+02	1.47E+01
c1	6.36E-03	1.40E-03
c2	2.98E-03	6.51E-04
c3	5.33E-03	1.20E-03
Covariance (c1,c2)	0.5953	--
Covariance (c1,c3)	0.5796	--
Degrees of Freedom	37	--

Goodness of Fit

Statistic	Estimate
F	89.273
p	< 0.001
Adjusted R <sup>2</sup>	0.8960
AIC	382.941

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.47	0.84
Lower bound	0.33	0.58
Upper bound	0.67	1.21
Standard Error	0.092*	0.171*

\*  $g \geq 0.05$ , estimate is uncertain

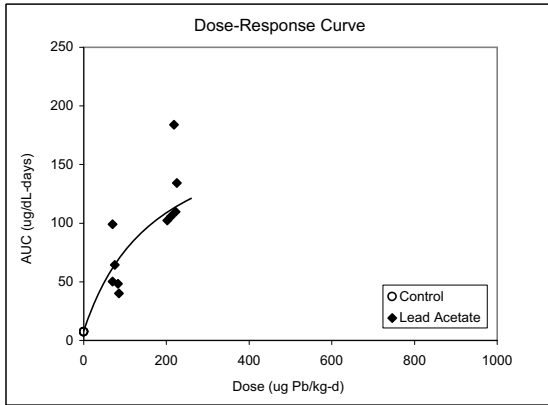
APPENDIX E

Figure 1c - All Data

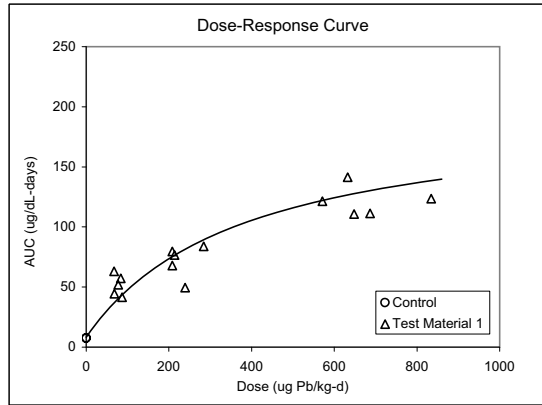
Phase II Experiment 4: Blood AUC

Michaelis-Menton Model:  $y = a + b*x1/(c1+x1) + b*x2/(c2+x2) + b*x3/(c3+x3)$

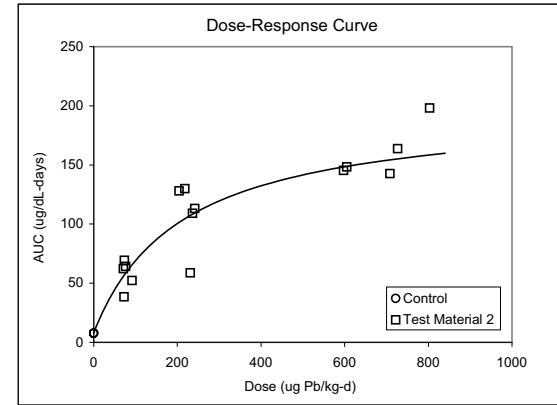
Reference Material (Lead Acetate)



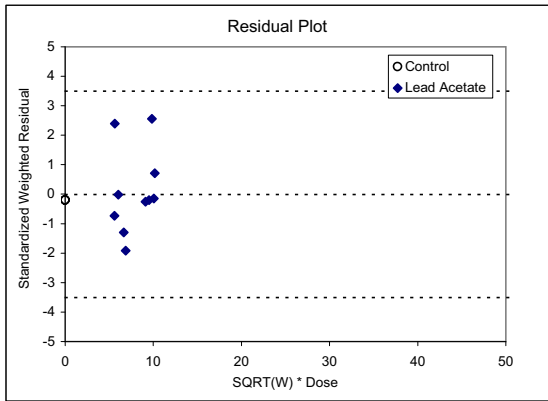
Test Material 1 (Murray Smelter Slag)



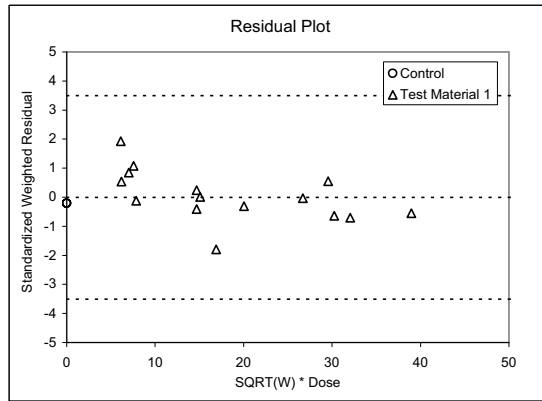
Test Material 2 (Jasper County High Lead Mill)



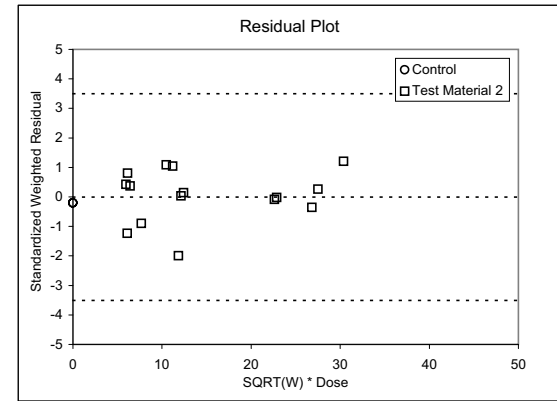
Residual Plot



Residual Plot



Residual Plot



Summary of Fitting

Parameter	Estimate	Standard Error
a	8.13E+00	2.28E+00
b	1.90E+02	2.47E+01
c1	1.77E+02	4.84E+01
c2	3.80E+02	1.03E+02
c3	2.11E+02	6.15E+01
Covariance (c1,c2)	0.7225	--
Covariance (c1,c3)	0.7236	--
Degrees of Freedom	37	--

Goodness of Fit

Statistic	Estimate
F	94.291
p	< 0.001
Adjusted R <sup>2</sup>	0.9010
AIC	379.665

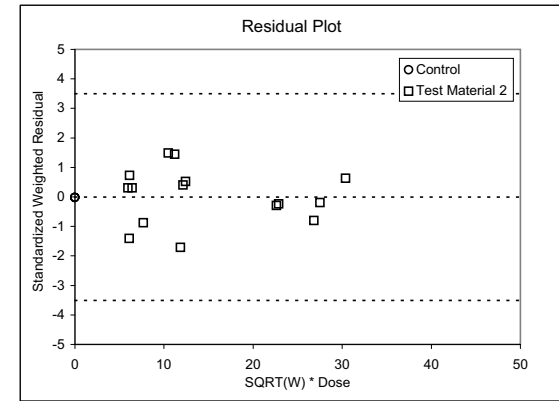
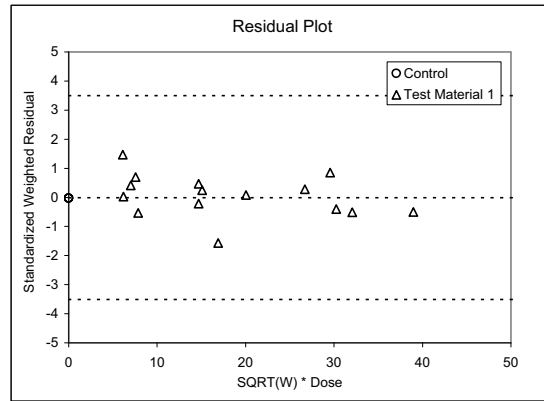
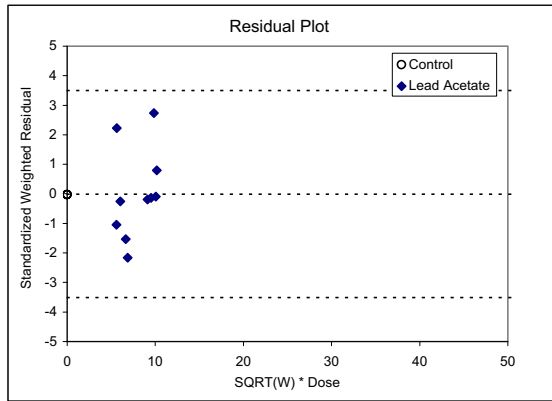
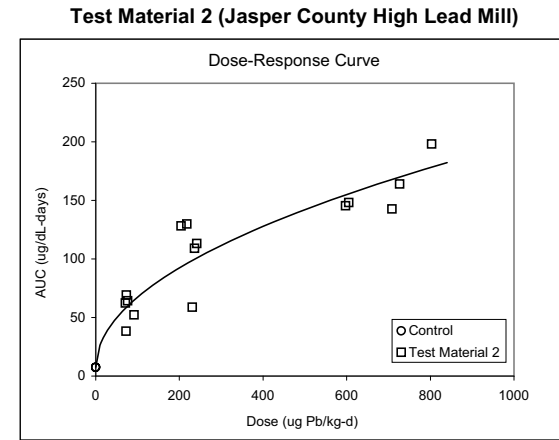
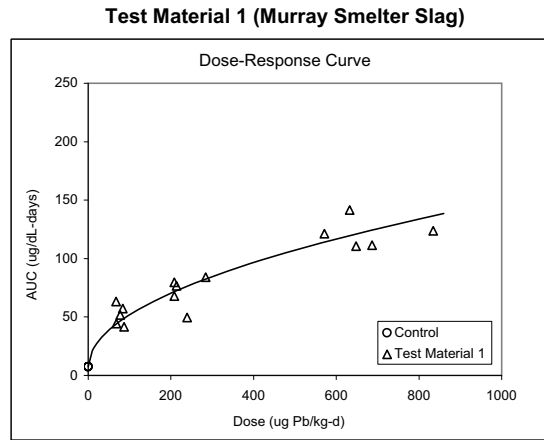
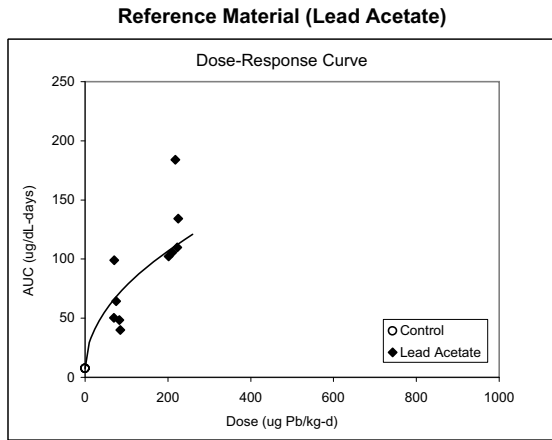
RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.47	0.84
Lower bound	0.32	0.57
Upper bound	0.68	1.28
Standard Error	0.094*	0.177*

\*  $g \geq 0.05$ , estimate is uncertain

APPENDIX E

**Figure 1d - All Data**  
**Phase II Experiment 4: Blood AUC**  
**Power Model:  $y = a + b_1 \cdot x_1^c + b_2 \cdot x_2^c + b_3 \cdot x_3^c$**



**Summary of Fitting**

Parameter	Estimate	Standard Error
a	7.57E+00	2.20E+00
b1	6.88E+00	1.92E+00
b2	4.35E+00	1.41E+00
b3	5.87E+00	1.86E+00
c	5.04E-01	5.34E-02
Covariance (b1,b2)	0.9315	--
Covariance (b1,b3)	0.9341	--
Degrees of Freedom	37	--

**Goodness of Fit**

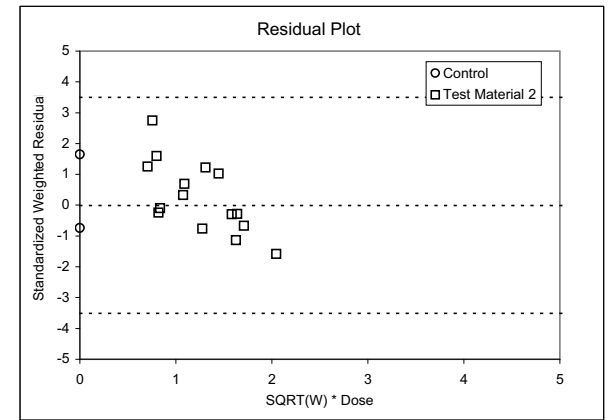
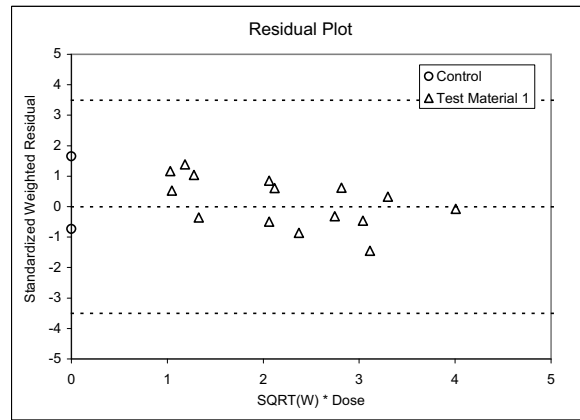
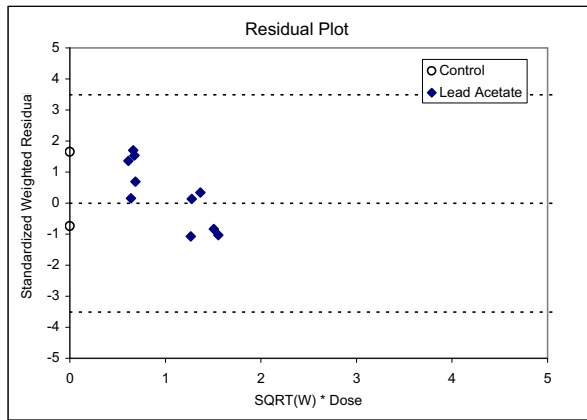
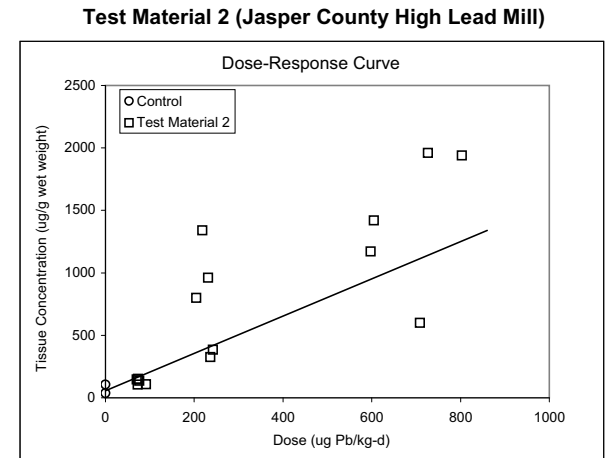
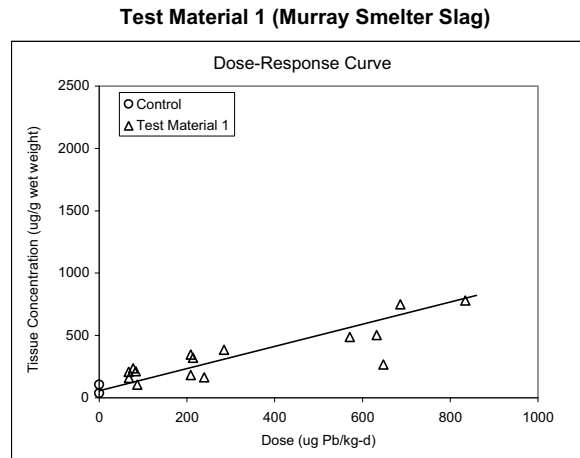
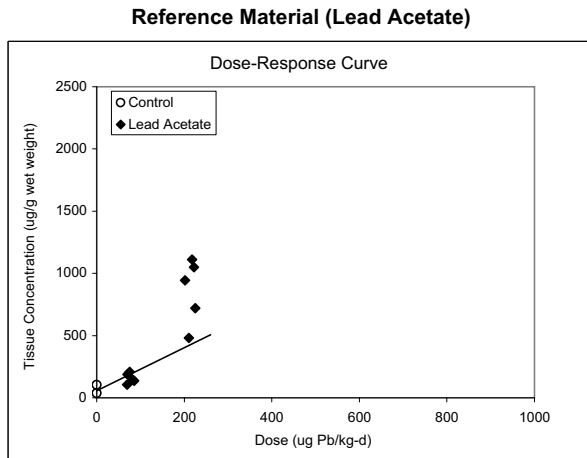
Statistic	Estimate
F	103.784
p	< 0.001
Adjusted R <sup>2</sup>	0.9093
AIC	374.263

**RBA and Uncertainty**

	Test Material 1	Test Material 2
RBA	0.40	0.73
Lower bound	0.23	0.43
Upper bound	0.59	1.06
Standard Error	--	--

APPENDIX E

**Figure 2a - All Data**  
**Phase II Experiment 4: Liver**  
**Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$**



**Summary of Fitting**

Parameter	Estimate	Standard Error
a	5.71E+01	1.77E+01
b1	1.73E+00	4.26E-01
b2	8.89E-01	1.50E-01
b3	1.49E+00	2.95E-01
Covariance (c1,c2)	0.1813	--
Covariance (c1,c3)	0.2399	--
Degrees of Freedom	38	--

**Goodness of Fit**

Statistic	Estimate
F	18.693
p	< 0.001
Adjusted R <sup>2</sup>	0.5642
AIC	558.553

**RBA and Uncertainty**

	Test Material 1	Test Material 2
RBA	0.51	0.86
Lower bound	0.33	0.54
Upper bound	0.88	1.47
Standard Error	0.140*	0.238*

\*  $g \geq 0.05$ , estimate is uncertain

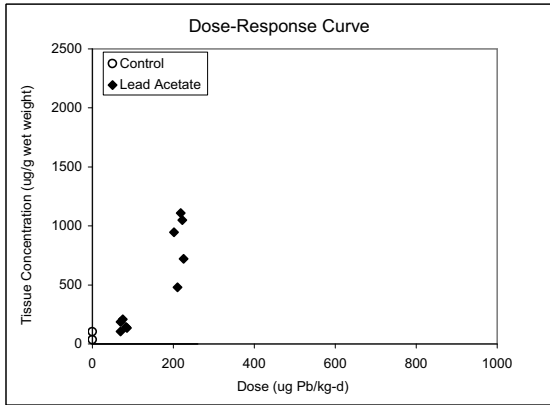
APPENDIX E

Figure 2b - All Data

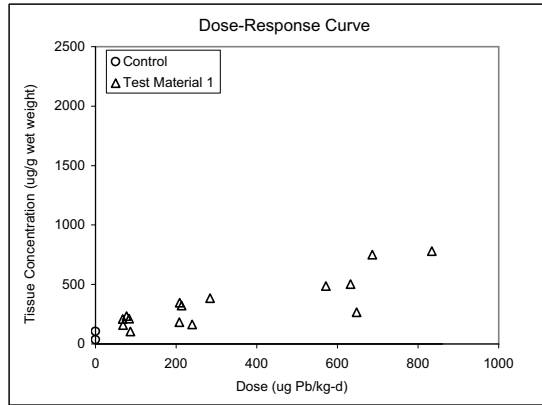
Phase II Experiment 4: Liver

Exponential Model:  $y = a + b*(1-\exp(-c1*x1)) + b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$

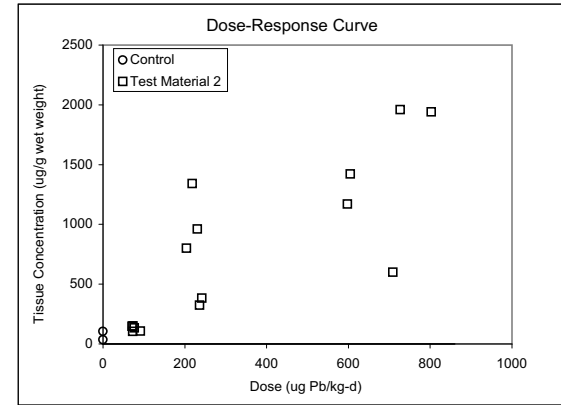
Reference Material (Lead Acetate)



Test Material 1 (Murray Smelter Slag)



Test Material 2 (Jasper County High Lead Mill)



**NO SOLUTION**

The software could not find a solution,  
or the solution was unstable and/or had unrealistic parameter estimates.

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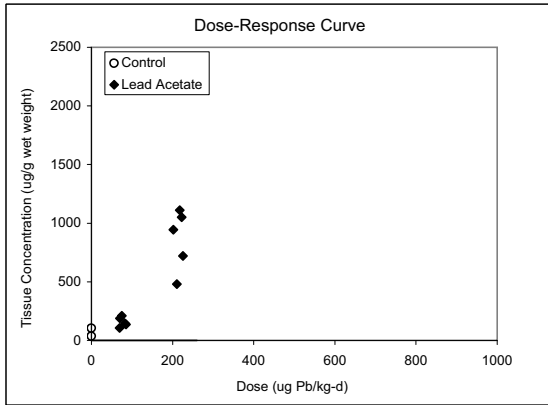
APPENDIX E

Figure 2c - All Data

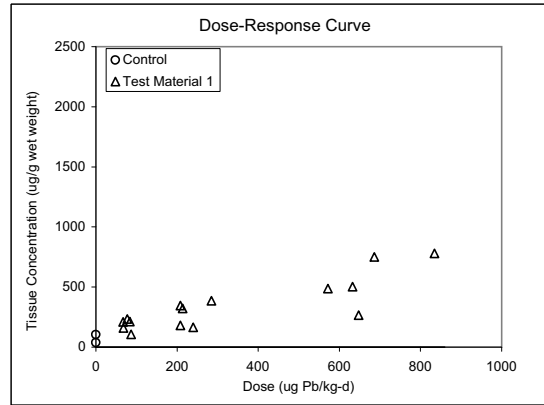
Phase II Experiment 4: Liver

Michaelis-Menton Model:  $y = a + b \cdot x_1 / (c_1 + x_1) + b \cdot x_2 / (c_2 + x_2) + b \cdot x_3 / (c_3 + x_3)$

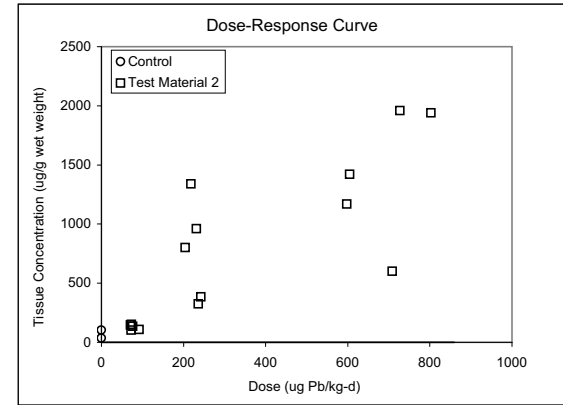
Reference Material (Lead Acetate)



Test Material 1 (Murray Smelter Slag)



Test Material 2 (Jasper County High Lead Mill)



**NO SOLUTION**

The software could not find a solution,  
or the solution was unstable and/or had unrealistic parameter estimates.

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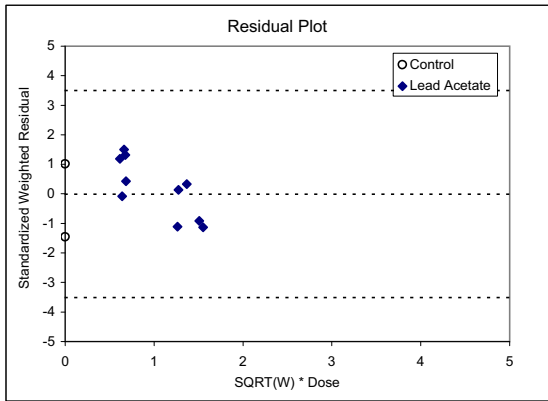
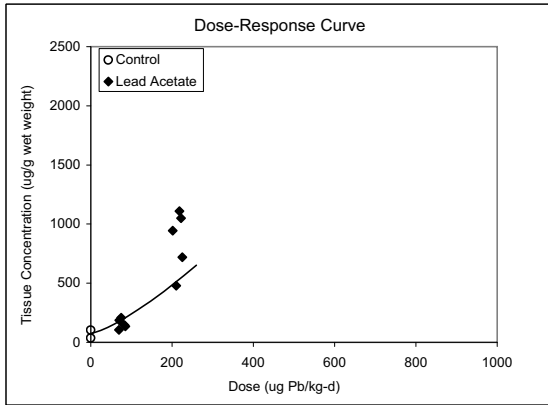
APPENDIX E

Figure 2d - All Data

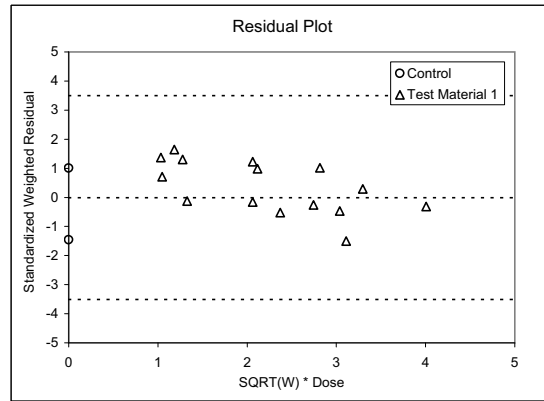
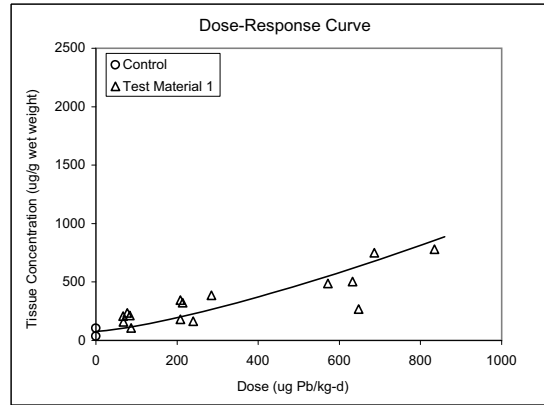
Phase II Experiment 4: Liver

Power Model:  $y = a + b_1 \cdot x_1^c + b_2 \cdot x_2^c + b_3 \cdot x_3^c$

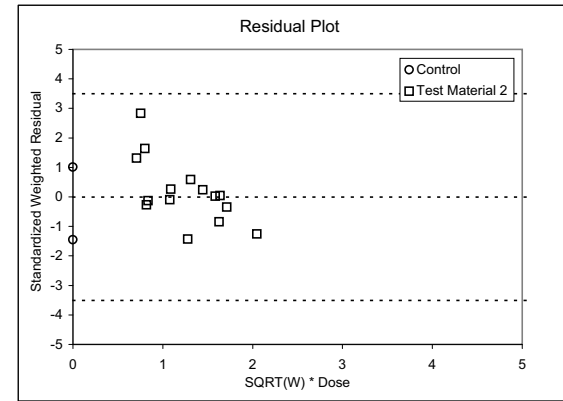
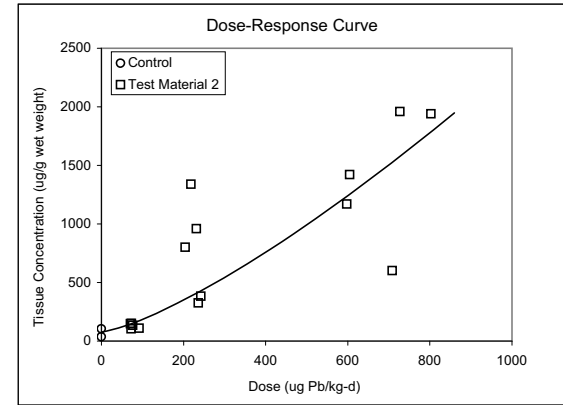
Reference Material (Lead Acetate)



Test Material 1 (Murray Smelter Slag)



Test Material 2 (Jasper County High Lead Mill)



Summary of Fitting

Parameter	Estimate	Standard Error
a	7.61E+01	1.98E+01
b1	3.76E-01	3.69E-01
b2	1.09E-01	1.34E-01
b3	2.52E-01	2.90E-01
c	1.32E+00	1.86E-01
Covariance (b1,b2)	0.9617	--
Covariance (b1,b3)	0.9615	--
Degrees of Freedom	37	--

Goodness of Fit

Statistic	Estimate
F	15.495
p	< 0.001
Adjusted R <sup>2</sup>	0.5858
AIC	555.816

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.39	0.74
Lower bound	?	?
Upper bound	?	?
Standard Error	--	--

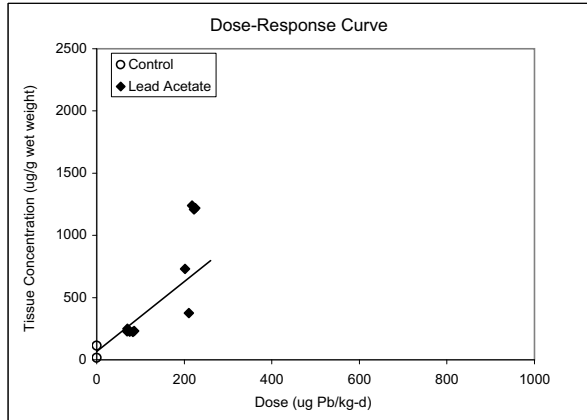
APPENDIX E

Figure 3a - All Data

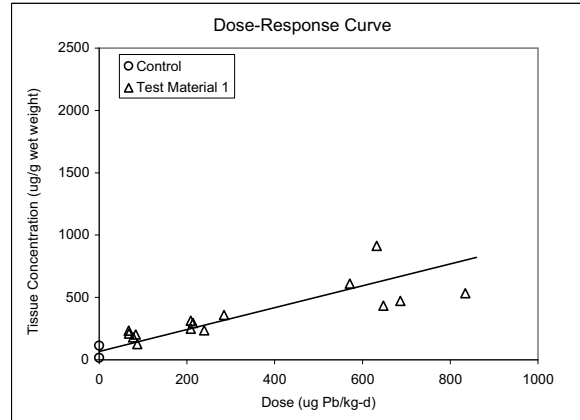
Phase II Experiment 4: Kidney

Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$

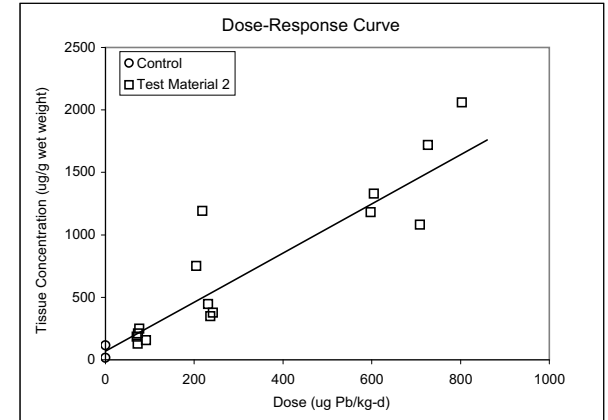
Reference Material (Lead Acetate)



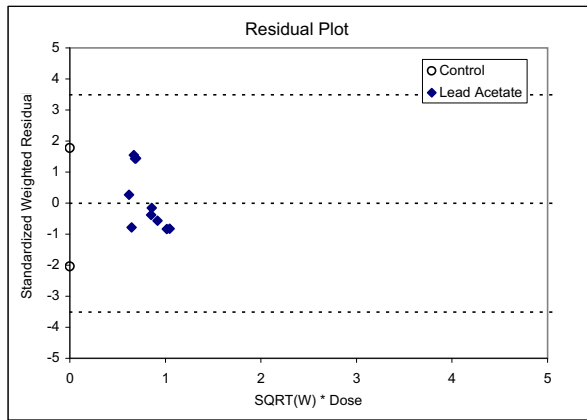
Test Material 1 (Murray Smelter Slag)



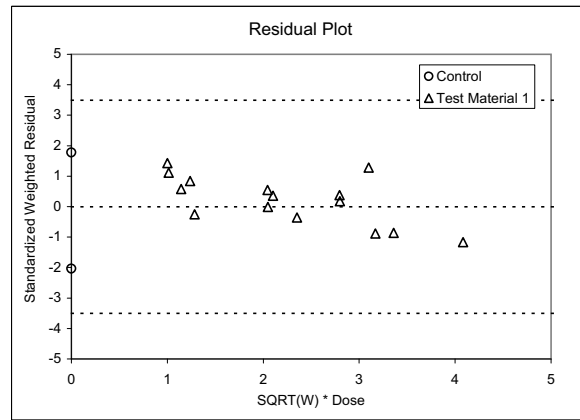
Test Material 2 (Jasper County High Lead Mill)



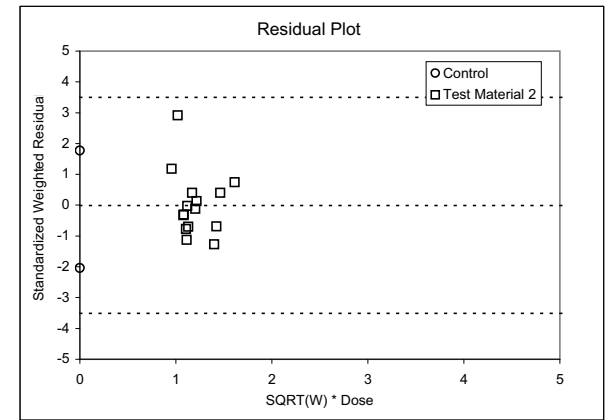
Residual Plot



Residual Plot



Residual Plot



Summary of Fitting

Parameter	Estimate	Standard Error
a	6.79E+01	1.62E+01
b1	2.80E+00	4.81E-01
b2	8.77E-01	1.34E-01
b3	1.97E+00	2.63E-01
Covariance (c1,c2)	0.1300	--
Covariance (c1,c3)	0.1213	--
Degrees of Freedom	38	--

Goodness of Fit

Statistic	Estimate
F	35.326
p	< 0.001
Adjusted R <sup>2</sup>	0.7152
AIC	550.107

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.31	0.70
Lower bound	0.22	0.50
Upper bound	0.46	1.02
Standard Error	0.067*	0.143*

\*  $g \geq 0.05$ , estimate is uncertain



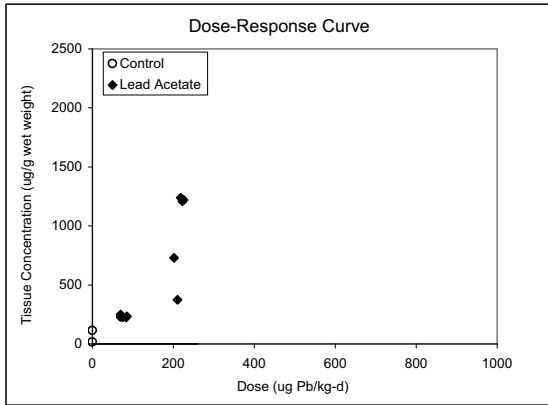
APPENDIX E

Figure 3b - All Data

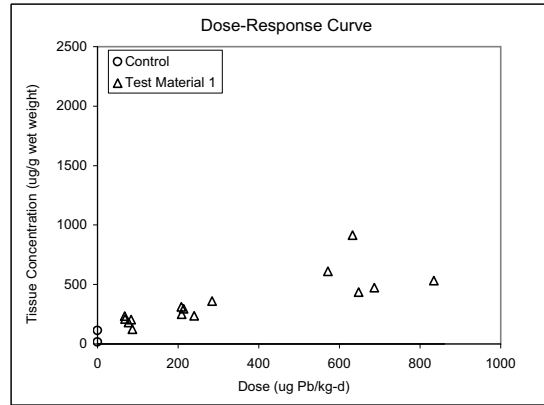
Phase II Experiment 4: Kidney

Exponential Model:  $y = a + b*(1-\exp(-c1*x1)) + b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$

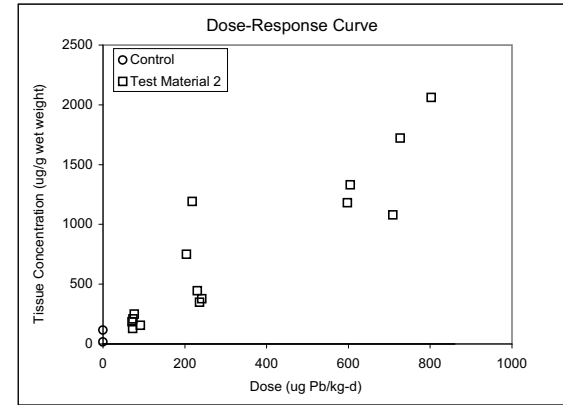
Reference Material (Lead Acetate)



Test Material 1 (Murray Smelter Slag)



Test Material 2 (Jasper County High Lead Mill)



**NO SOLUTION**

The software could not find a solution,  
or the solution was unstable and/or had unrealistic parameter estimates.

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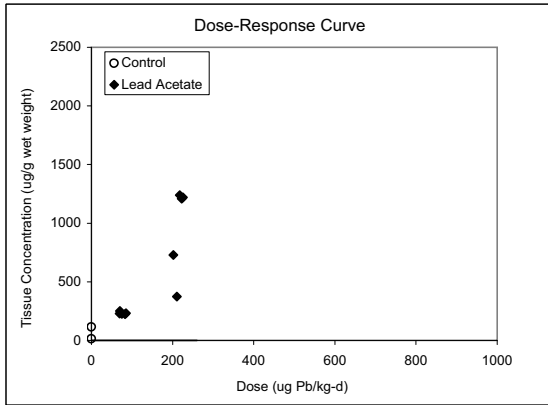
APPENDIX E

Figure 3c - All Data

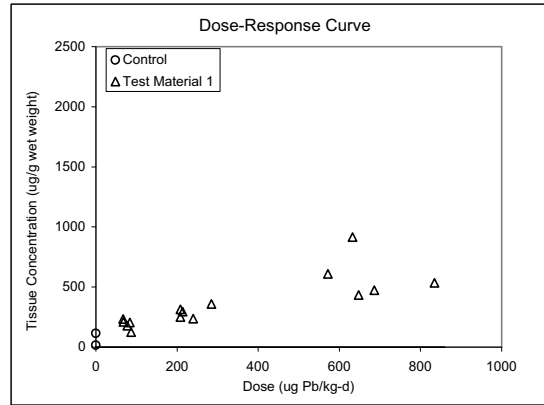
Phase II Experiment 4: Kidney

Michaelis-Menton Model:  $y = a + b \cdot x_1 / (c_1 + x_1) + b \cdot x_2 / (c_2 + x_2) + b \cdot x_3 / (c_3 + x_3)$

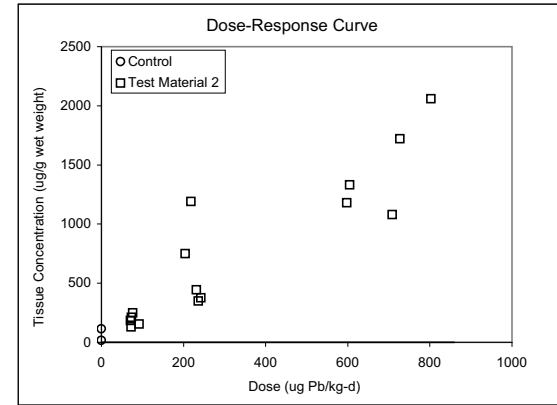
Reference Material (Lead Acetate)



Test Material 1 (Murray Smelter Slag)



Test Material 2 (Jasper County High Lead Mill)



**NO SOLUTION**

The software could not find a solution,  
or the solution was unstable and/or had unrealistic parameter estimates.

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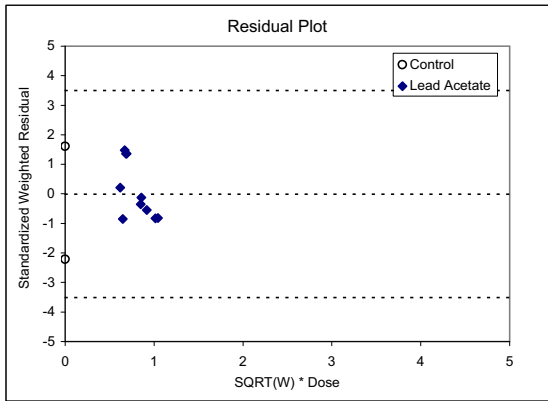
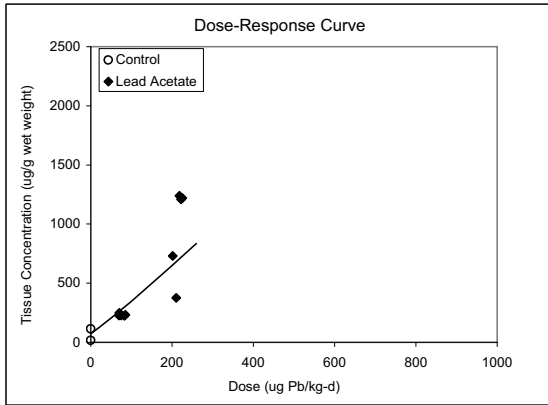
APPENDIX E

Figure 3d - All Data

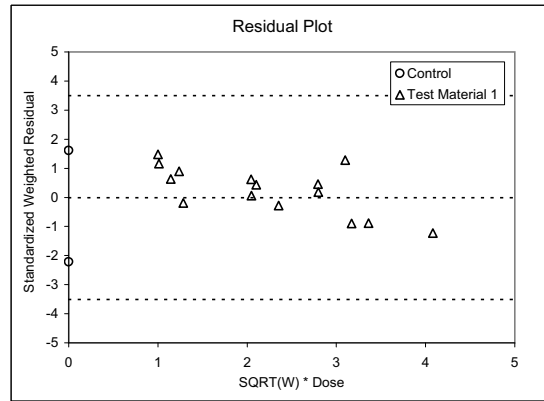
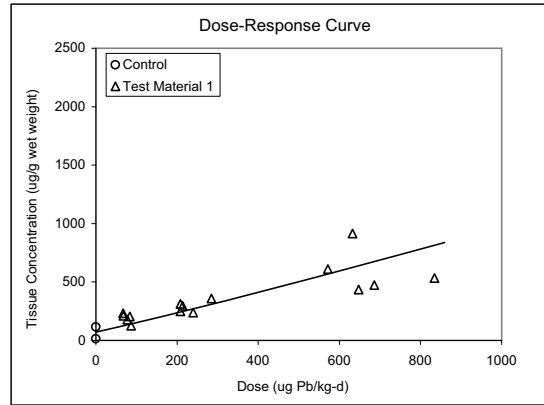
Phase II Experiment 4: Kidney

Power Model:  $y = a + b_1 \cdot x_1^c + b_2 \cdot x_2^c + b_3 \cdot x_3^c$

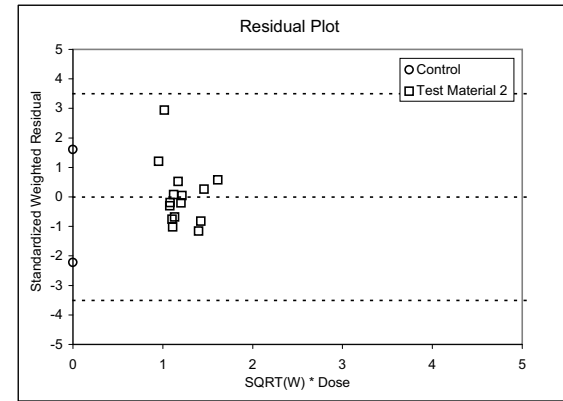
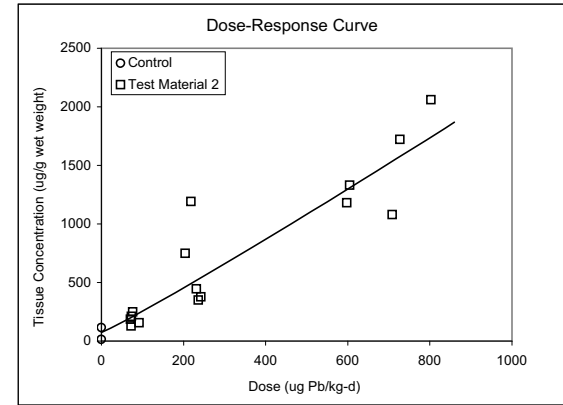
Reference Material (Lead Acetate)



Test Material 1 (Murray Smelter Slag)



Test Material 2 (Jasper County High Lead Mill)



Summary of Fitting

Parameter	Estimate	Standard Error
a	7.24E+01	1.86E+01
b1	2.09E+00	1.37E+00
b2	5.88E-01	4.86E-01
b3	1.38E+00	1.05E+00
c	1.06E+00	1.27E-01
Covariance (b1,b2)	0.9527	--
Covariance (b1,b3)	0.9542	--
Degrees of Freedom	37	--

Goodness of Fit

Statistic	Estimate
F	25.994
p	< 0.001
Adjusted R <sup>2</sup>	0.7092
AIC	551.821

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.30	0.68
Lower bound	0.69	?
Upper bound	0.50	?
Standard Error	--	--

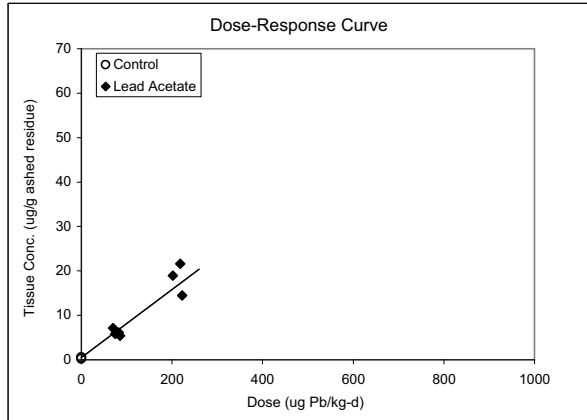
APPENDIX E

Figure 4a - All Data

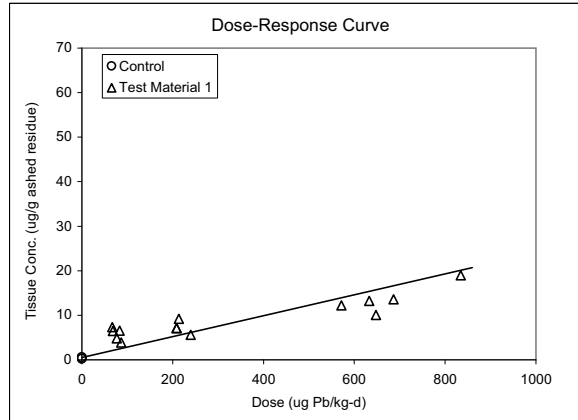
Phase II Experiment 4: Femur

Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$

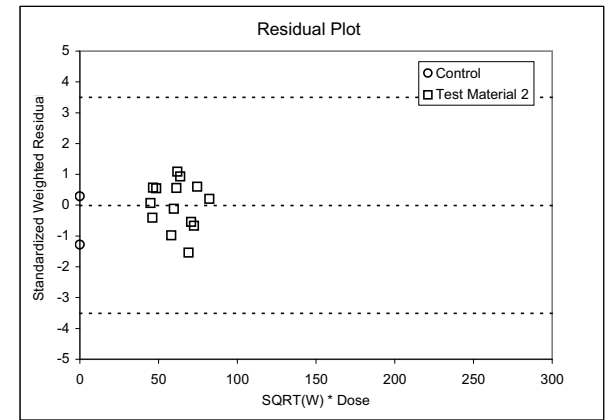
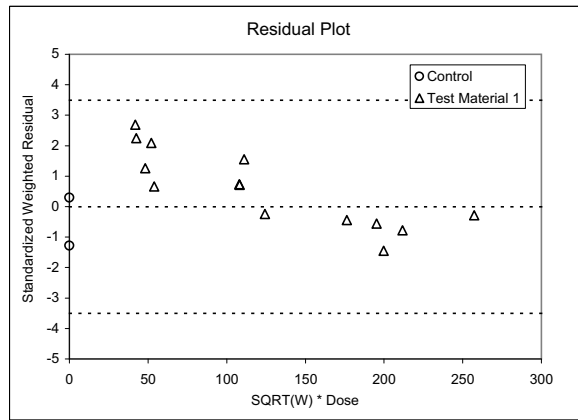
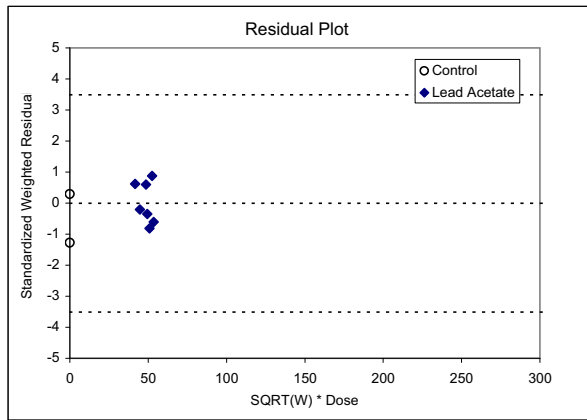
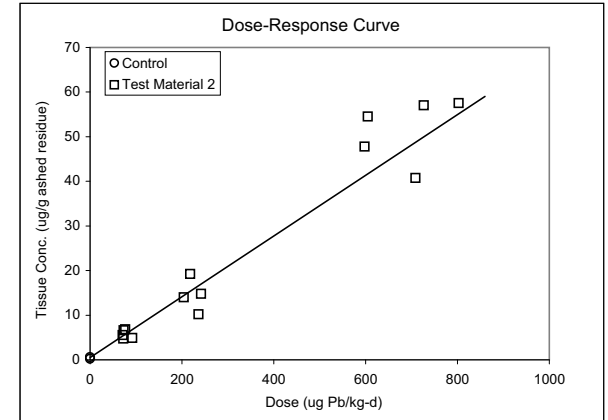
Reference Material (Lead Acetate)



Test Material 1 (Murray Smelter Slag)



Test Material 2 (Jasper County High Lead Mill)



Summary of Fitting

Parameter	Estimate	Standard Error
a	5.35E-01	1.64E-01
b1	7.65E-02	1.01E-02
b2	2.35E-02	2.47E-03
b3	6.80E-02	5.60E-03
Covariance (c1,c2)	0.0238	--
Covariance (c1,c3)	0.0207	--
Degrees of Freedom	33	--

Goodness of Fit

Statistic	Estimate
F	94.431
p	< 0.001
Adjusted R <sup>2</sup>	0.8862
AIC	196.118

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.31	0.89
Lower bound	0.23	0.69
Upper bound	0.41	1.18
Standard Error	0.051*	0.137*

\*  $g \geq 0.05$ , estimate is uncertain

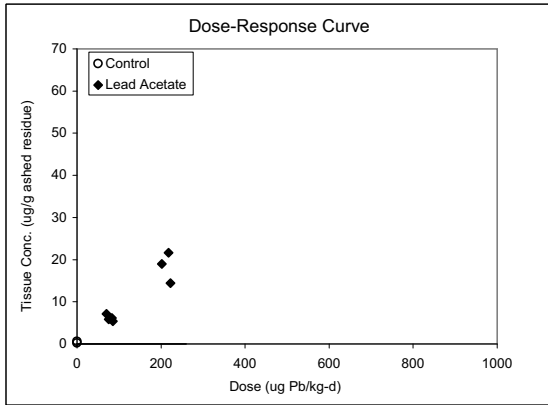
APPENDIX E

Figure 4b - All Data

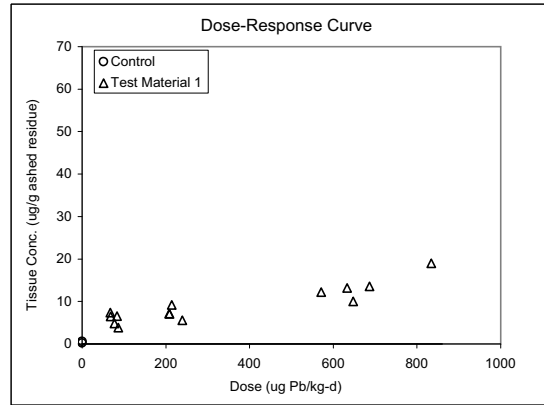
Phase II Experiment 4: Femur

Exponential Model:  $y = a + b*(1-\exp(-c1*x1))+b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$

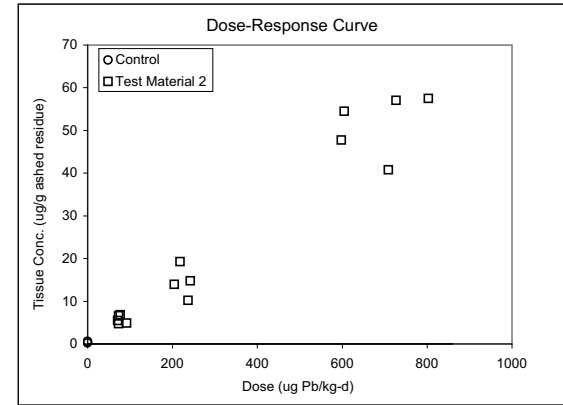
Reference Material (Lead Acetate)



Test Material 1 (Murray Smelter Slag)



Test Material 2 (Jasper County High Lead Mill)



**NO SOLUTION**

The software could not find a solution,  
or the solution was unstable and/or had unrealistic parameter estimates.

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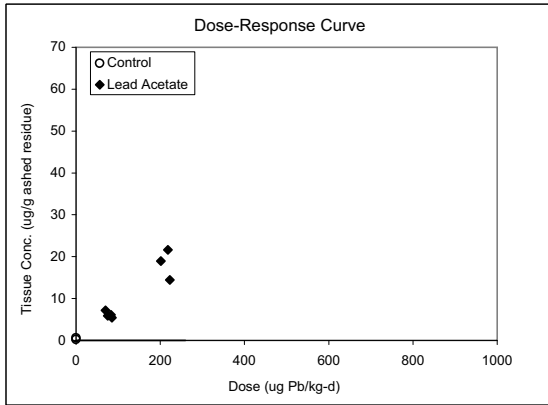
APPENDIX E

Figure 4c - All Data

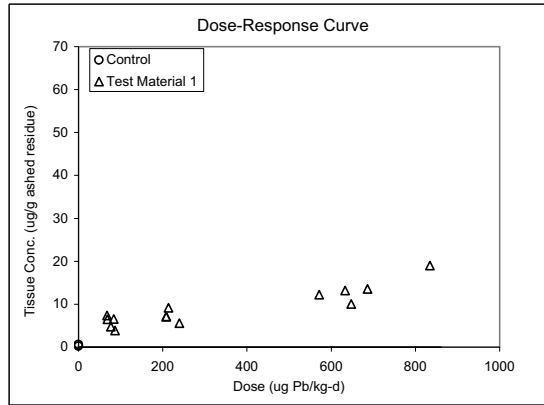
Phase II Experiment 4: Femur

Michaelis-Menton Model:  $y = a + b \cdot x_1 / (c_1 + x_1) + b \cdot x_2 / (c_2 + x_2) + b \cdot x_3 / (c_3 + x_3)$

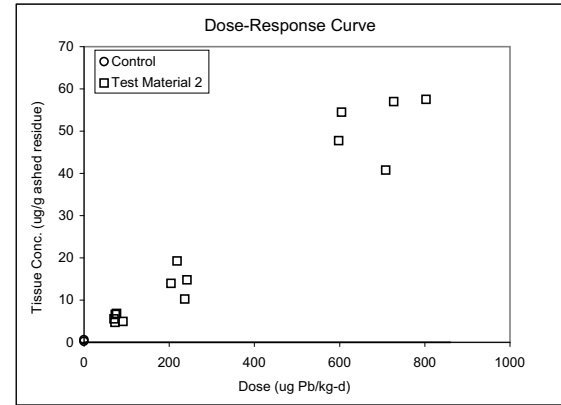
Reference Material (Lead Acetate)



Test Material 1 (Murray Smelter Slag)



Test Material 2 (Jasper County High Lead Mill)



**NO SOLUTION**

The software could not find a solution,  
or the solution was unstable and/or had unrealistic parameter estimates.

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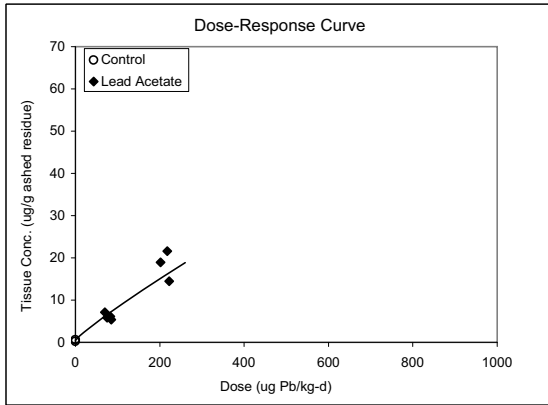
APPENDIX E

Figure 4d - All Data

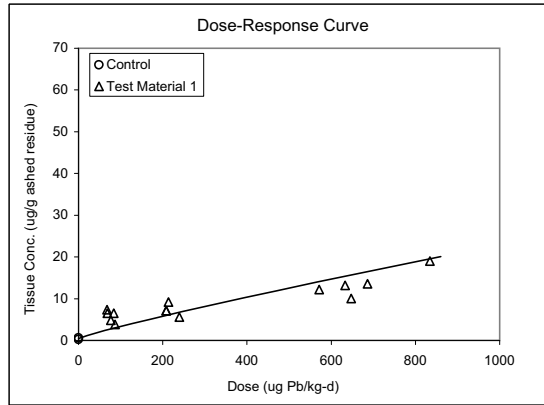
Phase II Experiment 4: Femur

Power Model:  $y = a + b_1 \cdot x_1^c + b_2 \cdot x_2^c + b_3 \cdot x_3^c$

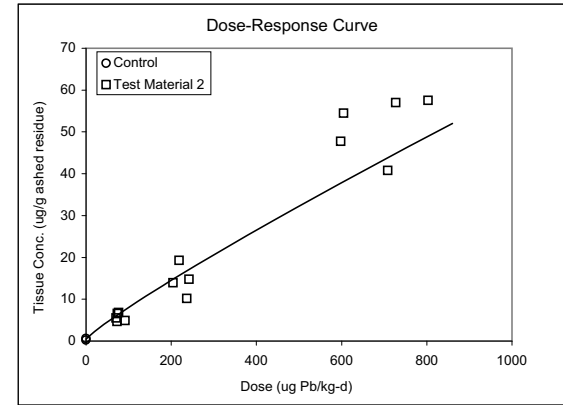
Reference Material (Lead Acetate)



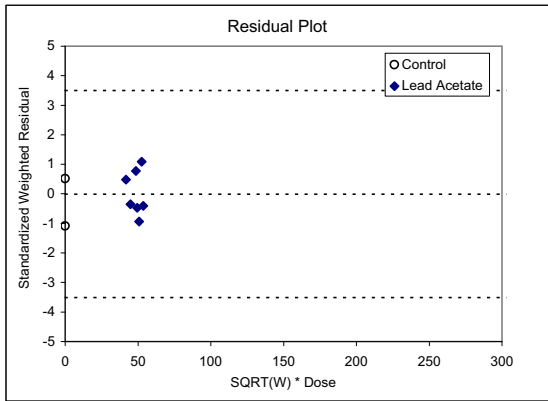
Test Material 1 (Murray Smelter Slag)



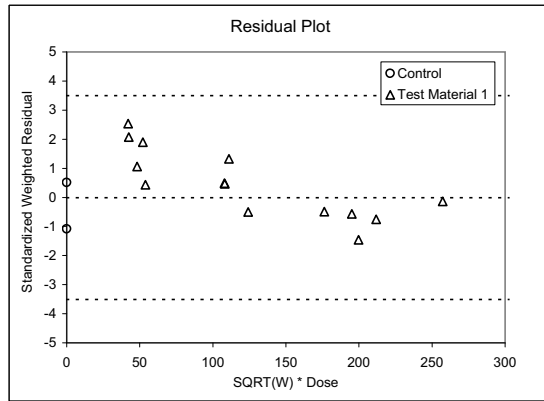
Test Material 2 (Jasper County High Lead Mill)



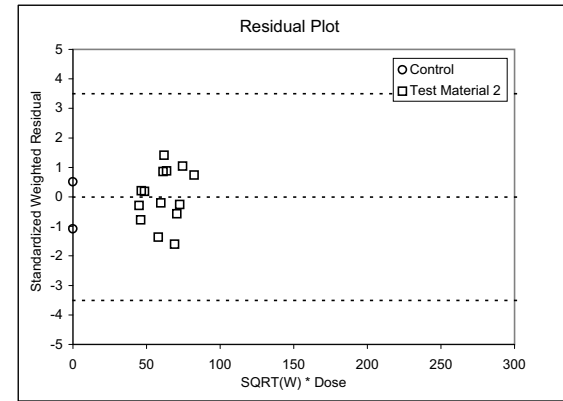
Residual Plot



Residual Plot



Residual Plot



Summary of Fitting

Parameter	Estimate	Standard Error
a	4.88E-01	1.66E-01
b1	1.29E-01	4.99E-02
b2	4.71E-02	2.26E-02
b3	1.24E-01	5.32E-02
c	8.92E-01	7.56E-02
Covariance (b1,b2)	0.9218	--
Covariance (b1,b3)	0.9254	--
Degrees of Freedom	32	--

Goodness of Fit

Statistic	Estimate
F	72.328
p	< 0.001
Adjusted R <sup>2</sup>	0.8880
AIC	195.603

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.32	0.96
Lower bound	0.13	0.56
Upper bound	0.45	1.34
Standard Error	--	--

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## APPENDIX E

### EXPERIMENT 5

Test Material 1: Aspen Berm  
Test Material 2: Aspen Residential

- Figure 1a Blood AUC - Linear Model
- Figure 1b Blood AUC - Exponential Model
- Figure 1c Blood AUC - Michaelis-Menton Model
- Figure 1d Blood AUC - Power Model
  
- Figure 2a Liver - Linear Model (All Data)
- Figure 2a Liver - Linear Model (Outlier Excluded)
- Figure 2b Liver - Exponential Model
- Figure 2c Liver - Michaelis-Menton Model
- Figure 2d Liver - Power Model
  
- Figure 3a Kidney - Linear Model
- Figure 3b Kidney - Exponential Model
- Figure 3c Kidney - Michaelis-Menton Model
- Figure 3d Kidney - Power Model
  
- Figure 4a Femur - Linear Model
- Figure 4b Femur - Exponential Model
- Figure 4c Femur - Michaelis-Menton Model
- Figure 4d Femur - Power Model

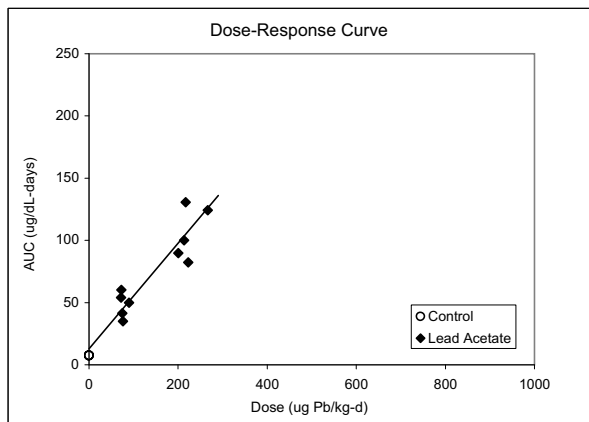
APPENDIX E

Figure 1a - All Data

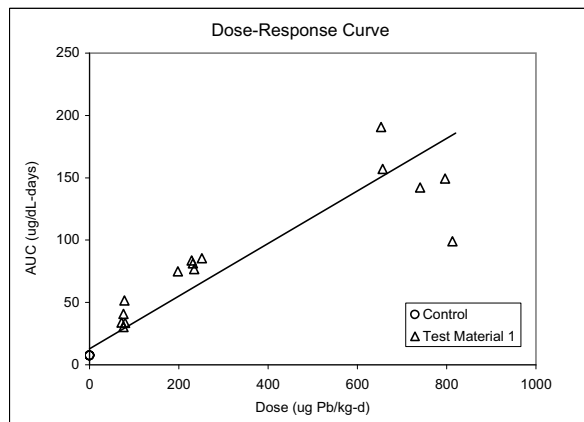
Phase II Experiment 5: Blood AUC

Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$

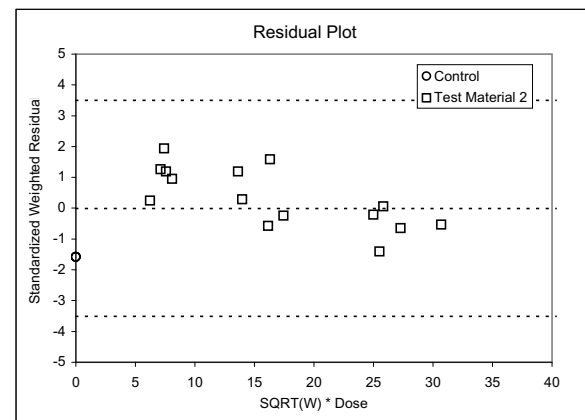
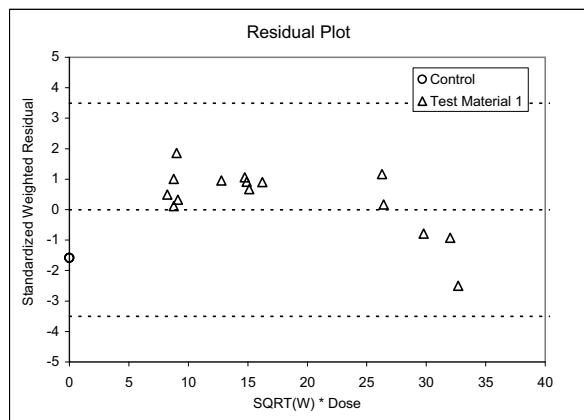
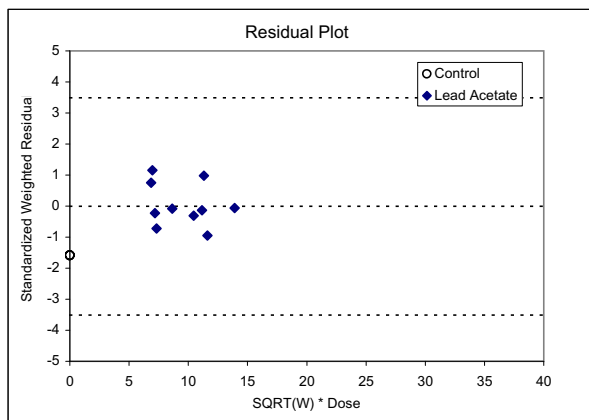
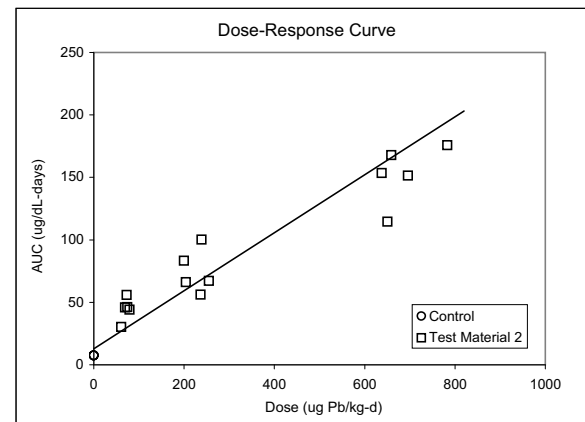
Reference Material (Lead Acetate)



Test Material 1 (Aspen Berm)



Test Material 2 (Aspen Residential)



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.29E+01	2.19E+00
b1	4.25E-01	4.90E-02
b2	2.11E-01	1.99E-02
b3	2.32E-01	2.12E-02
Covariance (c1,c2)	0.0903	--
Covariance (c1,c3)	0.0880	--
Degrees of Freedom	38	--

Goodness of Fit

Statistic	Estimate
F	87.459
p	< 0.001
Adjusted R <sup>2</sup>	0.8635
AIC	385.030

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.50	0.55
Lower bound	0.39	0.43
Upper bound	0.64	0.70
Standard Error	0.071	0.077

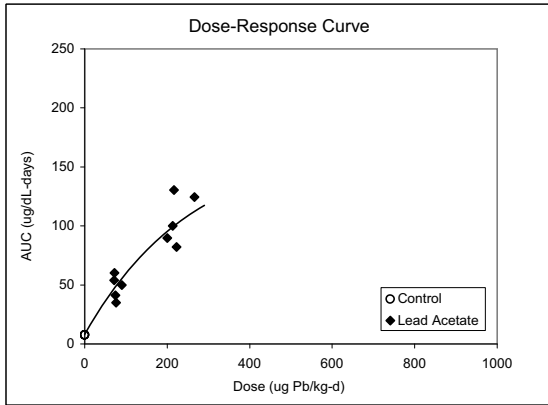
APPENDIX E

Figure 1b - All Data

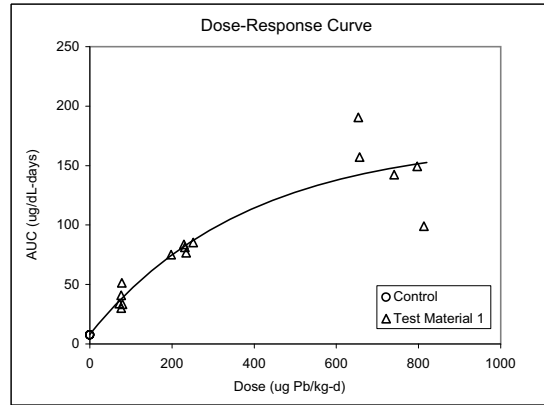
Phase II Experiment 5: Blood AUC

Exponential Model:  $y = a + b*(1-\exp(-c1*x1))+b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$

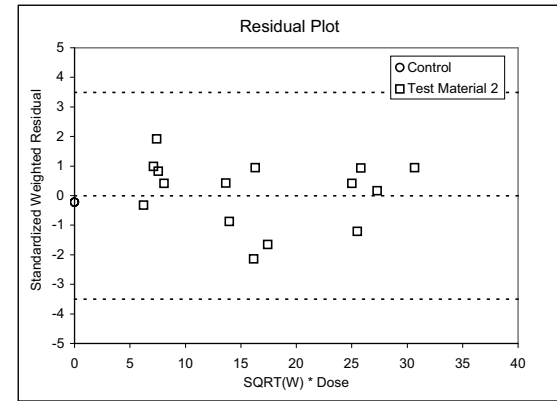
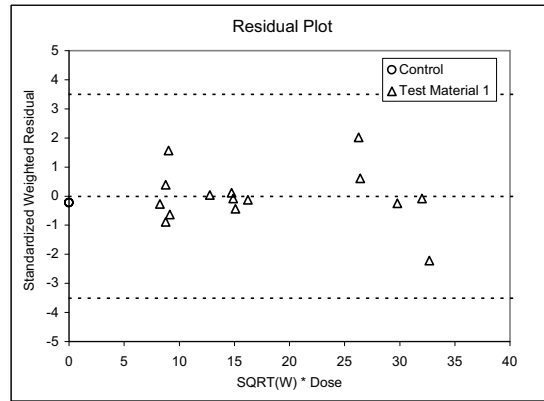
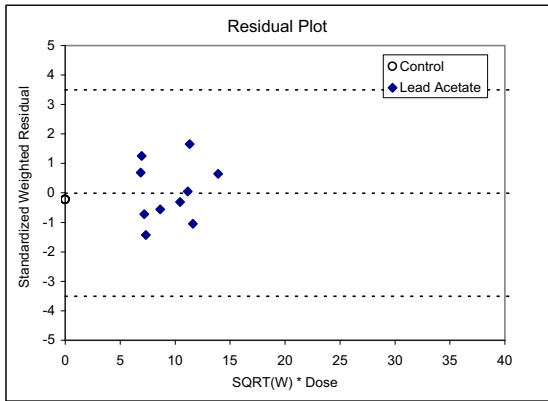
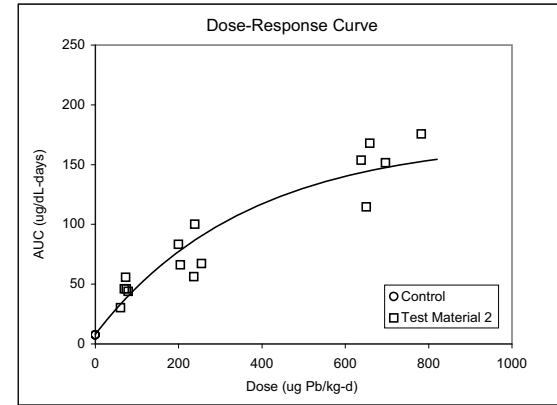
Reference Material (Lead Acetate)



Test Material 1 (Aspen Berm)



Test Material 2 (Aspen Residential)



Summary of Fitting

Parameter	Estimate	Standard Error
a	8.03E+00	1.72E+00
b	1.63E+02	1.69E+01
c1	3.82E-03	6.83E-04
c2	2.63E-03	4.97E-04
c3	2.76E-03	5.26E-04
Covariance (c1,c2)	0.7323	--
Covariance (c1,c3)	0.7322	--
Degrees of Freedom	37	--

Goodness of Fit

Statistic	Estimate
F	143.955
p	< 0.001
Adjusted R <sup>2</sup>	0.9331
AIC	345.170

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.69	0.72
Lower bound	0.54	0.56
Upper bound	0.87	0.91
Standard Error	0.093*	0.098*

\*  $g \geq 0.05$ , estimate is uncertain

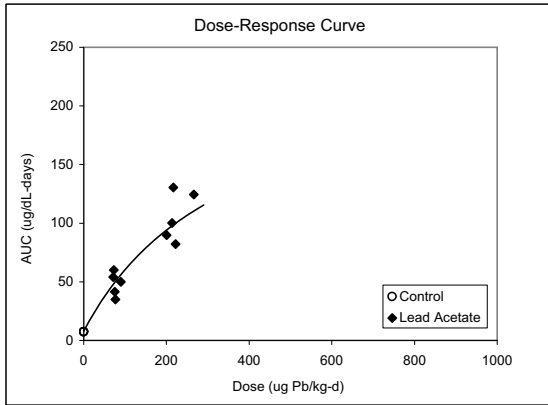
APPENDIX E

Figure 1c - All Data

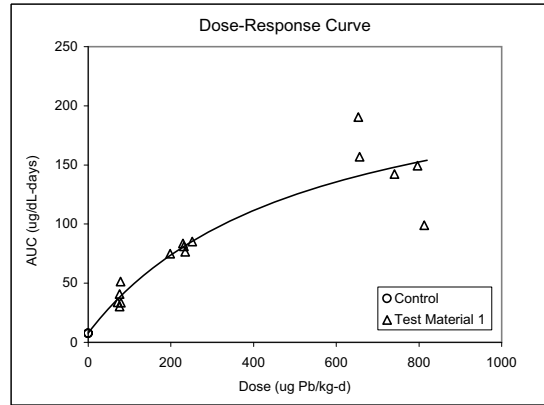
Phase II Experiment 5: Blood AUC

Michaelis-Menton Model:  $y = a + b*x1/(c1+x1) + b*x2/(c2+x2) + b*x3/(c3+x3)$

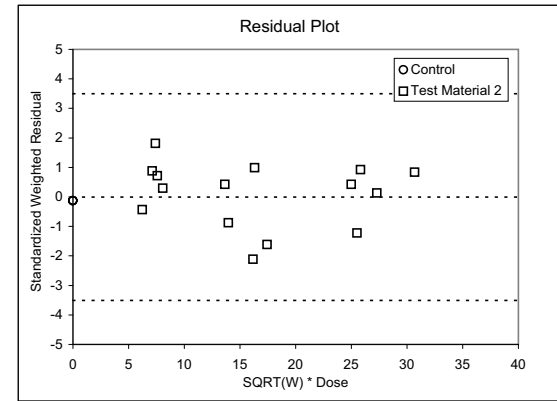
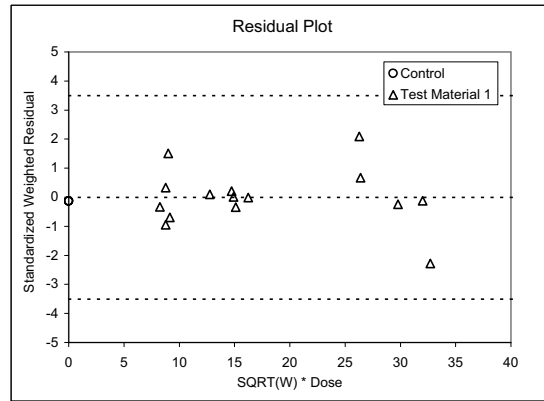
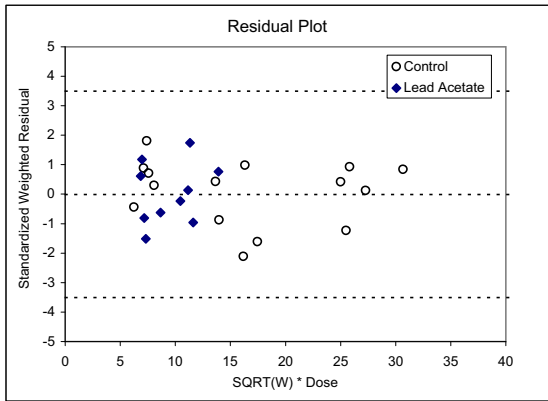
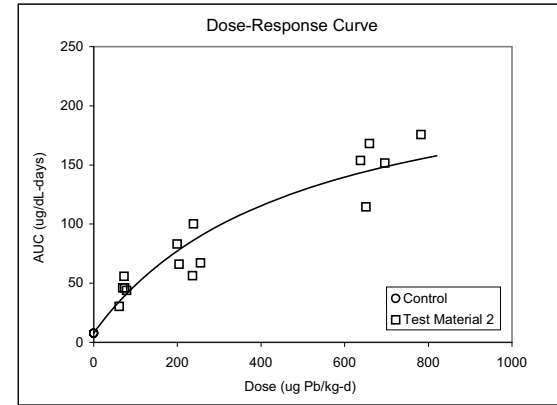
Reference Material (Lead Acetate)



Test Material 1 (Aspen Berm)



Test Material 2 (Aspen Residential)



Summary of Fitting

Parameter	Estimate	Standard Error
a	7.81E+00	1.73E+00
b	2.39E+02	3.23E+01
c1	3.55E+02	7.97E+01
c2	5.24E+02	1.24E+02
c3	4.89E+02	1.18E+02
Covariance (c1,c2)	0.8270	--
Covariance (c1,c3)	0.8275	--
Degrees of Freedom	37	--

Goodness of Fit

Statistic	Estimate
F	145.720
p	< 0.001
Adjusted R <sup>2</sup>	0.9339
AIC	344.735

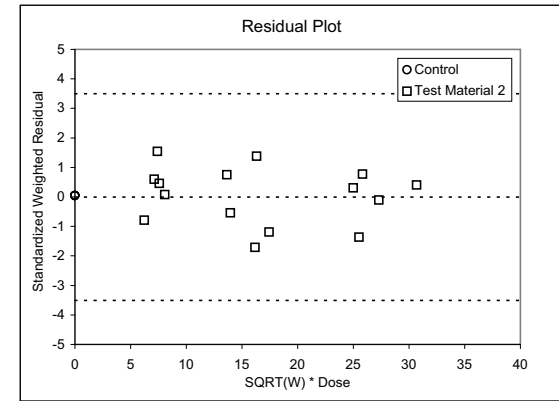
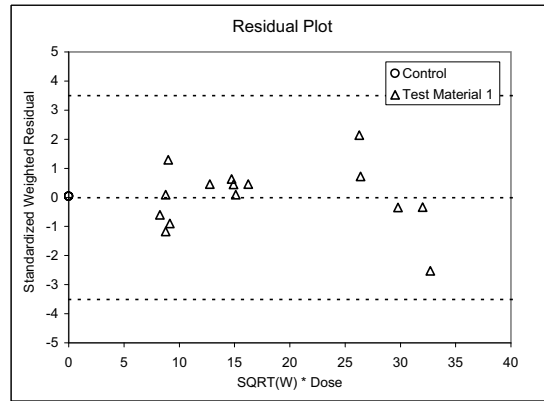
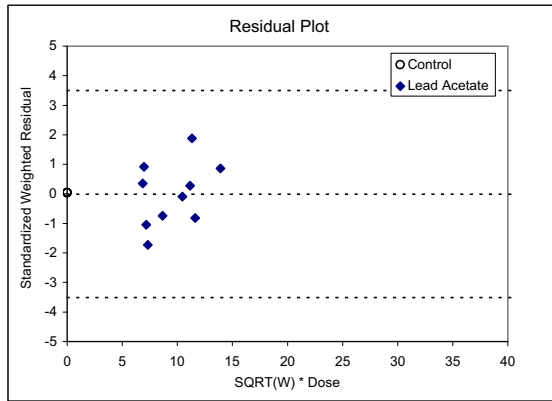
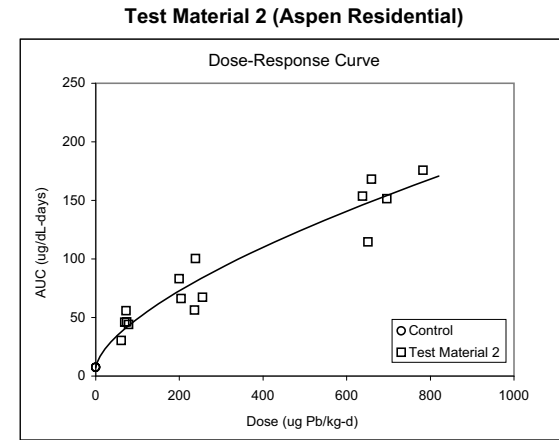
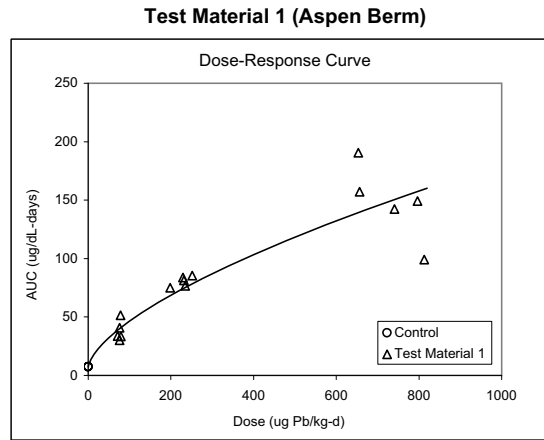
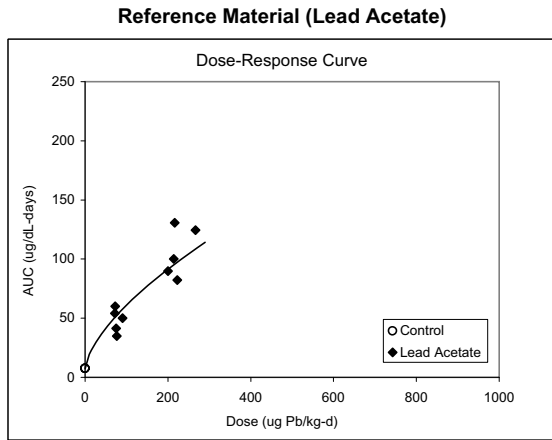
RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.68	0.73
Lower bound	0.53	0.57
Upper bound	0.88	0.95
Standard Error	0.093*	0.100*

\*  $g \geq 0.05$ , estimate is uncertain

APPENDIX E

**Figure 1d - All Data**  
**Phase II Experiment 5: Blood AUC**  
**Power Model:  $y = a + b_1 \cdot x_1^c + b_2 \cdot x_2^c + b_3 \cdot x_3^c$**



**Summary of Fitting**

Parameter	Estimate	Standard Error
a	7.41E+00	1.76E+00
b1	2.70E+00	6.67E-01
b2	1.97E+00	5.50E-01
b3	2.10E+00	5.84E-01
c	6.49E-01	4.56E-02
Covariance (b1,b2)	0.9387	--
Covariance (b1,b3)	0.9389	--
Degrees of Freedom	37	--

**Goodness of Fit**

Statistic	Estimate
F	144.915
p	< 0.001
Adjusted R <sup>2</sup>	0.9335
AIC	344.932

**RBA and Uncertainty**

	Test Material 1	Test Material 2
RBA	0.61	0.68
Lower bound	0.44	0.49
Upper bound	0.78	0.86
Standard Error	--	--

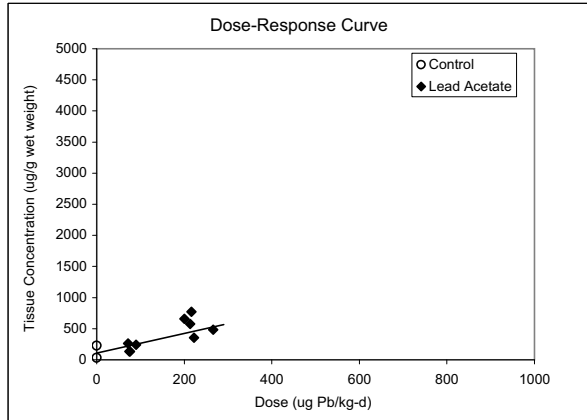
APPENDIX E

Figure 2a - All Data

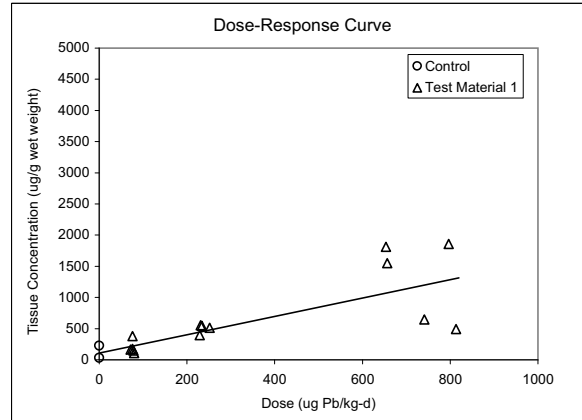
Phase II Experiment 5: Liver

Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$

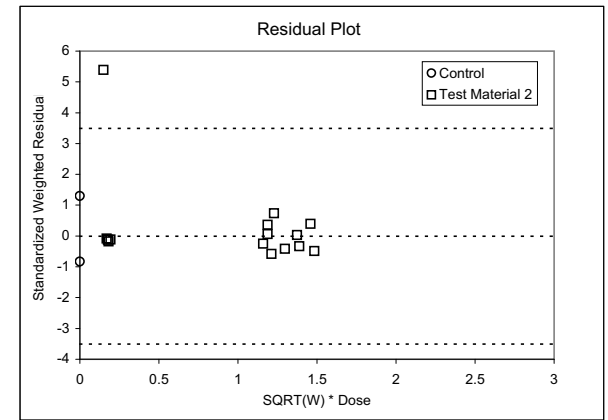
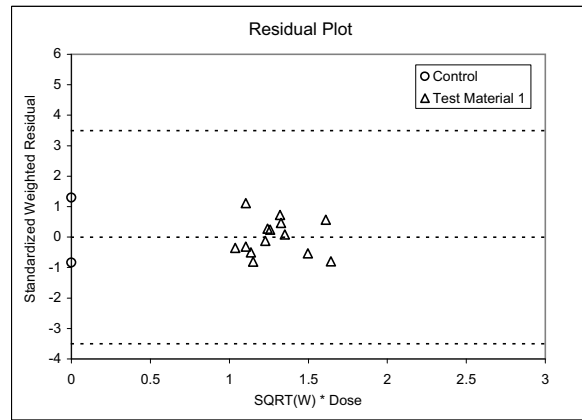
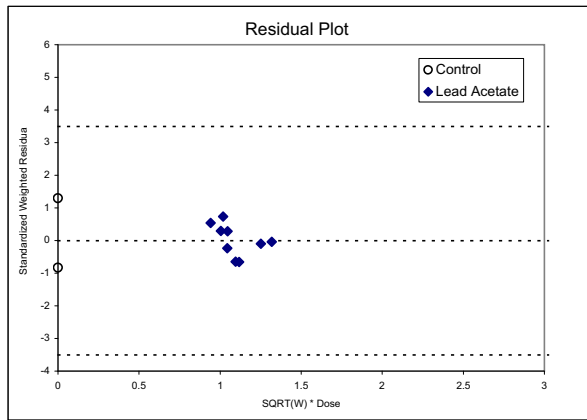
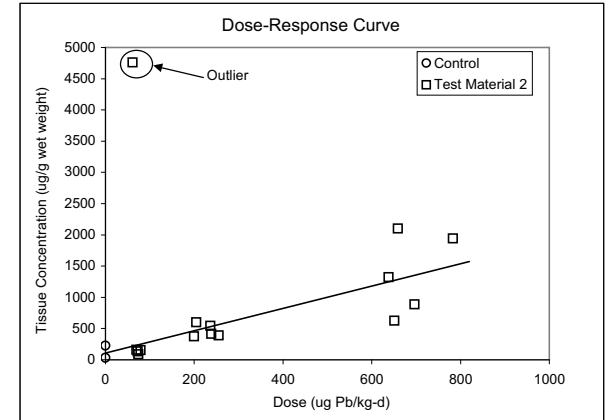
Reference Material (Lead Acetate)



Test Material 1 (Aspen Berm)



Test Material 2 (Aspen Residential)



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.07E+02	5.09E+01
b1	1.58E+00	7.86E-01
b2	1.47E+00	5.19E-01
b3	1.79E+00	5.47E-01
Covariance (c1,c2)	0.2781	--
Covariance (c1,c3)	0.1555	--
Degrees of Freedom	36	--

Goodness of Fit

Statistic	Estimate
F	5.754
p	0.0025
Adjusted R <sup>2</sup>	0.2678
AIC	674.409

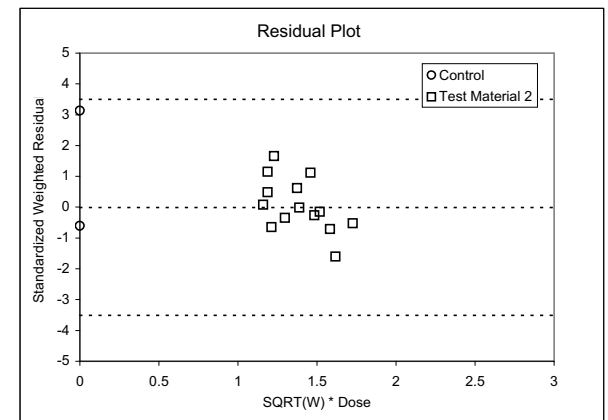
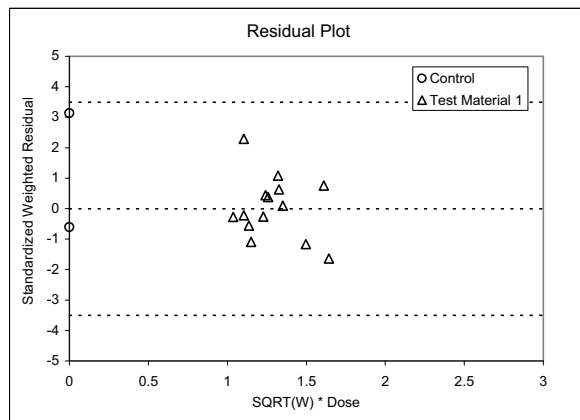
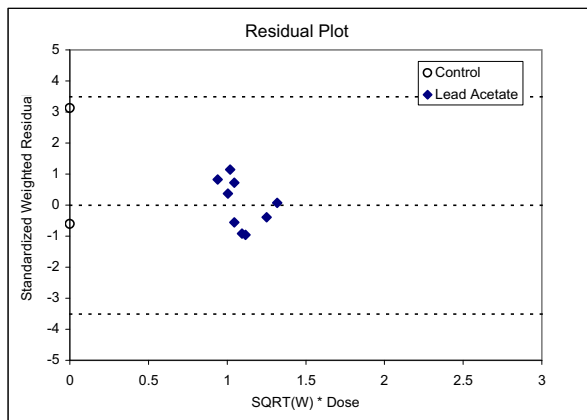
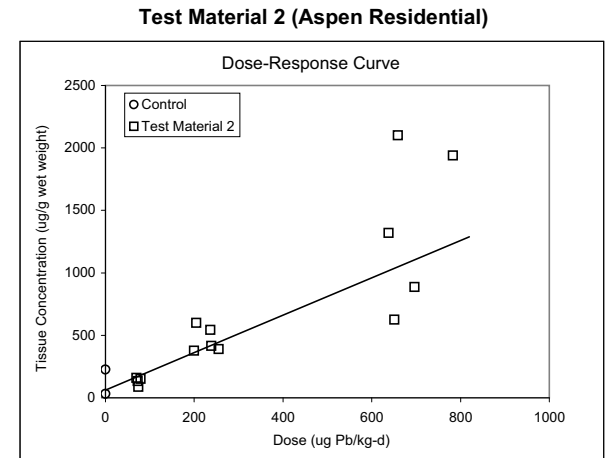
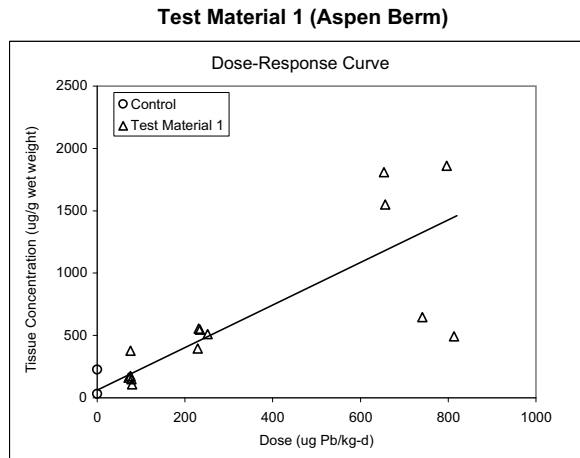
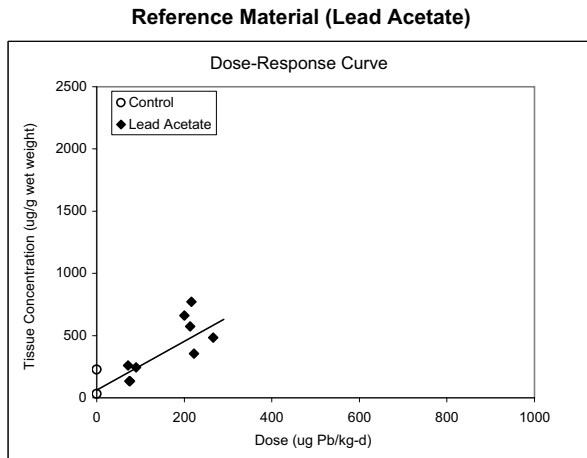
RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.93	1.13
Lower bound	0.38	0.48
Upper bound	5.14	6.78
Standard Error	0.490*	0.616*

\*  $g \geq 0.05$ , estimate is uncertain

APPENDIX E

**Figure 2a - Outlier Excluded**  
**Phase II Experiment 5: Liver**  
**Linear Model:  $y = a + b_1 \cdot x_1 + b_2 \cdot x_2 + b_3 \cdot x_3$**



**Summary of Fitting**

Parameter	Estimate	Standard Error
a	6.21E+01	2.46E+01
b1	1.96E+00	4.29E-01
b2	1.71E+00	2.85E-01
b3	1.50E+00	2.92E-01
Covariance (c1,c2)	0.2174	--
Covariance (c1,c3)	0.2847	--
Degrees of Freedom	35	--

**Goodness of Fit**

Statistic	Estimate
F	18.566
p	< 0.001
Adjusted R <sup>2</sup>	0.5810
AIC	526.951

**RBA and Uncertainty**

	Test Material 1	Test Material 2
RBA	0.87	0.77
Lower bound	0.58	0.50
Upper bound	1.39	1.21
Standard Error	0.214*	0.190*

\*  $g \geq 0.05$ , estimate is uncertain

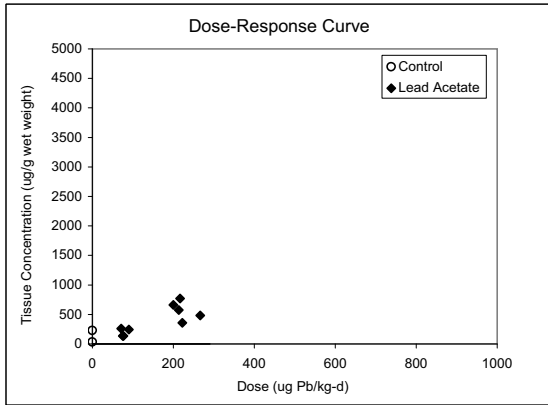
APPENDIX E

Figure 2b - All Data

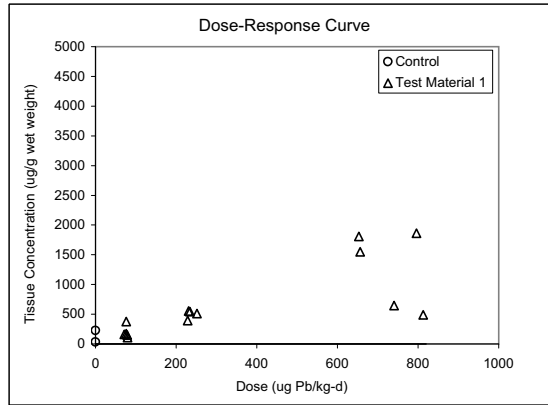
Phase II Experiment 5: Liver

Exponential Model:  $y = a + b*(1-\exp(-c1*x1)) + b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$

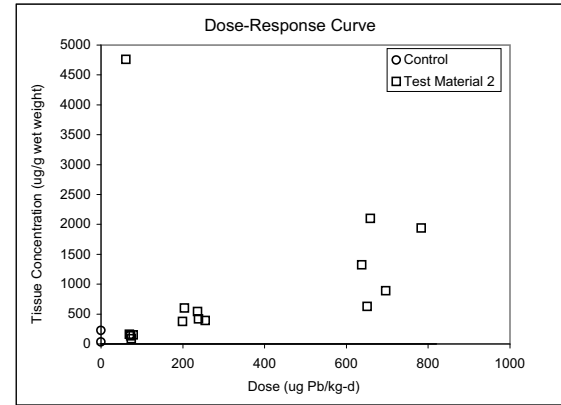
Reference Material (Lead Acetate)



Test Material 1 (Aspen Berm)



Test Material 2 (Aspen Residential)



**NO SOLUTION**

The software could not find a solution,  
or the solution was unstable and/or had unrealistic parameter estimates.

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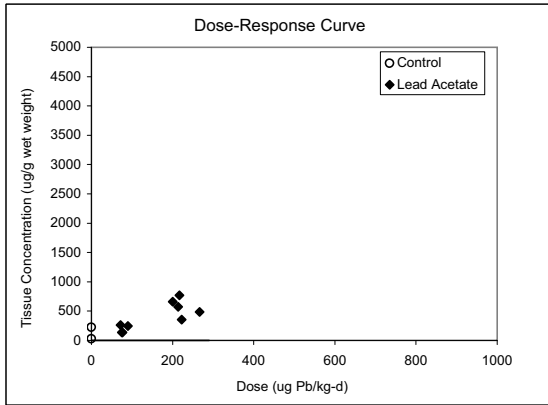
APPENDIX E

Figure 2c - All Data

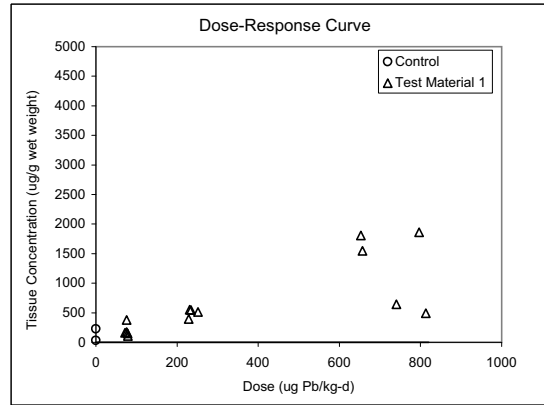
Phase II Experiment 5: Liver

Michaelis-Menton Model:  $y = a + b \cdot x_1 / (c_1 + x_1) + b \cdot x_2 / (c_2 + x_2) + b \cdot x_3 / (c_3 + x_3)$

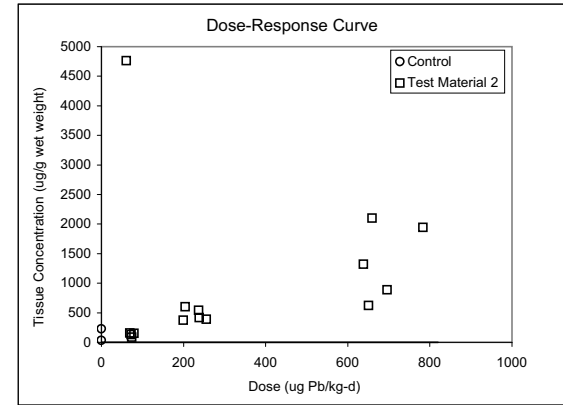
Reference Material (Lead Acetate)



Test Material 1 (Aspen Berm)



Test Material 2 (Aspen Residential)



**NO SOLUTION**

The software could not find a solution,  
or the solution was unstable and/or had unrealistic parameter estimates.

