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RELATIVE BIOAVAILABILITY OF ARSENIC IN BARBER ORCHARD SOILS

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EXECUTIVE SUMMARY

A study using juvenile swine as test animals was performed to measure the gastrointestinal absorption of arsenic from four Barber Orchard soil samples. The soil samples are identified as MS-1, MS-4, MS-5 and MS-8. The soil samples were collected from the Barber Orchard site located near Waynesville, Haywood County, NC. The property was used as a commercial apple orchard from 1903 until the mid-1980s. In 1999, elevated concentrations of arsenic, lead and organic pesticides were found in the soil.

The relative oral bioavailability of arsenic was assessed by comparing the absorption of arsenic from the Barber Orchard soils ("test materials") to that of sodium arsenate. Groups of four swine were given oral doses of sodium arsenate or the test material twice a day for 14 days. Groups of two or three non-treated swine served as a control.

The amount of arsenic absorbed by each animal was evaluated by measuring the amount of arsenic excreted in the urine (collected over 48-hour periods beginning on days 6, 9, and 12). The urinary excretion fraction (UEF) is the ratio of the amount excreted per 48 hours divided by the dose given per 48 hours. UEF was calculated for both test materials and sodium arsenate using simultaneous weighted linear regression. The relative bioavailability (RBA) of arsenic in each test material compared to sodium arsenate was calculated as follows:

$$RBA = \frac{UEF(test\ soil)}{UEF(sodium\ arsenate)}$$

Estimated RBA values (mean and 90% confidence interval) are shown below:

Time Interval	MS-1 Estimated RBA	MS-4 Estimated RBA	MS-5 Estimated RBA	MS-8 Estimated RBA
Days 6/7	0.38 (0.24 - 0.58)	0.43 (0.39 - 0.48)	0.62 (0.46 - 0.85)	0.53 (0.48 - 0.59)
Days 9/10	0.31 (0.20 - 0.45)	0.40 (0.36 - 0.45)	0.39 (0.29 - 0.53)	0.53 (0.47 - 0.59)
Days 12/13	0.27 (0.18 - 0.37)	0.39 (0.33 - 0.46)	0.44 (0.35 - 0.56)	0.53 (0.45 - 0.62)
All Days	0.31 (0.25 - 0.38)	0.41 (0.38 - 0.44)	0.49 (0.42 - 0.57)	0.53 (0.49 - 0.57)

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ACRONYMS AND ABBREVIATIONS

ABA	Absolute bioavailability
AF_o	Oral absorption fraction
As+3	Trivalent inorganic arsenic
As+5	Pentavalent inorganic arsenic
DMA	Dimethyl arsenic
D	Ingested dose
g	Gram
GLP	Good Laboratory Practices
kg	Kilogram
K_u	Fraction of absorbed arsenic which is excreted in urine
mL	Milliliter
MMA	Monomethyl arsenic
N	Number of data points
NaAs	Sodium arsenate
NIST	National Institute of Standards and Technology
NRCC	National Research Council of Canada
QC	Quality control
RBA	Relative bioavailability
ref	Reference material
RfD	Reference dose
SD	Standard deviation
SF	Slope factor
SRM	Standard reference material
TM	Test material
UEF	Urinary excretion fraction
USEPA	United States Environmental Protection Agency
µg	Microgram
µm	Micrometer
°C	Degrees Celsius

1.0 INTRODUCTION

1.1 Overview of Bioavailability

Reliable analysis of the potential hazard to humans from ingestion of a chemical depends upon accurate information on a number of key parameters, including the concentration of the chemical in environmental media (e.g., soil, dust, water, food, air, paint), intake rates of each medium, and the rate and extent of absorption ("bioavailability") of the chemical by the body from each ingested medium. The amount of a chemical that actually enters the body from an ingested medium depends on the physical-chemical properties of the chemical and of the medium. For example, some metals 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 influence (usually decrease) the absorption (bioavailability) of the metals when ingested. Thus, equal ingested doses of different forms of a chemical in different media may not be of equal health concern.