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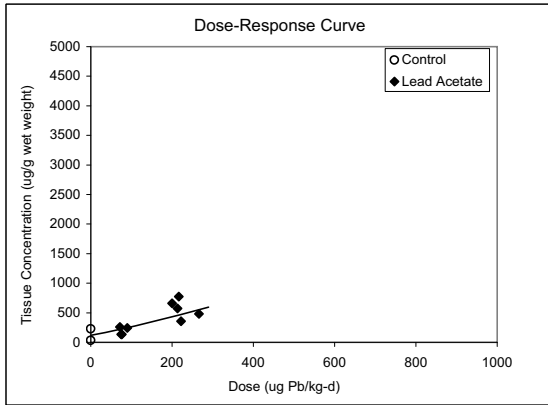
APPENDIX E

Figure 2d - All Data

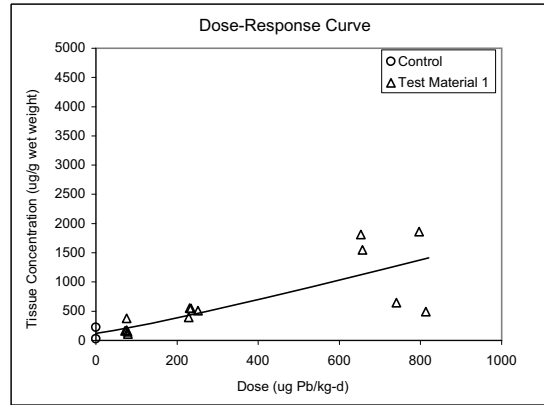
Phase II Experiment 5: Liver

Power Model:  $y = a + b1*x1^c + b2*x2^c + b3*x3^c$

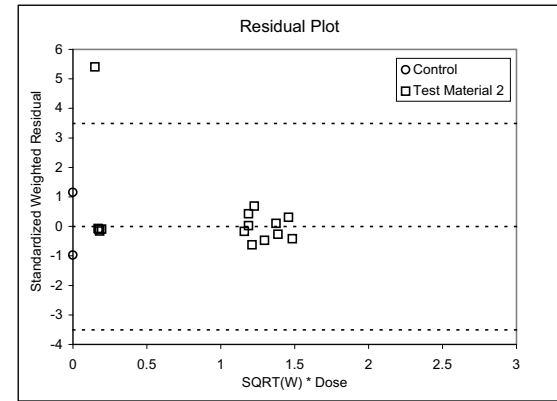
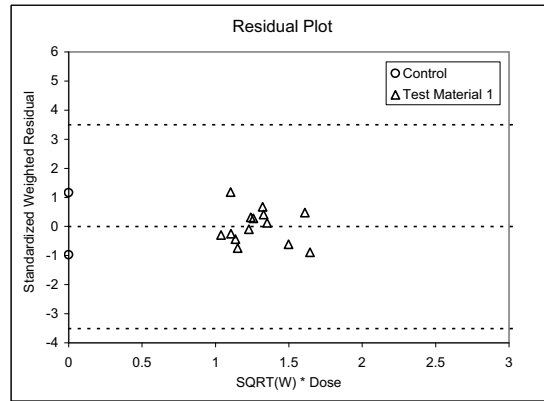
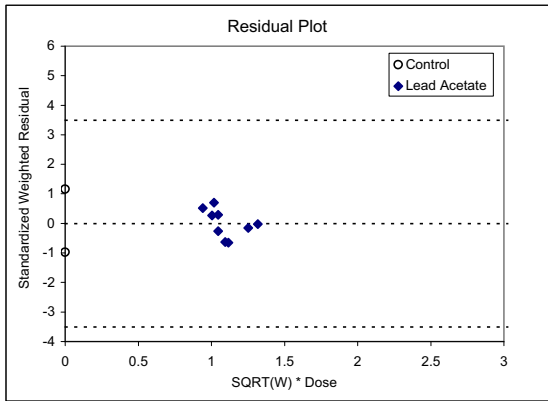
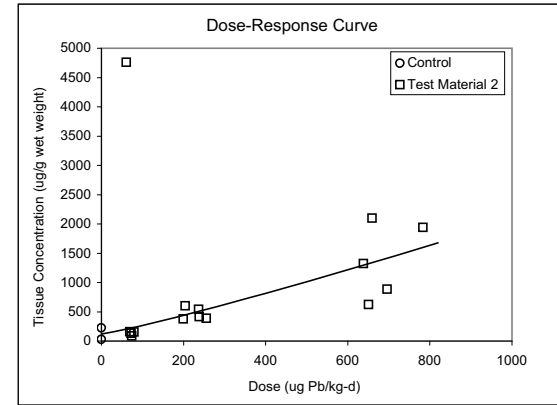
Reference Material (Lead Acetate)



Test Material 1 (Aspen Berm)



Test Material 2 (Aspen Residential)



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.20E+02	6.37E+01
b1	8.19E-01	1.73E+00
b2	6.98E-01	1.63E+00
b3	8.39E-01	1.93E+00
c	1.12E+00	3.67E-01
Covariance (b1,b2)	0.9666	--
Covariance (b1,b3)	0.9647	--
Degrees of Freedom	35	--

Goodness of Fit

Statistic	Estimate
F	4.240
p	0.0067
Adjusted R <sup>2</sup>	0.2494
AIC	675.820

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.87	1.02
Lower bound	?	?
Upper bound	?	?
Standard Error	--	--

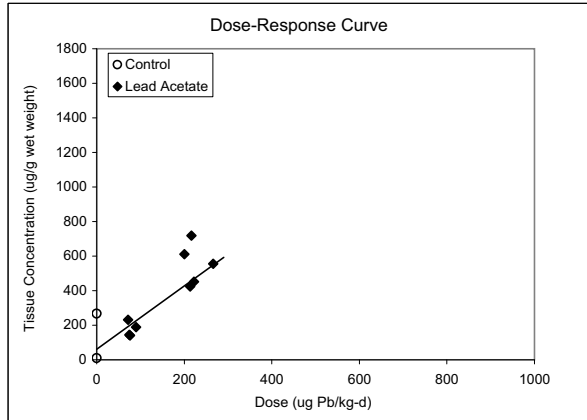
APPENDIX E

Figure 3a - All Data

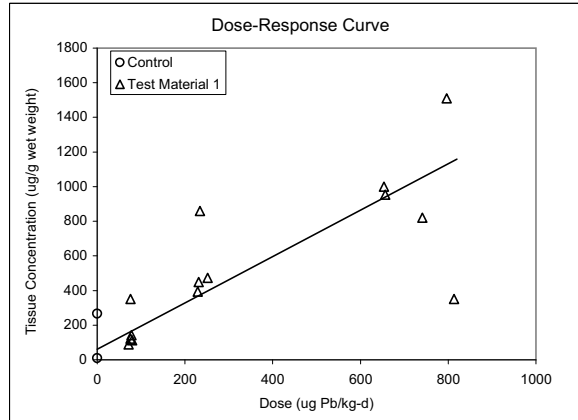
Phase II Experiment 5: Kidney

Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$

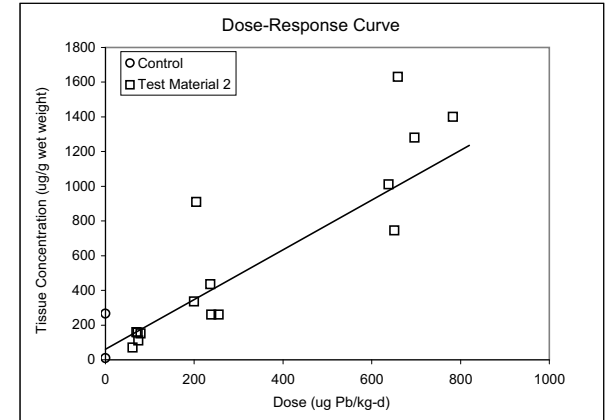
Reference Material (Lead Acetate)



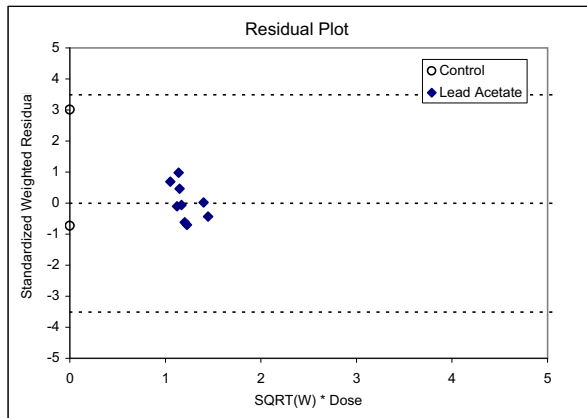
Test Material 1 (Aspen Berm)



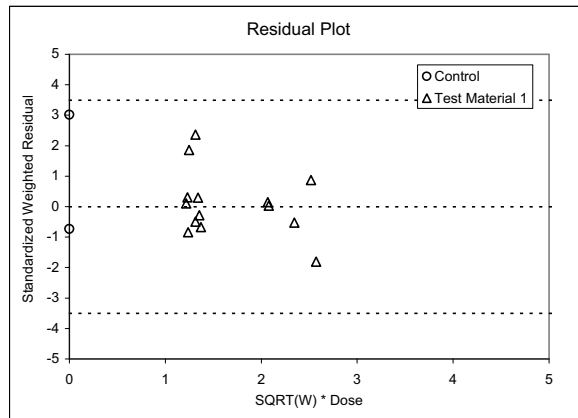
Test Material 2 (Aspen Residential)



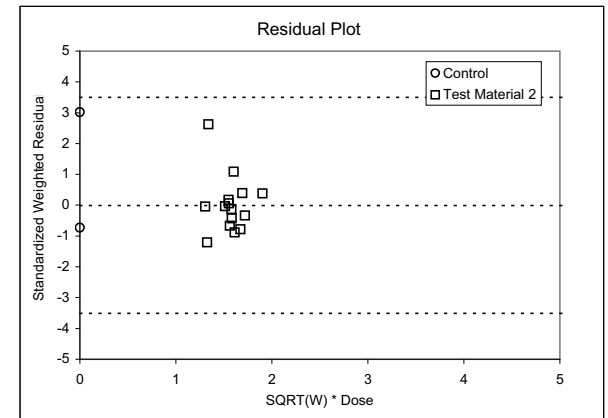
Residual Plot



Residual Plot



Residual Plot



Summary of Fitting

Parameter	Estimate	Standard Error
a	6.02E+01	2.63E+01
b1	1.84E+00	4.56E-01
b2	1.34E+00	2.50E-01
b3	1.43E+00	2.92E-01
Covariance (c1,c2)	0.2137	--
Covariance (c1,c3)	0.2775	--
Degrees of Freedom	36	--

Goodness of Fit

Statistic	Estimate
F	15.575
p	< 0.001
Adjusted R <sup>2</sup>	0.5286
AIC	547.820

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.73	0.78
Lower bound	0.46	0.49
Upper bound	1.26	1.33
Standard Error	0.202*	0.214*

\*  $g \geq 0.05$ , estimate is uncertain

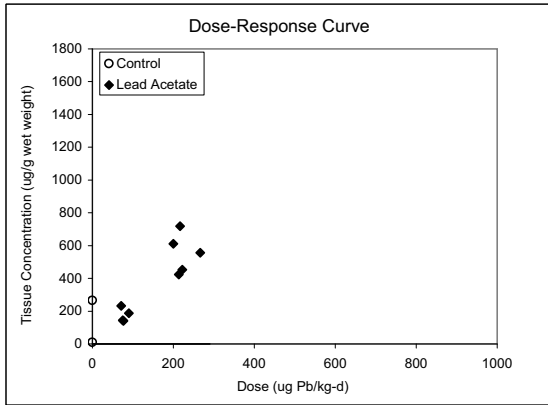
APPENDIX E

Figure 3b - All Data

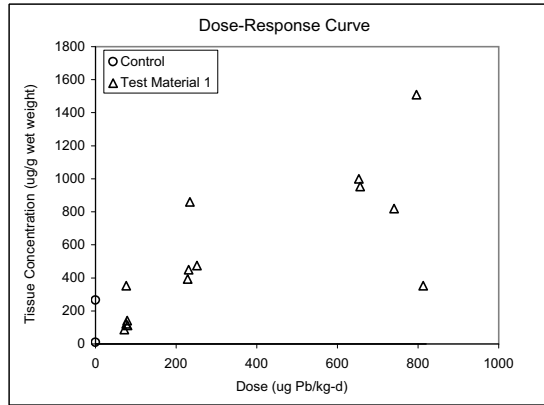
Phase II Experiment 5: Kidney

Exponential Model:  $y = a + b*(1-\exp(-c1*x1)) + b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$

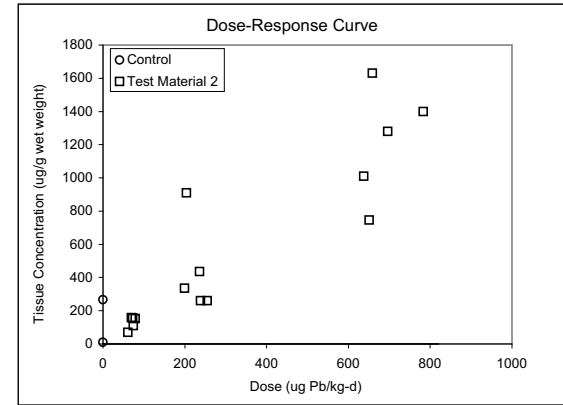
Reference Material (Lead Acetate)



Test Material 1 (Aspen Berm)



Test Material 2 (Aspen Residential)



**NO SOLUTION**

The software could not find a solution,  
or the solution was unstable and/or had unrealistic parameter estimates.

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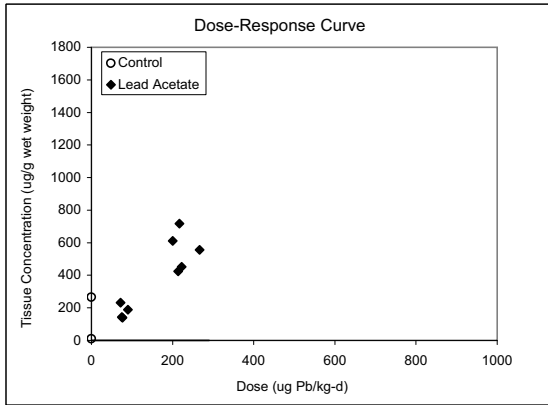
APPENDIX E

Figure 3c - All Data

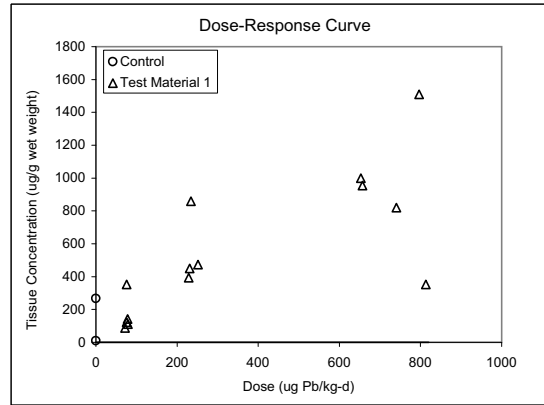
Phase II Experiment 5: Kidney

Michaelis-Menton Model:  $y = a + b \cdot x_1 / (c_1 + x_1) + b \cdot x_2 / (c_2 + x_2) + b \cdot x_3 / (c_3 + x_3)$

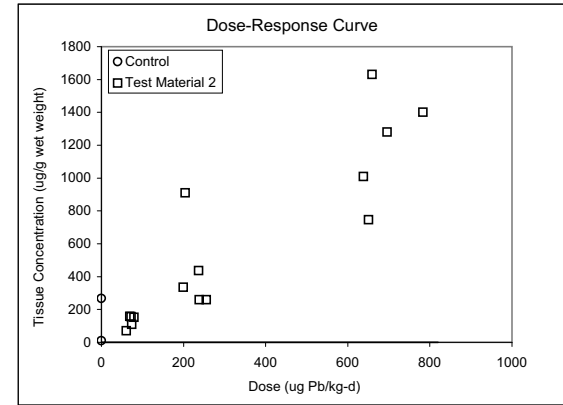
Reference Material (Lead Acetate)



Test Material 1 (Aspen Berm)



Test Material 2 (Aspen Residential)



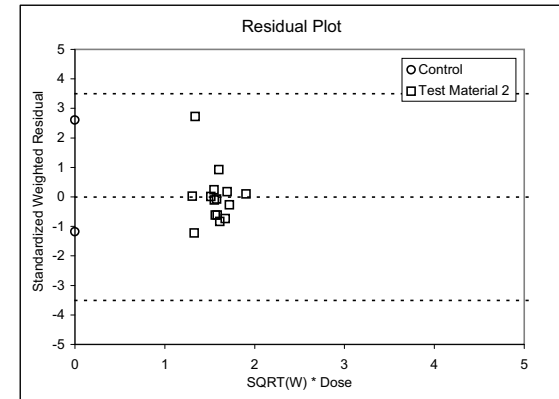
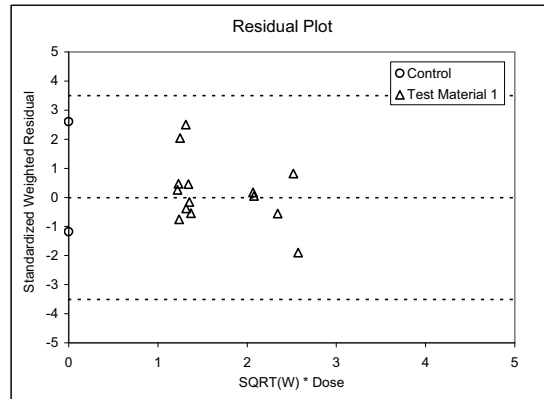
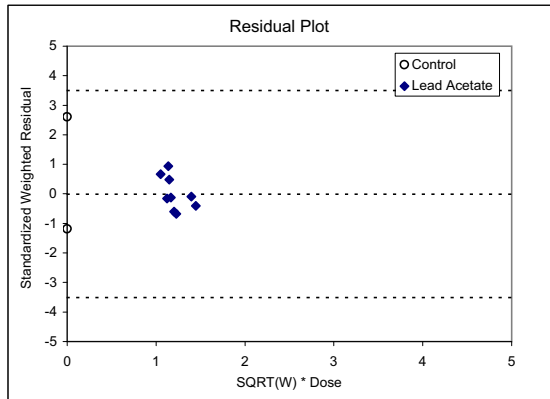
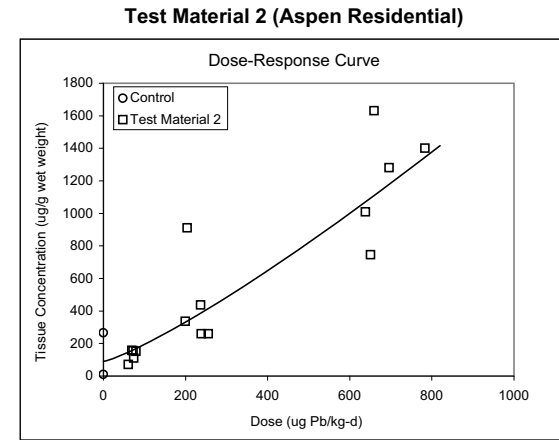
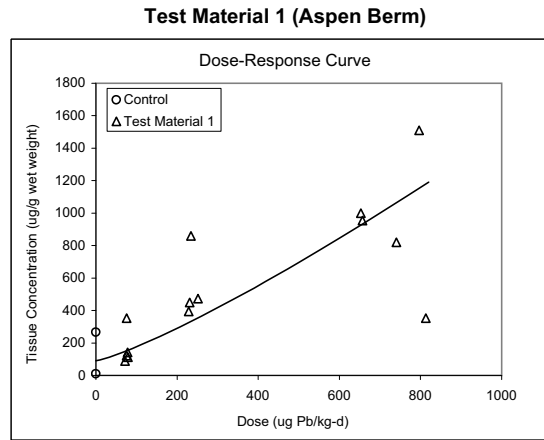
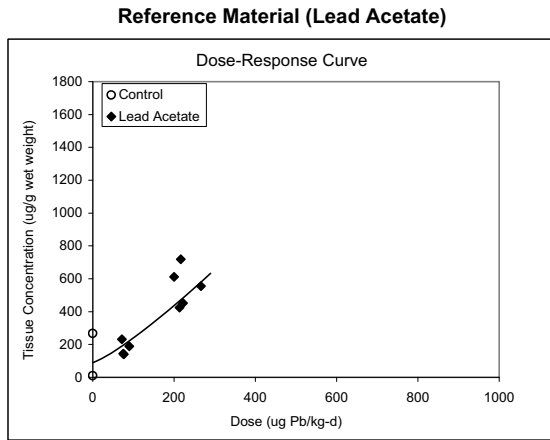
**NO SOLUTION**

The software could not find a solution,  
or the solution was unstable and/or had unrealistic parameter estimates.

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APPENDIX E

Figure 3d - All Data  
Phase II Experiment 5: Kidney  
Power Model:  $y = a + b_1 \cdot x_1^c + b_2 \cdot x_2^c + b_3 \cdot x_3^c$



**Summary of Fitting**

Parameter	Estimate	Standard Error
a	8.99E+01	4.32E+01
b1	5.81E-01	9.47E-01
b2	3.36E-01	6.35E-01
b3	4.05E-01	7.34E-01
c	1.21E+00	2.85E-01
Covariance (b1,b2)	0.9831	--
Covariance (b1,b3)	0.9834	--
Degrees of Freedom	35	--

**Goodness of Fit**

Statistic	Estimate
F	11.844
p	< 0.001
Adjusted R <sup>2</sup>	0.5266
AIC	548.008

**RBA and Uncertainty**

	Test Material 1	Test Material 2
RBA	0.64	0.74
Lower bound	?	?
Upper bound	?	?
Standard Error	--	--

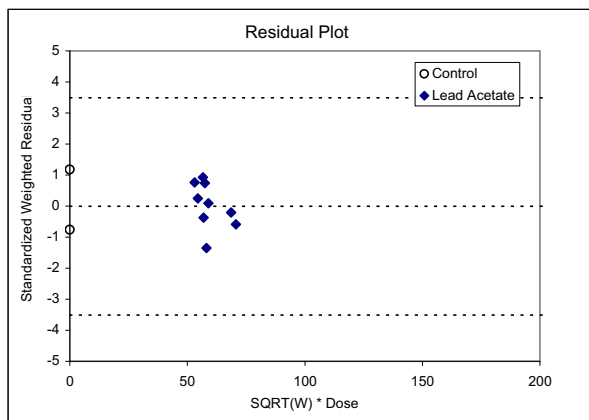
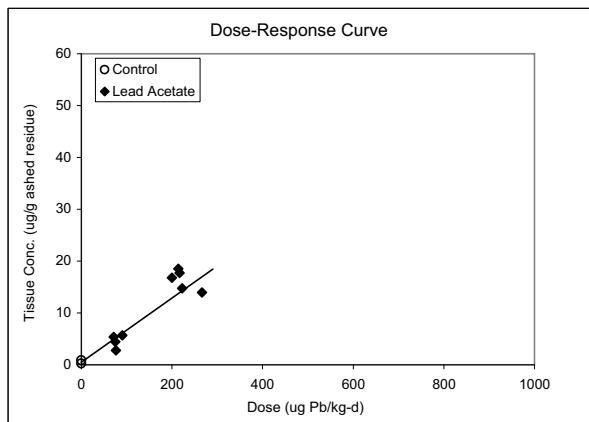
APPENDIX E

Figure 4a - All Data

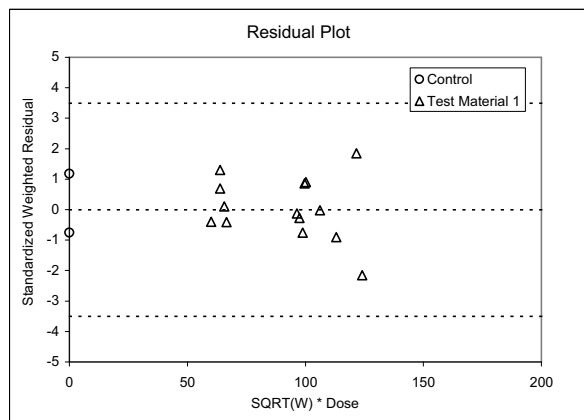
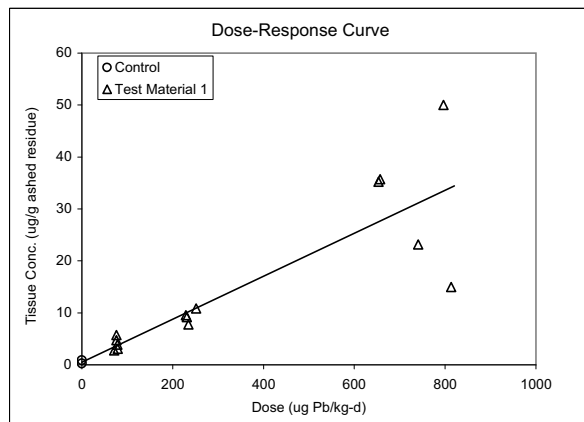
Phase II Experiment 5: Femur

Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$

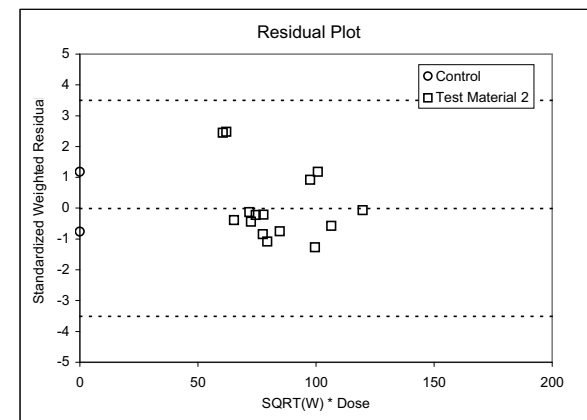
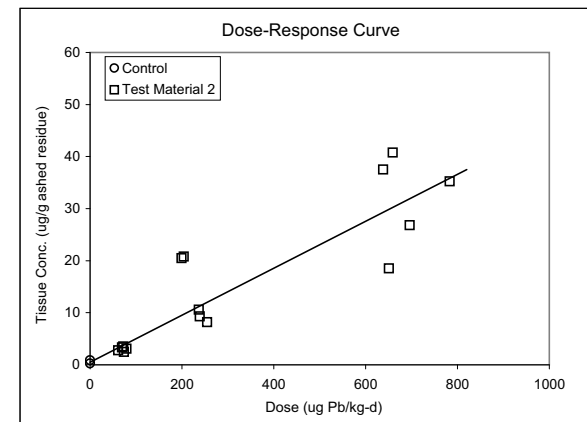
Reference Material (Lead Acetate)



Test Material 1 (Aspen Berm)



Test Material 2 (Aspen Residential)



Summary of Fitting

Parameter	Estimate	Standard Error
a	4.85E-01	2.13E-01
b1	6.19E-02	8.12E-03
b2	4.14E-02	4.15E-03
b3	4.51E-02	4.47E-03
Covariance (c1,c2)	0.0463	--
Covariance (c1,c3)	0.0555	--
Degrees of Freedom	36	--

Goodness of Fit

Statistic	Estimate
F	78.581
p	< 0.001
Adjusted R <sup>2</sup>	0.8565
AIC	221.181

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.67	0.73
Lower bound	0.51	0.56
Upper bound	0.89	0.97
Standard Error	0.108	0.117

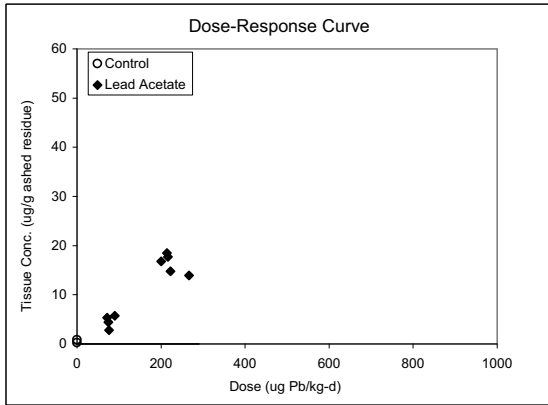
APPENDIX E

Figure 4b - All Data

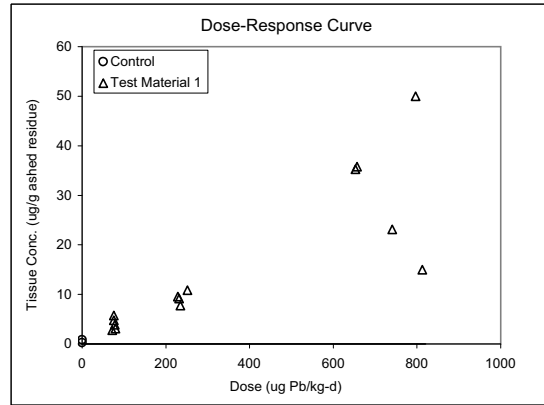
Phase II Experiment 5: Femur

Exponential Model:  $y = a + b*(1-\exp(-c1*x1))+b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$

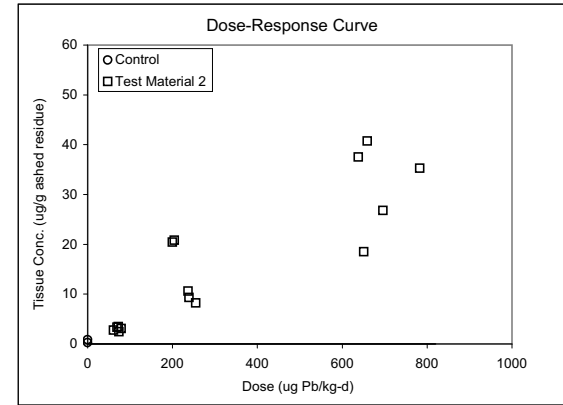
Reference Material (Lead Acetate)



Test Material 1 (Aspen Berm)



Test Material 2 (Aspen Residential)



**NO SOLUTION**

The software could not find a solution,  
or the solution was unstable and/or had unrealistic parameter estimates.

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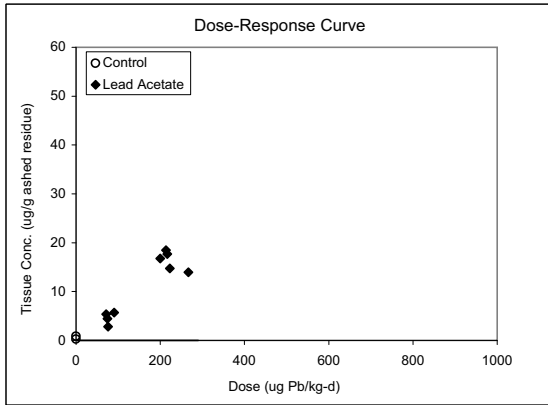
APPENDIX E

Figure 4c - All Data

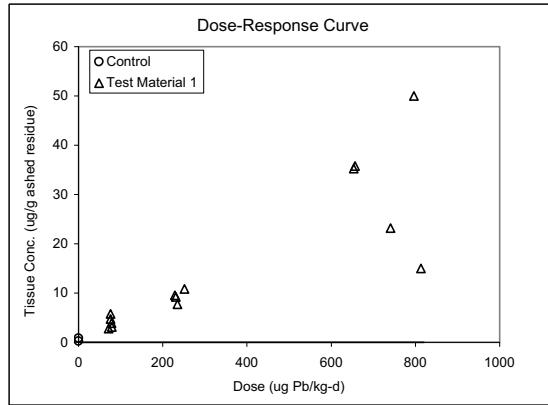
Phase II Experiment 5: Femur

Michaelis-Menton Model:  $y = a + b*x1/(c1+x1) + b*x2/(c2+x2) + b*x3/(c3+x3)$

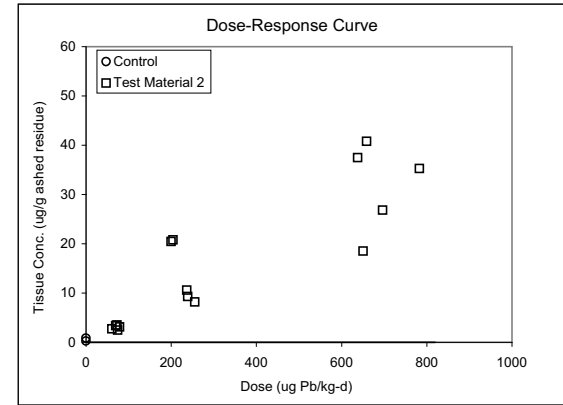
Reference Material (Lead Acetate)



Test Material 1 (Aspen Berm)



Test Material 2 (Aspen Residential)



**NO SOLUTION**

The software could not find a solution,  
or the solution was unstable and/or had unrealistic parameter estimates.

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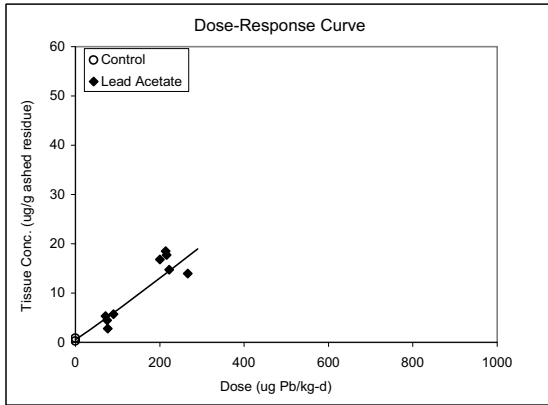
APPENDIX E

Figure 4d - All Data

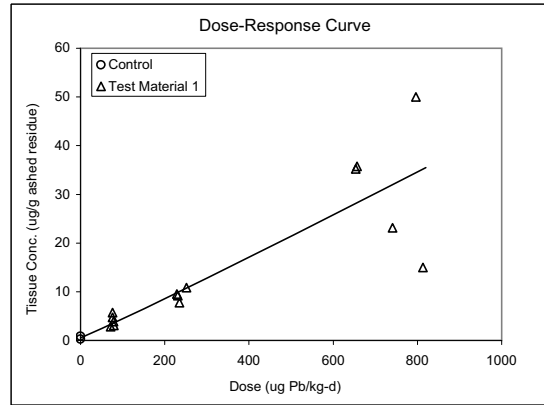
Phase II Experiment 5: Femur

Power Model:  $y = a + b1*x1^c + b2*x2^c + b3*x3^c$

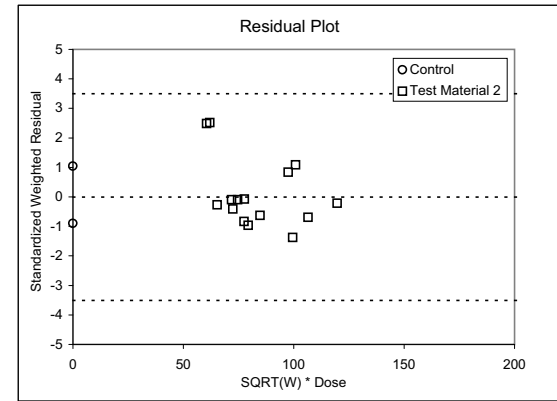
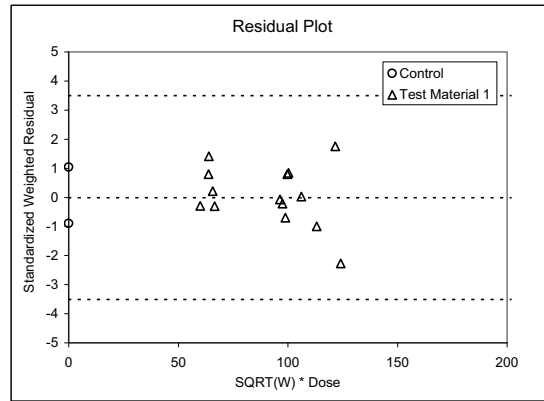
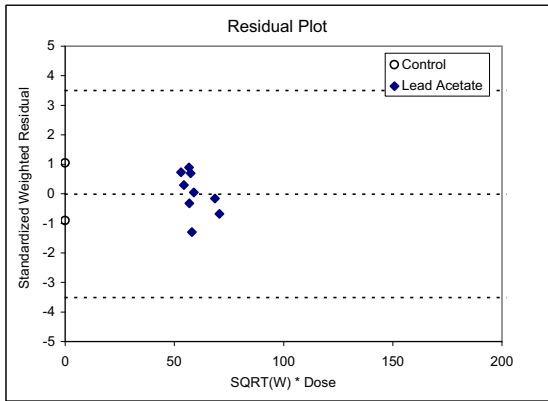
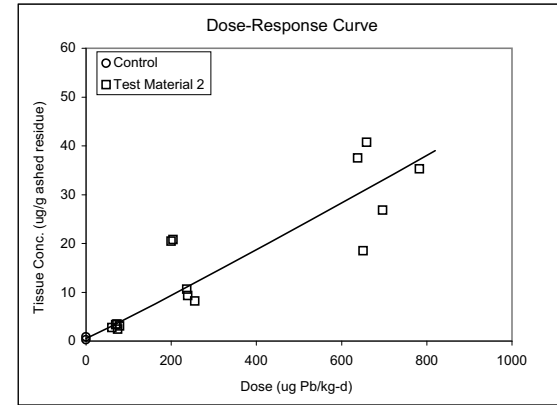
Reference Material (Lead Acetate)



Test Material 1 (Aspen Berm)



Test Material 2 (Aspen Residential)



Summary of Fitting

Parameter	Estimate	Standard Error
a	5.28E-01	2.29E-01
b1	5.00E-02	2.14E-02
b2	3.21E-02	1.57E-02
b3	3.53E-02	1.69E-02
c	1.04E+00	7.94E-02
Covariance (b1,b2)	0.9327	--
Covariance (b1,b3)	0.9328	--
Degrees of Freedom	35	--

Goodness of Fit

Statistic	Estimate
F	57.870
p	< 0.001
Adjusted R <sup>2</sup>	0.8536
AIC	222.558

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.65	0.72
Lower bound	0.33	0.39
Upper bound	0.88	0.97
Standard Error	--	--

## APPENDIX E

### EXPERIMENT 6

Test Material 1: Midvale Slag

Test Material 2: Butte Soil

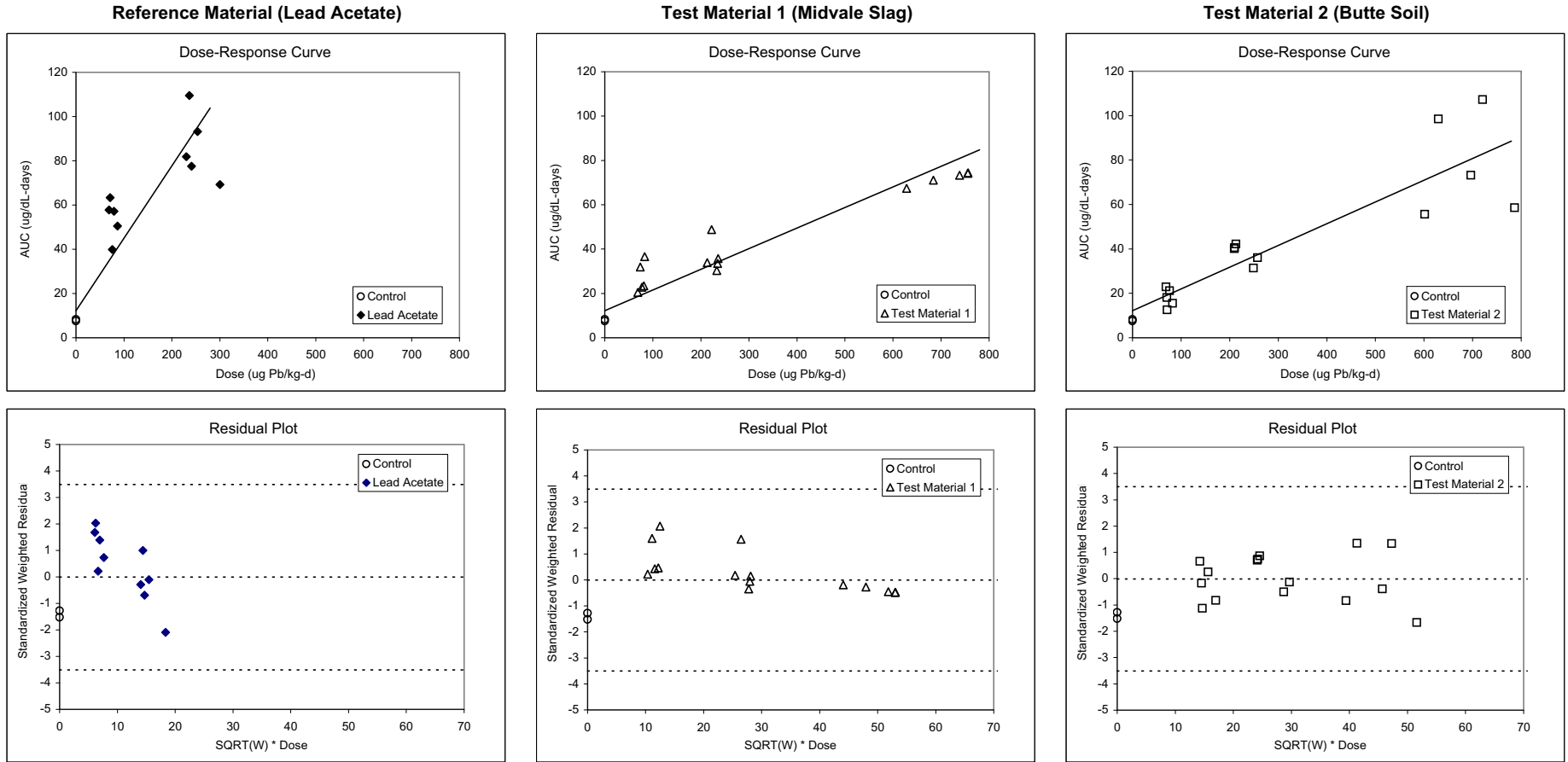
- Figure 1a Blood AUC - Linear Model
- Figure 1b Blood AUC - Exponential Model
- Figure 1c Blood AUC - Michaelis-Menton Model
- Figure 1d Blood AUC - Power Model
  
- Figure 2a Liver - Linear Model (All Data)
- Figure 2a Liver - Linear Model (Outlier Excluded)
- Figure 2b Liver - Exponential Model
- Figure 2c Liver - Michaelis-Menton Model
- Figure 2d Liver - Power Model
  
- Figure 3a Kidney - Linear Model (All Data)
- Figure 3a Kidney - Linear Model (Outlier Excluded)
- Figure 3b Kidney - Exponential Model
- Figure 3c Kidney - Michaelis-Menton Model
- Figure 3d Kidney - Power Model
  
- Figure 4a Femur - Linear Model
- Figure 4b Femur - Exponential Model
- Figure 4c Femur - Michaelis-Menton Model
- Figure 4d Femur - Power Model

APPENDIX E

Figure 1a - All Data

Phase II Experiment 6: Blood AUC

Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.22E+01	1.66E+00
b1	3.27E-01	3.47E-02
b2	9.31E-02	1.06E-02
b3	9.78E-02	1.15E-02
Covariance (c1,c2)	0.1007	--
Covariance (c1,c3)	0.1127	--
Degrees of Freedom	38	--

Goodness of Fit

Statistic	Estimate
F	63.445
p	< 0.001
Adjusted R <sup>2</sup>	0.8204
AIC	333.585

RBA and Uncertainty

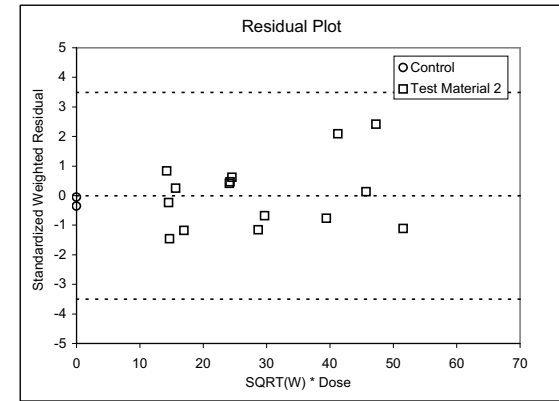
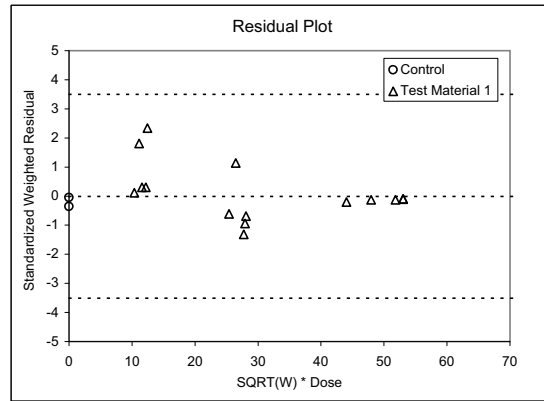
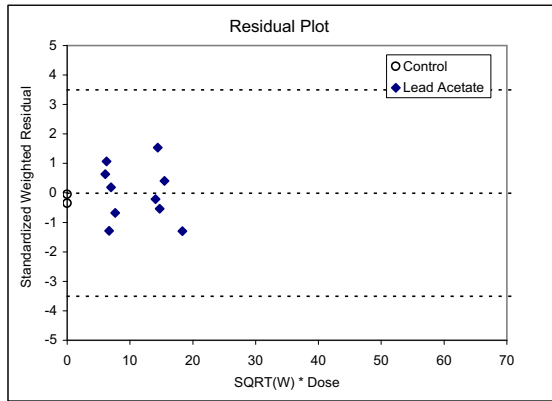
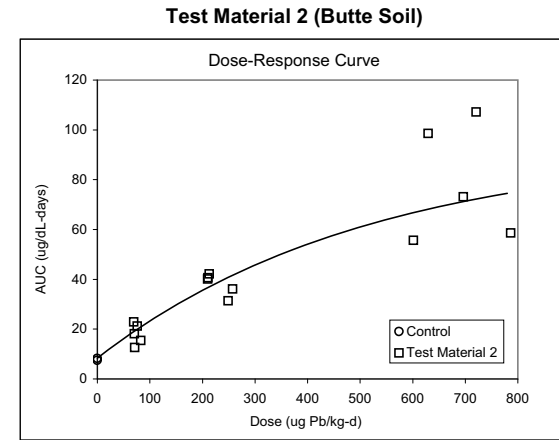
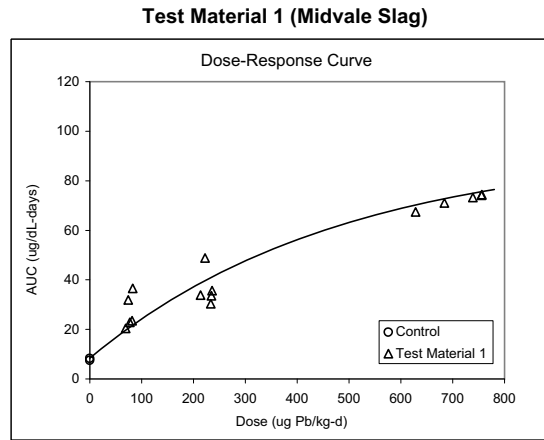
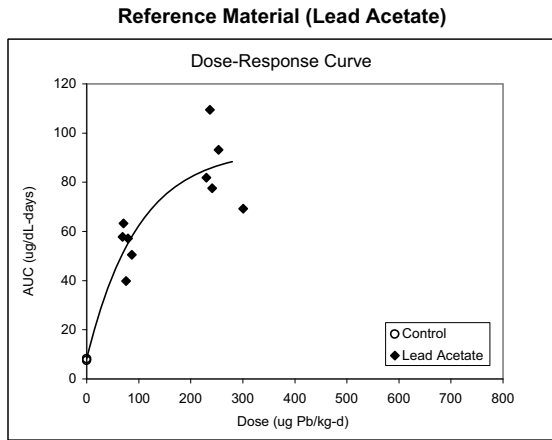
	Test Material 1	Test Material 2
RBA	0.28	0.30
Lower bound	0.22	0.23
Upper bound	0.36	0.38
Standard Error	0.042	0.045

APPENDIX E

Figure 1b - All Data

Phase II Experiment 6: Blood AUC

Exponential Model:  $y = a + b*(1-\exp(-c1*x1)) + b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$



Summary of Fitting

Parameter	Estimate	Standard Error
a	8.37E+00	1.61E+00
b	8.51E+01	9.89E+00
c1	1.01E-02	2.83E-03
c2	2.06E-03	4.66E-04
c3	1.93E-03	4.28E-04
Covariance (c1,c2)	0.7145	--
Covariance (c1,c3)	0.7021	--
Degrees of Freedom	37	--

Goodness of Fit

Statistic	Estimate
F	81.898
p	< 0.001
Adjusted R <sup>2</sup>	0.8875
AIC	311.830

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.21	0.19
Lower bound	0.15	0.14
Upper bound	0.31	0.29
Standard Error	0.041*	0.039*

\*  $g \geq 0.05$ , estimate is uncertain

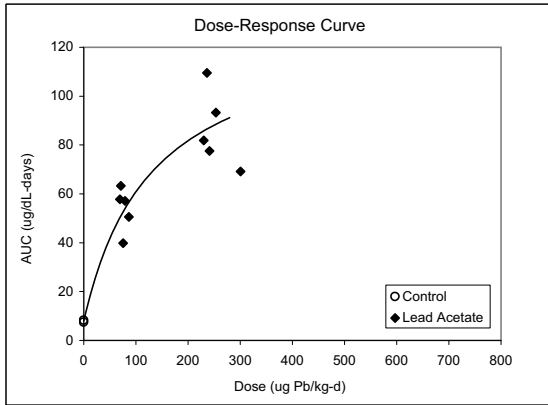
APPENDIX E

Figure 1c - All Data

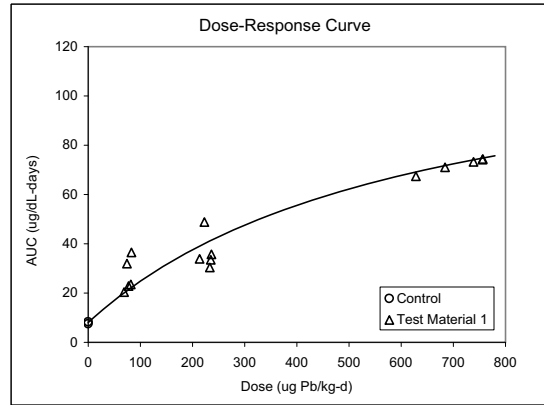
Phase II Experiment 6: Blood AUC

Michaelis-Menton Model:  $y = a + b \cdot x_1 / (c_1 + x_1) + b \cdot x_2 / (c_2 + x_2) + b \cdot x_3 / (c_3 + x_3)$

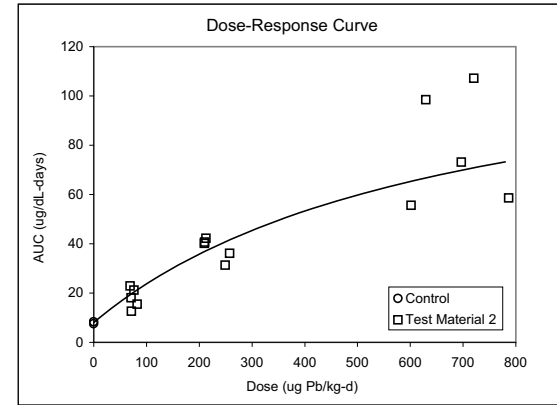
Reference Material (Lead Acetate)



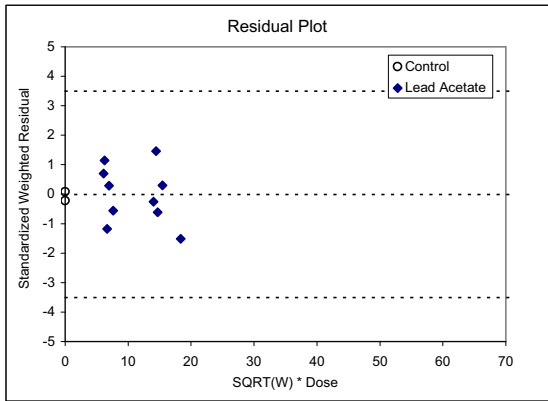
Test Material 1 (Midvale Slag)



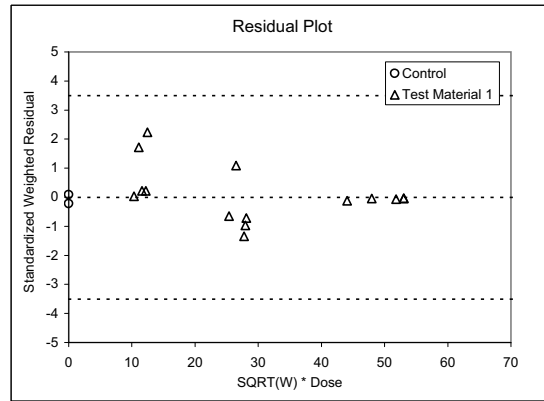
Test Material 2 (Butte Soil)



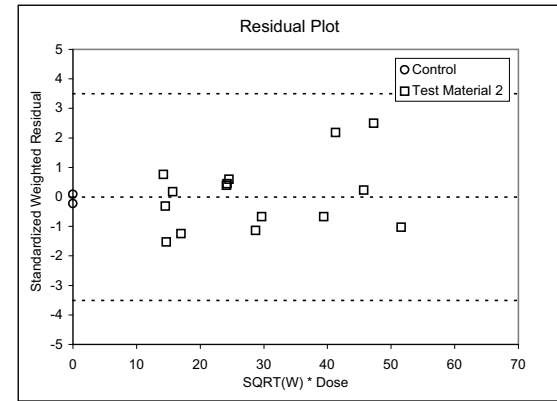
Residual Plot



Residual Plot



Residual Plot



Summary of Fitting

Parameter	Estimate	Standard Error
a	8.05E+00	1.68E+00
b	1.22E+02	2.01E+01
c1	1.31E+02	4.96E+01
c2	6.26E+02	1.91E+02
c3	6.79E+02	2.01E+02
Covariance (c1,c2)	0.8466	--
Covariance (c1,c3)	0.8359	--
Degrees of Freedom	37	--

Goodness of Fit

Statistic	Estimate
F	80.706
p	< 0.001
Adjusted R <sup>2</sup>	0.8861
AIC	312.322

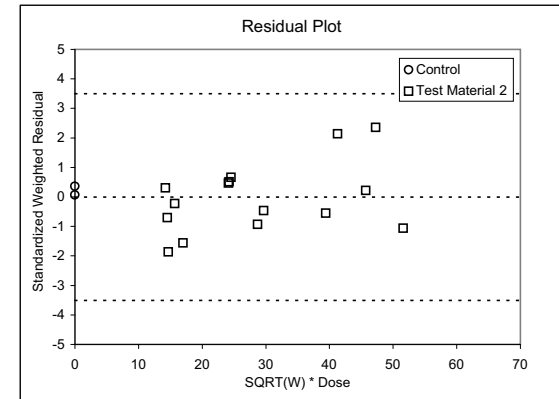
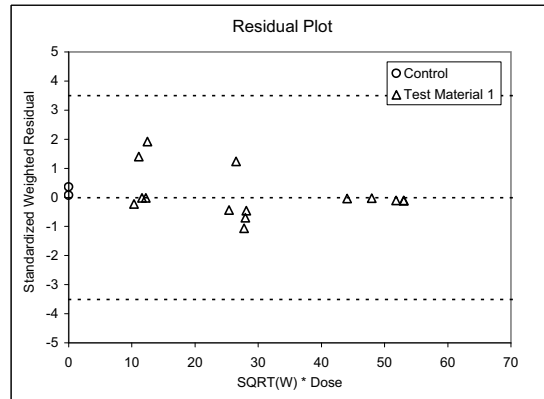
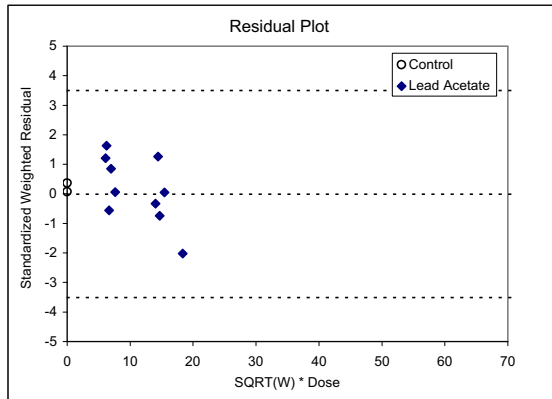
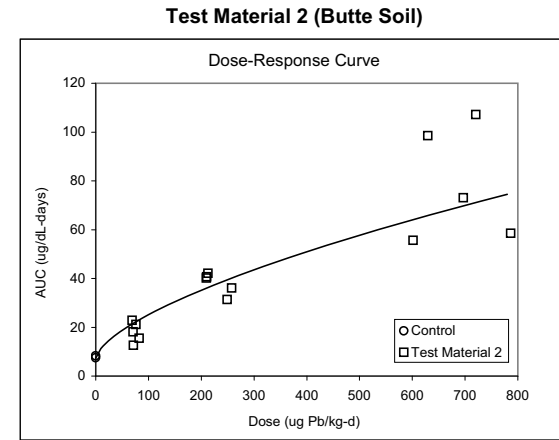
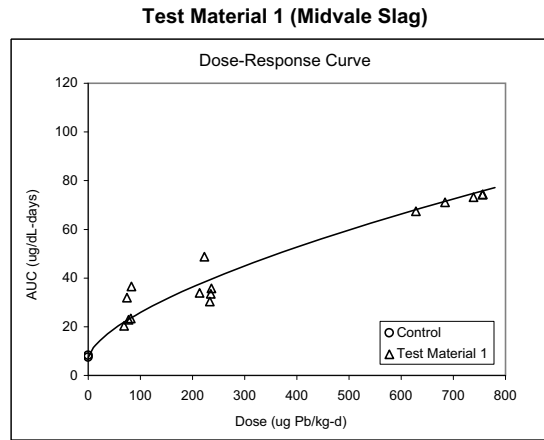
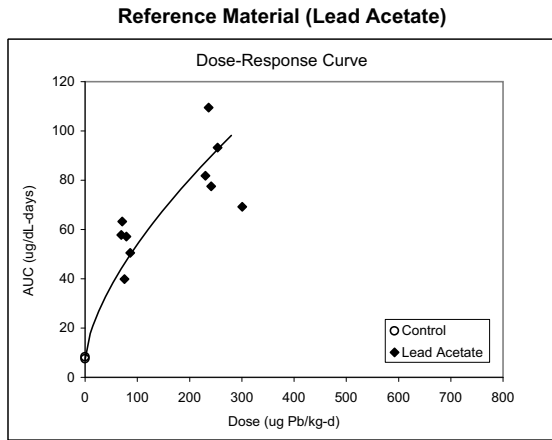
RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.21	0.19
Lower bound	0.12	0.11
Upper bound	0.29	0.27
Standard Error	0.042*	0.040*

\*  $g \geq 0.05$ , estimate is uncertain

APPENDIX E

**Figure 1d - All Data**  
**Phase II Experiment 6: Blood AUC**  
**Power Model:  $y = a + b_1 \cdot x_1^c + b_2 \cdot x_2^c + b_3 \cdot x_3^c$**



**Summary of Fitting**

Parameter	Estimate	Standard Error
a	7.32E+00	1.88E+00
b1	2.38E+00	8.92E-01
b2	9.43E-01	4.10E-01
b3	9.06E-01	3.88E-01
c	6.47E-01	6.78E-02
Covariance (b1,b2)	0.9646	--
Covariance (b1,b3)	0.9617	--
Degrees of Freedom	37	--

**Goodness of Fit**

Statistic	Estimate
F	72.563
p	< 0.001
Adjusted R <sup>2</sup>	0.8747
AIC	316.066

**RBA and Uncertainty**

	Test Material 1	Test Material 2
RBA	0.24	0.23
Lower bound	0.12	0.12
Upper bound	0.32	0.30
Standard Error	--	--

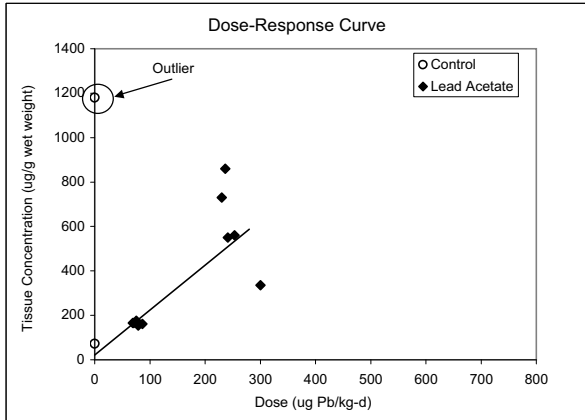
APPENDIX E

Figure 2a - All Data

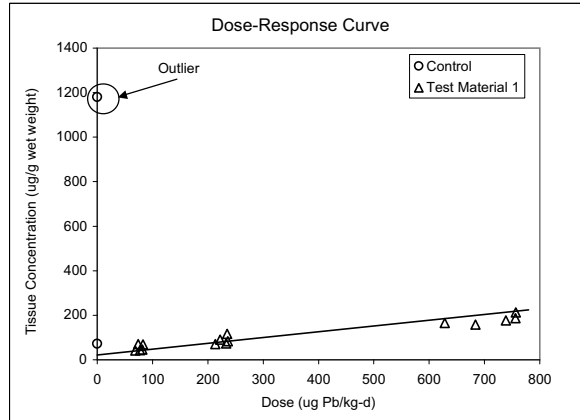
Phase II Experiment 6: Liver

Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$

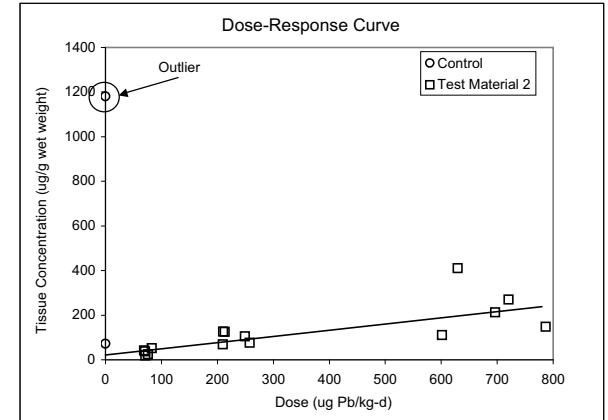
Reference Material (Lead Acetate)



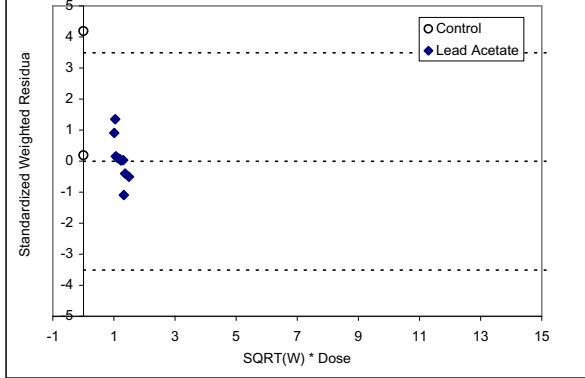
Test Material 1 (Midvale Slag)



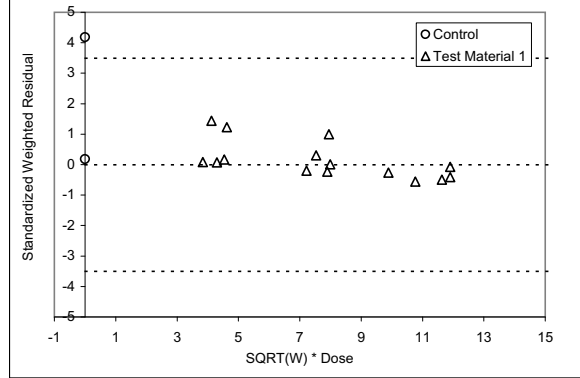
Test Material 2 (Butte Soil)



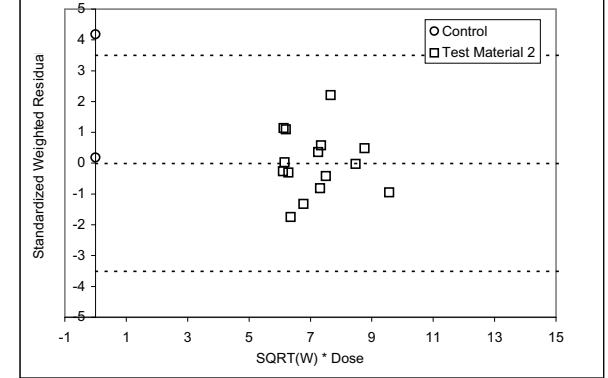
Residual Plot



Residual Plot



Residual Plot



Summary of Fitting

Parameter	Estimate	Standard Error
a	2.13E+01	6.97E+00
b1	2.02E+00	3.28E-01
b2	2.60E-01	4.52E-02
b3	2.78E-01	5.87E-02
Covariance (c1,c2)	0.1005	--
Covariance (c1,c3)	0.1298	--
Degrees of Freedom	38	--

Goodness of Fit

Statistic	Estimate
F	23.514
p	< 0.001
Adjusted R <sup>2</sup>	0.6223
AIC	468.374

RBA and Uncertainty

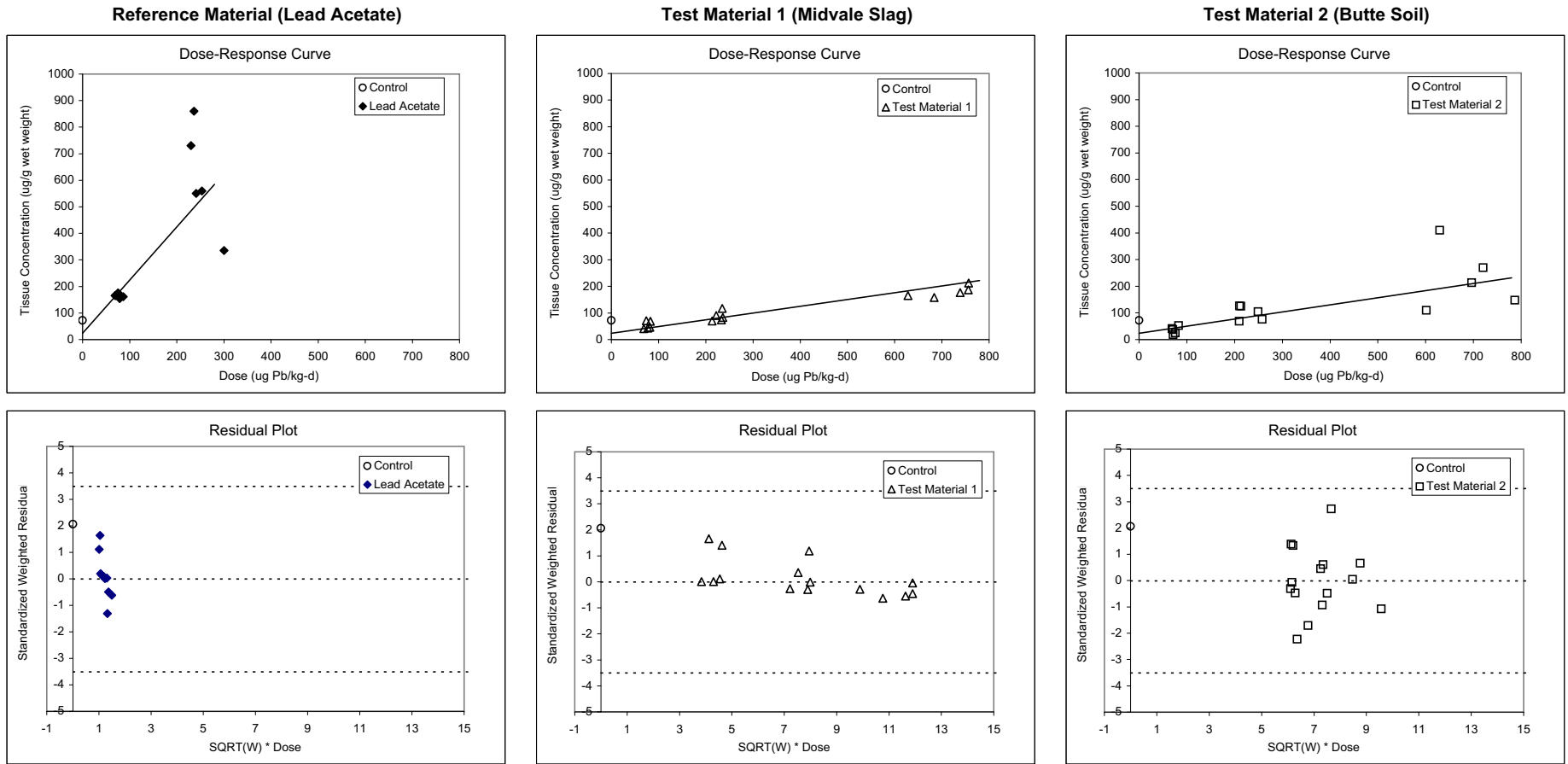
	Test Material 1	Test Material 2
RBA	0.13	0.14
Lower bound	0.09	0.09
Upper bound	0.19	0.21
Standard Error	0.029*	0.034*

\*  $g \geq 0.05$ , estimate is uncertain



APPENDIX E

**Figure 2a - Outlier Excluded**  
**Phase II Experiment 6: Liver**  
**Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$**



**Summary of Fitting**

Parameter	Estimate	Standard Error
a	2.33E+01	5.58E+00
b1	2.00E+00	2.69E-01
b2	2.54E-01	3.69E-02
b3	2.67E-01	4.77E-02
Covariance (c1,c2)	0.0962	--
Covariance (c1,c3)	0.1248	--
Degrees of Freedom	37	--

**Goodness of Fit**

Statistic	Estimate
F	34.108
p	< 0.001
Adjusted R <sup>2</sup>	0.7129
AIC	430.977

**RBA and Uncertainty**

	Test Material 1	Test Material 2
RBA	0.13	0.13
Lower bound	0.09	0.09
Upper bound	0.17	0.19
Standard Error	0.024*	0.028*

\*g ≥ 0.05, estimate is uncertain

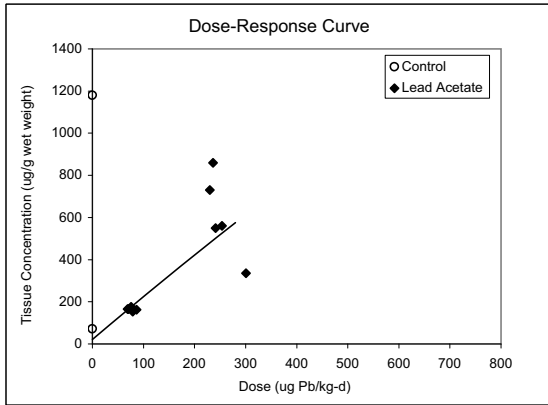
APPENDIX E

Figure 2b - All Data

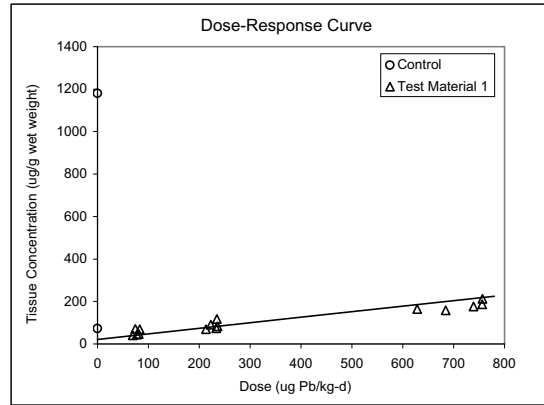
Phase II Experiment 6: Liver

Exponential Model:  $y = a + b*(1-\exp(-c1*x1))+b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$

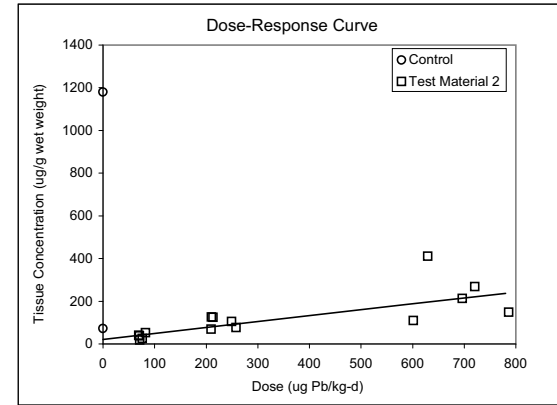
Reference Material (Lead Acetate)



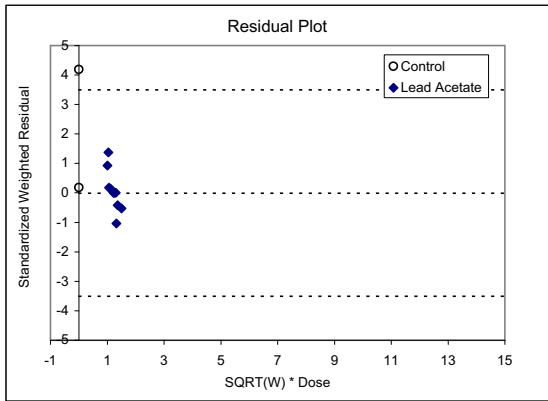
Test Material 1 (Midvale Slag)



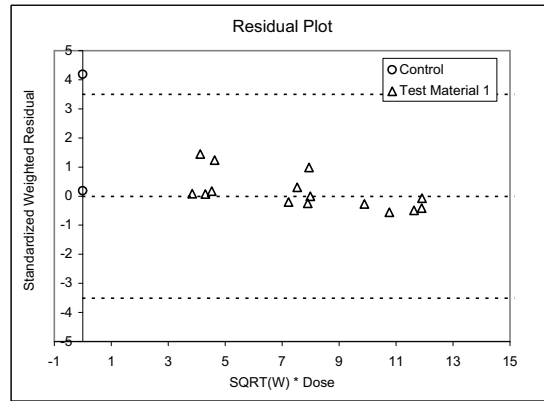
Test Material 2 (Butte Soil)



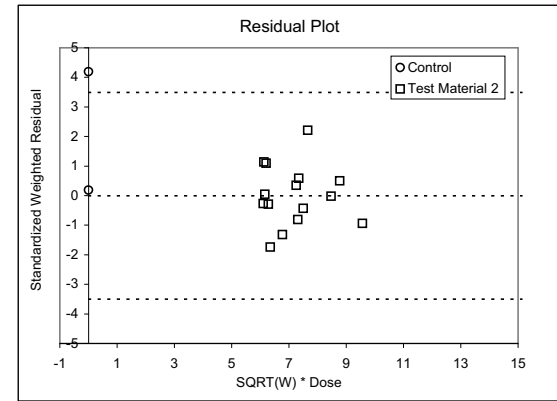
Residual Plot



Residual Plot



Residual Plot



Summary of Fitting

Parameter	Estimate	Standard Error
a	2.10E+01	8.24E+00
b	6.21E+03	6.55E+04
c1	3.33E-04	3.63E-03
c2	4.26E-05	4.60E-04
c3	4.55E-05	4.91E-04
Covariance (c1,c2)	0.9998	--
Covariance (c1,c3)	0.9997	--
Degrees of Freedom	37	--

Goodness of Fit

Statistic	Estimate
F	17.178
p	< 0.001
Adjusted R <sup>2</sup>	0.6121
AIC	470.359

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.13	0.14
Lower bound	?	?
Upper bound	?	?
Standard Error	0.031*	0.039*

\*  $g \geq 0.05$ , estimate is uncertain

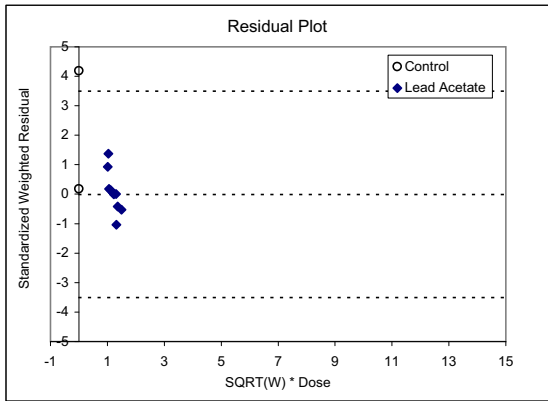
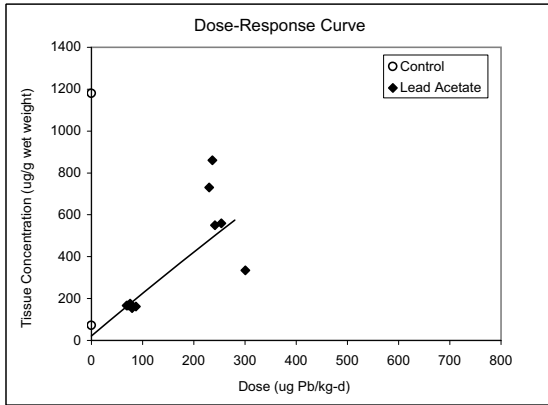
APPENDIX E

Figure 2c - All Data

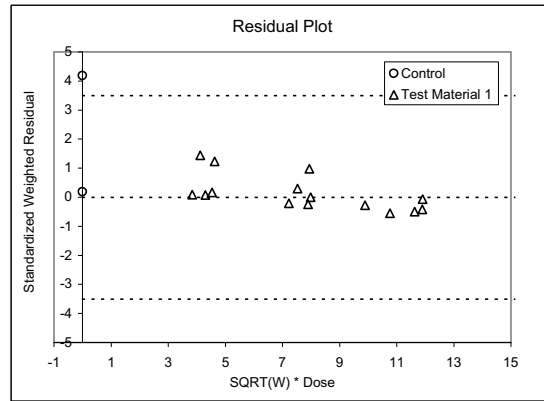
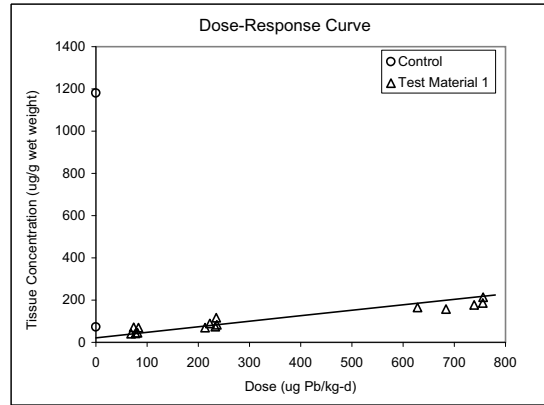
Phase II Experiment 6: Liver

Michaelis-Menton Model:  $y = a + b \cdot x_1 / (c_1 + x_1) + b \cdot x_2 / (c_2 + x_2) + b \cdot x_3 / (c_3 + x_3)$

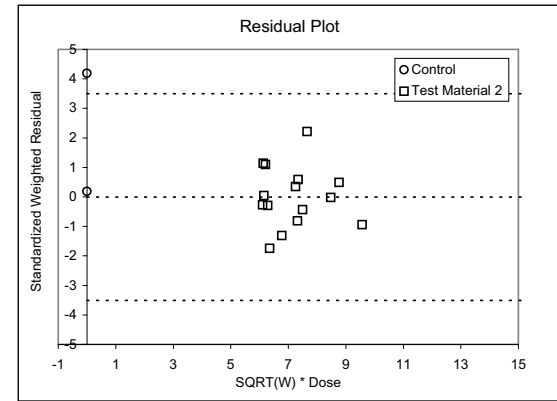
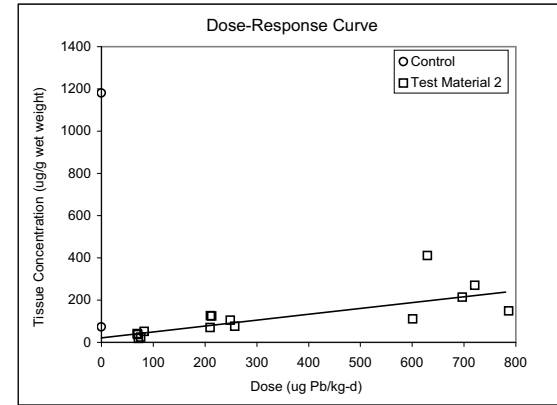
Reference Material (Lead Acetate)



Test Material 1 (Midvale Slag)



Test Material 2 (Butte Soil)



Summary of Fitting

Parameter	Estimate	Standard Error
a	2.09E+01	8.29E+00
b	1.21E+04	1.27E+05
c1	5.82E+03	6.29E+04
c2	4.55E+04	4.86E+05
c3	4.27E+04	4.57E+05
Covariance (c1,c2)	0.9998	--
Covariance (c1,c3)	0.9997	--
Degrees of Freedom	37	--

Goodness of Fit

Statistic	Estimate
F	17.178
p	< 0.001
Adjusted R <sup>2</sup>	0.6122
AIC	470.359

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.13	0.14
Lower bound	?	?
Upper bound	?	?
Standard Error	0.031*	0.039*

\*  $g \geq 0.05$ , estimate is uncertain

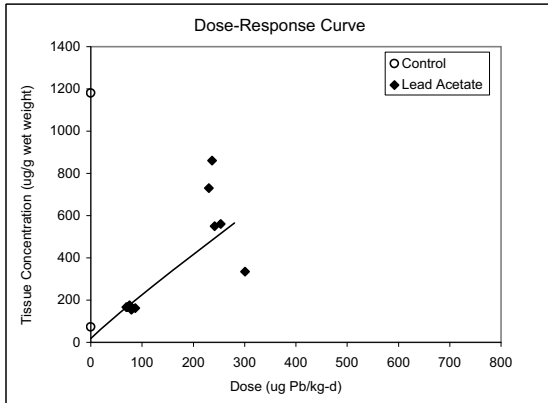
APPENDIX E

Figure 2d - All Data

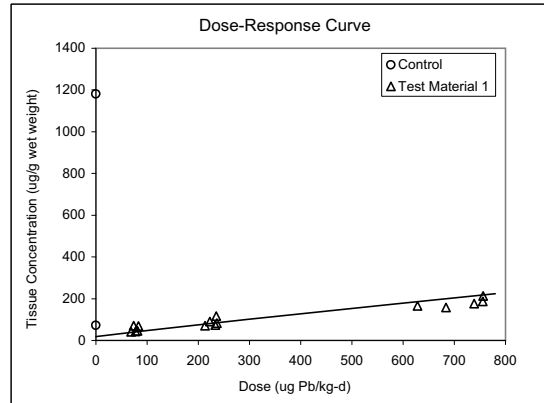
Phase II Experiment 6: Liver

Power Model:  $y = a + b_1 \cdot x_1^c + b_2 \cdot x_2^c + b_3 \cdot x_3^c$

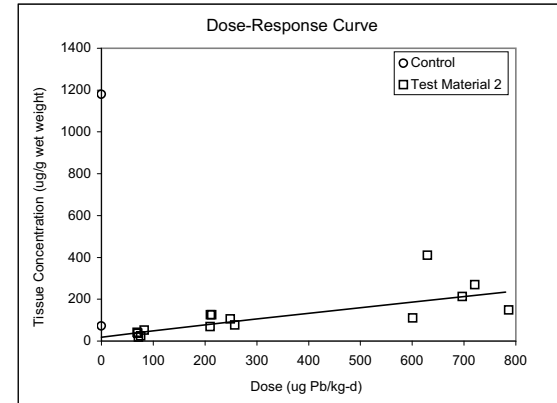
Reference Material (Lead Acetate)



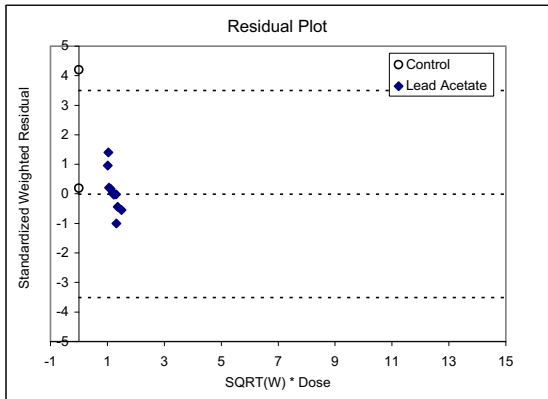
Test Material 1 (Midvale Slag)



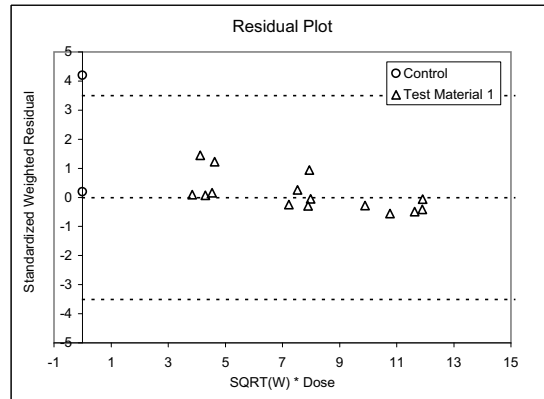
Test Material 2 (Butte Soil)



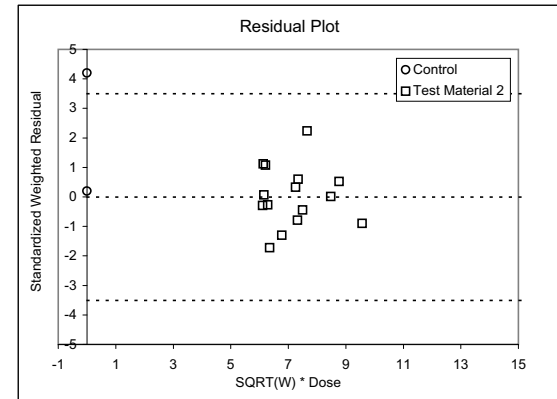
Residual Plot



Residual Plot



Residual Plot



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.81E+01	1.76E+01
b1	2.70E+00	3.63E+00
b2	3.86E-01	6.87E-01
b3	4.05E-01	7.20E-01
c	9.43E-01	2.62E-01
Covariance (b1,b2)	0.9893	--
Covariance (b1,b3)	0.9877	--
Degrees of Freedom	37	--

Goodness of Fit

Statistic	Estimate
F	17.205
p	< 0.001
Adjusted R <sup>2</sup>	0.6126
AIC	470.299

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.13	0.13
Lower bound	?	?
Upper bound	?	?
Standard Error	--	--

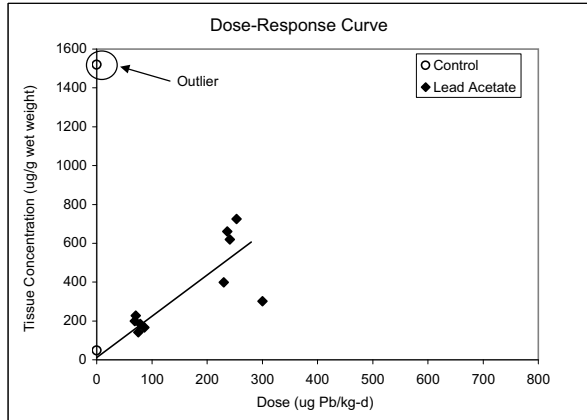
APPENDIX E

Figure 3a - All Data

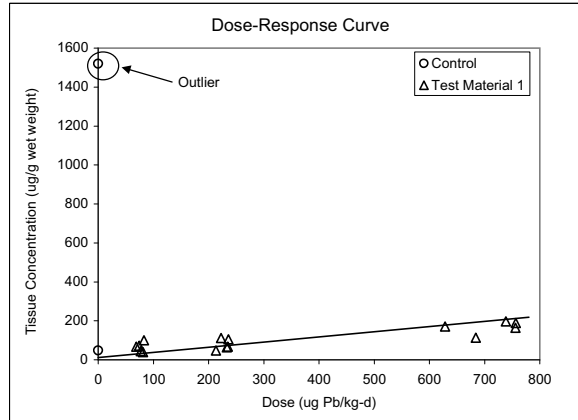
Phase II Experiment 6: Kidney

Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$

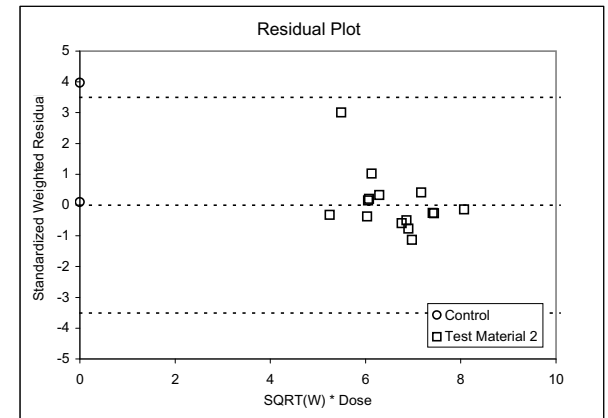
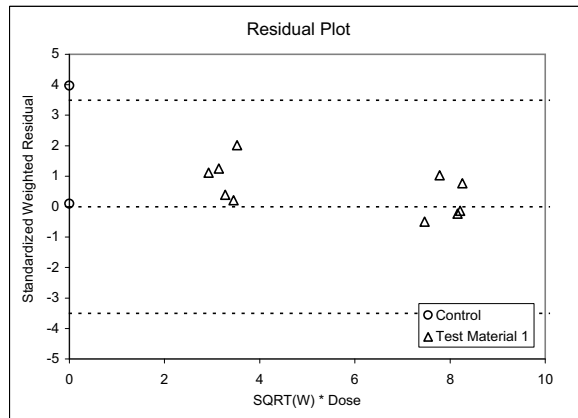
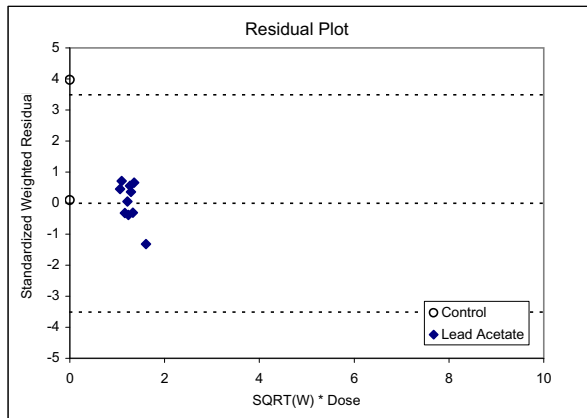
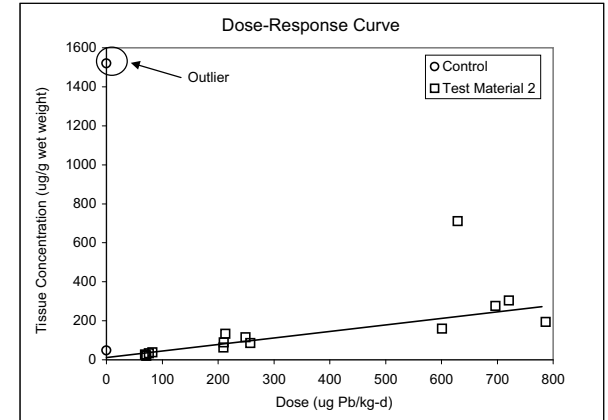
Reference Material (Lead Acetate)



Test Material 1 (Midvale Slag)



Test Material 2 (Butte Soil)



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.15E+01	9.29E+00
b1	2.12E+00	3.83E-01
b2	2.64E-01	5.24E-02
b3	3.34E-01	8.87E-02
Covariance (c1,c2)	0.0947	--
Covariance (c1,c3)	0.1423	--
Degrees of Freedom	38	--

Goodness of Fit

Statistic	Estimate
F	17.831
p	< 0.001
Adjusted R <sup>2</sup>	0.5519
AIC	500.260

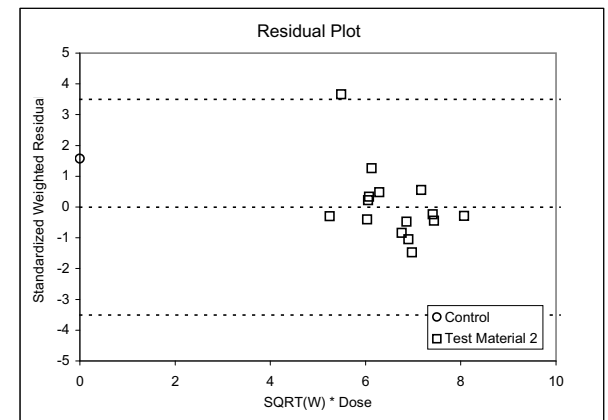
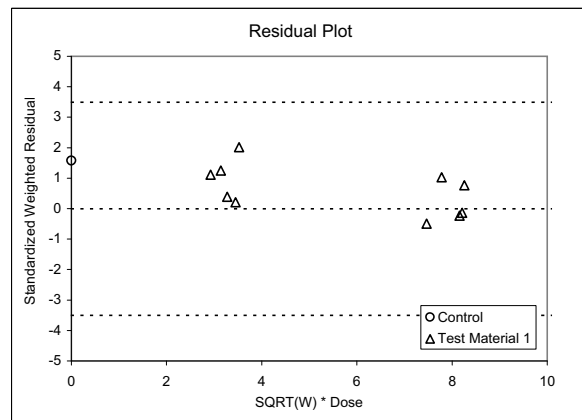
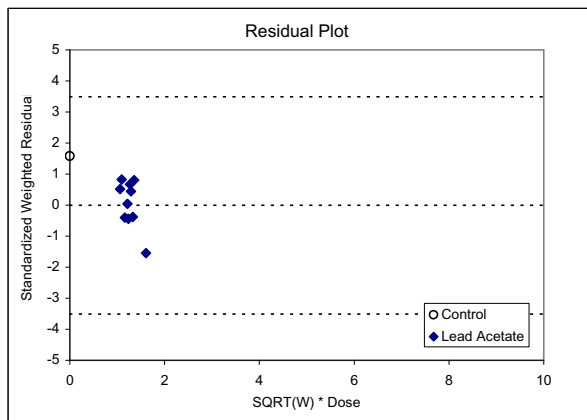
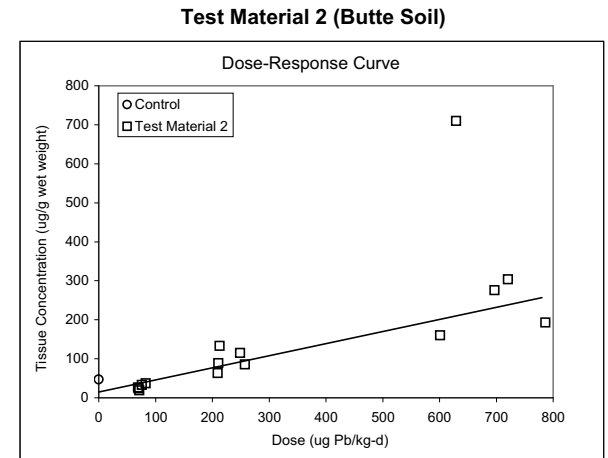
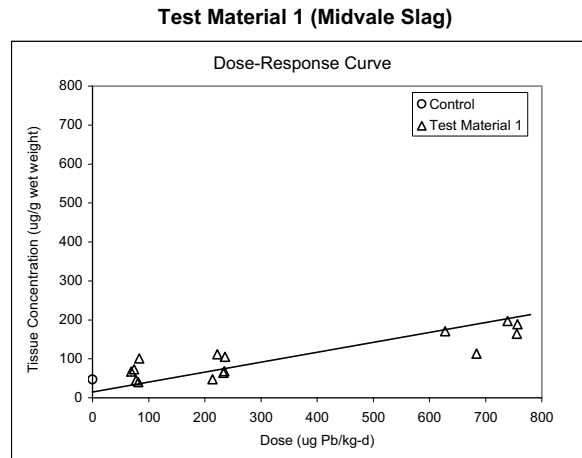
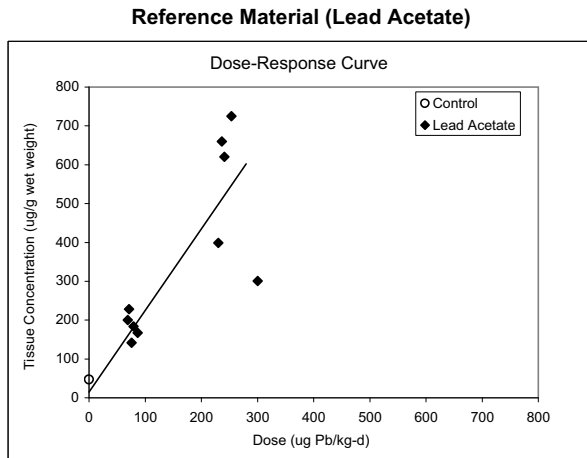
RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.12	0.16
Lower bound	0.08	0.09
Upper bound	0.19	0.25
Standard Error	0.032*	0.047*

\*  $g \geq 0.05$ , estimate is uncertain

APPENDIX E

**Figure 3a - Outlier Excluded**  
**Phase II Experiment 6: Kidney**  
**Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$**



**Summary of Fitting**

Parameter	Estimate	Standard Error
a	1.49E+01	7.31E+00
b1	2.10E+00	3.19E-01
b2	2.55E-01	4.32E-02
b3	3.10E-01	7.17E-02
Covariance (c1,c2)	0.0853	--
Covariance (c1,c3)	0.1306	--
Degrees of Freedom	37	--

**Goodness of Fit**

Statistic	Estimate
F	25.046
p	< 0.001
Adjusted R <sup>2</sup>	0.6433
AIC	454.018

**RBA and Uncertainty**

	Test Material 1	Test Material 2
RBA	0.12	0.15
Lower bound	0.08	0.09
Upper bound	0.18	0.22
Standard Error	0.026*	0.038*

\*  $g \geq 0.05$ , estimate is uncertain

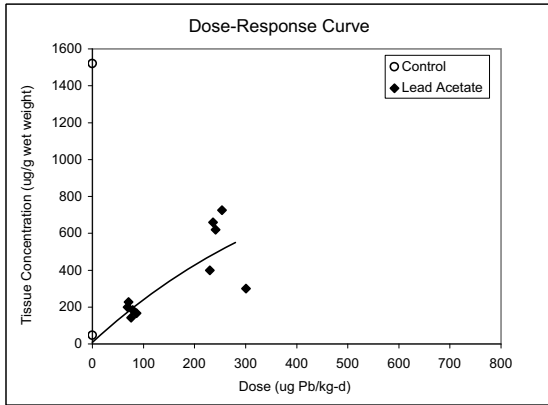
APPENDIX E

Figure 3b - All Data

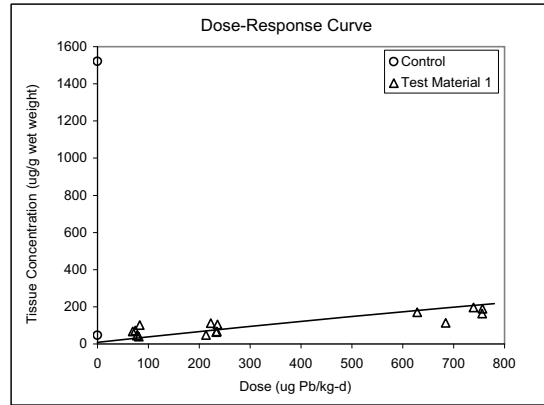
Phase II Experiment 6: Kidney

Exponential Model:  $y = a + b*(1-\exp(-c1*x1))+b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$

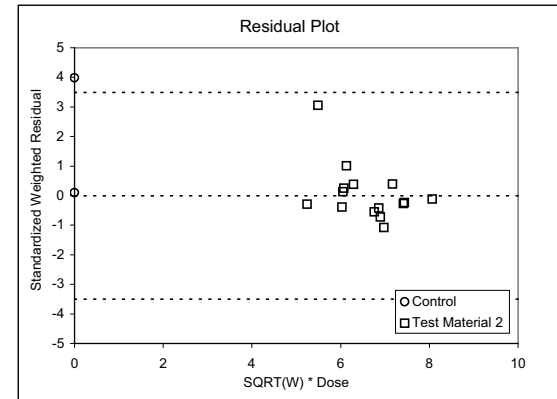
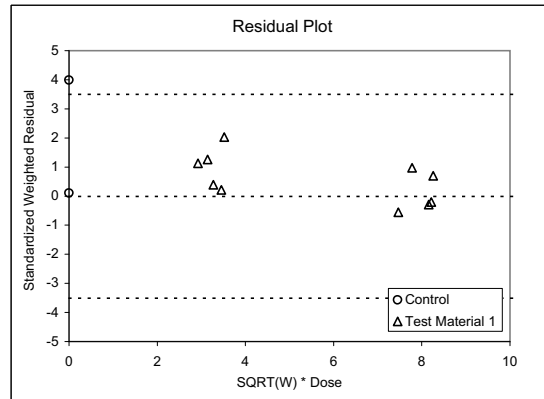
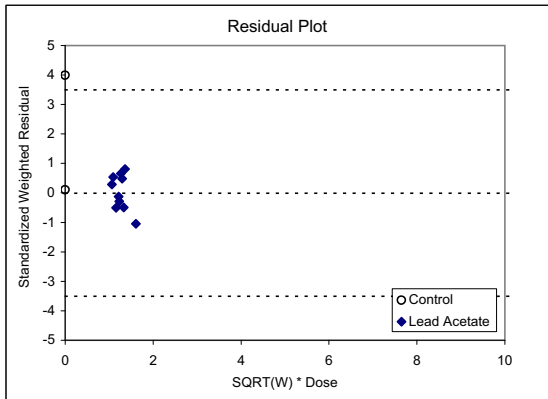
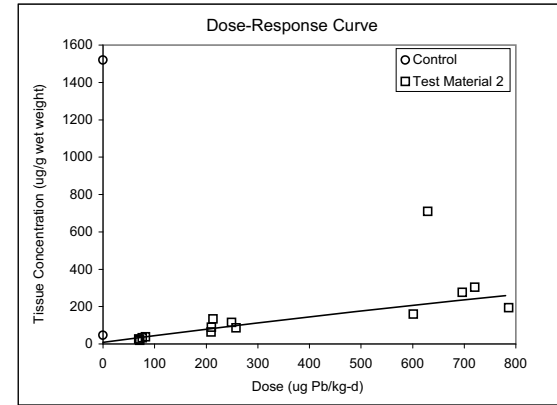
Reference Material (Lead Acetate)



Test Material 1 (Midvale Slag)



Test Material 2 (Butte Soil)



Summary of Fitting

Parameter	Estimate	Standard Error
a	9.36E+00	1.13E+01
b	1.21E+03	2.10E+03
c1	2.12E-03	4.39E-03
c2	2.42E-04	4.64E-04
c3	2.97E-04	5.74E-04
Covariance (c1,c2)	0.9899	--
Covariance (c1,c3)	0.9860	--
Degrees of Freedom	37	--

Goodness of Fit

Statistic	Estimate
F	13.189
p	< 0.001
Adjusted R <sup>2</sup>	0.5432
AIC	501.614

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.11	0.14
Lower bound	?	?
Upper bound	?	?
Standard Error	0.037*	0.051*

\*  $g \geq 0.05$ , estimate is uncertain

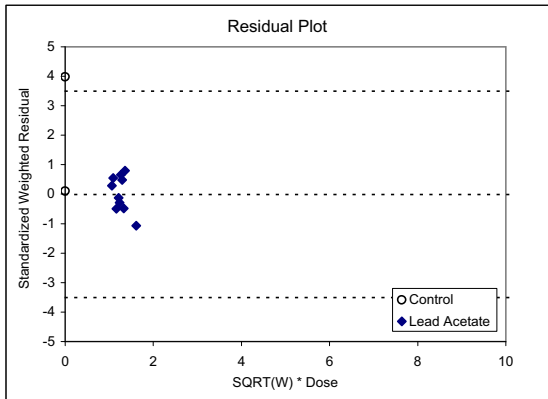
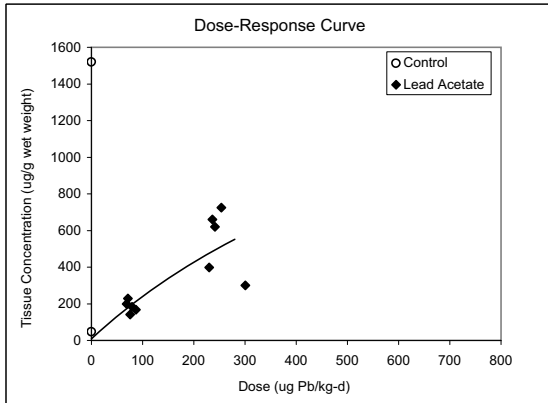
APPENDIX E

Figure 3c - All Data

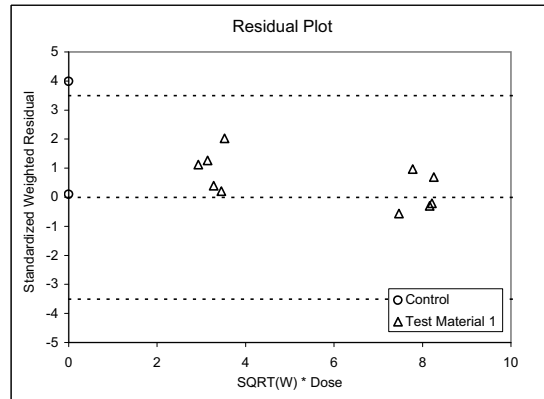
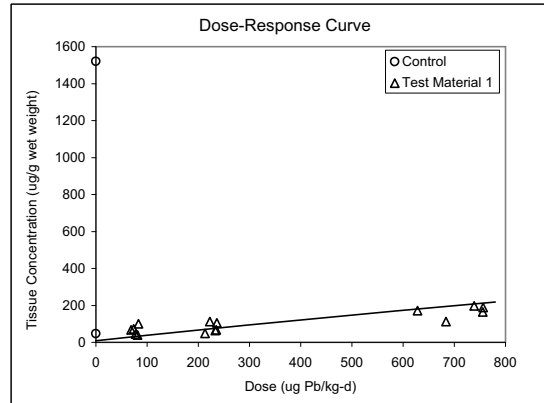
Phase II Experiment 6: Kidney

Michaelis-Menton Model:  $y = a + b \cdot x_1 / (c_1 + x_1) + b \cdot x_2 / (c_2 + x_2) + b \cdot x_3 / (c_3 + x_3)$

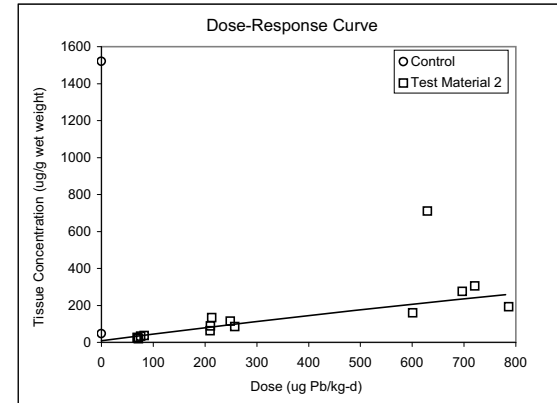
Reference Material (Lead Acetate)



Test Material 1 (Midvale Slag)



Test Material 2 (Butte Soil)



Summary of Fitting

Parameter	Estimate	Standard Error
a	9.28E+00	1.16E+01
b	2.22E+03	4.40E+03
c1	8.66E+02	2.04E+03
c2	7.54E+03	1.65E+04
c3	6.17E+03	1.36E+04
Covariance (c1,c2)	0.9923	--
Covariance (c1,c3)	0.9893	--
Degrees of Freedom	37	--

Goodness of Fit

Statistic	Estimate
F	13.183
p	< 0.001
Adjusted R <sup>2</sup>	0.5431
AIC	501.637

RBA and Uncertainty

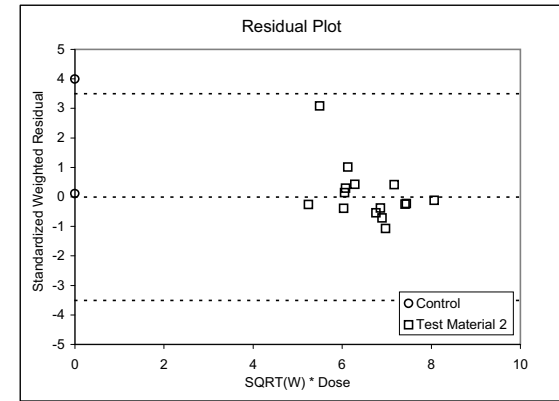
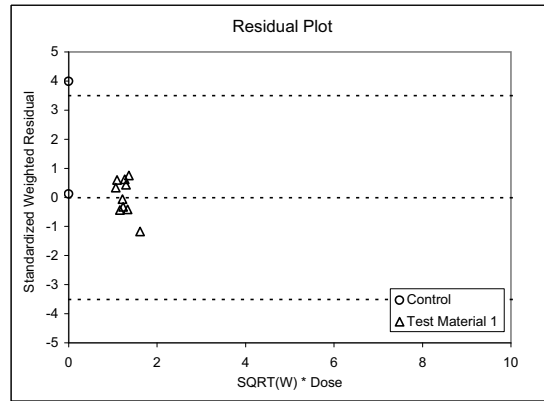
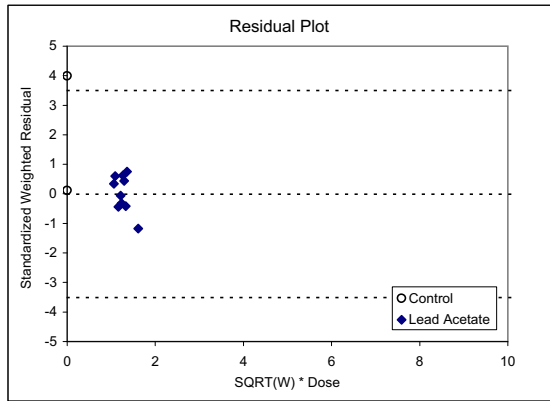
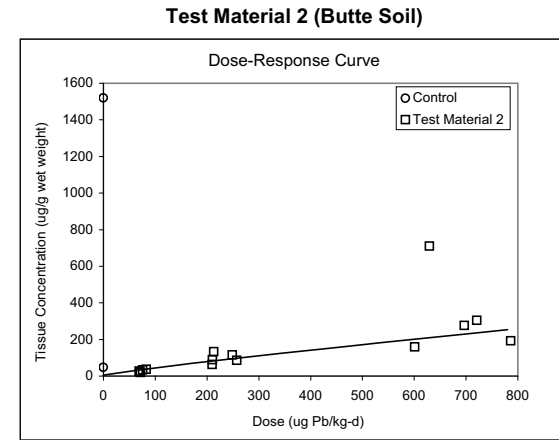
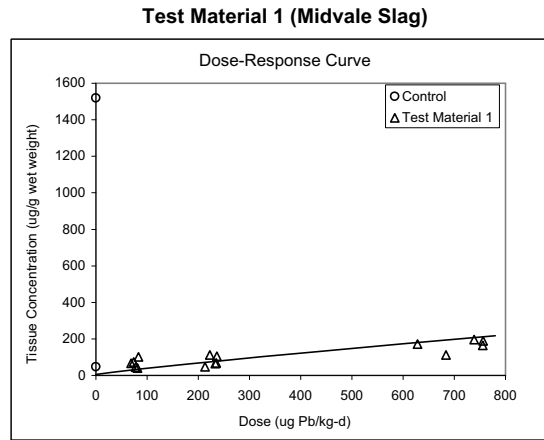
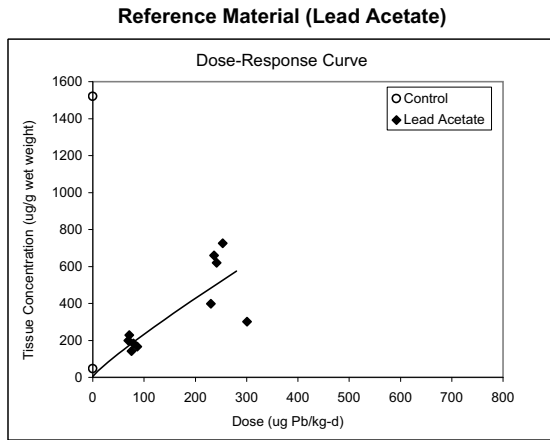
	Test Material 1	Test Material 2
RBA	0.11	0.14
Lower bound	?	?
Upper bound	?	?
Standard Error	0.037*	0.051*

\*  $g \geq 0.05$ , estimate is uncertain



APPENDIX E

**Figure 3d - All Data**  
**Phase II Experiment 6: Kidney**  
**Power Model:  $y = a + b_1 \cdot x_1^c + b_2 \cdot x_2^c + b_3 \cdot x_3^c$**



**Summary of Fitting**

Parameter	Estimate	Standard Error
a	5.15E+00	2.47E+01
b1	3.77E+00	5.85E+00
b2	5.63E-01	1.14E+00
b3	6.58E-01	1.31E+00
c	8.91E-01	2.94E-01
Covariance (b1,b2)	0.9901	--
Covariance (b1,b3)	0.9869	--
Degrees of Freedom	37	--

**Goodness of Fit**

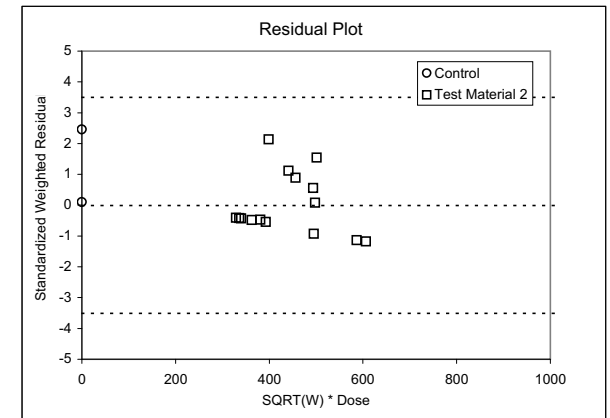
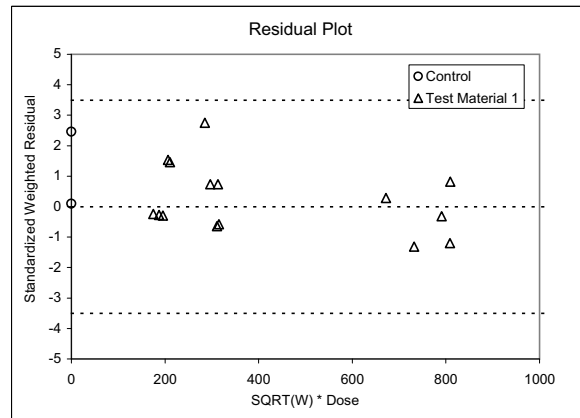
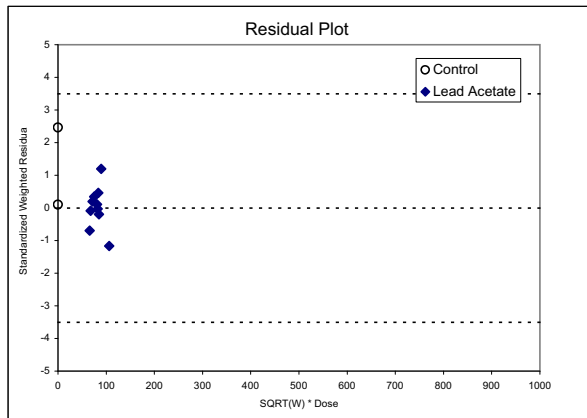
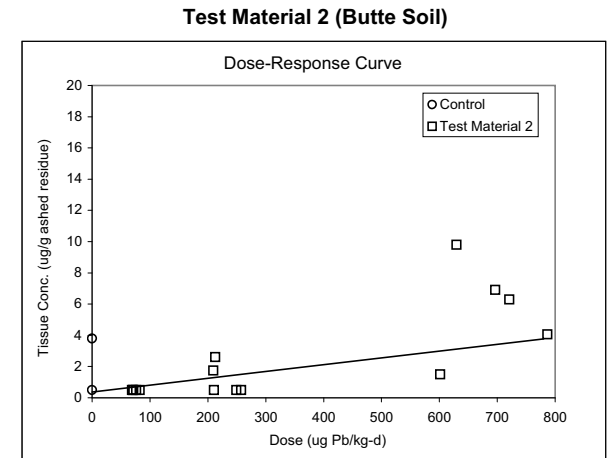
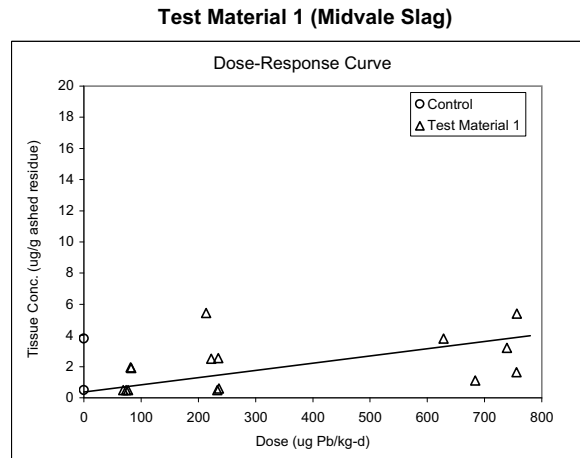
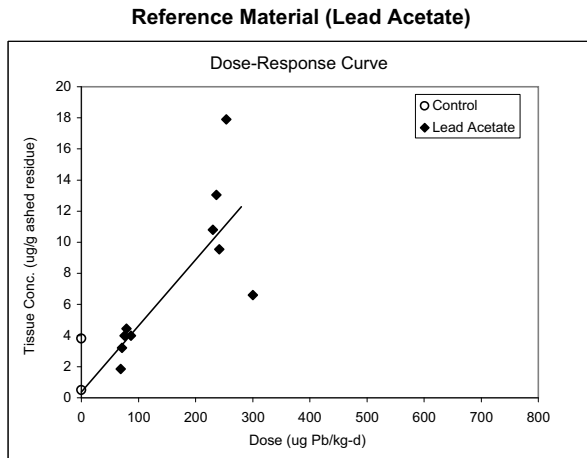
Statistic	Estimate
F	13.091
p	< 0.001
Adjusted R <sup>2</sup>	0.5412
AIC	501.991

**RBA and Uncertainty**

	Test Material 1	Test Material 2
RBA	0.12	0.14
Lower bound	?	?
Upper bound	?	?
Standard Error	--	--

APPENDIX E

**Figure 4a - All Data**  
**Phase II Experiment 6: Femur**  
**Linear Model:  $y = a + b_1 \cdot x_1 + b_2 \cdot x_2 + b_3 \cdot x_3$**



**Summary of Fitting**

Parameter	Estimate	Standard Error
a	3.69E-01	2.21E-01
b1	4.26E-02	8.27E-03
b2	4.63E-03	1.22E-03
b3	4.36E-03	1.68E-03
Covariance (c1,c2)	0.0873	--
Covariance (c1,c3)	0.1409	--
Degrees of Freedom	38	--

**Goodness of Fit**

Statistic	Estimate
F	12.878
p	< 0.001
Adjusted R <sup>2</sup>	0.4650
AIC	227.799

**RBA and Uncertainty**

	Test Material 1	Test Material 2
RBA	0.11	0.10
Lower bound	0.06	0.04
Upper bound	0.18	0.19
Standard Error	0.034*	0.042*

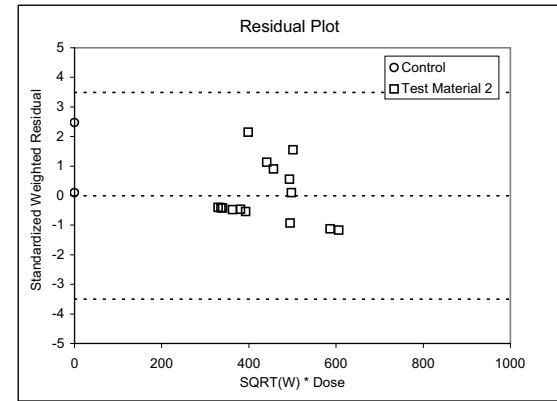
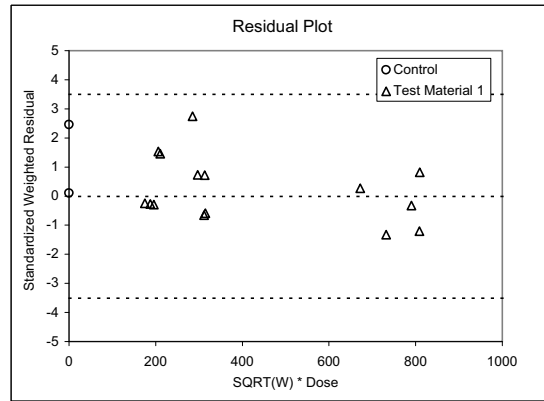
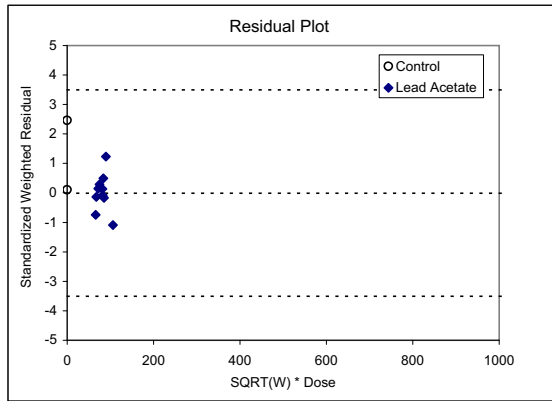
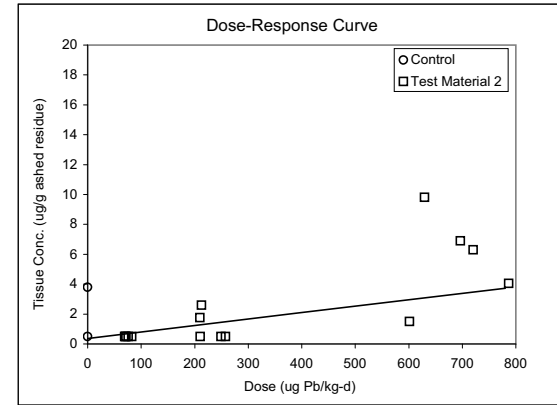
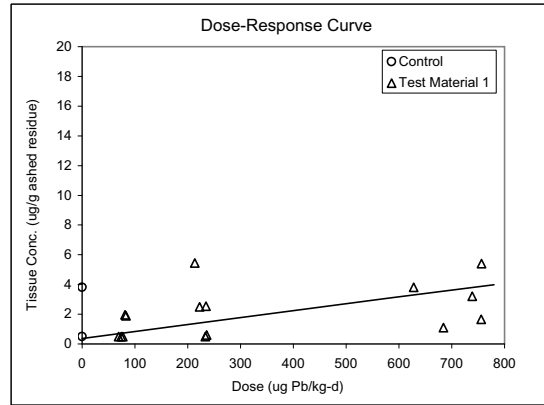
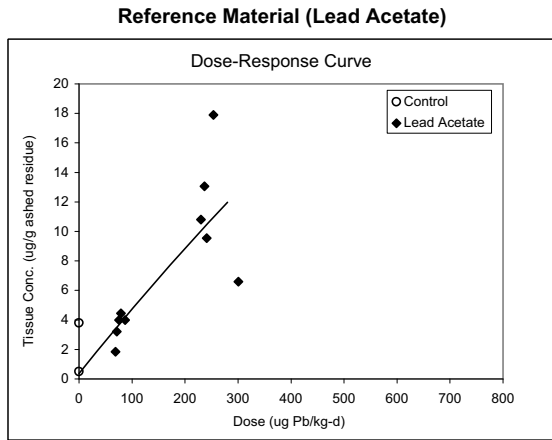
\*  $g \geq 0.05$ , estimate is uncertain

APPENDIX E

Figure 4b - All Data

Phase II Experiment 6: Femur

Exponential Model:  $y = a + b*(1-\exp(-c1*x1))+b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$



Summary of Fitting

Parameter	Estimate	Standard Error
a	3.62E-01	2.38E-01
b	7.38E+01	5.10E+02
c1	6.11E-04	4.43E-03
c2	6.46E-05	4.55E-04
c3	5.98E-05	4.20E-04
Covariance (c1,c2)	0.9990	--
Covariance (c1,c3)	0.9982	--
Degrees of Freedom	37	--

Goodness of Fit

Statistic	Estimate
F	9.415
p	< 0.001
Adjusted R <sup>2</sup>	0.4508
AIC	229.705

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.11	0.10
Lower bound	?	?
Upper bound	?	?
Standard Error	0.041*	0.048*

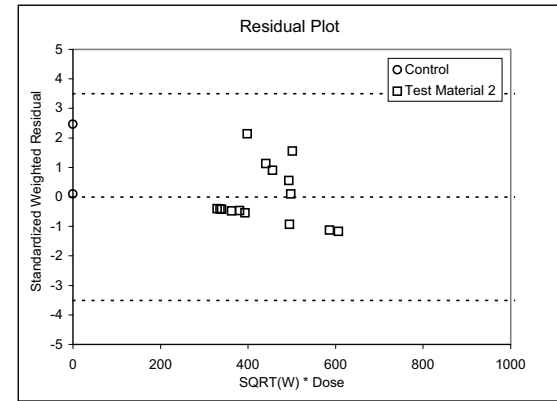
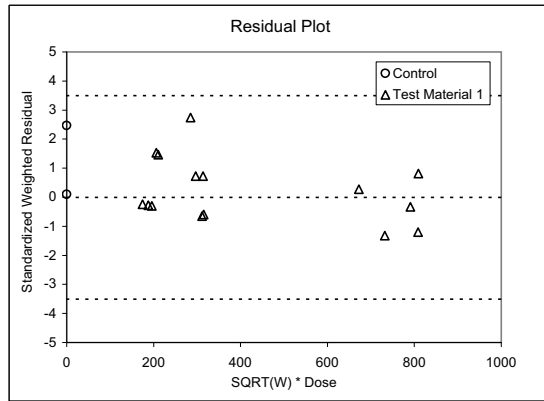
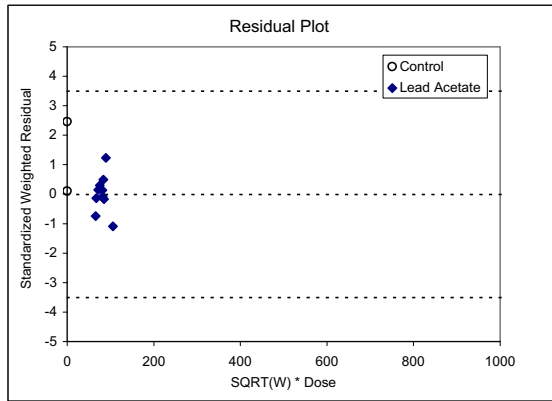
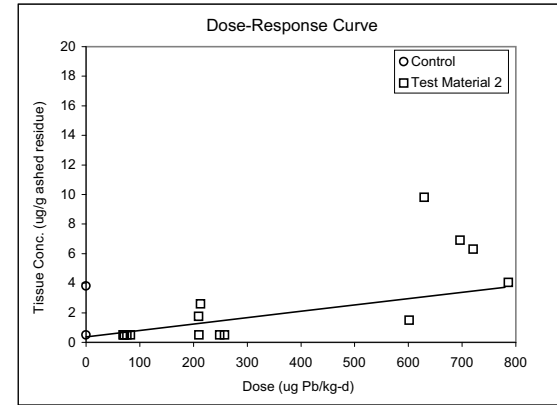
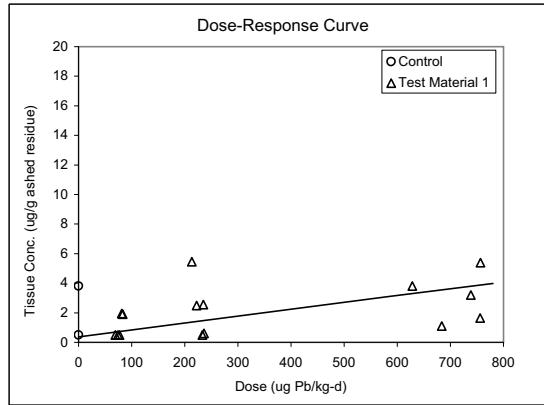
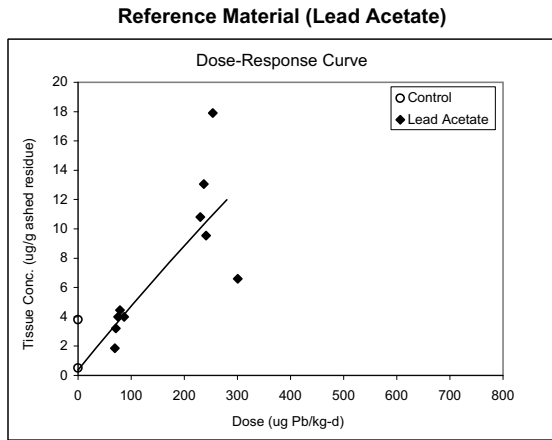
\*  $g \geq 0.05$ , estimate is uncertain

APPENDIX E

Figure 4c - All Data

Phase II Experiment 6: Femur

Michaelis-Menton Model:  $y = a + b \cdot x_1 / (c_1 + x_1) + b \cdot x_2 / (c_2 + x_2) + b \cdot x_3 / (c_3 + x_3)$



Summary of Fitting

Parameter	Estimate	Standard Error
a	3.62E-01	2.39E-01
b	1.52E+02	1.13E+03
c1	3.37E+03	2.65E+04
c2	3.18E+04	2.43E+05
c3	3.44E+04	2.62E+05
Covariance (c1,c2)	0.9991	--
Covariance (c1,c3)	0.9985	--
Degrees of Freedom	37	--

Goodness of Fit

Statistic	Estimate
F	9.414
p	< 0.001
Adjusted R <sup>2</sup>	0.4508
AIC	229.711

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.11	0.10
Lower bound	?	?
Upper bound	?	?
Standard Error	0.042*	0.047*

\* g ≥ 0.05, estimate is uncertain

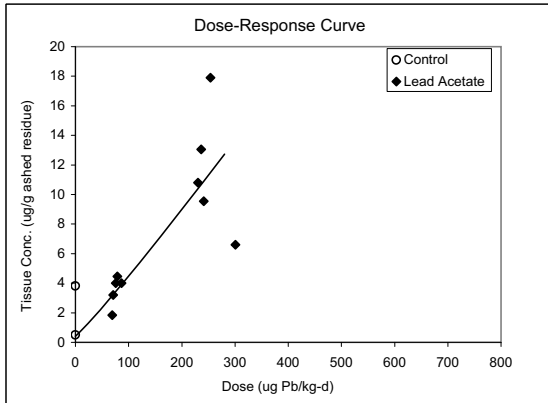
APPENDIX E

Figure 4d - All Data

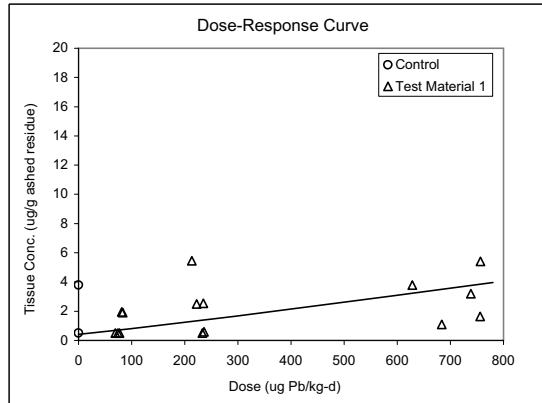
Phase II Experiment 6: Femur

Power Model:  $y = a + b_1 \cdot x_1^c + b_2 \cdot x_2^c + b_3 \cdot x_3^c$

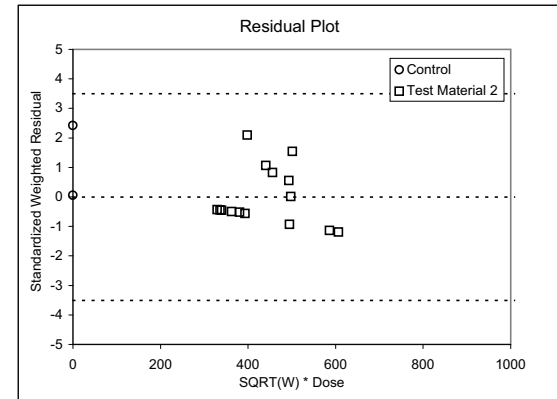
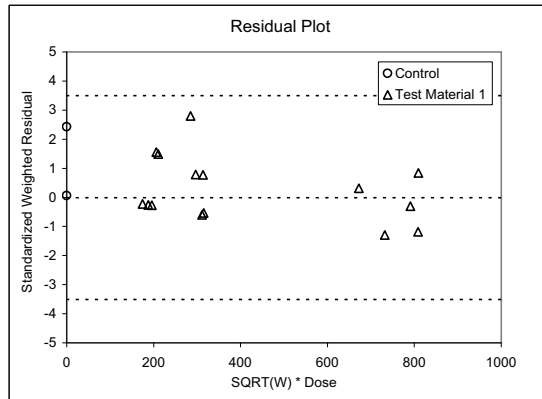
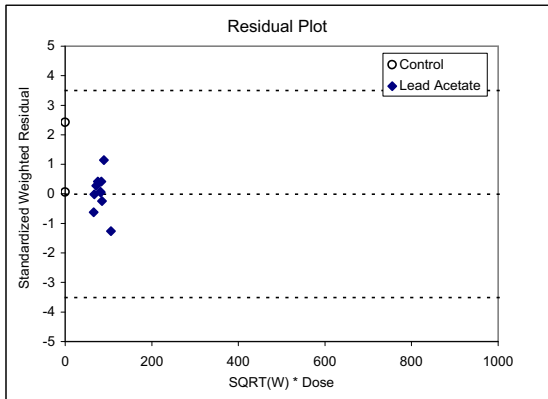
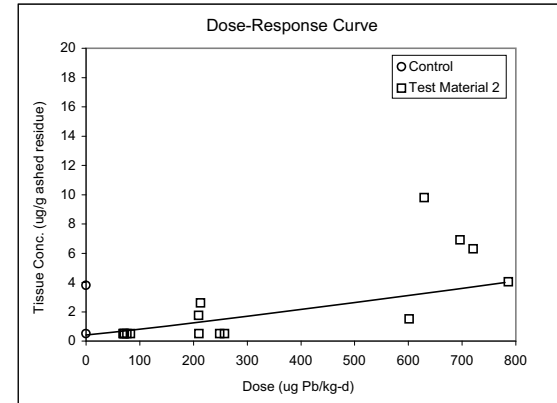
Reference Material (Lead Acetate)



Test Material 1 (Midvale Slag)



Test Material 2 (Butte Soil)



Summary of Fitting

Parameter	Estimate	Standard Error
a	4.18E-01	3.29E-01
b1	2.85E-02	5.08E-02
b2	2.73E-03	6.24E-03
b3	2.75E-03	6.16E-03
c	1.08E+00	3.36E-01
Covariance (b1,b2)	0.9875	--
Covariance (b1,b3)	0.9814	--
Degrees of Freedom	37	--

Goodness of Fit

Statistic	Estimate
F	9.426
p	< 0.001
Adjusted R <sup>2</sup>	0.4512
AIC	229.612

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.11	0.11
Lower bound	?	?
Upper bound	?	?
Standard Error	--	--

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## APPENDIX E

### EXPERIMENT 7

Test Material 1: California Gulch Phase I Residential Soil

Test Material 2: California Gulch Fe/Mn PbO

- Figure 1a Blood AUC - Linear Model (All Data)
- Figure 1a Blood AUC - Linear Model (Outlier Excluded)
- Figure 1b Blood AUC - Exponential Model
- Figure 1c Blood AUC - Michaelis-Menton Model
- Figure 1d Blood AUC - Power Model
  
- Figure 2a Liver - Linear Model (All Data)
- Figure 2a Liver - Linear Model (Outlier Excluded)
- Figure 2b Liver - Exponential Model
- Figure 2c Liver - Michaelis-Menton Model
- Figure 2d Liver - Power Model
  
- Figure 3a Kidney - Linear Model (All Data)
- Figure 3a Kidney - Linear Model (Outlier Excluded)
- Figure 3b Kidney - Exponential Model
- Figure 3c Kidney - Michaelis-Menton Model
- Figure 3d Kidney - Power Model
  
- Figure 4a Femur - Linear Model
- Figure 4b Femur - Exponential Model
- Figure 4c Femur - Michaelis-Menton Model
- Figure 4d Femur - Power Model

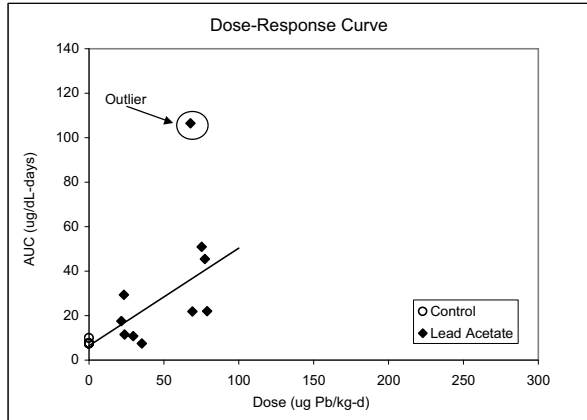
APPENDIX E

Figure 1a - All Data

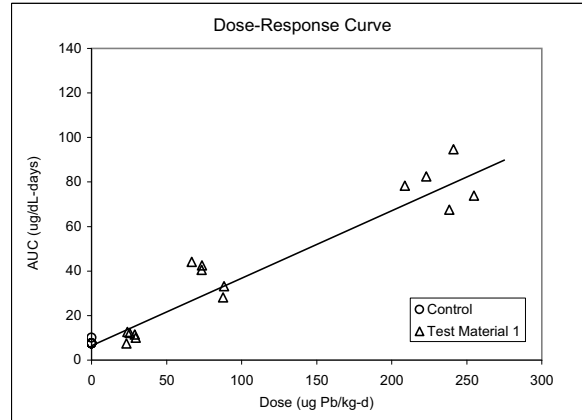
Phase II Experiment 7: Blood AUC

Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$

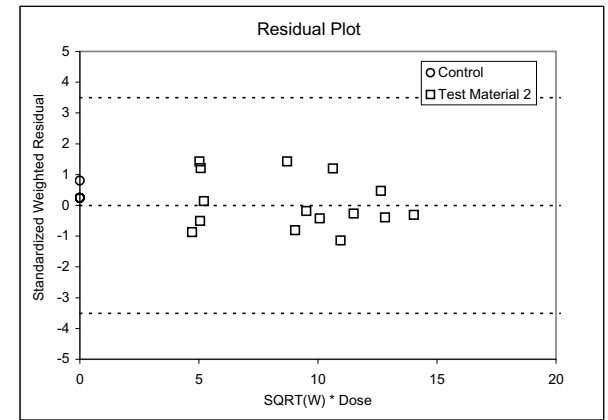
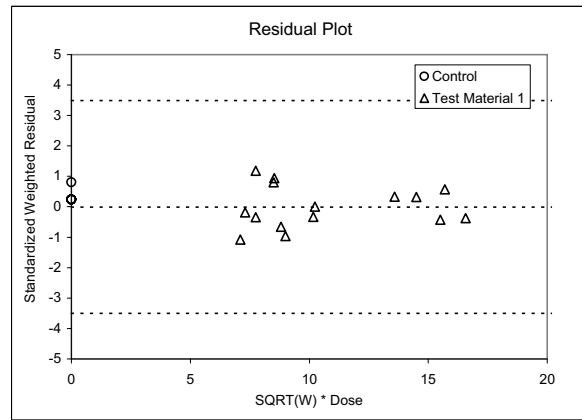
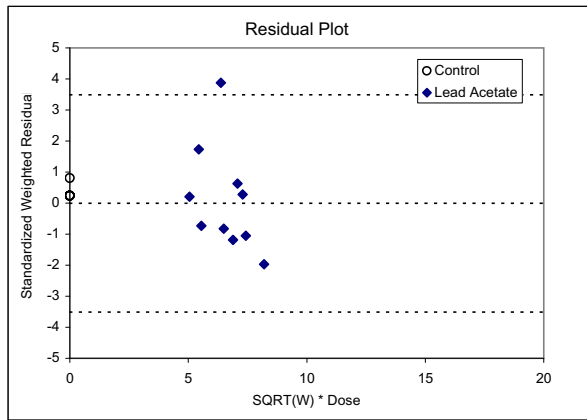
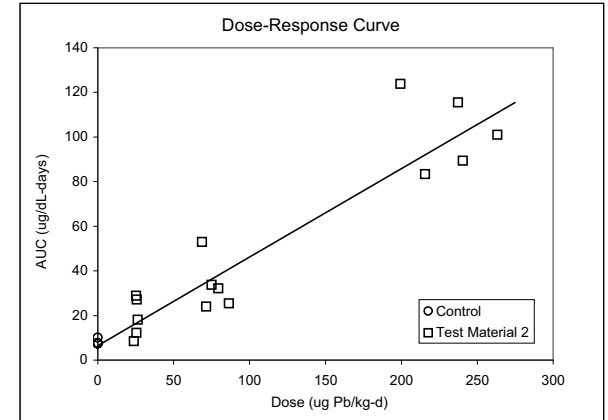
Reference Material (Lead Acetate)



Test Material 1 (California Gulch Phase I Residential Soil)



Test Material 2 (California Gulch Fe/Mn PbO)



Summary of Fitting

Parameter	Estimate	Standard Error
a	6.46E+00	1.59E+00
b1	4.39E-01	9.25E-02
b2	3.03E-01	4.49E-02
b3	3.97E-01	5.09E-02
Covariance (c1,c2)	0.1719	--
Covariance (c1,c3)	0.1351	--
Degrees of Freedom	41	--

Goodness of Fit

Statistic	Estimate
F	33.889
p	< 0.001
Adjusted R <sup>2</sup>	0.6916
AIC	394.354

RBA and Uncertainty

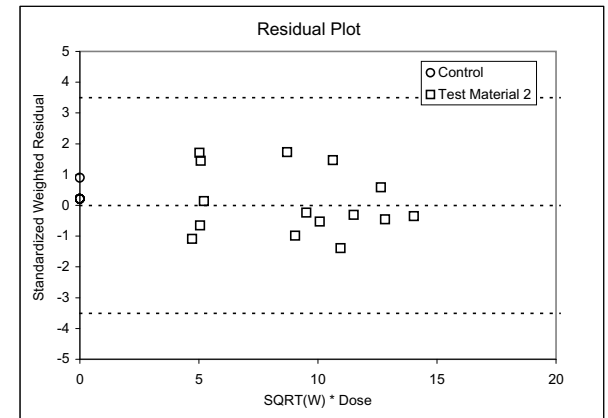
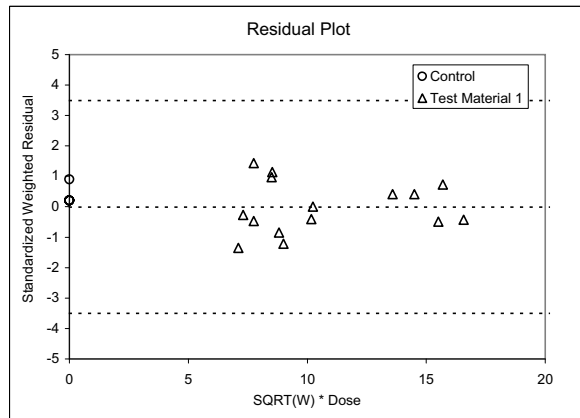
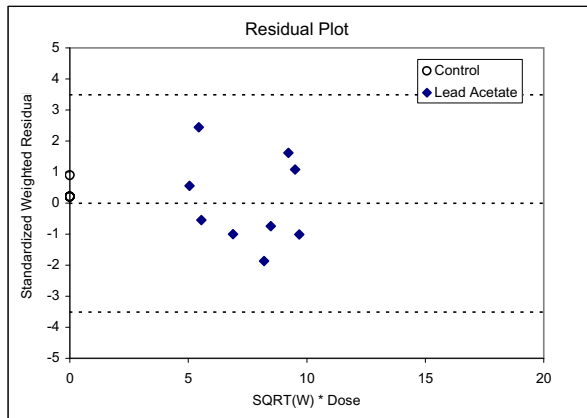
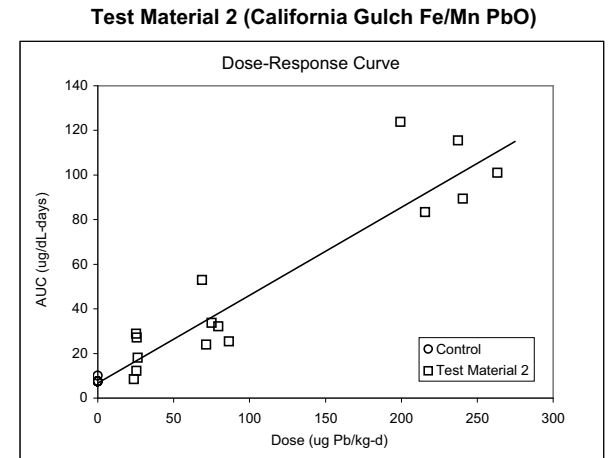
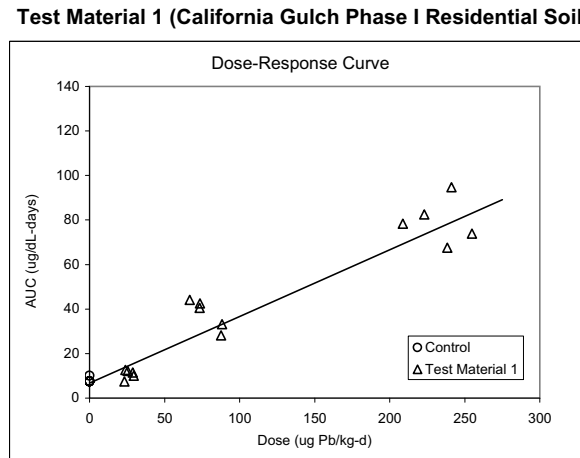
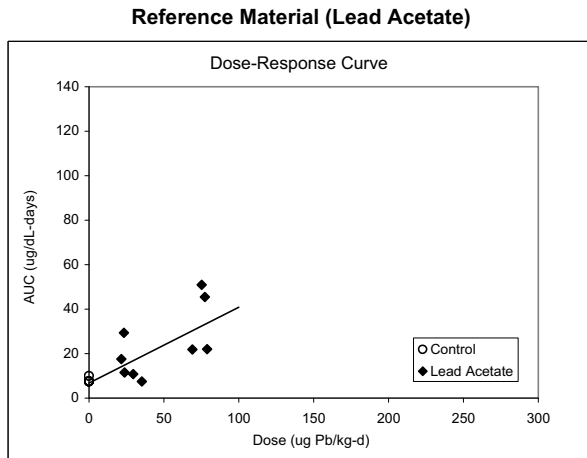
	Test Material 1	Test Material 2
RBA	0.69	0.90
Lower bound	0.47	0.63
Upper bound	1.08	1.42
Standard Error	0.163*	0.209*

\*  $g \geq 0.05$ , estimate is uncertain



APPENDIX E

**Figure 1a - Outlier Excluded**  
**Phase II Experiment 7: Blood AUC**  
**Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$**



**Summary of Fitting**

Parameter	Estimate	Standard Error
a	6.74E+00	1.30E+00
b1	3.40E-01	6.88E-02
b2	3.00E-01	3.69E-02
b3	3.94E-01	4.18E-02
Covariance (c1,c2)	0.1724	--
Covariance (c1,c3)	0.1355	--
Degrees of Freedom	40	--

**Goodness of Fit**

Statistic	Estimate
F	47.669
p	< 0.001
Adjusted R <sup>2</sup>	0.7650
AIC	341.729

**RBA and Uncertainty**

	Test Material 1	Test Material 2
RBA	0.88	1.16
Lower bound	0.62	0.83
Upper bound	1.34	1.76
Standard Error	0.192*	0.249*

\*  $g \geq 0.05$ , estimate is uncertain

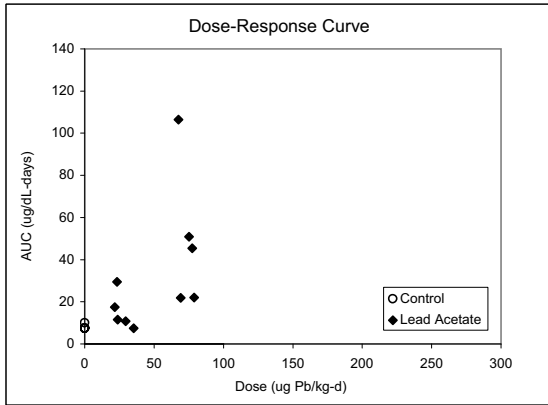
APPENDIX E

Figure 1b - All Data

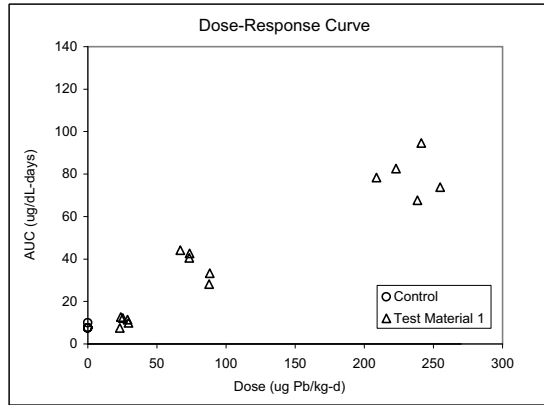
Phase II Experiment 7: Blood AUC

Exponential Model:  $y = a + b*(1-\exp(-c1*x1)) + b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$

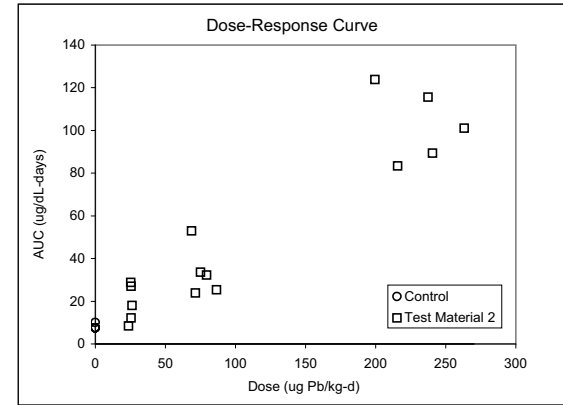
Reference Material (Lead Acetate)



Test Material 1 (California Gulch Phase I Residential Soil)



Test Material 2 (California Gulch Fe/Mn PbO)



**NO SOLUTION**

The software could not find a solution,  
or the solution was unstable and/or had unrealistic parameter estimates.

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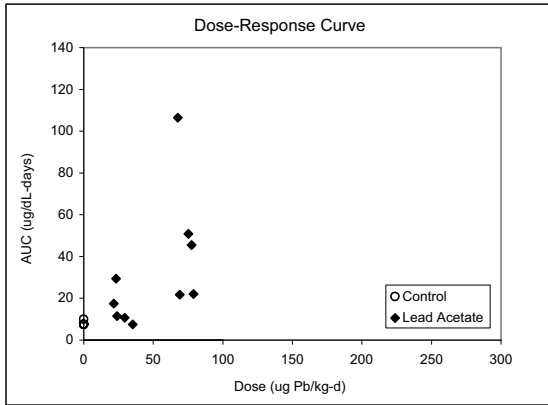
APPENDIX E

Figure 1c - All Data

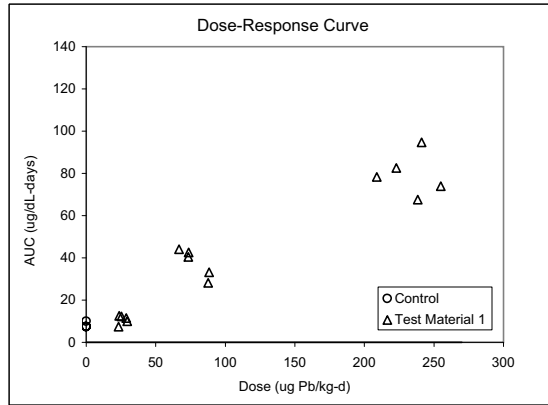
Phase II Experiment 7: Blood AUC

Michaelis-Menton Model:  $y = a + b \cdot x_1 / (c_1 + x_1) + b \cdot x_2 / (c_2 + x_2) + b \cdot x_3 / (c_3 + x_3)$

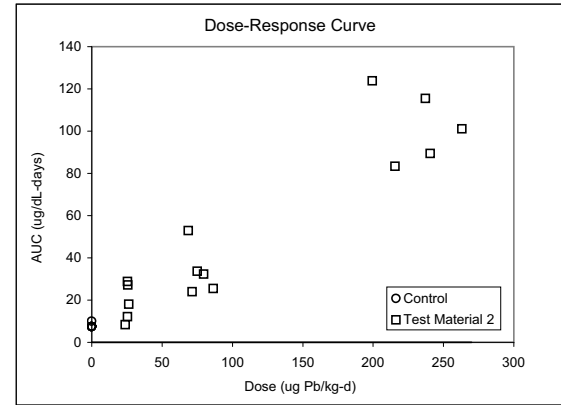
Reference Material (Lead Acetate)



Test Material 1 (California Gulch Phase I Residential Soil)



Test Material 2 (California Gulch Fe/Mn PbO)



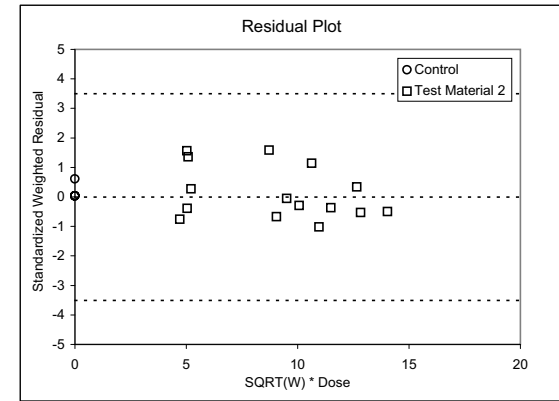
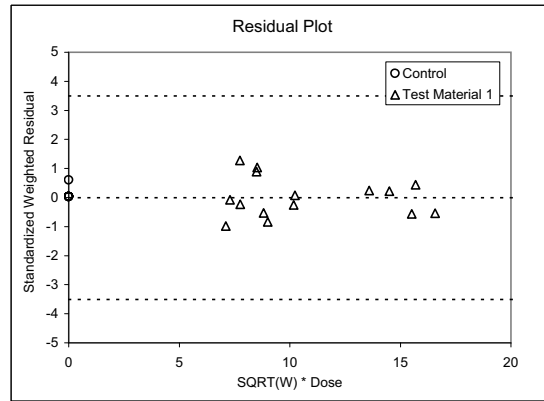
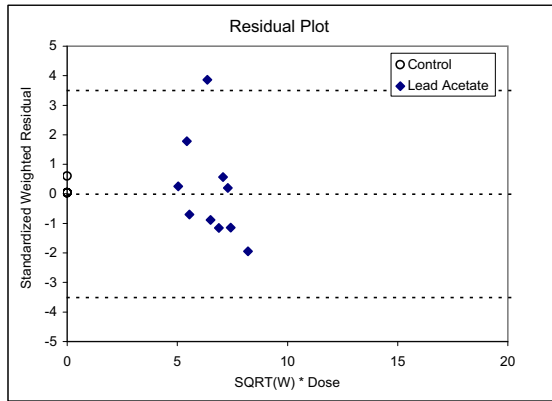
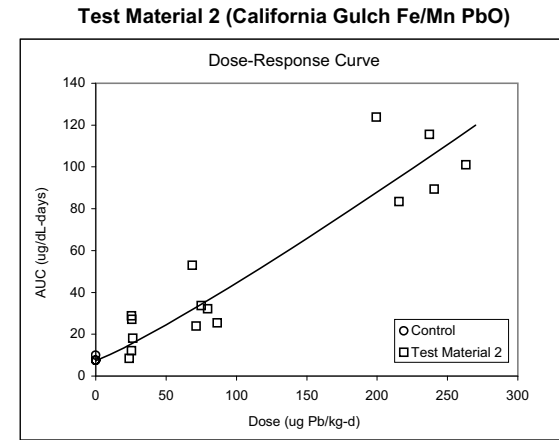
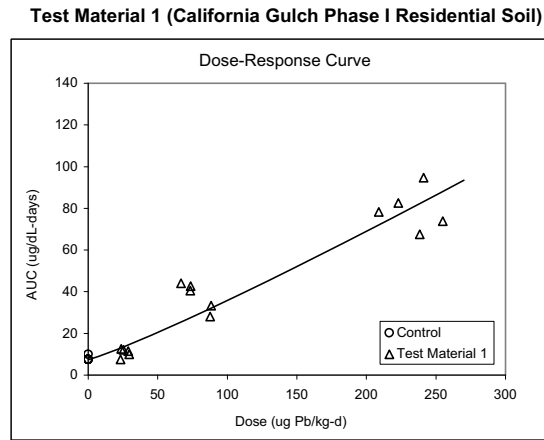
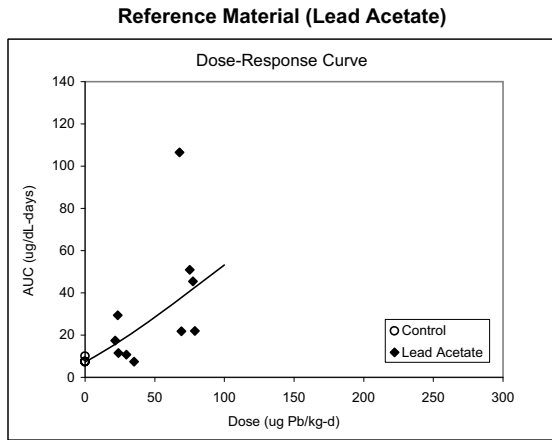
**NO SOLUTION**

The software could not find a solution,  
or the solution was unstable and/or had unrealistic parameter estimates.

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APPENDIX E

**Figure 1d - All Data**  
**Phase II Experiment 7: Blood AUC**  
**Power Model:  $y = a + b_1 \cdot x_1^c + b_2 \cdot x_2^c + b_3 \cdot x_3^c$**



**Summary of Fitting**

Parameter	Estimate	Standard Error
a	7.34E+00	1.95E+00
b1	2.70E-01	1.92E-01
b2	1.68E-01	1.40E-01
b3	2.19E-01	1.79E-01
c	1.11E+00	1.56E-01
Covariance (b1,b2)	0.9447	--
Covariance (b1,b3)	0.9455	--
Degrees of Freedom	40	--

**Goodness of Fit**

Statistic	Estimate
F	25.364
p	< 0.001
Adjusted R <sup>2</sup>	0.6890
AIC	394.283

**RBA and Uncertainty**

	Test Material 1	Test Material 2
RBA	0.65	0.83
Lower bound	?	?
Upper bound	?	?
Standard Error	--	--

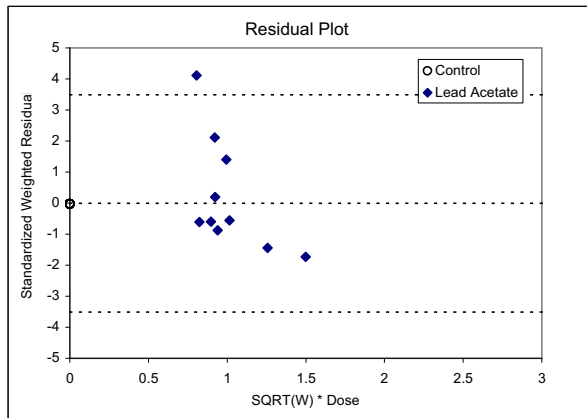
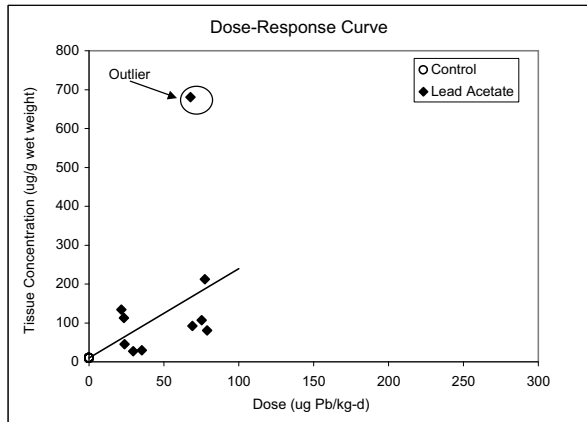
APPENDIX E

Figure 2a - All Data

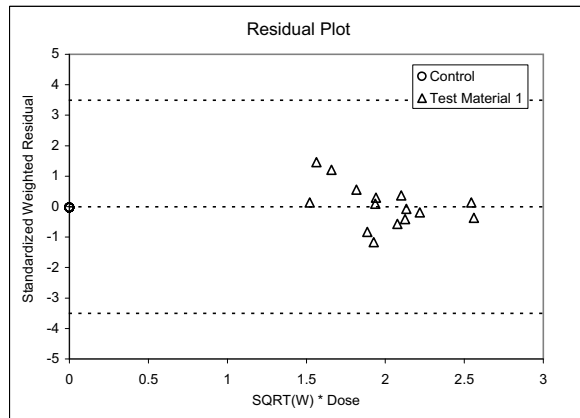
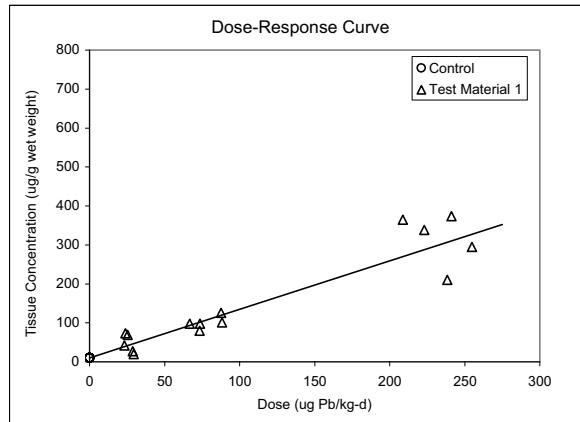
Phase II Experiment 7: Liver

Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$

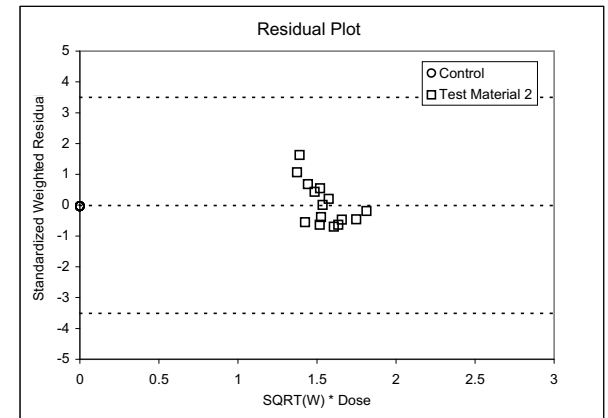
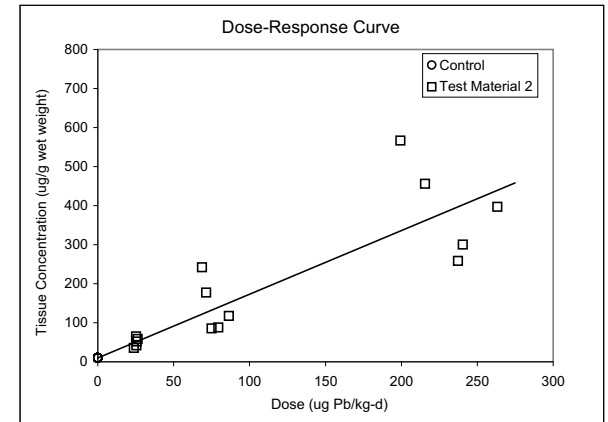
Reference Material (Lead Acetate)



Test Material 1 (California Gulch Phase I Residential Soil)



Test Material 2 (California Gulch Fe/Mn PbO)



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.02E+01	2.08E+00
b1	2.29E+00	4.81E-01
b2	1.24E+00	2.01E-01
b3	1.63E+00	2.60E-01
Covariance (c1,c2)	0.0199	--
Covariance (c1,c3)	0.0177	--
Degrees of Freedom	41	--

Goodness of Fit

Statistic	Estimate
F	32.074
p	< 0.001
Adjusted R <sup>2</sup>	0.6794
AIC	503.462

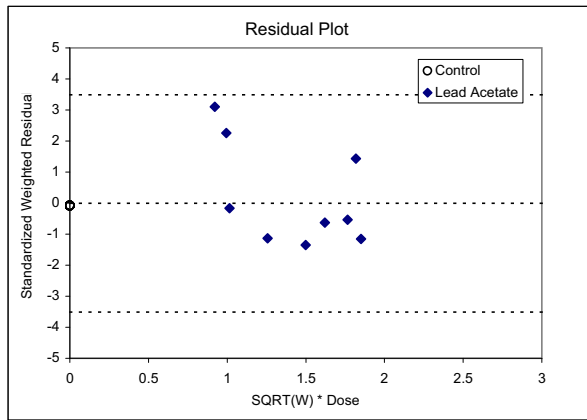
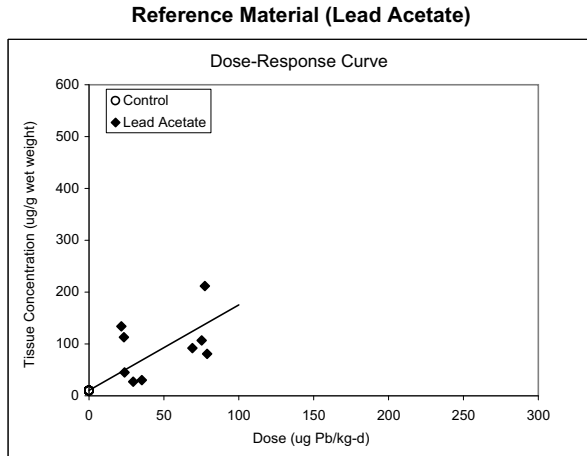
RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.54	0.71
Lower bound	0.35	0.46
Upper bound	0.89	1.16
Standard Error	0.142*	0.186*

\*  $g \geq 0.05$ , estimate is uncertain

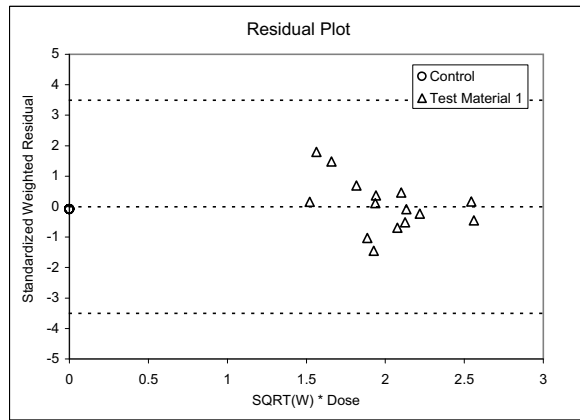
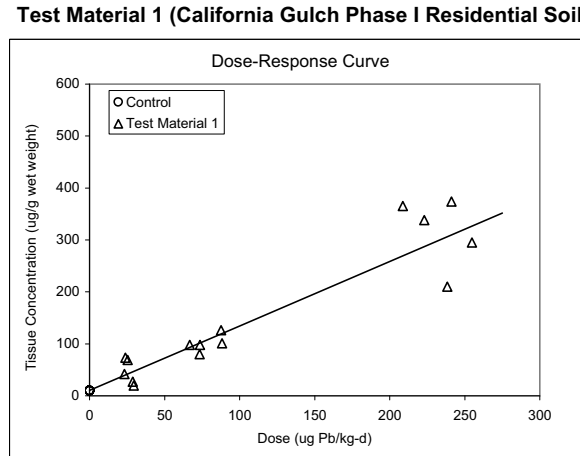
APPENDIX E

**Figure 2a - Outlier Excluded**  
**Phase II Experiment 7: Liver**  
**Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$**



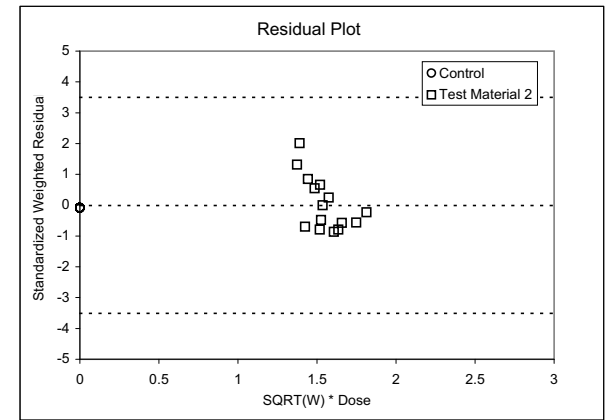
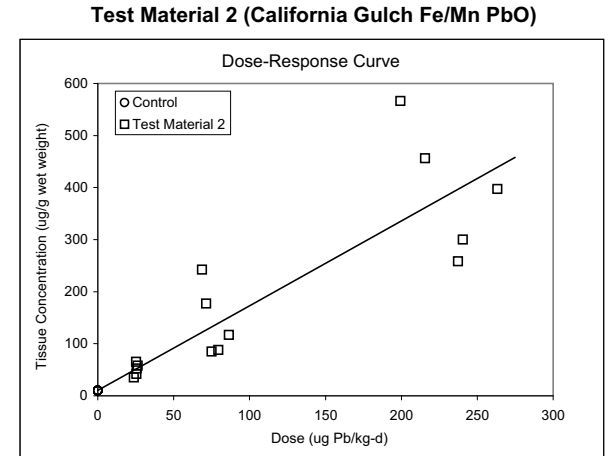
**Summary of Fitting**

Parameter	Estimate	Standard Error
a	1.03E+01	1.68E+00
b1	1.65E+00	2.89E-01
b2	1.24E+00	1.62E-01
b3	1.63E+00	2.11E-01
Covariance (c1,c2)	0.0204	--
Covariance (c1,c3)	0.0181	--
Degrees of Freedom	40	--



**Goodness of Fit**

Statistic	Estimate
F	48.222
p	< 0.001
Adjusted R <sup>2</sup>	0.7671
AIC	451.637



**RBA and Uncertainty**

	Test Material 1	Test Material 2
RBA	0.75	0.99
Lower bound	0.53	0.69
Upper bound	1.12	1.46
Standard Error	0.163*	0.213*

\*  $g \geq 0.05$ , estimate is uncertain

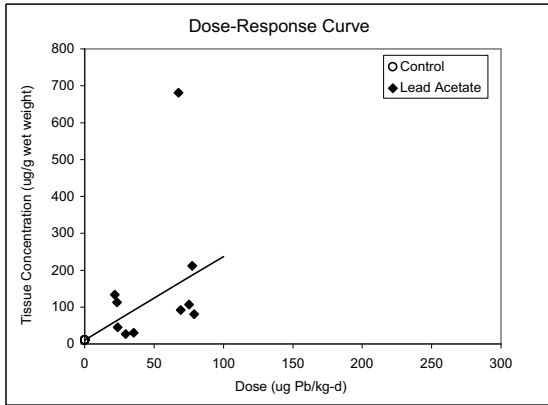
APPENDIX E

Figure 2b - All Data

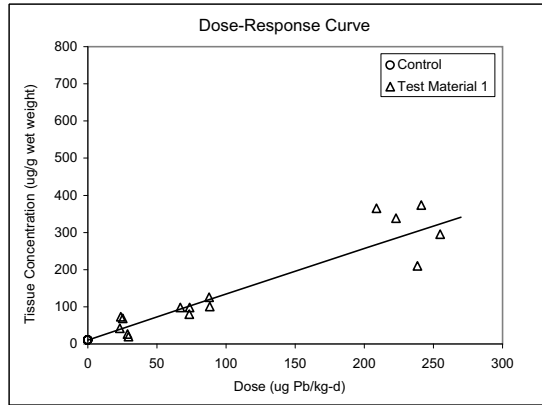
Phase II Experiment 7: Liver

Exponential Model:  $y = a + b*(1-\exp(-c1*x1)) + b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$

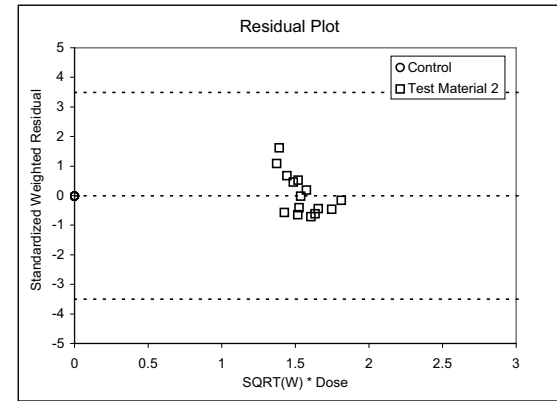
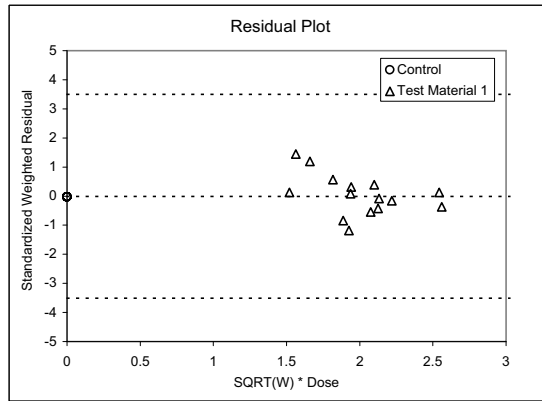
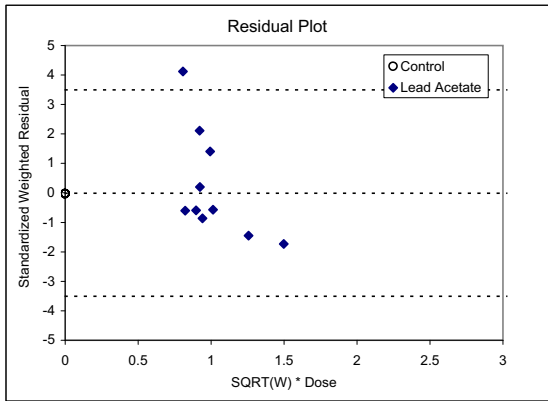
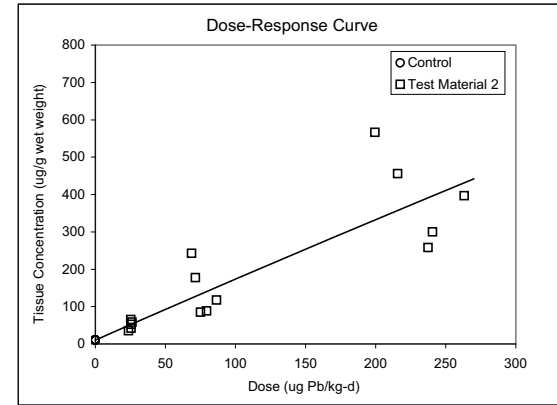
Reference Material (Lead Acetate)



Test Material 1 (California Gulch Phase I Residential Soil)



Test Material 2 (California Gulch Fe/Mn PbO)



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.01E+01	2.13E+00
b	6.22E+03	6.44E+04
c1	3.71E-04	3.99E-03
c2	2.02E-04	2.18E-03
c3	2.66E-04	2.88E-03
Covariance (c1,c2)	0.9997	--
Covariance (c1,c3)	0.9997	--
Degrees of Freedom	40	--

Goodness of Fit

Statistic	Estimate
F	23.468
p	< 0.001
Adjusted R <sup>2</sup>	0.6713
AIC	505.440

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.54	0.72
Lower bound	?	?
Upper bound	?	?
Standard Error	0.145*	0.196*

\*  $g \geq 0.05$ , estimate is uncertain

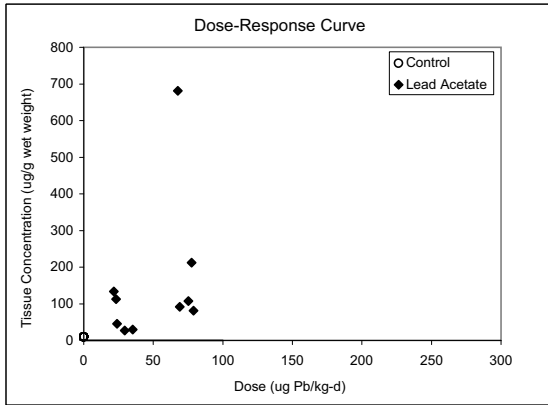
APPENDIX E

Figure 2c - All Data

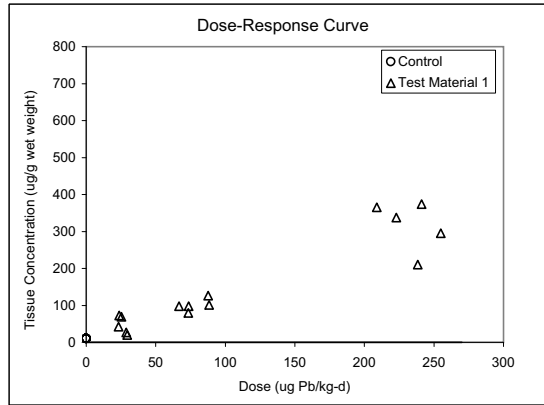
Phase II Experiment 7: Liver

Michaelis-Menton Model:  $y = a + b \cdot x_1 / (c_1 + x_1) + b \cdot x_2 / (c_2 + x_2) + b \cdot x_3 / (c_3 + x_3)$

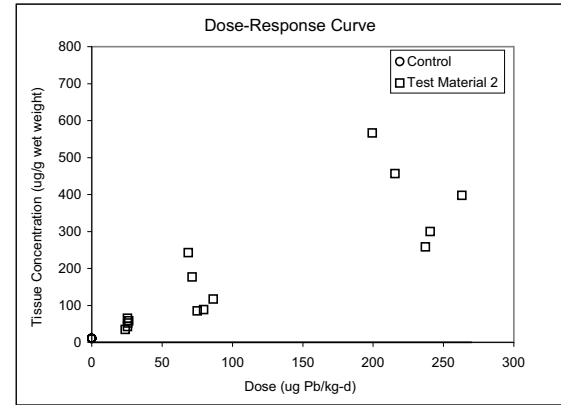
Reference Material (Lead Acetate)



Test Material 1 (California Gulch Phase I Residential Soil)



Test Material 2 (California Gulch Fe/Mn PbO)



**NO SOLUTION**

The software could not find a solution,  
or the solution was unstable and/or had unrealistic parameter estimates.

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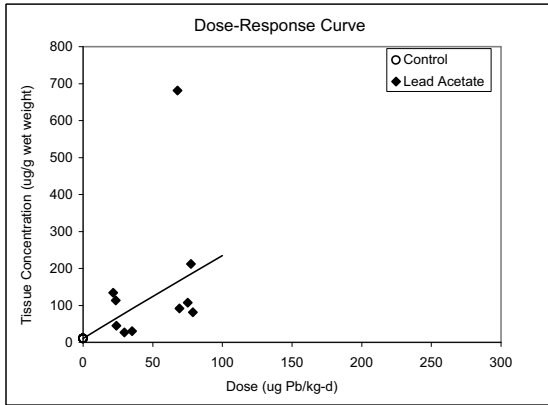
APPENDIX E

Figure 2d - All Data

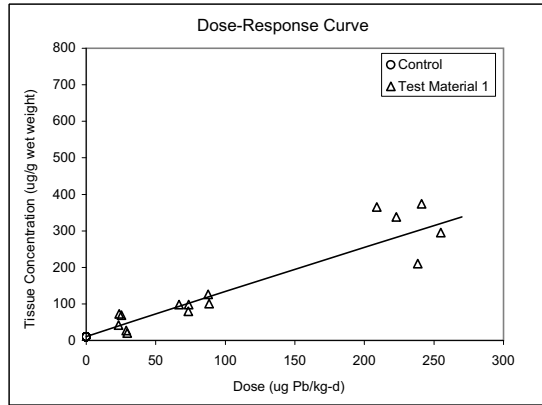
Phase II Experiment 7: Liver

Power Model:  $y = a + b1*x1^c + b2*x2^c + b3*x3^c$

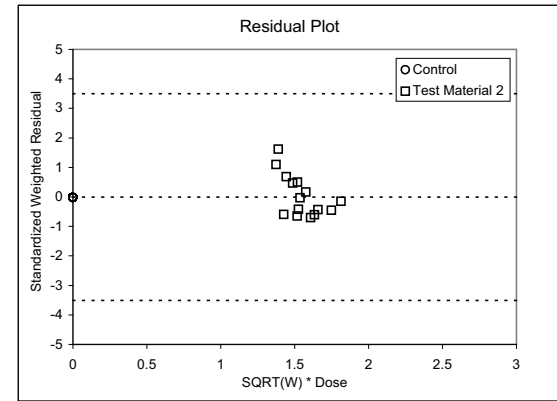
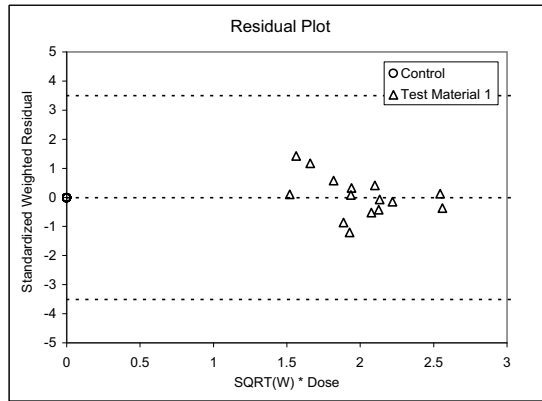
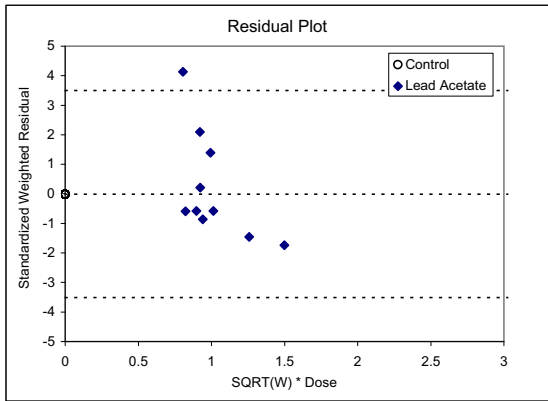
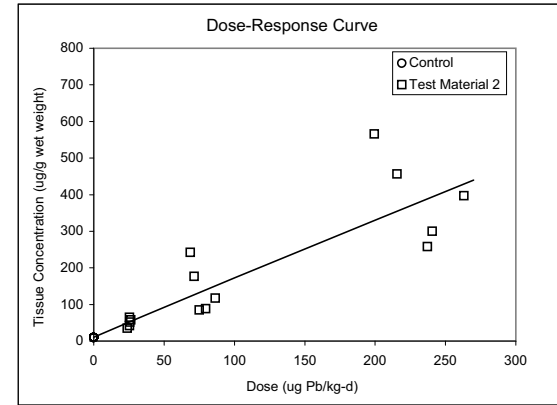
Reference Material (Lead Acetate)



Test Material 1 (California Gulch Phase I Residential Soil)



Test Material 2 (California Gulch Fe/Mn PbO)



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.01E+01	2.14E+00
b1	2.48E+00	1.28E+00
b2	1.37E+00	8.06E-01
b3	1.79E+00	1.03E+00
c	9.79E-01	1.26E-01
Covariance (b1,b2)	0.8779	--
Covariance (b1,b3)	0.8769	--
Degrees of Freedom	40	--

Goodness of Fit

Statistic	Estimate
F	23.491
p	< 0.001
Adjusted R <sup>2</sup>	0.6716
AIC	505.398

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.54	0.72
Lower bound	0.01	0.08
Upper bound	1.08	1.46
Standard Error	--	--

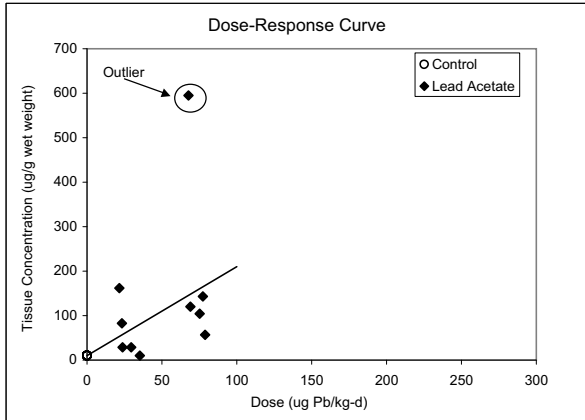
APPENDIX E

Figure 3a - All Data

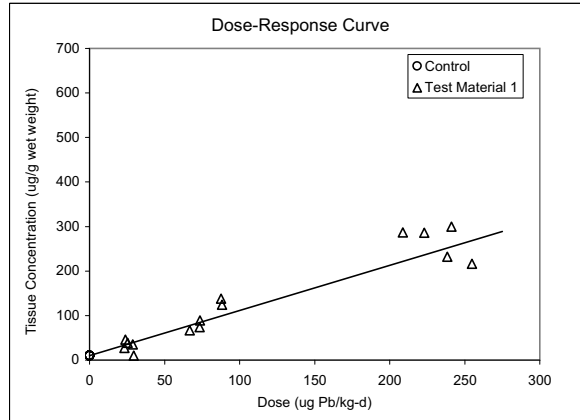
Phase II Experiment 7: Kidney

Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$

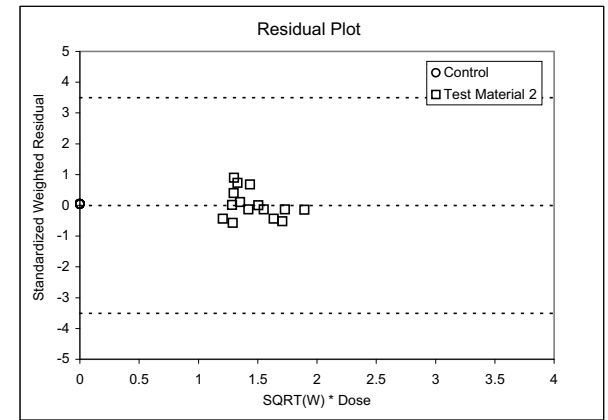
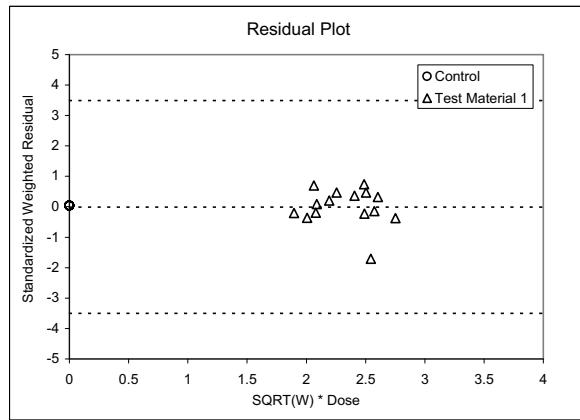
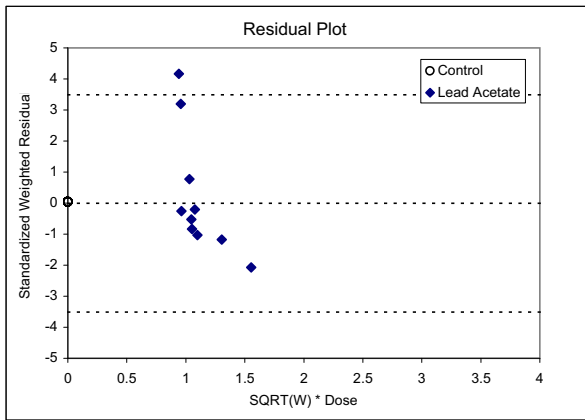
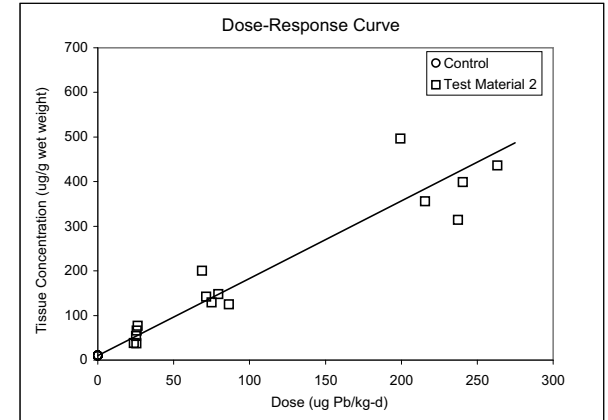
Reference Material (Lead Acetate)



Test Material 1 (California Gulch Phase I Residential Soil)



Test Material 2 (California Gulch Fe/Mn PbO)



Summary of Fitting

Parameter	Estimate	Standard Error
a	9.78E+00	2.53E+00
b1	2.01E+00	4.46E-01
b2	1.02E+00	1.77E-01
b3	1.73E+00	2.75E-01
Covariance (c1,c2)	0.0375	--
Covariance (c1,c3)	0.0222	--
Degrees of Freedom	41	--

Goodness of Fit

Statistic	Estimate
F	29.081
p	< 0.001
Adjusted R <sup>2</sup>	0.6569
AIC	501.595

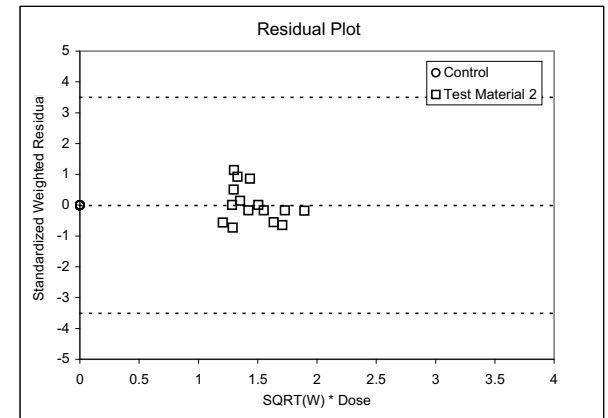
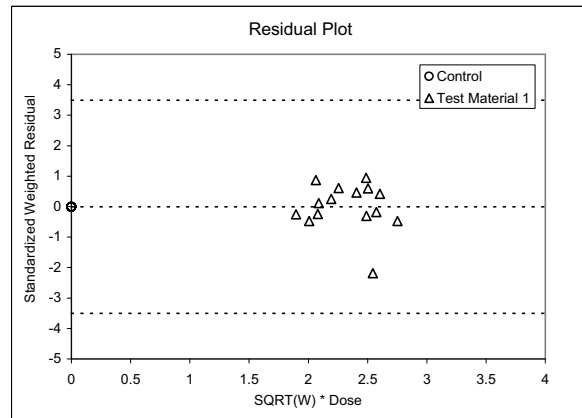
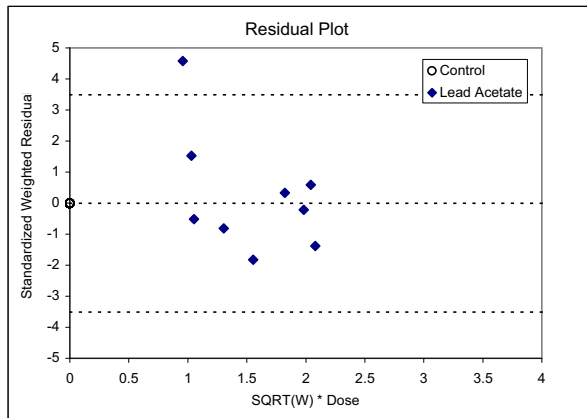
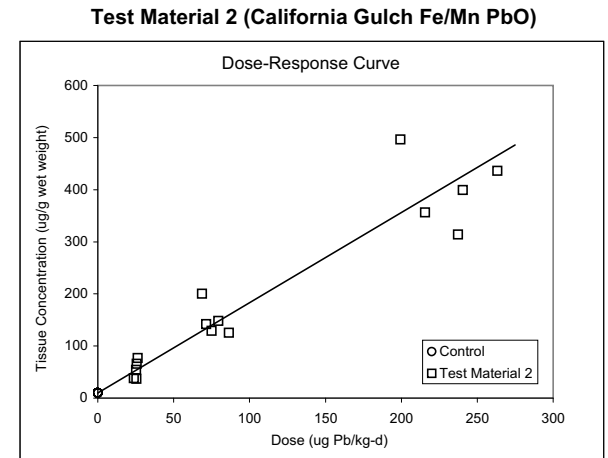
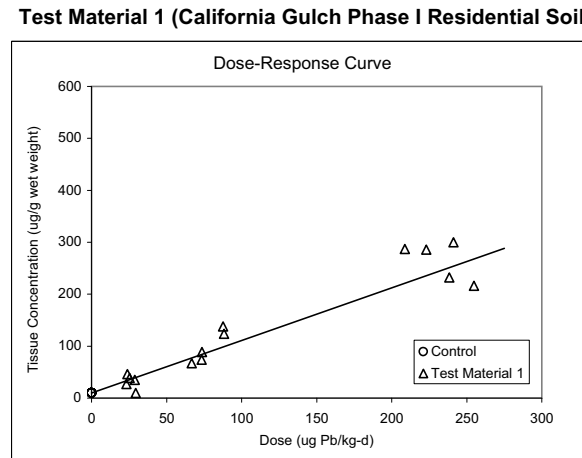
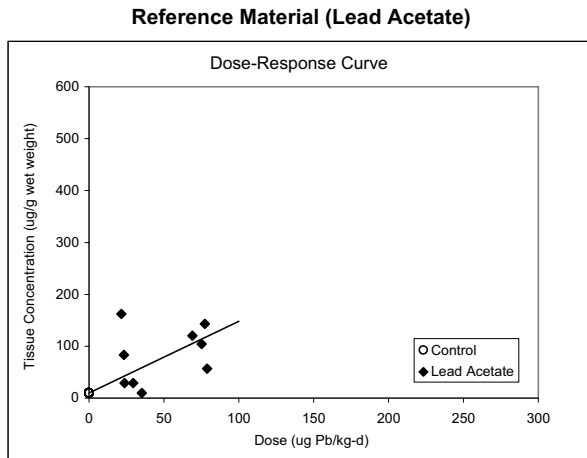
RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.51	0.86
Lower bound	0.32	0.56
Upper bound	0.85	1.45
Standard Error	0.141*	0.234*

\*  $g \geq 0.05$ , estimate is uncertain

APPENDIX E

**Figure 3a - Outlier Excluded**  
**Phase II Experiment 7: Kidney**  
**Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$**



**Summary of Fitting**

Parameter	Estimate	Standard Error
a	1.00E+01	1.99E+00
b1	1.38E+00	2.59E-01
b2	1.01E+00	1.39E-01
b3	1.73E+00	2.16E-01
Covariance (c1,c2)	0.0390	--
Covariance (c1,c3)	0.0230	--
Degrees of Freedom	40	--

**Goodness of Fit**

Statistic	Estimate
F	45.535
p	< 0.001
Adjusted R <sup>2</sup>	0.7565
AIC	446.484

**RBA and Uncertainty**

	Test Material 1	Test Material 2
RBA	0.73	1.25
Lower bound	0.50	0.88
Upper bound	1.12	1.91
Standard Error	0.167*	0.280*

\*  $g \geq 0.05$ , estimate is uncertain

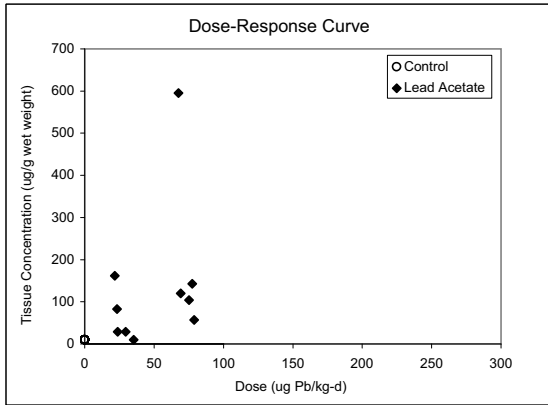
APPENDIX E

Figure 3b - All Data

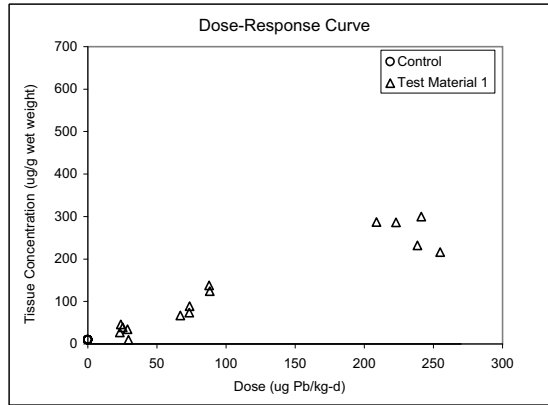
Phase II Experiment 7: Kidney

Exponential Model:  $y = a + b*(1-\exp(-c1*x1))+b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$

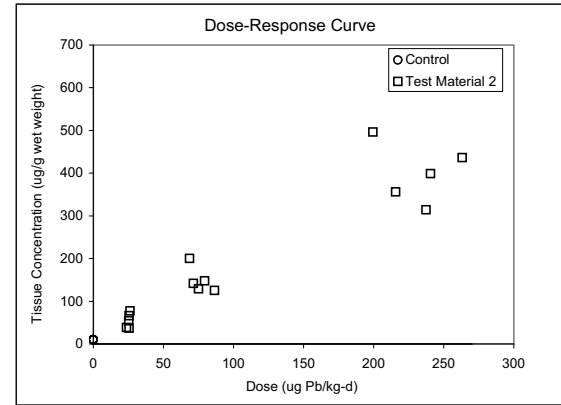
Reference Material (Lead Acetate)



Test Material 1 (California Gulch Phase I Residential Soil)



Test Material 2 (California Gulch Fe/Mn PbO)



**NO SOLUTION**

The software could not find a solution,  
or the solution was unstable and/or had unrealistic parameter estimates.

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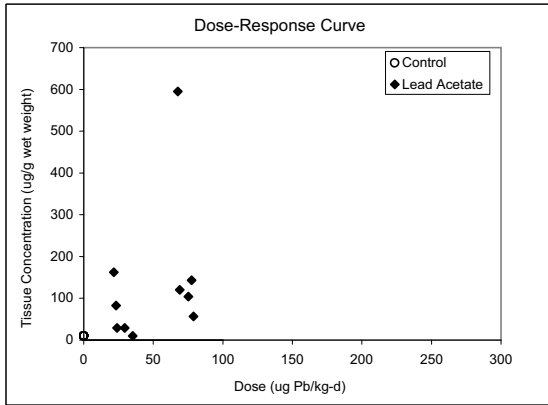
APPENDIX E

Figure 3c - All Data

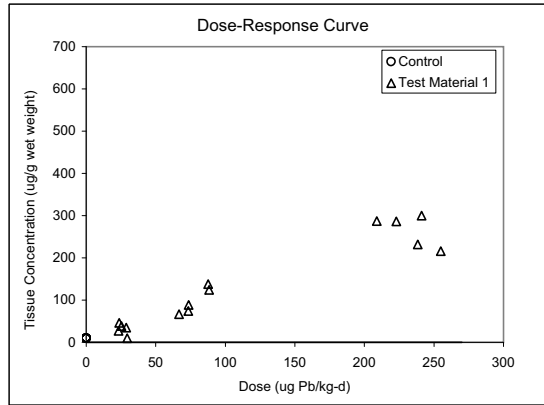
Phase II Experiment 7: Kidney

Michaelis-Menton Model:  $y = a + b \cdot x_1 / (c_1 + x_1) + b \cdot x_2 / (c_2 + x_2) + b \cdot x_3 / (c_3 + x_3)$

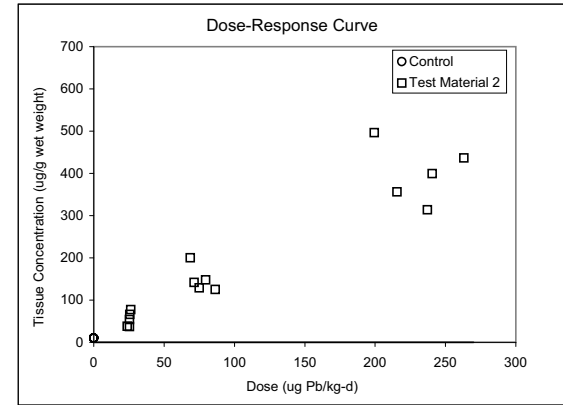
Reference Material (Lead Acetate)



Test Material 1 (California Gulch Phase I Residential Soil)



Test Material 2 (California Gulch Fe/Mn PbO)



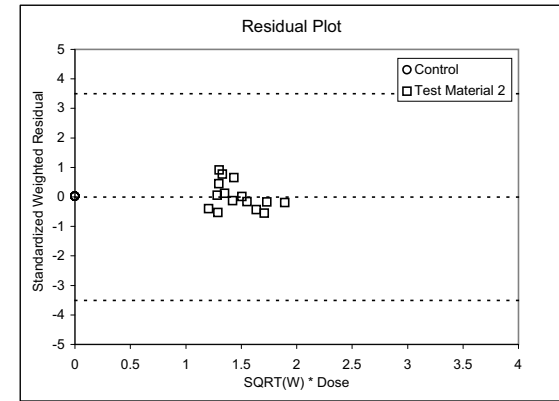
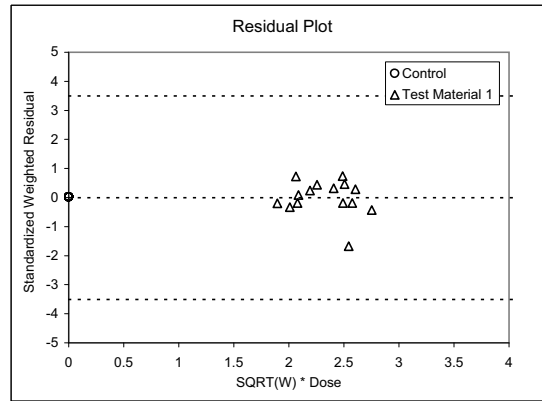
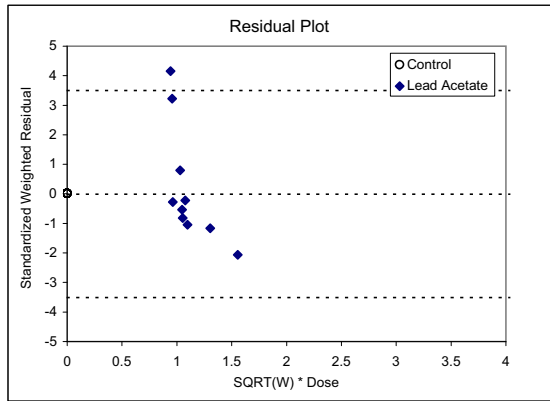
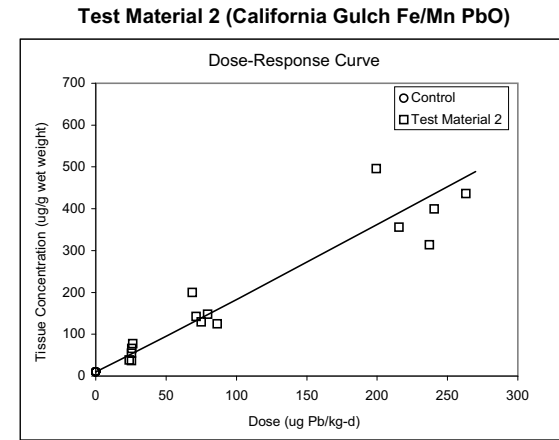
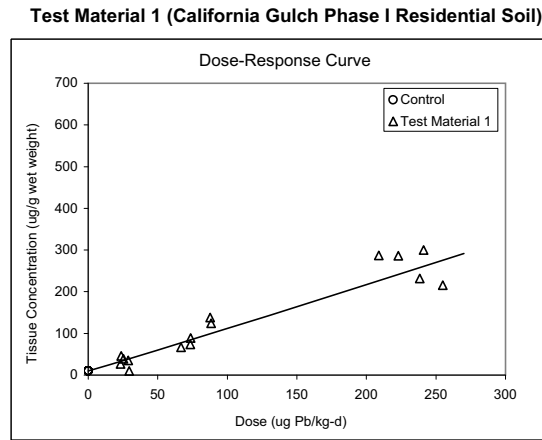
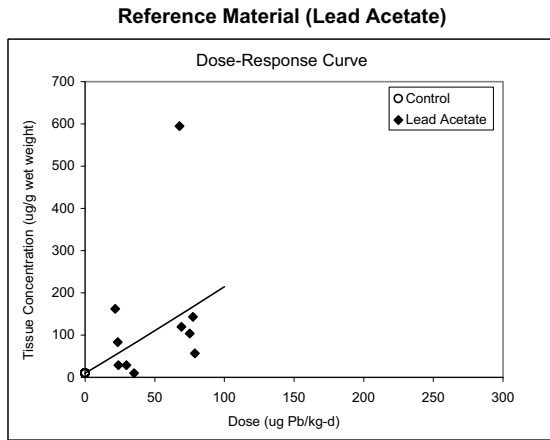
**NO SOLUTION**

The software could not find a solution,  
or the solution was unstable and/or had unrealistic parameter estimates.