Bioavailability of a chemical 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 the chemical absorbed to the amount ingested:

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

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

Relative bioavailability (RBA) is the ratio of the AF_o of the chemical present in some test material (*test*) to the AF_o of the chemical in some appropriate reference material (e.g., either the chemical dissolved in water or a solid form that is expected to fully dissolve in the stomach) (*ref*):

$$RBA(test\ vs\ ref) = \frac{AF_o(test)}{AF_o(ref)}$$

For example, if 100 micrograms (µg) of a chemical (e.g., arsenic) dissolved in drinking water were ingested and a total of 50 µg were absorbed into the body, the AF_o would be 50/100, or 0.50 (50%). Likewise, if 100 µg of a chemical contained in soil were ingested and 30 µg were absorbed into the body, the AF_o for this chemical in soil would be 30/100, or 0.30 (30%). If the chemical dissolved in water were used as the frame of reference for describing the relative amount of the same chemical 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), and/or Klaassen et al. (1996).

1.2 Using RBA Data to Improve Risk Calculations

When reliable data are available on the relative bioavailability (RBA) of a chemical in a site medium (e.g., soil), the information can be used to improve the accuracy of exposure and risk calculations at that site. RBA data can be used to adjust default oral toxicity values (reference dose and slope factor) to account for differences in absorption between the chemical ingested in water and the chemical ingested in site media, assuming the toxicity factors are based on a readily soluble form of the chemical. For non-cancer effects, the default reference dose ($RfD_{default}$) can be adjusted ($RfD_{adjusted}$) as follows:

$$RfD_{adjusted} = \frac{RfD_{default}}{RBA}$$

For potential carcinogenic effects, the default slope factor ($SF_{default}$) can be adjusted ($SF_{adjusted}$) as follows:

$$SF_{adjusted} = SF_{default} \cdot RBA$$

Alternatively, it is also acceptable to adjust the dose (rather than the toxicity factors) as follows:

$$Dose_{adjusted} = Dose_{default} \cdot RBA$$

This dose adjustment is mathematically equivalent to adjusting the toxicity factors as described above.

1.3 Purpose of this Study

The objective of this study was to use juvenile swine as a test system in order to determine the RBA of arsenic in Barber Orchard soil samples compared to a soluble form of arsenic (sodium arsenate).

2.0 STUDY DESIGN

Test materials and a reference material (sodium arsenate, NaAs) were administered to groups of juvenile swine at two or three different dose levels for 14 days. Due to space constraints of the animal laboratory, the test materials were evaluated in three separate studies: (1) Study 1 (MS-1 test material); (2) Study 2 (MS-5 test material); and (3) Study 3 (MS-4 and MS-8 test materials).

Each study evaluated one or two test materials and a reference material, and included a non-treated group of two or three animals to serve as a control for determining background arsenic levels. The design for each of the studies is presented in Table 2-1. All doses were administered orally.

The study was performed as nearly as possible within the spirit and guidelines of Good Laboratory Practices (GLP: 40 CFR 792).

2.1 Test Materials

2.1.1 Sample Description

The test materials used in these investigations included Barber Orchard soil samples MS-1, MS-4, MS-5 and MS-8. The samples were collected from the Barber Orchard site located near Waynesville, Haywood County, NC. The property was used as a commercial apple orchard from 1903 until the mid-1980s. In the late 1980s, some of the land was parceled off and sold for residential properties, church properties, and commercial or light industrial property. The majority of the remaining acreage is slated for residential development. In 1999, elevated concentrations of arsenic, lead and organic pesticides were found in the soil.

2.1.2 Sample Preparation and Analysis

USEPA Region 4 collected the soil from the Barber Orchard site. The soil was placed in a large stainless steel mixing bowl and then homogenized. Homogenized soil was then shipped to USEPA's Office of Research and Development, National Exposure Research Laboratory (NERL) for processing. Soil was spread out in drying trays, placed in an air-drying oven and dried for about 4 days at <40 ºC. The soil was then added to a vibrating 2 mm stainless steel sieve screen to remove plant material, rocks and large chunks of aggregated soil. Material remaining on the screen was deaggregated and rescreened.

Bulk soil samples (unsieved) were measured at USEPA's laboratory in Athens, GA by inductively coupled plasma mass spectrometry (ICP-MS) following method EPA 200.8. Subsamples were then sieved to <250 µm by the Florida Department of Environmental Protection (FDEP) laboratory in Tallahassee, FL, prepared following method EPA 3050B, and analyzed following method EPA 6020. Total arsenic concentration in the unsieved and <250-µm sieved test materials are:

Sample Type	MS-1	MS-4	MS-5	MS-8
Bulk soil[1]	280 ppm	300 ppm	370 ppm	310 ppm
Sieved soil[2]	290 ppm	388 ppm	382 ppm	364 ppm

[1] Measured before sieving by EPA lab in Athens, GA. EPA method 200.8 was used for sample analysis.
[2] Measured on sieved (<250 µm) fractions by the FDEP lab. EPA method 3050B was used for sample preparation, and EPA Method 6020 (similar to EPA method 200.8) was used for sample analysis.