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APPENDIX E

**Figure 3d - All Data**  
**Phase II Experiment 7: Kidney**  
**Power Model:  $y = a + b1*x1^c + b2*x2^c + b3*x3^c$**



**Summary of Fitting**

Parameter	Estimate	Standard Error
a	9.90E+00	2.64E+00
b1	1.83E+00	9.89E-01
b2	9.14E-01	5.60E-01
b3	1.55E+00	9.55E-01
c	1.02E+00	1.28E-01
Covariance (b1,b2)	0.8746	--
Covariance (b1,b3)	0.8793	--
Degrees of Freedom	40	--

**Goodness of Fit**

Statistic	Estimate
F	21.305
p	< 0.001
Adjusted R <sup>2</sup>	0.6486
AIC	503.510

**RBA and Uncertainty**

	Test Material 1	Test Material 2
RBA	0.51	0.85
Lower bound	?	?
Upper bound	1.12	1.83
Standard Error	--	--

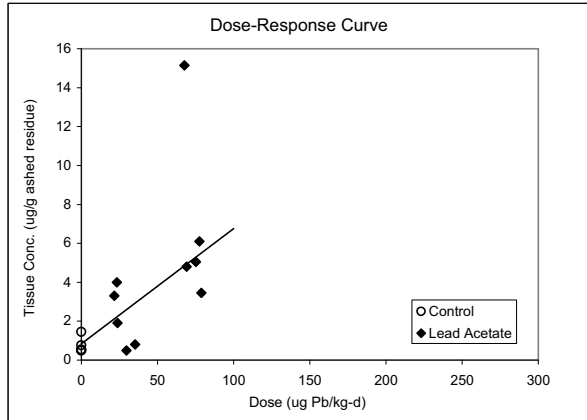
APPENDIX E

Figure 4a - All Data

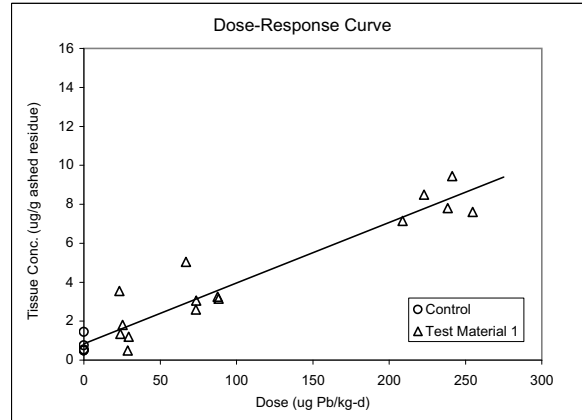
Phase II Experiment 7: Femur

Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$

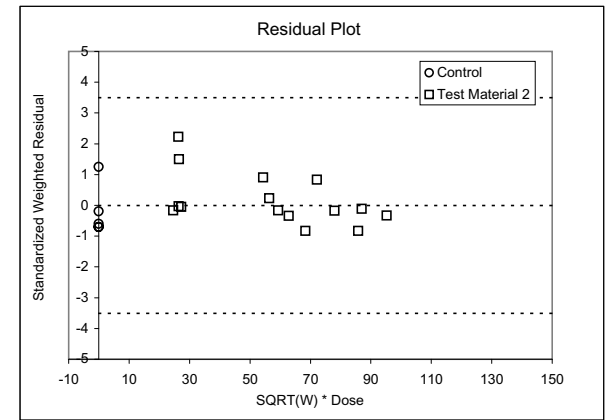
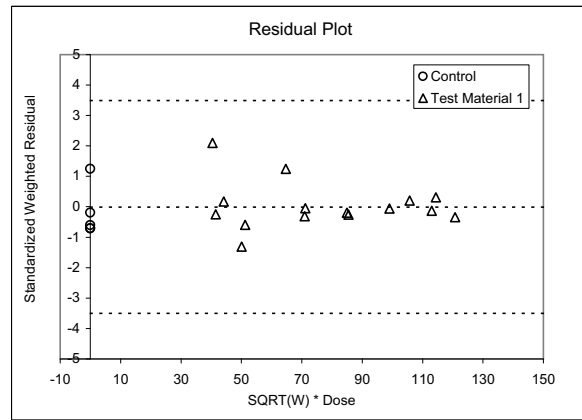
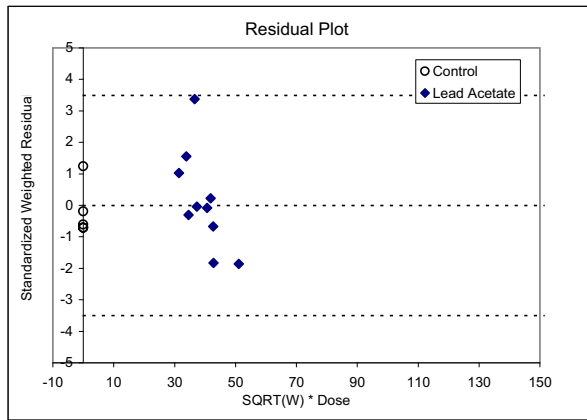
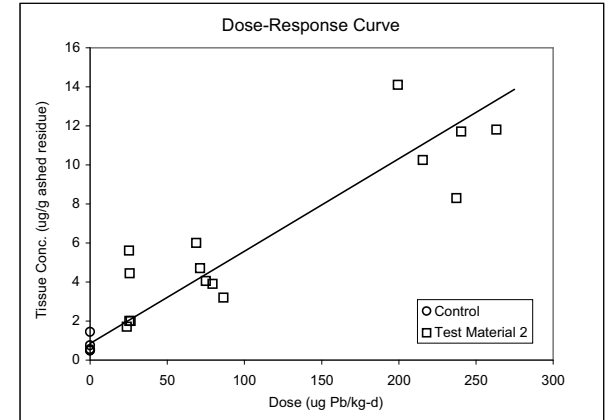
Reference Material (Lead Acetate)



Test Material 1 (California Gulch Phase I Residential Soil)



Test Material 2 (California Gulch Fe/Mn PbO)



Summary of Fitting

Parameter	Estimate	Standard Error
a	8.45E-01	1.98E-01
b1	5.91E-02	1.46E-02
b2	3.11E-02	5.78E-03
b3	4.73E-02	7.42E-03
Covariance (c1,c2)	0.1175	--
Covariance (c1,c3)	0.0828	--
Degrees of Freedom	41	--

Goodness of Fit

Statistic	Estimate
F	24.456
p	< 0.001
Adjusted R <sup>2</sup>	0.6153
AIC	216.348

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.53	0.80
Lower bound	0.33	0.51
Upper bound	0.93	1.40
Standard Error	0.153*	0.225*

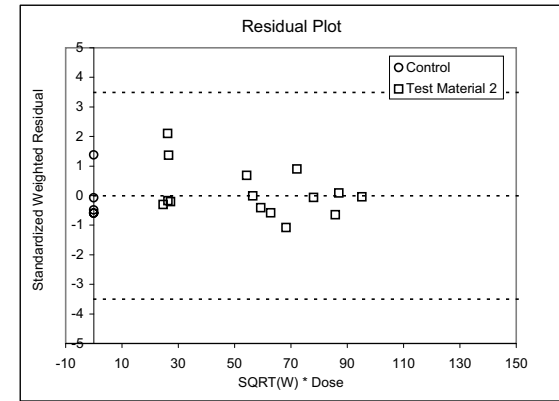
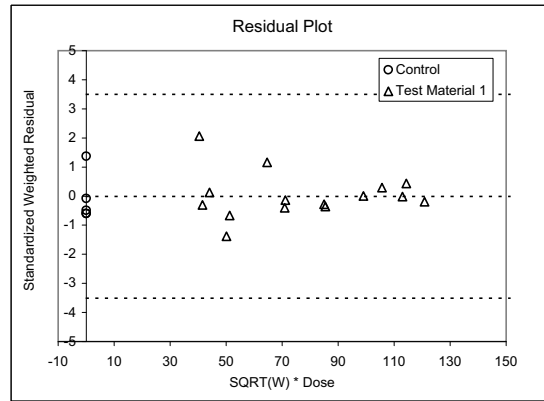
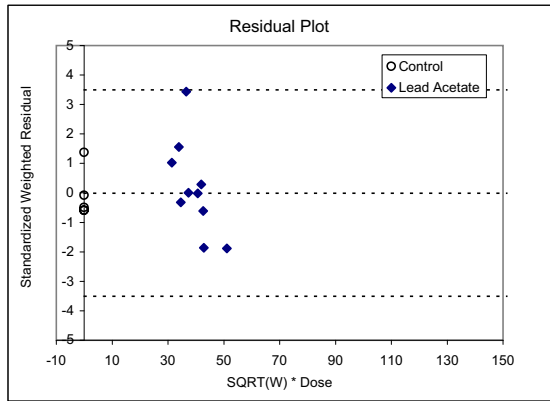
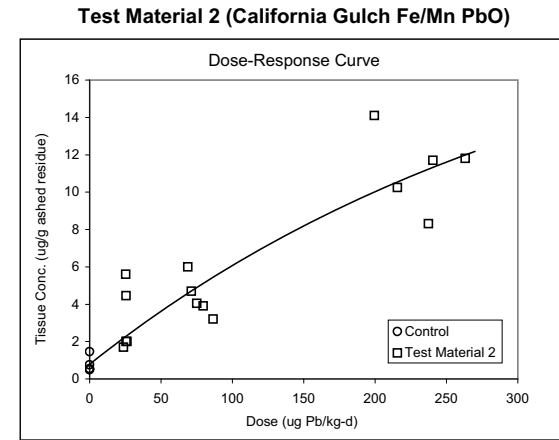
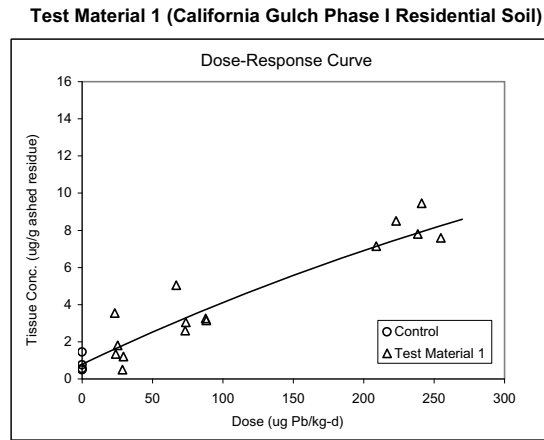
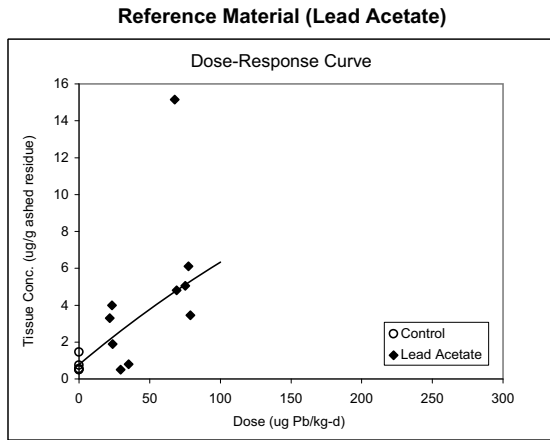
\*  $g \geq 0.05$ , estimate is uncertain

APPENDIX E

Figure 4b - All Data

Phase II Experiment 7: Femur

Exponential Model:  $y = a + b*(1-\exp(-c1*x1))+b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$



**Summary of Fitting**

Parameter	Estimate	Standard Error
a	7.87E-01	2.14E-01
b	2.09E+01	2.14E+01
c1	3.08E-03	3.58E-03
c2	1.73E-03	2.09E-03
c3	2.91E-03	3.75E-03
Covariance (c1,c2)	0.9636	--
Covariance (c1,c3)	0.9659	--
Degrees of Freedom	40	--

**Goodness of Fit**

Statistic	Estimate
F	18.305
p	< 0.001
Adjusted R <sup>2</sup>	0.6114
AIC	216.591

**RBA and Uncertainty**

	Test Material 1	Test Material 2
RBA	0.56	0.95
Lower bound	?	?
Upper bound	?	?
Standard Error	0.181*	0.324*

\*  $g \geq 0.05$ , estimate is uncertain



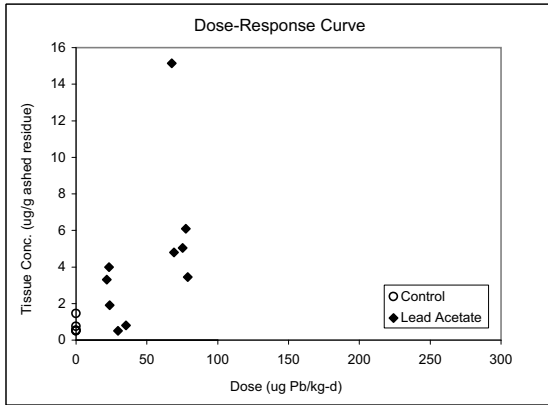
APPENDIX E

Figure 4c - All Data

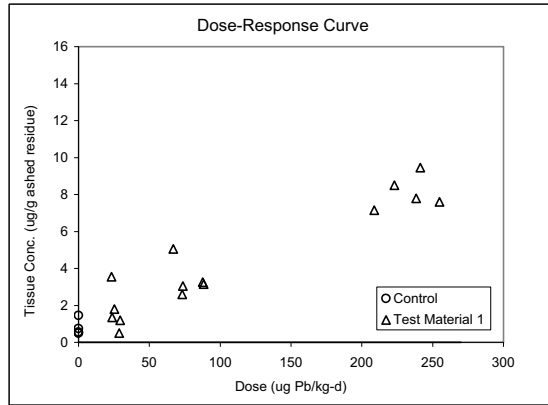
Phase II Experiment 7: Femur

Michaelis-Menton Model:  $y = a + b \cdot x1 / (c1 + x1) + b \cdot x2 / (c2 + x2) + b \cdot x3 / (c3 + x3)$

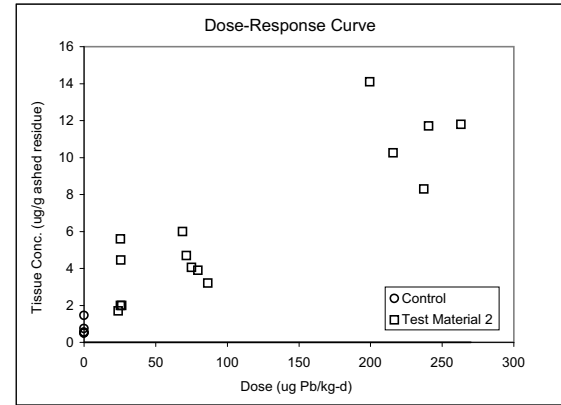
Reference Material (Lead Acetate)



Test Material 1 (California Gulch Phase I Residential Soil)



Test Material 2 (California Gulch Fe/Mn PbO)



**NO SOLUTION**

The software could not find a solution,  
or the solution was unstable and/or had unrealistic parameter estimates.

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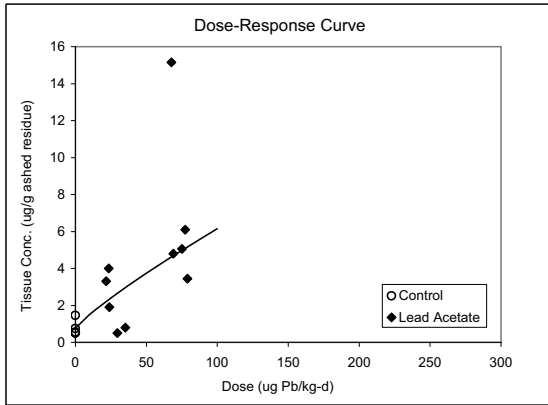
APPENDIX E

Figure 4d - All Data

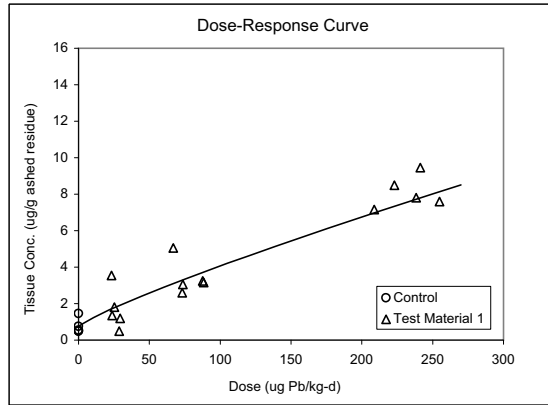
Phase II Experiment 7: Femur

Power Model:  $y = a + b1*x1^c + b2*x2^c + b3*x3^c$

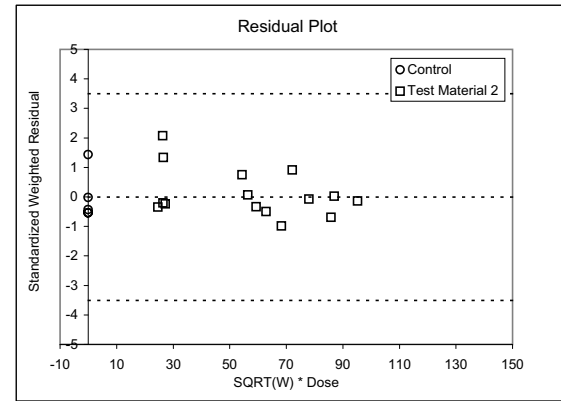
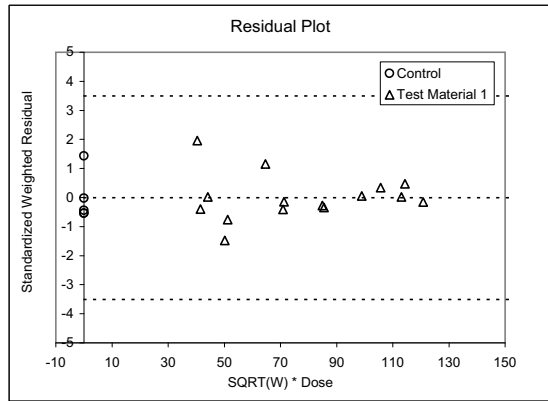
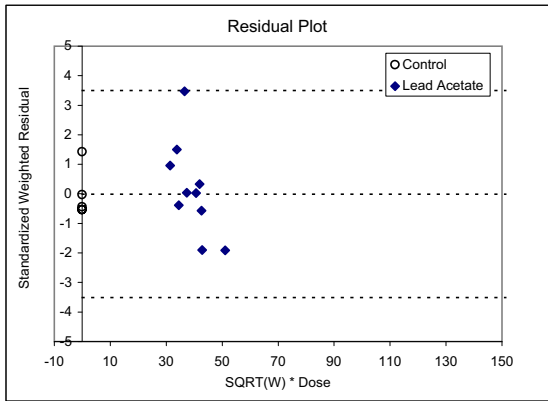
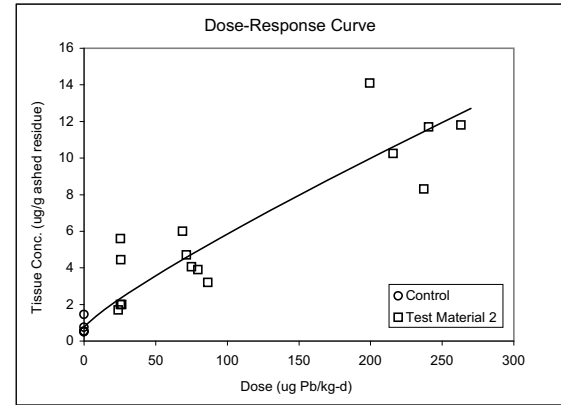
Reference Material (Lead Acetate)



Test Material 1 (California Gulch Phase I Residential Soil)



Test Material 2 (California Gulch Fe/Mn PbO)



Summary of Fitting

Parameter	Estimate	Standard Error
a	7.61E-01	2.24E-01
b1	1.03E-01	6.71E-02
b2	6.31E-02	4.86E-02
b3	9.73E-02	7.39E-02
c	8.59E-01	1.51E-01
Covariance (b1,b2)	0.9128	--
Covariance (b1,b3)	0.9157	--
Degrees of Freedom	40	--

Goodness of Fit

Statistic	Estimate
F	18.357
p	< 0.001
Adjusted R <sup>2</sup>	0.6121
AIC	216.374

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.56	0.93
Lower bound	?	?
Upper bound	?	?
Standard Error	--	--

## APPENDIX E

### EXPERIMENT 8

Test Material 1: California Gulch AV Slag  
Test Material 2: Lead Acetate - IV (for ABA determination)

- Figure 1a Blood AUC - Linear Model
- Figure 1b Blood AUC - Exponential Model
- Figure 1c Blood AUC - Michaelis-Menton Model
- Figure 1d Blood AUC - Power Model
  
- Figure 2a Liver - Linear Model (All Data)
- Figure 2a Liver - Linear Model (Outlier Excluded)
- Figure 2b Liver - Exponential Model
- Figure 2c Liver - Michaelis-Menton Model
- Figure 2d Liver - Power Model
  
- Figure 3a Kidney - Linear Model (All Data)
- Figure 3a Kidney - Linear Model (Outlier Excluded)
- Figure 3b Kidney - Exponential Model
- Figure 3c Kidney - Michaelis-Menton Model
- Figure 3d Kidney - Power Model
  
- Figure 4a Femur - Linear Model
- Figure 4b Femur - Exponential Model
- Figure 4c Femur - Michaelis-Menton Model
- Figure 4d Femur - Power Model

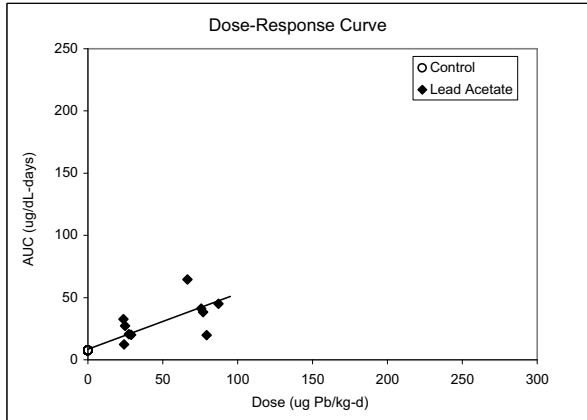
APPENDIX E

Figure 1a - All Data

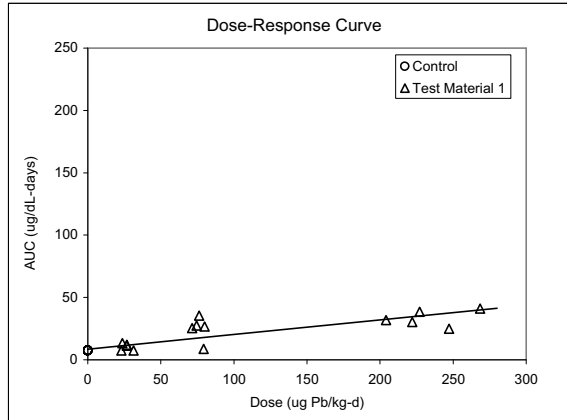
Phase II Experiment 8: Blood AUC

Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$

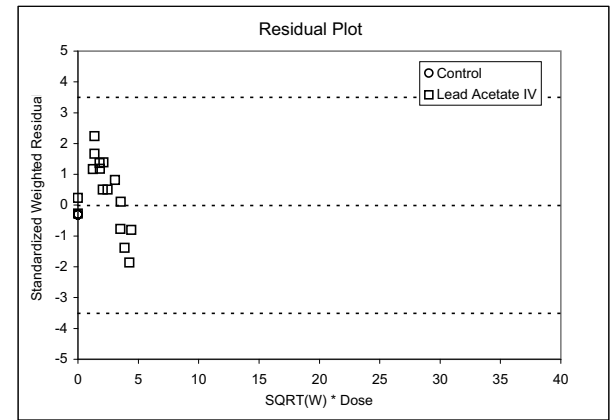
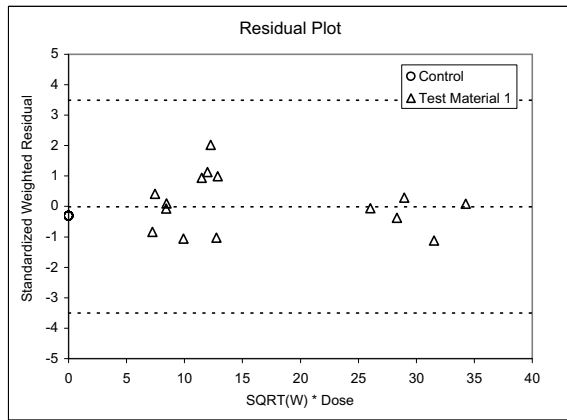
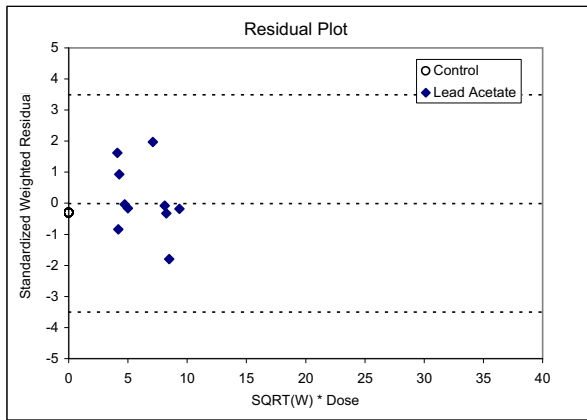
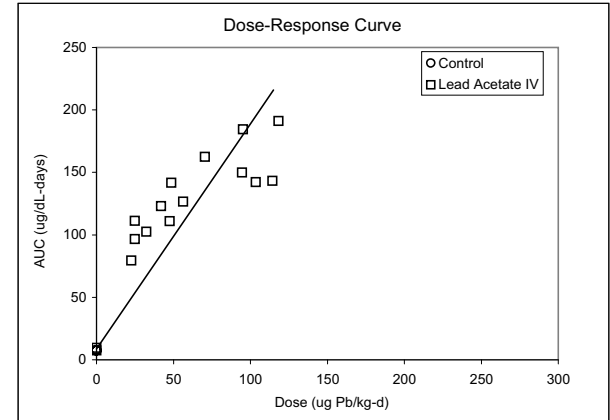
Reference Material (Lead Acetate - Oral)



Test Material 1 (California Gulch AV Slag)



Lead Acetate - IV



Summary of Fitting

Parameter	Estimate	Standard Error
a	8.59E+00	1.20E+00
b1	4.44E-01	7.45E-02
b2	1.17E-01	2.20E-02
b3	1.80E+00	1.41E-01
Covariance (c1,c2)	0.1238	--
Covariance (c1,c3)	0.0351	--
Degrees of Freedom	42	--

Goodness of Fit

Statistic	Estimate
F	70.263
p	< 0.001
Adjusted R <sup>2</sup>	0.8220
AIC	377.196

RBA and Uncertainty

	Test Material 1
RBA	0.26
Lower bound	0.17
Upper bound	0.39
Standard Error	0.062*

\*  $g \geq 0.05$ , estimate is uncertain

ABA and Uncertainty

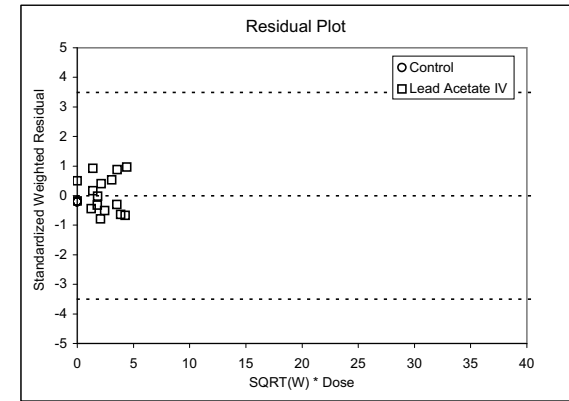
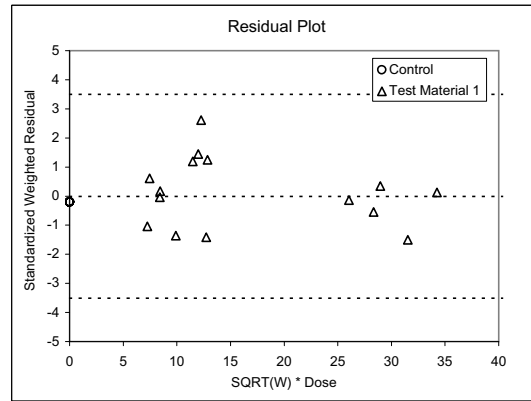
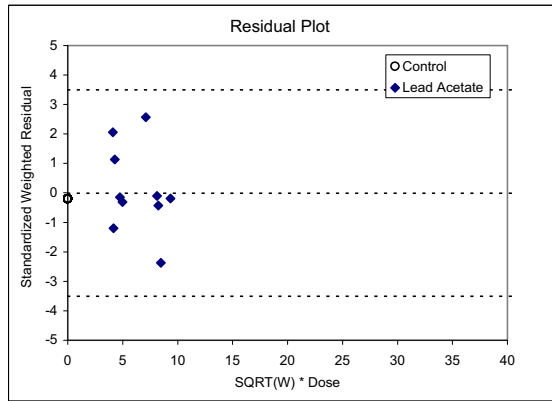
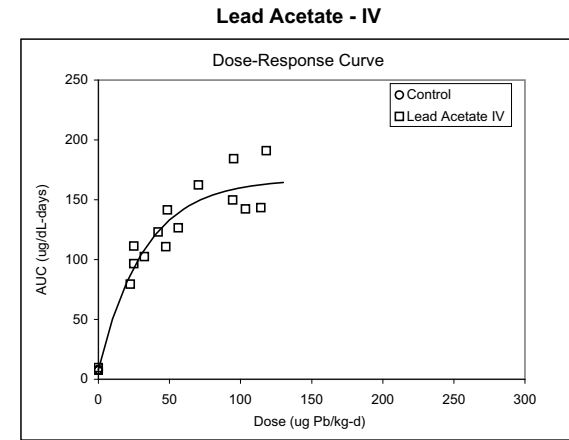
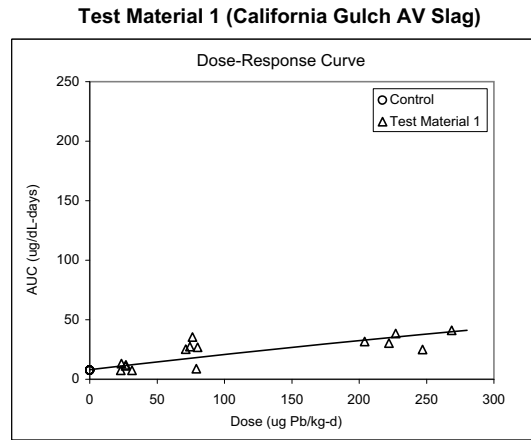
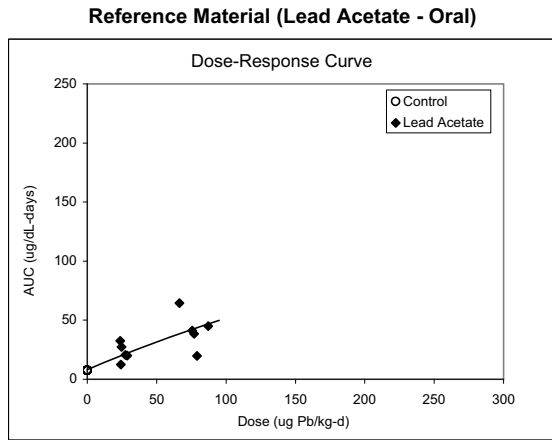
	Lead Acetate
ABA	0.25
Lower bound	0.17
Upper bound	0.33
Standard Error	0.045

APPENDIX E

Figure 1b - All Data

Phase II Experiment 8: Blood AUC

Exponential Model:  $y = a + b*(1-\exp(-c1*x1))+b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$



Summary of Fitting

Parameter	Estimate	Standard Error
a	8.04E+00	9.29E-01
b	1.59E+02	1.76E+01
c1	3.20E-03	5.86E-04
c2	8.34E-04	1.59E-04
c3	3.08E-02	8.40E-03
Covariance (c1,c2)	0.4920	--
Covariance (c1,c3)	0.5858	--
Degrees of Freedom	41	--

Goodness of Fit

Statistic	Estimate
F	99.719
p	< 0.001
Adjusted R <sup>2</sup>	0.8977
AIC	337.913

RBA and Uncertainty

	Test Material 1
RBA	0.26
Lower bound	0.19
Upper bound	0.36
Standard Error	0.049*

\*  $g \geq 0.05$ , estimate is uncertain

ABA and Uncertainty

	Lead Acetate
ABA	0.10
Lower bound	0.07
Upper bound	0.17
Standard Error	0.023*

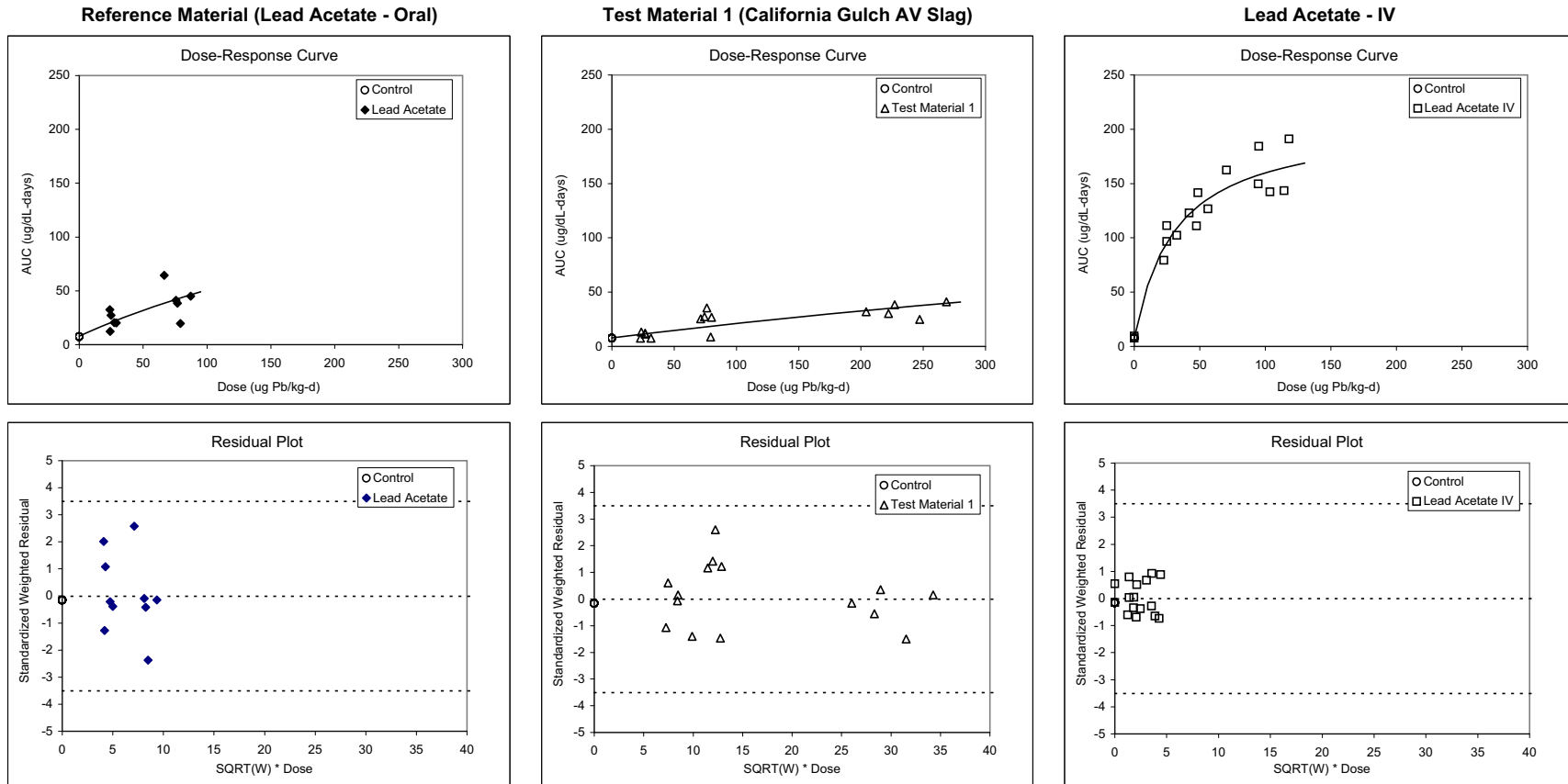
\*  $g \geq 0.05$ , estimate is uncertain

APPENDIX E

Figure 1c - All Data

Phase II Experiment 8: Blood AUC

Michaelis-Menton Model:  $y = a + b \cdot x_1 / (c_1 + x_1) + b \cdot x_2 / (c_2 + x_2) + b \cdot x_3 / (c_3 + x_3)$



Summary of Fitting

Parameter	Estimate	Standard Error
a	7.93E+00	9.30E-01
b	2.00E+02	3.32E+01
c1	3.67E+02	8.85E+01
c2	1.42E+03	3.47E+02
c3	3.18E+01	1.39E+01
Covariance (c1,c2)	0.6808	--
Covariance (c1,c3)	0.7694	--
Degrees of Freedom	41	--

Goodness of Fit

Statistic	Estimate
F	101.785
p	< 0.001
Adjusted R <sup>2</sup>	0.8996
AIC	336.939

RBA and Uncertainty

	Test Material 1
RBA	0.26
Lower bound	0.18
Upper bound	0.37
Standard Error	0.050*

\* g ≥ 0.05, estimate is uncertain

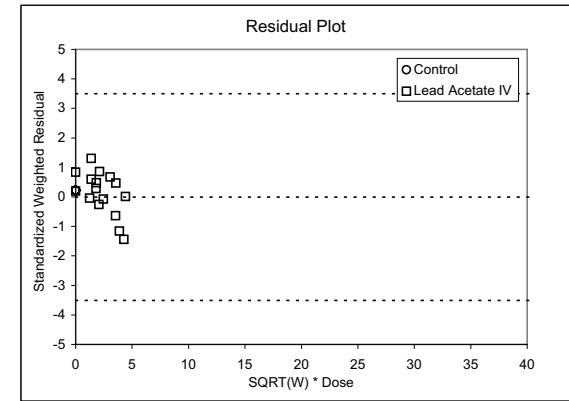
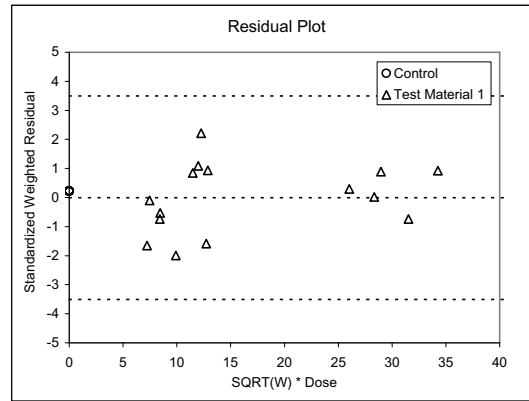
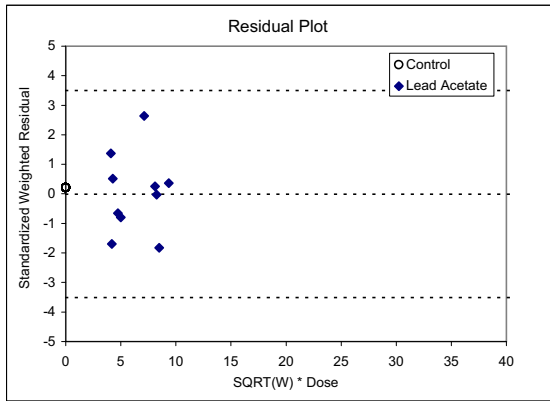
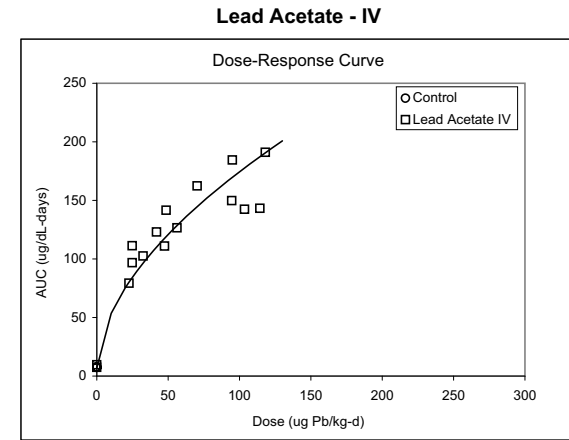
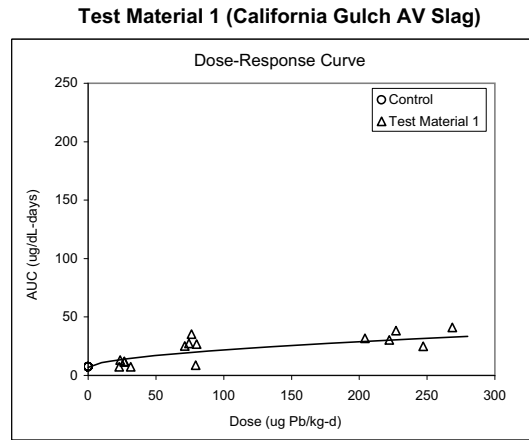
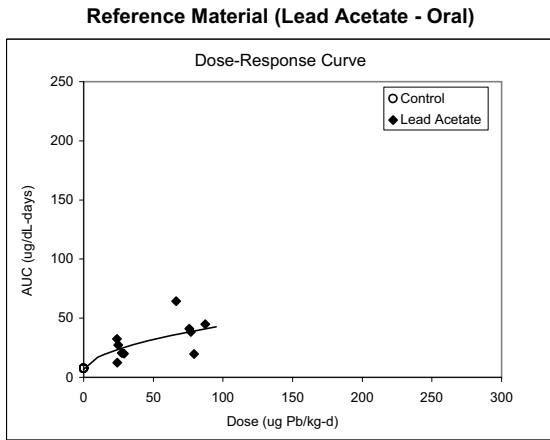
ABA and Uncertainty

	Lead Acetate
ABA	0.09
Lower bound	0.03
Upper bound	0.13
Standard Error	0.026*

\* g ≥ 0.05, estimate is uncertain

APPENDIX E

**Figure 1d - All Data**  
**Phase II Experiment 8: Blood AUC**  
**Power Model:  $y = a + b1*x1^c + b2*x2^c + b3*x3^c$**



**Summary of Fitting**

Parameter	Estimate	Standard Error
a	6.89E+00	1.11E+00
b1	2.86E+00	1.01E+00
b2	1.16E+00	4.93E-01
b3	1.30E+01	4.52E+00
c	5.56E-01	8.15E-02
Covariance (b1,b2)	0.8993	--
Covariance (b1,b3)	0.9228	--
Degrees of Freedom	41	--

**Goodness of Fit**

Statistic	Estimate
F	87.734
p	< 0.001
Adjusted R <sup>2</sup>	0.8852
AIC	344.366

**RBA and Uncertainty**

	Test Material 1
RBA	0.20
Lower bound	0.07
Upper bound	0.34
Standard Error	--

**ABA and Uncertainty**

	Lead Acetate
ABA	0.07
Lower bound	0.04
Upper bound	0.11
Standard Error	--

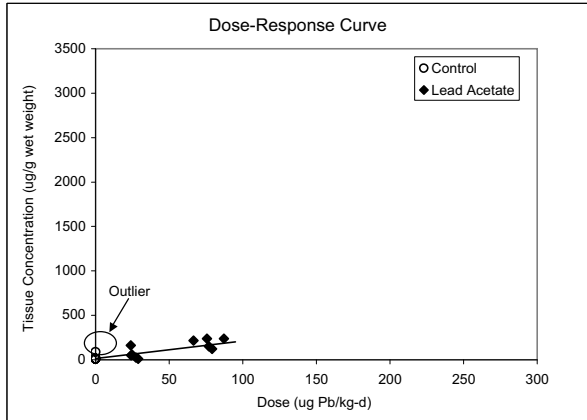
APPENDIX E

Figure 2a - All Data

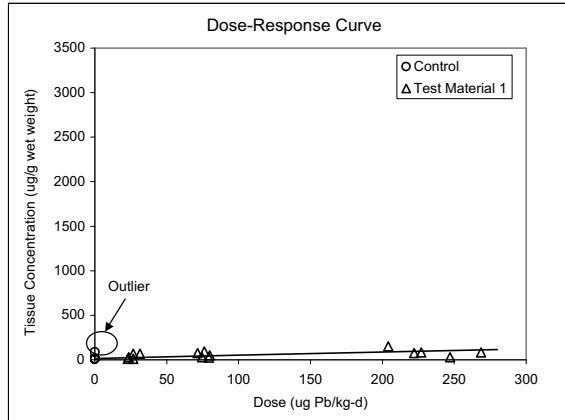
Phase II Experiment 8: Liver

Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$

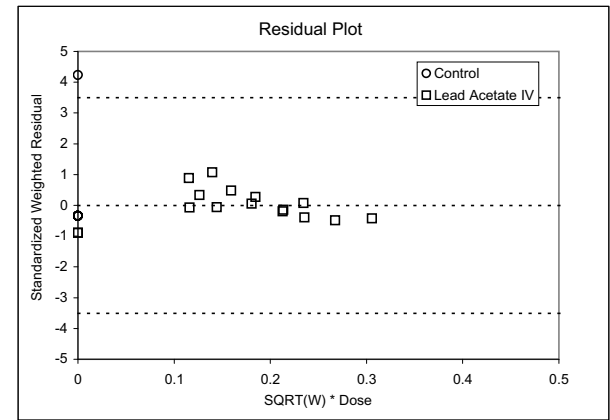
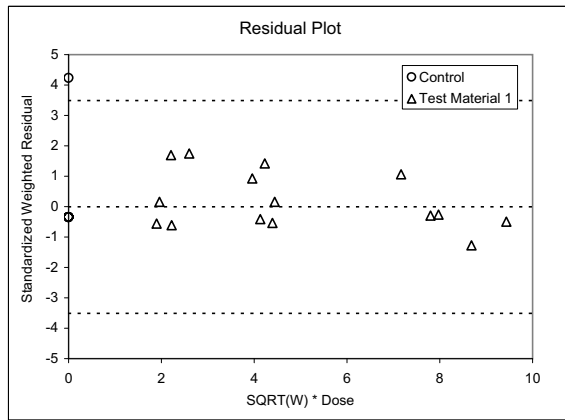
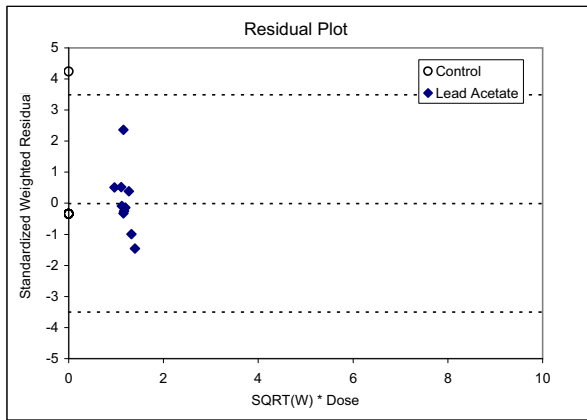
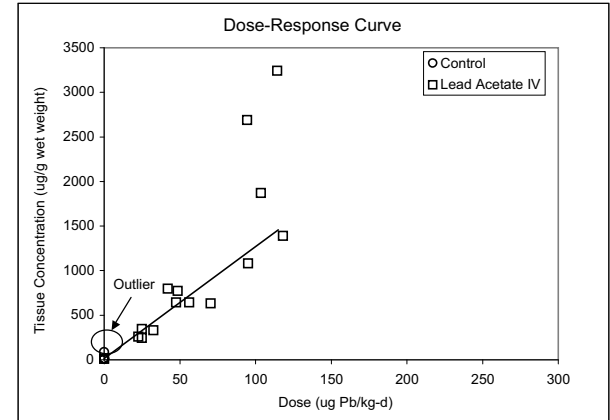
Reference Material (Lead Acetate - Oral)



Test Material 1 (California Gulch AV Slag)



Lead Acetate - IV



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.56E+01	3.76E+00
b1	1.94E+00	5.76E-01
b2	3.55E-01	1.04E-01
b3	1.25E+01	2.91E+00
Covariance (c1,c2)	0.0491	--
Covariance (c1,c3)	0.0059	--
Degrees of Freedom	42	--

Goodness of Fit

Statistic	Estimate
F	13.353
p	< 0.001
Adjusted R <sup>2</sup>	0.4516
AIC	629.699

RBA and Uncertainty

	Test Material 1
RBA	0.18
Lower bound	0.08
Upper bound	0.40
Standard Error	0.074*

\* g ≥ 0.05, estimate is uncertain

ABA and Uncertainty

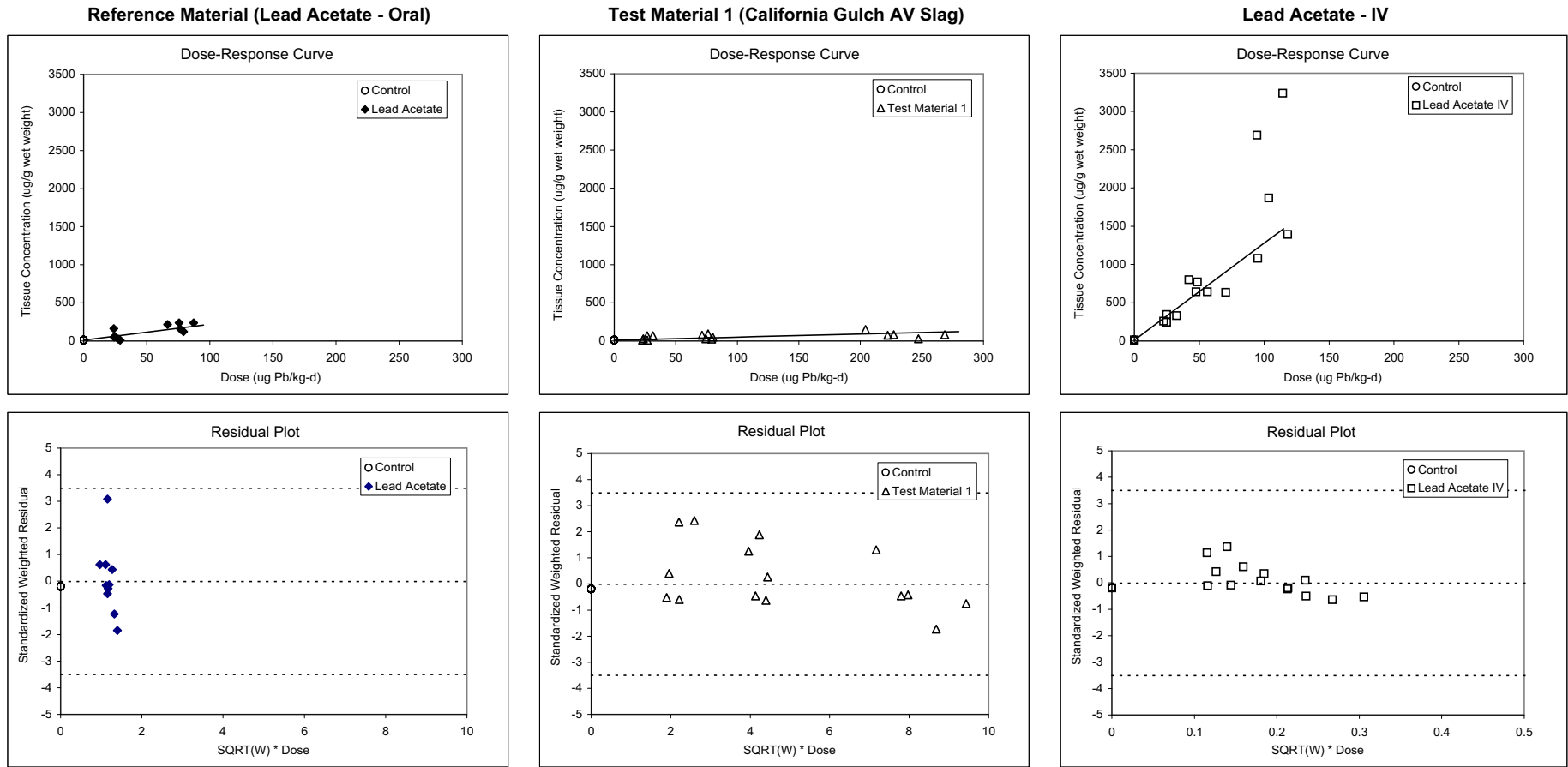
	Lead Acetate
ABA	0.15
Lower bound	0.07
Upper bound	0.29
Standard Error	0.058*

\* g ≥ 0.05, estimate is uncertain



APPENDIX E

**Figure 2a - Outlier Excluded**  
**Phase II Experiment 8: Liver**  
**Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$**



**Summary of Fitting**

Parameter	Estimate	Standard Error
a	1.10E+01	2.03E+00
b1	2.07E+00	4.45E-01
b2	3.91E-01	7.97E-02
b3	1.27E+01	2.26E+00
Covariance (c1,c2)	0.0243	--
Covariance (c1,c3)	0.0028	--
Degrees of Freedom	41	--

**Goodness of Fit**

Statistic	Estimate
F	25.206
p	< 0.001
Adjusted R <sup>2</sup>	0.6227
AIC	537.628

**RBA and Uncertainty**

	Test Material 1
RBA	0.19
Lower bound	0.11
Upper bound	0.32
Standard Error	0.055*

\* g ≥ 0.05, estimate is uncertain

**ABA and Uncertainty**

	Lead Acetate
ABA	0.16
Lower bound	0.10
Upper bound	0.26
Standard Error	0.046*

\* g ≥ 0.05, estimate is uncertain

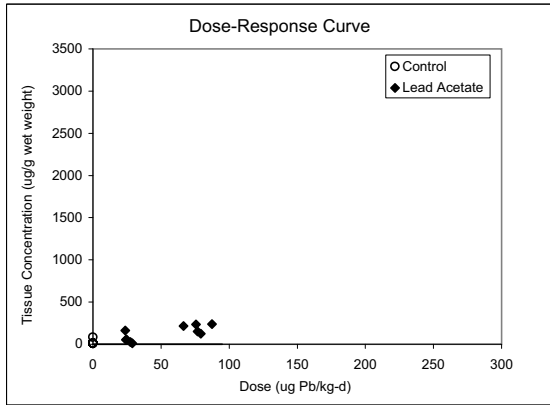
APPENDIX E

Figure 2b - All Data

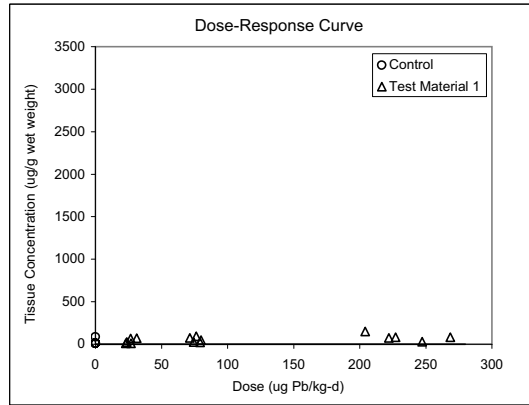
Phase II Experiment 8: Liver

Exponential Model:  $y = a + b*(1-\exp(-c1*x1)) + b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$

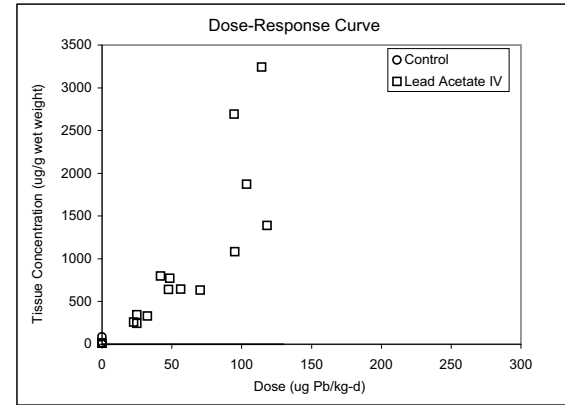
Reference Material (Lead Acetate - Oral)



Test Material 1 (California Gulch AV Slag)



Lead Acetate - IV



**NO SOLUTION**

The software could not find a solution,  
or the solution was unstable and/or had unrealistic parameter estimates.

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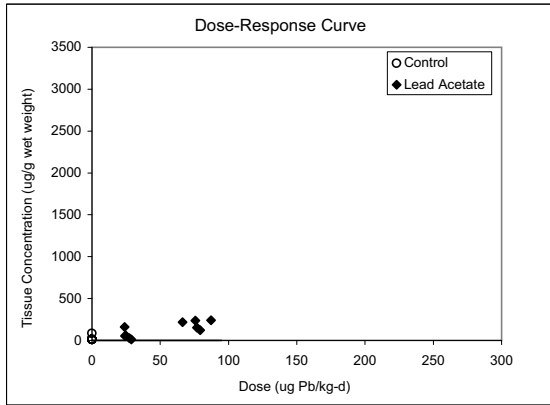
APPENDIX E

Figure 2c - All Data

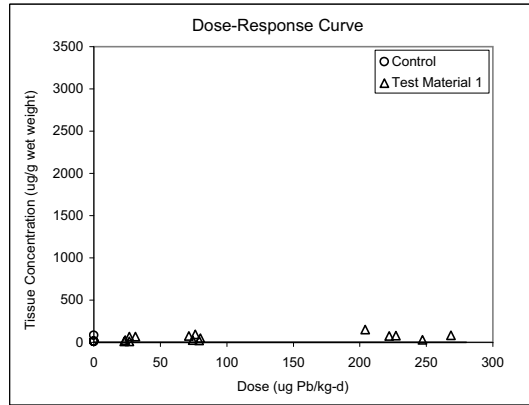
Phase II Experiment 8: Liver

Michaelis-Menton Model:  $y = a + \frac{b \cdot x_1}{c_1 + x_1} + \frac{b \cdot x_2}{c_2 + x_2} + \frac{b \cdot x_3}{c_3 + x_3}$

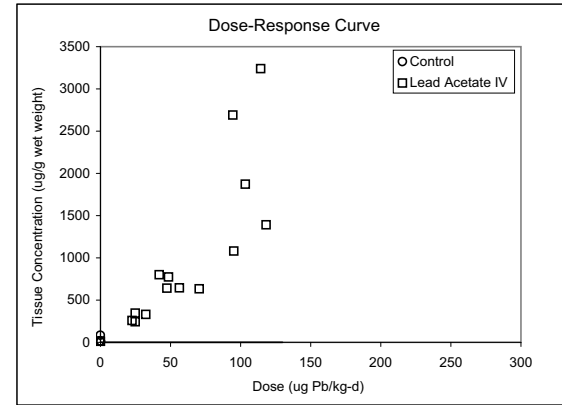
Reference Material (Lead Acetate - Oral)



Test Material 1 (California Gulch AV Slag)



Lead Acetate - IV



**NO SOLUTION**

The software could not find a solution,  
or the solution was unstable and/or had unrealistic parameter estimates.

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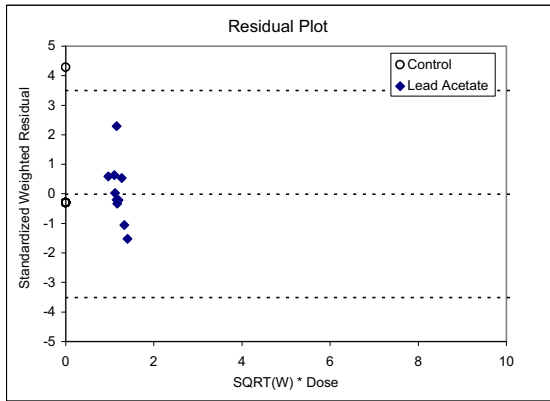
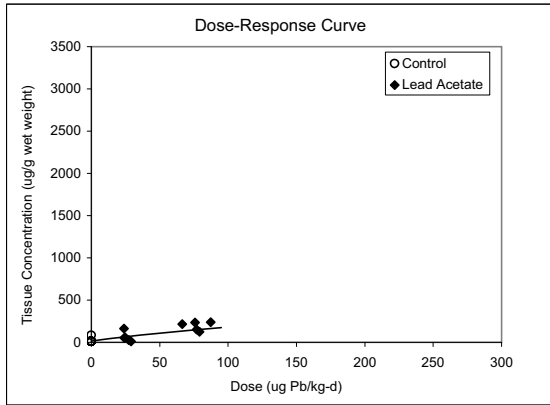
APPENDIX E

Figure 2d - All Data

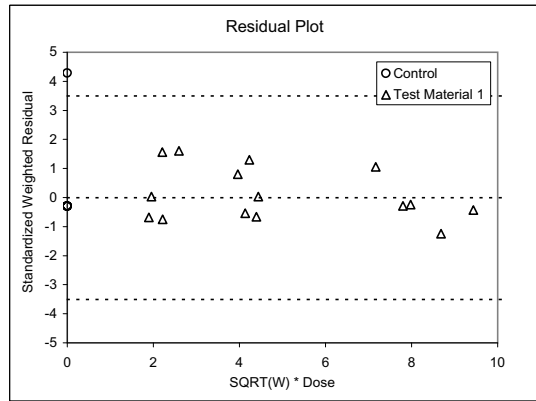
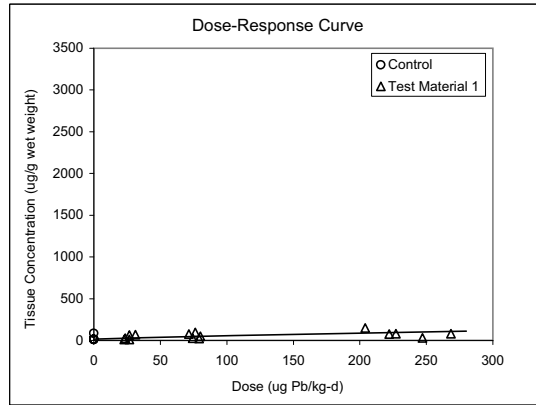
Phase II Experiment 8: Liver

Power Model:  $y = a + b1*x1^c + b2*x2^c + b3*x3^c$

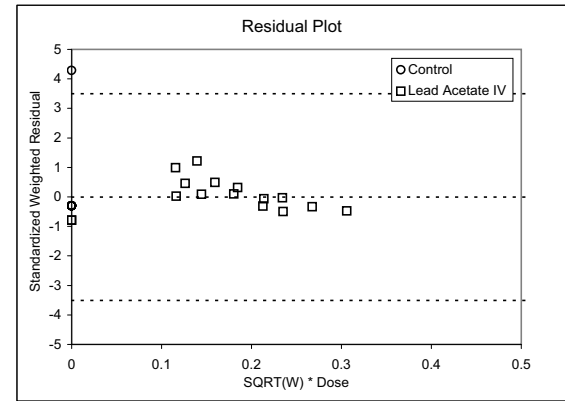
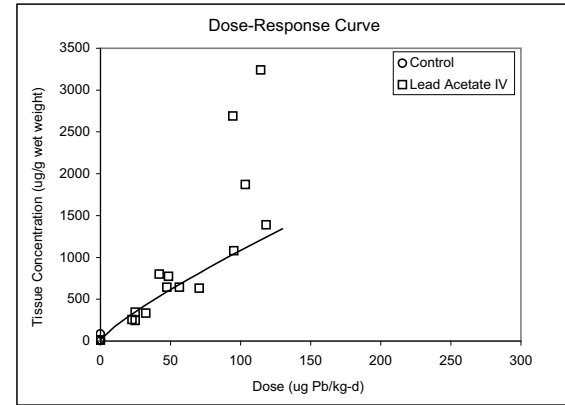
Reference Material (Lead Acetate - Oral)



Test Material 1 (California Gulch AV Slag)



Lead Acetate - IV



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.49E+01	3.93E+00
b1	3.60E+00	3.67E+00
b2	8.77E-01	1.19E+00
b3	2.31E+01	2.32E+01
c	8.33E-01	2.63E-01
Covariance (b1,b2)	0.9380	--
Covariance (b1,b3)	0.9287	--
Degrees of Freedom	41	--

Goodness of Fit

Statistic	Estimate
F	9.890
p	< 0.001
Adjusted R <sup>2</sup>	0.4414
AIC	630.613

RBA and Uncertainty

	Test Material 1
RBA	0.18
Lower bound	?
Upper bound	?
Standard Error	--

ABA and Uncertainty

	Lead Acetate
ABA	0.11
Lower bound	?
Upper bound	?
Standard Error	--

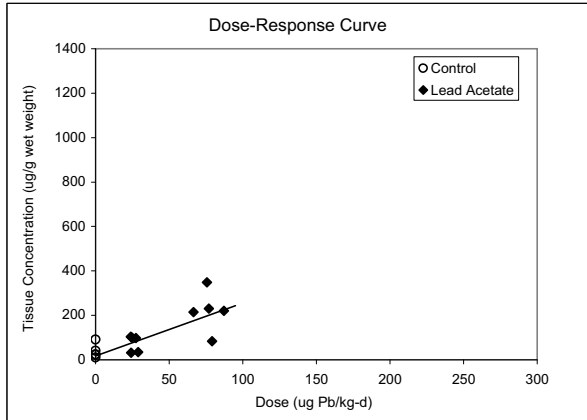
APPENDIX E

Figure 3a - All Data

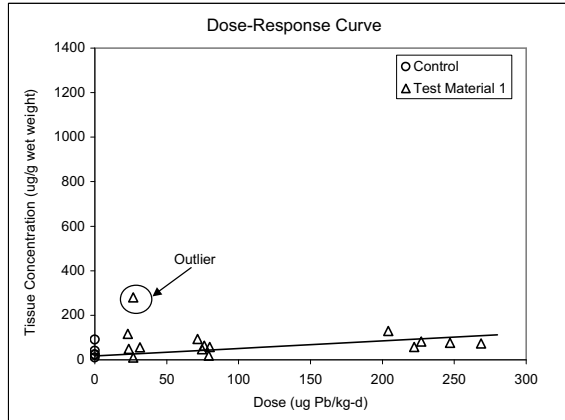
Phase II Experiment 8: Kidney

Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$

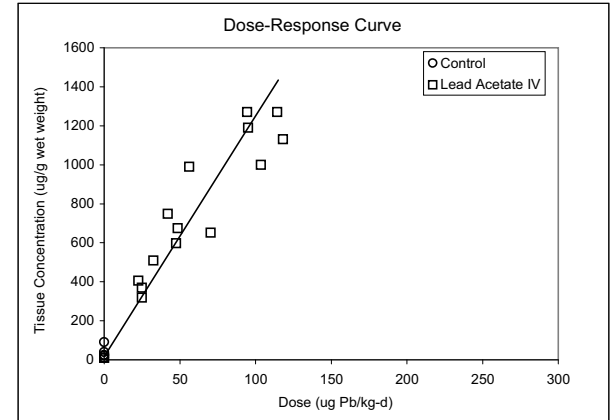
Reference Material (Lead Acetate - Oral)



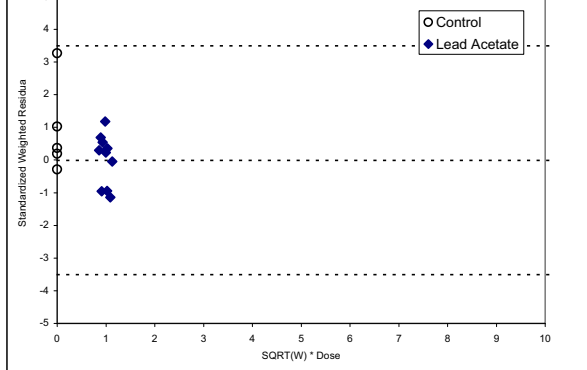
Test Material 1 (California Gulch AV Slag)



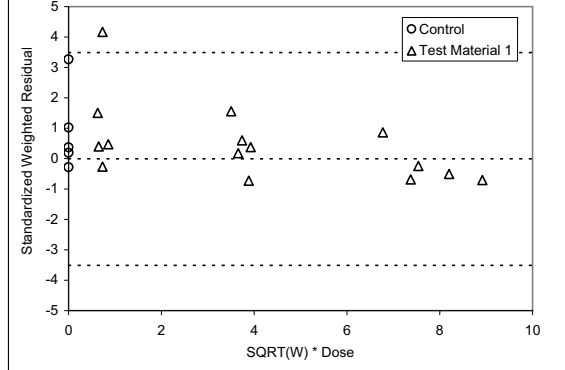
Lead Acetate - IV



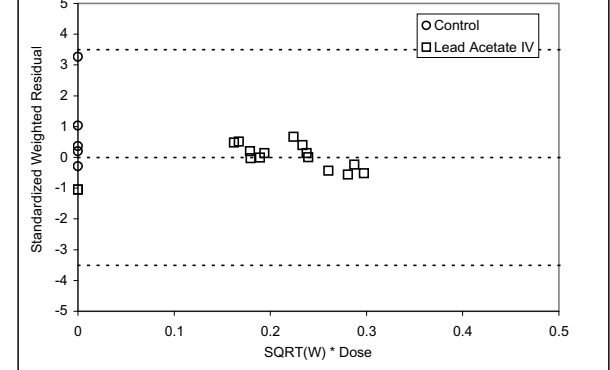
Residual Plot



Residual Plot



Residual Plot



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.66E+01	4.21E+00
b1	2.39E+00	5.76E-01
b2	3.42E-01	9.48E-02
b3	1.23E+01	2.07E+00
Covariance (c1,c2)	0.0503	--
Covariance (c1,c3)	0.0067	--
Degrees of Freedom	42	--

Goodness of Fit

Statistic	Estimate
F	21.139
p	< 0.001
Adjusted R <sup>2</sup>	0.5731
AIC	586.555

RBA and Uncertainty

Statistic	Test Material 1
RBA	0.14
Lower bound	0.07
Upper bound	0.27
Standard Error	0.051*

\* g ≥ 0.05, estimate is uncertain

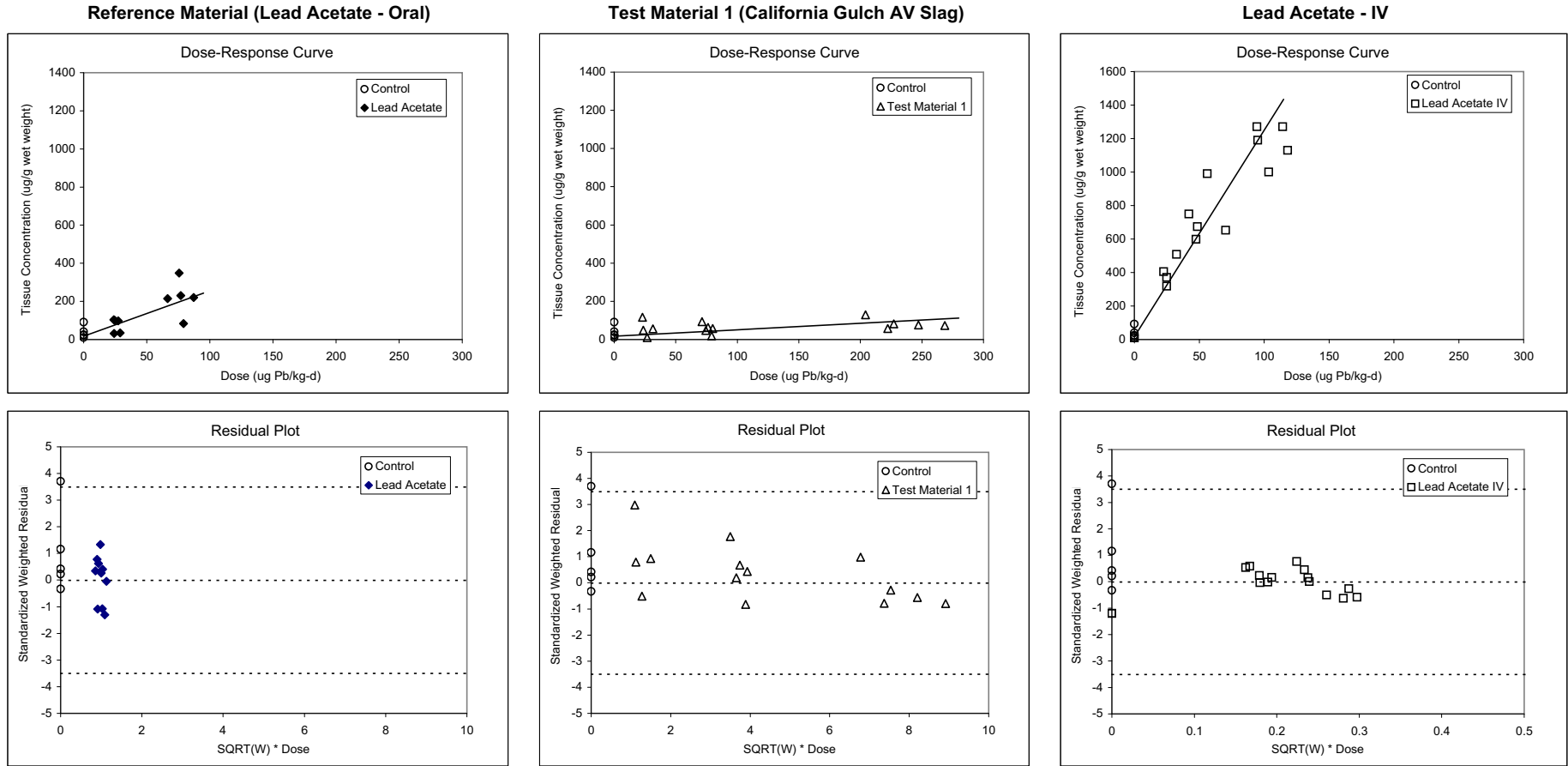
ABA and Uncertainty

Statistic	Lead Acetate
ABA	0.19
Lower bound	0.11
Upper bound	0.31
Standard Error	0.057*

\* g ≥ 0.05, estimate is uncertain

APPENDIX E

**Figure 3a - Outlier Excluded**  
**Phase II Experiment 8: Kidney**  
**Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$**



**Summary of Fitting**

Parameter	Estimate	Standard Error
a	1.67E+01	3.65E+00
b1	2.39E+00	5.05E-01
b2	3.41E-01	8.29E-02
b3	1.23E+01	1.82E+00
Covariance (c1,c2)	0.0519	--
Covariance (c1,c3)	0.0065	--
Degrees of Freedom	41	--

**Goodness of Fit**

Statistic	Estimate
F	27.487
p	< 0.001
Adjusted R <sup>2</sup>	0.6436
AIC	540.150

**RBA and Uncertainty**

	Test Material 1
RBA	0.14
Lower bound	0.08
Upper bound	0.25
Standard Error	0.045*

\* g ≥ 0.05, estimate is uncertain

**ABA and Uncertainty**

	Lead Acetate
ABA	0.19
Lower bound	0.12
Upper bound	0.29
Standard Error	0.050*

\* g ≥ 0.05, estimate is uncertain

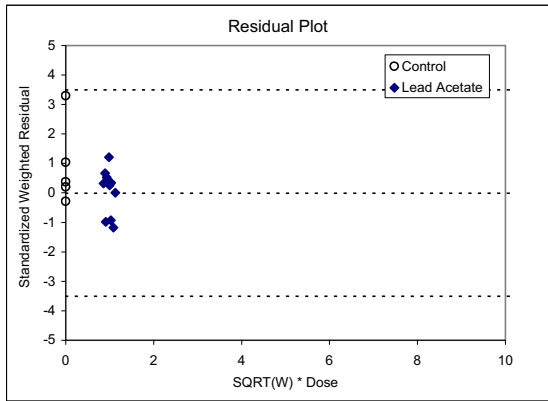
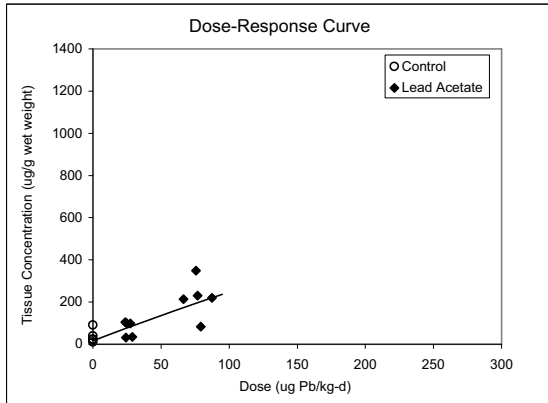
APPENDIX E

Figure 3b - All Data

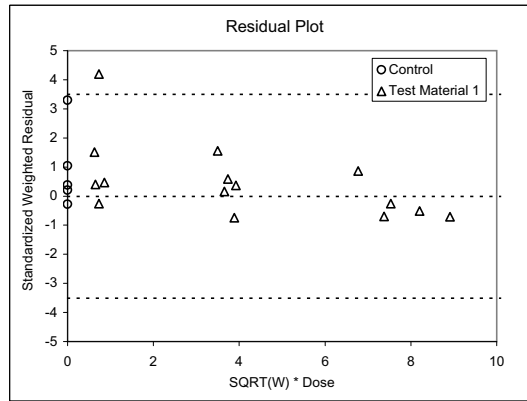
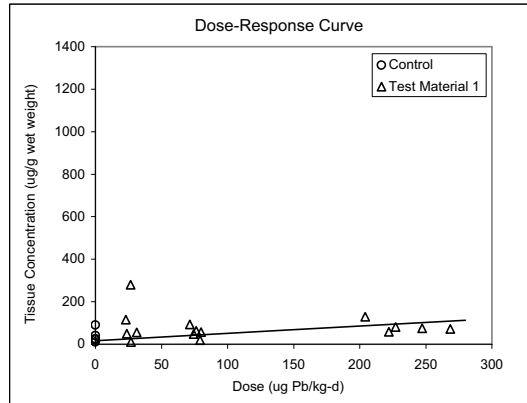
Phase II Experiment 8: Kidney

Exponential Model:  $y = a + b*(1-\exp(-c1*x1))+b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$

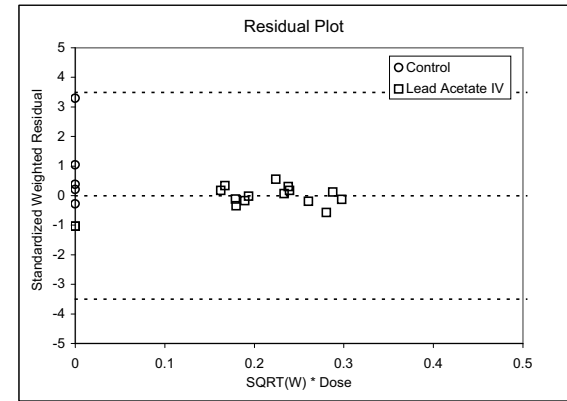
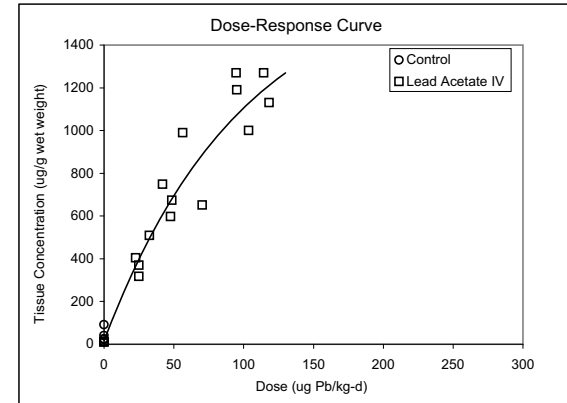
Reference Material (Lead Acetate - Oral)



Test Material 1 (California Gulch AV Slag)



Lead Acetate - IV



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.65E+01	4.23E+00
b	1.72E+03	1.60E+03
c1	1.44E-03	1.44E-03
c2	2.05E-04	2.04E-04
c3	1.00E-02	1.29E-02
Covariance (c1,c2)	0.9322	--
Covariance (c1,c3)	0.9527	--
Degrees of Freedom	41	--

Goodness of Fit

Statistic	Estimate
F	15.994
p	< 0.001
Adjusted R <sup>2</sup>	0.5713
AIC	585.963

RBA and Uncertainty

	Test Material 1
RBA	0.14
Lower bound	?
Upper bound	?
Standard Error	0.052*

\*  $g \geq 0.05$ , estimate is uncertain

ABA and Uncertainty

	Lead Acetate
ABA	0.14
Lower bound	?
Upper bound	?
Standard Error	0.064*

\*  $g \geq 0.05$ , estimate is uncertain

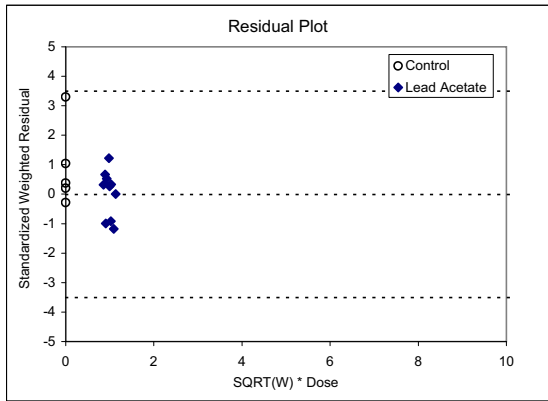
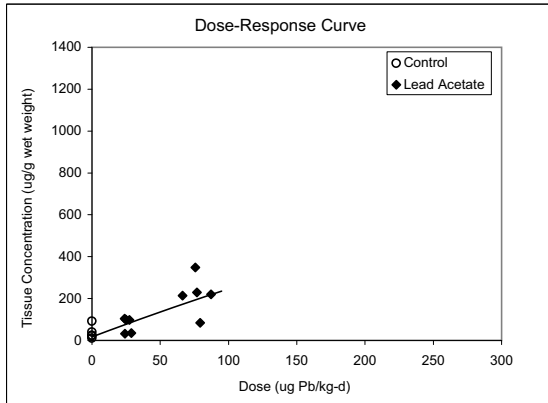
APPENDIX E

Figure 3c - All Data

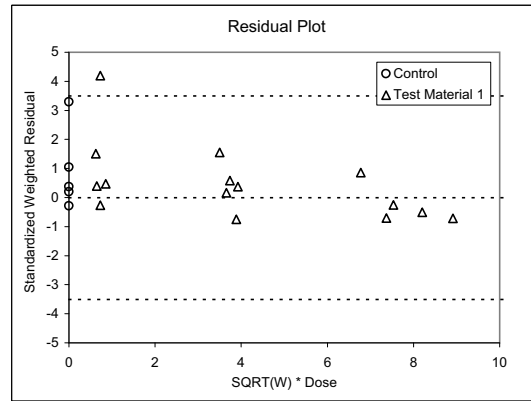
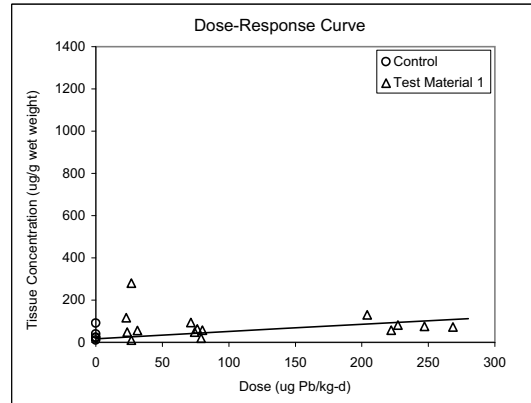
Phase II Experiment 8: Kidney

Michaelis-Menton Model:  $y = a + b*x1/(c1+x1) + b*x2/(c2+x2) + b*x3/(c3+x3)$

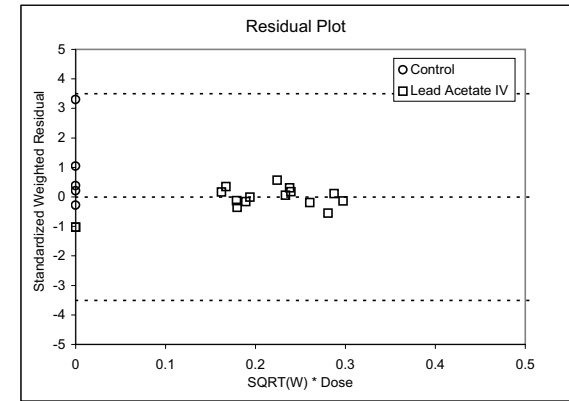
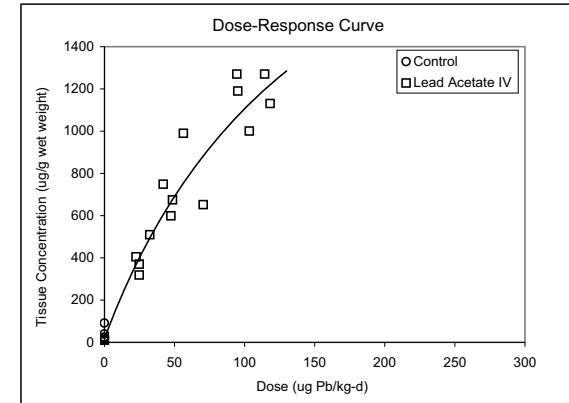
Reference Material (Lead Acetate - Oral)



Test Material 1 (California Gulch AV Slag)



Lead Acetate - IV



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.64E+01	4.23E+00
b	2.81E+03	3.20E+03
c1	1.13E+03	1.37E+03
c2	7.92E+03	9.53E+03
c3	1.58E+02	2.46E+02
Covariance (c1,c2)	0.9535	--
Covariance (c1,c3)	0.9679	--
Degrees of Freedom	41	--

Goodness of Fit

Statistic	Estimate
F	15.996
p	< 0.001
Adjusted R <sup>2</sup>	0.5714
AIC	585.953

RBA and Uncertainty

	Test Material 1
RBA	0.14
Lower bound	?
Upper bound	?
Standard Error	0.053*

\*  $g \geq 0.05$ , estimate is uncertain

ABA and Uncertainty

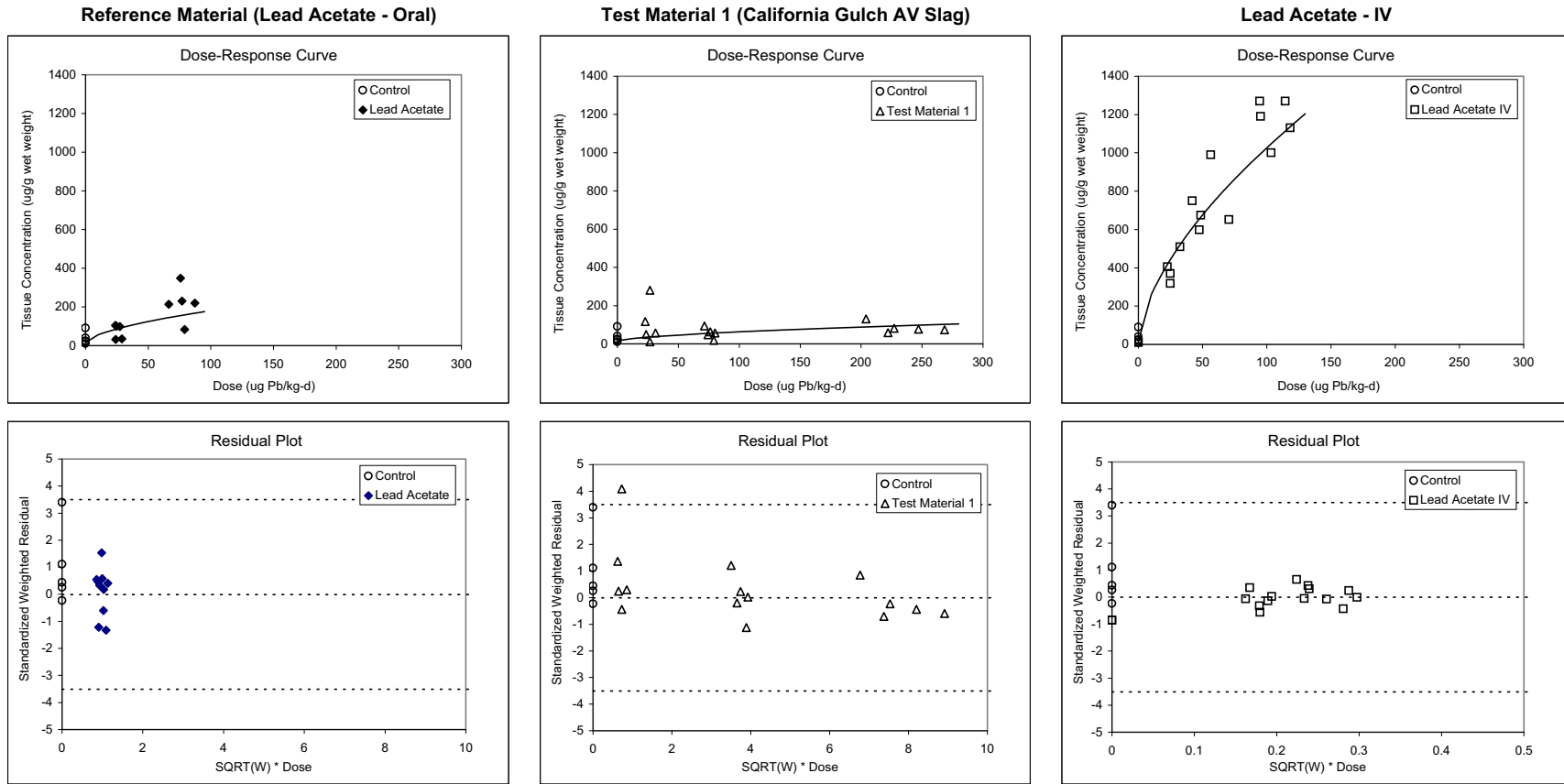
	Lead Acetate
ABA	0.14
Lower bound	?
Upper bound	?
Standard Error	0.068*

\*  $g \geq 0.05$ , estimate is uncertain



APPENDIX E

**Figure 3d - All Data**  
**Phase II Experiment 8: Kidney**  
**Power Model:  $y = a + b1*x1^c + b2*x2^c + b3*x3^c$**



**Summary of Fitting**

Parameter	Estimate	Standard Error
a	1.53E+01	4.23E+00
b1	9.75E+00	7.60E+00
b2	2.77E+00	2.94E+00
b3	5.93E+01	4.88E+01
c	6.16E-01	2.04E-01
Covariance (b1,b2)	0.9292	--
Covariance (b1,b3)	0.9318	--
Degrees of Freedom	41	--

**Goodness of Fit**

Statistic	Estimate
F	16.981
p	< 0.001
Adjusted R <sup>2</sup>	0.5869
AIC	581.290

**RBA and Uncertainty**

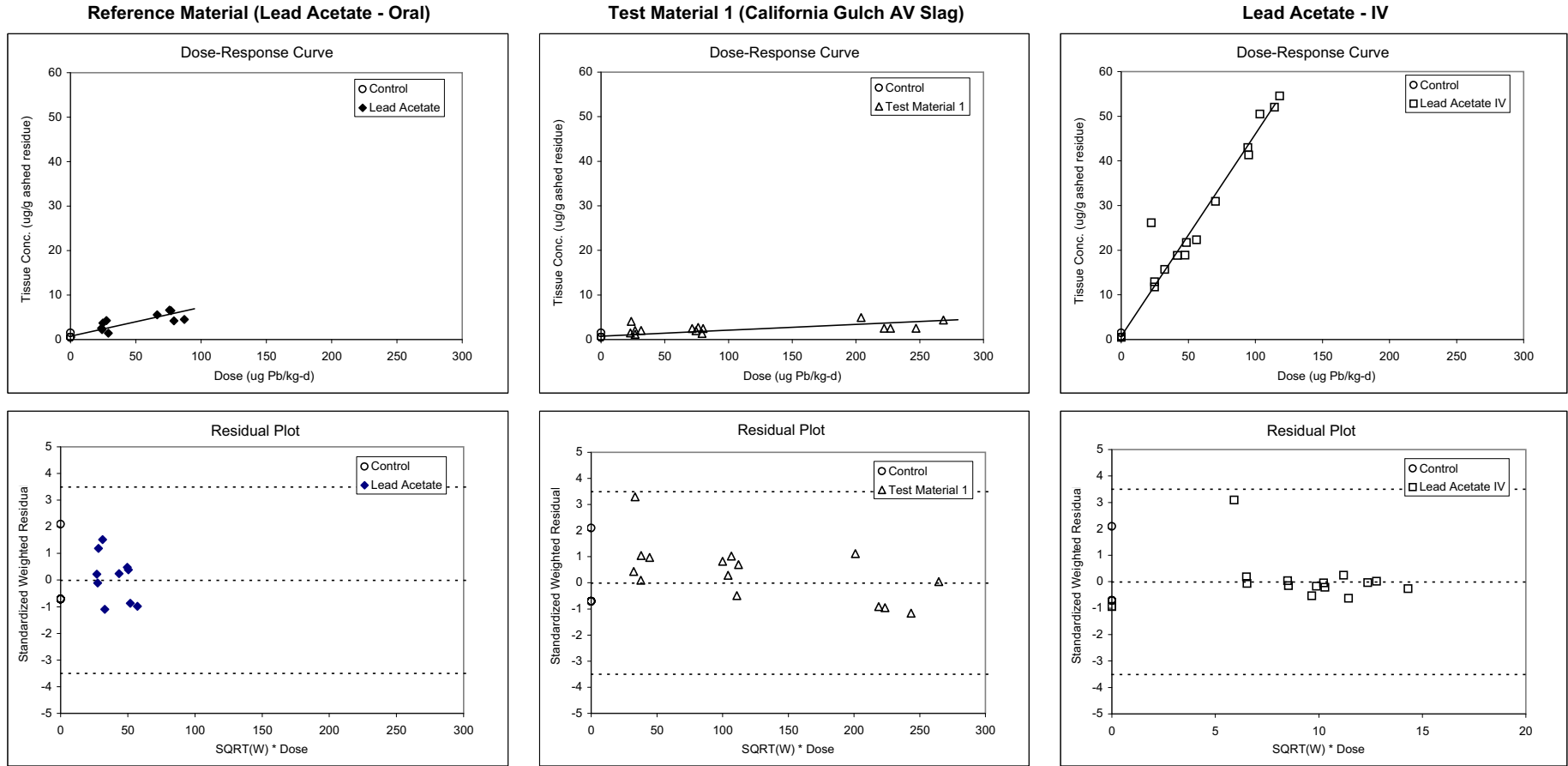
	Test Material 1
RBA	0.13
Lower bound	?
Upper bound	?
Standard Error	--

**ABA and Uncertainty**

	Lead Acetate
ABA	0.05
Lower bound	?
Upper bound	?
Standard Error	--

APPENDIX E

Figure 4a - All Data  
Phase II Experiment 8: Femur  
Linear Model:  $y = a + b_1*x_1 + b_2*x_2 + b_3*x_3$



Summary of Fitting

Parameter	Estimate	Standard Error
a	7.54E-01	1.21E-01
b1	6.49E-02	1.05E-02
b2	1.32E-02	2.45E-03
b3	4.53E-01	3.53E-02
Covariance (c1,c2)	0.0708	--
Covariance (c1,c3)	0.0128	--
Degrees of Freedom	42	--

Goodness of Fit

Statistic	Estimate
F	74.474
p	< 0.001
Adjusted R <sup>2</sup>	0.8305
AIC	193.909

RBA and Uncertainty

	Test Material 1
RBA	0.20
Lower bound	0.13
Upper bound	0.30
Standard Error	0.048*

\*  $g \geq 0.05$ , estimate is uncertain

ABA and Uncertainty

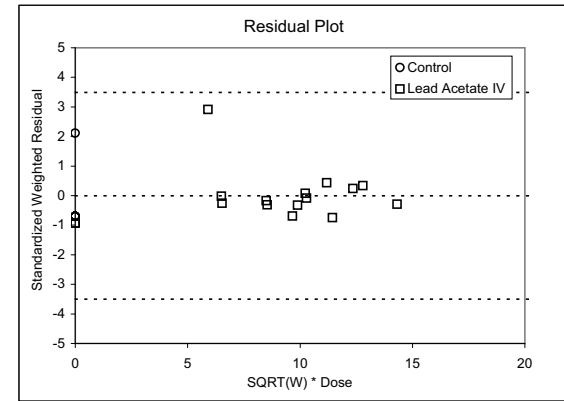
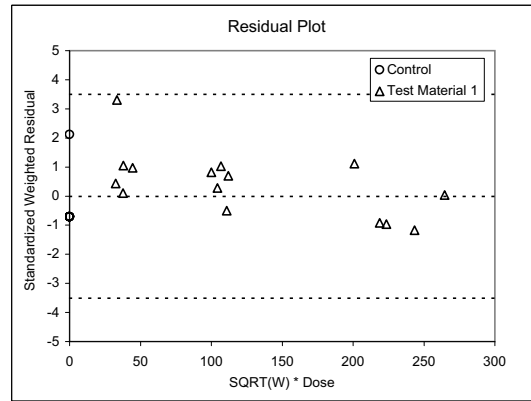
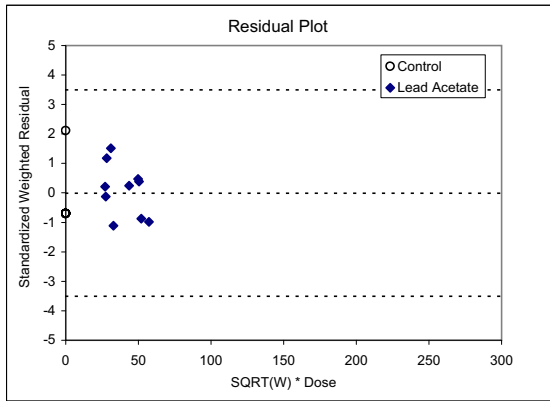
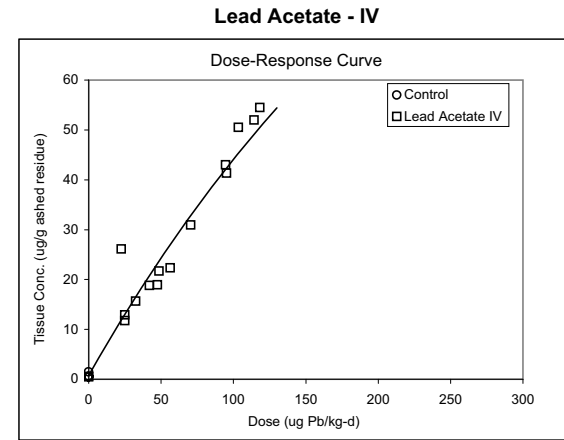
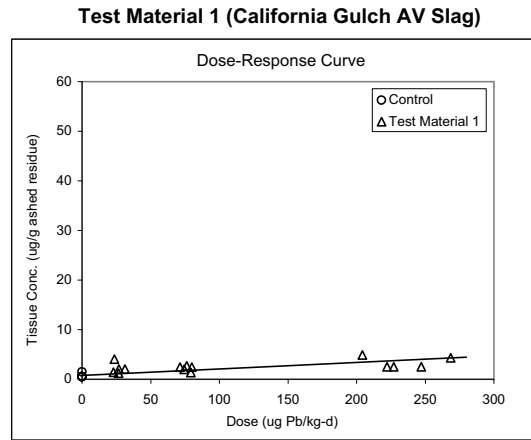
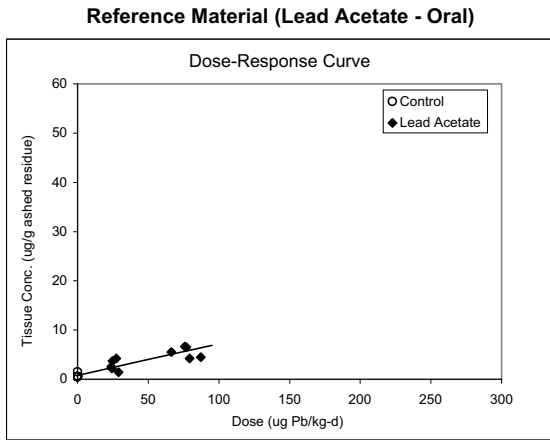
	Lead Acetate
ABA	0.14
Lower bound	0.10
Upper bound	0.19
Standard Error	0.026

APPENDIX E

Figure 4b - All Data

Phase II Experiment 8: Femur

Exponential Model:  $y = a + b*(1-\exp(-c1*x1))+b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$



Summary of Fitting

Parameter	Estimate	Standard Error
a	7.50E-01	1.22E-01
b	1.48E+02	2.03E+02
c1	4.47E-04	6.30E-04
c2	9.03E-05	1.27E-04
c3	3.47E-03	5.42E-03
Covariance (c1,c2)	0.9853	--
Covariance (c1,c3)	0.9917	--
Degrees of Freedom	41	--

Goodness of Fit

Statistic	Estimate
F	55.160
p	< 0.001
Adjusted R <sup>2</sup>	0.8280
AIC	195.180

RBA and Uncertainty

	Test Material 1
RBA	0.20
Lower bound	?
Upper bound	?
Standard Error	0.049*

\* g ≥ 0.05, estimate is uncertain

ABA and Uncertainty

	Lead Acetate
ABA	0.13
Lower bound	?
Upper bound	?
Standard Error	0.032*

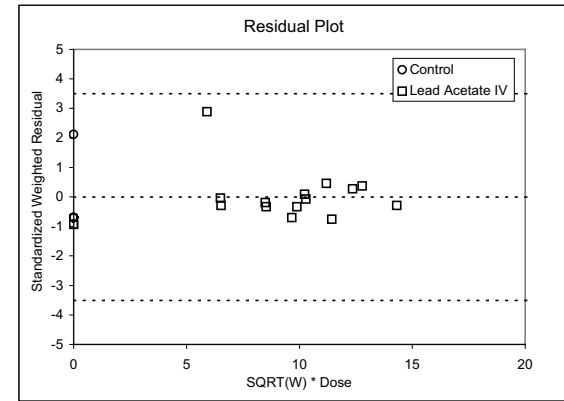
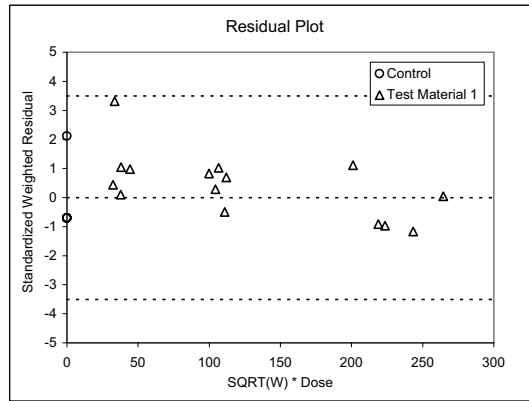
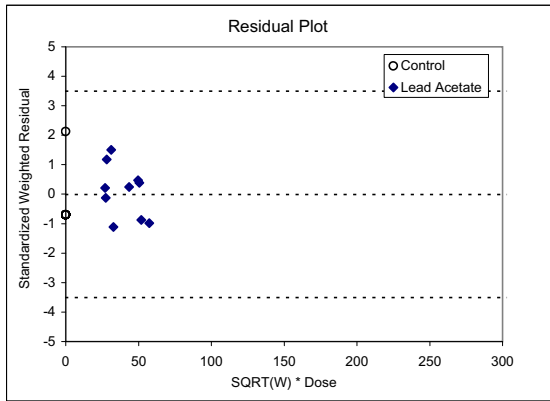
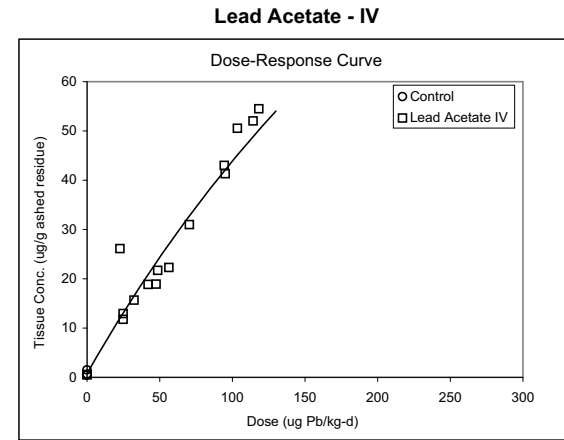
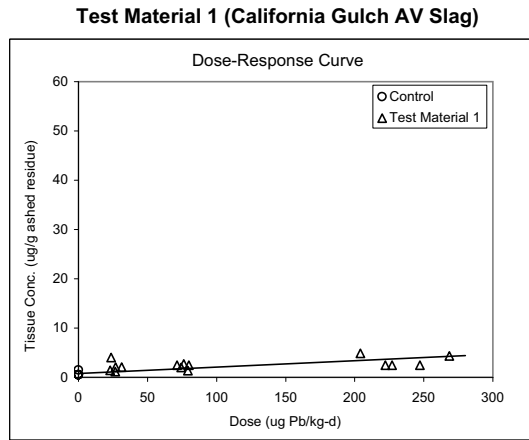
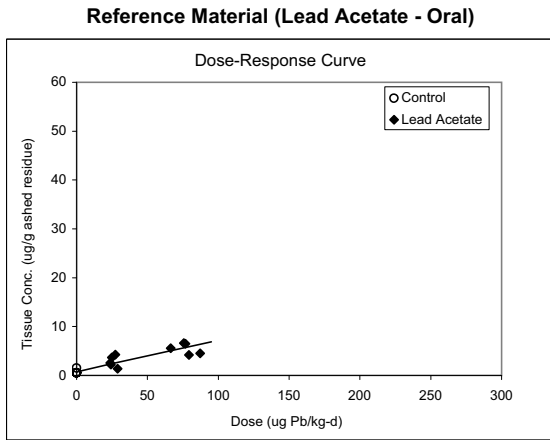
\* g ≥ 0.05, estimate is uncertain