The sieved soil concentrations were used to calculate doses in these swine RBA studies.

X-ray absorption spectroscopy was conducted on the test materials to characterize the arsenic mineralogy (Miller and Scheckel, 2012).

2.2 Experimental Animals

Juvenile swine were selected for use because they are considered to be a good physiological model for gastrointestinal absorption in children (Weis and LaVelle, 1991; Casteel et al., 1996). The animals were intact males of the Pig Improvement Corporation genetically defined Line 26, and were purchased from Chinn Farms, Clarence, Missouri.

The number of animals purchased for each study was several more than required by the protocol. These animals were purchased at an age of about 5-6 weeks (weaning occurs at age 3 weeks) and housed in individual stainless steel cages. The animals were then held under quarantine for one week to observe their health before beginning exposure to dosing materials. Each animal was examined by a certified veterinary clinician (swine specialist) and any animals that appeared to be in poor health during this quarantine period were excluded from the study. To minimize weight variations among animals and groups, extra animals most different in body weight (either heavier or lighter) five days prior to exposure (day -5) were also excluded from the study. The remaining animals were assigned to dose groups at random (group assignments are presented in Appendix A).

When exposure began (day zero), the animals were about 6-7 weeks old. The animals were weighed at the beginning of the study and every three days during the course of the study. In each study, the rate of weight gain was comparable in all dosing groups. Body weight data are presented in Appendix B.

All animals were examined daily by an attending veterinarian while on study and were subjected to detailed examination at necropsy by a certified veterinary pathologist in order to assess overall animal health.

2.3 Diet

Animals were weaned onto standard pig chow (made at the University of Missouri Animal Science Feed Mill). The feed was nutritionally complete. The ingredients of the feed are presented in Table 2-2. Arsenic concentration in randomly selected feed samples measured <0.3 µg/g (Table 2-3).

Prior to the start of dosing and throughout the dosing period, each day every animal was given an amount of feed equal to 4.0% of the mean body weight of all animals on study. Feed amounts were adjusted every three days, when animals were weighed. Feed was administered in two equal portions, at 11:00 AM and 5:00 PM daily.

Drinking water was provided *ad libitum* via self-activated watering nozzles within each cage. Arsenic concentration of water samples from randomly selected drinking water nozzles were <1 μg/L (Table 2-3).

2.4 Dosing

Animals were exposed to dosing materials (sodium arsenate or sieved test material) for 14 days, with the dose for each day being administered in two equal portions beginning at 9:00 AM and 3:00 PM (two hours before feeding). Pigs were dosed two hours before feeding to ensure that they were in a semi-fasted state because the presence of food in the stomach is known to reduce arsenic absorption. To facilitate dose administration, dosing materials were placed in a small depression in a ball of dough consisting of moistened feed (typically about 5g) and the dough was pinched shut. This was then placed in the feeder at dosing time.

Target arsenic doses (expressed as μg of arsenic per kg of body weight per day) for animals in each group were determined in the study design (Table 2-1). The daily mass of arsenic administered (either as sodium arsenate or as sieved test material) to animals in each group was calculated by multiplying the target dose (μg/kg-day) for that group by the anticipated average weight of the animals (kg) over the course of the study:

$$Mass\ (\mu g\ /\ day) = Dose\ (\mu g\ /\ kg - day) \cdot Average\ Body\ Weight\ (kg)$$

The average body weight expected during the course of the study was estimated by measuring the average body weight of all animals one day before the study began, and then assuming an average weight gain of 0.5 kg/day during the study. After completion of the study, the true mean body weight was calculated using the actual body weights (measured every three days during the study), and the resulting true mean body weight was used to calculate the actual doses achieved. These calculations included adjustments for any partial or missed doses (see Appendix C). Actual doses for each group are shown in Table 2-1.

2.5 Collection and Preservation of Urine Samples

Samples of urine were collected from each animal for 48-hour periods on days 6 to 7 (U-1), 9 to 10 (U-2), and 12 to 13 (U-3) of the study. Collection began at 9:00 AM and ended 48 hours later. The urine was collected in a plastic bucket placed beneath each cage, which was emptied into a plastic storage bottle. Aluminum screens were placed under the cages to minimize contamination with feces, spilled food, or other debris. Due to the length of the collection period, collection containers were emptied periodically (typically twice daily) into a separate plastic bottles to ensure that there was no loss of sample due to overflow.

At the end of each collection period, the total urine volume for each animal was measured (Appendix D) and three 60-mL portions were removed and acidified with 0.6 mL concentrated nitric acid. All samples were refrigerated. Two of the aliquots were archived and one aliquot was sent for arsenic analysis (refrigeration was maintained until arsenic analysis).

2.6 Arsenic Analysis

Urine samples were assigned random chain-of-custody tag numbers and submitted to the analytical laboratory for analysis in a blind fashion. The samples were analyzed for arsenic by L. E. T., Inc., (Columbia, Missouri). In brief, 25-mL samples of urine were digested by refluxing and then heating to dryness in the presence of magnesium nitrate and concentrated nitric acid. Following magnesium nitrate digestion, samples were transferred to a muffle furnace and ashed at 500°C. The digested and ashed residue was dissolved in hydrochloric acid and analyzed by the hydride generation technique using a PerkinElmer 3100 atomic absorption spectrometer. Preliminary tests of this method established that each of the different forms of arsenic that may occur in urine, including trivalent inorganic arsenic (As+3), pentavalent inorganic arsenic (As+5), monomethyl arsenic (MMA), and dimethyl arsenic (DMA) are all recovered with high efficiency.

Analytical results for the urine samples are presented in Appendix E.

2.7 Quality Control

A number of quality control (QC) steps were taken during this project to evaluate the accuracy of the analytical procedures. The results for QC samples are presented in Appendix F, and are summarized below.

<u>Blind Duplicates (Sample Preparation Replicates)</u>

A random selection of about 20% of all urine samples generated during each study were prepared for laboratory analysis in duplicate (i.e., two separate subsamples of urine were digested) and submitted to the laboratory in a blind fashion. There was generally good agreement between results for the duplicate pairs (Figure F-1 and Table F-1).

<u>Spike Recovery</u>

During arsenic analysis for each study, every tenth sample was spiked with known amounts of arsenic (sodium arsenate) and the recovery of the added arsenic was measured. Mean arsenic concentrations recovered from spiked samples were within 10% of actual arsenic concentrations (Table F-2).

<u>Laboratory Duplicates</u>

During arsenic analysis, every tenth sample was analyzed in duplicate (Table F-3). For urine samples, duplicate results agreed within ±1 times the detection limit or less than 10% relative percent difference (RPD). Most duplicate water samples were below the detection limit. Duplicate analysis for feed samples showed deviations between 35% (Study 1 and Study 2) and 67% (Study 3).

Laboratory Control Standards

Laboratory control standards (samples of reference materials for which a certified concentration of specific analytes has been established) were tested periodically during sample analysis. Recovery of arsenic from these standards was generally good and within the acceptable range (Table F-4).

Blanks

Blank samples run along with each batch of samples (N ≥ 6) never yielded a measurable level of arsenic (Table F-5). The detection limit was 1 µg/L.

Summary of QC Results

Based on the results of all of the QC samples and steps described above, it is concluded that the analytical results are of sufficient quality for derivation of reliable estimates of arsenic absorption from the test materials.

3.0 DATA ANALYSIS

3.1 Overview

Figure 3-1 shows a conceptual model for the toxicokinetic fate of ingested arsenic. Key points of this model are as follows:

- In most animals (including humans), absorbed arsenic is excreted mainly in the urine over the course of several days. Thus, the UEF, defined as the amount excreted in the urine divided by the amount given, is usually a reasonable approximation of the AF_o or ABA. However, this ratio will underestimate total absorption, because some absorbed arsenic is excreted in the feces via the bile, and some absorbed arsenic enters tissue compartments (e.g., skin, hair) from which it is cleared very slowly or not at all. Thus, the urinary excretion fraction should not be equated with the absolute absorption fraction.