APPENDIX E

Figure 4c - All Data

Phase II Experiment 8: Femur

Michaelis-Menton Model:  $y = a + b \cdot x_1 / (c_1 + x_1) + b \cdot x_2 / (c_2 + x_2) + b \cdot x_3 / (c_3 + x_3)$



Summary of Fitting

Parameter	Estimate	Standard Error
a	7.49E-01	1.22E-01
b	2.47E+02	3.32E+02
c1	3.72E+03	5.14E+03
c2	1.84E+04	2.54E+04
c3	4.72E+02	7.29E+02
Covariance (c1,c2)	0.9848	--
Covariance (c1,c3)	0.9913	--
Degrees of Freedom	41	--

Goodness of Fit

Statistic	Estimate
F	55.226
p	< 0.001
Adjusted R <sup>2</sup>	0.8282
AIC	195.104

RBA and Uncertainty

	Test Material 1
RBA	0.20
Lower bound	?
Upper bound	?
Standard Error	0.049*

\* g ≥ 0.05, estimate is uncertain

ABA and Uncertainty

	Lead Acetate
ABA	0.13
Lower bound	?
Upper bound	?
Standard Error	0.032*

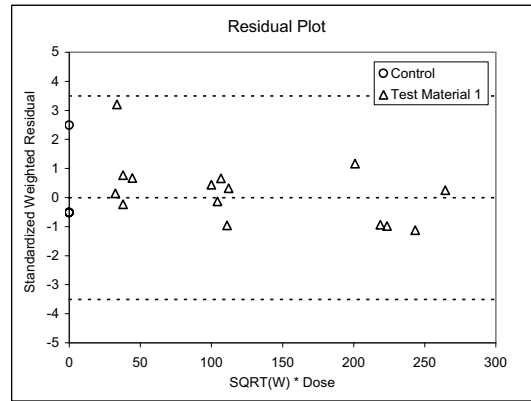
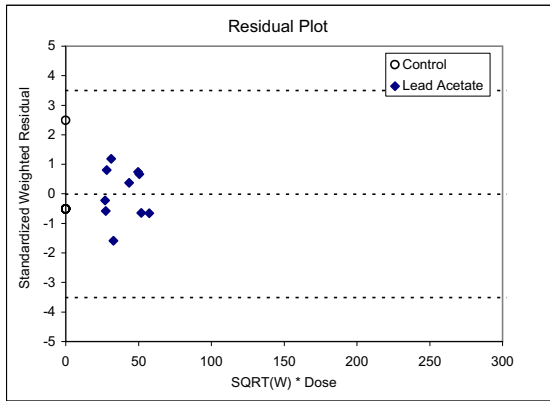
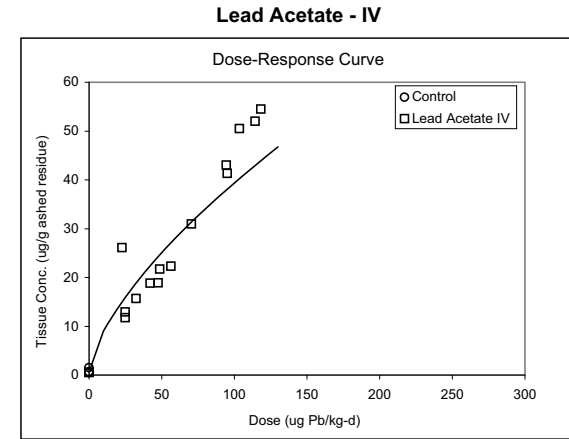
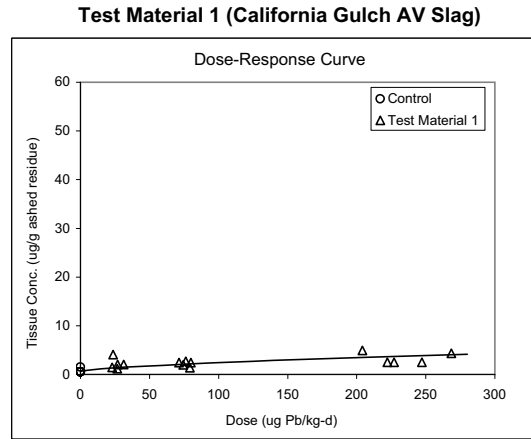
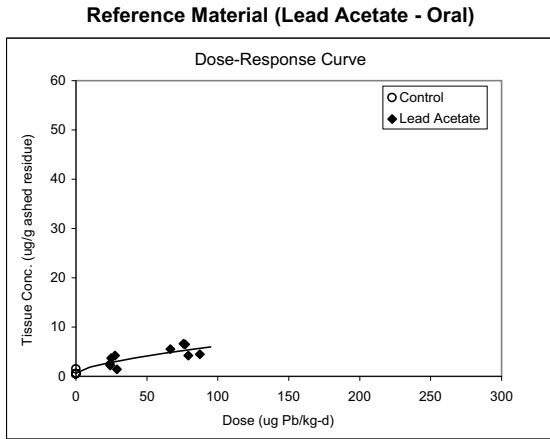
\* g ≥ 0.05, estimate is uncertain

APPENDIX E

Figure 4d - All Data

Phase II Experiment 8: Femur

Power Model:  $y = a + b1 \cdot x1^c + b2 \cdot x2^c + b3 \cdot x3^c$



Summary of Fitting

Parameter	Estimate	Standard Error
a	6.72E-01	1.18E-01
b1	2.56E-01	1.15E-01
b2	8.15E-02	4.63E-02
b3	1.81E+00	7.96E-01
c	6.66E-01	1.07E-01
Covariance (b1,b2)	0.9154	--
Covariance (b1,b3)	0.9329	--
Degrees of Freedom	41	--

Goodness of Fit

Statistic	Estimate
F	64.812
p	< 0.001
Adjusted R <sup>2</sup>	0.8501
AIC	185.595

RBA and Uncertainty

	Test Material 1
RBA	0.18
Lower bound	0.01
Upper bound	0.31
Standard Error	--

ABA and Uncertainty

	Lead Acetate
ABA	0.05
Lower bound	0.03
Upper bound	0.10
Standard Error	--

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## APPENDIX E

### EXPERIMENT 9

Test Material 1: Palmerton Location 2

Test Material 2: Palmerton Location 4

- Figure 1a Blood AUC - Linear Model
- Figure 1b Blood AUC - Exponential Model
- Figure 1c Blood AUC - Michaelis-Menton Model
- Figure 1d Blood AUC - Power Model
  
- Figure 2a Liver - Linear Model
- Figure 2b Liver - Exponential Model
- Figure 2c Liver - Michaelis-Menton Model
- Figure 2d Liver - Power Model
  
- Figure 3a Kidney - Linear Model
- Figure 3b Kidney - Exponential Model
- Figure 3c Kidney - Michaelis-Menton Model
- Figure 3d Kidney - Power Model
  
- Figure 4a Femur - Linear Model
- Figure 4b Femur - Exponential Model
- Figure 4c Femur - Michaelis-Menton Model
- Figure 4d Femur - Power Model

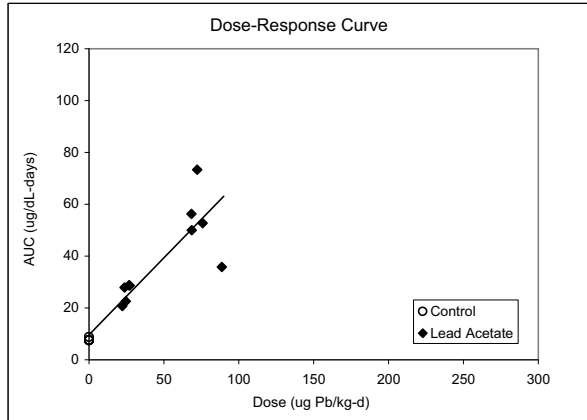
APPENDIX E

Figure 1a - All Data

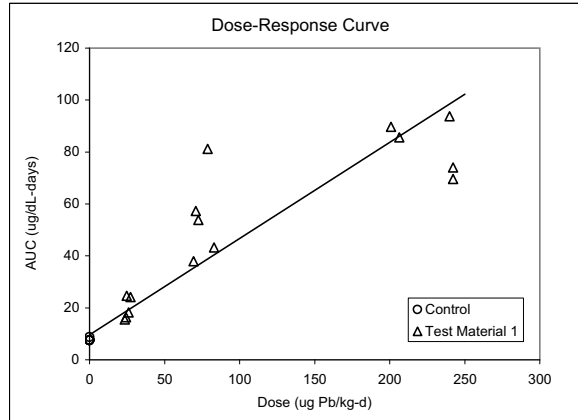
Phase II Experiment 9: Blood AUC

Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$

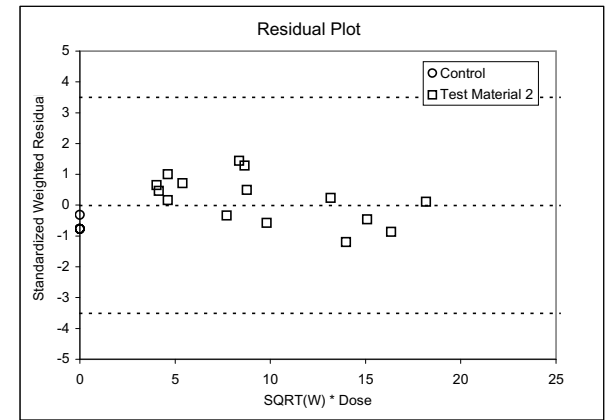
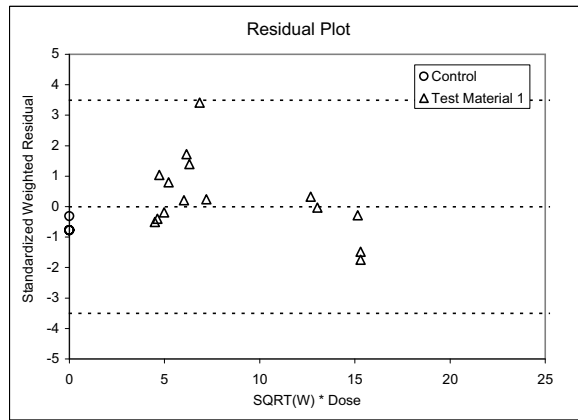
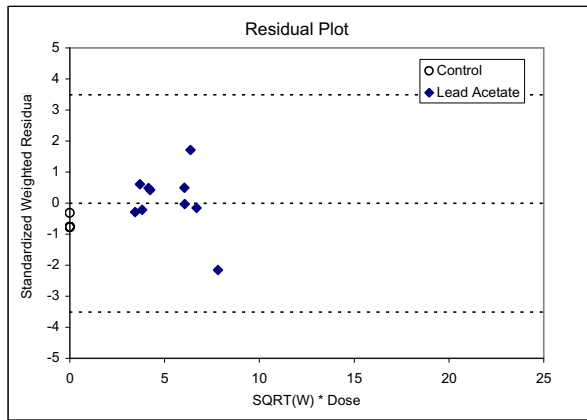
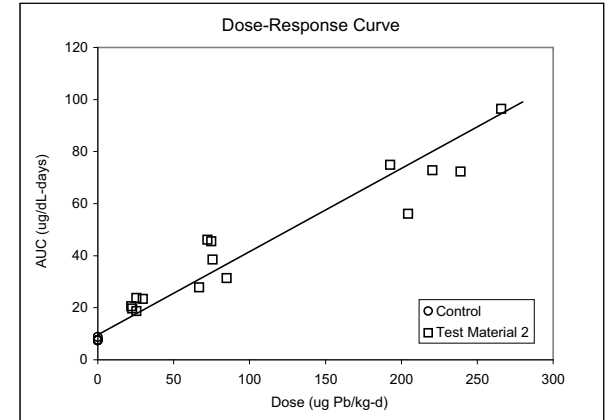
Reference Material (Lead Acetate)



Test Material 1 (Palmerston Location 2)



Test Material 2 (Palmerston Location 4)



Summary of Fitting

Parameter	Estimate	Standard Error
a	9.61E+00	1.08E+00
b1	5.94E-01	6.90E-02
b2	3.71E-01	3.20E-02
b3	3.20E-01	2.90E-02
Covariance (c1,c2)	0.0930	--
Covariance (c1,c3)	0.1000	--
Degrees of Freedom	41	--

Goodness of Fit

Statistic	Estimate
F	92.835
p	< 0.001
Adjusted R <sup>2</sup>	0.8623
AIC	328.763

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.62	0.54
Lower bound	0.50	0.43
Upper bound	0.80	0.69
Standard Error	0.086	0.075



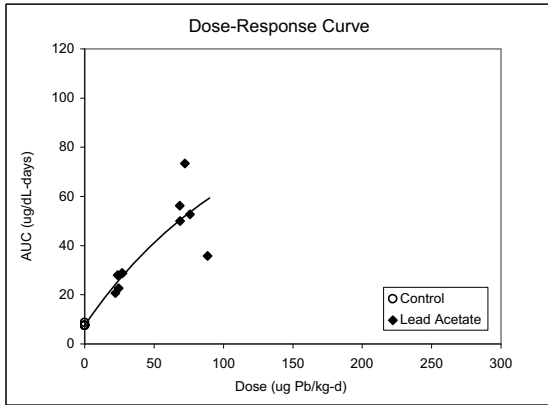
APPENDIX E

Figure 1b - All Data

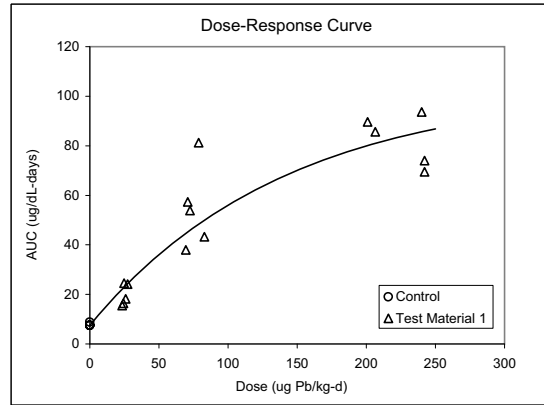
Phase II Experiment 9: Blood AUC

Exponential Model:  $y = a + b*(1-\exp(-c1*x1)) + b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$

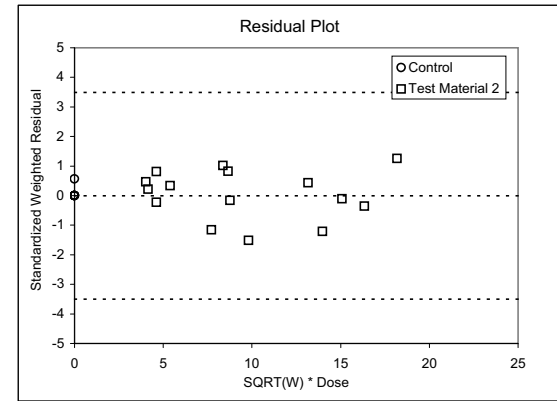
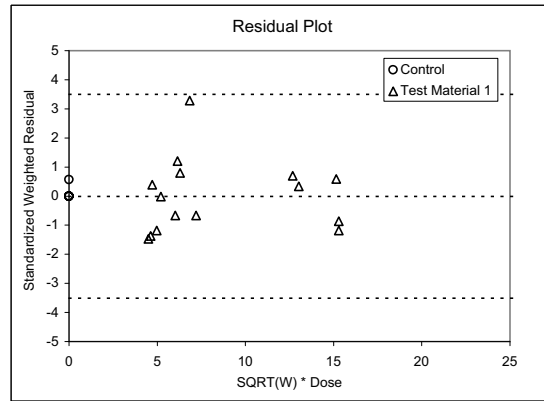
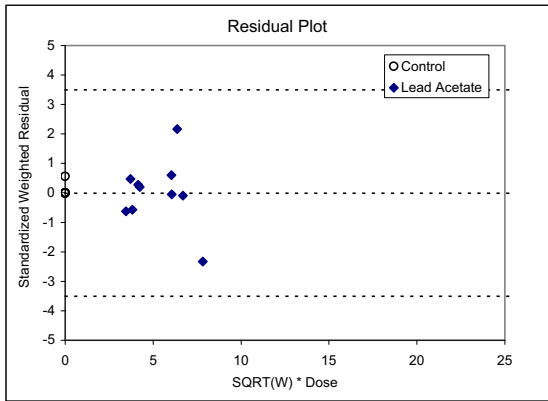
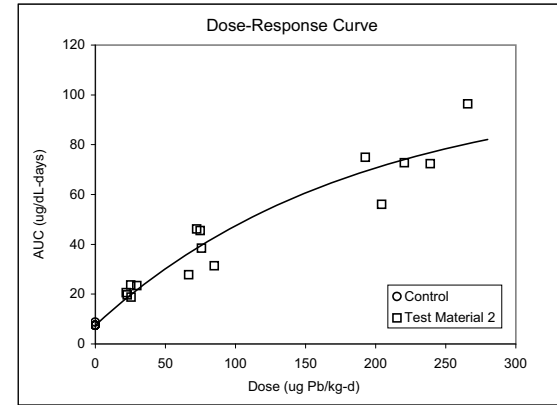
Reference Material (Lead Acetate)



Test Material 1 (Palmerston Location 2)



Test Material 2 (Palmerston Location 4)



Summary of Fitting

Parameter	Estimate	Standard Error
a	7.51E+00	9.94E-01
b	9.55E+01	1.41E+01
c1	8.68E-03	1.98E-03
c2	7.09E-03	1.78E-03
c3	5.41E-03	1.31E-03
Covariance (c1,c2)	0.8172	--
Covariance (c1,c3)	0.8147	--
Degrees of Freedom	40	--

Goodness of Fit

Statistic	Estimate
F	111.320
p	< 0.001
Adjusted R <sup>2</sup>	0.9093
AIC	312.220

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.82	0.62
Lower bound	0.61	0.47
Upper bound	1.05	0.80
Standard Error	0.119*	0.089*

\*  $g \geq 0.05$ , estimate is uncertain

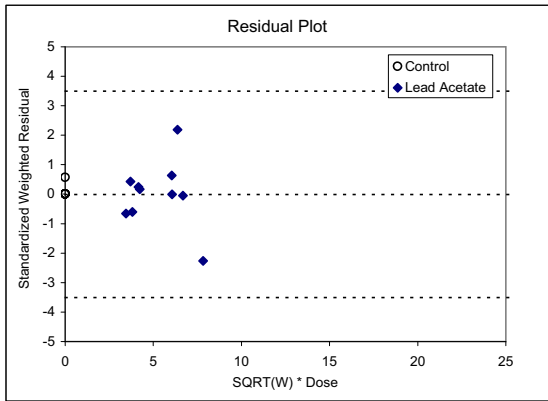
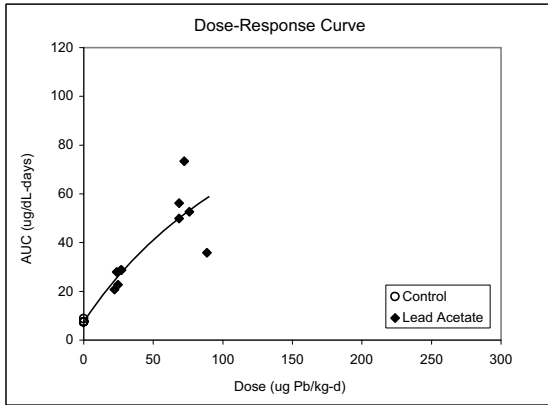
APPENDIX E

Figure 1c - All Data

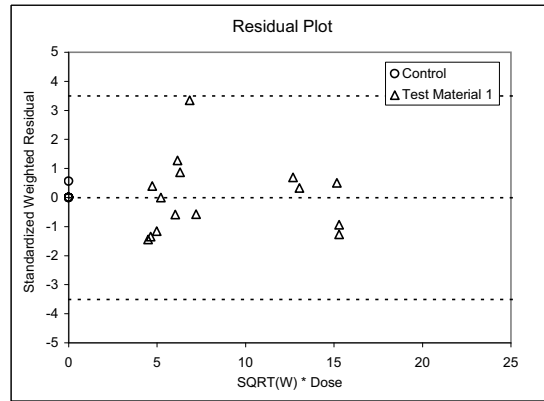
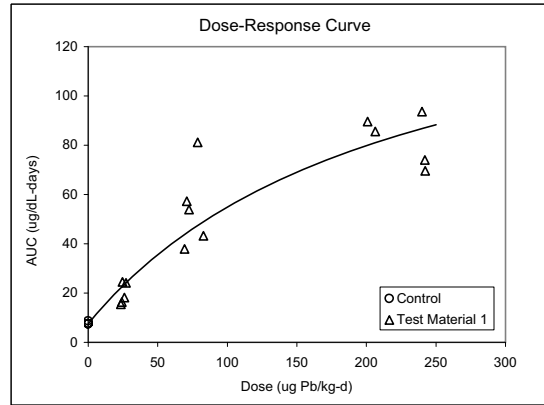
Phase II Experiment 9: Blood AUC

Michaelis-Menton Model:  $y = a + b \cdot x_1 / (c_1 + x_1) + b \cdot x_2 / (c_2 + x_2) + b \cdot x_3 / (c_3 + x_3)$

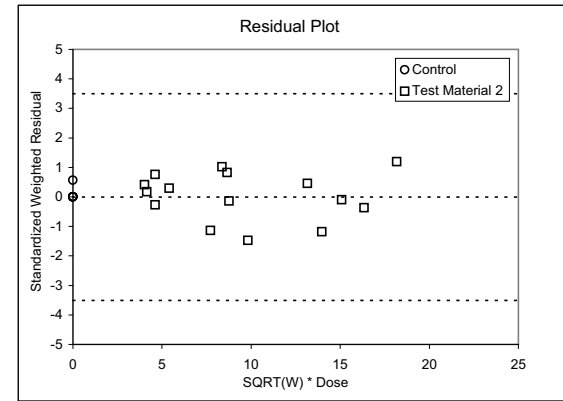
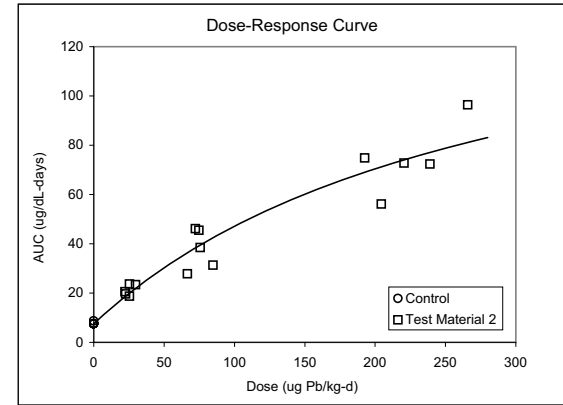
Reference Material (Lead Acetate)



Test Material 1 (Palmerston Location 2)



Test Material 2 (Palmerston Location 4)



Summary of Fitting

Parameter	Estimate	Standard Error
a	7.50E+00	1.01E+00
b	1.52E+02	2.98E+01
c1	1.77E+02	5.15E+01
c2	2.21E+02	7.00E+01
c3	2.84E+02	8.70E+01
Covariance (c1,c2)	0.8860	--
Covariance (c1,c3)	0.8834	--
Degrees of Freedom	40	--

Goodness of Fit

Statistic	Estimate
F	109.669
p	< 0.001
Adjusted R <sup>2</sup>	0.9081
AIC	312.679

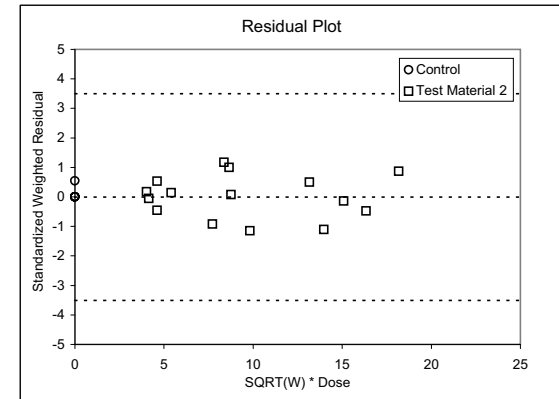
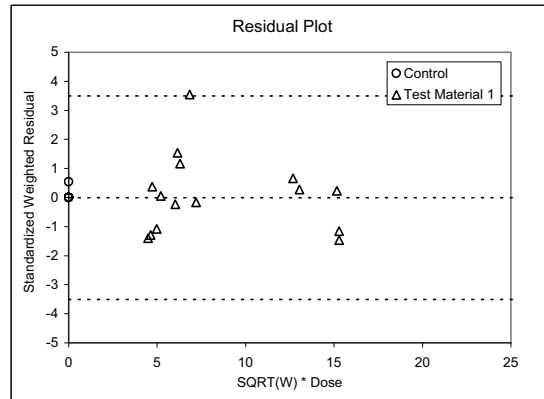
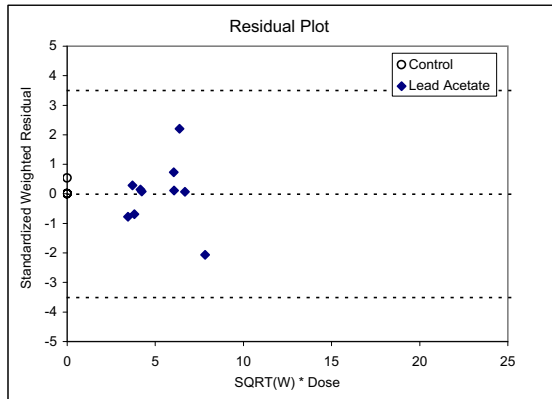
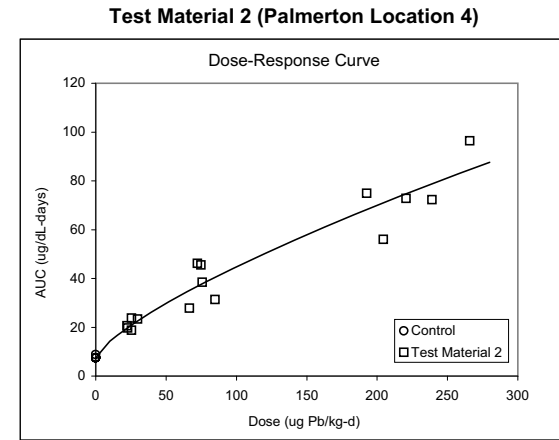
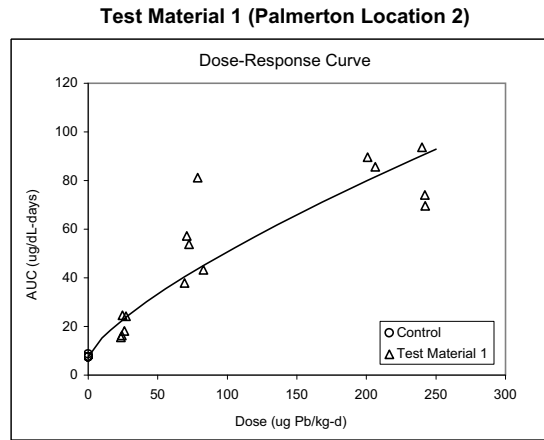
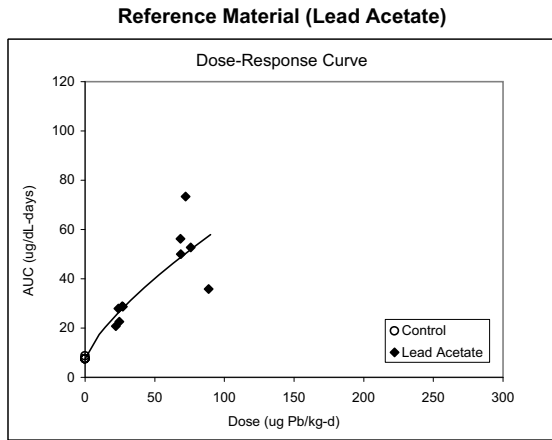
RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.80	0.62
Lower bound	0.62	0.48
Upper bound	1.10	0.84
Standard Error	0.118*	0.090*

\*  $g \geq 0.05$ , estimate is uncertain

APPENDIX E

**Figure 1d - All Data**  
**Phase II Experiment 9: Blood AUC**  
**Power Model:  $y = a + b_1 \cdot x_1^c + b_2 \cdot x_2^c + b_3 \cdot x_3^c$**



**Summary of Fitting**

Parameter	Estimate	Standard Error
a	7.49E+00	1.08E+00
b1	1.78E+00	4.67E-01
b2	1.41E+00	4.22E-01
b3	1.22E+00	3.68E-01
c	7.43E-01	5.86E-02
Covariance (b1,b2)	0.9184	--
Covariance (b1,b3)	0.9173	--
Degrees of Freedom	40	--

**Goodness of Fit**

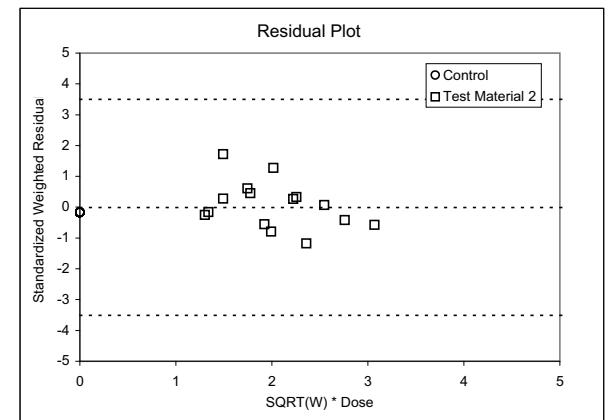
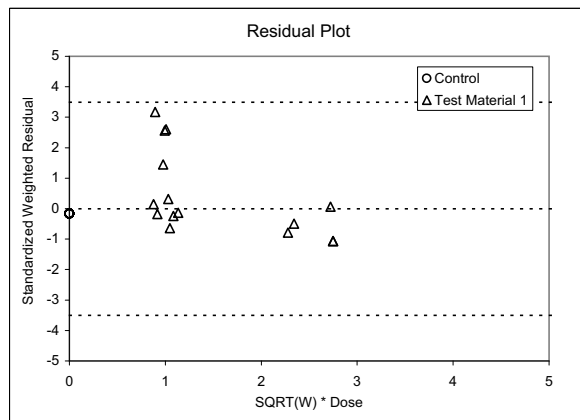
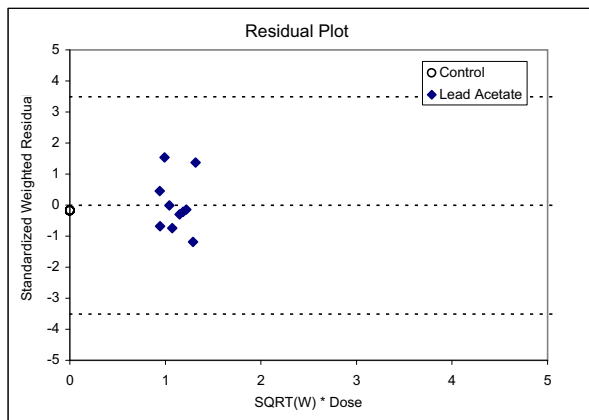
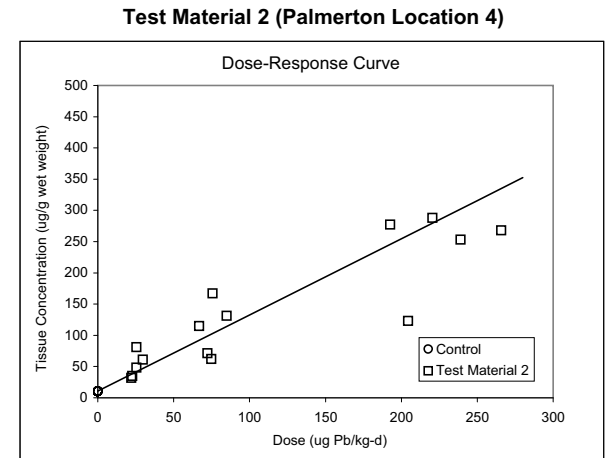
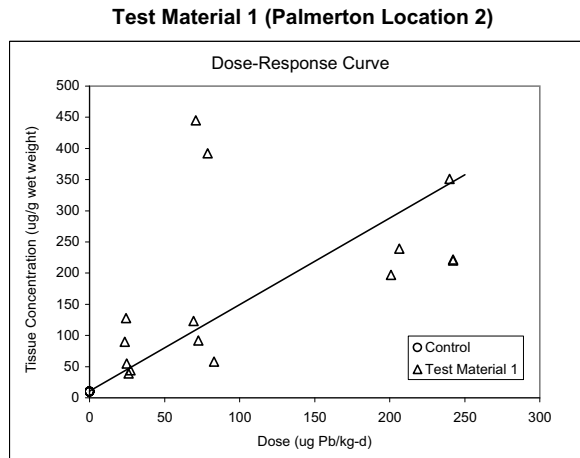
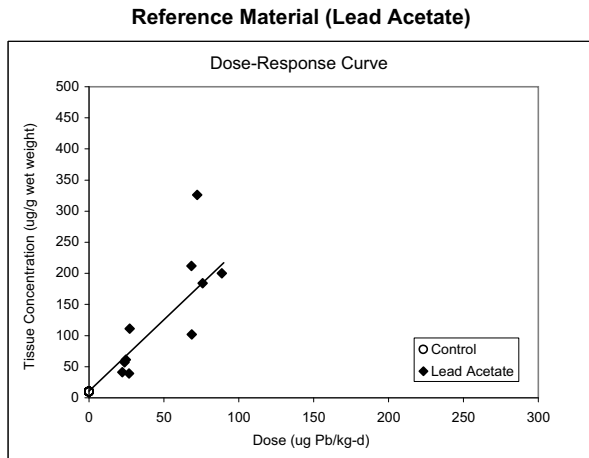
Statistic	Estimate
F	98.378
p	< 0.001
Adjusted R <sup>2</sup>	0.8985
AIC	316.197

**RBA and Uncertainty**

	Test Material 1	Test Material 2
RBA	0.73	0.60
Lower bound	0.51	0.41
Upper bound	0.95	0.78
Standard Error	--	--

APPENDIX E

**Figure 2a - All Data**  
**Phase II Experiment 9: Liver**  
**Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$**



**Summary of Fitting**

Parameter	Estimate	Standard Error
a	1.07E+01	1.88E+00
b1	2.30E+00	3.98E-01
b2	1.39E+00	2.14E-01
b3	1.22E+00	1.75E-01
Covariance (c1,c2)	0.0117	--
Covariance (c1,c3)	0.0189	--
Degrees of Freedom	41	--

**Goodness of Fit**

Statistic	Estimate
F	40.132
p	< 0.001
Adjusted R <sup>2</sup>	0.7274
AIC	484.924

**RBA and Uncertainty**

	Test Material 1	Test Material 2
RBA	0.60	0.53
Lower bound	0.41	0.37
Upper bound	0.91	0.79
Standard Error	0.139*	0.119*

\*  $g \geq 0.05$ , estimate is uncertain

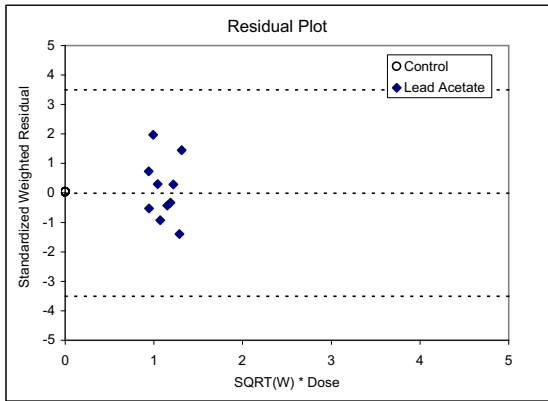
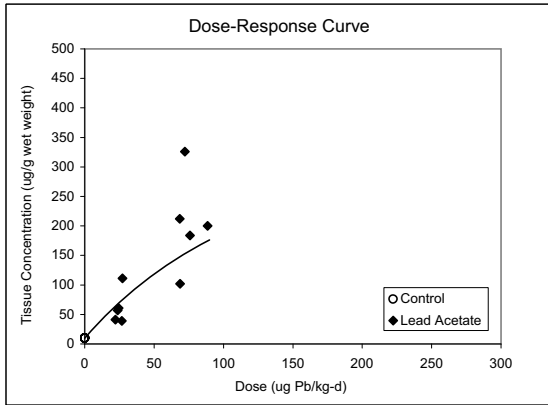
APPENDIX E

Figure 2b - All Data

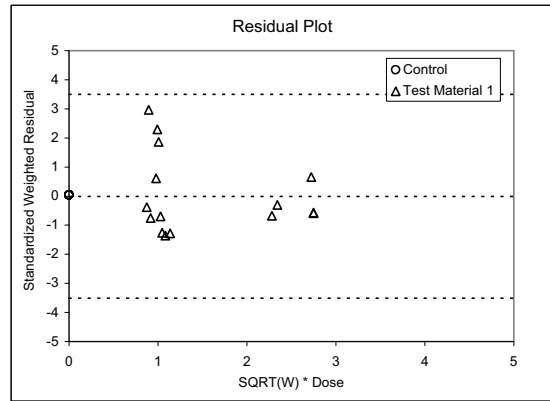
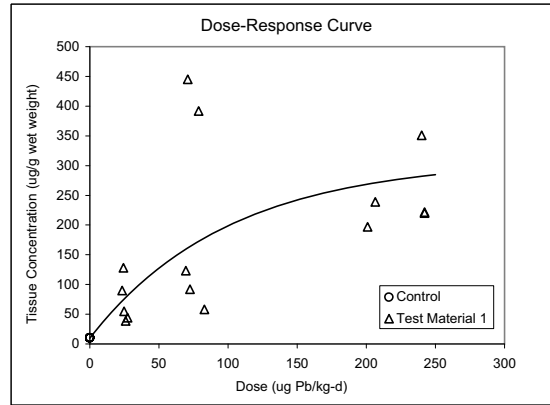
Phase II Experiment 9: Liver

Exponential Model:  $y = a + b \cdot (1 - \exp(-c_1 \cdot x_1)) + b \cdot (1 - \exp(-c_2 \cdot x_2)) + b \cdot (1 - \exp(-c_3 \cdot x_3))$

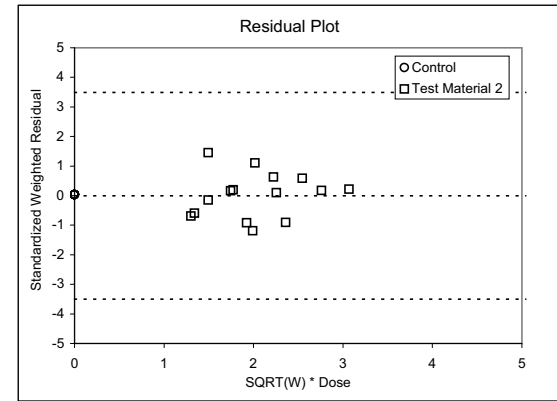
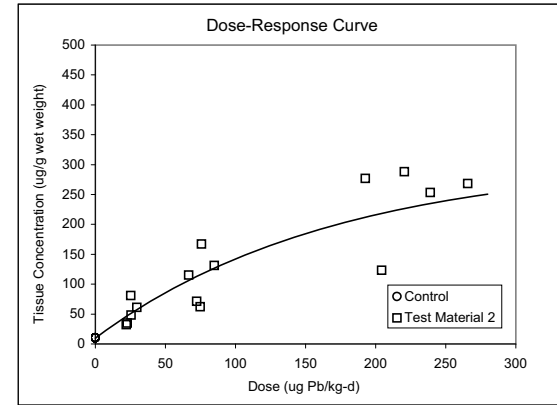
Reference Material (Lead Acetate)



Test Material 1 (Palmerston Location 2)



Test Material 2 (Palmerston Location 4)



Summary of Fitting

Parameter	Estimate	Standard Error
a	9.87E+00	1.72E+00
b	2.99E+02	7.29E+01
c1	9.01E-03	3.15E-03
c2	9.97E-03	3.96E-03
c3	5.83E-03	2.08E-03
Covariance (c1,c2)	0.7276	--
Covariance (c1,c3)	0.7387	--
Degrees of Freedom	40	--

Goodness of Fit

Statistic	Estimate
F	39.356
p	< 0.001
Adjusted R <sup>2</sup>	0.7771
AIC	470.653

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	1.11	0.65
Lower bound	0.56	0.38
Upper bound	1.86	1.09
Standard Error	0.309*	0.165*

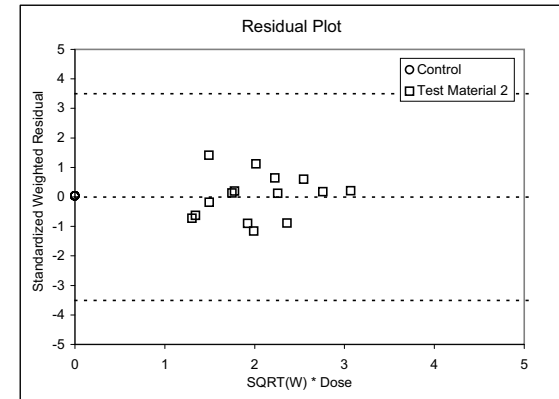
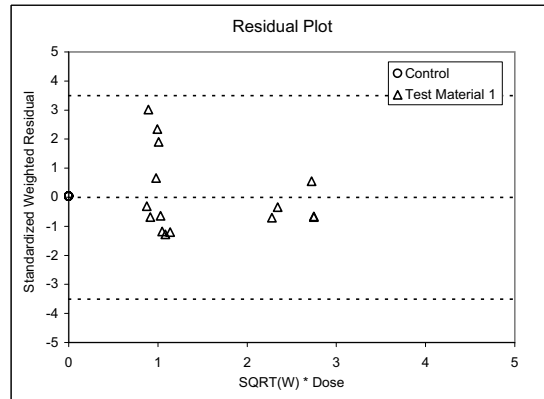
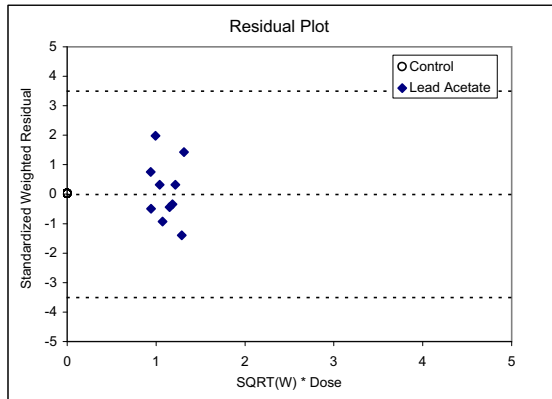
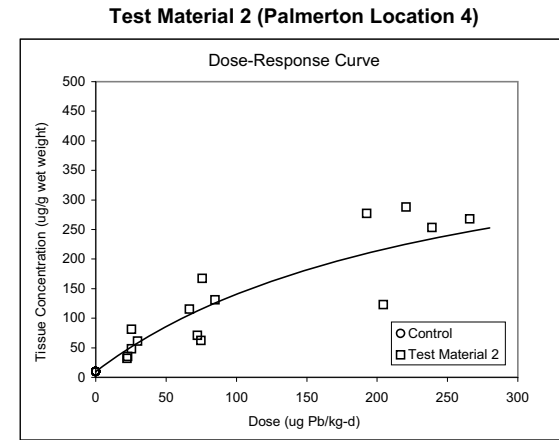
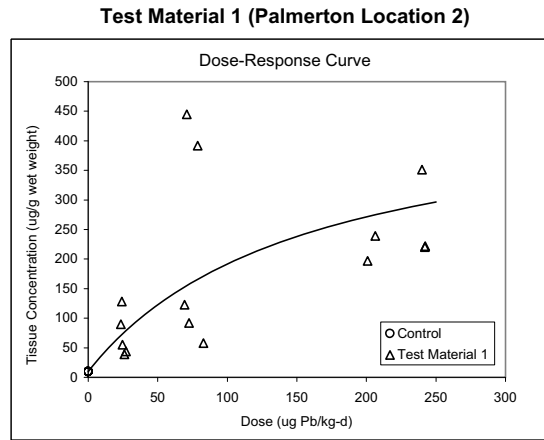
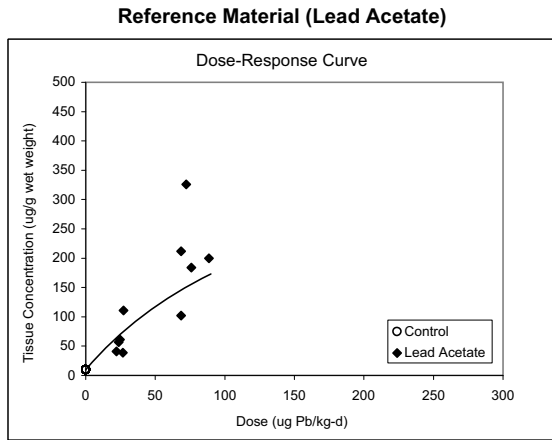
\*  $g \geq 0.05$ , estimate is uncertain

APPENDIX E

Figure 2c - All Data

Phase II Experiment 9: Liver

Michaelis-Menton Model:  $y = a + b \cdot x_1 / (c_1 + x_1) + b \cdot x_2 / (c_2 + x_2) + b \cdot x_3 / (c_3 + x_3)$



Summary of Fitting

Parameter	Estimate	Standard Error
a	9.88E+00	1.74E+00
b	4.66E+02	1.53E+02
c1	1.67E+02	7.50E+01
c2	1.56E+02	8.13E+01
c3	2.57E+02	1.19E+02
Covariance (c1,c2)	0.8328	--
Covariance (c1,c3)	0.8354	--
Degrees of Freedom	40	--

Goodness of Fit

Statistic	Estimate
F	38.613
p	< 0.001
Adjusted R <sup>2</sup>	0.7737
AIC	471.634

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	1.07	0.65
Lower bound	0.60	0.35
Upper bound	3.55	1.33
Standard Error	0.309*	0.170*

\*  $g \geq 0.05$ , estimate is uncertain

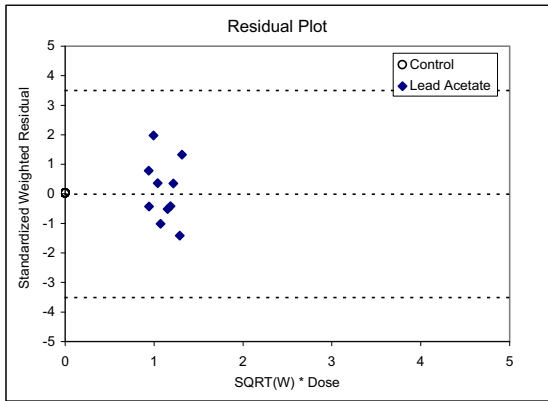
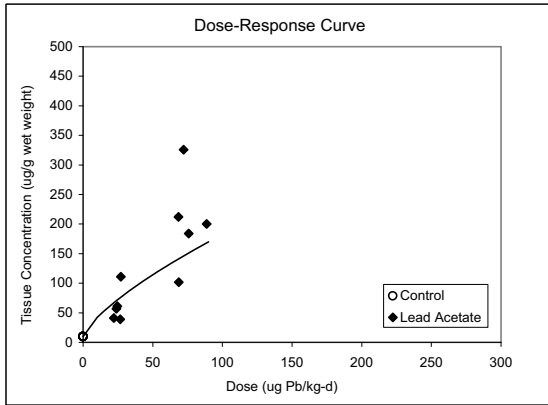
APPENDIX E

Figure 2d - All Data

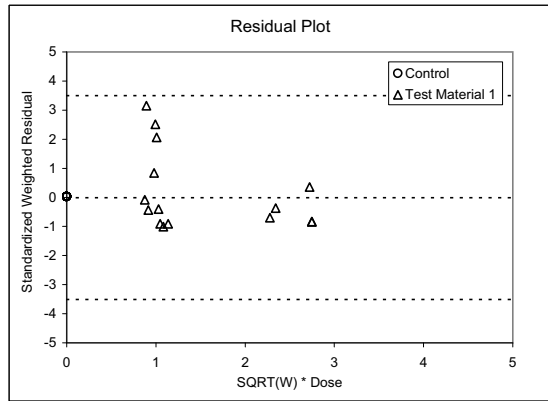
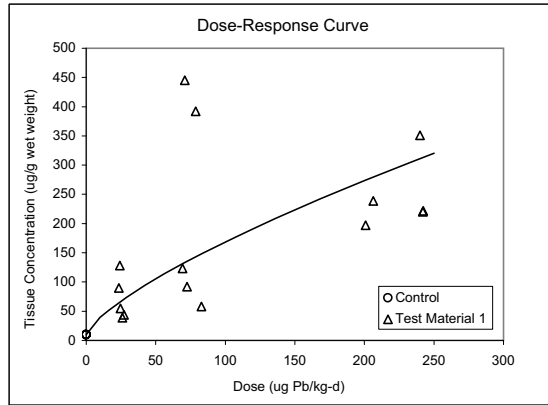
Phase II Experiment 9: Liver

Power Model:  $y = a + b1*x1^c + b2*x2^c + b3*x3^c$

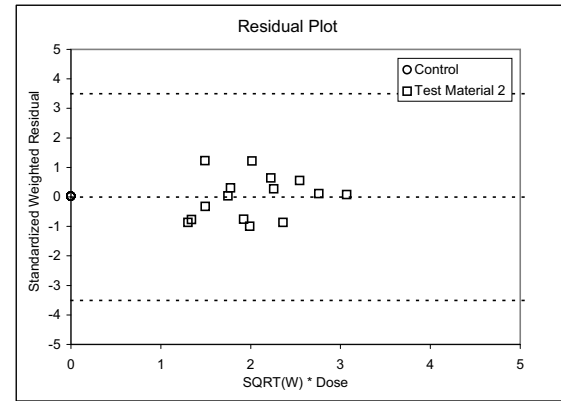
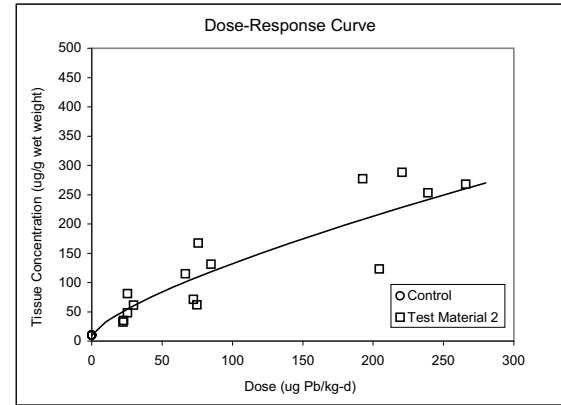
Reference Material (Lead Acetate)



Test Material 1 (Palmerston Location 2)



Test Material 2 (Palmerston Location 4)



Summary of Fitting

Parameter	Estimate	Standard Error
a	9.91E+00	1.80E+00
b1	5.94E+00	2.26E+00
b2	5.45E+00	2.53E+00
b3	4.20E+00	1.84E+00
c	7.32E-01	9.60E-02
Covariance (b1,b2)	0.8634	--
Covariance (b1,b3)	0.8614	--
Degrees of Freedom	40	--

Goodness of Fit

Statistic	Estimate
F	35.748
p	< 0.001
Adjusted R <sup>2</sup>	0.7595
AIC	475.710

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.89	0.62
Lower bound	0.29	0.25
Upper bound	1.52	1.08
Standard Error	--	--

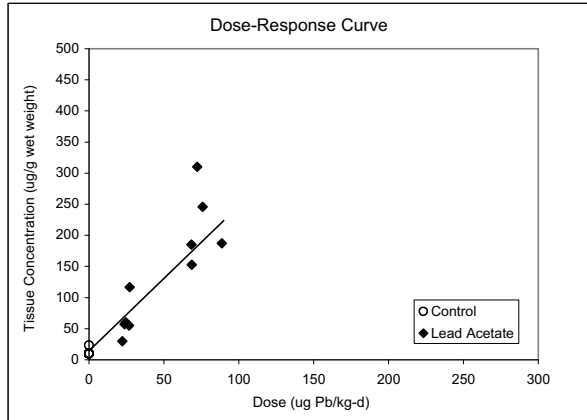
APPENDIX E

Figure 3a - All Data

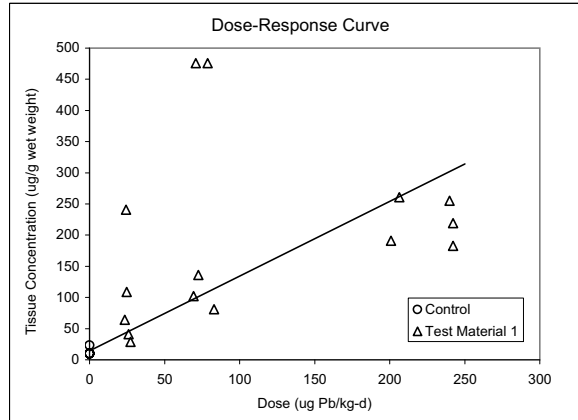
Phase II Experiment 9: Kidney

Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$

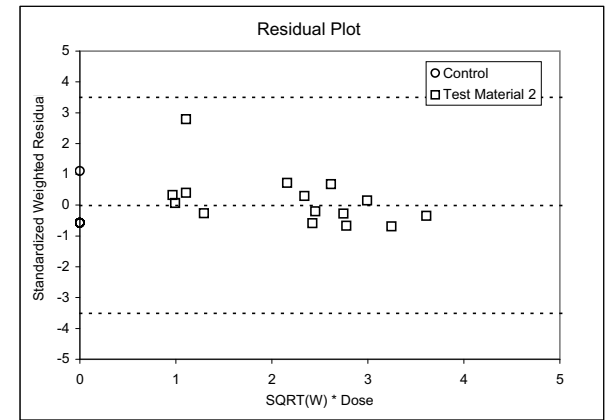
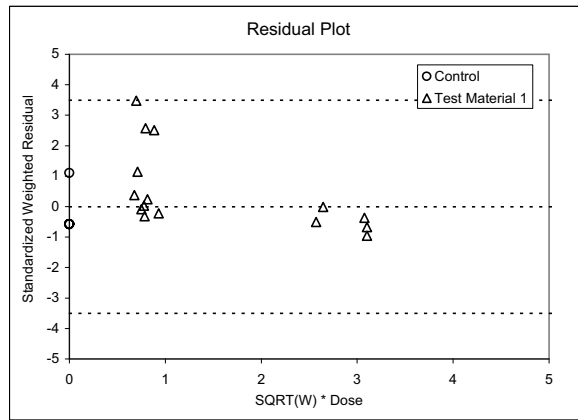
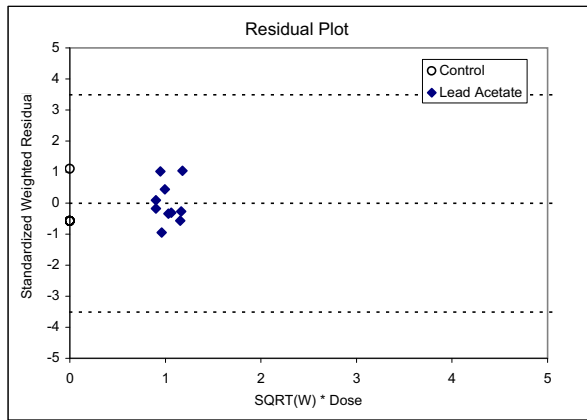
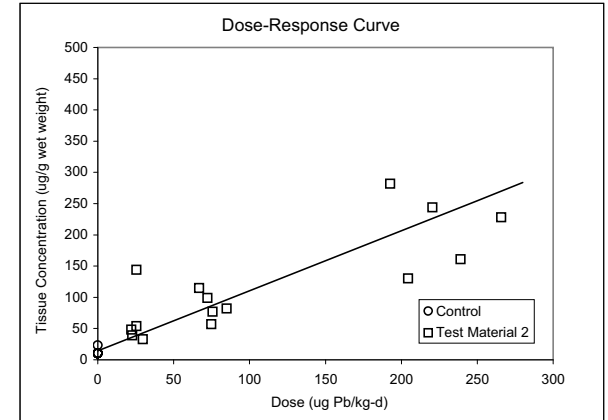
Reference Material (Lead Acetate)



Test Material 1 (Palmerston Location 2)



Test Material 2 (Palmerston Location 4)



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.45E+01	3.55E+00
b1	2.33E+00	5.37E-01
b2	1.20E+00	2.49E-01
b3	9.61E-01	1.93E-01
Covariance (c1,c2)	0.0182	--
Covariance (c1,c3)	0.0342	--
Degrees of Freedom	41	--

Goodness of Fit

Statistic	Estimate
F	21.21
p	< 0.001
Adjusted R <sup>2</sup>	0.579
AIC	535.863

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.51	0.41
Lower bound	0.30	0.25
Upper bound	0.91	0.72
Standard Error	0.158*	0.124*

\*  $g \geq 0.05$ , estimate is uncertain



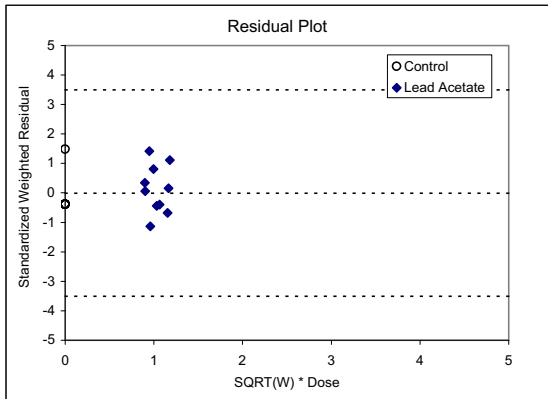
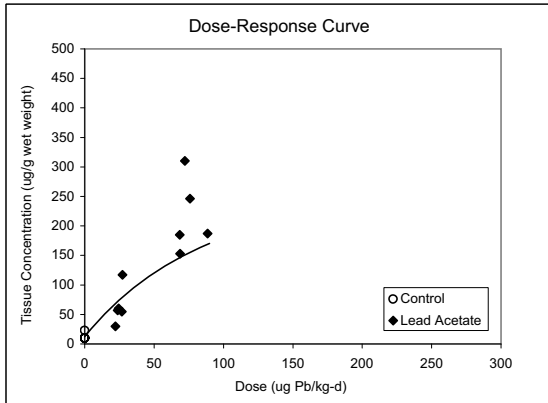
APPENDIX E

Figure 3b - All Data

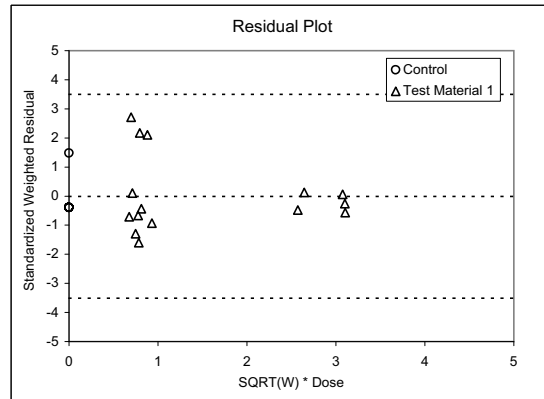
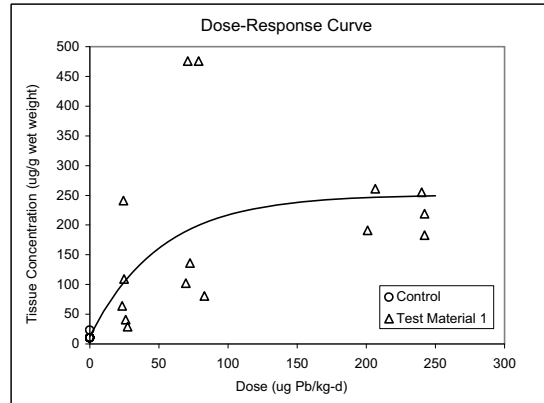
Phase II Experiment 9: Kidney

Exponential Model:  $y = a + b*(1-\exp(-c1*x1)) + b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$

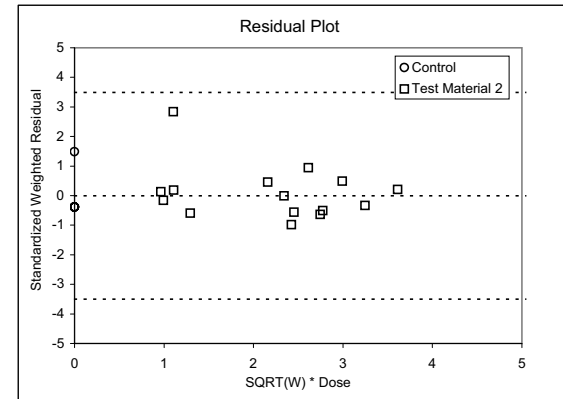
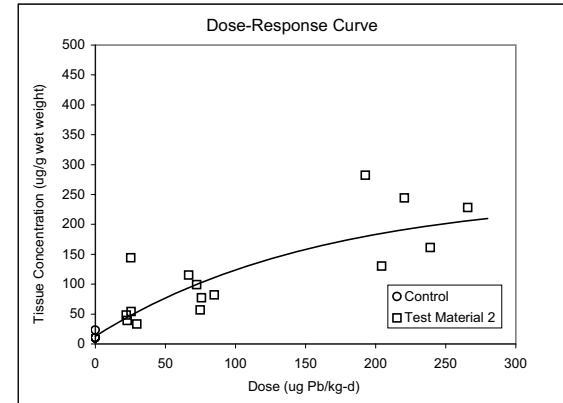
Reference Material (Lead Acetate)



Test Material 1 (Palmerston Location 2)



Test Material 2 (Palmerston Location 4)



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.27E+01	3.25E+00
b	2.38E+02	5.33E+01
c1	1.20E-02	4.75E-03
c2	1.95E-02	9.03E-03
c3	6.28E-03	2.47E-03
Covariance (c1,c2)	0.5421	--
Covariance (c1,c3)	0.5740	--
Degrees of Freedom	40	--

Goodness of Fit

Statistic	Estimate
F	22.48
p	< 0.001
Adjusted R <sup>2</sup>	0.661
AIC	511.641

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	1.62	0.52
Lower bound	0.50	0.24
Upper bound	3.66	1.16
Standard Error	0.672*	0.190*

\*  $g \geq 0.05$ , estimate is uncertain

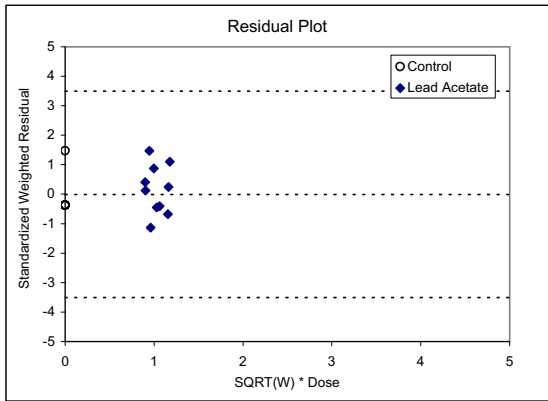
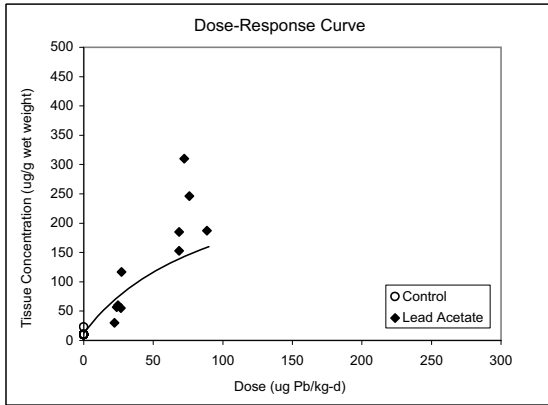
APPENDIX E

Figure 3c - All Data

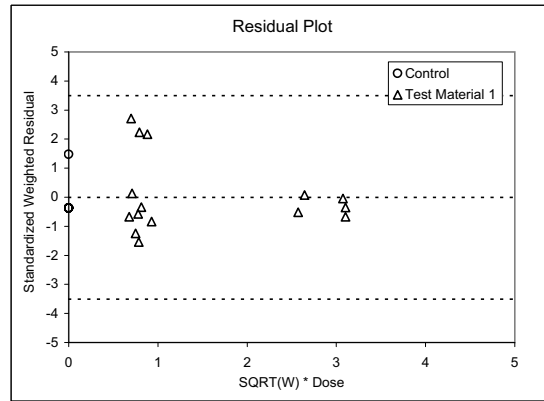
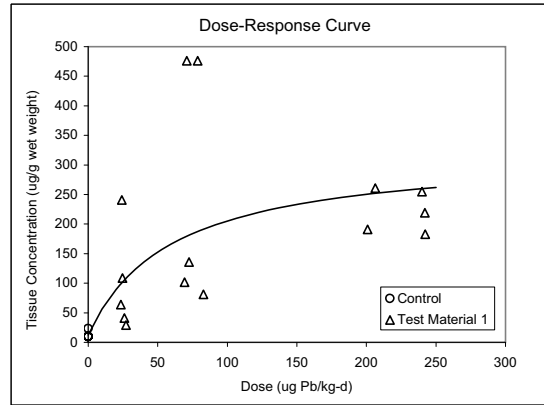
Phase II Experiment 9: Kidney

Michaelis-Menton Model:  $y = a + b \cdot x_1 / (c_1 + x_1) + b \cdot x_2 / (c_2 + x_2) + b \cdot x_3 / (c_3 + x_3)$

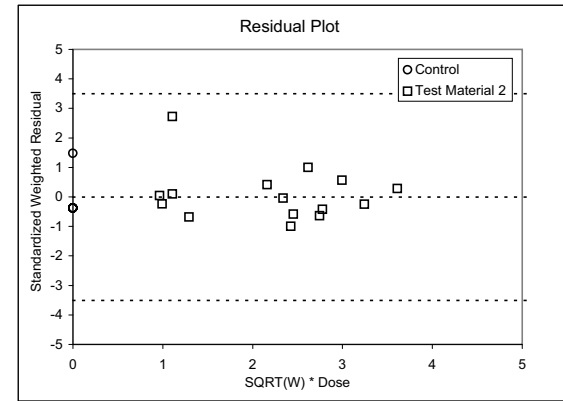
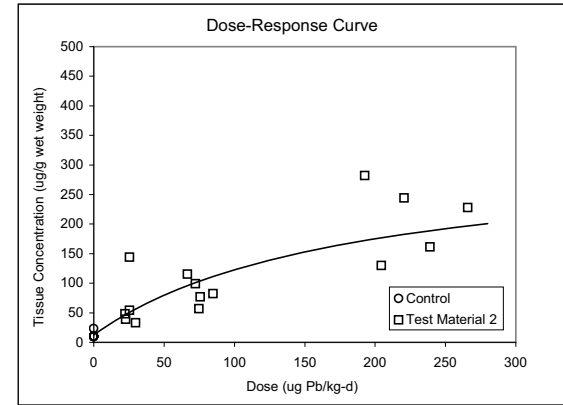
Reference Material (Lead Acetate)



Test Material 1 (Palmerston Location 2)



Test Material 2 (Palmerston Location 4)



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.26E+01	3.29E+00
b	3.10E+02	9.28E+01
c1	9.94E+01	5.00E+01
c2	6.09E+01	3.95E+01
c3	1.82E+02	9.29E+01
Covariance (c1,c2)	0.6978	--
Covariance (c1,c3)	0.6997	--
Degrees of Freedom	40	--

Goodness of Fit

Statistic	Estimate
F	21.85
p	< 0.001
Adjusted R <sup>2</sup>	0.655
AIC	513.547

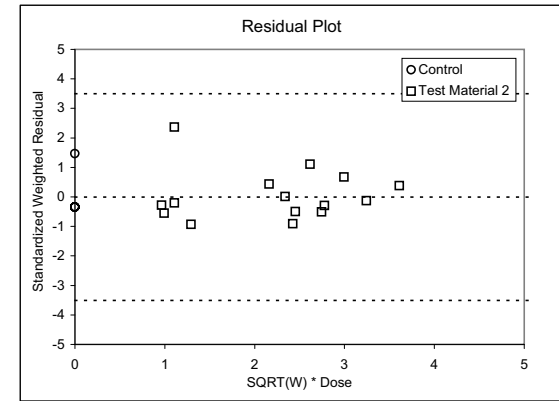
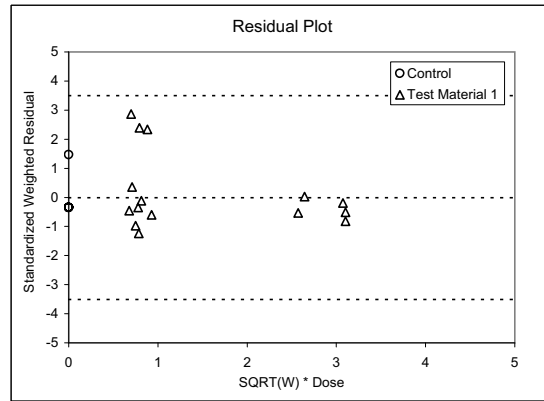
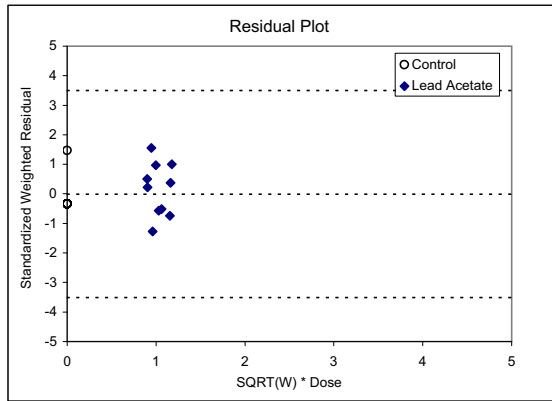
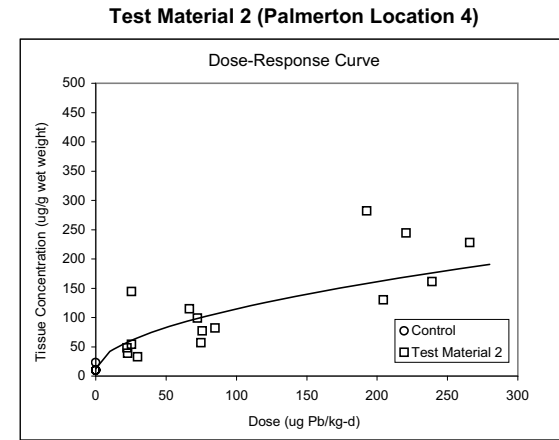
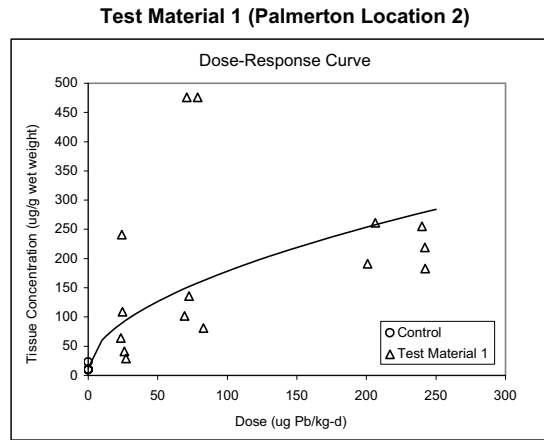
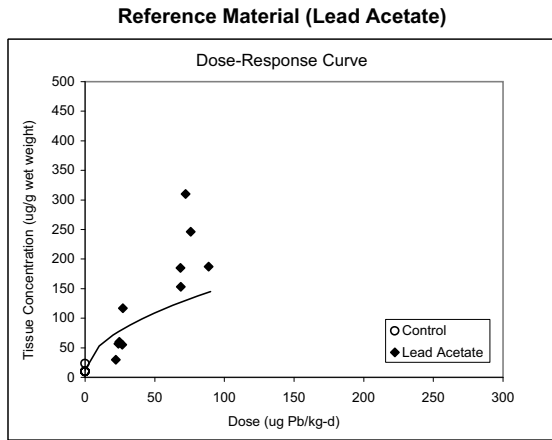
RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	1.63	0.55
Lower bound	0.59	0.17
Upper bound	-6.63	1.89
Standard Error	0.763*	0.215*

\*  $g \geq 0.05$ , estimate is uncertain

APPENDIX E

**Figure 3d - All Data**  
**Phase II Experiment 9: Kidney**  
**Power Model:  $y = a + b_1 \cdot x_1^c + b_2 \cdot x_2^c + b_3 \cdot x_3^c$**



**Summary of Fitting**

Parameter	Estimate	Standard Error
a	1.25E+01	3.39E+00
b1	1.17E+01	5.96E+00
b2	1.38E+01	8.75E+00
b3	8.50E+00	5.09E+00
c	5.40E-01	1.31E-01
Covariance (b1,b2)	0.8697	--
Covariance (b1,b3)	0.8638	--
Degrees of Freedom	40	--

**Goodness of Fit**

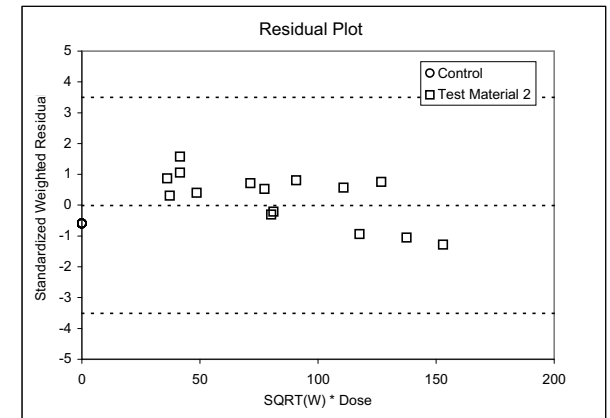
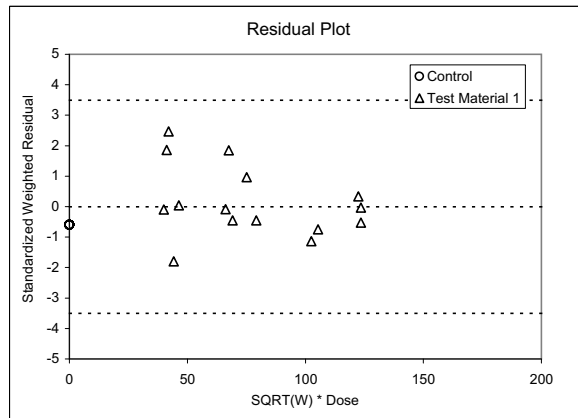
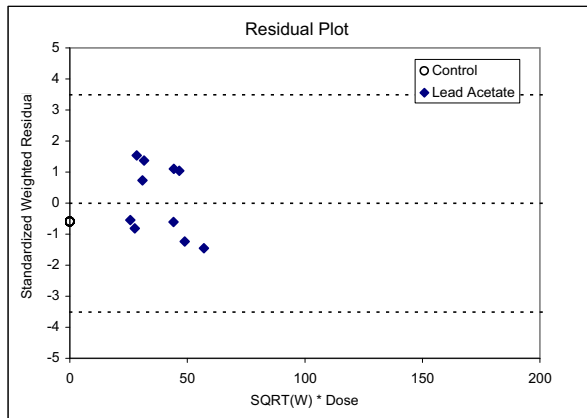
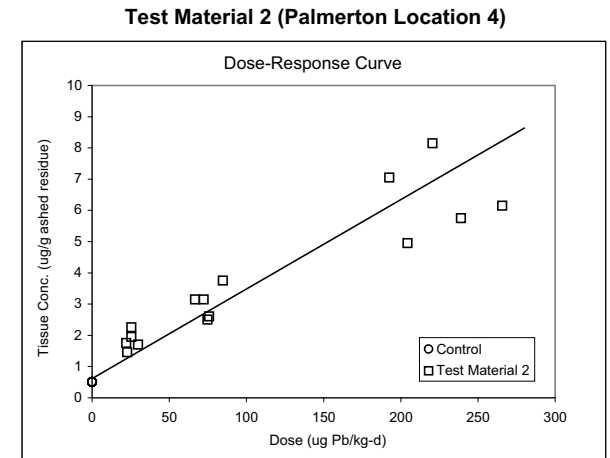
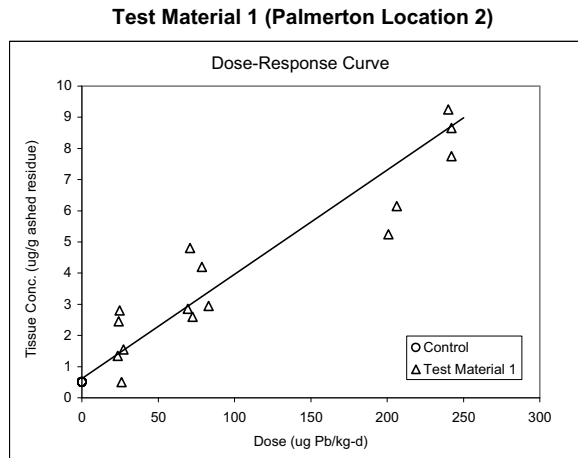
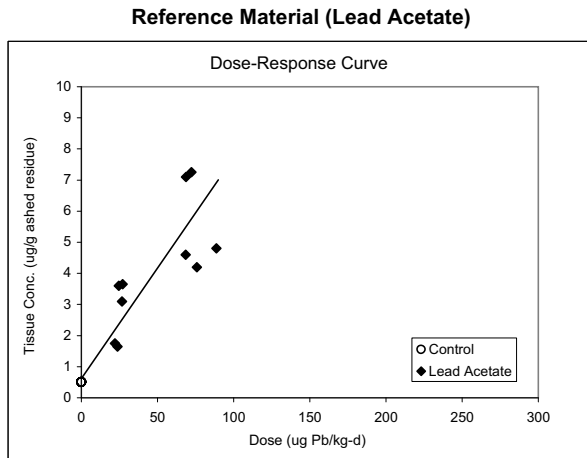
Statistic	Estimate
F	20.25
p	< 0.001
Adjusted R <sup>2</sup>	0.636
AIC	518.750

**RBA and Uncertainty**

	Test Material 1	Test Material 2
RBA	1.36	0.56
Lower bound	?	?
Upper bound	4.22	1.94
Standard Error	--	--

APPENDIX E

**Figure 4a - All Data**  
**Phase II Experiment 9: Femur**  
**Linear Model:  $y = a + b_1 \cdot x_1 + b_2 \cdot x_2 + b_3 \cdot x_3$**



**Summary of Fitting**

Parameter	Estimate	Standard Error
a	6.17E-01	8.33E-02
b1	7.10E-02	7.90E-03
b2	3.34E-02	3.15E-03
b3	2.87E-02	2.85E-03
Covariance (c1,c2)	0.0554	--
Covariance (c1,c3)	0.0566	--
Degrees of Freedom	41	--

**Goodness of Fit**

Statistic	Estimate
F	87.669
p	< 0.001
Adjusted R <sup>2</sup>	0.8553
AIC	118.621

**RBA and Uncertainty**

	Test Material 1	Test Material 2
RBA	0.47	0.40
Lower bound	0.37	0.32
Upper bound	0.60	0.52
Standard Error	0.067	0.058

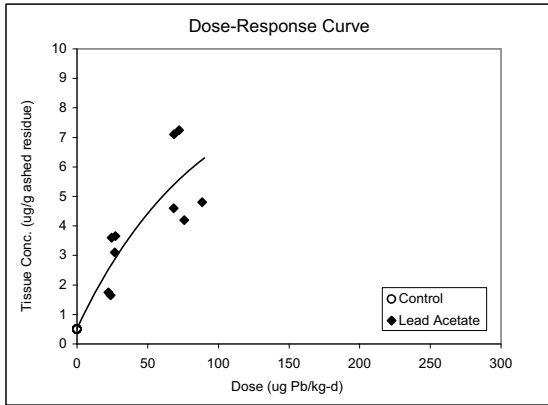
APPENDIX E

Figure 4b - All Data

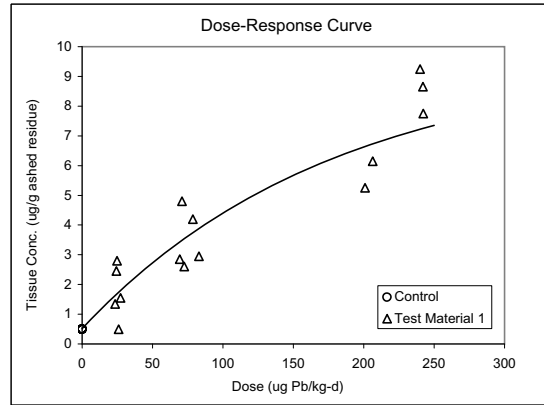
Phase II Experiment 9: Femur

Exponential Model:  $y = a + b*(1-\exp(-c1*x1)) + b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$

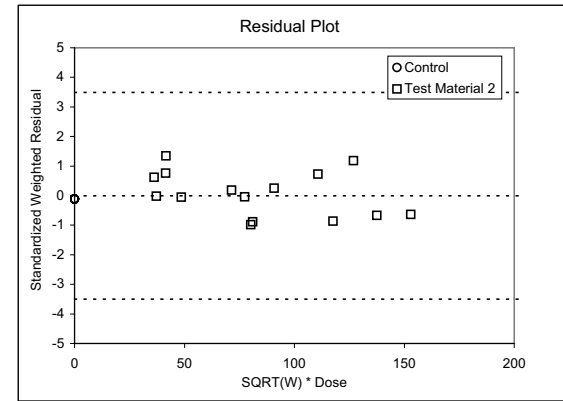
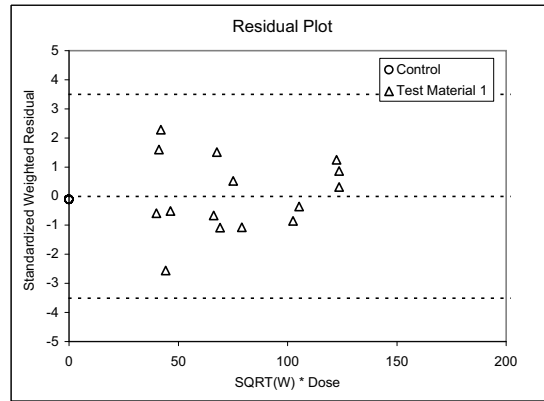
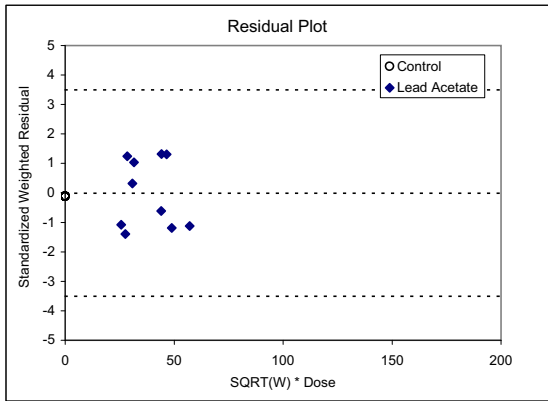
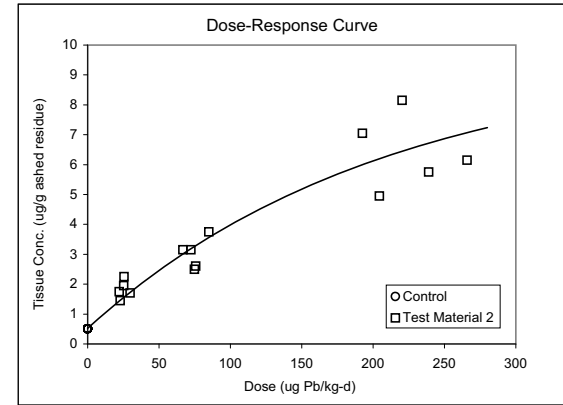
Reference Material (Lead Acetate)



Test Material 1 (Palmerston Location 2)



Test Material 2 (Palmerston Location 4)



Summary of Fitting

Parameter	Estimate	Standard Error
a	5.20E-01	8.02E-02
b	9.08E+00	2.03E+00
c1	1.12E-02	3.77E-03
c2	5.58E-03	1.87E-03
c3	4.80E-03	1.60E-03
Covariance (c1,c2)	0.8717	--
Covariance (c1,c3)	0.8714	--
Degrees of Freedom	40	--

Goodness of Fit

Statistic	Estimate
F	84.798
p	< 0.001
Adjusted R <sup>2</sup>	0.8840
AIC	112.175

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.50	0.43
Lower bound	0.35	0.30
Upper bound	0.70	0.60
Standard Error	0.084*	0.072*

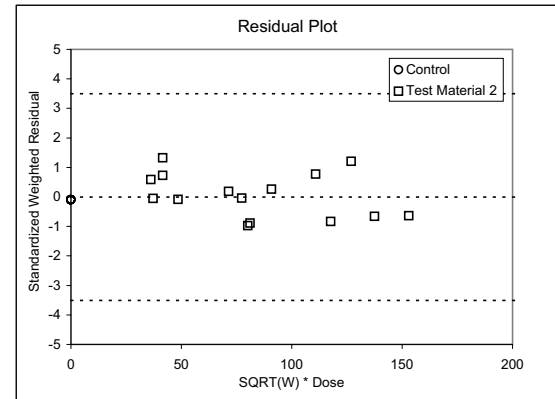
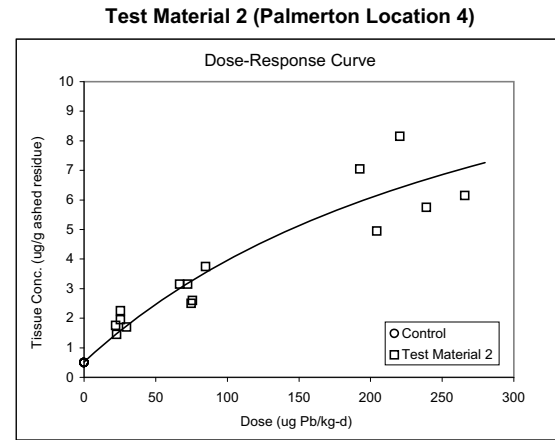
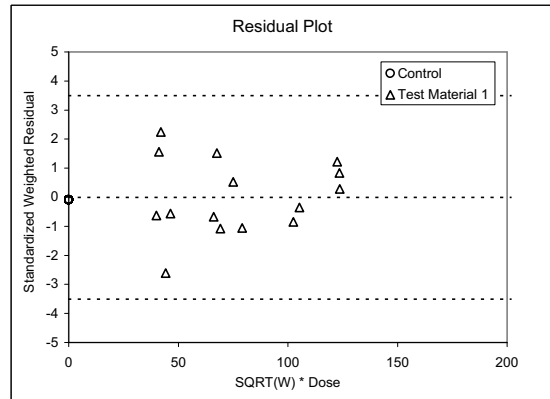
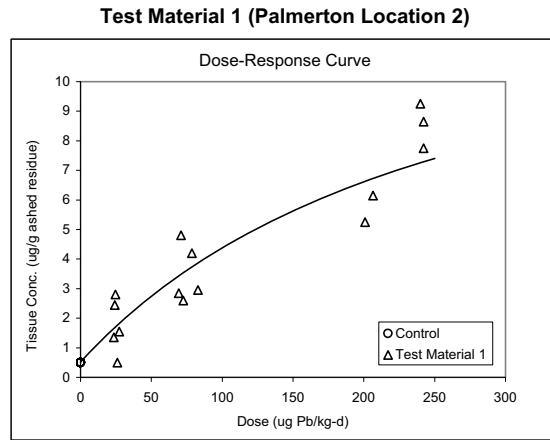
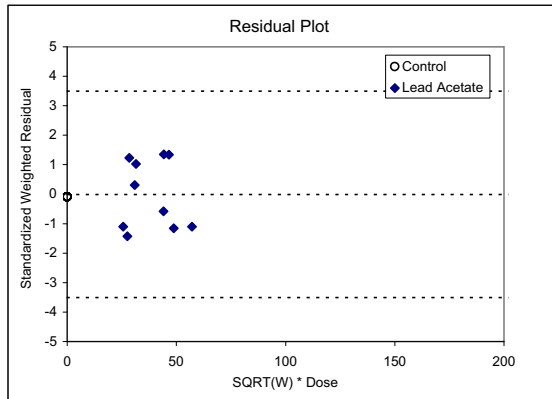
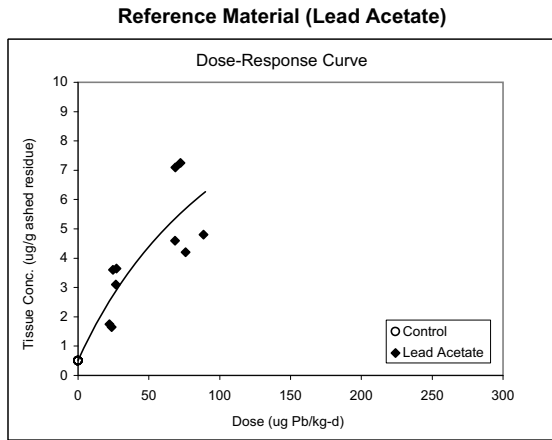
\*  $g \geq 0.05$ , estimate is uncertain

APPENDIX E

Figure 4c - All Data

Phase II Experiment 9: Femur

Michaelis-Menton Model:  $y = a + b \cdot x_1 / (c_1 + x_1) + b \cdot x_2 / (c_2 + x_2) + b \cdot x_3 / (c_3 + x_3)$



**Summary of Fitting**

Parameter	Estimate	Standard Error
a	5.16E-01	8.03E-02
b	1.45E+01	3.90E+00
c1	1.36E+02	5.41E+01
c2	2.74E+02	1.09E+02
c3	3.20E+02	1.26E+02
Covariance (c1,c2)	0.9096	--
Covariance (c1,c3)	0.9088	--
Degrees of Freedom	40	--

**Goodness of Fit**

Statistic	Estimate
F	85.458
p	< 0.001
Adjusted R <sup>2</sup>	0.8848
AIC	111.965

**RBA and Uncertainty**

	Test Material 1	Test Material 2
RBA	0.50	0.43
Lower bound	0.34	0.29
Upper bound	0.72	0.62
Standard Error	0.084*	0.072*

\*  $g \geq 0.05$ , estimate is uncertain

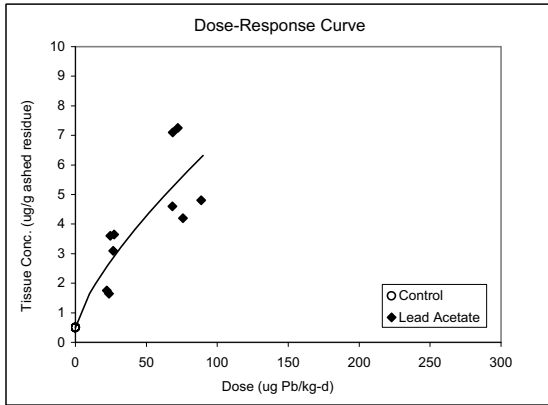
APPENDIX E

Figure 4d - All Data

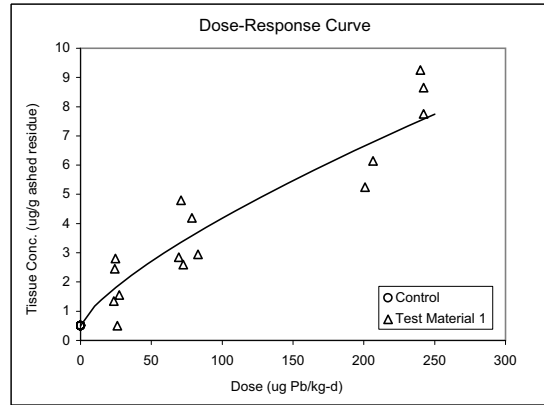
Phase II Experiment 9: Femur

Power Model:  $y = a + b1*x1^c + b2*x2^c + b3*x3^c$

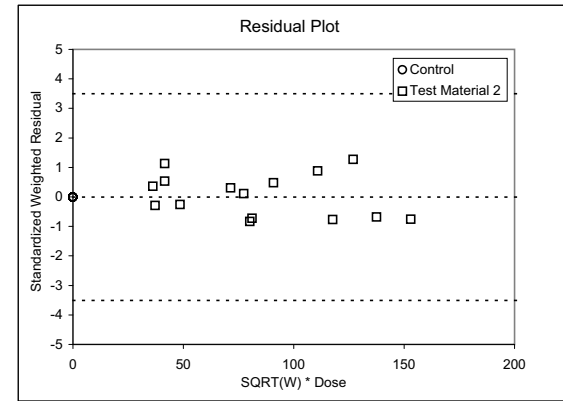
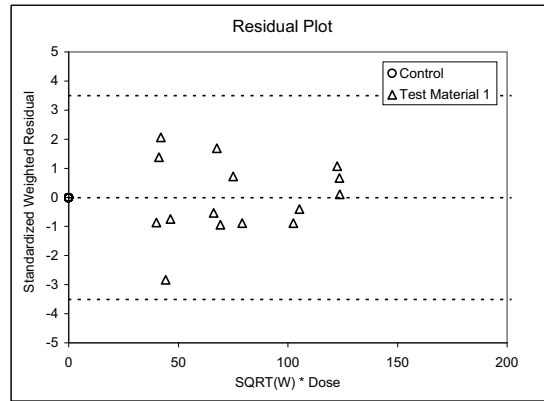
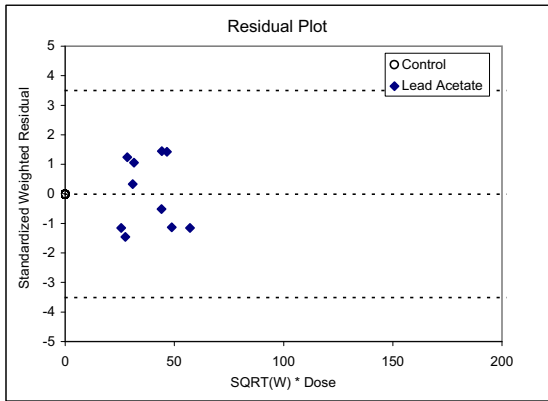
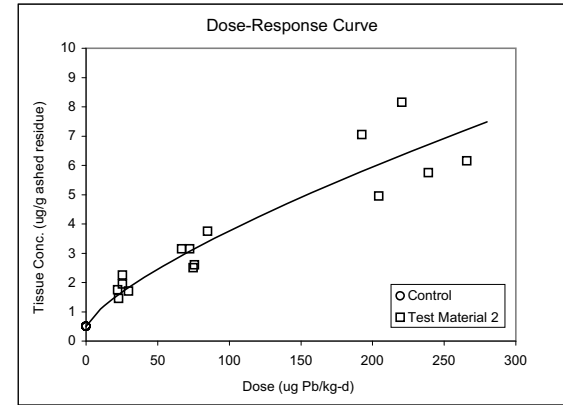
Reference Material (Lead Acetate)



Test Material 1 (Palmerston Location 2)



Test Material 2 (Palmerston Location 4)



Summary of Fitting

Parameter	Estimate	Standard Error
a	5.02E-01	8.02E-02
b1	2.09E-01	5.76E-02
b2	1.22E-01	3.88E-02
b3	1.08E-01	3.51E-02
c	7.40E-01	6.47E-02
Covariance (b1,b2)	0.9159	--
Covariance (b1,b3)	0.9151	--
Degrees of Freedom	40	--

Goodness of Fit

Statistic	Estimate
F	88.101
p	< 0.001
Adjusted R <sup>2</sup>	0.8879
AIC	111.154

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.48	0.41
Lower bound	0.32	0.27
Upper bound	0.64	0.55
Standard Error	--	--

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## APPENDIX E

### EXPERIMENT 11

Test Material 1: Murray Smelter Soil

Test Material 2: NIST Paint

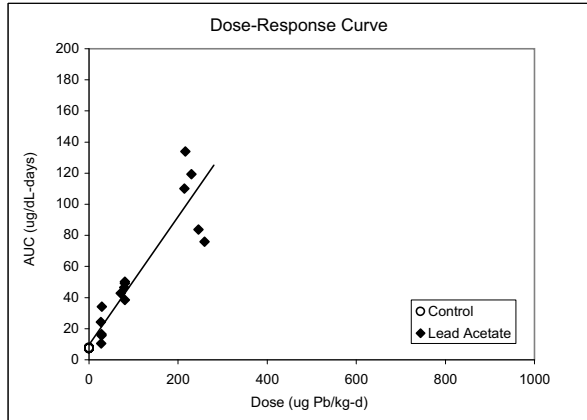
- Figure 1a Blood AUC - Linear Model
- Figure 1b Blood AUC - Exponential Model
- Figure 1c Blood AUC - Michaelis-Menton Model
- Figure 1d Blood AUC - Power Model
  
- Figure 2a Liver - Linear Model
- Figure 2b Liver - Exponential Model
- Figure 2c Liver - Michaelis-Menton Model
- Figure 2d Liver - Power Model
  
- Figure 3a Kidney - Linear Model
- Figure 3b Kidney - Exponential Model
- Figure 3c Kidney - Michaelis-Menton Model
- Figure 3d Kidney - Power Model
  
- Figure 4a Femur - Linear Model
- Figure 4b Femur - Exponential Model
- Figure 4c Femur - Michaelis-Menton Model
- Figure 4d Femur - Power Model

APPENDIX E

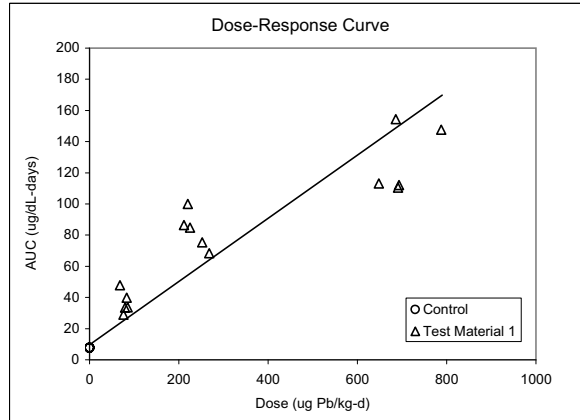
Figure 1a - All Data

Phase II Experiment 11: Blood AUC  
 Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$

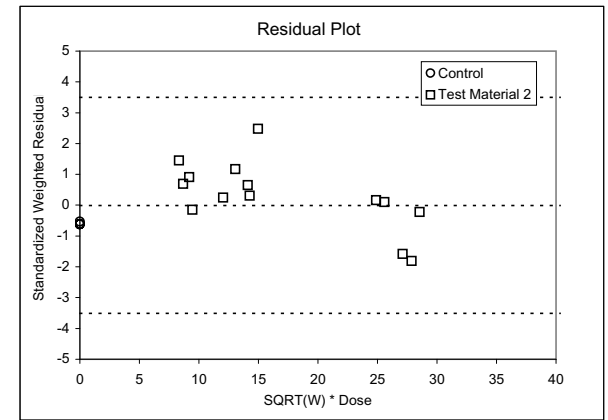
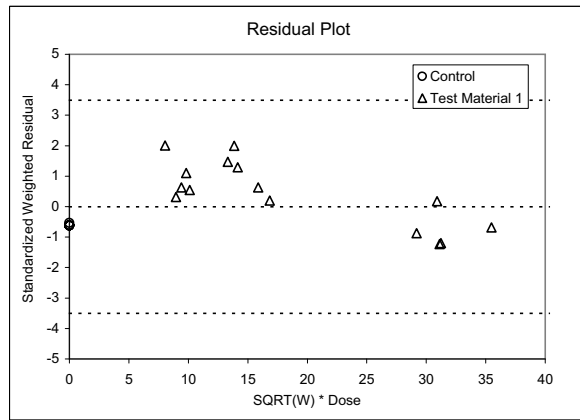
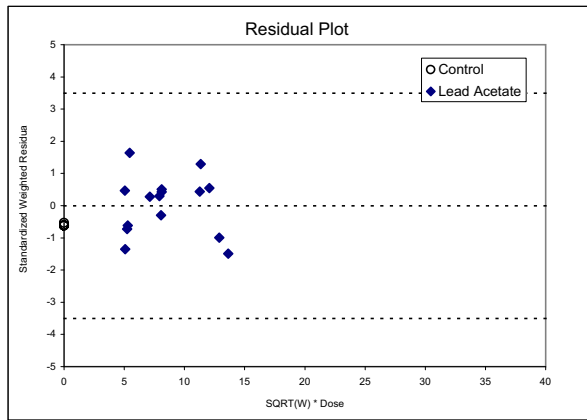
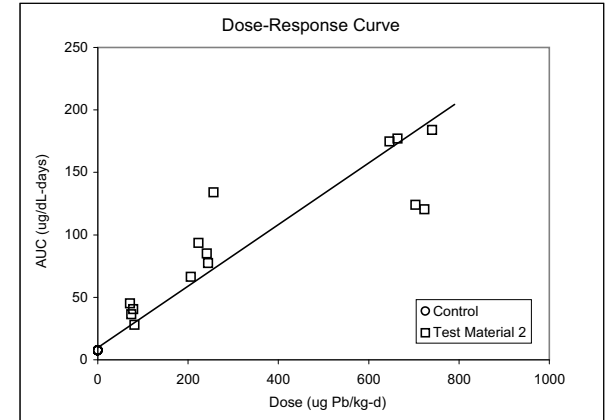
Reference Material (Lead Acetate)



Test Material 1 (Murray Smelter Soil)



Test Material 2 (NIST Paint)



Summary of Fitting

Parameter	Estimate	Standard Error
a	9.70E+00	1.48E+00
b1	4.12E-01	4.59E-02
b2	2.03E-01	1.90E-02
b3	2.46E-01	2.20E-02
Covariance (c1,c2)	0.0667	--
Covariance (c1,c3)	0.0600	--
Degrees of Freedom	45	--