- The RBA of two orally administered materials (i.e., a test material and reference material) can be calculated from the ratio of the urinary excretion fraction of the two materials. This calculation is independent of the extent of tissue binding and of biliary excretion:

$$RBA(test\ vs\ ref) = \frac{AF_o(test)}{AF_o(ref)} = \frac{D \cdot AF_o(test) \cdot K_u}{D \cdot AF_o(ref) \cdot K_u} = \frac{UEF(test)}{UEF(ref)}$$

  where:

  D = Ingested dose (µg)

  K_u = Fraction of absorbed arsenic that is excreted in the urine

Based on the conceptual model above, the basic method used to estimate the RBA of arsenic in a particular test material compared to arsenic in a reference material (sodium arsenate) is as follows:

1. Plot the amount of arsenic excreted in the urine (µg per 48 hours) as a function of the administered amount of arsenic (µg per 48 hours), both for reference material and for test material.

2. Find the best fit linear regression line through the each data set. The slope of each line (µg per 48 hours excreted per µg per 48 hours ingested) is the best estimate of the urinary excretion fraction (UEF) for each material.

3. Calculate RBA for each test material as the ratio of the UEF for test material compared to UEF for reference material:

$$RBA(test\ vs\ ref) = \frac{UEF(test)}{UEF(ref)}$$

A detailed description of the curve-fitting methods and rationale and the methods used to quantify uncertainty in the arsenic RBA estimates for a test material are summarized below. All model fitting was performed in Microsoft Excel® using matrix functions.

3.2 Dose-Response Model

Simultaneous Regression

The techniques used to derive linear regression fits to the dose-response data are based on the methods recommended by Finney (1978). 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, 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).

When a study consists of a reference group and two test materials (e.g., see Study 3), the same approach is used, except that all three curves are fit simultaneously:

$$\mu(i) = a + b_r \cdot x_r(i) + b_{t1} \cdot x_{t1}(i) + b_{t2} \cdot x_{t2}(i)$$

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). It has previously been shown that this assumption is generally not satisfied in swine-based RBA studies, where there is a tendency toward increasing variance in response as a function of increasing dose (heteroscedasticity) (USEPA, 2005). 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*

σ_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 alternative strategies for assigning weights. The method used in this study estimates the value of σ_i^2 using an "external" variance model based on an analysis of the relationship between variance and mean response using data consolidated across many different swine-based arsenic RBA studies. The data used to derive the variance model are shown in Figure 3-2. As seen, log-variance increases as an approximately linear function of log-mean response:

$$\ln(s_i^2) = k1 + k2 \cdot \ln(\bar{y}_i)$$

where:

s_i^2 = observed variance of responses of animals in dose group *i*
$\bar{y}_i$ = mean observed response of animals in dose group *i*

Based on these data, values of *k*1 and *k*2 were derived using ordinary least squares minimization. The resulting values were -1.10 for *k*1 and 1.64 for *k*2.

Goodness of Fit

The goodness-of-fit of each dose-response model was assessed using the F test statistic and the adjusted coefficient of multiple determination (Adj R^2) as described by Draper and Smith (1998). A fit is considered acceptable if the p-value is less than 0.05.

Assessment of 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. In this study, 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 values were calculated both with and without the potential outlier(s) excluded, and the result with the outlier(s) excluded was used as the preferred estimate.

3.3 Calculation of RBA Estimates

The arsenic RBA values were calculated as the ratio of the slope term for the test material data set (b_t) and the reference material data set (b_r):

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

The uncertainly range about the RBA ratio was calculated using Fieller's Theorem as described by Finney (1978).

4.0 RESULTS

4.1 Clinical Signs

The doses of arsenic administered in this study are below a level that is expected to cause toxicological responses in swine. No clinical signs of arsenic-induced toxicity were noted in any of the animals used in the studies.

4.2 Background Arsenic Excretion

Measured values for urinary arsenic excretion (mean and standard deviation) for control animals from days 6 to 13 are shown below:

Study	Arsenic mass in urine (µg/48 hours)	Number of samples
Study 1 (MS-1)	66.0 ± 14.5	8
Study 2 (MS-5)	73.3 ± 35.8	6
Study 3 (MS-4 & MS-8)	85.0 ± 35.5	9

These values are representative of endogenous background levels in food and water and support the view that the animals were not exposed to any significant exogenous sources of arsenic throughout the study.

4.3 Urinary Arsenic Variance

As discussed in Section 3.2, the urinary arsenic dose-response data are analyzed using weighted least squares regression and the weights are assigned using an "external" variance model. To ensure that the variance model was valid, the variance values from each of dose groups in each of the Barber Orchard studies were superimposed on the historic data set (Figures 4-1 through 4-3). As seen, the variances of the urinary arsenic data from these studies are consistent with the data used to generate the variance model.