Goodness of Fit

Statistic	Estimate
F	96.525
p	< 0.001
Adjusted R <sup>2</sup>	0.8565
AIC	436.433

RBA and Uncertainty

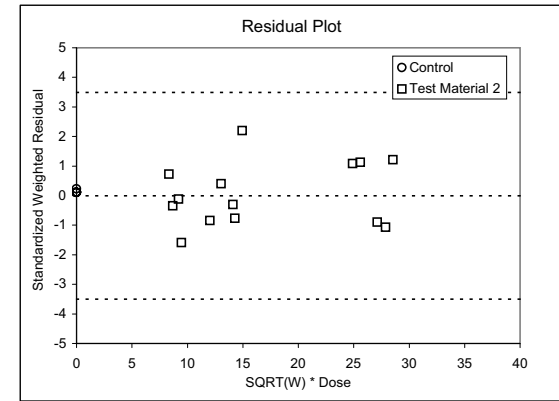
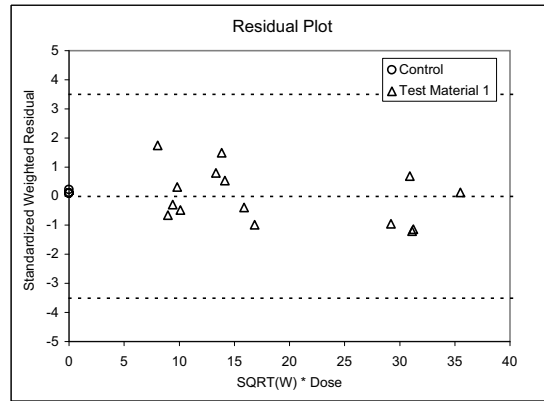
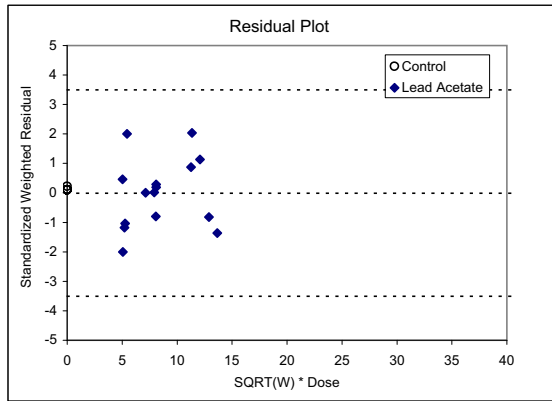
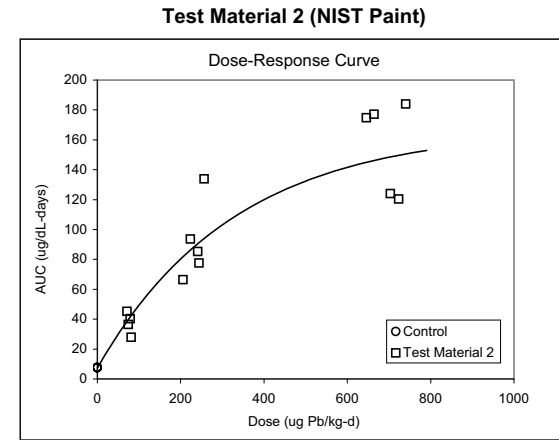
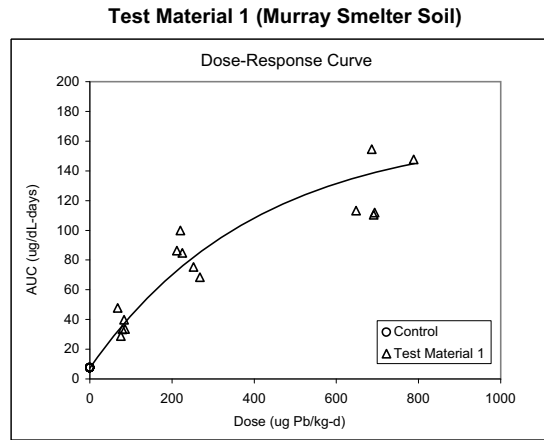
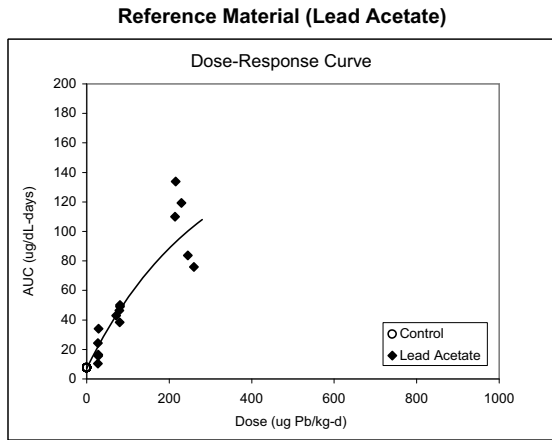
	Test Material 1	Test Material 2
RBA	0.49	0.60
Lower bound	0.39	0.48
Upper bound	0.63	0.76
Standard Error	0.069	0.083

APPENDIX E

Figure 1b - All Data

Phase II Experiment 11: Blood AUC

Exponential Model:  $y = a + b*(1-\exp(-c1*x1)) + b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$



Summary of Fitting

Parameter	Estimate	Standard Error
a	7.21E+00	1.18E+00
b	1.60E+02	1.75E+01
c1	3.54E-03	6.21E-04
c2	2.49E-03	4.96E-04
c3	3.04E-03	6.15E-04
Covariance (c1,c2)	0.7274	--
Covariance (c1,c3)	0.7186	--
Degrees of Freedom	44	--

Goodness of Fit

Statistic	Estimate
F	143.605
p	< 0.001
Adjusted R <sup>2</sup>	0.9224
AIC	390.414

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.70	0.86
Lower bound	0.54	0.66
Upper bound	0.89	1.09
Standard Error	0.098*	0.123*

\*  $g \geq 0.05$ , estimate is uncertain

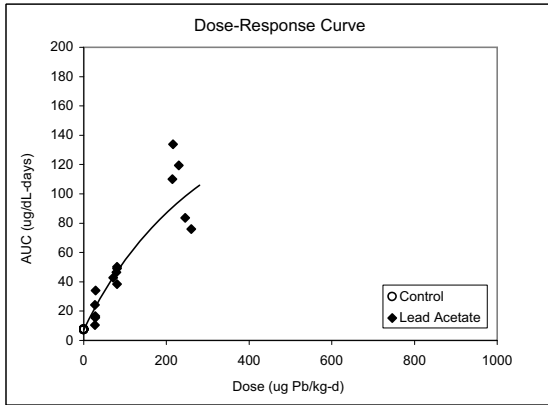
APPENDIX E

Figure 1c - All Data

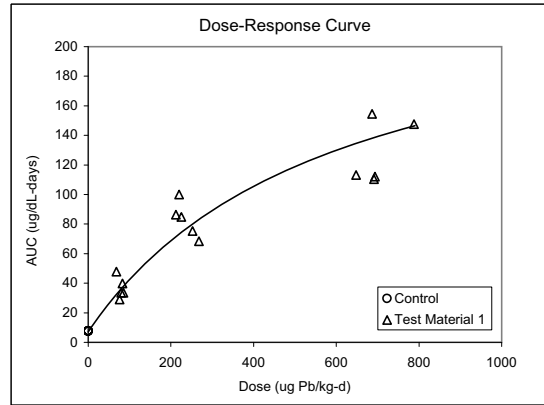
Phase II Experiment 11: Blood AUC

Michaelis-Menton Model:  $y = a + b*x1/(c1+x1) + b*x2/(c2+x2) + b*x3/(c3+x3)$

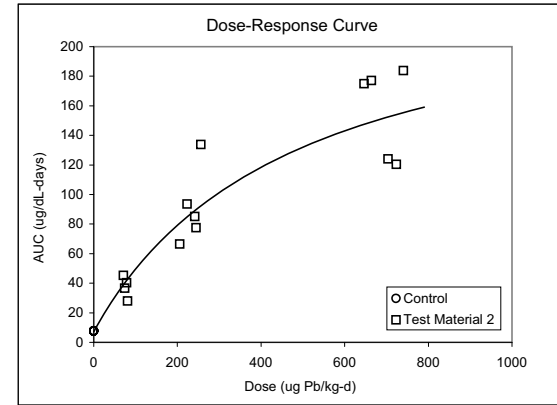
Reference Material (Lead Acetate)



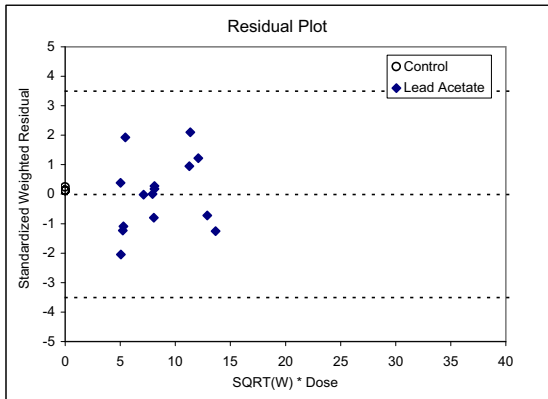
Test Material 1 (Murray Smelter Soil)



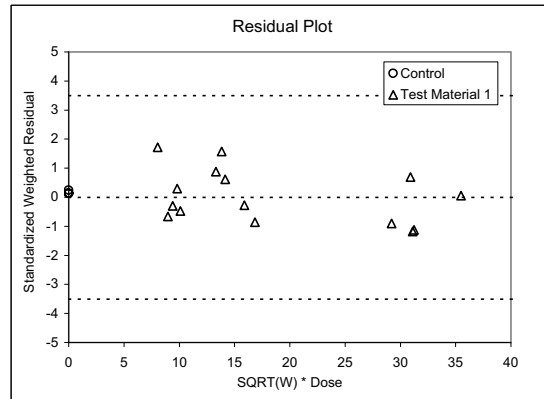
Test Material 2 (NIST Paint)



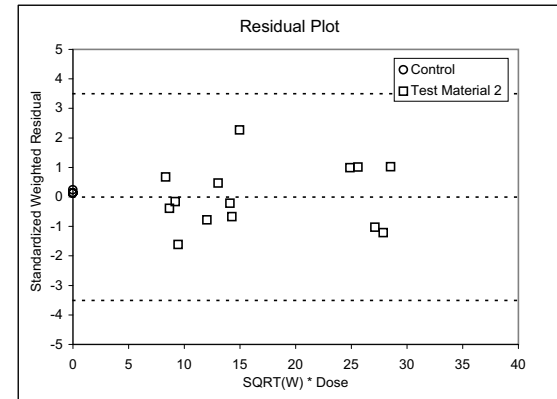
Residual Plot



Residual Plot



Residual Plot



Summary of Fitting

Parameter	Estimate	Standard Error
a	7.16E+00	1.20E+00
b	2.44E+02	3.62E+01
c1	4.11E+02	9.21E+01
c2	5.91E+02	1.50E+02
c3	4.76E+02	1.24E+02
Covariance (c1,c2)	0.8303	--
Covariance (c1,c3)	0.8277	--
Degrees of Freedom	44	--

Goodness of Fit

Statistic	Estimate
F	141.020
p	< 0.001
Adjusted R <sup>2</sup>	0.9211
AIC	391.331

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.70	0.86
Lower bound	0.55	0.68
Upper bound	0.93	1.17
Standard Error	0.099*	0.126*

\* g ≥ 0.05, estimate is uncertain

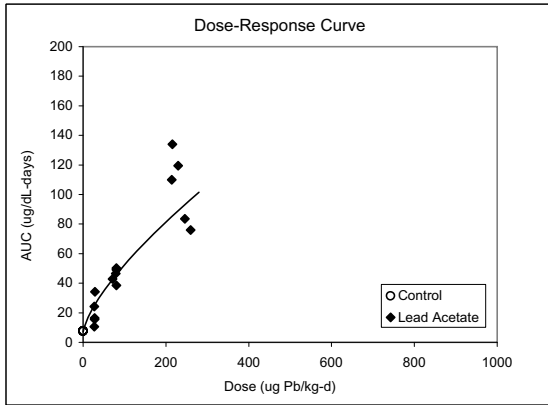
APPENDIX E

Figure 1d - All Data

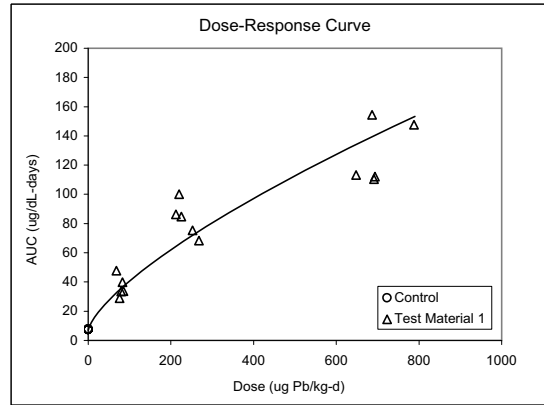
Phase II Experiment 11: Blood AUC

Power Model:  $y = a + b_1 \cdot x_1^c + b_2 \cdot x_2^c + b_3 \cdot x_3^c$

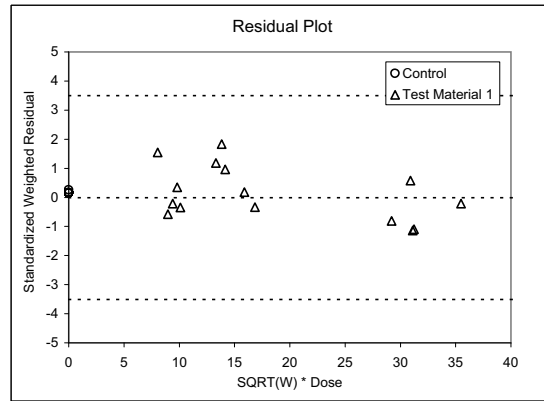
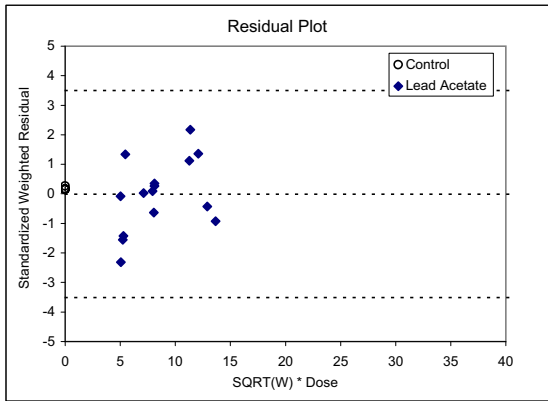
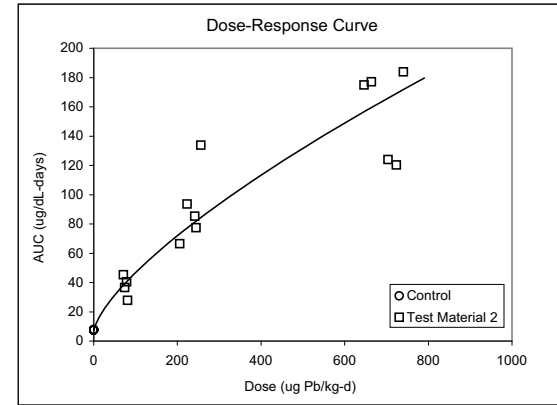
Reference Material (Lead Acetate)



Test Material 1 (Murray Smelter Soil)



Test Material 2 (NIST Paint)



Summary of Fitting

Parameter	Estimate	Standard Error
a	7.04E+00	1.34E+00
b1	1.71E+00	4.52E-01
b2	1.27E+00	4.06E-01
b3	1.49E+00	4.74E-01
c	7.12E-01	5.18E-02
Covariance (b1,b2)	0.9262	--
Covariance (b1,b3)	0.9264	--
Degrees of Freedom	44	--

Goodness of Fit

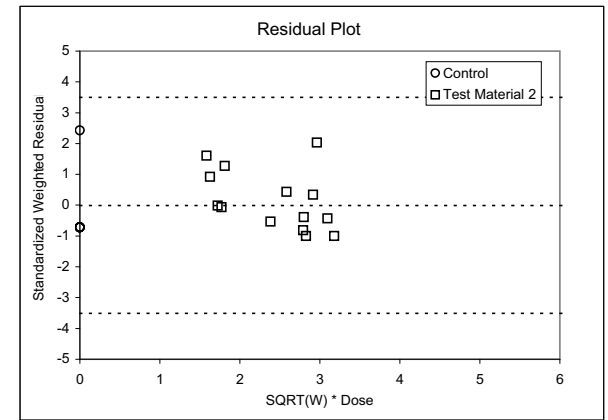
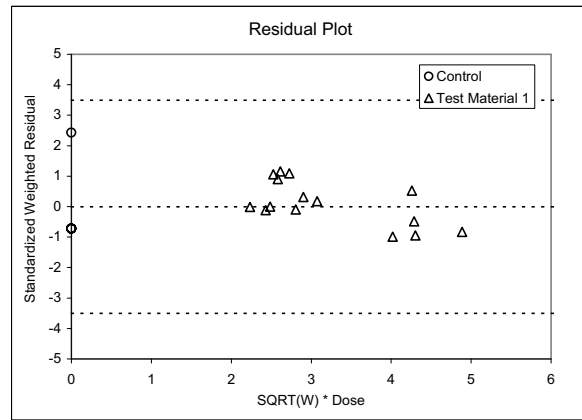
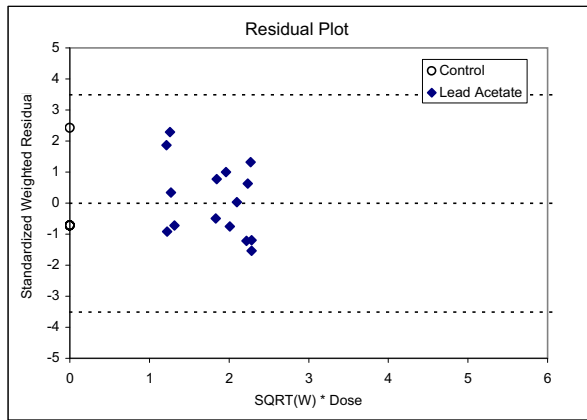
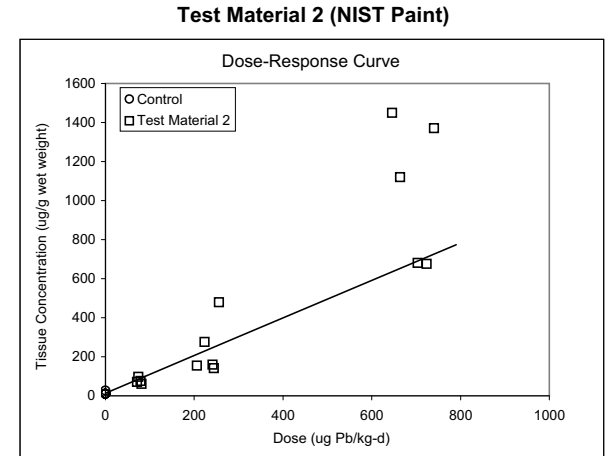
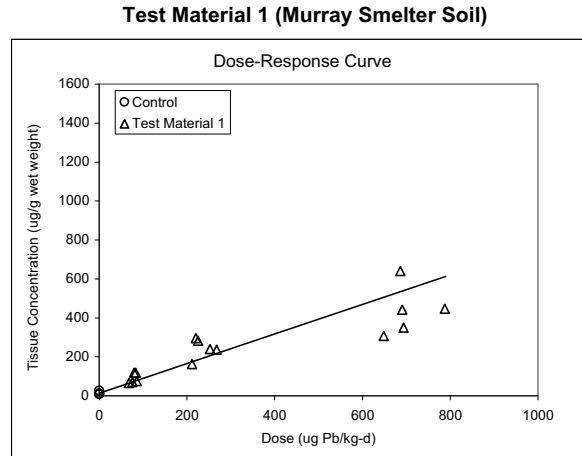
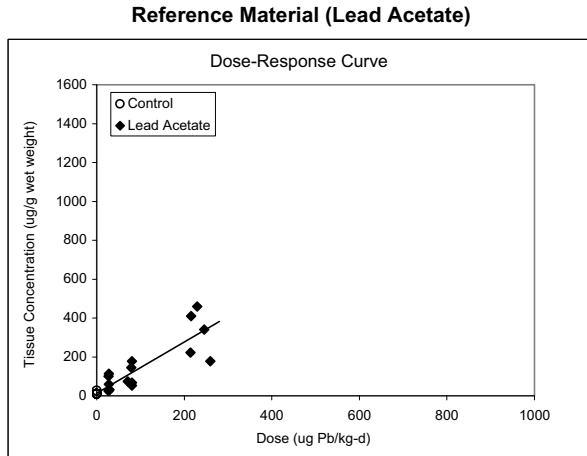
Statistic	Estimate
F	115.506
p	< 0.001
Adjusted R <sup>2</sup>	0.9051
AIC	402.393

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.66	0.83
Lower bound	0.42	0.54
Upper bound	0.85	1.07
Standard Error	--	--

APPENDIX E

**Figure 2a - All Data**  
**Phase II Experiment 11: Liver**  
**Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$**



**Summary of Fitting**

Parameter	Estimate	Standard Error
a	1.37E+01	2.30E+00
b1	1.31E+00	1.80E-01
b2	7.59E-01	1.00E-01
b3	9.62E-01	1.41E-01
Covariance (c1,c2)	0.0165	--
Covariance (c1,c3)	0.0209	--
Degrees of Freedom	44	--

**Goodness of Fit**

Statistic	Estimate
F	50.849
p	< 0.001
Adjusted R <sup>2</sup>	0.7570
AIC	561.444

**RBA and Uncertainty**

	Test Material 1	Test Material 2
RBA	0.58	0.73
Lower bound	0.42	0.52
Upper bound	0.80	1.03
Standard Error	0.109*	0.145*

\*  $g \geq 0.05$ , estimate is uncertain

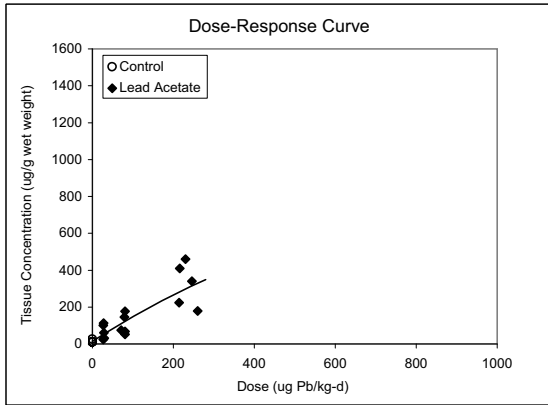
APPENDIX E

Figure 2b - All Data

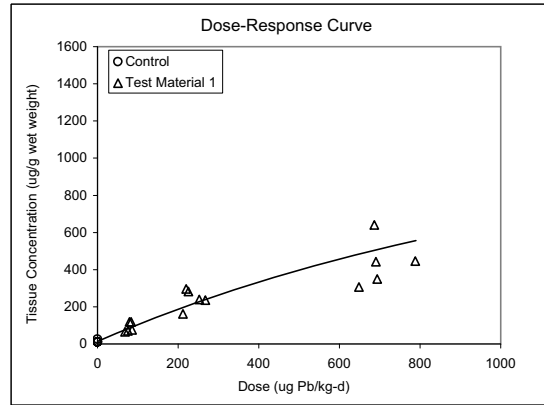
Phase II Experiment 11: Liver

Exponential Model:  $y = a + b*(1-\exp(-c1*x1))+b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$

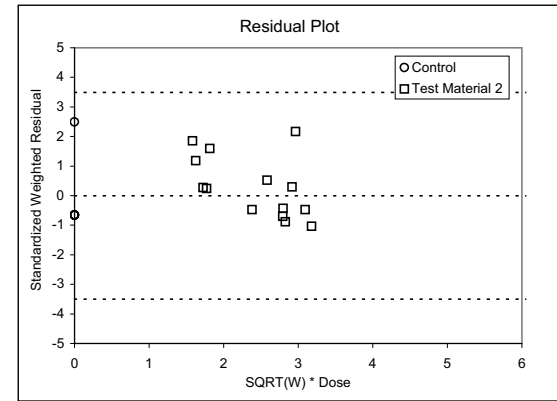
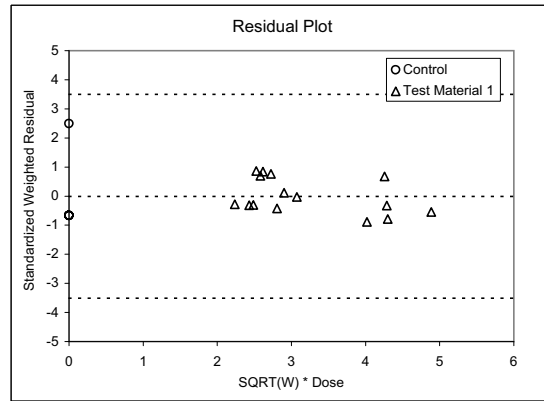
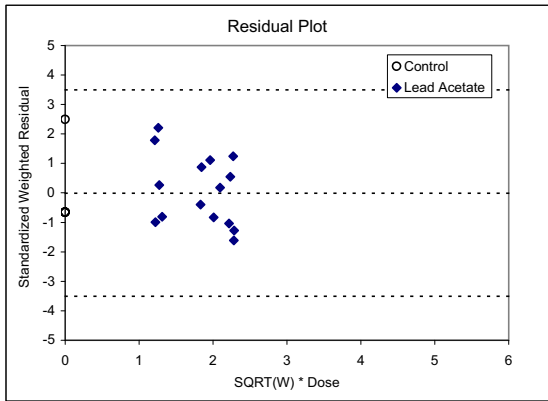
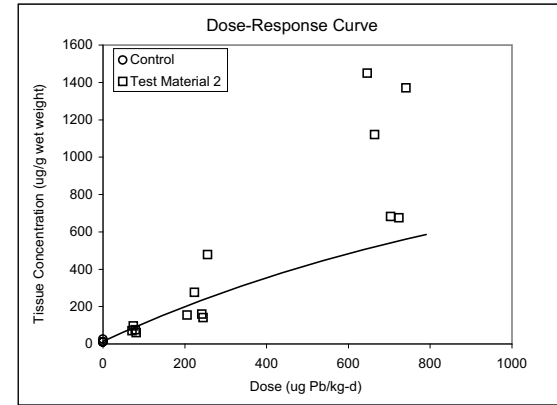
Reference Material (Lead Acetate)



Test Material 1 (Murray Smelter Soil)



Test Material 2 (NIST Paint)



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.34E+01	2.33E+00
b	1.11E+03	9.46E+02
c1	1.29E-03	1.21E-03
c2	8.53E-04	8.65E-04
c3	9.21E-04	8.71E-04
Covariance (c1,c2)	0.9770	--
Covariance (c1,c3)	0.9728	--
Degrees of Freedom	43	--

Goodness of Fit

Statistic	Estimate
F	50.761
p	< 0.001
Adjusted R <sup>2</sup>	0.7567
AIC	561.591

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.66	0.71
Lower bound	?	?
Upper bound	?	?
Standard Error	0.147*	0.156*

\*  $g \geq 0.05$ , estimate is uncertain

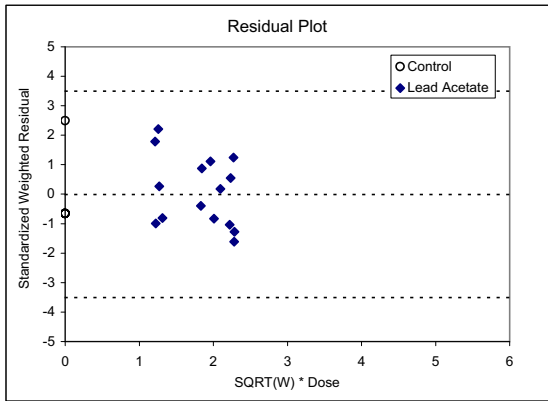
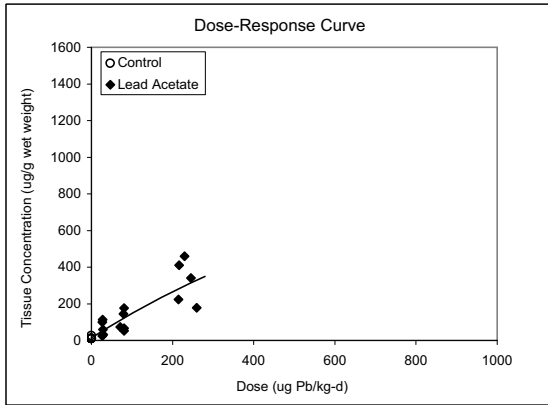
APPENDIX E

Figure 2c - All Data

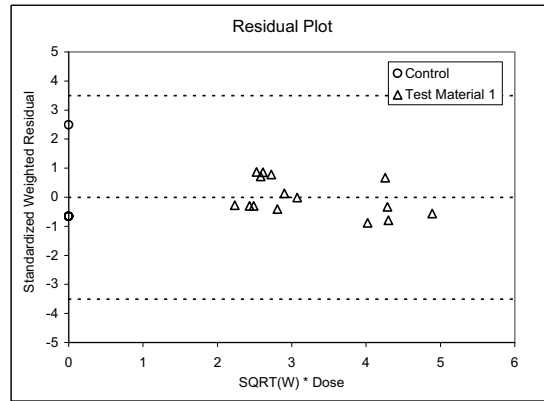
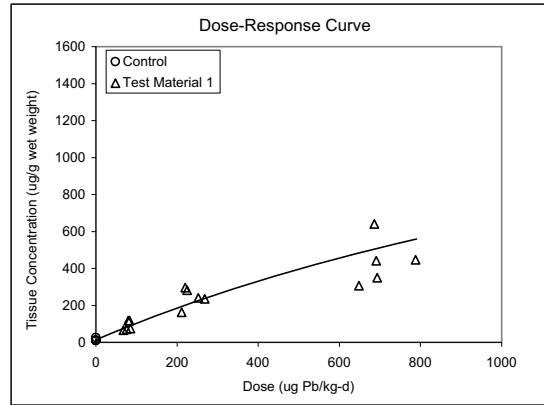
Phase II Experiment 11: Liver

Michaelis-Menton Model:  $y = a + b \cdot x_1 / (c_1 + x_1) + b \cdot x_2 / (c_2 + x_2) + b \cdot x_3 / (c_3 + x_3)$

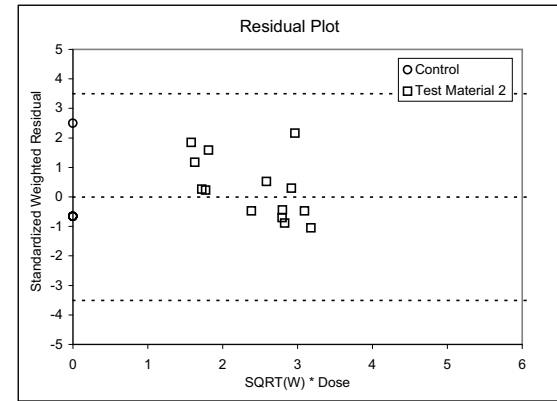
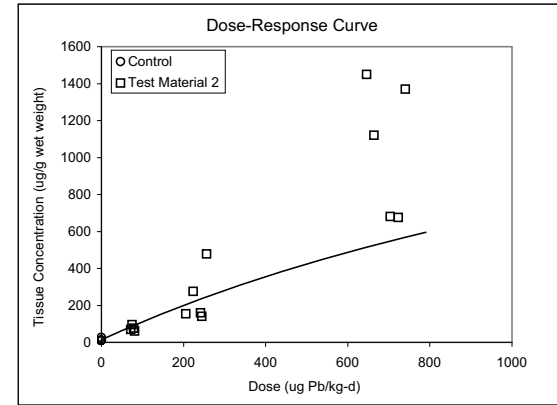
Reference Material (Lead Acetate)



Test Material 1 (Murray Smelter Soil)



Test Material 2 (NIST Paint)



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.34E+01	2.34E+00
b	2.07E+03	2.04E+03
c1	1.44E+03	1.55E+03
c2	2.21E+03	2.54E+03
c3	2.02E+03	2.19E+03
Covariance (c1,c2)	0.9824	--
Covariance (c1,c3)	0.9793	--
Degrees of Freedom	43	--

Goodness of Fit

Statistic	Estimate
F	50.798
p	< 0.001
Adjusted R <sup>2</sup>	0.7568
AIC	561.543

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.65	0.71
Lower bound	?	?
Upper bound	?	?
Standard Error	0.146*	0.157*

\* g ≥ 0.05, estimate is uncertain



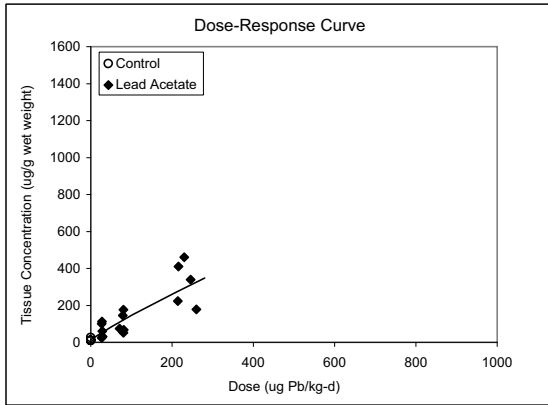
APPENDIX E

Figure 2d - All Data

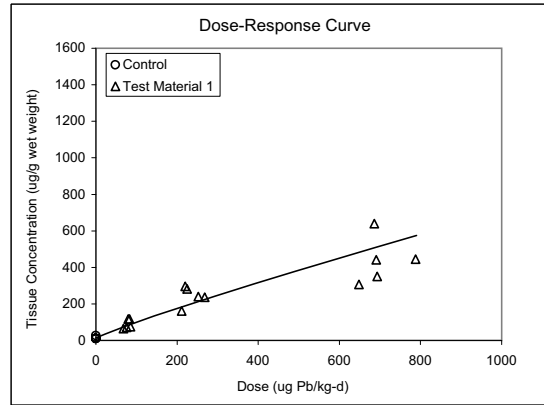
Phase II Experiment 11: Liver

Power Model:  $y = a + b1*x1^c + b2*x2^c + b3*x3^c$

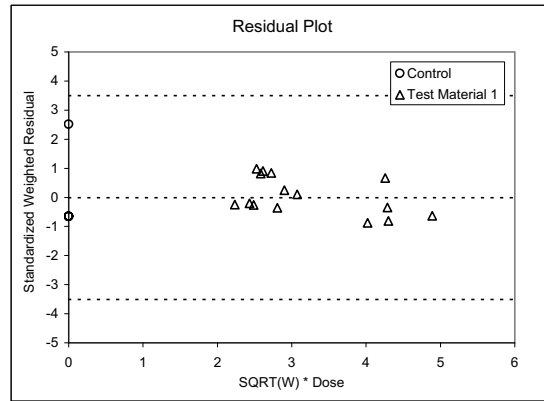
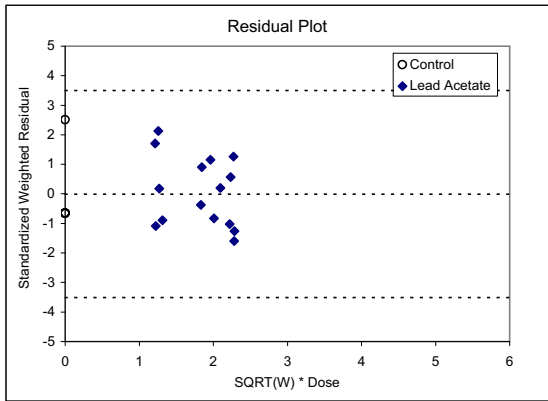
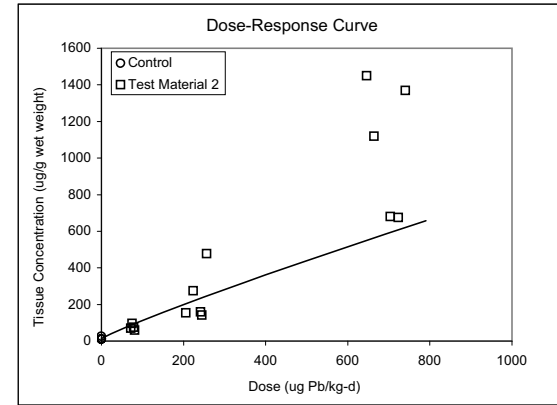
Reference Material (Lead Acetate)



Test Material 1 (Murray Smelter Soil)



Test Material 2 (NIST Paint)



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.33E+01	2.34E+00
b1	2.05E+00	9.53E-01
b2	1.34E+00	7.73E-01
b3	1.54E+00	7.93E-01
c	9.05E-01	9.76E-02
Covariance (b1,b2)	0.9327	--
Covariance (b1,b3)	0.9175	--
Degrees of Freedom	43	--

Goodness of Fit

Statistic	Estimate
F	51.275
p	< 0.001
Adjusted R <sup>2</sup>	0.7586
AIC	560.976

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.63	0.73
Lower bound	0.06	0.28
Upper bound	0.91	1.17
Standard Error	--	--

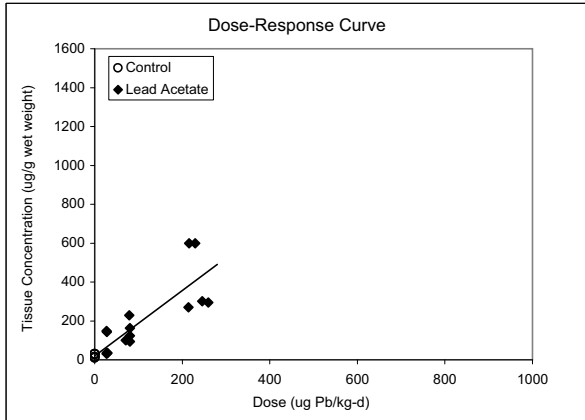
APPENDIX E

Figure 3a - All Data

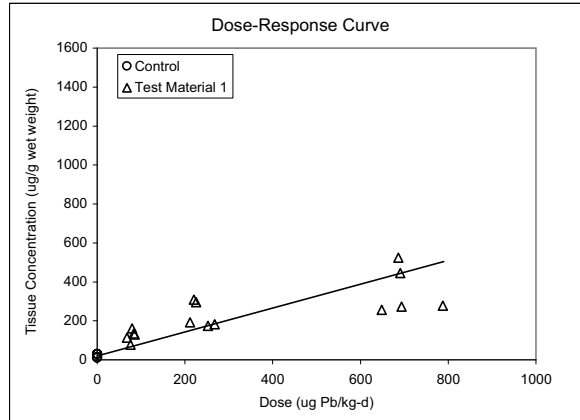
Phase II Experiment 11: Kidney

Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$

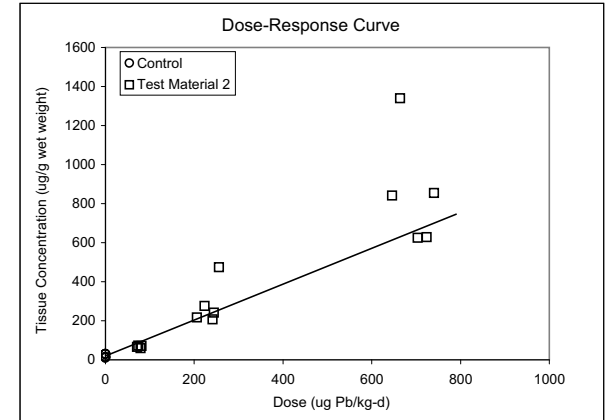
Reference Material (Lead Acetate)



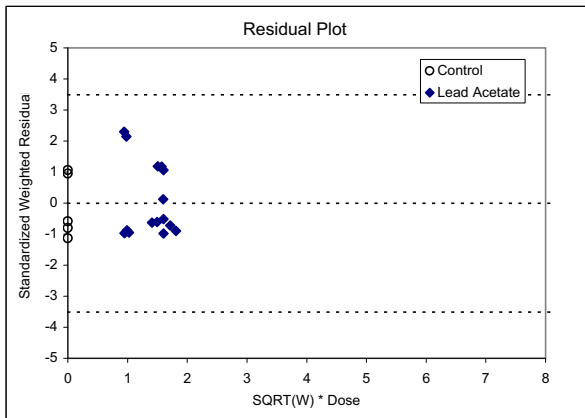
Test Material 1 (Murray Smelter Soil)



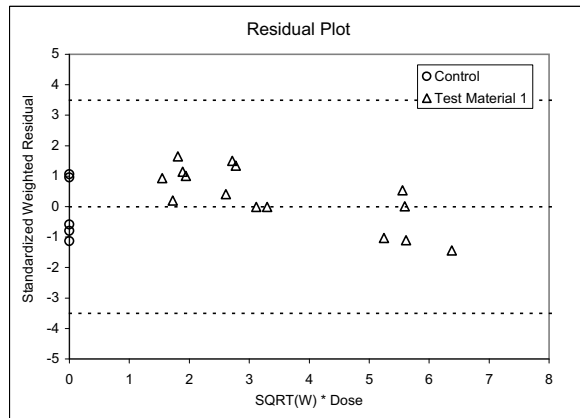
Test Material 2 (NIST Paint)



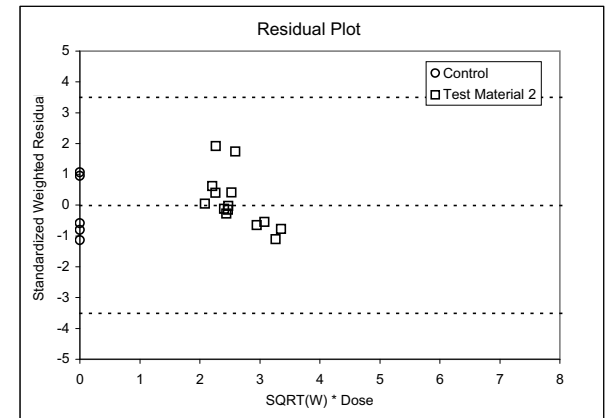
Residual Plot



Residual Plot



Residual Plot



Summary of Fitting

Parameter	Estimate	Standard Error
a	2.03E+01	4.13E+00
b1	1.68E+00	2.48E-01
b2	6.12E-01	9.05E-02
b3	9.18E-01	1.44E-01
Covariance (c1,c2)	0.0267	--
Covariance (c1,c3)	0.0454	--
Degrees of Freedom	44	--

Goodness of Fit

Statistic	Estimate
F	43.248
p	< 0.001
Adjusted R <sup>2</sup>	0.7253
AIC	576.648

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.36	0.55
Lower bound	0.25	0.38
Upper bound	0.52	0.78
Standard Error	0.075*	0.115*

\*  $g \geq 0.05$ , estimate is uncertain

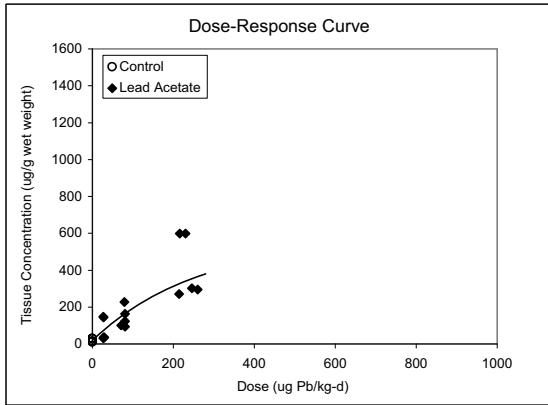
APPENDIX E

Figure 3b - All Data

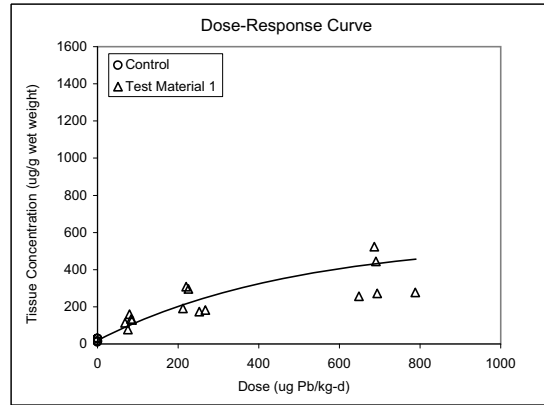
Phase II Experiment 11: Kidney

Exponential Model:  $y = a + b*(1-\exp(-c1*x1)) + b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$

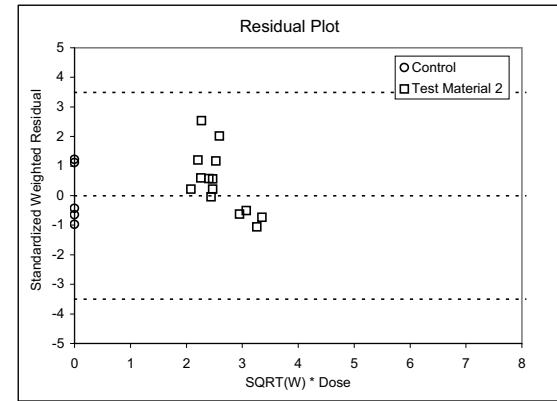
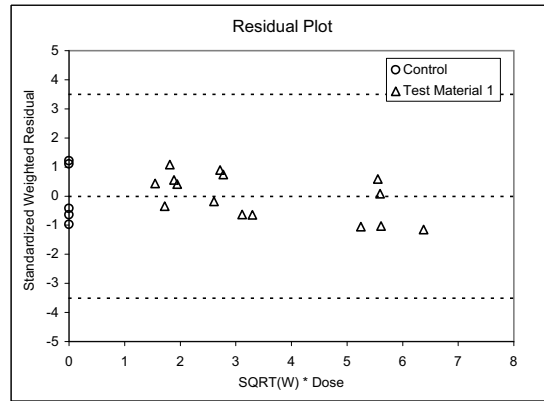
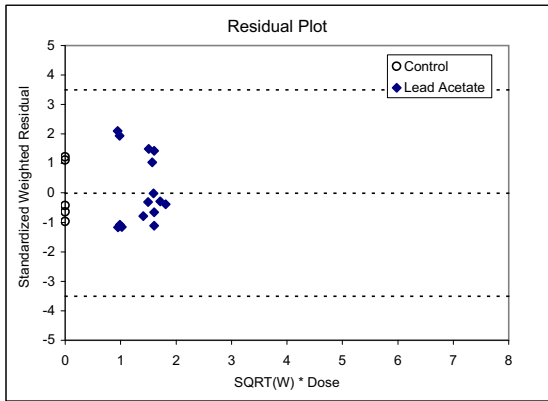
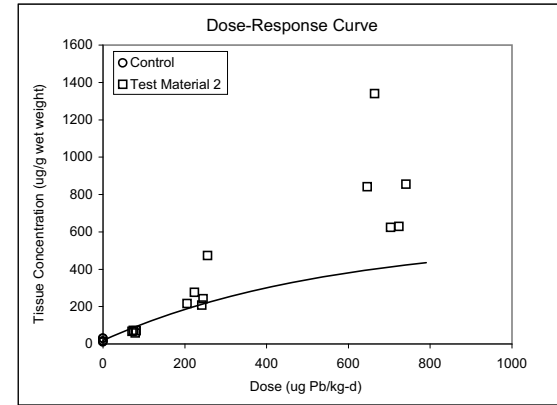
Reference Material (Lead Acetate)



Test Material 1 (Murray Smelter Soil)



Test Material 2 (NIST Paint)



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.89E+01	4.24E+00
b	5.49E+02	2.04E+02
c1	3.83E-03	1.88E-03
c2	2.03E-03	1.17E-03
c3	1.80E-03	8.67E-04
Covariance (c1,c2)	0.8761	--
Covariance (c1,c3)	0.8456	--
Degrees of Freedom	43	--

Goodness of Fit

Statistic	Estimate
F	31.501
p	< 0.001
Adjusted R <sup>2</sup>	0.7177
AIC	578.650

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.53	0.47
Lower bound	0.05	0.22
Upper bound	0.93	1.04
Standard Error	0.148*	0.127*

\*  $g \geq 0.05$ , estimate is uncertain

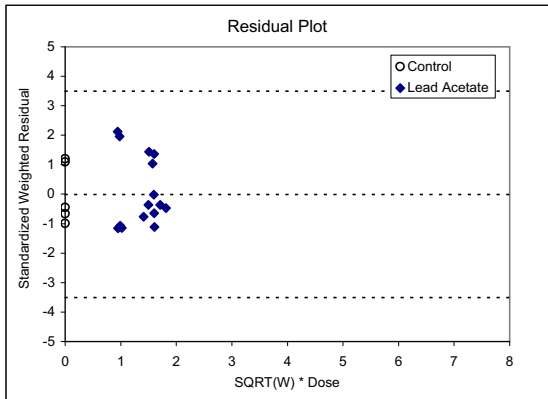
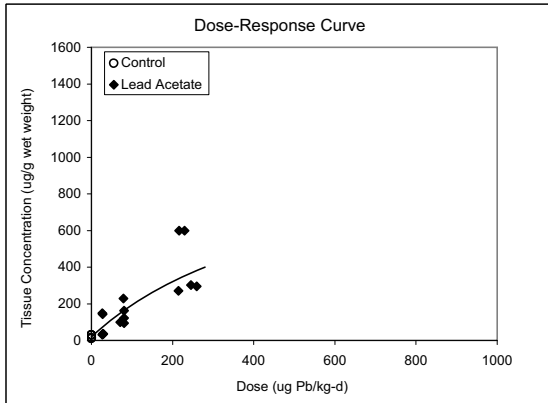
APPENDIX E

Figure 3c - All Data

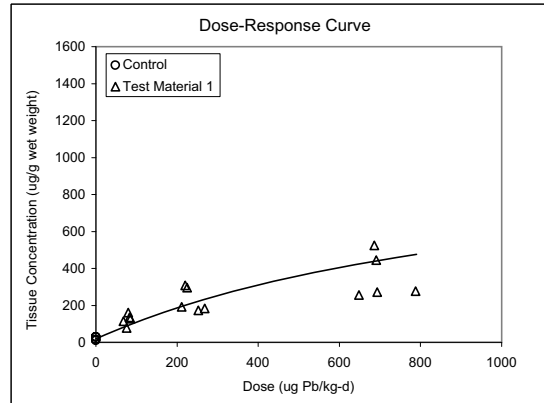
Phase II Experiment 11: Kidney

Michaelis-Menton Model:  $y = a + b \cdot x1 / (c1 + x1) + b \cdot x2 / (c2 + x2) + b \cdot x3 / (c3 + x3)$

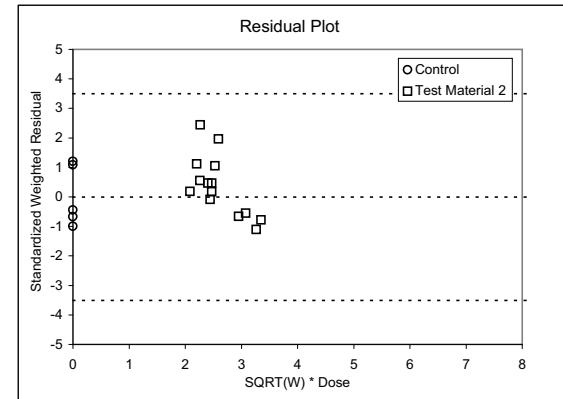
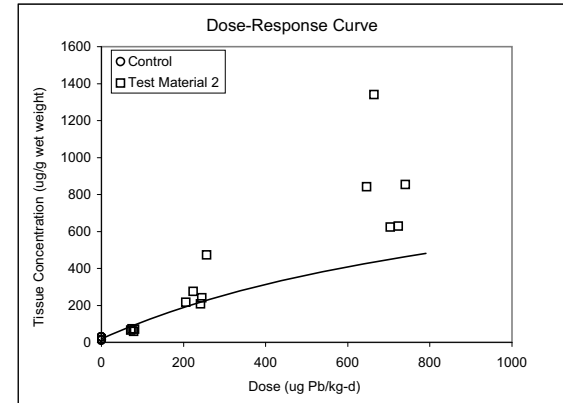
Reference Material (Lead Acetate)



Test Material 1 (Murray Smelter Soil)



Test Material 2 (NIST Paint)



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.91E+01	4.26E+00
b	1.11E+03	6.56E+02
c1	5.34E+02	3.90E+02
c2	1.12E+03	9.29E+02
c3	1.11E+03	7.91E+02
Covariance (c1,c2)	0.9475	--
Covariance (c1,c3)	0.9350	--
Degrees of Freedom	43	--

Goodness of Fit

Statistic	Estimate
F	31.472
p	< 0.001
Adjusted R <sup>2</sup>	0.7175
AIC	578.702

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.48	0.48
Lower bound	?	?
Upper bound	?	?
Standard Error	0.128*	0.126*

\*  $g \geq 0.05$ , estimate is uncertain

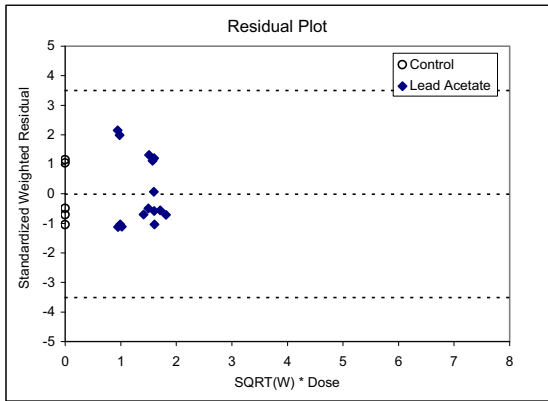
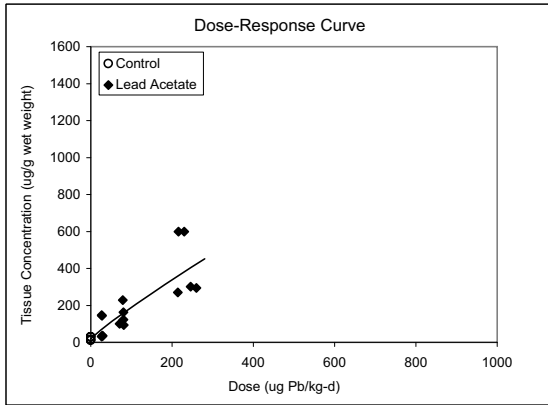
APPENDIX E

Figure 3d - All Data

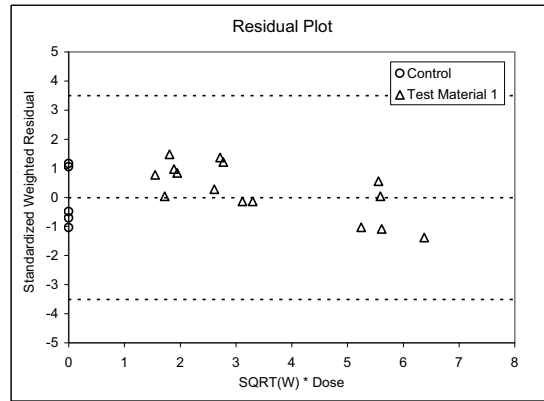
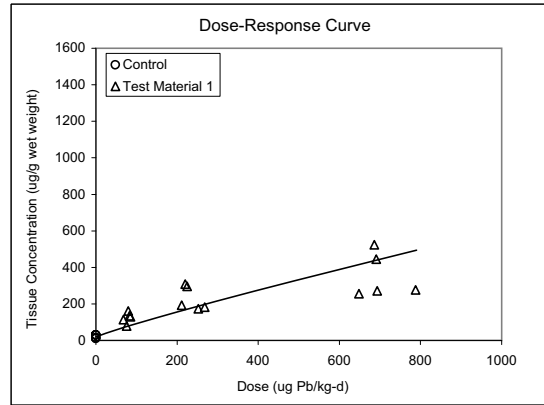
Phase II Experiment 11: Kidney

Power Model:  $y = a + b_1 \cdot x_1^c + b_2 \cdot x_2^c + b_3 \cdot x_3^c$

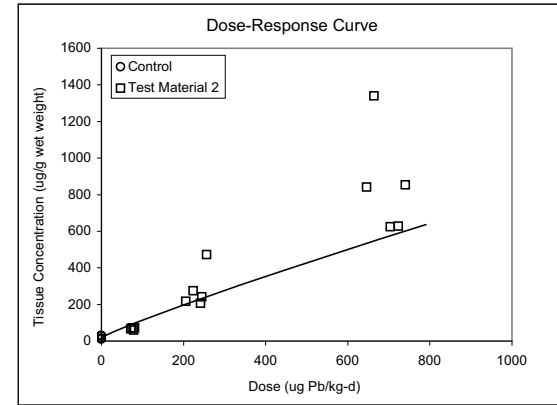
Reference Material (Lead Acetate)



Test Material 1 (Murray Smelter Soil)



Test Material 2 (NIST Paint)



Summary of Fitting

Parameter	Estimate	Standard Error
a	1.95E+01	4.30E+00
b1	2.61E+00	1.40E+00
b2	1.12E+00	7.79E-01
b3	1.46E+00	8.67E-01
c	9.07E-01	1.11E-01
Covariance (b1,b2)	0.9422	--
Covariance (b1,b3)	0.9294	--
Degrees of Freedom	43	--

Goodness of Fit

Statistic	Estimate
F	31.801
p	< 0.001
Adjusted R <sup>2</sup>	0.7196
AIC	578.247

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.39	0.52
Lower bound	?	?
Upper bound	0.58	0.96
Standard Error	--	--

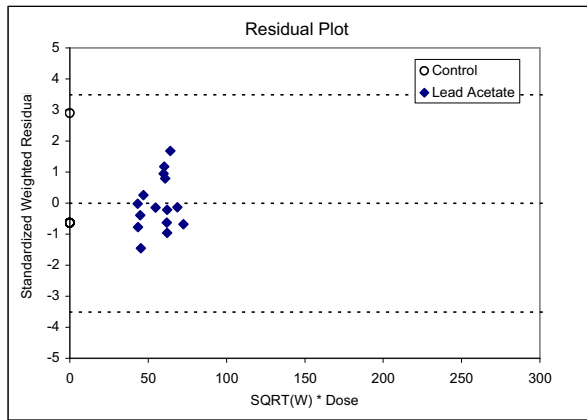
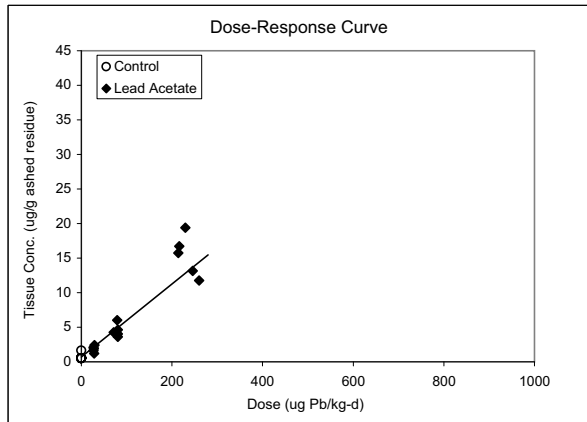
APPENDIX E

Figure 4a - All Data

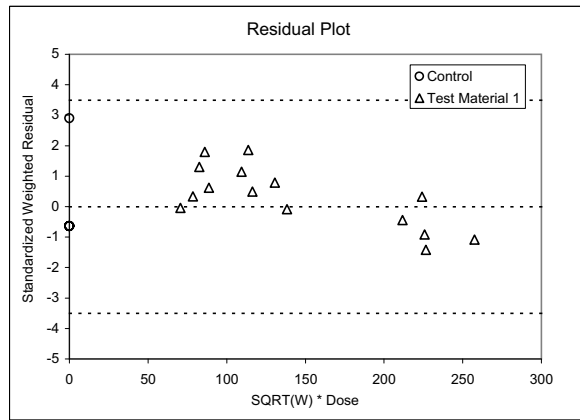
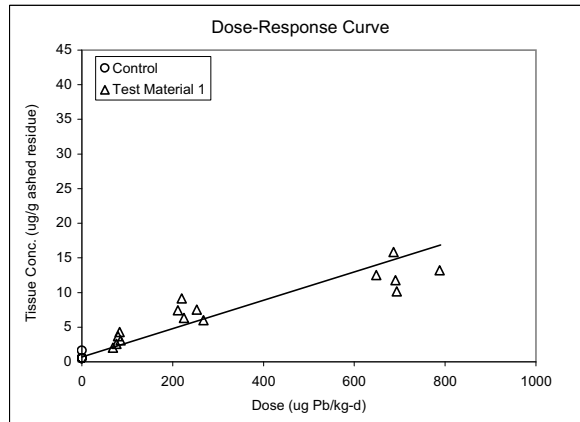
Phase II Experiment 11: Femur

Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$

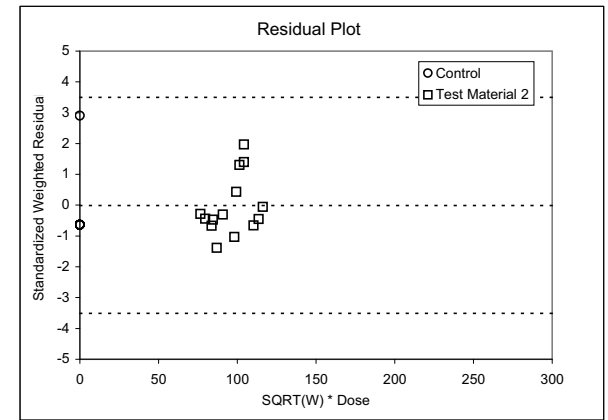
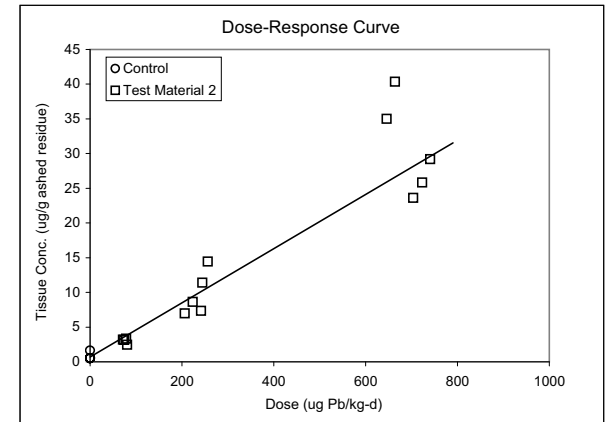
Reference Material (Lead Acetate)



Test Material 1 (Murray Smelter Soil)



Test Material 2 (NIST Paint)



Summary of Fitting

Parameter	Estimate	Standard Error
a	6.98E-01	1.32E-01
b1	5.28E-02	5.46E-03
b2	2.05E-02	1.92E-03
b3	3.90E-02	3.39E-03
Covariance (c1,c2)	0.0688	--
Covariance (c1,c3)	0.0673	--
Degrees of Freedom	44	--

Goodness of Fit

Statistic	Estimate
F	108.800
p	< 0.001
Adjusted R <sup>2</sup>	0.8708
AIC	198.208

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.39	0.74
Lower bound	0.31	0.59
Upper bound	0.49	0.93
Standard Error	0.052	0.096

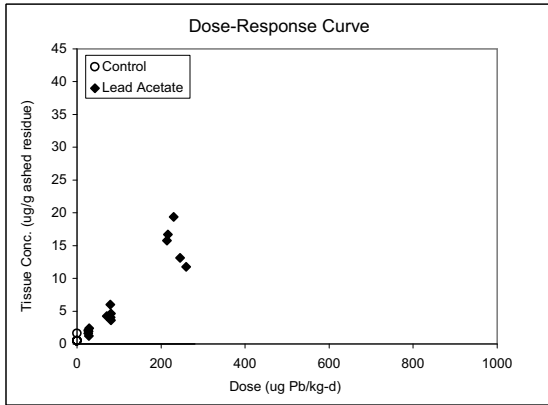
APPENDIX E

Figure 4b - All Data

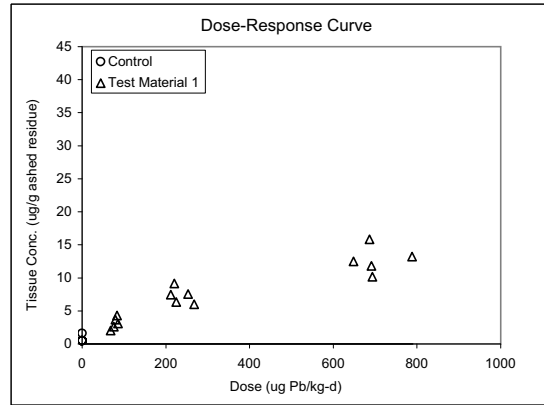
Phase II Experiment 11: Femur

Exponential Model:  $y = a + b*(1-\exp(-c1*x1)) + b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$

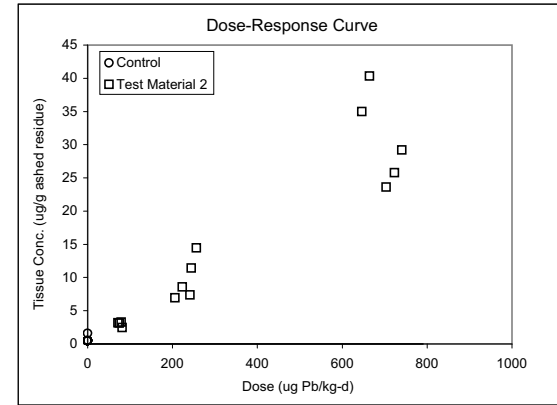
Reference Material (Lead Acetate)



Test Material 1 (Murray Smelter Soil)



Test Material 2 (NIST Paint)



**NO SOLUTION**

The software could not find a solution,  
or the solution was unstable and/or had unrealistic parameter estimates.

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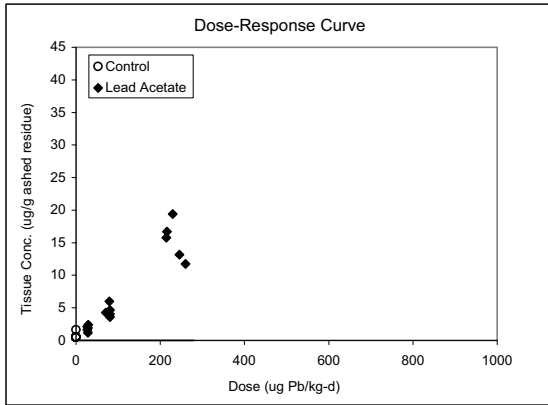
APPENDIX E

Figure 4c - All Data

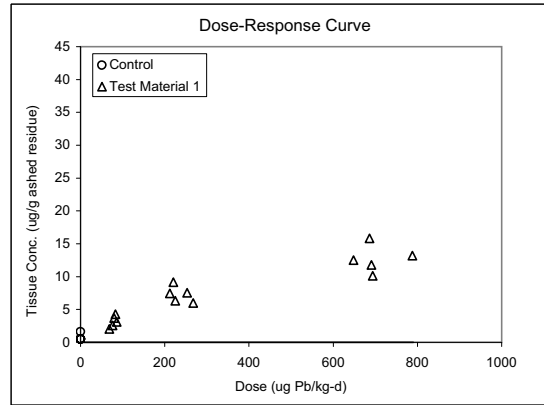
Phase II Experiment 11: Femur

Michaelis-Menton Model:  $y = a + b \cdot x1 / (c1 + x1) + b \cdot x2 / (c2 + x2) + b \cdot x3 / (c3 + x3)$

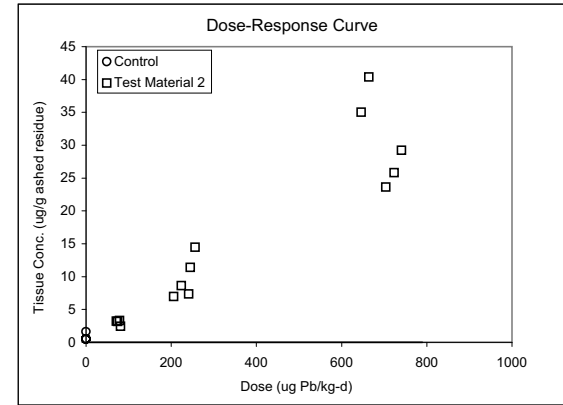
Reference Material (Lead Acetate)



Test Material 1 (Murray Smelter Soil)



Test Material 2 (NIST Paint)



**NO SOLUTION**

The software could not find a solution,  
or the solution was unstable and/or had unrealistic parameter estimates.

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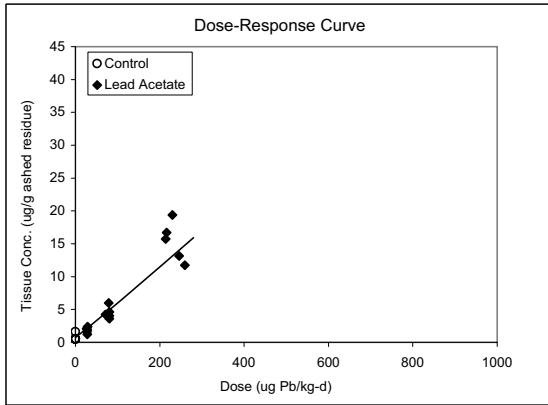
APPENDIX E

Figure 4d - All Data

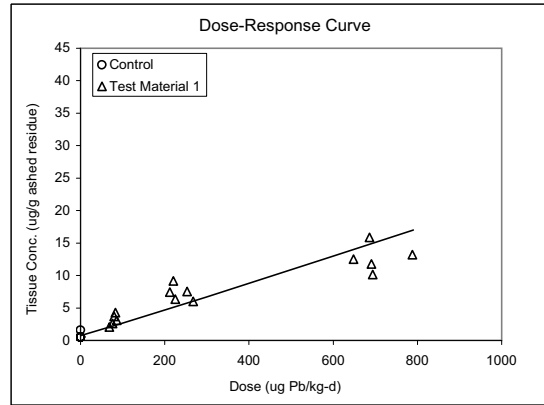
Phase II Experiment 11: Femur

Power Model:  $y = a + b1*x1^c + b2*x2^c + b3*x3^c$

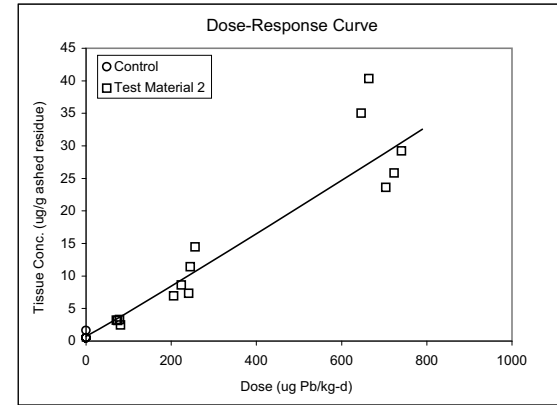
Reference Material (Lead Acetate)



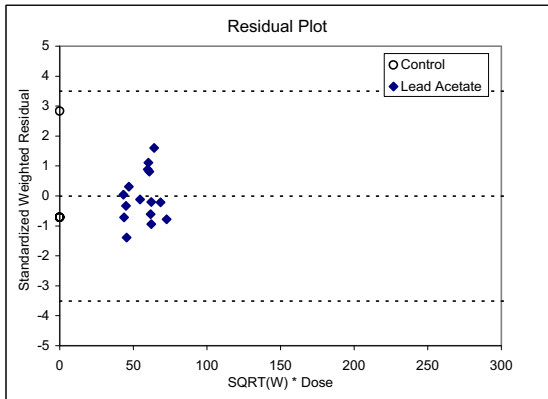
Test Material 1 (Murray Smelter Soil)



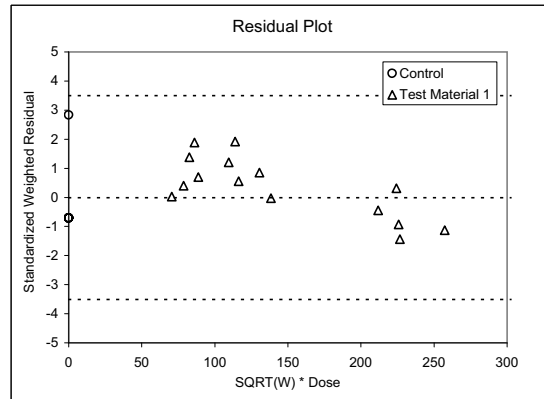
Test Material 2 (NIST Paint)



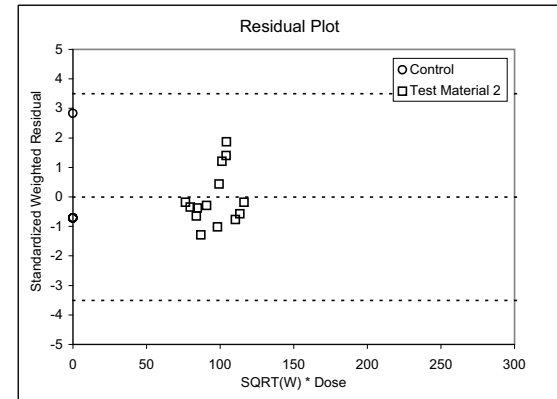
Residual Plot



Residual Plot



Residual Plot



Summary of Fitting

Parameter	Estimate	Standard Error
a	7.21E-01	1.44E-01
b1	4.56E-02	1.71E-02
b2	1.67E-02	7.95E-03
b3	3.27E-02	1.43E-02
c	1.03E+00	7.40E-02
Covariance (b1,b2)	0.9444	--
Covariance (b1,b3)	0.9443	--
Degrees of Freedom	43	--

Goodness of Fit

Statistic	Estimate
F	80.328
p	< 0.001
Adjusted R <sup>2</sup>	0.8686
AIC	200.024

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.38	0.73
Lower bound	0.18	0.45
Upper bound	0.48	0.91
Standard Error	--	--

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## APPENDIX E

### EXPERIMENT 12

Test Material 1: Galena-enriched Soil

Test Material 2: Palmerton Location 2 (Reproducibility Study)

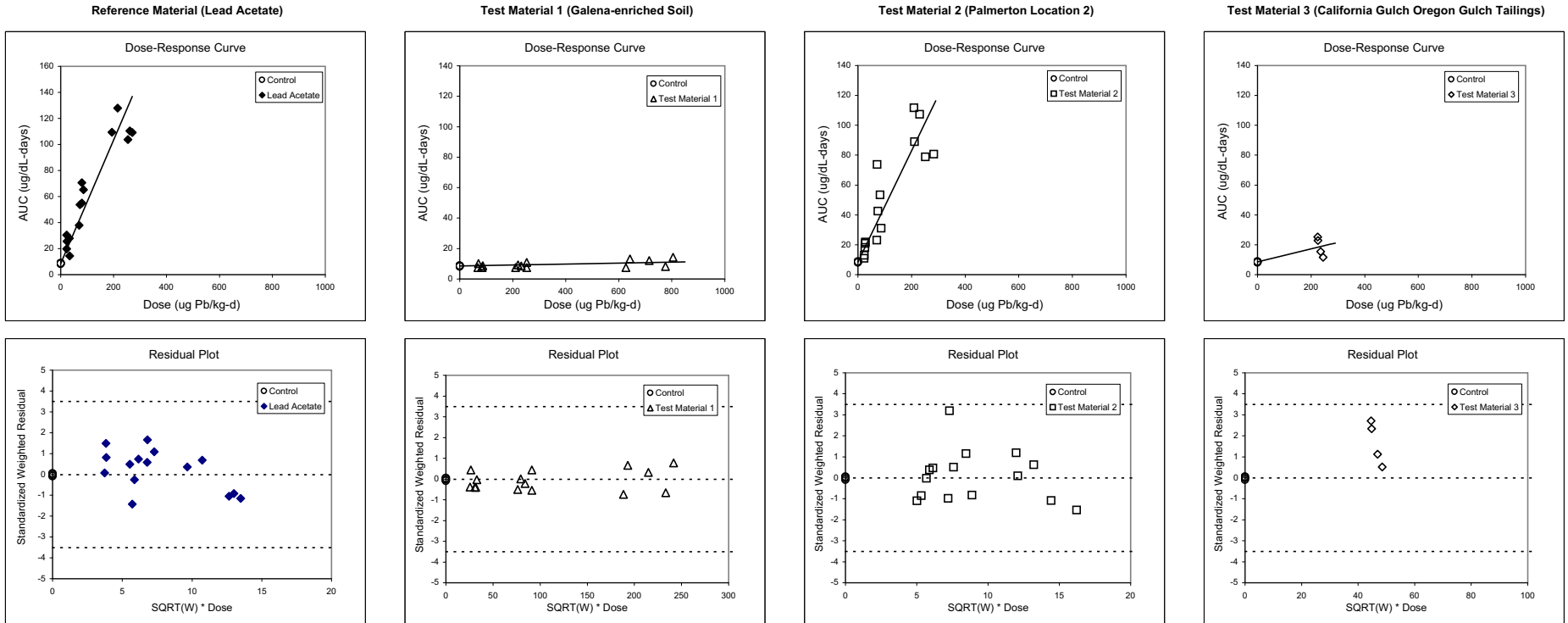
Test Material 3: California Gulch Oregon Gulch Tailings

- Figure 1a Blood AUC - Linear Model
- Figure 1b Blood AUC - Exponential Model
- Figure 1c Blood AUC - Michaelis-Menton Model
- Figure 1d Blood AUC - Power Model
  
- Figure 2a Liver - Linear Model
- Figure 2b Liver - Exponential Model
- Figure 2c Liver - Michaelis-Menton Model
- Figure 2d Liver - Power Model
  
- Figure 3a Kidney - Linear Model (All Data)
- Figure 3a Kidney - Linear Model (Outliers Excluded)
- Figure 3b Kidney - Exponential Model
- Figure 3c Kidney - Michaelis-Menton Model
- Figure 3d Kidney - Power Model
  
- Figure 4a Femur - Linear Model
- Figure 4b Femur - Exponential Model
- Figure 4c Femur - Michaelis-Menton Model
- Figure 4d Femur - Power Model

APPENDIX E

Figure 1a - All Data

Phase II Experiment 12: Blood AUC  
 Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$



Summary of Fitting

Parameter	Estimate	Standard Error
a	8.55E+00	9.63E-01
b1	4.76E-01	3.69E-02
b2	3.10E-03	2.91E-03
b3	3.72E-01	3.24E-02
b4	4.34E-02	1.32E-02
Covariance (c1,c2)	0.1535	--
Covariance (c1,c3)	0.0703	--
Covariance (c1,c4)	0.0746	--
Degrees of Freedom	47	--

Goodness of Fit

Statistic	Estimate
F	124.227
p	< 0.001
Adjusted R <sup>2</sup>	0.9062
AIC	375.135

RBA and Uncertainty

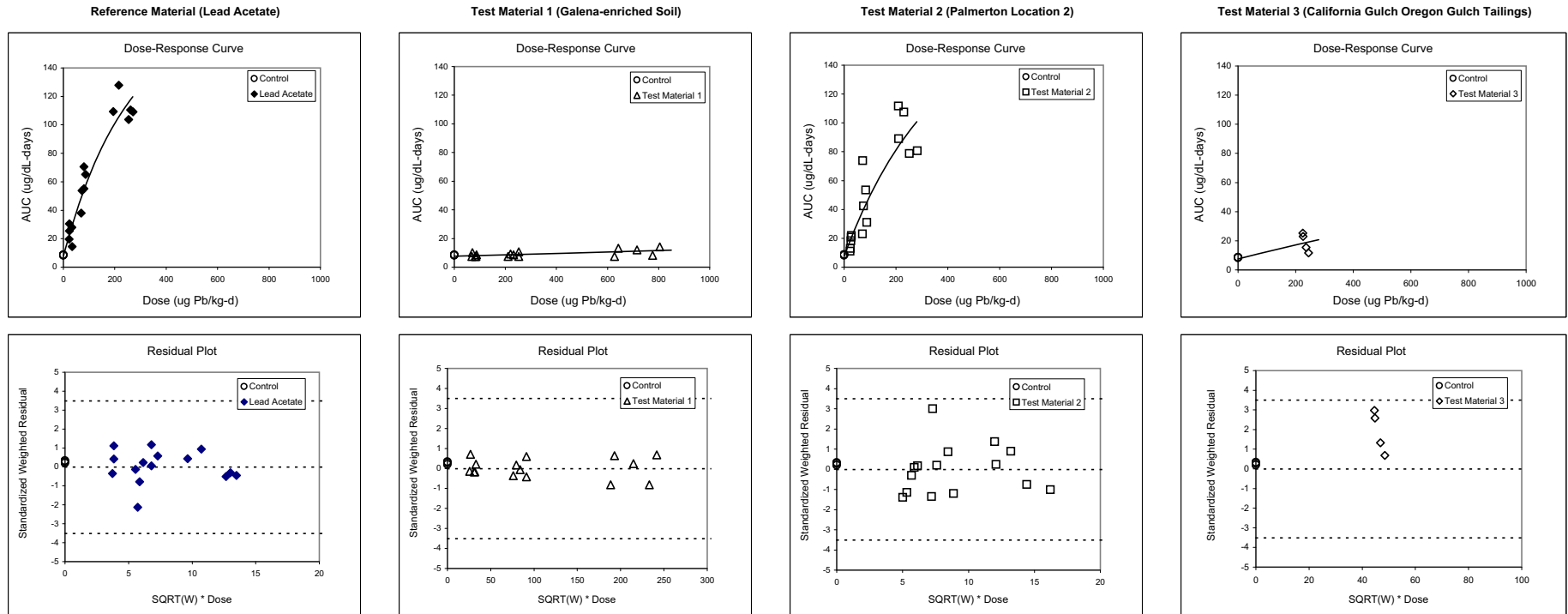
	Test Material 1	Test Material 2	Test Material 3
RBA	0.01	0.78	0.09
Lower bound	0.00	0.64	0.04
Upper bound	0.02	0.94	0.14
Standard Error	0.006	0.088	0.028

APPENDIX E

Figure 1b - All Data

Phase II Experiment 12: Blood AUC

Exponential Model:  $y = a + b \cdot (1 - \exp(-c_1 \cdot x_1)) + b \cdot (1 - \exp(-c_2 \cdot x_2)) + b \cdot (1 - \exp(-c_3 \cdot x_3))$



Summary of Fitting

Parameter	Estimate	Standard Error
a	7.62E+00	9.62E-01
b	1.69E+02	4.82E+01
c1	4.02E-03	1.59E-03
c2	2.93E-05	2.00E-05
c3	2.86E-03	1.07E-03
Covariance (c1,c2)	0.5770	--
Covariance (c1,c3)	0.9418	--
Degrees of Freedom	46	--

Goodness of Fit

Statistic	Estimate
F	104.665
p	< 0.001
Adjusted R <sup>2</sup>	0.9104
AIC	370.380

RBA and Uncertainty

	Test Material 1	Test Material 2	Test Material 3
RBA	0.01	0.71	0.07
Lower bound	0.00	0.55	0.04
Upper bound	0.02	0.99	0.13
Standard Error	0.004*	0.094*	0.020*

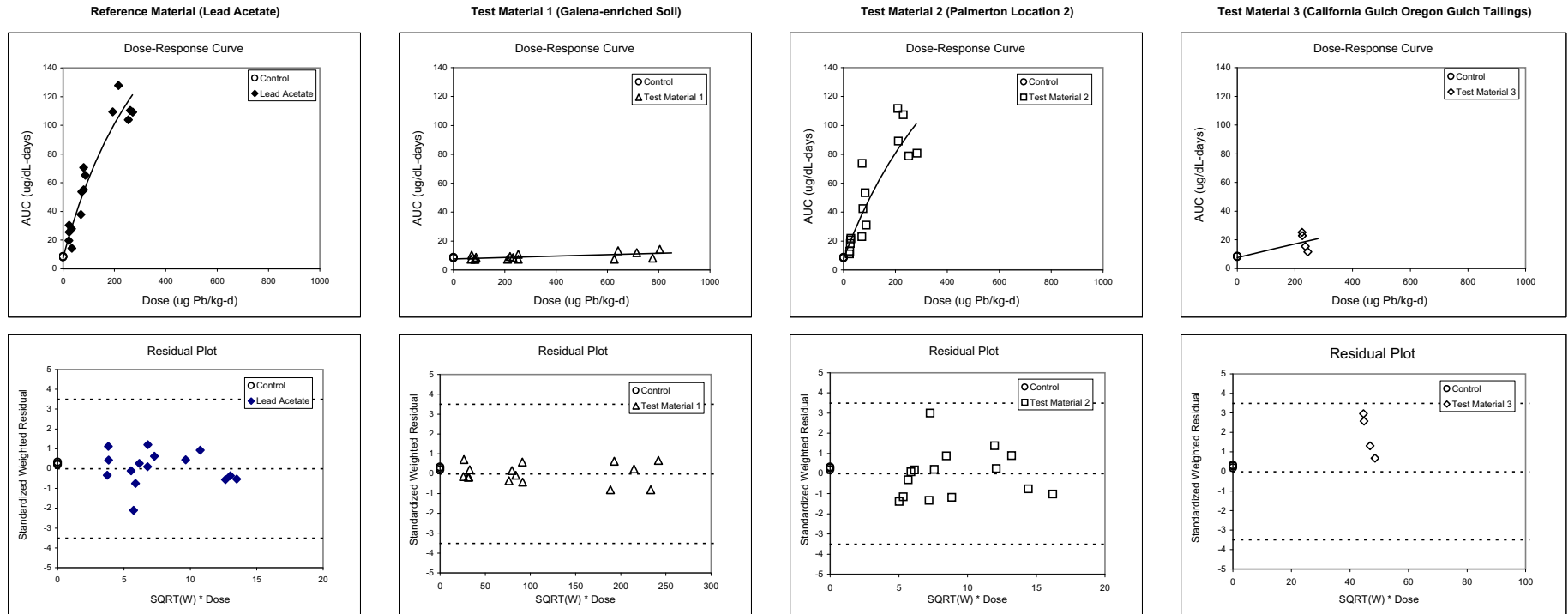
\*  $g \geq 0.05$ , estimate is uncertain

APPENDIX E

Figure 1c - All Data

Phase II Experiment 12: Blood AUC

Michaelis-Menton Model:  $y = a + b \cdot x_1 / (c_1 + x_1) + b \cdot x_2 / (c_2 + x_2) + b \cdot x_3 / (c_3 + x_3)$



Summary of Fitting

Parameter	Estimate	Standard Error
a	7.64E+00	9.71E-01
b	2.98E+02	1.06E+02
c1	4.38E+02	2.08E+02
c2	6.04E+04	4.45E+04
c3	6.12E+02	2.78E+02
Covariance (c1,c2)	0.6443	--
Covariance (c1,c3)	0.9615	--
Degrees of Freedom	46	--

Goodness of Fit

Statistic	Estimate
F	104.126
p	< 0.001
Adjusted R <sup>2</sup>	0.9100
AIC	370.760

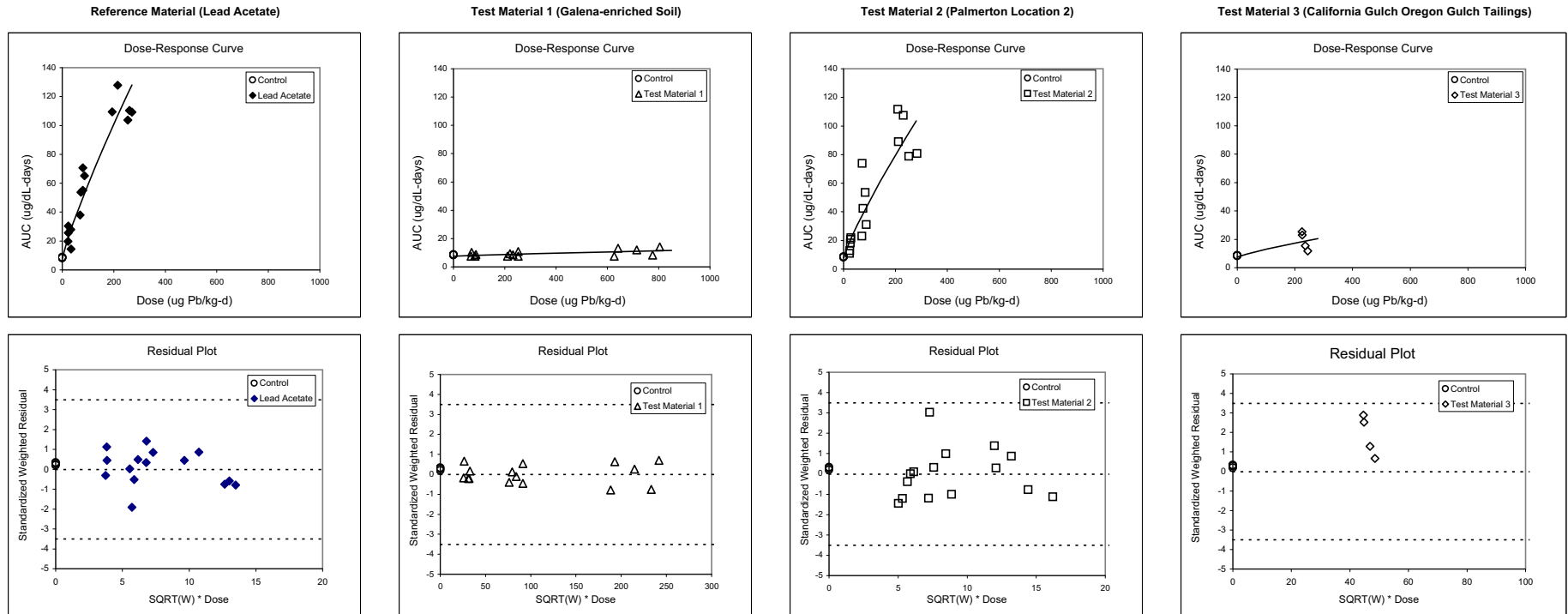
RBA and Uncertainty

	Test Material 1	Test Material 2	Test Material 3
RBA	0.01	0.72	0.07
Lower bound	0.00	0.46	0.03
Upper bound	-0.01	0.95	0.16
Standard Error	0.004*	0.094*	0.021*

\*  $g \geq 0.05$ , estimate is uncertain

APPENDIX E

**Figure 1d - All Data**  
**Phase II Experiment 12: Blood AUC**  
**Power Model:  $y = a + b1*x1^c + b2*x2^c + b3*x3^c$**



**Summary of Fitting**

Parameter	Estimate	Standard Error
a	7.61E+00	1.10E+00
b1	1.01E+00	3.55E-01
b2	1.24E-02	1.09E-02
b3	7.78E-01	2.75E-01
c	8.55E-01	5.23E-02
Covariance (b1,b2)	0.7381	--
Covariance (b1,b3)	0.9551	--
Degrees of Freedom	46	--

**Goodness of Fit**

Statistic	Estimate
F	98.107
p	< 0.001
Adjusted R <sup>2</sup>	0.9049
AIC	374.839

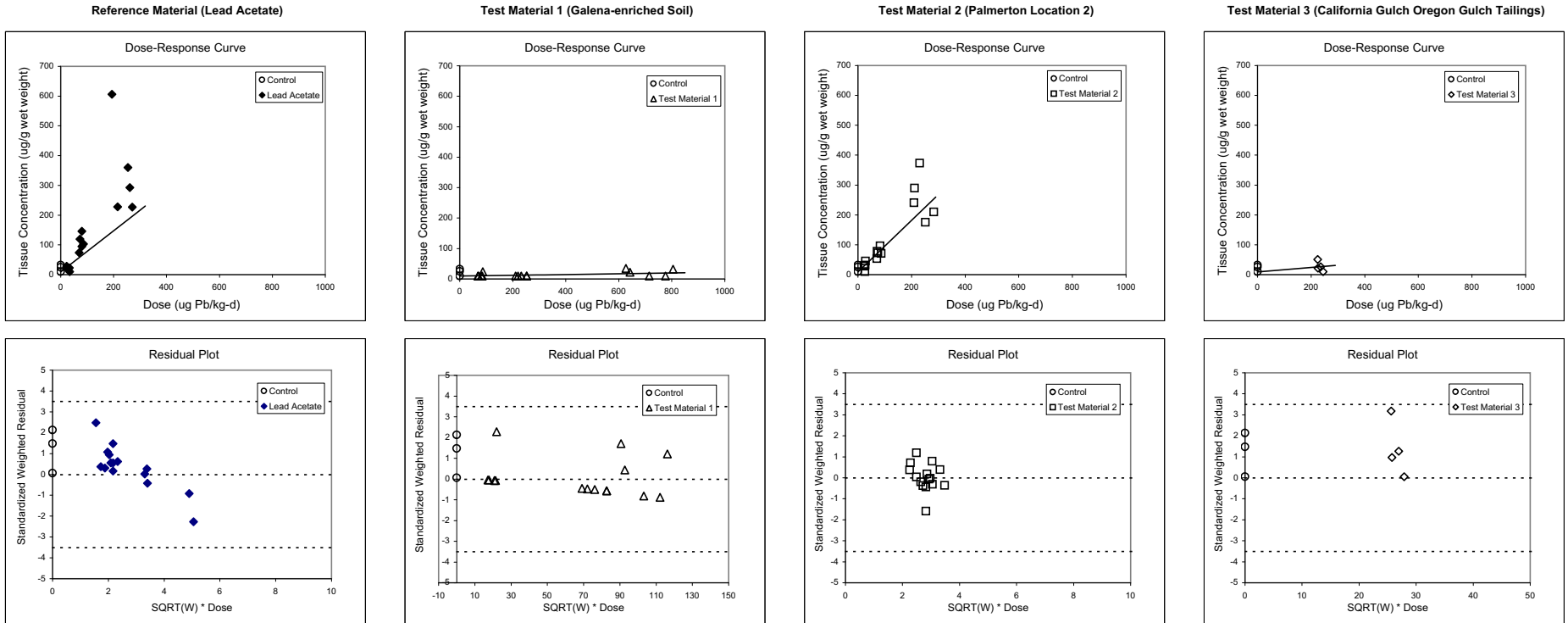
**RBA and Uncertainty**

	Test Material 1	Test Material 2	Test Material 3
RBA	0.01	0.74	0.07
Lower bound	?	0.57	?
Upper bound	0.01	0.95	0.12
Standard Error	--	--	--

APPENDIX E

Figure 2a - All Data

Phase II Experiment 12: Liver  
 Linear Model:  $y = a + b_1*x_1 + b_2*x_2 + b_3*x_3$



Summary of Fitting

Parameter	Estimate	Standard Error
a	9.38E+00	2.21E+00
b1	6.90E-01	1.49E-01
b2	1.26E-02	7.84E-03
b3	8.63E-01	1.45E-01
b4	7.51E-02	3.01E-02
Covariance (c1,c2)	0.2961	--
Covariance (c1,c3)	0.1132	--
Covariance (c1,c4)	0.1251	--
Degrees of Freedom	47	--

Goodness of Fit

Statistic	Estimate
F	33.199
p	< 0.001
Adjusted R <sup>2</sup>	0.7163
AIC	506.975

RBA and Uncertainty

	Test Material 1	Test Material 2	Test Material 3
RBA	0.02	1.25	0.11
Lower bound	0.00	0.82	0.04
Upper bound	0.04	2.03	0.21
Standard Error	0.011*	0.322*	0.047*

\*  $g \geq 0.05$ , estimate is uncertain

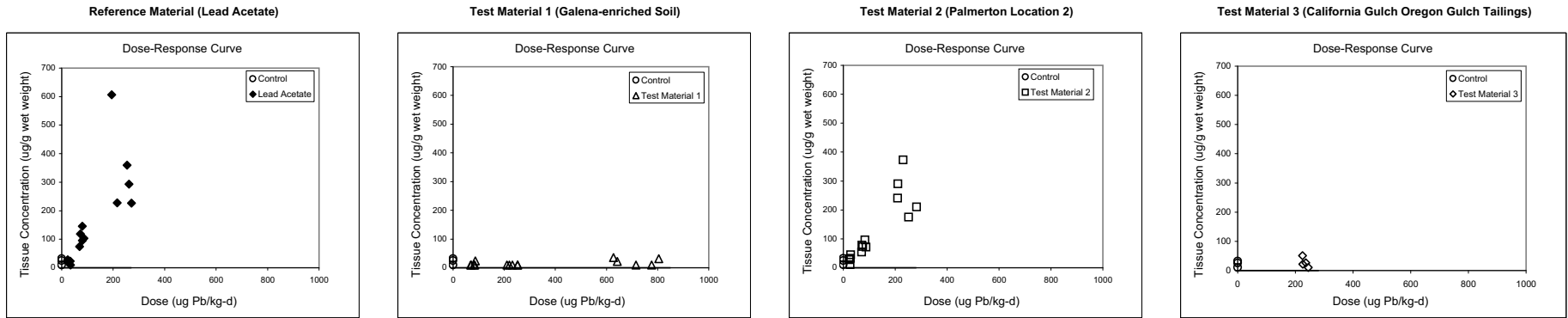


APPENDIX E

Figure 2b - All Data

Phase II Experiment 12: Liver

Exponential Model:  $y = a + b*(1-\exp(-c1*x1))+b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$



**NO SOLUTION**

The software could not find a solution,  
or the solution was unstable and/or had unrealistic parameter estimates.

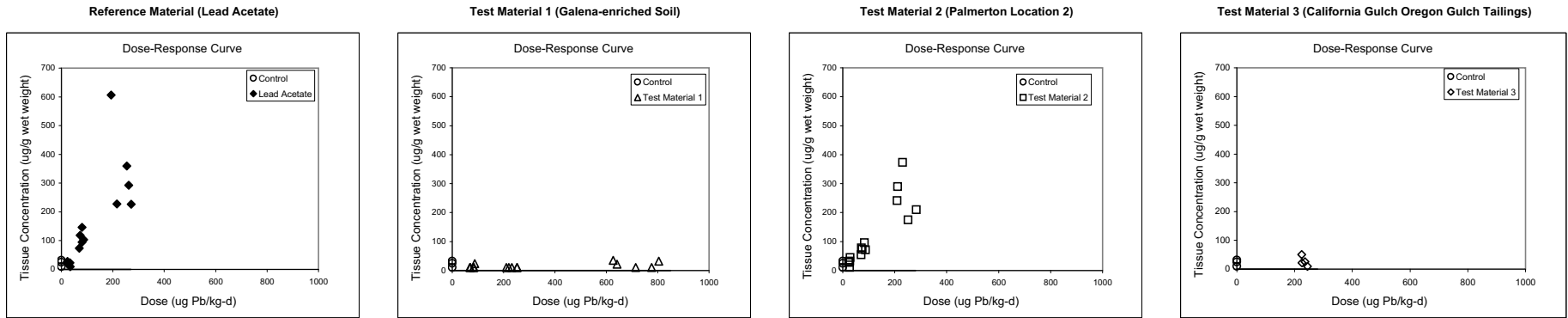
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APPENDIX E

Figure 2c - All Data

Phase II Experiment 12: Liver

Michaelis-Menton Model:  $y = a + b \cdot x_1 / (c_1 + x_1) + b \cdot x_2 / (c_2 + x_2) + b \cdot x_3 / (c_3 + x_3)$

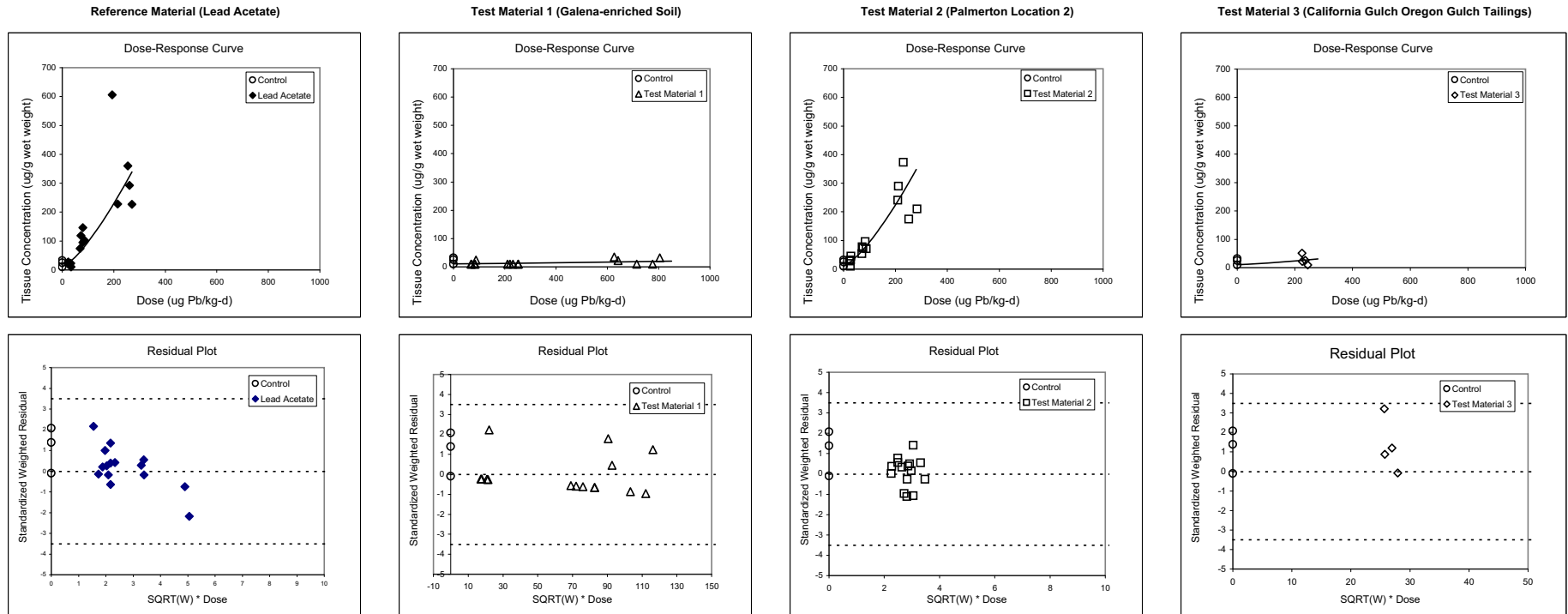


**NO SOLUTION**  
 The software could not find a solution,  
 or the solution was unstable and/or had unrealistic parameter estimates.

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APPENDIX E

**Figure 2d - All Data**  
**Phase II Experiment 12: Liver**  
**Power Model:  $y = a + b1*x1^c + b2*x2^c + b3*x3^c$**



**Summary of Fitting**

Parameter	Estimate	Standard Error
a	1.10E+01	1.94E+00
b1	1.67E-01	1.21E-01
b2	1.03E-03	1.38E-03
b3	1.64E-01	1.25E-01
c	1.35E+00	1.52E-01
Covariance (b1,b2)	0.8593	--
Covariance (b1,b3)	0.9467	--
Degrees of Freedom	46	--

**Goodness of Fit**

Statistic	Estimate
F	31.031
p	< 0.001
Adjusted R <sup>2</sup>	0.7465
AIC	493.797

**RBA and Uncertainty**

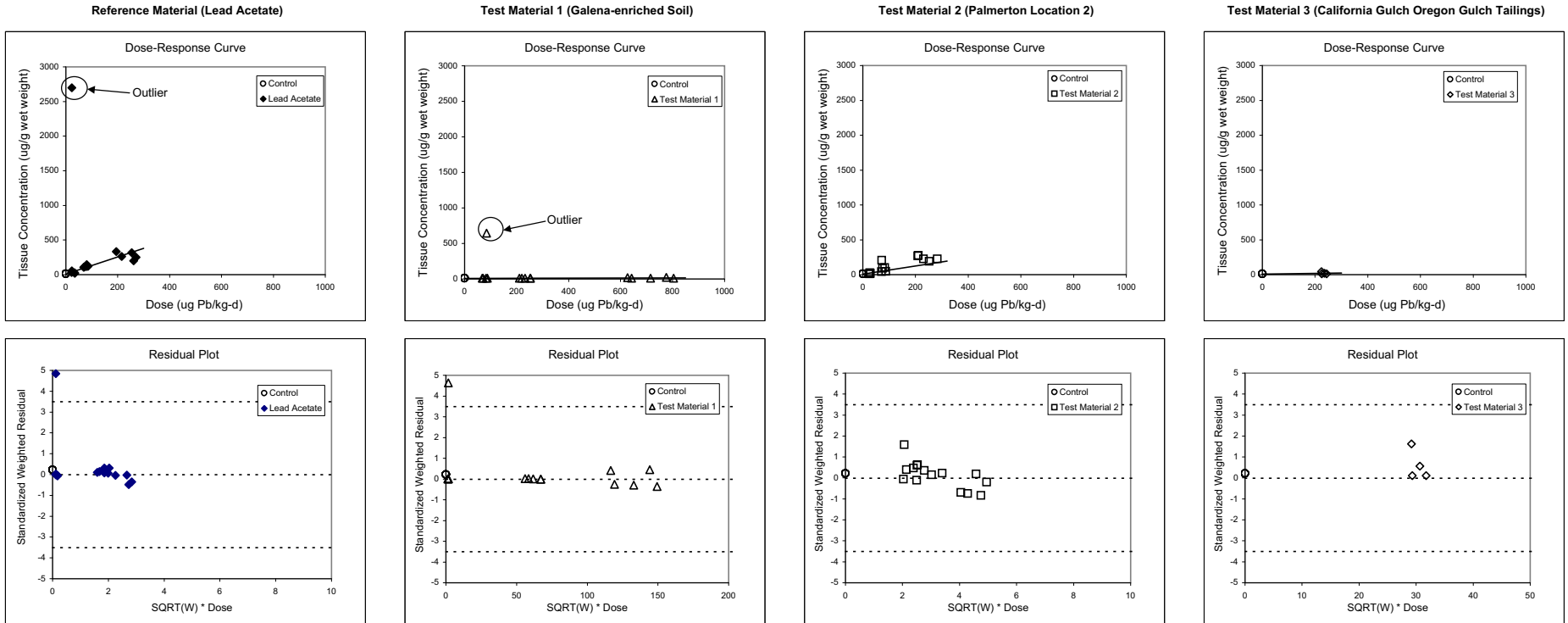
	Test Material 1	Test Material 2	Test Material 3
RBA	0.02	0.98	0.12
Lower bound	?	?	?
Upper bound	?	?	?
Standard Error	--	--	--

APPENDIX E

Figure 3a - All Data

Phase II Experiment 12: Kidney

Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$



Summary of Fitting

Parameter	Estimate	Standard Error
a	7.71E+00	4.83E+00
b1	1.24E+00	4.35E-01
b2	9.56E-03	1.30E-02
b3	5.80E-01	2.64E-01
b4	5.49E-02	5.39E-02
Covariance (c1,c2)	0.0560	--
Covariance (c1,c3)	0.0379	--
Covariance (c1,c4)	0.0304	--
Degrees of Freedom	47	--

Goodness of Fit

Statistic	Estimate
F	7.238
p	< 0.001
Adjusted R <sup>2</sup>	0.3285
AIC	868.907

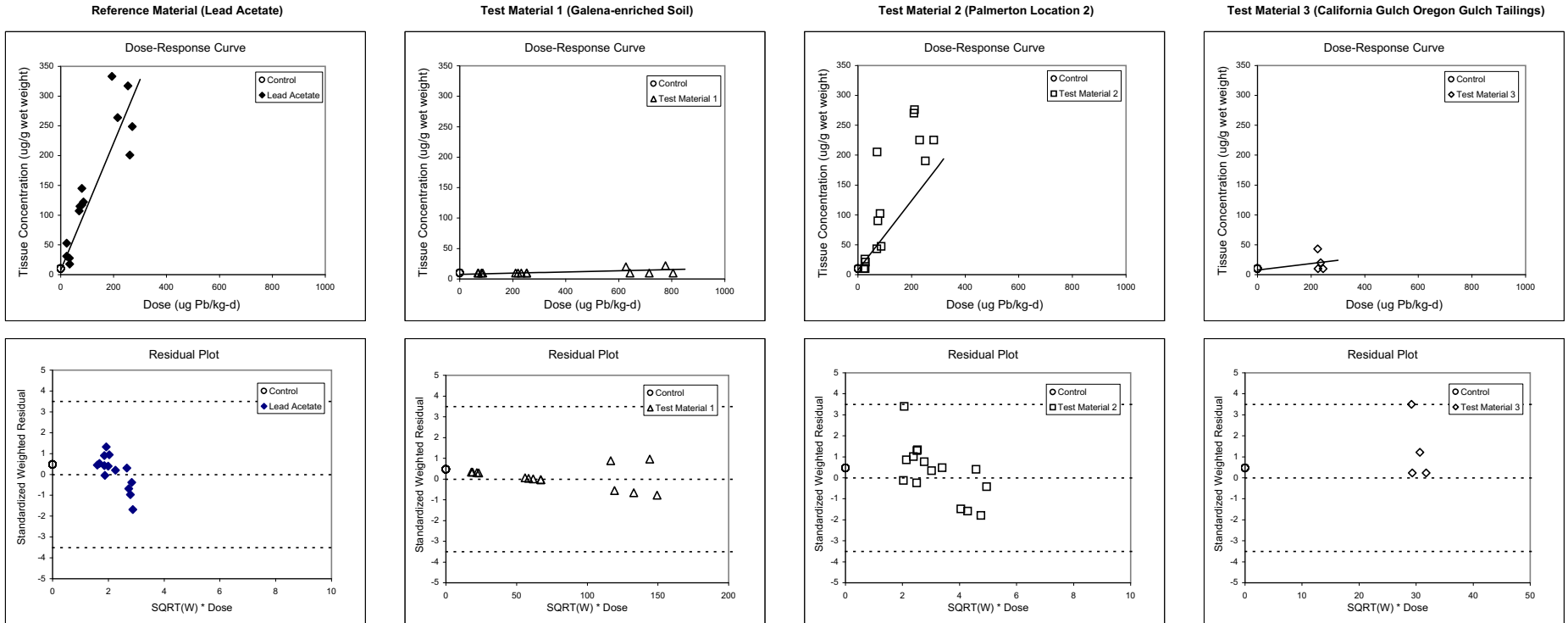
RBA and Uncertainty

	Test Material 1	Test Material 2	Test Material 3
RBA	0.01	0.47	0.04
Lower bound	-0.01	0.11	-0.03
Upper bound	0.03	1.30	0.16
Standard Error	0.011*	0.264*	0.046*

\*  $g \geq 0.05$ , estimate is uncertain

APPENDIX E

**Figure 3a - Outliers Excluded**  
**Phase II Experiment 12: Kidney**  
**Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$**



**Summary of Fitting**

Parameter	Estimate	Standard Error
a	7.68E+00	1.72E+00
b1	1.07E+00	1.60E-01
b2	9.72E-03	5.37E-03
b3	5.81E-01	1.12E-01
b4	5.51E-02	2.32E-02
Covariance (c1,c2)	0.1129	--
Covariance (c1,c3)	0.0686	--
Covariance (c1,c4)	0.0542	--
Degrees of Freedom	45	--

**Goodness of Fit**

Statistic	Estimate
F	37.309
p	< 0.001
Adjusted R <sup>2</sup>	0.7477
AIC	458.069

**RBA and Uncertainty**

	Test Material 1	Test Material 2	Test Material 3
RBA	0.01	0.54	0.05
Lower bound	< 0.001	0.35	0.02
Upper bound	0.02	0.80	0.09
Standard Error	0.005*	0.128*	0.023*

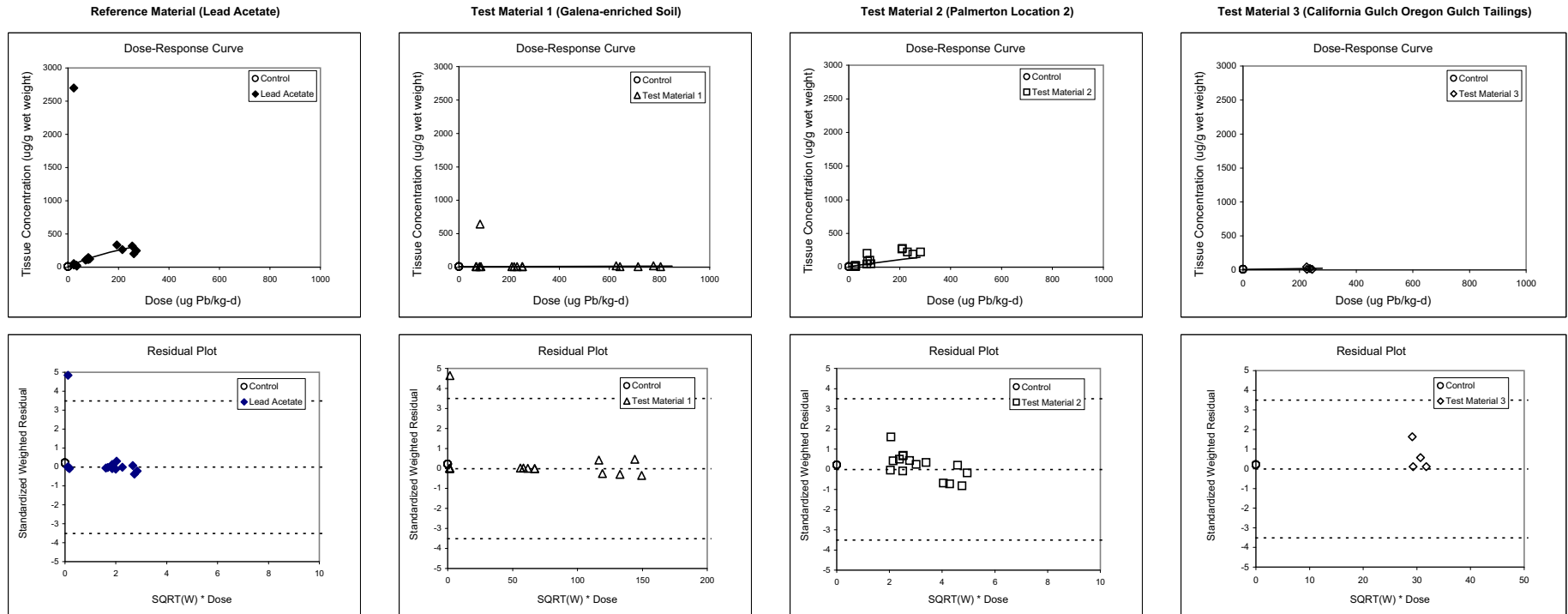
\*  $g \geq 0.05$ , estimate is uncertain

APPENDIX E

Figure 3b - All Data

Phase II Experiment 12: Kidney

Exponential Model:  $y = a + b*(1-\exp(-c1*x1))+b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$



Summary of Fitting

Parameter	Estimate	Standard Error
a	7.72E+00	4.99E+00
b	4.89E+02	1.01E+03
c1	3.53E-03	9.63E-03
c2	1.96E-05	5.03E-05
c3	1.19E-03	2.63E-03
Covariance (c1,c2)	0.8332	--
Covariance (c1,c3)	0.9615	--
Degrees of Freedom	46	--

Goodness of Fit

Statistic	Estimate
F	5.696
p	< 0.001
Adjusted R <sup>2</sup>	0.3152
AIC	870.070

RBA and Uncertainty

	Test Material 1	Test Material 2	Test Material 3
RBA	0.01	0.34	0.03
Lower bound	?	?	?
Upper bound	?	?	?
Standard Error	0.009*	0.285*	0.040*

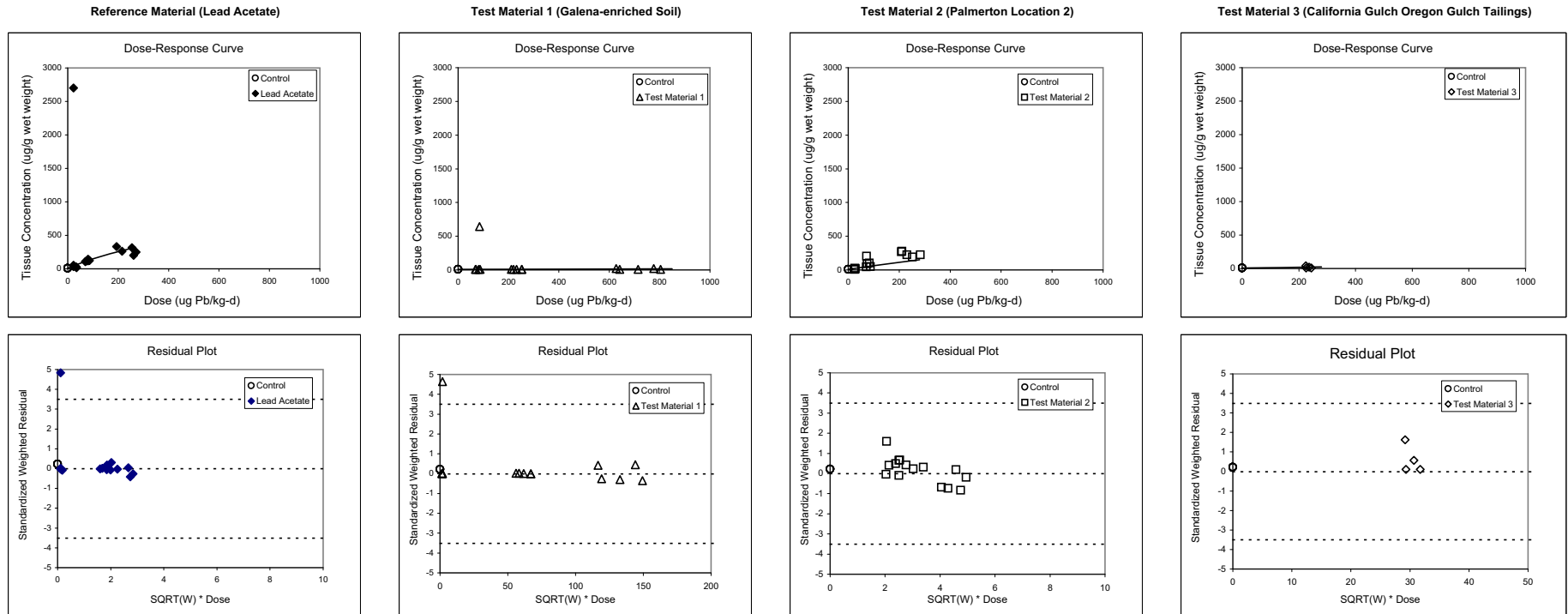
\*  $g \geq 0.05$ , estimate is uncertain

APPENDIX E

Figure 3c - All Data

Phase II Experiment 12: Kidney

Michaelis-Menton Model:  $y = a + b \cdot x_1 / (c_1 + x_1) + b \cdot x_2 / (c_2 + x_2) + b \cdot x_3 / (c_3 + x_3)$



Summary of Fitting

Parameter	Estimate	Standard Error
a	7.72E+00	4.99E+00
b	1.08E+03	3.46E+03
c1	6.69E+02	2.65E+03
c2	1.13E+05	4.07E+05
c3	1.86E+03	6.31E+03
Covariance (c1,c2)	0.9197	--
Covariance (c1,c3)	0.9839	--
Degrees of Freedom	46	--

Goodness of Fit

Statistic	Estimate
F	5.687
p	< 0.001
Adjusted R <sup>2</sup>	0.3148
AIC	870.320

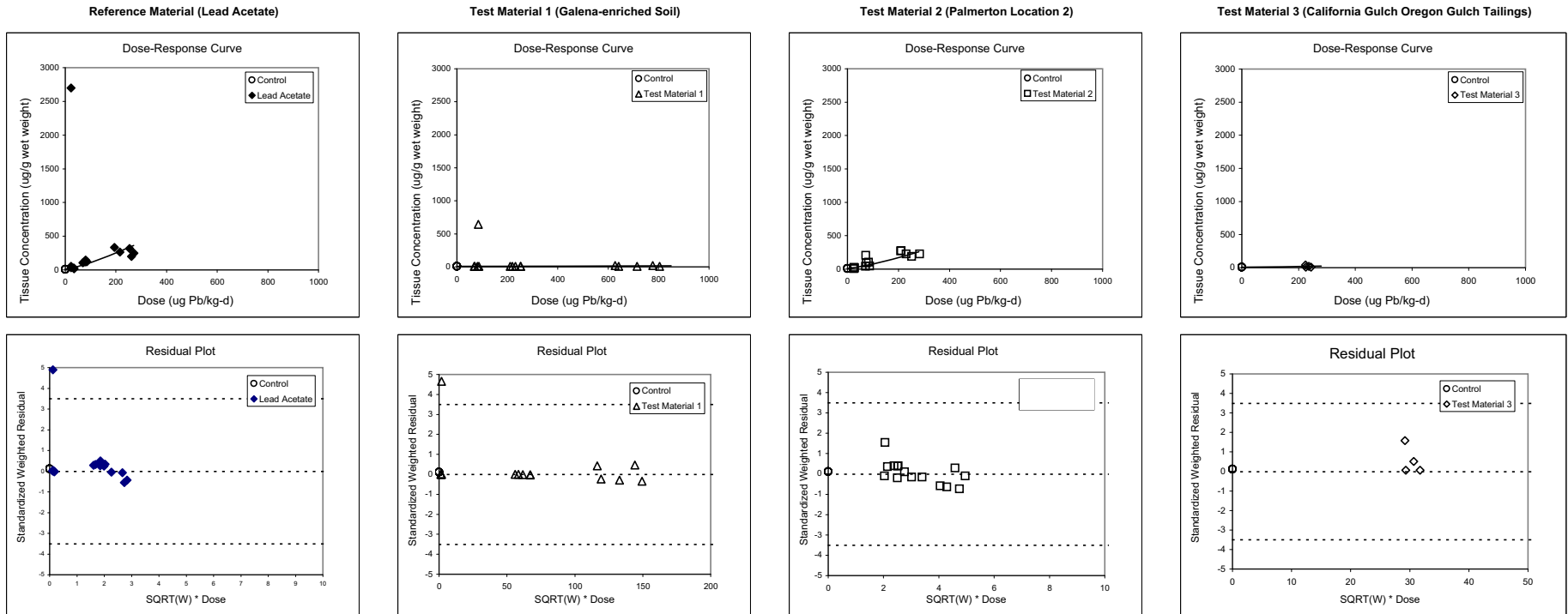
RBA and Uncertainty

	Test Material 1	Test Material 2	Test Material 3
RBA	0.01	0.36	0.03
Lower bound	?	?	?
Upper bound	?	?	?
Standard Error	0.009*	0.315*	0.044*

\*  $g \geq 0.05$ , estimate is uncertain

APPENDIX E

**Figure 3d - All Data**  
**Phase II Experiment 12: Kidney**  
**Power Model:  $y = a + b1*x1^c + b2*x2^c + b3*x3^c$**



**Summary of Fitting**

Parameter	Estimate	Standard Error
a	8.77E+00	4.86E+00
b1	2.98E-01	5.94E-01
b2	1.36E-03	4.51E-03
b3	1.99E-01	3.56E-01
c	1.26E+00	3.71E-01
Covariance (b1,b2)	0.8626	--
Covariance (b1,b3)	0.9574	--
Degrees of Freedom	46	--

**Goodness of Fit**

Statistic	Estimate
F	5.929
p	< 0.001
Adjusted R <sup>2</sup>	0.3258
AIC	864.518

**RBA and Uncertainty**

	Test Material 1	Test Material 2	Test Material 3
RBA	0.01	0.73	0.08
Lower bound	?	?	?
Upper bound	?	?	?
Standard Error	--	--	--

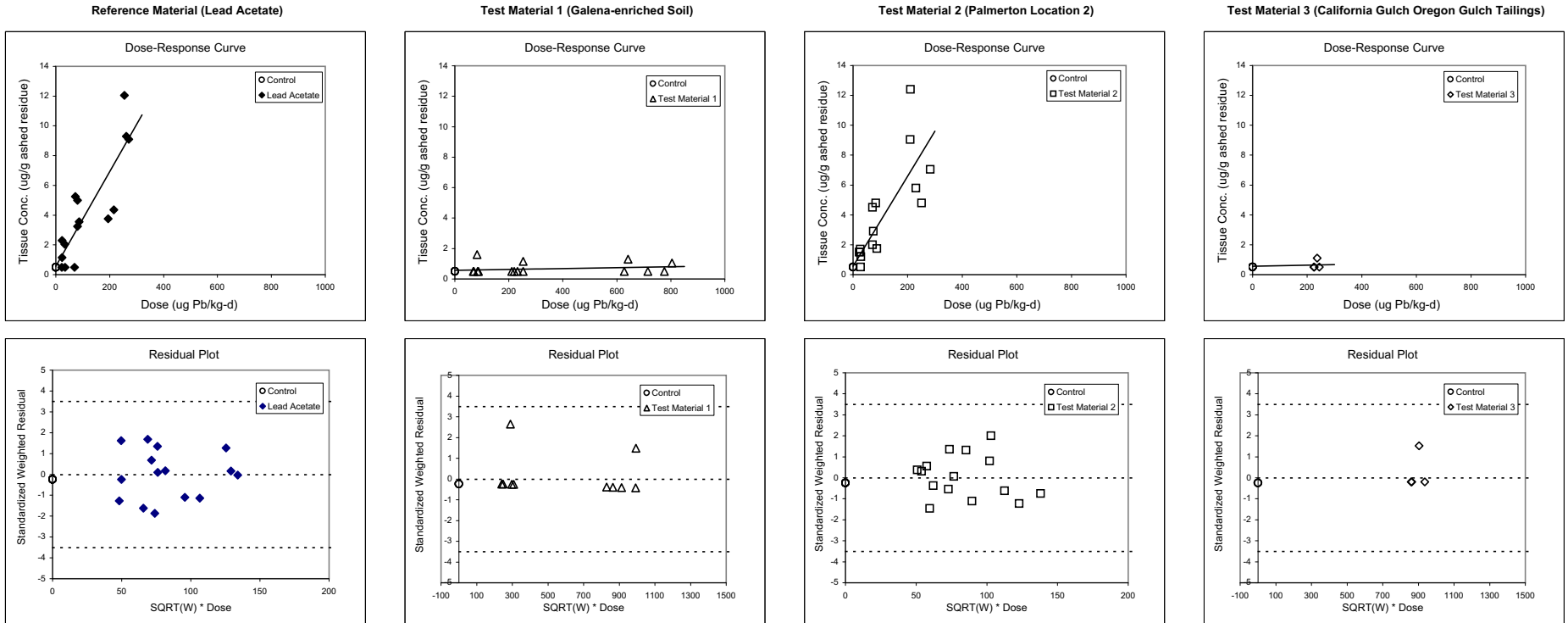


APPENDIX E

Figure 4a - All Data

Phase II Experiment 12: Femur

Linear Model:  $y = a + b1*x1 + b2*x2 + b3*x3$



Summary of Fitting

Parameter	Estimate	Standard Error
a	5.69E-01	1.05E-01
b1	3.18E-02	4.24E-03
b2	3.01E-04	3.12E-04
b3	3.01E-02	4.25E-03
b4	3.58E-04	9.00E-04
Covariance (c1,c2)	0.1724	--
Covariance (c1,c3)	0.0760	--
Covariance (c1,c4)	0.1361	--
Degrees of Freedom	47	--

Goodness of Fit

Statistic	Estimate
F	82.424
p	< 0.001
Adjusted R <sup>2</sup>	0.8646
AIC	137.166

RBA and Uncertainty

	Test Material 1	Test Material 2	Test Material 3
RBA	0.01	0.95	0.01
Lower bound	-0.01	0.69	-0.04
Upper bound	0.03	1.30	0.06
Standard Error	0.010*	0.177*	0.028*

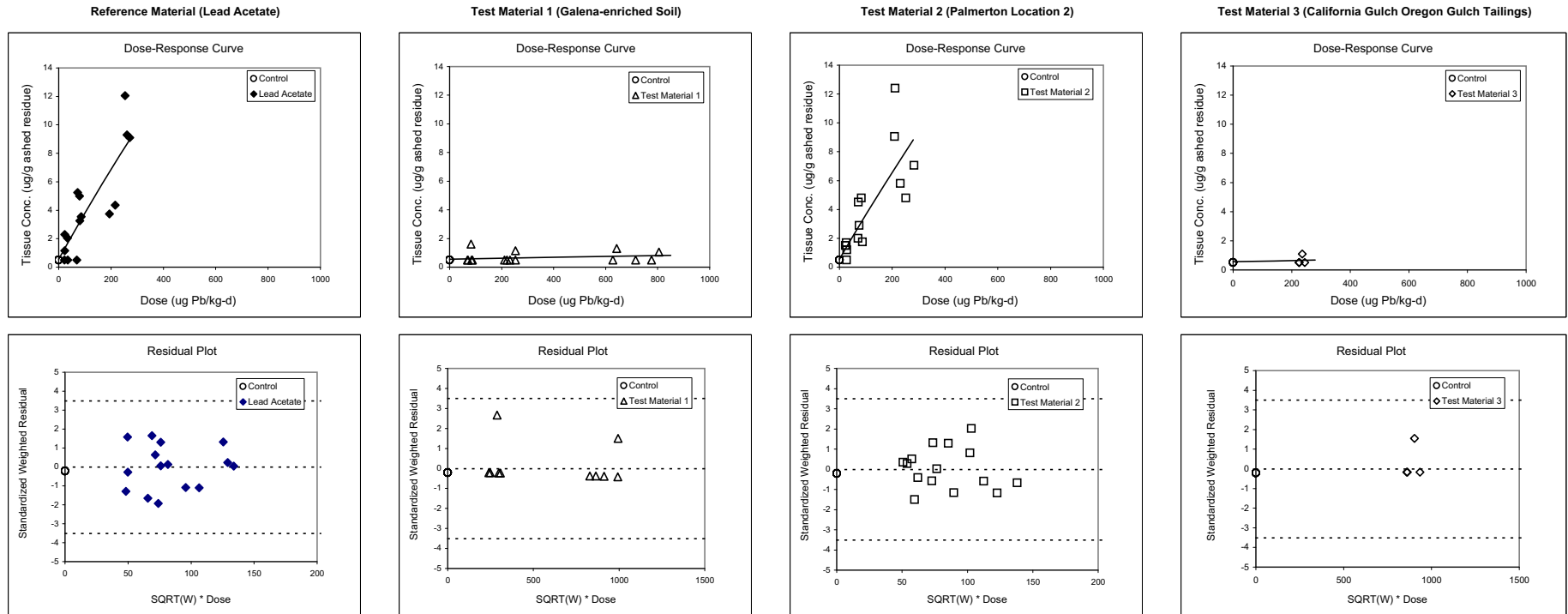
\*  $g \geq 0.05$ , estimate is uncertain

APPENDIX E

Figure 4b - All Data

Phase II Experiment 12: Femur

Exponential Model:  $y = a + b*(1-\exp(-c1*x1))+b*(1-\exp(-c2*x2)) + b*(1-\exp(-c3*x3))$



Summary of Fitting

Parameter	Estimate	Standard Error
a	5.60E-01	1.13E-01
b	6.55E+01	2.73E+02
c1	5.07E-04	2.21E-03
c2	4.87E-06	2.19E-05
c3	4.82E-04	2.09E-03
Covariance (c1,c2)	0.9760	--
Covariance (c1,c3)	0.9990	--
Degrees of Freedom	46	--

Goodness of Fit

Statistic	Estimate
F	61.801
p	< 0.001
Adjusted R <sup>2</sup>	0.8563
AIC	139.150

RBA and Uncertainty

	Test Material 1	Test Material 2	Test Material 3
RBA	0.01	0.95	0.01
Lower bound	?	?	?
Upper bound	?	?	?
Standard Error	0.009*	0.185*	0.027*

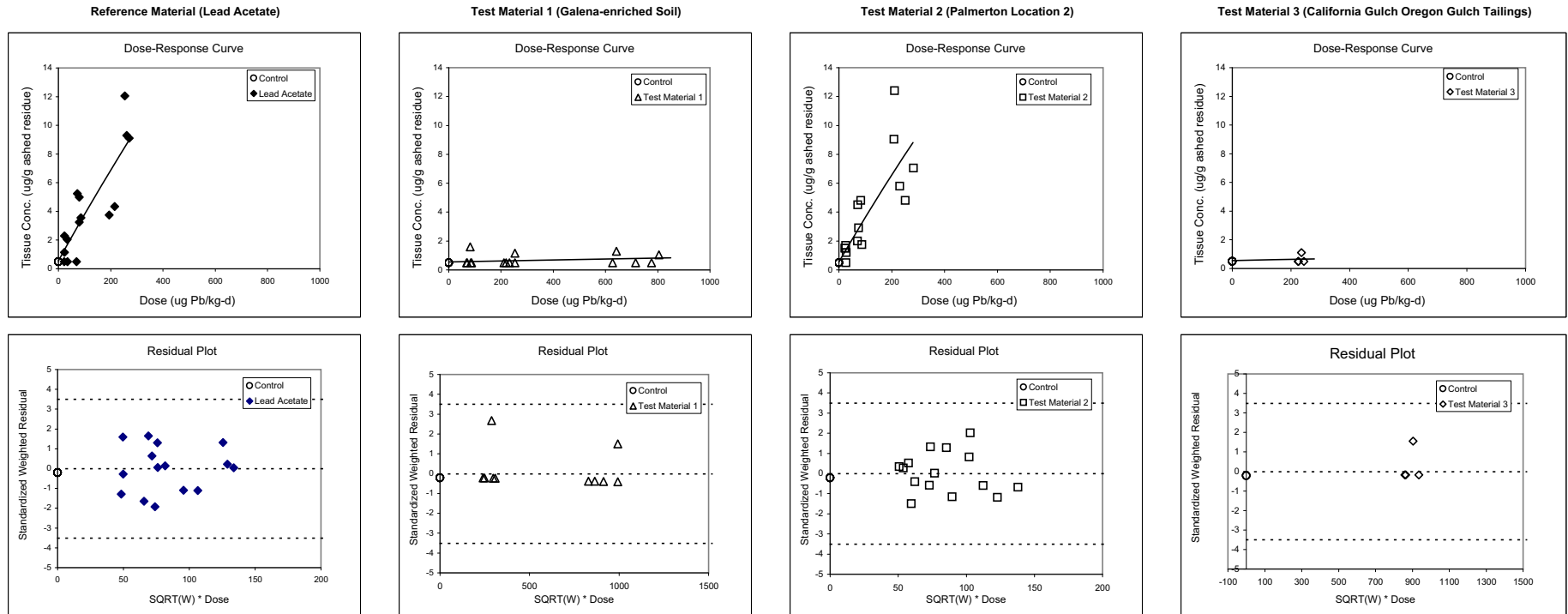
\*  $g \geq 0.05$ , estimate is uncertain

APPENDIX E

Figure 4c - All Data

Phase II Experiment 12: Femur

Michaelis-Menton Model:  $y = a + b \cdot x_1 / (c_1 + x_1) + b \cdot x_2 / (c_2 + x_2) + b \cdot x_3 / (c_3 + x_3)$



Summary of Fitting

Parameter	Estimate	Standard Error
a	5.60E-01	1.13E-01
b	1.31E+02	5.71E+02
c1	3.94E+03	1.80E+04
c2	4.10E+05	1.93E+06
c3	4.15E+03	1.89E+04
Covariance (c1,c2)	0.9781	--
Covariance (c1,c3)	0.9991	--
Degrees of Freedom	46	--

Goodness of Fit

Statistic	Estimate
F	61.857
p	< 0.001
Adjusted R <sup>2</sup>	0.8565
AIC	139.151

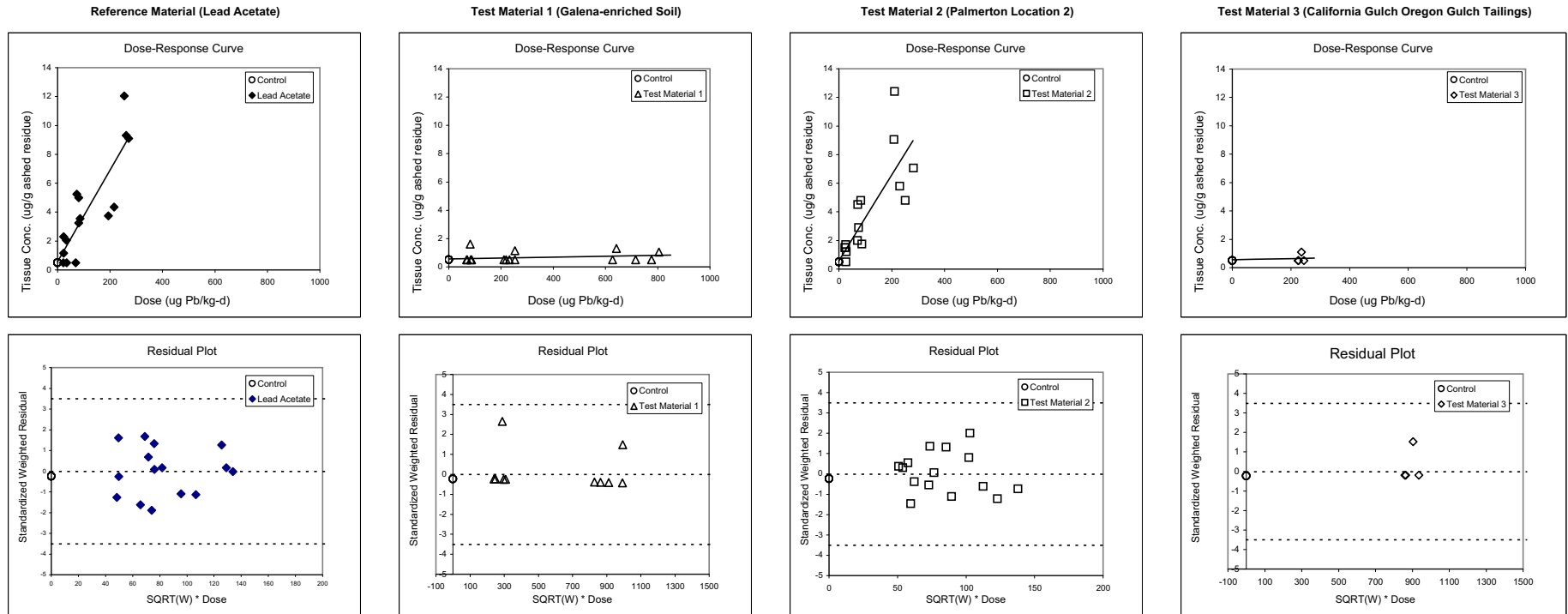
RBA and Uncertainty

	Test Material 1	Test Material 2	Test Material 3
RBA	0.01	0.95	0.01
Lower bound	?	?	?
Upper bound	?	?	?
Standard Error	0.009*	0.184*	0.027*

\*  $g \geq 0.05$ , estimate is uncertain

APPENDIX E

**Figure 4d - All Data**  
**Phase II Experiment 12: Femur**  
**Power Model:  $y = a + b1*x1^c + b2*x2^c + b3*x3^c$**



**Summary of Fitting**

Parameter	Estimate	Standard Error
a	5.67E-01	1.18E-01
b1	3.25E-02	2.13E-02
b2	3.14E-04	4.82E-04
b3	3.08E-02	2.01E-02
c	9.95E-01	1.27E-01
Covariance (b1,b2)	0.7455	--
Covariance (b1,b3)	0.9584	--
Degrees of Freedom	46	--

**Goodness of Fit**

Statistic	Estimate
F	63.930
p	< 0.001
Adjusted R <sup>2</sup>	0.8605
AIC	139.183

**RBA and Uncertainty**

	Test Material 1	Test Material 2	Test Material 3
RBA	0.01	0.95	0.01
Lower bound	0.06	?	?
Upper bound	0.04	?	?
Standard Error	--	--	--

**APPENDIX F**

**DETAILED LEAD SPECIATION DATA  
FOR TEST MATERIALS**

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APPENDIX F

METAL CONTENT OF TEST MATERIALS

Experiment	Test Material	Concentration (ppm)																							
		Al	As	Au	Ba	Be	Ca	Cd	Co	Cr	Cu	Fe	Hg	K	Mg	Mn	Na	Ni	Pb	Sb	Se	Tl	V	Zn	
2	Bingham Creek Residential	10,600	51.2	4.1	143	0.71	13,600	4.2	7.5	16.6	691	16,100	-	4,340	7,020	466	362	15.0	1,590	10 U	<17	<17	20.8	903	
	Bingham Creek Channel Soil	10,100	149.0	17.2	152	0.73	8,500	8.7	7.9	17.9	1,720	22,500	-	4,150	5,970	376	314	15.1	6,330	18.7	<17	<17	22.0	-	
3	Jasper County High Lead Smelter	8,850	25.1	1.3	284	1.70	45,800	33.7	19.3	23.8	94	40,200	0.64	1,490	7,860	784	399	44.8	10,800	4.90	1.0U	1.4U	22.5	10,000	
	Jasper County Low Lead Yard	4,370	10.7	0.6	94	1.00	81,800	188.0	6.4	15.2	144	18,000	1.30	927	1,390	240	403	30.1	4,050	1.0 U	1.0U	1.80	14.8	50,000	
4	Murray Smelter Slag	9,370	710	18.3	2,140	0.86	89,600	30.9	45.4	34.0	2,100	170,000	1.00	2,430	11,200	2,640	836	16.7	11,700	55.7	43.90	12.60	73.6	49,500	
	Jasper County High Lead Mill	9,380	16.4	18.8	211	1.40	19,900	139.0	34.3	64.6	96	26,600	12.10	1,400	2,280	1,270	339	110.0	6,940	1.0 U	1.0U	1.4U	23.0	17,200	
5	Aspen Berm	5,070	66.9	92.3	1,640	1.30	37,200	41.9	17.1	7.7	145	33,700	0.77	1,090	14,300	2,220	249	29.8	14,200	5.20	2.00	1.80	11.5	6,580	
	Aspen Residential	8,440	16.7	18.9	1,030	0.82	17,300	47.4	11.1	10.4	52	23,000	0.23	2,140	6,890	934	114	21.9	3,870	11.4	0.38	0.27	16.0	4,110	
6	Midvale Slag	10,500	619	.11U	637	0.58	93,200	24.5	33.0	142.0	1,330	202,000	0.74	4,250	6,180	1,640	7,910	.31U	8,170	71.9	39.70	8.10	10.1U	33,300	
	Butte Soil	7,540	226	40.5	134	0.56	15,700	42.2	9.2	6.9	838	48,500	2.20	3,560	2,950	12,800	530	8.0	8,530	10.60	0.27	1.80	27.0	12,100	
7	California Gulch Phase I Residential Soil	8,670	203	43.0	605	0.60	20,100	59.9	2.0	9.1	657	68,120	1.26	1,500	9,521	7,090	6,560	5.6	7,510	1.80	1.90	<0.5	33.7	13,738	
	California Gulch Fe/Mn PbO	11,900	110	16.7	266	1.00	3,930	38.5	6.9	7.5	165	27,500	4.90	1,770	2,520	1,190	279	7.5	4,320	6.00	0.80	3.70	17.9	2,650	
8	California Gulch AV Slag	20,800	1,050	21.2	2,430	1.20	117,000	12.8	53.8	43.1	2,080	207,000	0.11	7,390	6,360	6,910	4,080	7.1	10,600	57.2	61.30	1.80	37.2	67,300	
9	Palmerton Location 2	7,750	110	9.5	6,850	1.40	1,160	195.0	18.8	30.3	462	25,900	1.70	515	725	6,320	667	15.0	3,230	6.00	11.80	1.90	53.1	6,500	
	Palmerton Location 4	7,850	134.0	5.1	1,090	2.00	2,480	319.0	17.4	26.6	350	26,700	1.10	512	684	9,230	2,100	26.8	2,150	7.40	6.90	0.85	49.8	19,100	
11	Murray Smelter Soil	6,520	310	11.1	584	0.48b	69,000	23.8	11.5	16.4	856	38,700	0.52	2,040	15,000	863	532.0b	10.4	3,200	20.0	6.80	4.80	28.3	10,400	
	NIST Paint	5,850	4.8	0.63U	1,320	0.47b	11,800	4.0	8.3	20.8	12	8,890	0.92	1,360	2,900	272	81.9b	5.80b	8,350	8.7 U	0.61U	0.87U	11.6	1,880	
12	Galena-enriched Soil	6,340	4.9	0.63U	112	0.49b	2,650	0.8	3.1	10.2	11	10,000	0.06b	1,460	2,790	293	31.20b	3.80b	11,200	8.70	0.61U	0.87U	12.60b	107	
	California Gulch Oregon Gulch Tailings	248	1,290	41.7	14	2.00	8,290	4.0	10.1	8.0	350	391,000	0.24	451	118	126	34	28.2	1,270	74.4	0.53	0.86	47.7	441	

All samples were analyzed by inductively coupled plasma-atomic emission spectrometry (ICP-AES) in accord with USEPA Method 200.7.

APPENDIX F

**EXPERIMENT 2 - BINGHAM CREEK RESIDENTIAL**

**Lead Speciation Summary Statistics**

Mineral	Counts		Particle Size			Count Freq (%)		LW Freq (%)		Density	Lead Fraction	Relative Lead Mass (%)	
	Total	Lib	Avg	Min	Max	Total	Lib	Total	Lib			Total	Lib
Cerussite	2	2	4	2	5	1.0%	1.0%	0.28%	0.28%	6.6	0.776	1.8%	1.8%
Fe-Pb Oxide	30	30	15	2	75	15.1%	15.1%	17.93%	17.93%	4	0.052	4.6%	4.6%
Fe-Pb Silicate*	14	14	10	8	20	7.0%	7.0%	5.52%	5.52%	3.5	0.052	1.2%	1.2%
Mn-Pb Oxide	21	21	22	2	110	10.6%	10.6%	18.13%	18.13%	5.1	0.159	18.1%	18.1%
Pb-As Oxide	3	3	4	2	8	1.5%	1.5%	0.52%	0.52%	6	0.5	1.9%	1.9%
Pb Phosphate	43	43	13	1	110	21.6%	21.6%	21.70%	21.70%	5.1	0.37	50.4%	50.4%
Fe-Pb Sulfate	86	86	10	1	120	43.2%	43.2%	35.91%	35.91%	3.7	0.134	21.9%	21.9%
<b>TOTAL</b>	<b>199</b>	<b>199</b>	<b>13</b>			<b>100.0%</b>	<b>100.0%</b>	<b>100.00%</b>	<b>100.00%</b>			<b>100.0%</b>	<b>100.0%</b>

\*This mineral is now considered to be equivalent to Fe-Pb Oxide.

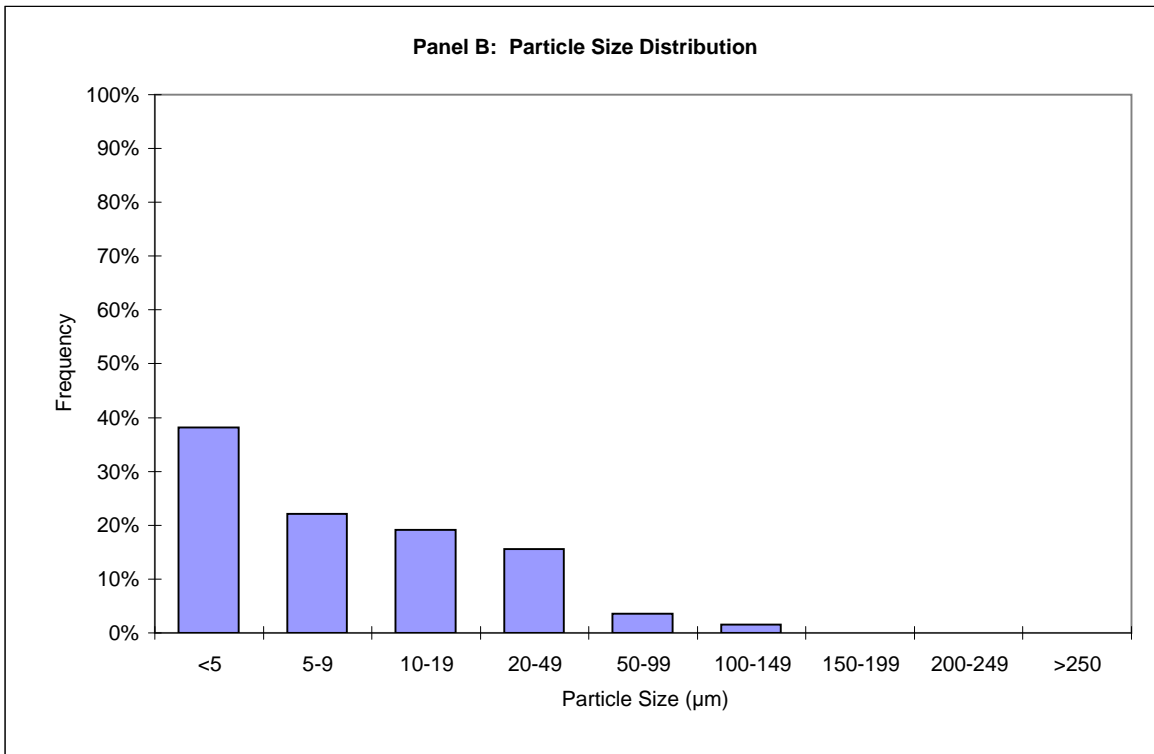
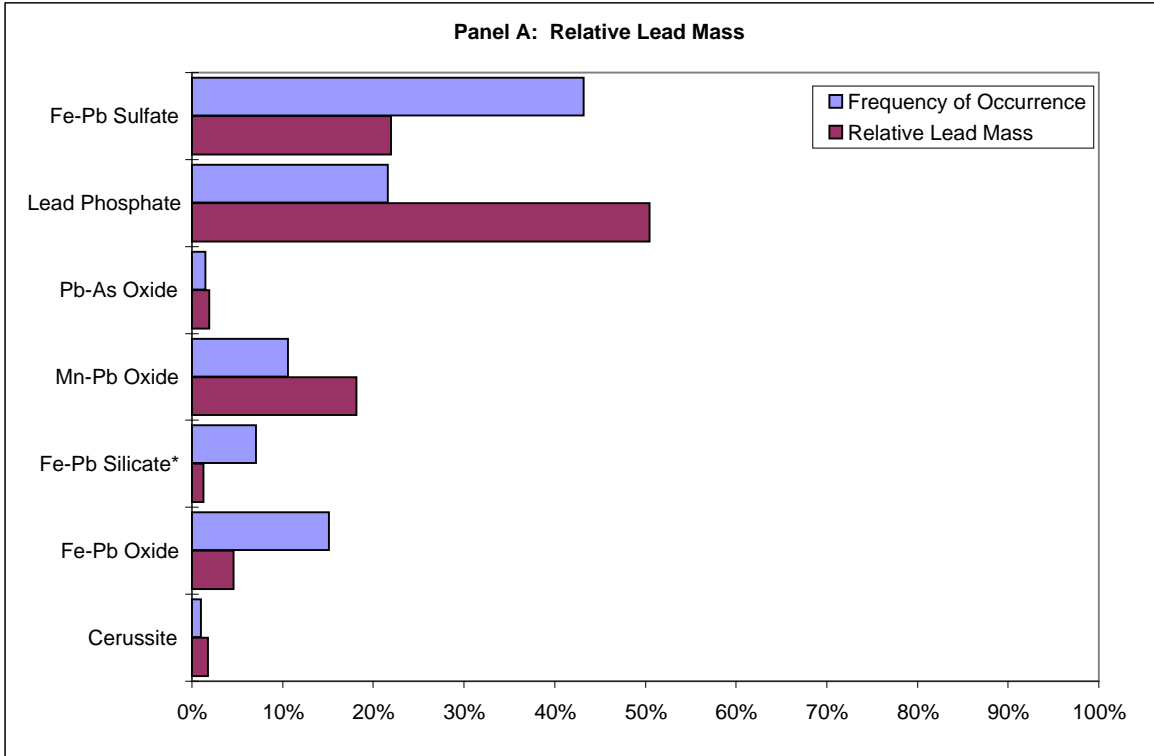
**Particle Size Distribution**

Size	Total Freq	Lib Freq	Total RLM	Lib RLM
<5	38.2%	38.2%	8.2%	8.2%
5-9	22.1%	22.1%	12.2%	12.2%
10-19	19.1%	19.1%	13.0%	13.0%
20-49	15.6%	15.6%	30.3%	30.3%
50-99	3.5%	3.5%	18.8%	18.8%
100-149	1.5%	1.5%	17.6%	17.6%
150-199	0.0%	0.0%	0.0%	0.0%
200-249	0.0%	0.0%	0.0%	0.0%
≥250	0.0%	0.0%	0.0%	0.0%
<b>TOTAL</b>	<b>100%</b>	<b>100%</b>	<b>100%</b>	<b>100%</b>



EXPERIMENT 2 - BINGHAM CREEK RESIDENTIAL

Speciation and Particle Size Data



\*This mineral is now considered to be equivalent to Fe-Pb Oxid

APPENDIX F

**EXPERIMENT 2 - BINGHAM CREEK CHANNEL SOIL**

**Lead Speciation Summary Statistics**

Mineral	Counts		Particle Size			Count Freq (%)		LW Freq (%)		Density	Lead Fraction	Relative Lead Mass (%)	
	Total	Lib	Avg	Min	Max	Total	Lib	Total	Lib			Total	Lib
Anglesite	57	56	4	1	30	11.6%	11.4%	6.26%	6.23%	6.3	0.684	28.4%	28.3%
Cerussite	1	1	2	2	2	0.2%	0.2%	0.05%	0.05%	6.6	0.776	0.3%	0.3%
Fe-Pb Oxide	25	25	17	4	60	5.1%	5.1%	10.88%	10.88%	4.0	0.053	2.4%	2.4%
FeSbO	1	1	5	5	5	0.2%	0.2%	0.13%	0.13%			0.0%	0.0%
Fe-Pb Silicate*	4	4	15	10	20	0.8%	0.8%	1.56%	1.56%	3.5	0.057	0.3%	0.3%
Galena	1	1	50	50	50	0.2%	0.2%	1.30%	1.30%	7.5	0.866	8.9%	8.9%
Mn-Pb Oxide	5	5	21	5	50	1.0%	1.0%	2.67%	2.67%	5.1	0.159	2.3%	2.3%
Lead Organic	2	2	105	100	110	0.4%	0.4%	5.45%	5.45%	1.3	0.037	0.3%	0.3%
Pb-As Oxide	3	3	4	1	8	0.6%	0.6%	0.29%	0.29%	6.0	0.500	0.9%	0.9%
Lead Barite	1	1	10	10	10	0.2%	0.2%	0.26%	0.26%	4.5	0.031	0.0%	0.0%
Lead Phosphate	42	42	12	1	100	8.6%	8.6%	13.01%	13.01%	5.1	0.370	25.8%	25.8%
Fe-Pb Sulfate	349	349	6	1	110	71.1%	71.1%	58.15%	58.15%	3.7	0.134	30.4%	30.4%
<b>TOTAL</b>	<b>491</b>	<b>490</b>	<b>8</b>			<b>100.0%</b>	<b>99.8%</b>	<b>100.00%</b>	<b>99.97%</b>			<b>100.0%</b>	<b>99.9%</b>

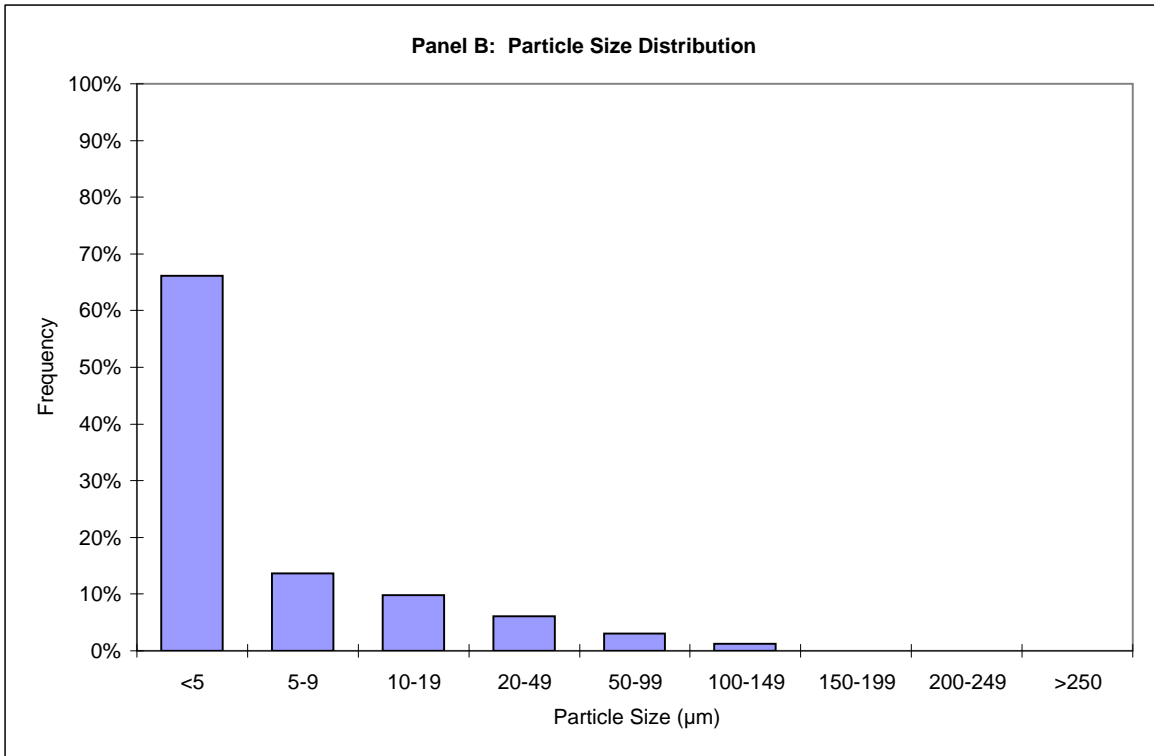
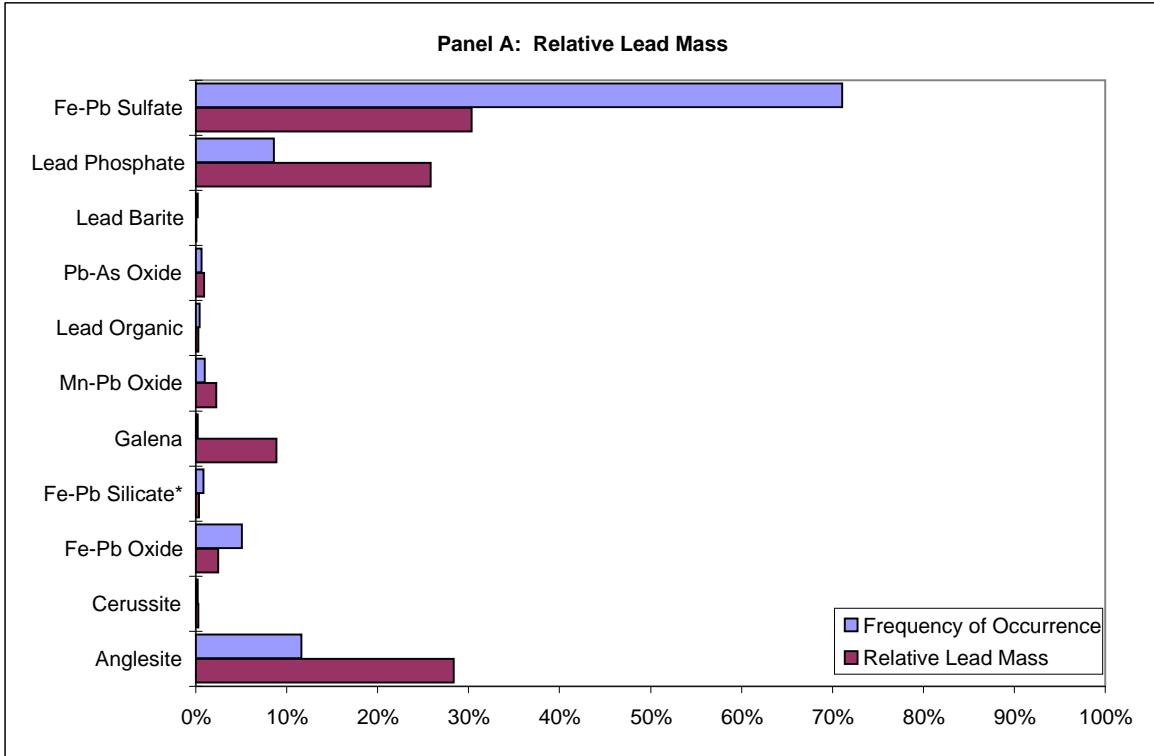
\*This mineral is now considered to be equivalent to Fe-Pb Oxide.

**Particle Size Distribution**

Size	Total Freq	Lib Freq	Total RLM	Lib RLM
<5	66.2%	66.0%	13.9%	13.8%
5-9	13.6%	13.6%	17.5%	17.5%
10-19	9.8%	9.8%	18.4%	18.4%
20-49	6.1%	6.1%	20.0%	20.0%
50-99	3.1%	3.1%	20.5%	20.5%
100-149	1.2%	1.2%	9.6%	9.6%
150-199	0.0%	0.0%	0.0%	0.0%
200-249	0.0%	0.0%	0.0%	0.0%
≥250	0.0%	0.0%	0.0%	0.0%
<b>TOTAL</b>	<b>100%</b>	<b>100%</b>	<b>100%</b>	<b>100%</b>

EXPERIMENT 2 - BINGHAM CREEK CHANNEL SOIL

Speciation and Particle Size Data



\*This mineral is now considered to be equivalent to Fe-Pb Oxid

APPENDIX F

**EXPERIMENT 3 - JASPER COUNTY HIGH LEAD SMELTER**

**Lead Speciation Summary Statistics**

Mineral	Counts		Particle Size			Count Freq (%)		LW Freq (%)		Density	Lead Fraction	Relative Lead Mass (%)	
	Total	Lib	Avg	Min	Max	Total	Lib	Total	Lib			Total	Lib
Anglesite	1	1	12	12	12	0.25%	0.25%	0.11%	0.11%	6.3	0.684	0.9%	0.9%
Calcite	2	2	48	35	60	0.50%	0.50%	0.87%	0.87%	2.8	0.050	0.2%	0.2%
Cerussite	12	11	31	8	90	3.0%	2.8%	3.39%	3.26%	6.6	0.776	32.1%	30.7%
Clay	2	2	35	10	60	0.50%	0.50%	0.64%	0.64%	3.1	0.005	0.02%	0.02%
Fe-Pb Oxide	24	24	45	10	150	6.0%	6.0%	10.04%	10.04%	4.0	0.037	2.7%	2.7%
Fe-Pb Silicate*	22	22	83	4	175	5.5%	5.5%	16.80%	16.80%	3.7	0.100	11.5%	11.5%
Mn-Pb Oxide	5	5	47	12	100	1.3%	1.3%	2.18%	2.18%	5.1	0.112	2.3%	2.3%
Native Lead	56	0	2	1	9	14.0%	0.0%	1.07%	0.00%	11.3	1.000	22.2%	0.0%
Lead Oxide	6	1	6	1	10	1.5%	0.3%	0.31%	0.02%	4.0	0.037	0.09%	0.01%
Lead Phosphate	117	117	7	1	90	29.3%	29.3%	7.25%	7.25%	5.1	0.310	21.1%	21.1%
Slag	62	62	94	15	300	15.5%	15.5%	53.58%	53.58%	3.7	0.012	4.3%	4.3%
Fe-Pb Sulfate	90	75	5	1	10	22.6%	18.8%	3.75%	3.20%	3.7	0.100	2.6%	2.2%
<b>TOTAL</b>	<b>399</b>	<b>322</b>	<b>27</b>			<b>100.0%</b>	<b>80.7%</b>	<b>100.00%</b>	<b>97.95%</b>			<b>100.0%</b>	<b>76.0%</b>

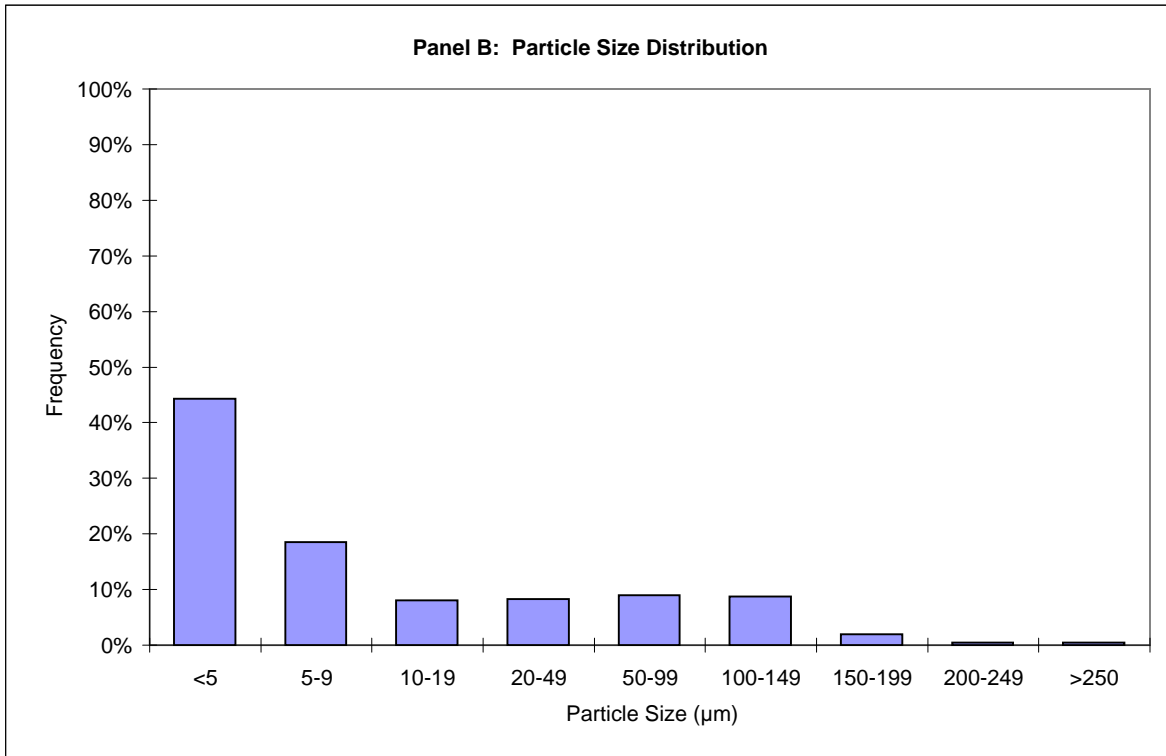
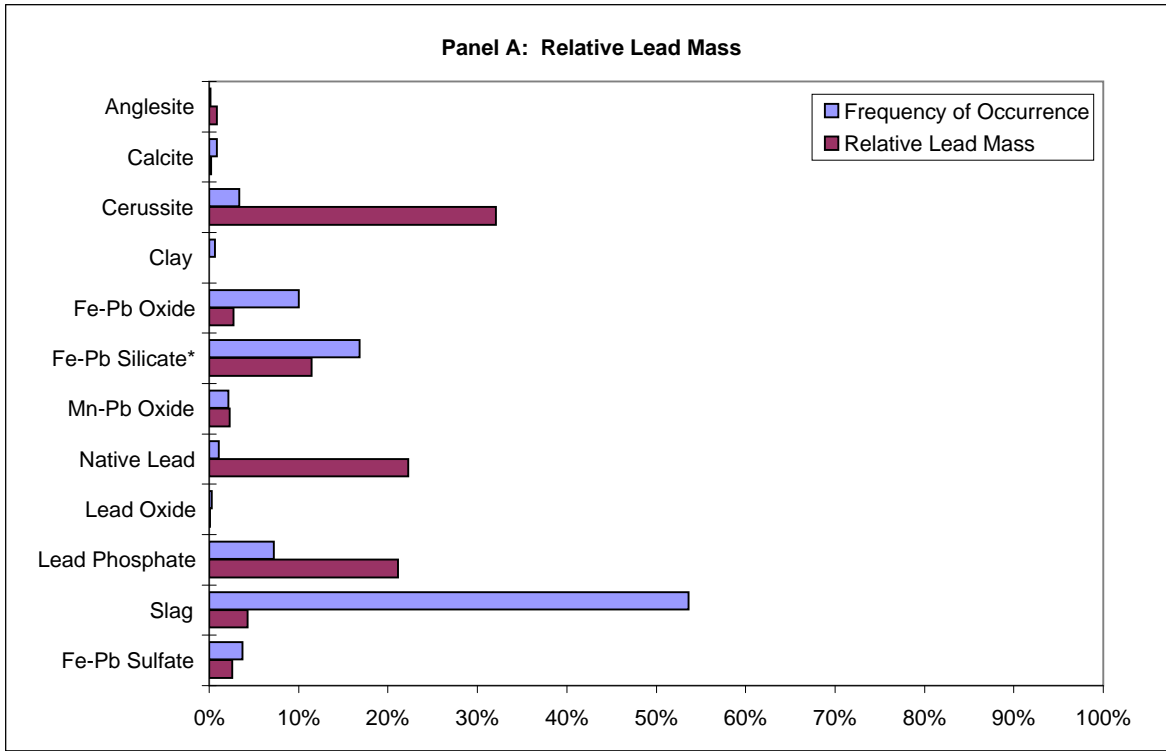
\*This mineral is now considered to be equivalent to Fe-Pb Oxide.

**Particle Size Distribution**

Size	Total Freq	Lib Freq	Total RLM	Lib RLM
<5	44.4%	28.1%	17.2%	3.8%
5-9	18.5%	16.0%	15.0%	5.7%
10-19	8.0%	7.5%	7.8%	6.4%
20-49	8.3%	8.3%	14.0%	14.0%
50-99	9.0%	9.0%	31.9%	31.9%
100-149	8.8%	8.8%	9.6%	9.6%
150-199	2.0%	2.0%	3.8%	3.8%
200-249	0.5%	0.5%	0.3%	0.3%
≥250	0.5%	0.5%	0.4%	0.4%
<b>TOTAL</b>	<b>100%</b>	<b>81%</b>	<b>100%</b>	<b>76%</b>

**EXPERIMENT 3 - JASPER COUNTY HIGH LEAD SMELTER**

**Speciation and Particle Size Data**



\*This mineral is now considered to be equivalent to Fe-Pb Oxid

APPENDIX F

**EXPERIMENT 3 - JASPER COUNTY LOW LEAD YARD**

**Lead Speciation Summary Statistics**

Mineral	Counts		Particle Size			Count Freq (%)		LW Freq (%)		Density	Lead Fraction	Relative Lead Mass (%)	
	Total	Lib	Avg	Min	Max	Total	Lib	Total	Lib			Total	Lib
Anglesite	3	3	3	2	6	1.6%	1.6%	0.31%	0.31%	6.3	0.684	0.48%	0.48%
Cerussite	95	95	15	1	130	52.2%	52.2%	43.37%	43.37%	6.6	0.776	81.1%	81.1%
Clay	1	1	15	15	15	0.5%	0.5%	0.46%	0.46%	3.1	0.005	0.003%	0.003%
Fe-Pb Oxide	18	18	36	8	100	9.9%	9.9%	19.53%	19.53%	4	0.037	1.1%	1.1%
Fe-Pb Silicate*	9	9	33	5	100	4.9%	4.9%	9.11%	9.11%	3.7	0.1	1.2%	1.2%
Galena	2	1	53	25	80	1.1%	0.5%	3.21%	0.76%	7.5	0.866	7.6%	1.8%
Mn-Pb Oxide	10	10	25	8	55	5.5%	5.5%	7.73%	7.73%	5.1	0.112	1.6%	1.6%
Pb-As Oxide	1	1	8	8	8	0.5%	0.5%	0.24%	0.24%	7.1	0.243	0.15%	0.15%
Lead Silicate	2	2	2	1	2	1.1%	1.1%	0.09%	0.09%	8	0.167	0.04%	0.04%
Lead Phosphate	32	32	11	1	80	17.6%	17.6%	10.42%	10.42%	5.1	0.31	6.0%	6.0%
Fe-Pb Sulfate	9	9	20	1	100	4.9%	4.9%	5.53%	5.53%	3.7	0.1	0.75%	0.75%
<b>TOTAL</b>	<b>182</b>	<b>181</b>	<b>18</b>			<b>100.0%</b>	<b>99.5%</b>	<b>100.00%</b>	<b>97.56%</b>			<b>100.0%</b>	<b>94.2%</b>

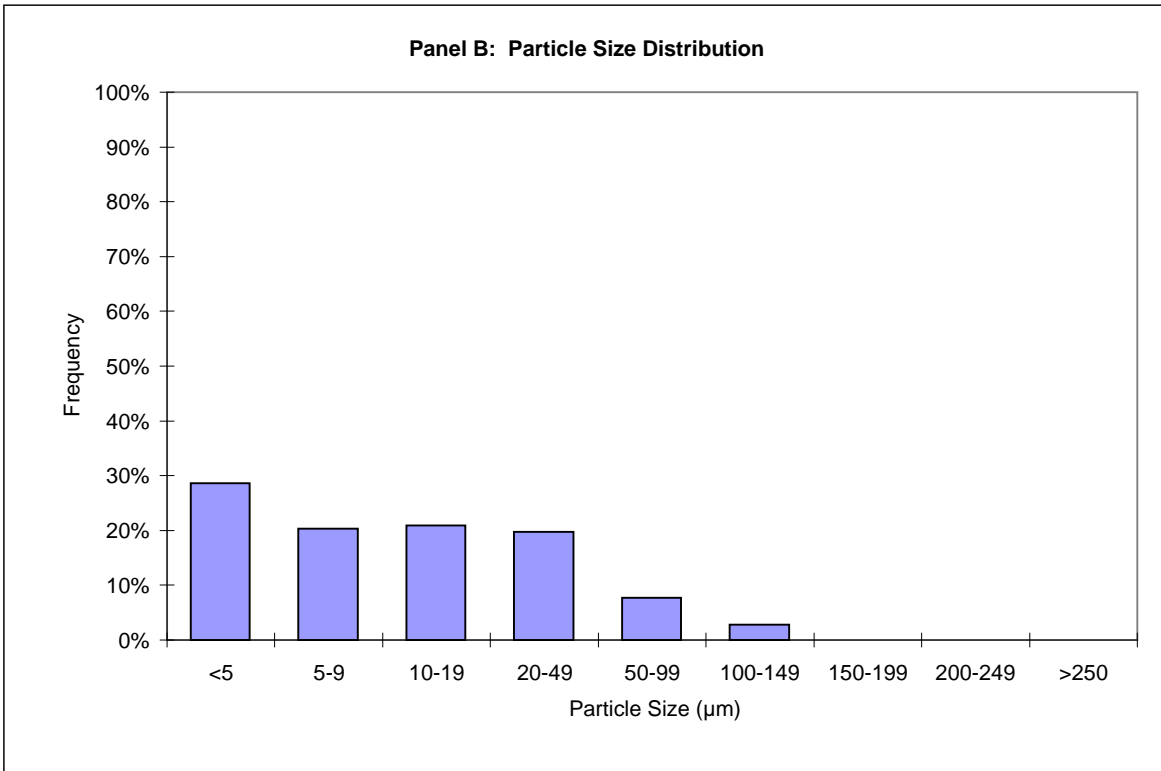
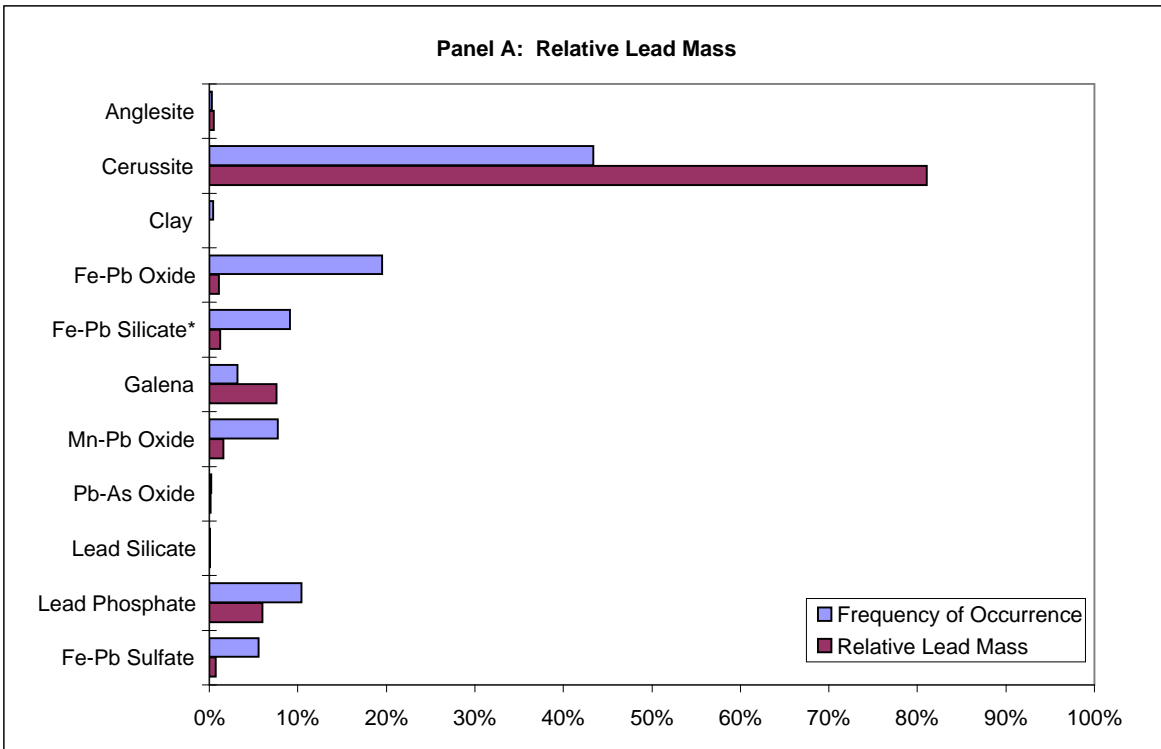
\*This mineral is now considered to be equivalent to Fe-Pb Oxide.

**Particle Size Distribution**

Size	Total Freq	Lib Freq	Total RLM	Lib RLM
<5	28.6%	28.6%	5.0%	5.0%
5-9	20.3%	20.3%	8.5%	8.5%
10-19	20.9%	20.9%	17.1%	17.1%
20-49	19.8%	19.8%	30.2%	30.2%
50-99	7.7%	7.1%	23.6%	17.8%
100-149	2.7%	2.7%	15.6%	15.6%
150-199	0.0%	0.0%	0.0%	0.0%
200-249	0.0%	0.0%	0.0%	0.0%
≥250	0.0%	0.0%	0.0%	0.0%
<b>TOTAL</b>	<b>100%</b>	<b>99%</b>	<b>100%</b>	<b>94%</b>

EXPERIMENT 3 - JASPER COUNTY LOW LEAD YARD

Speciation and Particle Size Data



\*This mineral is now considered to be equivalent to Fe-Pb Oxid

APPENDIX F

**EXPERIMENT 4 - MURRAY SMELTER SLAG**

**Lead Speciation Summary Statistics**

Mineral	Counts		Particle Size			Count Freq (%)		LW Freq (%)		Density	Lead Fraction	Relative Lead Mass (%)	
	Total	Lib	Avg	Min	Max	Total	Lib	Total	Lib			Total	Lib
Anglesite	3	0	12	10	15	0.2%	0.0%	0.04%	0.00%	6.3	0.684	1.0%	0.0%
Cerussite	4	3	8	3	15	0.3%	0.2%	0.04%	0.04%	6.6	0.776	1.1%	1.0%
Fe-Pb Oxide	3	3	18	8	35	0.2%	0.2%	0.07%	0.07%	4	0.031	0.04%	0.04%
Fe-As Oxide	3	3	17	4	35	0.2%	0.2%	0.06%	0.06%			0.0%	0.0%
Fe-Pb Silicate*	9	9	28	8	80	0.7%	0.7%	0.32%	0.32%	4	0.22	1.5%	1.5%
Galena	98	7	2	1	15	7.2%	0.5%	0.27%	0.08%	7.5	0.866	9.2%	2.6%
Mn-Pb Oxide	7	7	31	8	110	0.5%	0.5%	0.28%	0.28%	5.1	0.112	0.8%	0.8%
Native Lead	3	2	3	2	4	0.2%	0.1%	0.01%	0.01%	11.3	1	0.7%	0.5%
Pb-As Oxide	39	31	6	1	60	2.9%	2.3%	0.30%	0.27%	7.1	0.5	5.7%	5.1%
Pb(M)O	8	3	18	2	110	0.6%	0.2%	0.19%	0.16%	8	0.5	3.9%	3.3%
Lead Oxide	143	79	8	1	100	10.5%	5.8%	1.48%	1.18%	9.5	0.93	68.7%	54.6%
Slag	1037	1037	73	5	310	76.1%	76.1%	96.71%	96.71%	3.65	0.0038	7.0%	7.0%
Fe-Pb Sulfate	2	2	55	10	100	0.1%	0.1%	0.14%	0.14%	3.7	0.1	0.3%	0.3%
Zn-Pb Silicate	4	3	16	10	30	0.3%	0.2%	0.08%	0.07%	5.1	0.014	0.03%	0.03%
<b>TOTAL</b>	<b>1363</b>	<b>1189</b>	<b>58</b>			<b>100.0%</b>	<b>87.2%</b>	<b>100.00%</b>	<b>99.38%</b>			<b>100.0%</b>	<b>76.8%</b>

\*This mineral is now considered to be equivalent to Fe-Pb Oxide.

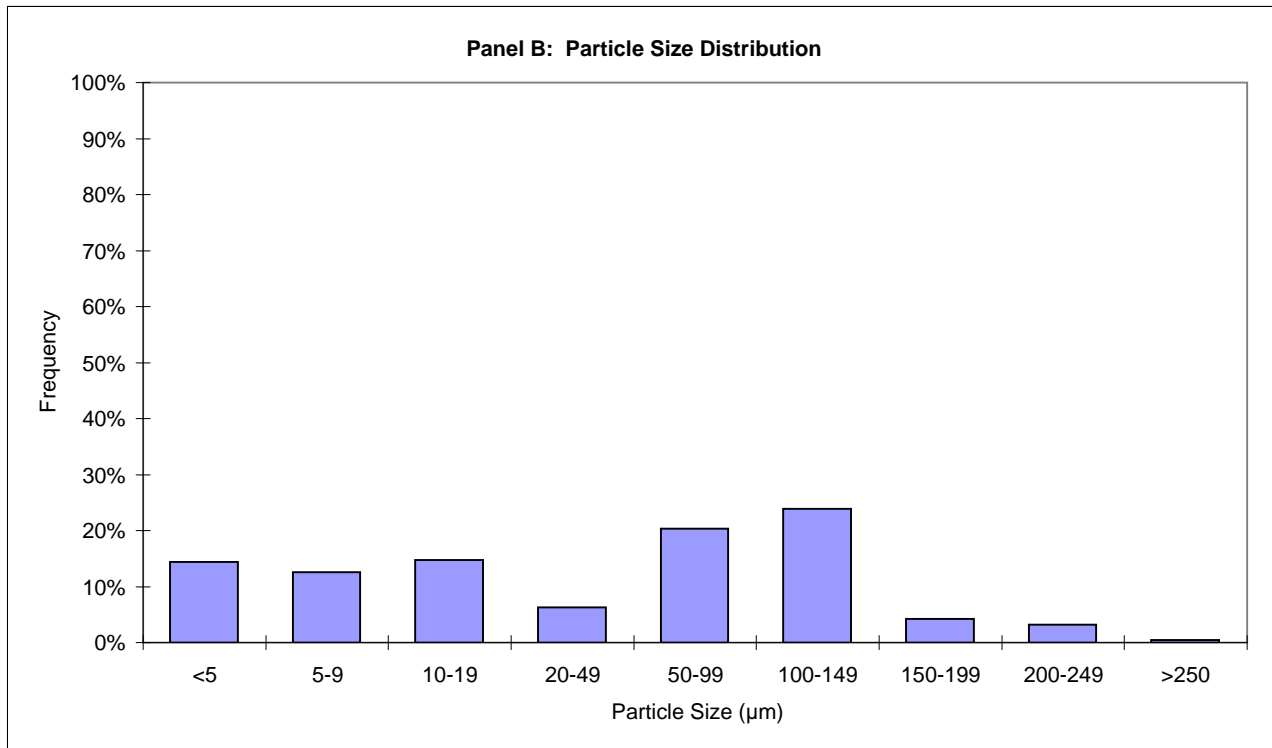
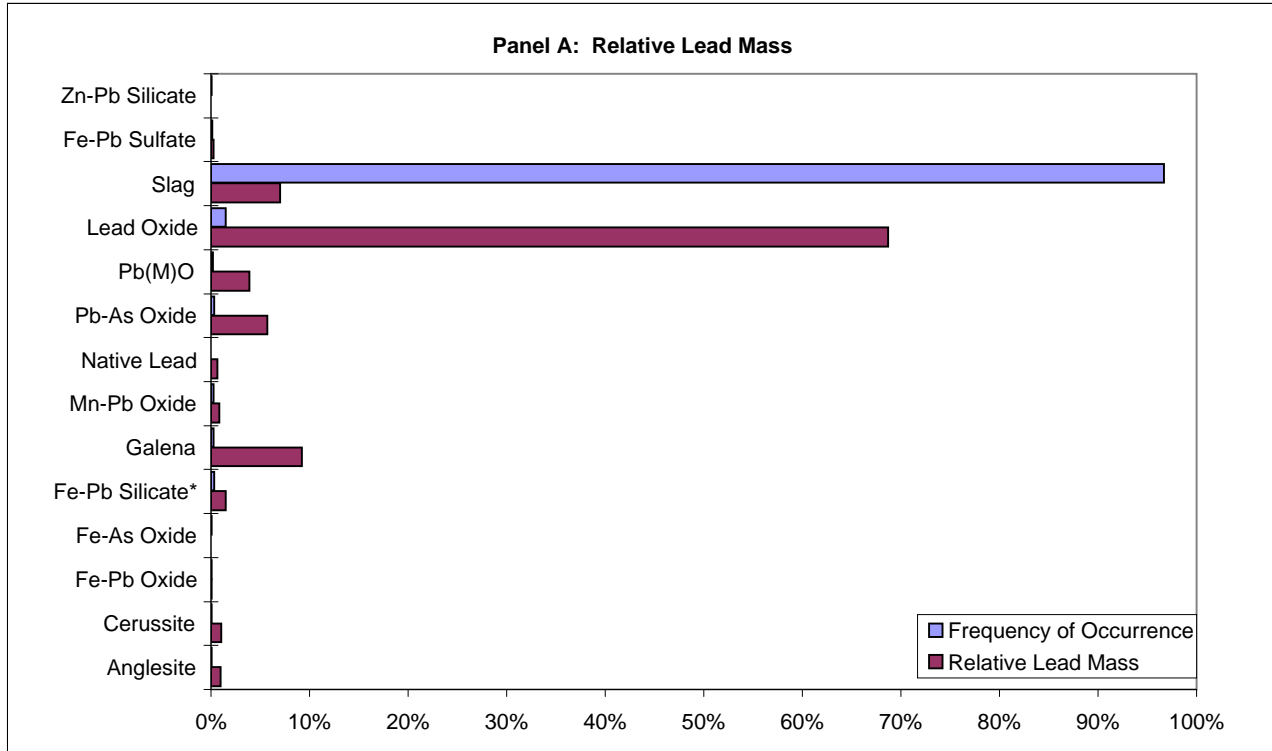
**Particle Size Distribution**

Size	Total Freq	Lib Freq	Total RLM	Lib RLM
<5	14.5%	4.1%	15.6%	5.4%
5-9	12.6%	11.2%	13.7%	7.9%
10-19	14.7%	13.9%	22.9%	17.3%
20-49	6.2%	6.2%	17.1%	15.3%
50-99	20.3%	20.3%	16.2%	16.2%
100-149	23.8%	23.8%	12.8%	12.8%
150-199	4.2%	4.2%	0.8%	0.8%
200-249	3.2%	3.2%	0.8%	0.8%
≥250	0.4%	0.4%	0.1%	0.1%
<b>TOTAL</b>	<b>100%</b>	<b>87%</b>	<b>100%</b>	<b>77%</b>



**EXPERIMENT 4 - MURRAY SMELTER SLAG**

**Speciation and Particle Size Data**



\*This mineral is now considered to be equivalent to Fe-Pb Oxid

APPENDIX F

**EXPERIMENT 4 - JASPER COUNTY HIGH LEAD MILL**

**Lead Speciation Summary Statistics**

Mineral	Counts		Particle Size			Count Freq (%)		LW Freq (%)		Density	Lead Fraction	Relative Lead Mass (%)	
	Total	Lib	Avg	Min	Max	Total	Lib	Total	Lib			Total	Lib
Anglesite	1	1	25	25	25	0.36%	0.36%	0.36%	0.36%	6.3	0.684	1.6%	1.6%
Lead Barite	1	1	3	3	3	0.36%	0.36%	0.04%	0.04%	4.5	0.045	0.01%	0.01%
Calcite	1	1	25	25	25	0.36%	0.36%	0.36%	0.36%	2.8	0.05	0.1%	0.1%
Cerussite	90	90	8	1	70	32.0%	32.0%	10.74%	10.74%	6.6	0.776	57.0%	57.0%
Clay	3	3	24	8	40	1.1%	1.1%	1.04%	1.04%	3.1	0.005	0.02%	0.02%
Fe-Pb Oxide	33	33	22	3	110	11.7%	11.7%	10.44%	10.44%	4	0.037	1.6%	1.6%
Fe-Pb Silicate*	41	41	36	1	210	14.6%	14.6%	21.16%	21.16%	3.7	0.1	8.1%	8.1%
Galena	6	0	6	1	30	2.1%	0.0%	0.51%	0.00%	7.5	0.866	3.4%	0.0%
Mn-Pb Oxide	39	39	27	3	125	13.9%	13.9%	14.77%	14.77%	5.1	0.112	8.7%	8.7%
Native Lead	3	0	4	1	10	1.1%	0.0%	0.18%	0.00%	11.3	1	2.2%	0.0%
Lead Oxide	3	1	17	5	40	1.07%	0.36%	0.71%	0.57%	9.5	0.93	6.5%	5.2%
Lead Silicate	1	1	10	10	10	0.36%	0.36%	0.14%	0.14%	8	0.45	0.53%	0.53%
Lead Phosphate	15	15	21	2	100	5.3%	5.3%	4.53%	4.53%	5.1	0.31	7.4%	7.4%
Slag	24	24	92	15	210	8.5%	8.5%	31.45%	31.45%	3.65	0.012	1.4%	1.4%
Fe-Pb Sulfate	20	20	13	3	60	7.1%	7.1%	3.58%	3.58%	3.7	0.1	1.4%	1.4%
<b>TOTAL</b>	<b>281</b>	<b>270</b>	<b>25</b>			<b>100.0%</b>	<b>96.1%</b>	<b>100.00%</b>	<b>99.16%</b>			<b>100.0%</b>	<b>93.1%</b>

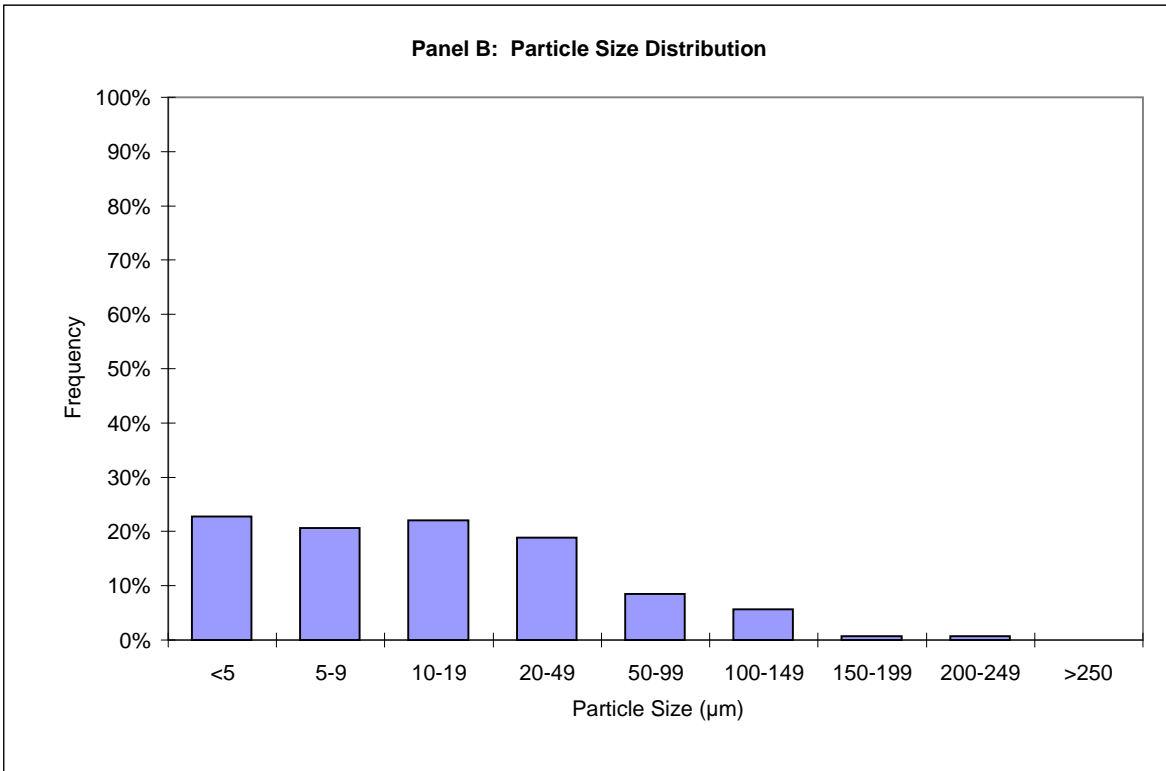
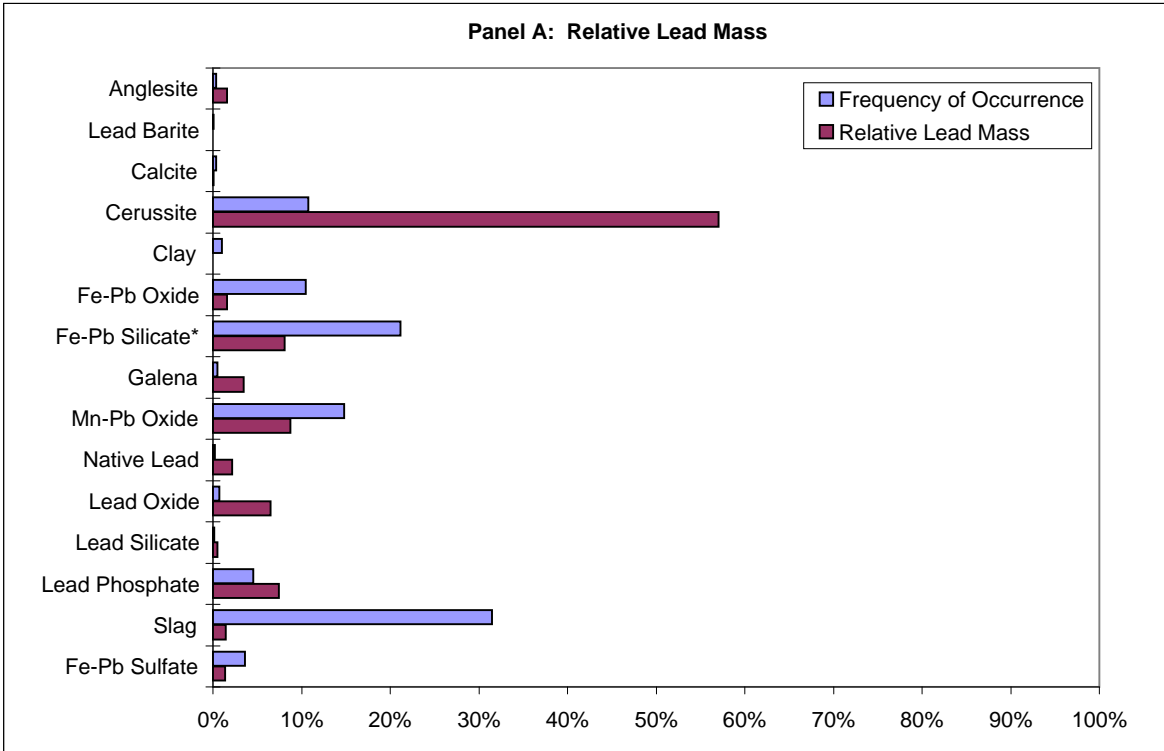
\*This mineral is now considered to be equivalent to Fe-Pb Oxide.