4.4 Dose-Response Modeling

Outlier Identification

For each study, the dose-response data for arsenic in urine were initially modeled using all data, and outliers were identified as discussed above. These results are shown in Appendix G.

STUDY 1

Initial modeling indicated that data collected from days 9/10 and 12/13 from pig 374 were outliers (standardized weighted residuals > 3.5) (see Appendix G, Figures G-1 through G-4). The residual calculated from urine data collected from the same pig on days 6/7 was 3.2, just below the criterion for outlier identification. Further review of the data for this pig showed that the urine output on all days was at least 10-times that of the other pigs. Based on the high urine output and the poor agreement of the data from this animal with other animals in the same dose group, data for pig 374 were excluded from the final evaluation for arsenic RBA. Figures 4-4 (days 6/7), 4-5 (days 9/10), 4-6 (days 12/13) and 4-7 (all days combined) show the revised fittings with the outlier excluded from the analysis.

STUDY 2

Initial modeling indicated that data collected on days 9/10 from pig 464 were outliers based on the standardized weighted residuals greater than 3.5 (see Appendix G, Figures G-5 through G-9). Based on this analysis, data for pig 464 on days 9/10 were excluded from the final evaluation for arsenic RBA. Final regression fittings are shown in Figures 4-8 through 4-11.

STUDY 3

Initial modeling using all the data did not indicate the presence of any outliers. Therefore, all data were included in the final analysis. Final regression fittings are shown in Figures 4-12 through 4-15.

Best Fit Results After Outlier Exclusion

After exclusion of outliers, all of the dose-response curves were approximately linear, with the slope of the best-fit straight line being equal to the best estimate of the UEF. Table 4-1 summarizes the resulting slopes (UEF estimates) for the final fittings of each test material and corresponding reference material.

4.5 Calculated RBA Values

Estimated RBA values (mean and 90% confidence interval) are shown below:

Time Interval	MS-1 Estimated RBA	MS-4 Estimated RBA	MS-5 Estimated RBA	MS-8 Estimated RBA
Days 6/7	0.38 (0.24 - 0.58)	0.43 (0.39 - 0.48)	0.62 (0.46 - 0.85)	0.53 (0.48 - 0.59)
Days 9/10	0.31 (0.20 - 0.45)	0.40 (0.36 - 0.45)	0.39 (0.29 - 0.53)	0.53 (0.47 - 0.59)
Days 12/13	0.27 (0.18 - 0.37)	0.39 (0.33 - 0.46)	0.44 (0.35 - 0.56)	0.53 (0.45 - 0.62)
All Days	0.31 (0.25 - 0.38)	0.41 (0.38 - 0.44)	0.49 (0.42 - 0.57)	0.53 (0.49 - 0.57)

4.6 Uncertainty

The bioavailability estimates above are subject to uncertainty that arises from several different sources. One source of uncertainty is the inherent biological variability between different animals in a dose group, which in turn causes variability in the amount of arsenic absorbed by the exposed animals. The between-animal variability results in statistical uncertainty in the best-fit dose-response curves and, hence, uncertainty in the calculated values of RBA. Such statistical uncertainty is accounted for by the statistical models used above and is characterized by the uncertainty range around the RBA estimates.

However, there is also uncertainty in the extrapolation of RBA values measured in juvenile swine to young children or adults, and this uncertainty is not included in the statistical confidence bounds above. Even though the immature swine is believed to be a useful and meaningful animal model for gastrointestinal absorption in humans, it is possible that there are differences in physiological parameters that may influence RBA; therefore, RBA values in swine may not be identical to values in children. In addition, RBA may depend on the amount and type of food in the stomach, since the presence of food can influence stomach pH, holding time, and possibly other factors that may influence solubilization of arsenic. In this regard, it is important to recall that RBA values measured in this study are based on animals that have little or no food in their stomach at the time of exposure and, hence, are likely to yield high-end values of RBA. Thus, these RBA values may be somewhat conservative for humans who ingest the site soils along with food. The magnitude of this bias is not known.