**Particle Size Distribution**

Size	Total Freq	Lib Freq	Total RLM	Lib RLM
<5	22.8%	20.3%	8.3%	7.2%
5-9	20.6%	19.9%	12.9%	11.6%
10-19	22.1%	21.7%	24.3%	22.7%
20-49	18.9%	18.5%	33.7%	30.9%
50-99	8.5%	8.5%	12.8%	12.8%
100-149	5.7%	5.7%	6.5%	6.5%
150-199	0.7%	0.7%	0.2%	0.2%
200-249	0.7%	0.7%	1.3%	1.3%
≥250	0.0%	0.0%	0.0%	0.0%
<b>TOTAL</b>	<b>100%</b>	<b>96%</b>	<b>100%</b>	<b>93%</b>

**EXPERIMENT 4 - JASPER COUNTY HIGH LEAD MILL**

**Speciation and Particle Size Data**



\*This mineral is now considered to be equivalent to Fe-Pb Oxid

APPENDIX F

**EXPERIMENT 5 - ASPEN BERM**

**Lead Speciation Summary Statistics**

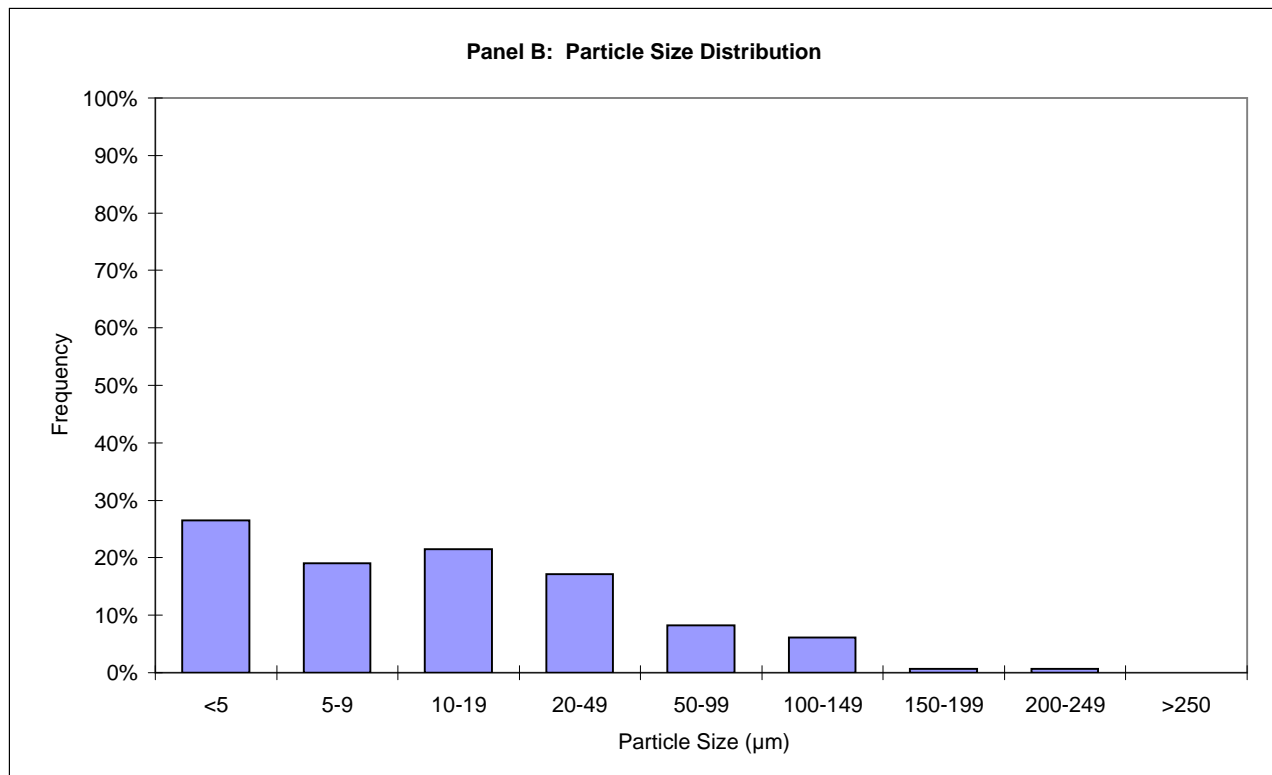
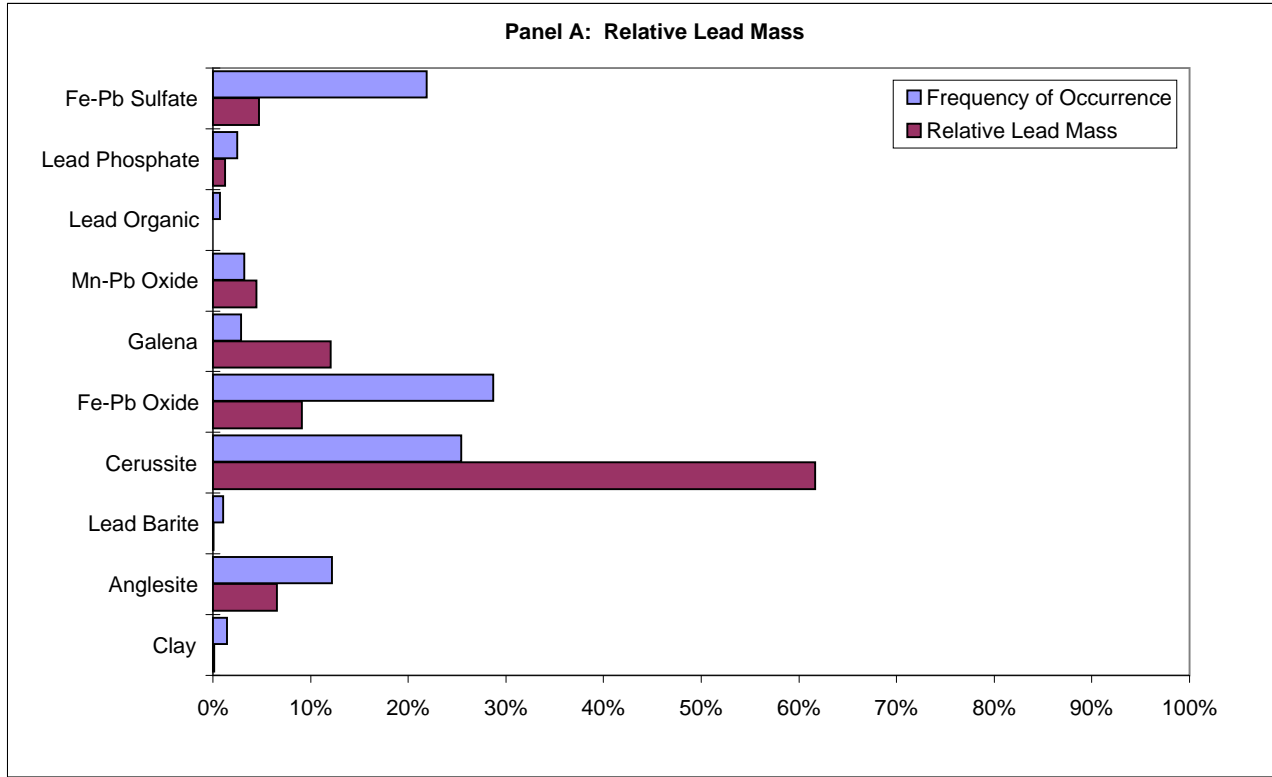
Mineral	Counts		Particle Size			Count Freq (%)		LW Freq (%)		Density	Lead Fraction	Relative Lead Mass (%)	
	Total	Lib	Avg	Min	Max	Total	Lib	Total	Lib			Total	Lib
Clay	4	4	55	10	120	1.4%	1.4%	3.30%	3.30%	2.6	0.02	0.1%	0.1%
Anglesite	34	34	5	1	90	12.2%	12.2%	2.63%	2.63%	6.3	0.684	6.6%	6.6%
Lead Barite	3	3	10	2	25	1.1%	1.1%	0.45%	0.45%	4.5	0.05	0.1%	0.1%
Cerussite	71	68	20	1	110	25.4%	24.4%	20.80%	20.11%	6.6	0.776	61.7%	59.6%
Fe-Pb Oxide	80	69	35	2	210	28.7%	24.7%	41.43%	36.09%	4	0.095	9.1%	7.9%
Galena	8	6	27	10	50	2.9%	2.2%	3.23%	2.70%	7.5	0.86	12.0%	10.1%
Mn-Pb Oxide	9	9	56	10	150	3.2%	3.2%	7.58%	7.58%	5.1	0.2	4.5%	4.5%
Lead Organic	2	2	70	40	100	0.7%	0.7%	2.10%	2.10%	1.3	0.018	0.0%	0.0%
Lead Phosphate	7	7	45	10	110	2.5%	2.5%	4.73%	4.73%	5.1	0.09	1.3%	1.3%
Fe-Pb Sulfate	61	39	15	4	90	21.9%	14.0%	13.75%	6.87%	3.7	0.16	4.7%	2.4%
<b>TOTAL</b>	<b>279</b>	<b>241</b>	<b>24</b>			<b>100.0%</b>	<b>86.4%</b>	<b>100.00%</b>	<b>86.57%</b>			<b>100.0%</b>	<b>92.5%</b>

**Particle Size Distribution**

Size	Total Freq	Lib Freq	Total RLM	Lib RLM
<5	26.5%	25.4%	2.5%	2.3%
5-9	19.0%	15.8%	5.9%	5.6%
10-19	21.5%	17.6%	14.4%	12.6%
20-49	17.2%	14.3%	29.7%	26.3%
50-99	8.2%	5.7%	25.3%	23.4%
100-149	6.1%	6.1%	19.0%	19.0%
150-199	0.7%	0.7%	1.8%	1.8%
200-249	0.7%	0.7%	1.4%	1.4%
≥250	0.0%	0.0%	0.0%	0.0%
<b>TOTAL</b>	<b>100%</b>	<b>86%</b>	<b>100%</b>	<b>92%</b>

**EXPERIMENT 5 - ASPEN BERM**

**Speciation and Particle Size Data**



APPENDIX F

**EXPERIMENT 5 - ASPEN RESIDENTIAL**

**Lead Speciation Summary Statistics**

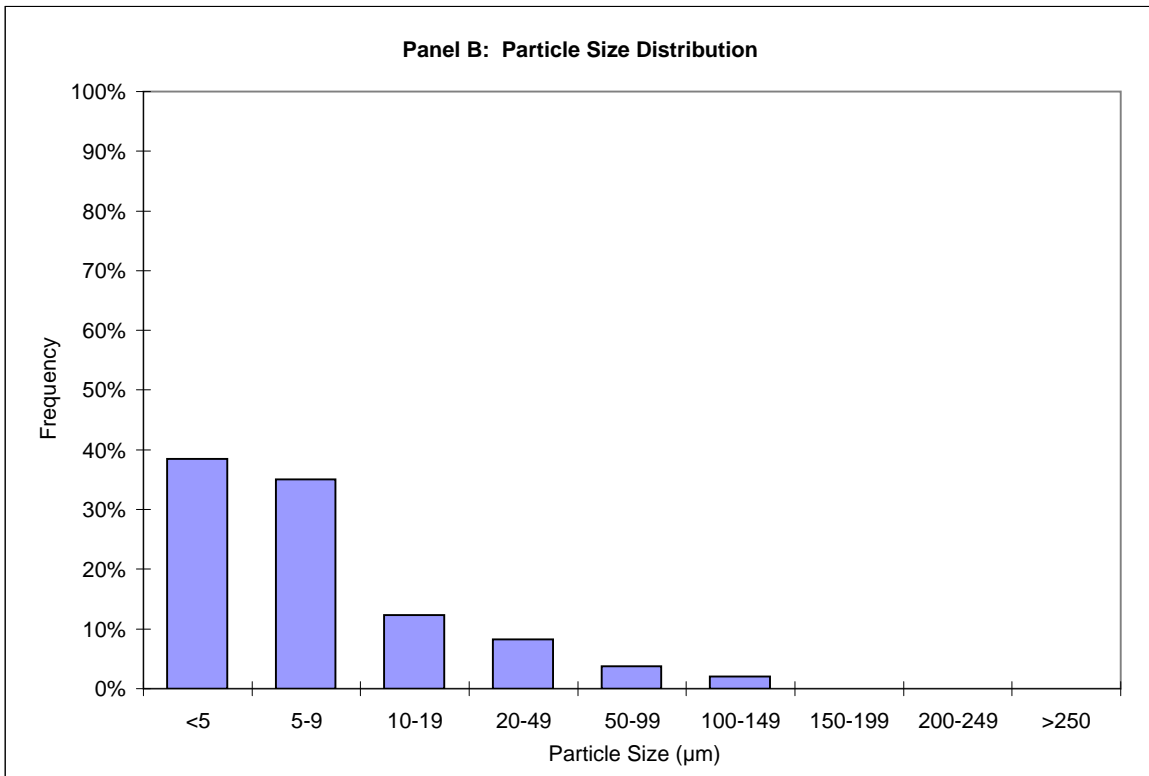
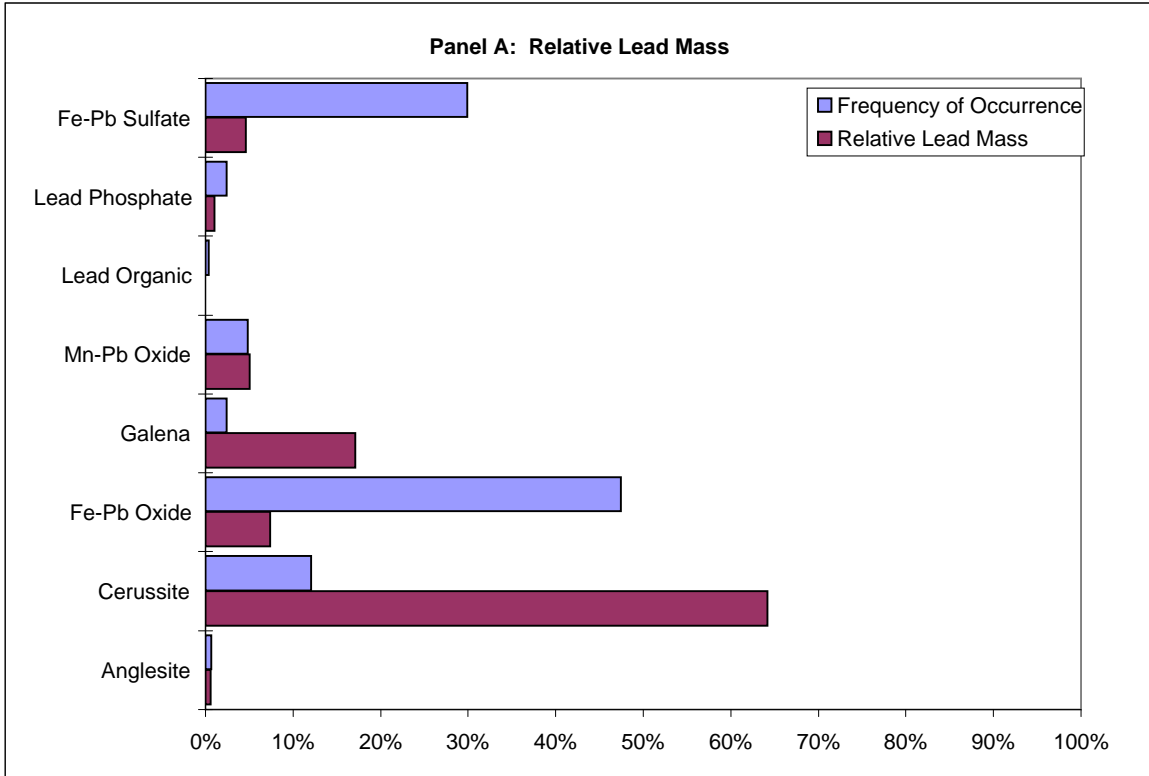
Mineral	Counts		Particle Size			Count Freq (%)		LW Freq (%)		Density	Lead Fraction	Relative Lead Mass (%)	
	Total	Lib	Avg	Min	Max	Total	Lib	Total	Lib			Total	Lib
Anglesite	2	2	5	4	5	0.7%	0.7%	0.27%	0.27%	6.3	0.684	0.6%	0.6%
Cerussite	35	35	23	2	125	12.0%	12.0%	24.57%	24.57%	6.6	0.776	64.2%	64.2%
Fe-Pb Oxide	138	138	9	1	100	47.4%	47.4%	38.18%	38.18%	4	0.095	7.4%	7.4%
Galena	7	1	25	5	110	2.4%	0.3%	5.21%	3.31%	7.5	0.86	17.1%	10.9%
Mn-Pb Oxide	14	14	23	5	80	4.8%	4.8%	9.73%	9.73%	5.1	0.2	5.1%	5.1%
Lead Organic	1	1	80	80	80	0.3%	0.3%	2.41%	2.41%	1.3	0.018	0.0%	0.0%
Lead Phosphate	7	7	21	3	60	2.4%	2.4%	4.49%	4.49%	5.1	0.09	1.1%	1.1%
Fe-Pb Sulfate	87	87	6	1	60	29.9%	29.9%	15.15%	15.15%	3.7	0.16	4.6%	4.6%
<b>TOTAL</b>	<b>291</b>	<b>285</b>	<b>11</b>			<b>100.0%</b>	<b>97.9%</b>	<b>100.00%</b>	<b>98.10%</b>			<b>100.0%</b>	<b>93.8%</b>

**Particle Size Distribution**

Size	Total Freq	Lib Freq	Total RLM	Lib RLM
<5	38.5%	38.5%	4.5%	4.5%
5-9	35.1%	34.0%	9.3%	7.5%
10-19	12.4%	11.7%	9.2%	7.2%
20-49	8.2%	7.9%	22.7%	20.2%
50-99	3.8%	3.8%	8.6%	8.6%
100-149	2.1%	2.1%	45.7%	45.7%
150-199	0.0%	0.0%	0.0%	0.0%
200-249	0.0%	0.0%	0.0%	0.0%
≥250	0.0%	0.0%	0.0%	0.0%
<b>TOTAL</b>	<b>100%</b>	<b>98%</b>	<b>100%</b>	<b>94%</b>

**EXPERIMENT 5 - ASPEN RESIDENTIAL**

**Speciation and Particle Size Data**



## APPENDIX F

## EXPERIMENT 6 - MIDVALE SLAG

## Lead Speciation Summary Statistics

Mineral	Counts		Particle Size			Count Freq (%)		LW Freq (%)		Density	Lead Fraction	Relative Lead Mass (%)	
	Total	Lib	Avg	Min	Max	Total	Lib	Total	Lib			Total	Lib
Cerussite	7	7	22	10	45	0.4%	0.4%	0.07%	0.07%	6.6	0.776	3.8%	3.8%
Fe-Pb Oxide	4	4	26	12	45	0.2%	0.2%	0.04%	0.04%	4	0.15	0.3%	0.3%
Galena	2	2	90	80	100	0.1%	0.1%	0.08%	0.08%	7.5	0.866	5.7%	5.7%
Native Lead	67	6	4	1	40	3.4%	0.3%	0.12%	0.04%	11.3	1	15.4%	5.0%
Pb-As Oxide	119	41	16	1	100	6.0%	2.1%	0.82%	0.61%	7.1	0.5	32.6%	24.2%
Lead Oxide	61	29	12	1	55	3.1%	1.5%	0.31%	0.26%	9	0.83	25.9%	21.6%
Slag	1721	1721	131	10	600	86.7%	86.7%	98.52%	98.52%	3.65	0.004	16.0%	16.0%
Sulfosalts	1	1	50	50	50	0.1%	0.1%	0.02%	0.02%	6	0.25	0.4%	0.4%
Fe-Pb Sulfate	2	2	15	15	15	0.1%	0.1%	0.01%	0.01%	3.7	0.14	0.1%	0.1%
TOTAL	1984	1813	115			100.0%	91.4%	100.00%	99.65%			100.0%	77.0%

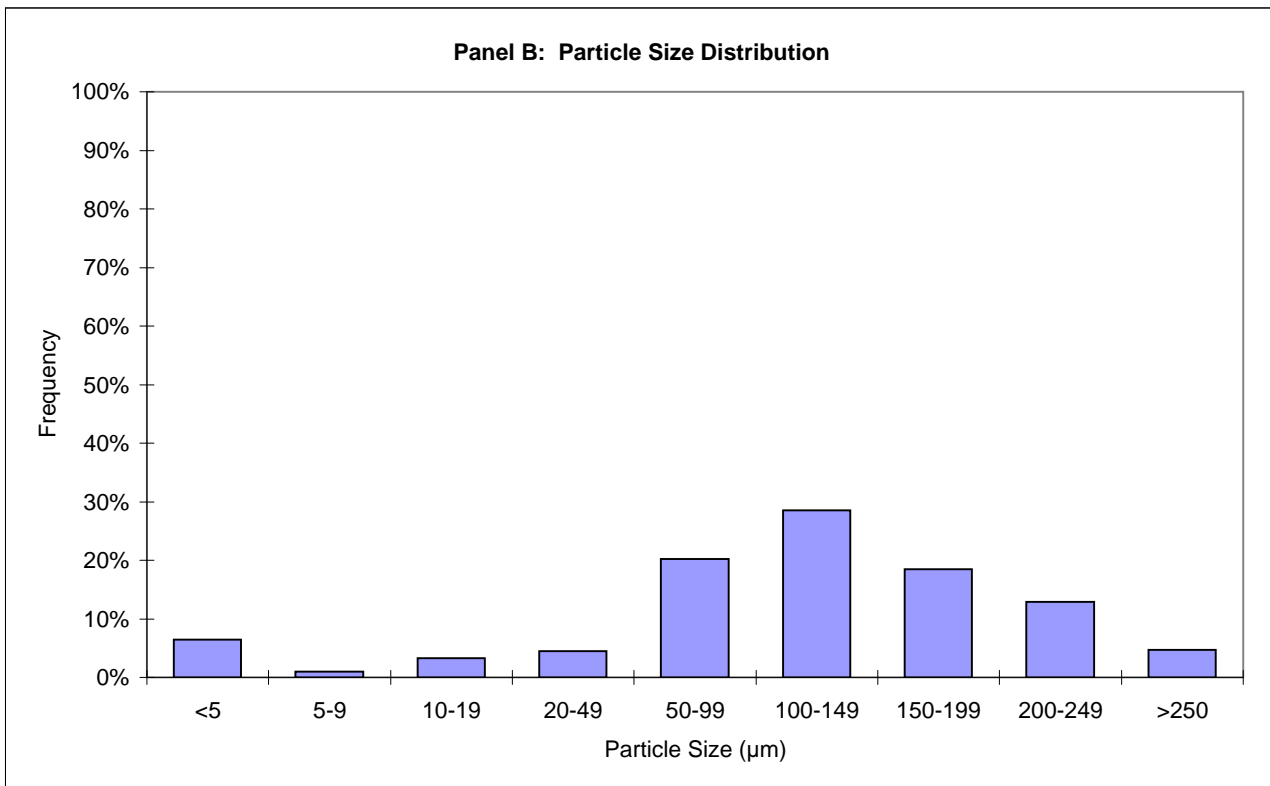
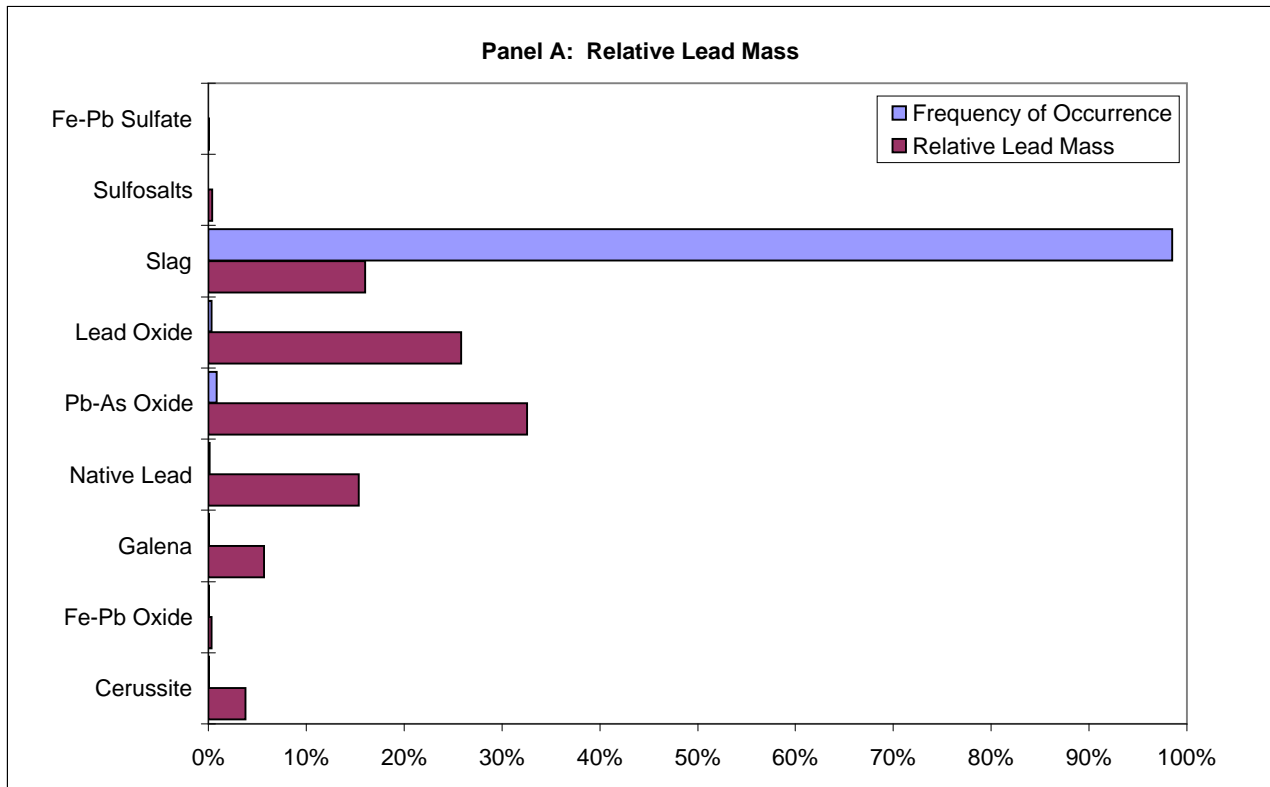
## Particle Size Distribution

Size	Total Freq	Lib Freq	Total RLM	Lib RLM
<5	6.5%	0.1%	8.4%	0.2%
5-9	1.0%	0.5%	3.5%	2.2%
10-19	3.2%	1.8%	17.7%	8.7%
20-49	4.4%	4.1%	33.7%	29.2%
50-99	20.3%	20.3%	17.7%	17.7%
100-149	28.6%	28.6%	9.4%	9.4%
150-199	18.5%	18.5%	4.0%	4.0%
200-249	12.9%	12.9%	3.8%	3.8%
≥250	4.7%	4.7%	1.8%	1.8%
TOTAL	100%	91%	100%	77%



**EXPERIMENT 6 - MIDVALE SLAG**

**Speciation and Particle Size Data**



APPENDIX F

**EXPERIMENT 6 - BUTTE SOIL**

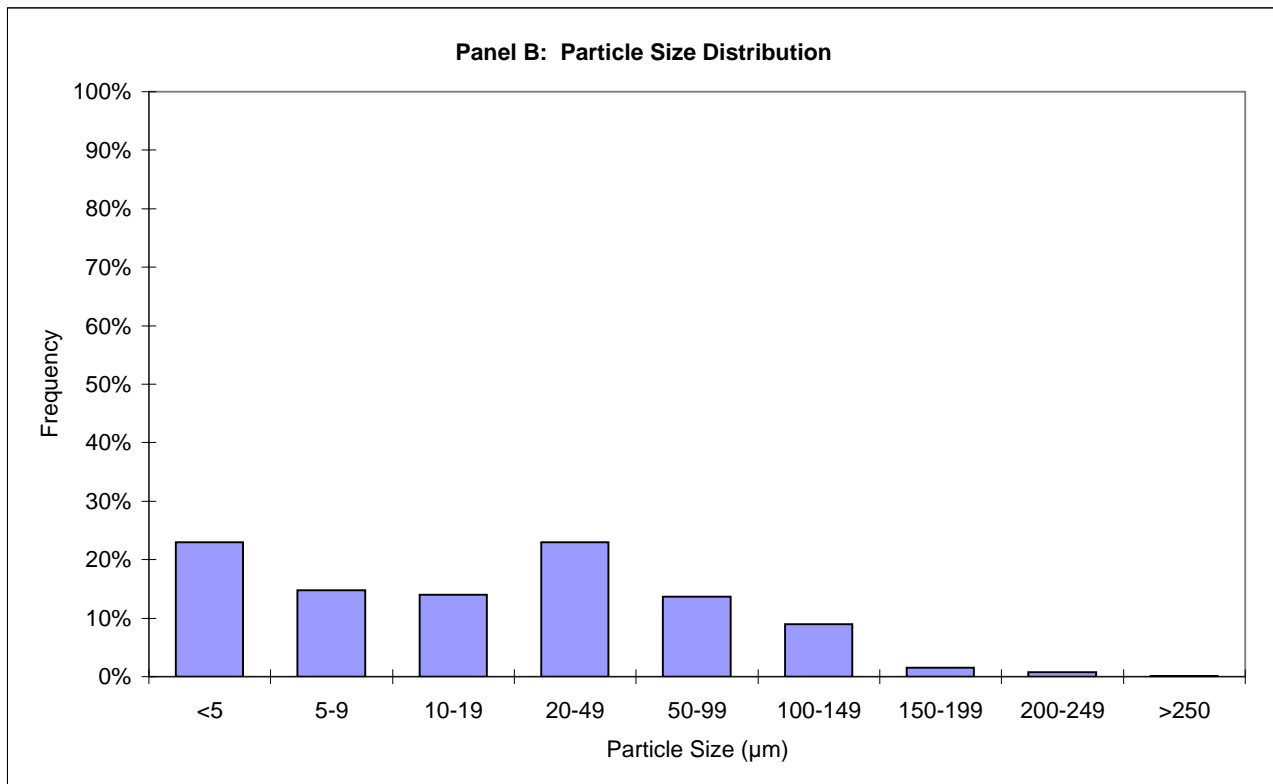
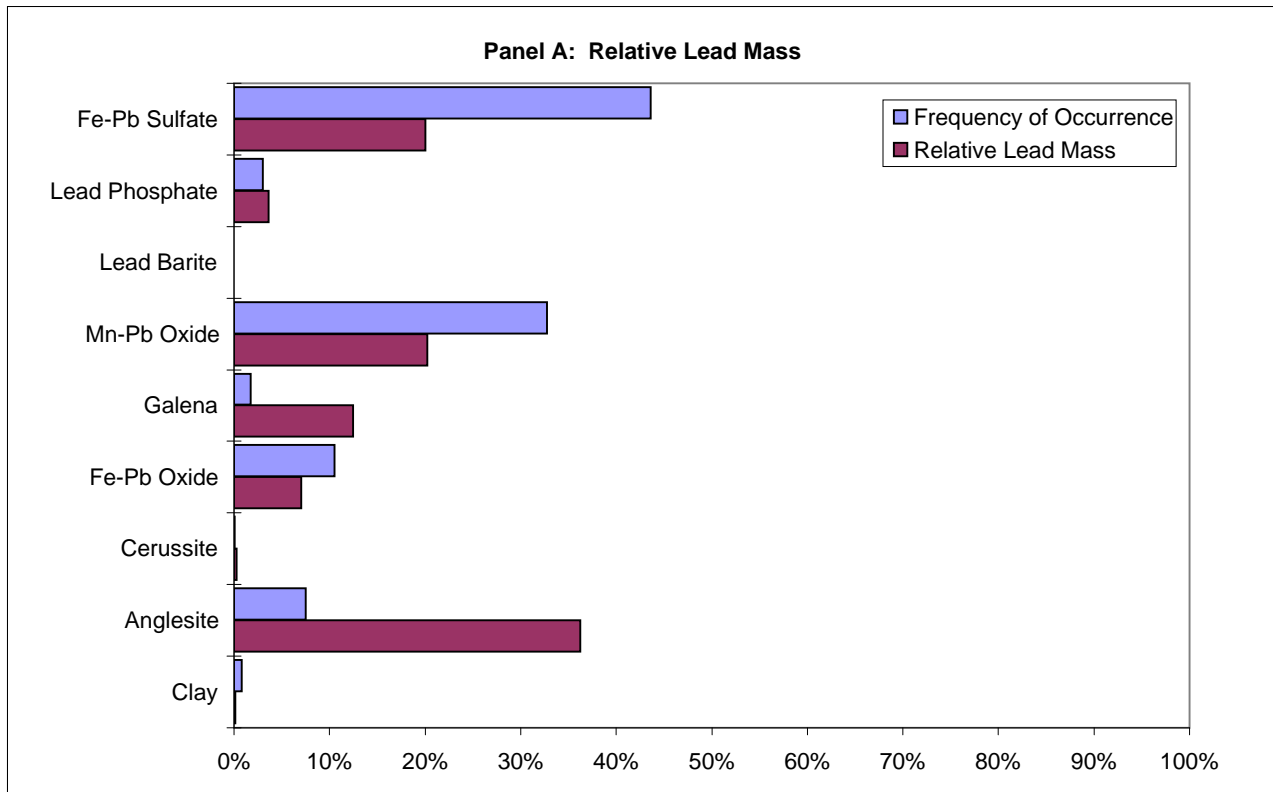
**Lead Speciation Summary Statistics**

Mineral	Counts		Particle Size			Count Freq (%)		LW Freq (%)		Density	Lead Fraction	Relative Lead Mass (%)	
	Total	Lib	Avg	Min	Max	Total	Lib	Total	Lib			Total	Lib
Clay	3	3	58	30	100	0.5%	0.5%	0.82%	0.82%	3.2	0.039	0.1%	0.1%
Anglesite	138	134	12	1	100	21.7%	21.1%	7.51%	7.37%	6.3	0.684	36.2%	35.6%
Cerussite	1	1	10	10	10	0.2%	0.2%	0.05%	0.05%	6.6	0.776	0.3%	0.3%
Fe-Pb Oxide	37	27	61	4	180	5.8%	4.3%	10.48%	8.28%	4	0.15	7.0%	5.6%
Galena	37	35	10	1	55	5.8%	5.5%	1.72%	1.70%	7.5	0.866	12.5%	12.4%
Mn-Pb Oxide	161	150	44	3	200	25.4%	23.6%	32.77%	29.29%	5.1	0.108	20.2%	18.1%
Lead Barite	1	1	5	5	5	0.2%	0.2%	0.02%	0.02%	4.5	0.058	0.0%	0.0%
Lead Phosphate	12	1	54	5	200	1.9%	0.2%	3.03%	0.06%	5.1	0.208	3.6%	0.1%
Fe-Pb Sulfate	245	226	38	2	250	38.6%	35.6%	43.61%	40.55%	3.7	0.111	20.1%	18.6%
<b>TOTAL</b>	<b>635</b>	<b>578</b>	<b>34</b>			<b>100.0%</b>	<b>91.0%</b>	<b>100.00%</b>	<b>88.13%</b>			<b>100.0%</b>	<b>90.7%</b>

**Particle Size Distribution**

Size	Total Freq	Lib Freq	Total RLM	Lib RLM
<5	23.0%	22.2%	3.4%	3.3%
5-9	14.8%	13.2%	9.8%	9.5%
10-19	14.0%	12.4%	11.4%	10.7%
20-49	23.0%	21.7%	26.5%	25.8%
50-99	13.7%	11.3%	25.0%	22.1%
100-149	9.0%	8.0%	17.0%	15.1%
150-199	1.6%	1.4%	2.9%	2.9%
200-249	0.8%	0.5%	3.3%	1.5%
≥250	0.2%	0.2%	0.6%	0.6%
<b>TOTAL</b>	<b>100%</b>	<b>91%</b>	<b>100%</b>	<b>91%</b>

**EXPERIMENT 6 - BUTTE SOIL**  
**Speciation and Particle Size Data**



APPENDIX F

**EXPERIMENT 7 - CALIFORNIA GULCH PHASE I RESIDENTIAL SOIL**

**Lead Speciation Summary Statistics**

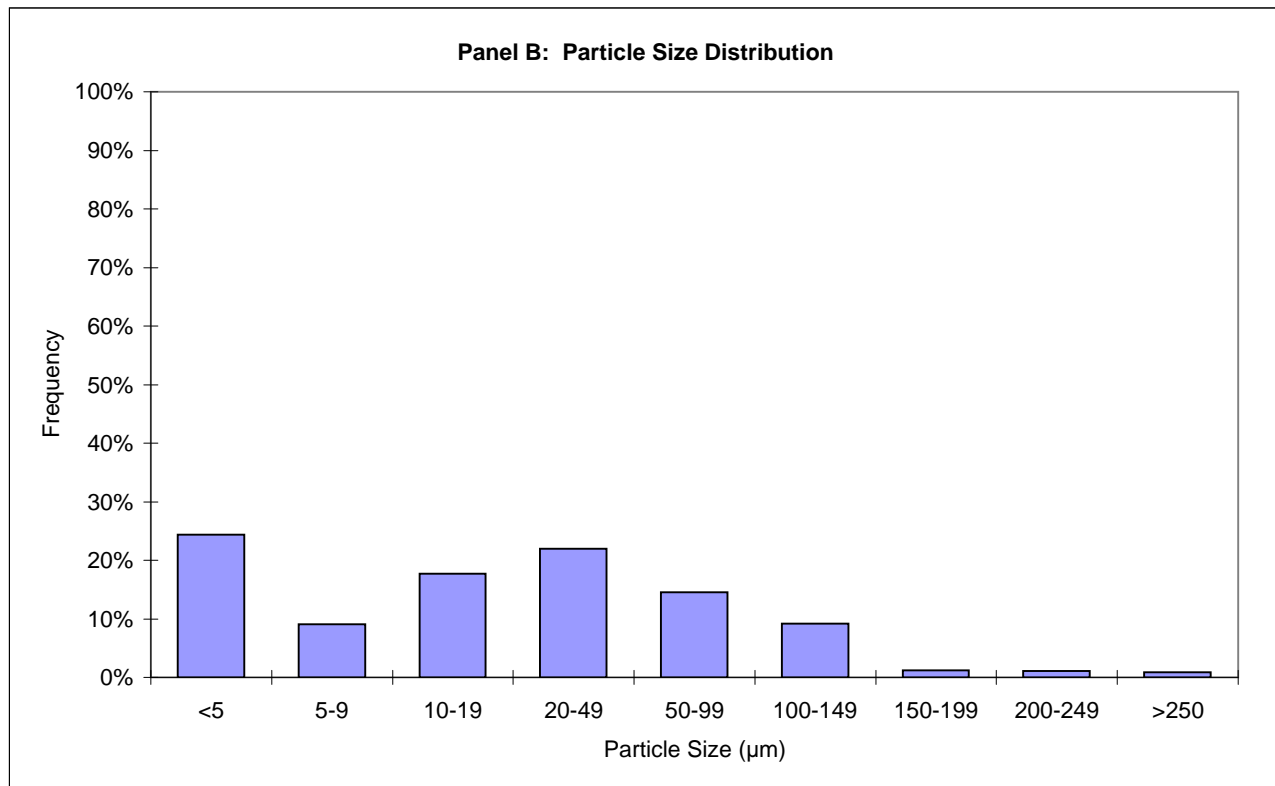
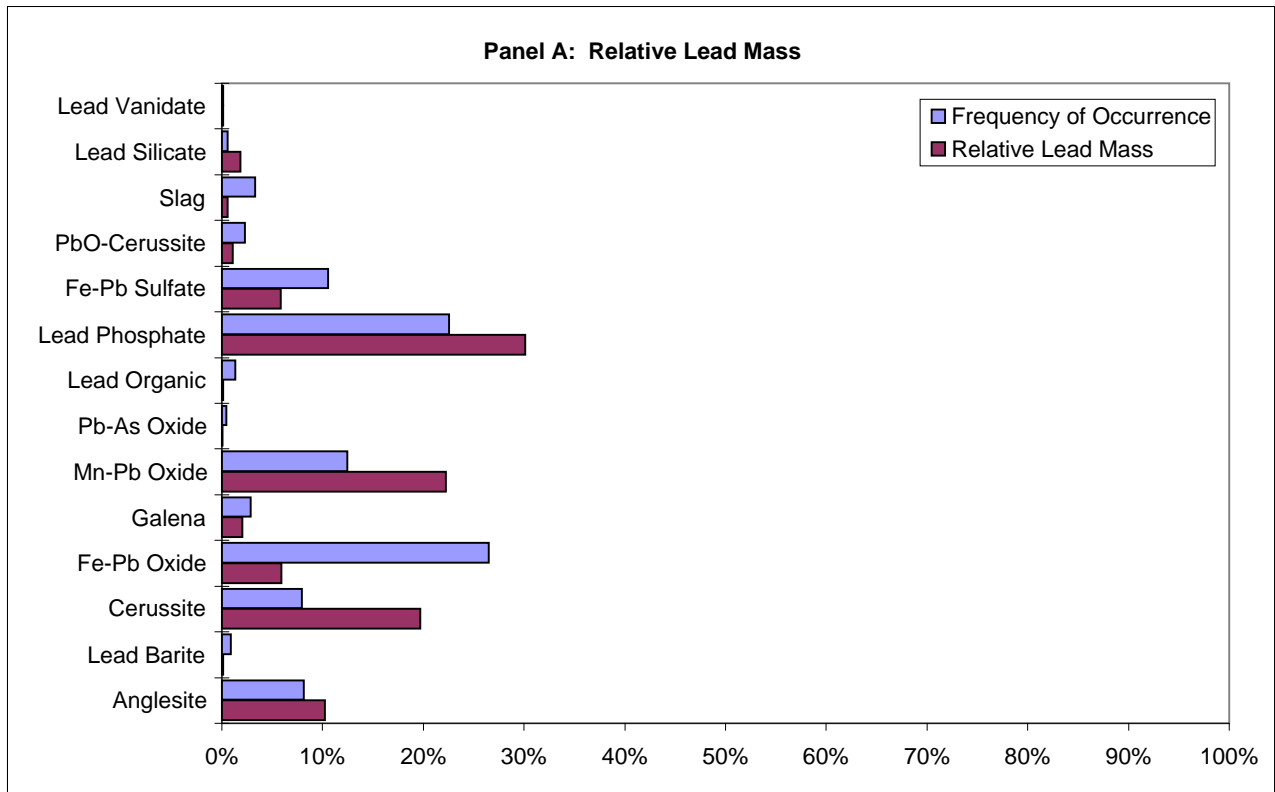
Mineral	Counts		Particle Size			Count Freq (%)		LW Freq (%)		Density	Lead Fraction	Relative Lead Mass (%)	
	Total	Lib	Avg	Min	Max	Total	Lib	Total	Lib			Total	Lib
Anglesite	54	28	9	1	45	8.1%	4.2%	2.02%	1.58%	6.3	0.684	10.2%	8.0%
Cerussite	53	33	14	1	125	8.0%	5.0%	3.28%	3.11%	6.6	0.776	19.7%	18.7%
Fe-Pb Sulfate	70	65	31	1	120	10.5%	9.8%	9.59%	9.56%	3.7	0.14	5.8%	5.8%
Mn-Pb Oxide	83	83	43	1	250	12.5%	12.5%	15.77%	15.77%	5	0.24	22.2%	22.2%
Lead Phosphate	150	115	19	1	150	22.6%	17.3%	12.57%	11.96%	5.1	0.4	30.1%	28.6%
Pb-As Oxide	3	0	3	1	5	0.5%	0.0%	0.04%	0.00%	7.1	0.24	0.1%	0.0%
Lead Barite	6	1	18	2	100	0.9%	0.2%	0.48%	0.44%	4.5	0.058	0.1%	0.1%
Fe-Pb Oxide	176	166	52	1	300	26.5%	25.0%	40.45%	40.40%	4	0.031	5.9%	5.9%
PbO-Cerussite	15	0	3	1	10	2.3%	0.0%	0.18%	0.00%	6.6	0.776	1.1%	0.0%
Lead Organic	9	9	78	20	110	1.4%	1.4%	3.08%	3.08%	1.3	0.023	0.1%	0.1%
Galena	19	0	3	1	10	2.9%	0.0%	0.27%	0.00%	7.5	0.866	2.0%	0.0%
Lead Silicate	4	4	30	10	50	0.6%	0.6%	0.53%	0.53%	6	0.5	1.9%	1.9%
Lead Vanidate	1	1	10	10	10	0.2%	0.2%	0.04%	0.04%	6.4	0.32	0.1%	0.1%
Slag	22	22	121	25	250	3.3%	3.3%	11.71%	11.71%	3.65	0.012	0.6%	0.6%
<b>TOTAL</b>	<b>665</b>	<b>527</b>	<b>34</b>			<b>100.0%</b>	<b>79.2%</b>	<b>100.00%</b>	<b>98.18%</b>			<b>100.0%</b>	<b>92.0%</b>

**Particle Size Distribution**

Size	Total Freq	Lib Freq	Total RLM	Lib RLM
<5	24.4%	8.3%	5.1%	1.7%
5-9	9.0%	5.0%	5.3%	2.0%
10-19	17.7%	17.3%	11.9%	11.2%
20-49	22.0%	22.0%	22.3%	22.3%
50-99	14.6%	14.4%	22.4%	21.7%
100-149	9.2%	9.2%	27.4%	27.4%
150-199	1.2%	1.2%	3.0%	3.0%
200-249	1.1%	1.1%	0.6%	0.6%
≥250	0.9%	0.9%	2.1%	2.1%
<b>TOTAL</b>	<b>100%</b>	<b>79%</b>	<b>100%</b>	<b>92%</b>

**EXPERIMENT 7 - CALIFORNIA GULCH PHASE I RESIDENTIAL SOIL**

**Speciation and Particle Size Data**



APPENDIX F

**EXPERIMENT 7 - CALIFORNIA GULCH Fe/Mn PbO**

**Lead Speciation Summary Statistics**

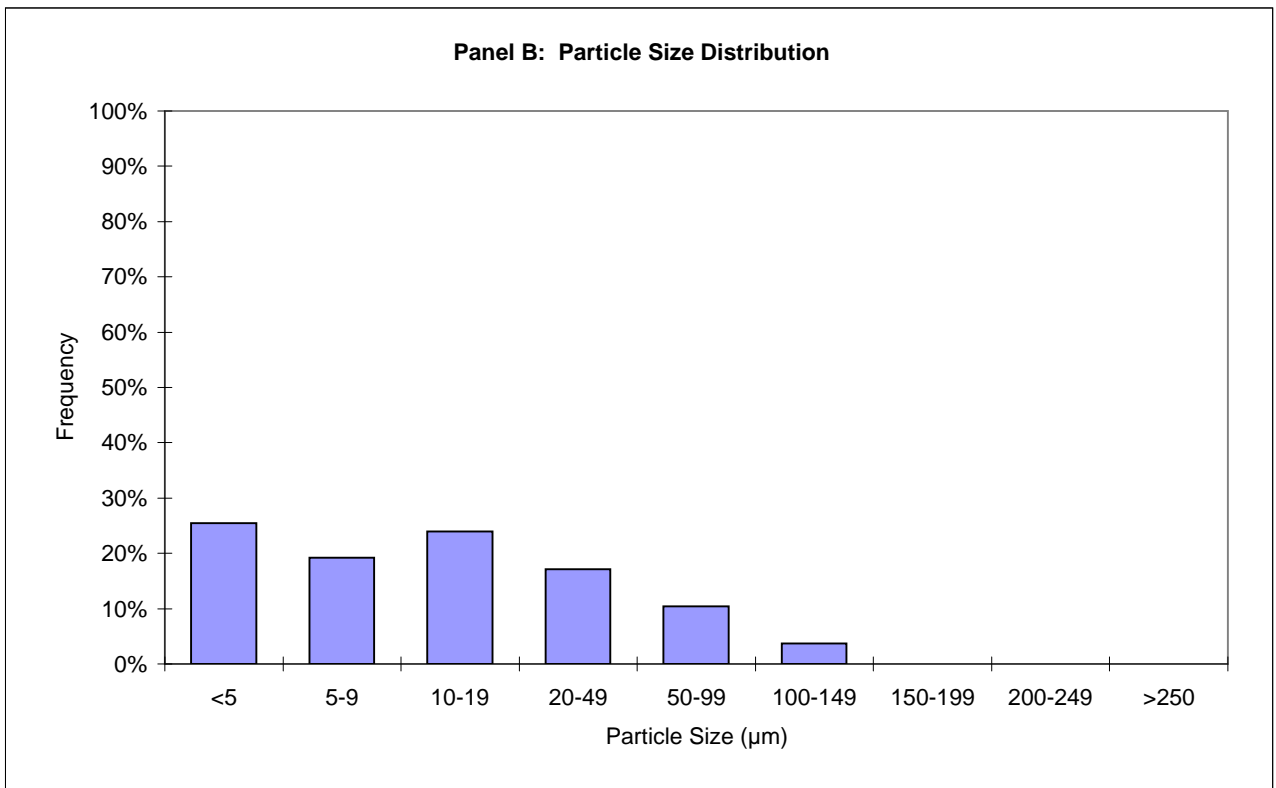
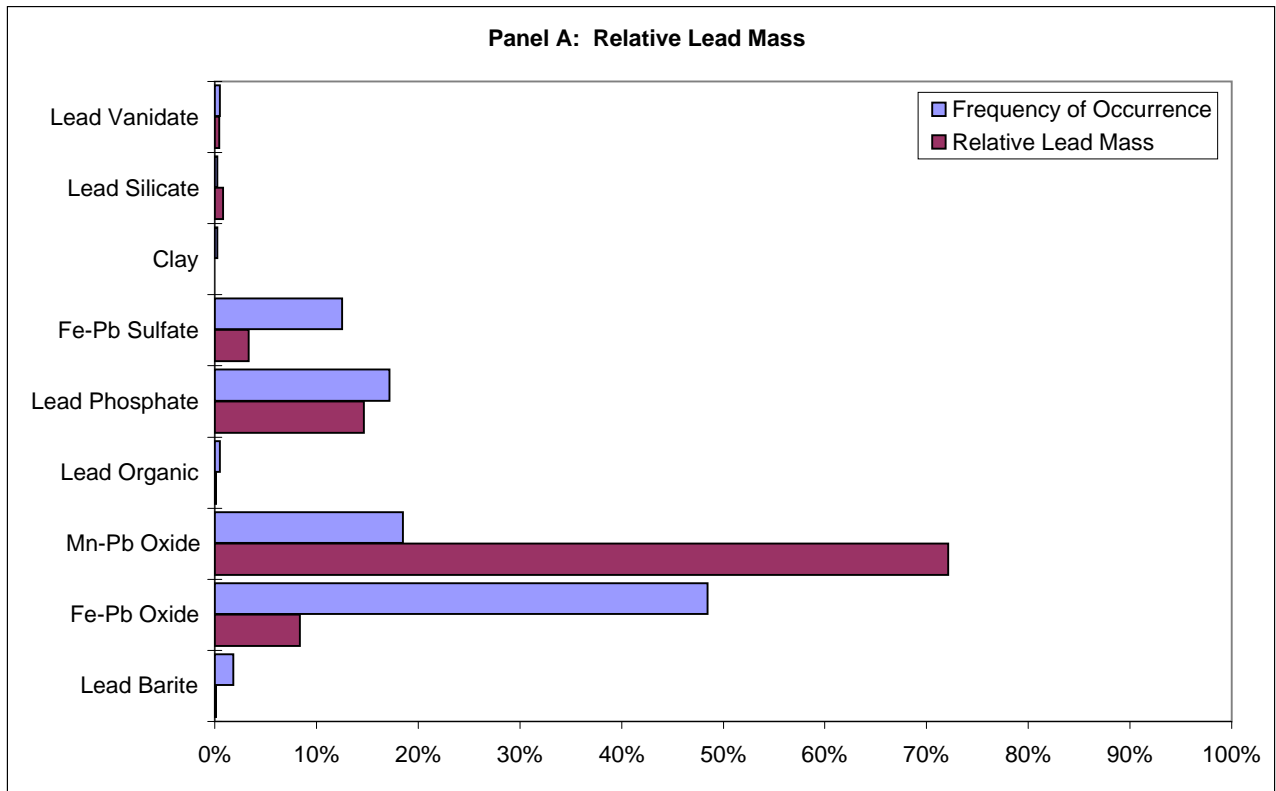
Mineral	Counts		Particle Size			Count Freq (%)		LW Freq (%)		Density	Lead Fraction	Relative Lead Mass (%)	
	Total	Lib	Avg	Min	Max	Total	Lib	Total	Lib			Total	Lib
Lead Barite	7	1	5	2	10	1.8%	0.3%	0.40%	0.10%	4.5	0.05	0.1%	0.0%
Clay	1	1	50	50	50	0.3%	0.3%	0.61%	0.61%	3.1	0.005	0.0%	0.0%
Fe-Pb Oxide	186	186	20	0	130	48.4%	48.4%	44.85%	44.85%	4	0.031	8.4%	8.4%
Mn-Pb Oxide	71	71	45	2	125	18.5%	18.5%	39.14%	39.14%	5.1	0.24	72.1%	72.1%
Lead Organic	2	2	103	80	125	0.5%	0.5%	2.49%	2.49%	1.3	0.0232	0.1%	0.1%
Lead Silicate	1	1	15	15	15	0.3%	0.3%	0.18%	0.18%	6	0.5	0.8%	0.8%
Lead Vanadate	2	2	6	3	8	0.5%	0.5%	0.13%	0.13%	6.4	0.32	0.4%	0.4%
Lead Phosphate	66	64	8	1	60	17.2%	16.7%	6.16%	6.09%	5.1	0.31	14.7%	14.5%
Fe-Pb Sulfate	48	48	10	3	100	12.5%	12.5%	6.03%	6.03%	3.7	0.1	3.4%	3.4%
<b>TOTAL</b>	<b>384</b>	<b>376</b>	<b>21</b>			<b>100.0%</b>	<b>97.9%</b>	<b>100.00%</b>	<b>99.62%</b>			<b>100.0%</b>	<b>99.7%</b>

**Particle Size Distribution**

Size	Total Freq	Lib Freq	Total RLM	Lib RLM
<5	25.5%	24.0%	4.0%	3.8%
5-9	19.3%	19.0%	4.8%	4.7%
10-19	24.0%	23.7%	10.9%	10.8%
20-49	17.2%	17.2%	23.4%	23.4%
50-99	10.4%	10.4%	41.7%	41.7%
100-149	3.6%	3.6%	15.3%	15.3%
150-199	0.0%	0.0%	0.0%	0.0%
200-249	0.0%	0.0%	0.0%	0.0%
≥250	0.0%	0.0%	0.0%	0.0%
<b>TOTAL</b>	<b>100%</b>	<b>98%</b>	<b>100%</b>	<b>99.7%</b>

EXPERIMENT 7 - CALIFORNIA GULCH Fe/Mn PbO

Speciation and Particle Size Data



## APPENDIX F

## EXPERIMENT 8 - CALIFORNIA GULCH AV SLAG

## Lead Speciation Summary Statistics

Mineral	Counts		Particle Size			Count Freq (%)		LW Freq (%)		Density	Lead Fraction	Relative Lead Mass (%)	
	Total	Lib	Avg	Min	Max	Total	Lib	Total	Lib			Total	Lib
Anglesite	3	3	37	30	45	0.2%	0.2%	0.07%	0.07%	6.3	0.684	2.4%	2.4%
Cerussite	3	3	11	8	15	0.2%	0.2%	0.02%	0.02%	6.6	0.776	0.9%	0.9%
Galena	6	1	16	1	80	0.4%	0.1%	0.06%	0.05%	7.5	0.866	3.1%	2.7%
Native Lead	4	1	6	2	15	0.2%	0.1%	0.02%	0.01%	11.34	1	1.4%	0.9%
Pb-As Oxide	253	34	8	1	125	15.6%	2.1%	1.30%	0.90%	6	0.5	30.9%	21.4%
Lead Oxide	139	18	8	1	125	8.6%	1.1%	0.73%	0.59%	9.5	0.930	51.0%	41.5%
Slag	1206	1206	126	5	450	74.5%	74.5%	97.68%	97.68%	3.65	0.0035	9.9%	9.9%
Fe-Pb Sulfate	5	1	37	10	55	0.3%	0.1%	0.12%	0.04%	3.7	0.091	0.3%	0.1%
TOTAL	1619	1267	96			100.0%	78.3%	100.00%	99.36%			100.0%	79.6%

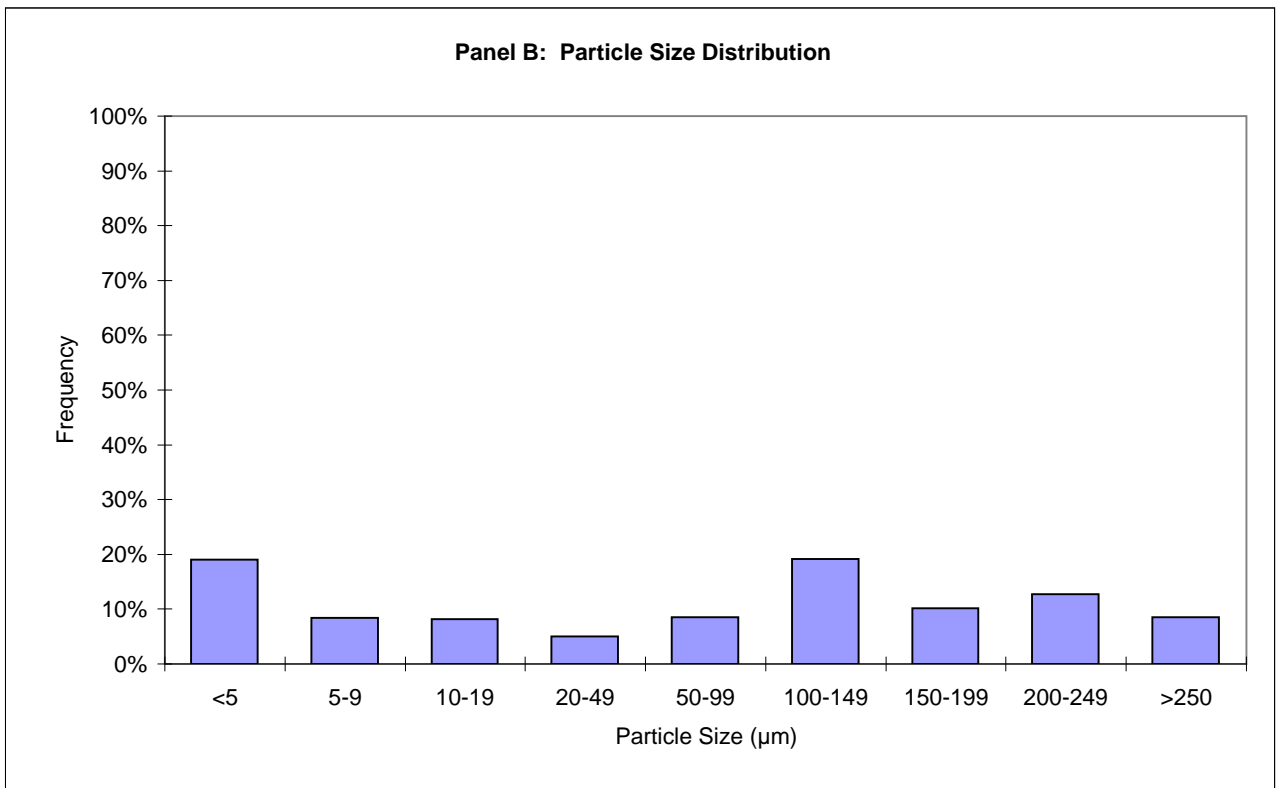
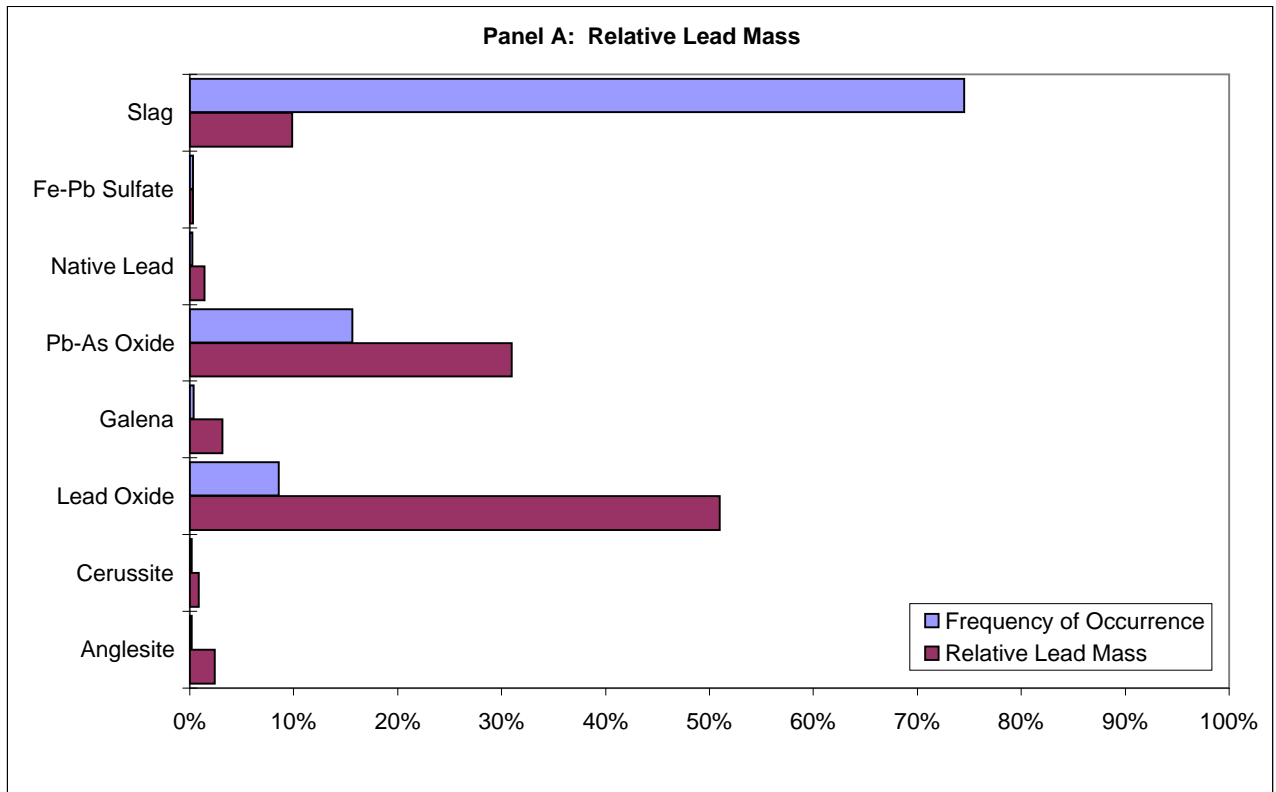
## Particle Size Distribution

Size	Total Freq	Lib Freq	Total RLM	Lib RLM
<5	19.1%	0.1%	11.3%	0.1%
5-9	8.5%	6.9%	4.7%	0.6%
10-19	8.2%	7.4%	6.8%	4.4%
20-49	5.0%	4.6%	23.5%	20.9%
50-99	8.6%	8.6%	24.2%	24.2%
100-149	19.2%	19.2%	22.4%	22.4%
150-199	10.1%	10.1%	1.7%	1.7%
200-249	12.8%	12.8%	2.7%	2.7%
≥250	8.6%	8.6%	2.7%	2.7%
TOTAL	100%	78%	100%	80%



EXPERIMENT 8 - CALIFORNIA GULCH AV SLAG

Speciation and Particle Size Data



APPENDIX F

**EXPERIMENT 9 - PALMERTON LOCATION 2**

**Lead Speciation Summary Statistics**

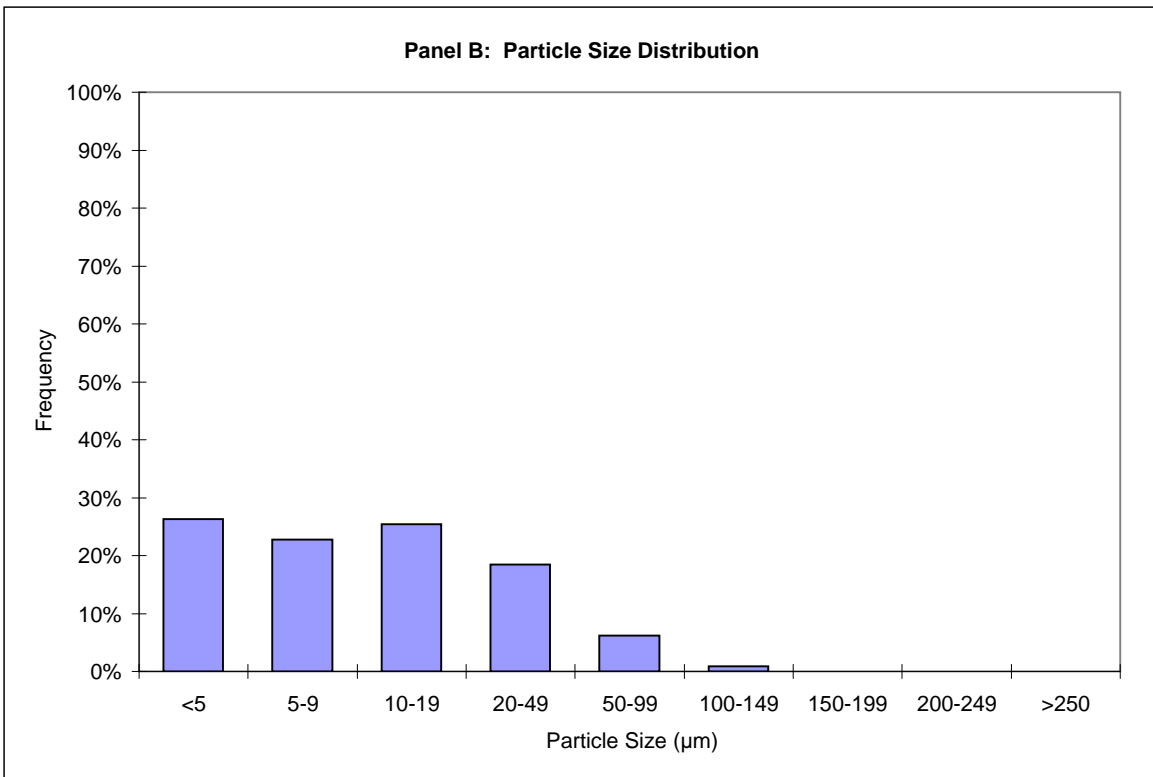
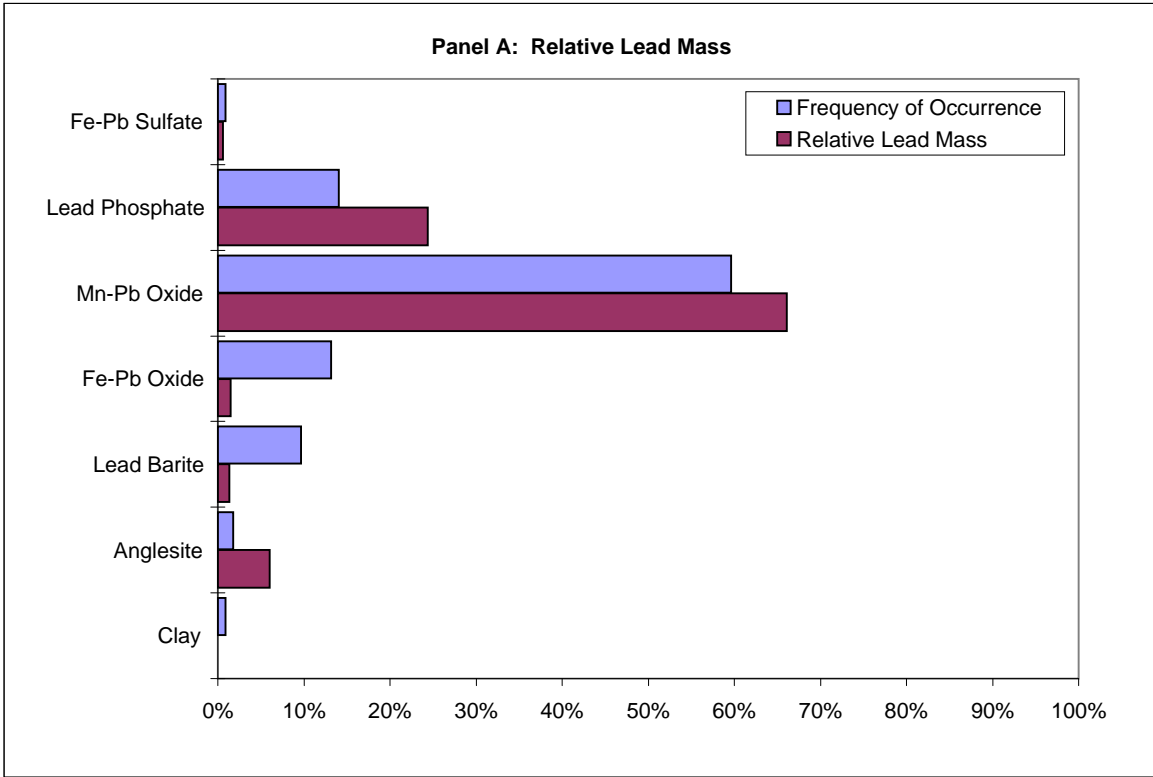
Mineral	Counts		Particle Size			Count Freq (%)		LW Freq (%)		Density	Lead Fraction	Relative Lead Mass (%)	
	Total	Lib	Avg	Min	Max	Total	Lib	Total	Lib			Total	Lib
Clay	1	1	10	10	10	0.9%	0.9%	0.6%	0.6%	3.1	0.005	0.0%	0.0%
Anglesite	2	2	4	3	4	1.8%	1.8%	0.4%	0.4%	6.3	0.684	6.0%	6.0%
Lead Barite	11	11	8	1	41	9.6%	9.6%	5.0%	5.0%	4.5	0.018	1.4%	1.4%
Fe-Pb oxide	15	15	8	3	20	13.2%	13.2%	7.4%	7.4%	4	0.015	1.5%	1.5%
Mn-Pb Oxide	68	68	17	2	100	59.6%	59.6%	68.8%	68.8%	5.1	0.055	66.1%	66.1%
Lead Phosphate	16	16	19	1	45	14.0%	14.0%	17.4%	17.4%	5.1	0.08	24.4%	24.4%
Fe-Pb Sulfate	1	1	8	8	8	0.9%	0.9%	0.5%	0.5%	3.7	0.1	0.6%	0.6%
<b>TOTAL</b>	<b>114</b>	<b>114</b>	<b>11</b>			<b>100.0%</b>	<b>100.0%</b>	<b>100.0%</b>	<b>100.0%</b>			<b>100.0%</b>	<b>100.0%</b>

**Particle Size Distribution**

Size	Total Freq	Lib Freq	Total RLM	Lib RLM
<5	26.3%	26.3%	10.8%	10.8%
5-9	22.8%	22.8%	5.4%	5.4%
10-19	25.4%	25.4%	16.7%	16.7%
20-49	18.4%	18.4%	27.6%	27.6%
50-99	6.1%	6.1%	32.4%	32.4%
100-149	0.9%	0.9%	7.1%	7.1%
150-199	0.0%	0.0%	0.0%	0.0%
200-249	0.0%	0.0%	0.0%	0.0%
≥250	0.0%	0.0%	0.0%	0.0%
<b>TOTAL</b>	<b>100%</b>	<b>100%</b>	<b>100%</b>	<b>100%</b>

EXPERIMENT 9 - PALMERTON LOCATION 2

Speciation and Particle Size Data



APPENDIX F

**EXPERIMENT 9 - PALMERTON LOCATION 4**

**Lead Speciation Summary Statistics**

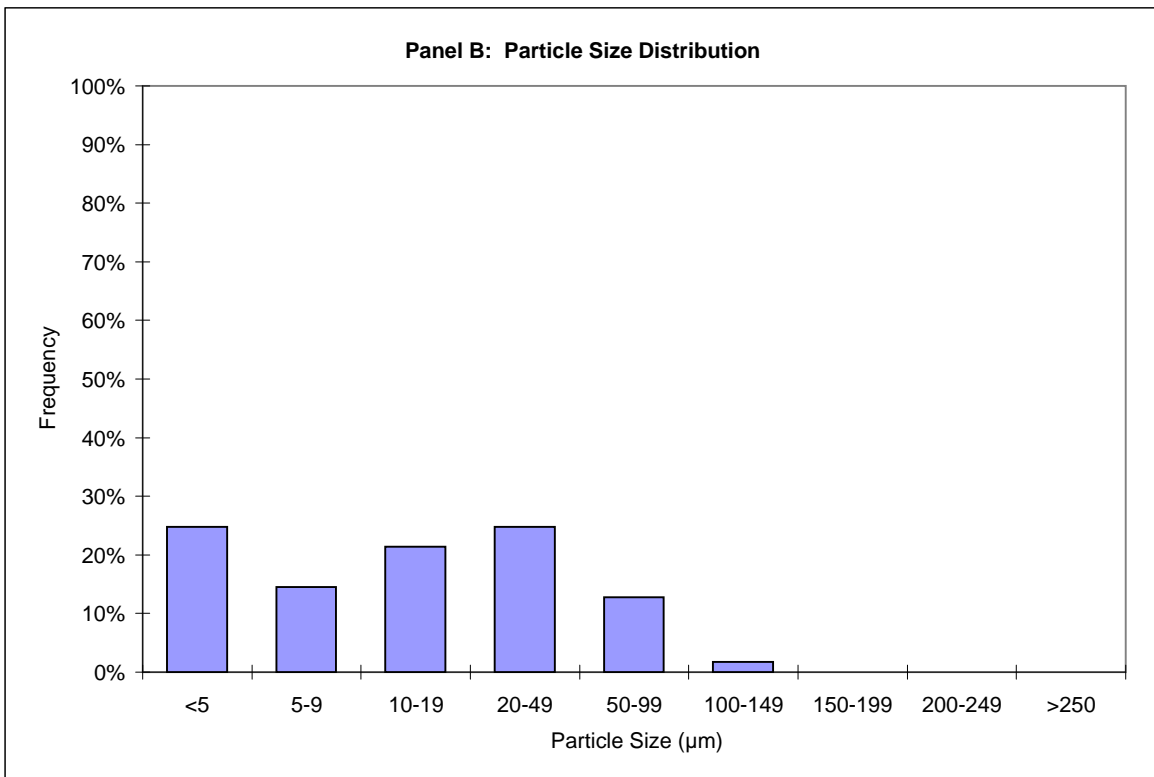
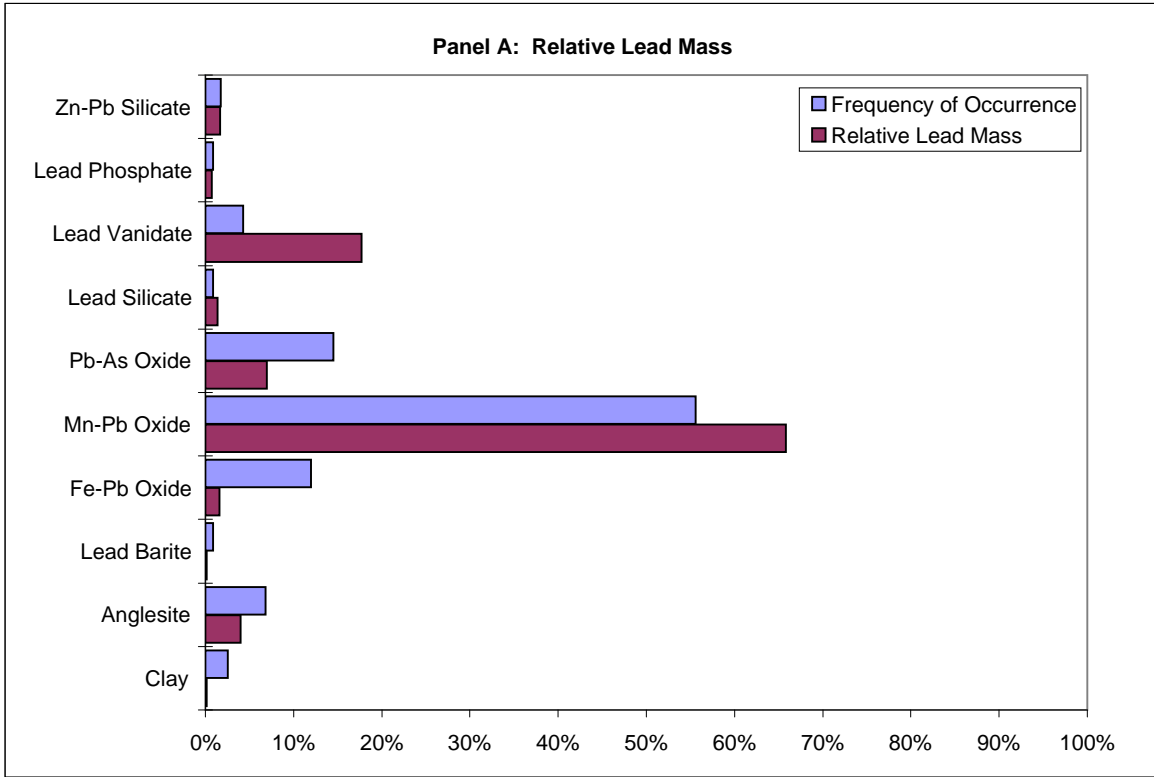
Mineral	Counts		Particle Size			Count Freq (%)		LW Freq (%)		Density	Lead Fraction	Relative Lead Mass (%)	
	Total	Lib	Avg	Min	Max	Total	Lib	Total	Lib			Total	Lib
Clay	3	3	24	8	45	2.6%	2.6%	2.90%	2.90%	3.1	0.005	0.1%	0.1%
Anglesite	8	0	1	1	1	6.8%	0.0%	0.32%	0.00%	6.3	0.684	4.0%	0.0%
Lead Barite	1	1	12	12	12	0.9%	0.9%	0.48%	0.48%	4.5	0.018	0.1%	0.1%
Fe-Pb Oxide	14	14	16	8	40	12.0%	12.0%	9.02%	9.02%	4	0.015	1.6%	1.6%
Mn-Pb Oxide	65	65	31	4	110	55.6%	55.6%	80.82%	80.82%	5.1	0.055	65.8%	65.8%
Pb-As Oxide	17	0	1	1	1	14.5%	0.0%	0.68%	0.00%	7.1	0.5	7.0%	0.0%
Lead Silicate	1	1	4	4	4	0.9%	0.9%	0.16%	0.16%	6	0.5	1.4%	1.4%
Lead Vanadate	5	5	15	5	35	4.3%	4.3%	2.98%	2.98%	6.4	0.32	17.7%	17.7%
Lead Phosphate	1	1	15	15	15	0.9%	0.9%	0.60%	0.60%	5.1	0.08	0.7%	0.7%
Zn-Pb Silicate	2	2	26	12	40	1.7%	1.7%	2.07%	2.07%	5.5	0.05	1.6%	1.6%
<b>TOTAL</b>	<b>117</b>	<b>92</b>	<b>15</b>			<b>100.0%</b>	<b>78.6%</b>	<b>100.0%</b>	<b>99.0%</b>			<b>100.0%</b>	<b>89.1%</b>

**Particle Size Distribution**

Size	Total Freq	Lib Freq	Total RLM	Lib RLM
<5	24.8%	3.4%	12.7%	1.8%
5-9	14.5%	14.5%	5.0%	5.0%
10-19	21.4%	21.4%	8.8%	8.8%
20-49	24.8%	24.8%	34.4%	34.4%
50-99	12.8%	12.8%	32.3%	32.3%
100-149	1.7%	1.7%	6.8%	6.8%
150-199	0.0%	0.0%	0.0%	0.0%
200-249	0.0%	0.0%	0.0%	0.0%
≥250	0.0%	0.0%	0.0%	0.0%
<b>TOTAL</b>	<b>100%</b>	<b>79%</b>	<b>100%</b>	<b>89%</b>

EXPERIMENT 9 - PALMERTON LOCATION 4

Speciation and Particle Size Data



APPENDIX F

**EXPERIMENT 11 - MURRAY SMELTER SOIL**

**Lead Speciation Summary Statistics**

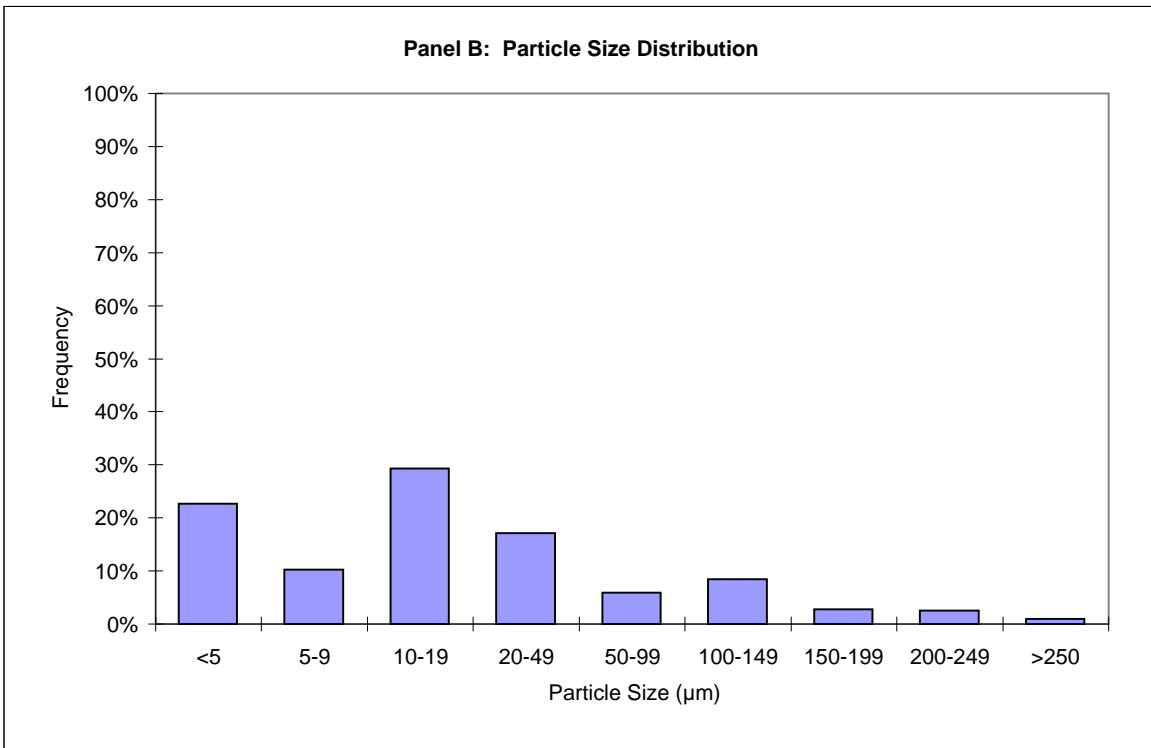
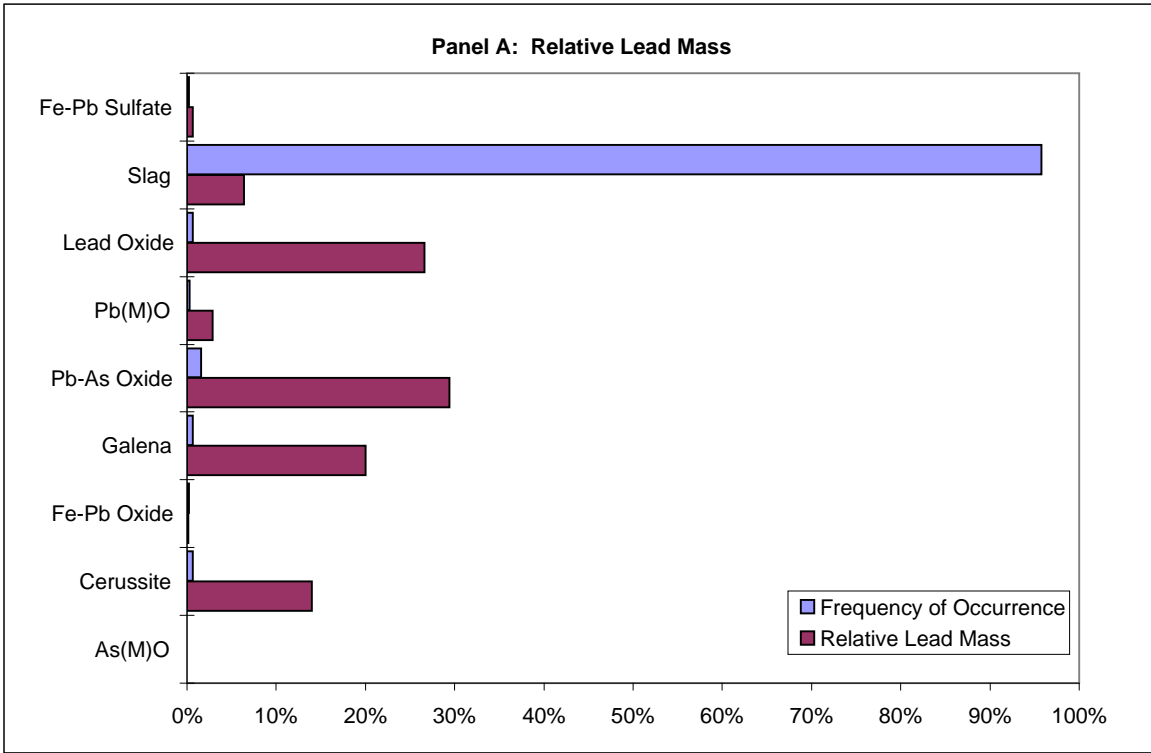
Mineral	Counts		Particle Size			Count Freq (%)		LW Freq (%)		Density	Lead Fraction	Relative Lead Mass (%)	
	Total	Lib	Avg	Min	Max	Total	Lib	Total	Lib			Total	Lib
As(M)O	1	1	3	3	3	0.2%	0.2%	0.02%	0.02%	6.5	0.005	0.0%	0.0%
Cerussite	7	6	14	5	40	1.6%	1.4%	0.66%	0.38%	6.3	0.684	14.0%	8.2%
Fe-Pb Oxide	4	4	8	8	8	0.9%	0.9%	0.22%	0.22%	4	0.031	0.1%	0.1%
Galena	55	1	2	1	30	12.9%	0.2%	0.62%	0.21%	7.5	0.866	20.0%	6.6%
Pb-As Oxide	44	16	5	1	55	10.3%	3.7%	1.59%	1.22%	7.1	0.527	29.4%	22.4%
Pb(M)O	6	4	7	2	15	1.4%	0.9%	0.27%	0.18%	7	0.3	2.8%	1.8%
Lead Oxide	10	8	9	2	25	2.3%	1.9%	0.61%	0.56%	9.5	0.93	26.6%	24.2%
Slag	299	299	47	5	310	70.0%	70.0%	95.76%	95.76%	3.65	0.0037	6.4%	6.4%
Fe-Pb Sulfate	1	1	35	35	35	0.2%	0.2%	0.24%	0.24%	3.7	0.14	0.6%	0.6%
<b>TOTAL</b>	<b>427</b>	<b>340</b>	<b>34</b>			<b>100.0%</b>	<b>79.6%</b>	<b>100.00%</b>	<b>98.78%</b>			<b>100.0%</b>	<b>70.4%</b>

**Particle Size Distribution**

Size	Total Freq	Lib Freq	Total RLM	Lib RLM
<5	22.7%	3.3%	26.5%	5.2%
5-9	10.3%	9.8%	10.6%	8.8%
10-19	29.3%	29.0%	17.6%	16.9%
20-49	17.1%	16.9%	33.4%	27.5%
50-99	5.9%	5.9%	7.8%	7.8%
100-149	8.4%	8.4%	1.8%	1.8%
150-199	2.8%	2.8%	0.8%	0.8%
200-249	2.6%	2.6%	1.0%	1.0%
≥250	0.9%	0.9%	0.5%	0.5%
<b>TOTAL</b>	<b>100%</b>	<b>80%</b>	<b>100%</b>	<b>70%</b>

EXPERIMENT 11 - MURRAY SMELTER SOIL

Speciation and Particle Size Data



\*This mineral is now considered to be equivalent to Fe-Pb Oxid

APPENDIX F

**EXPERIMENT 11 - NIST PAINT**

**Lead Speciation Summary Statistics**

Mineral	Counts		Particle Size			Count Freq (%)		LW Freq (%)		Density	Lead Fraction	Relative Lead Mass (%)	
	Total	Lib	Avg	Min	Max	Total	Lib	Total	Lib			Total	Lib
Anglesite	3	3	7	4	12	1.1%	1.1%	0.87%	0.87%	6.3	0.684	0.6%	0.6%
Cerussite	183	183	9	1	110	66.8%	66.8%	67.80%	67.80%	6.6	0.776	55.3%	55.3%
Lead Oxide	88	88	9	1	80	32.1%	32.1%	31.32%	31.32%	9.5	0.93	44.1%	44.1%
<b>TOTAL</b>	<b>274</b>	<b>274</b>	<b>9</b>			<b>100.0%</b>	<b>100.0%</b>	<b>100.00%</b>	<b>100.00%</b>			<b>100.0%</b>	<b>100.0%</b>

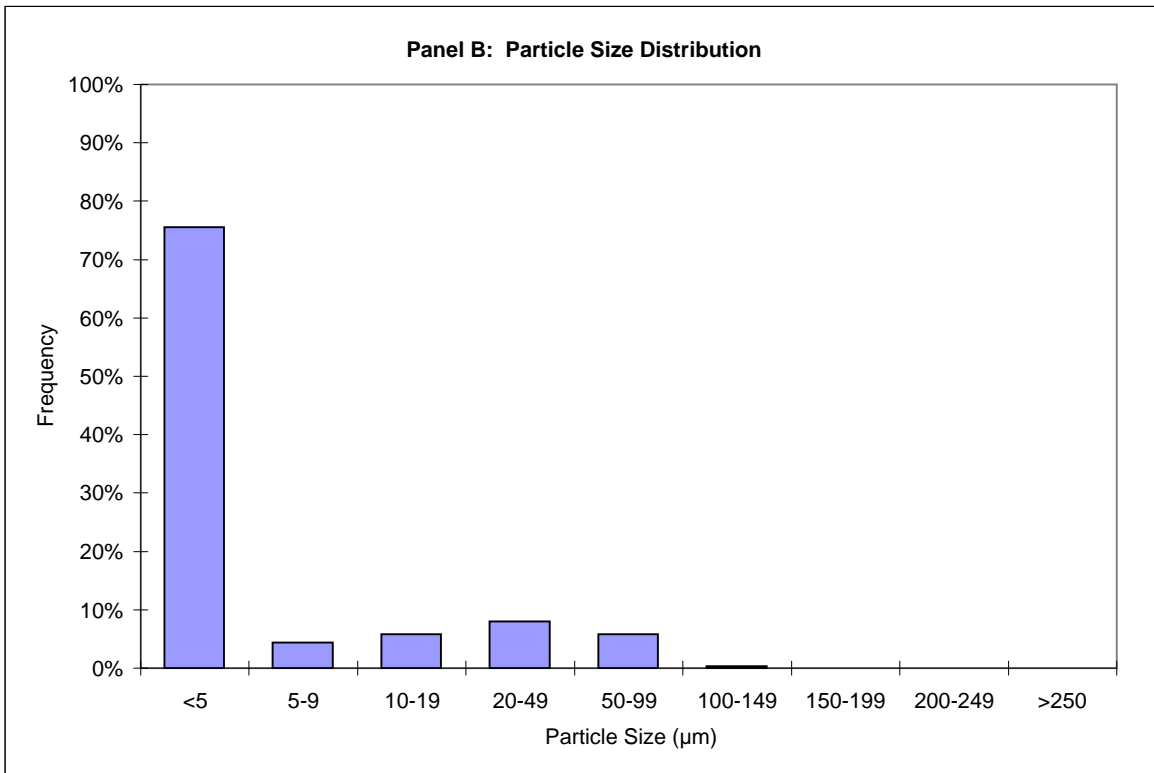
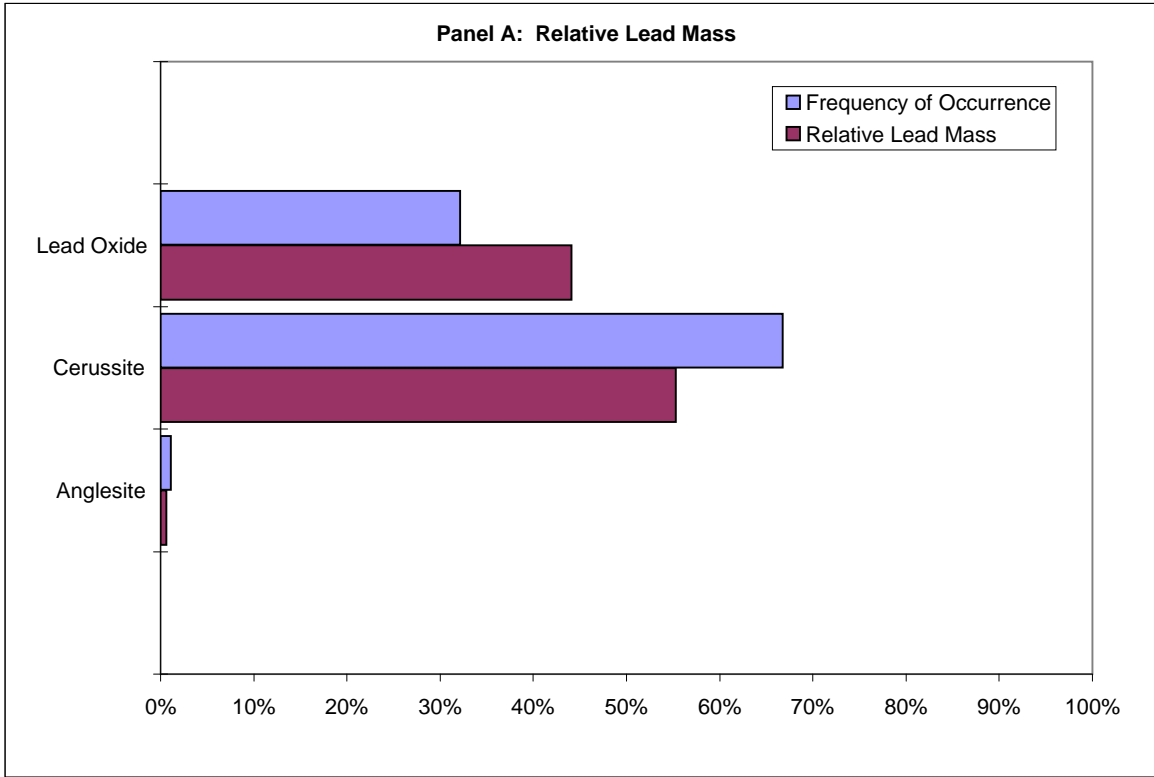
**Particle Size Distribution**

Size	Total Freq	Lib Freq	Total RLM	Lib RLM
<5	75.5%	75.5%	15.0%	15.0%
5-9	4.4%	4.4%	3.1%	3.1%
10-19	5.8%	5.8%	6.4%	6.4%
20-49	8.0%	8.0%	27.8%	27.8%
50-99	5.8%	5.8%	43.9%	43.9%
100-149	0.4%	0.4%	3.7%	3.7%
150-199	0.0%	0.0%	0.0%	0.0%
200-249	0.0%	0.0%	0.0%	0.0%
≥250	0.0%	0.0%	0.0%	0.0%
<b>TOTAL</b>	<b>100%</b>	<b>100%</b>	<b>100%</b>	<b>100%</b>



EXPERIMENT 11 - NIST PAINT

Speciation and Particle Size Data



APPENDIX F

**EXPERIMENT 12 - GALENA-ENRICHED SOIL**

**Lead Speciation Summary Statistics**

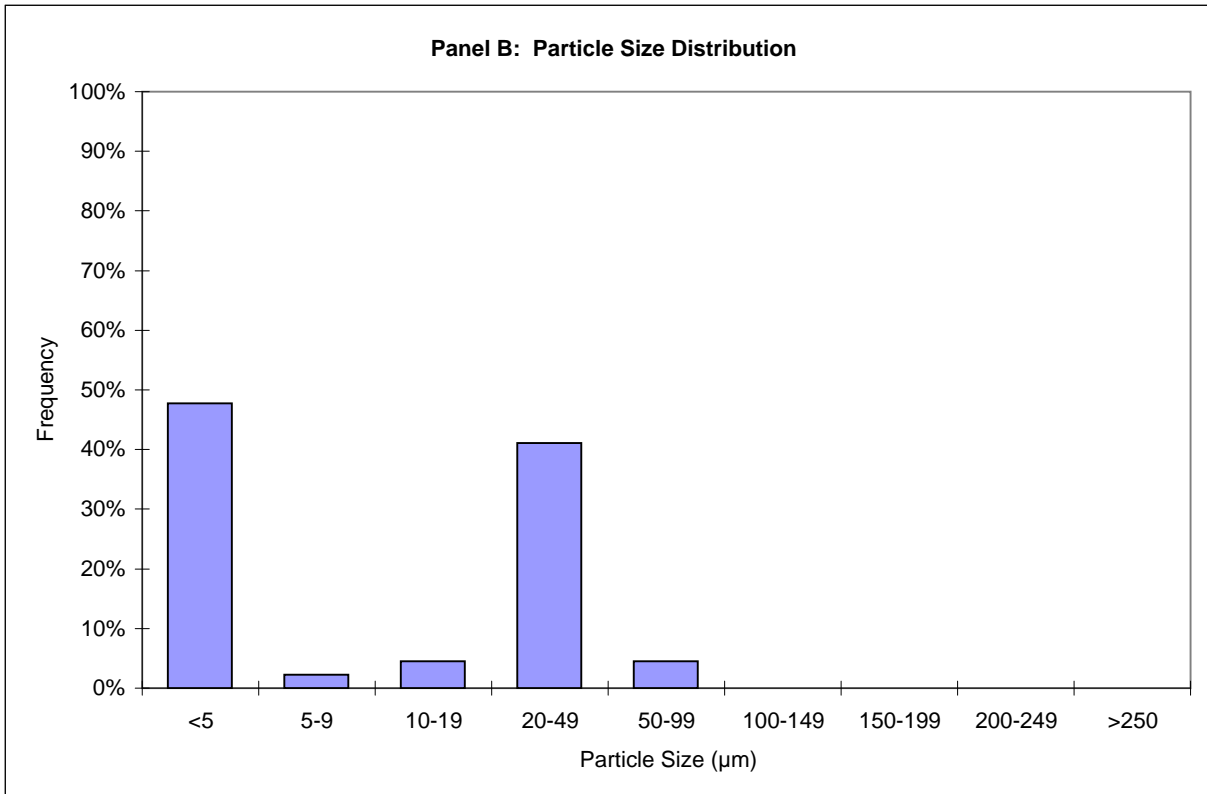
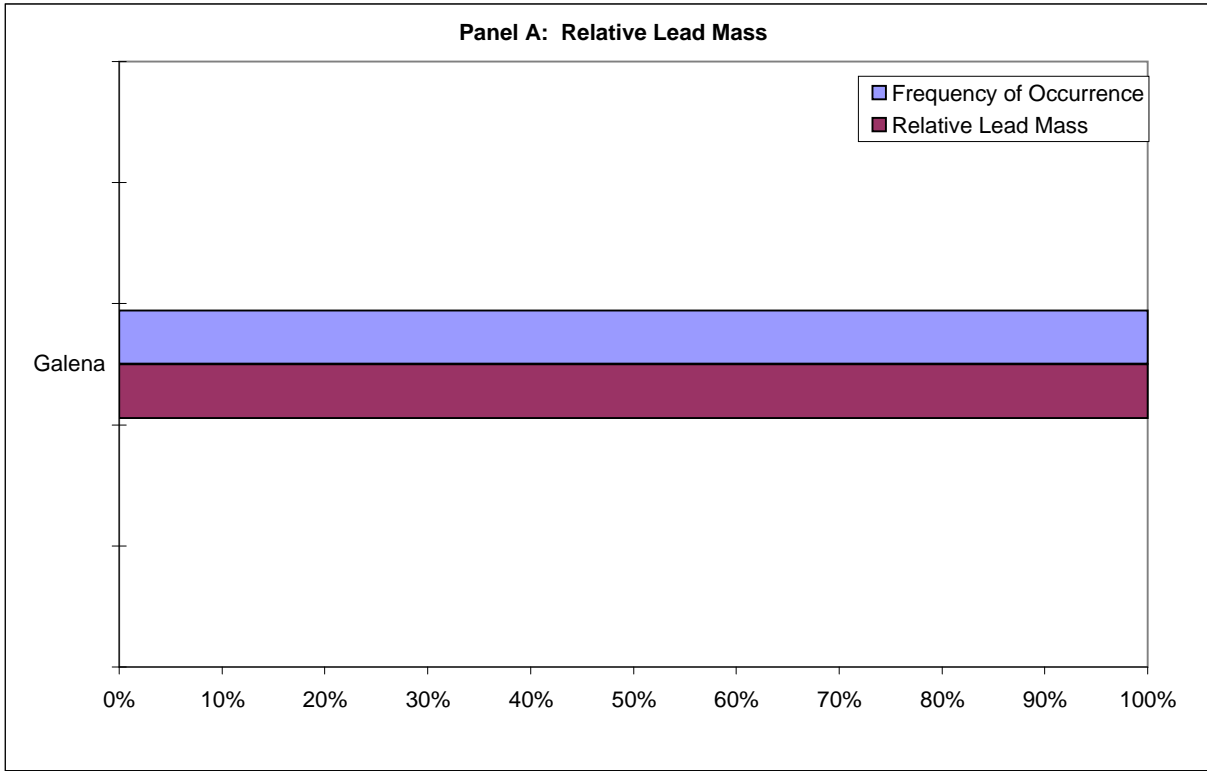
Mineral	Counts		Avg	Particle Size		Count Freq (%)		LW Freq (%)		Density	Lead Fraction	Relative Lead Mass (%)	
	Total	Lib		Min	Max	Total	Lib	Total	Lib			Total	Lib
Galena	224	224	17	1	80	100.0%	100.0%	100.00%	100.00%	7.5	0.866	100.0%	100.0%
TOTAL	224	224	17			100.0%	100.0%	100.00%	100.00%			100.0%	100.0%

**Particle Size Distribution**

Size	Total Freq	Lib Freq	Total RLM	Lib RLM
<5	47.8%	47.8%	4.9%	4.9%
5-9	2.2%	2.2%	0.7%	0.7%
10-19	4.5%	4.5%	3.3%	3.3%
20-49	41.1%	41.1%	75.9%	75.9%
50-99	4.5%	4.5%	15.3%	15.3%
100-149	0.0%	0.0%	0.0%	0.0%
150-199	0.0%	0.0%	0.0%	0.0%
200-249	0.0%	0.0%	0.0%	0.0%
≥250	0.0%	0.0%	0.0%	0.0%
TOTAL	100%	100%	100%	100%

### EXPERIMENT 12 - GALENA-ENRICHED SOIL

#### Speciation and Particle Size Data



APPENDIX F

**EXPERIMENT 12 - CALIFORNIA GULCH OREGON GULCH TAILINGS**

**Lead Speciation Summary Statistics**

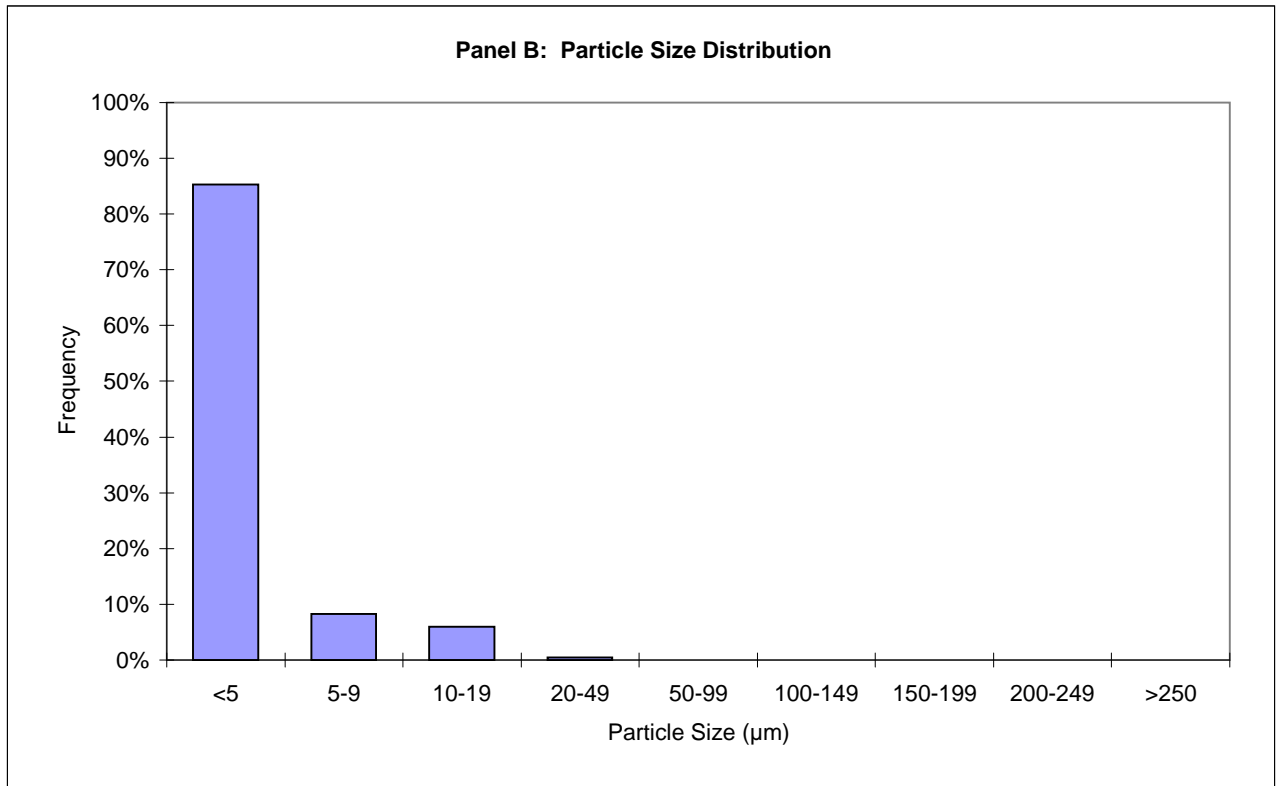
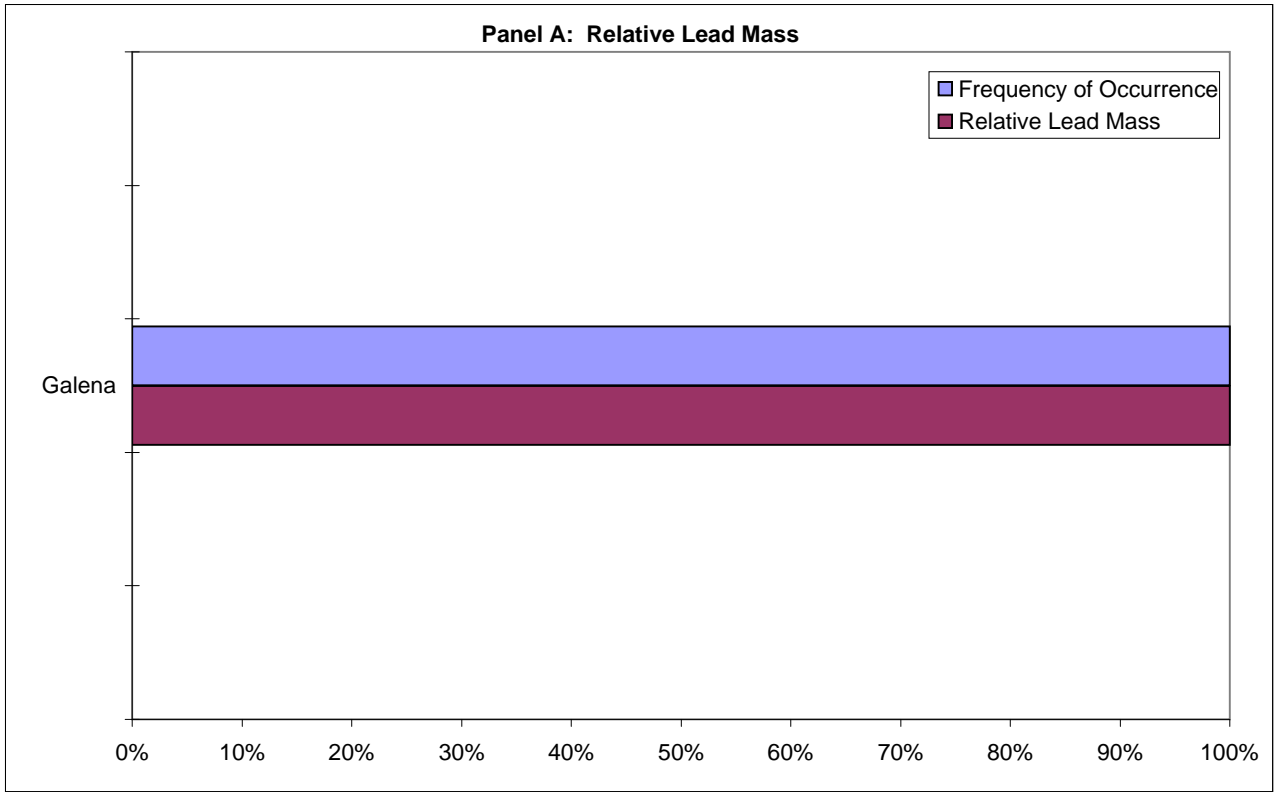
Mineral	Counts		Avg	Particle Size		Count Freq (%)		LW Freq (%)		Density	Lead Fraction	Relative Lead Mass (%)	
	Total	Lib		Min	Max	Total	Lib	Total	Lib			Total	Lib
Galena	217	4	2	1	25	100.0%	1.8%	100.00%	5.14%	7.5	0.866	100.0%	5.1%
TOTAL	217	4	2			100.0%	1.8%	100.00%	5.14%			100.0%	5.1%

**Particle Size Distribution**

Size	Total Freq	Lib Freq	Total RLM	Lib RLM
<5	85.3%	0.9%	46.8%	1.2%
5-9	8.3%	0.0%	21.5%	0.0%
10-19	6.0%	0.9%	26.7%	4.0%
20-49	0.5%	0.0%	4.9%	0.0%
50-99	0.0%	0.0%	0.0%	0.0%
100-149	0.0%	0.0%	0.0%	0.0%
150-199	0.0%	0.0%	0.0%	0.0%
200-249	0.0%	0.0%	0.0%	0.0%
≥250	0.0%	0.0%	0.0%	0.0%
TOTAL	100%	2%	100%	5%

### EXPERIMENT 12 - CALIFORNIA GULCH OREGON GULCH TAILINGS

#### Speciation and Particle Size Data



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