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TABLES AND FIGURES

TABLE 2-1 STUDY DESIGNS AND DOSING INFORMATION

STUDY 1

Group	Group Name Abbreviation	Dose Material Administered	As Conc of the material (ug/g or ug/uL)	No. Pigs in Group	Arsenic Dose (µg/kg BW-day)	
					Target	Actual [a]
1	Control	(none)	0	3	0	0.0
2	NaAs	Sodium Arsenate	2	4	25	32.0
3	NaAs	Sodium Arsenate	10	4	50	55.7
4	NaAs	Sodium Arsenate	10	4	100	125.2
5	TM1	Barber Orchard Soil MS-1	290	4	60	72.9
6	TM1	Barber Orchard Soil MS-1	290	4	120	145.7

STUDY 2

Group	Group Name Abbreviation	Dose Material Administered	As Conc of the material (ug/g or ug/uL)	No. Pigs in Group	Arsenic Dose (µg/kg BW-day)	
					Target	Actual [a]
1	NaAs	Sodium Arsenate	2	4	25	29.7
2	NaAs	Sodium Arsenate	10	4	50	57.3
3	TM1	Barber orchard Soil MS-5	382	4	40	46.0
4	TM1	Barber orchard Soil MS-5	382	4	60	71.0
5	TM1	Barber orchard Soil MS-5	382	4	120	138.9
6	Control	(none)	0	2	0	0.0

TABLE 2-1 STUDY DESIGNS AND DOSING INFORMATION

STUDY 3

Group	Group Name Abbreviation	Dose Material Administered	As Conc of the material (ug/g or ug/uL)	No. Pigs in Group	Arsenic Dose (µg/kg BW-day)	
					Target	Actual [a]
1	NaAs	Sodium Arsenate	10.00	4	25	25.4
2	NaAs	Sodium Arsenate	10.00	4	50	53.6
3	NaAs	Sodium Arsenate	10.00	4	100	104.6
4	TM1	Barber Orchard Soil MS-4	300	4	40	52.6
5	TM1	Barber Orchard Soil MS-4	300	4	60	77.3
6	TM1	Barber Orchard Soil MS-4	300	4	120	144.4
7	TM2	Barber Orchard Soil MS-8	310	4	40	44.6
8	TM2	Barber Orchard Soil MS-8	310	4	60	72.0
9	TM2	Barber Orchard Soil MS-8	310	4	120	155.0
10	Control	(none)	0	3	0	0.0

[a] Calculated as the administered daily dose divided by the measured or extrapolated daily body weight, averaged over days 0-14 for each animal and each group.

Doses were administered in two equal portions given at 9:00 AM and 3:00 PM each day. Doses were held constant based on the expected mean weight during the exposure interval (14 days).

TABLE 2-2 TYPICAL FEED COMPOSITION

Purina TestDiet® 5TXP: Porcine Grower Purified Diet with Low Lead[1]

INGREDIENTS

Corn Starch, %	25.2	Potassium Phosphate, %	0.87
Sucrose, %	20.9648	Calcium Carbonate, %	0.7487
Glucose, %	16	Salt, %	0.501
Soy Protein Isolate, %	14.9899	Magnesium Sulfate, %	0.1245
Casein - Vitamin Free, %	8.5	DL-Methionine, %	0.0762
Powdered Cellulose, %	6.7208	Choline Chloride, %	0.0586
Corn Oil, %	3.4046	Vitamin/Mineral Premix, %	0.0577
Dicalcium Phosphate, %	1.7399	Sodium Selenite, %	0.0433

NUTRITIONAL PROFILE[2]

Protein, %	**21**	**Fat, %**		**3.5**
Arginine, %	1.42	Cholesterol, ppm		0
Histidine, %	0.61	Linoleic Acid, %		1.95
Isoleucine, %	1.14	Linolenic Acid, %		0.03
Leucine, %	1.95	Arachidonic Acid, %		0
Lysine, %	1.56	Omega-3 Fatty Acids, %		0.03
Methionine, %	0.49	Total Saturated Fatty Acids, %		0.43
Cystine, %	0.23	Total Monounsaturated Fatty Acids, %		0.82
Phenylalanine, %	1.22	Polyunsaturated Fatty Acids, %		1.98
Tyrosine, %	1.03			
Threonine, %	0.88			
Tryptophan, %	0.32	**Fiber (max), %**		**6.8**
Valine, %	1.16			
Alanine, %	0.95	**Carbohydrates, %**		**62.2**
Aspartic Acid, %	2.33			
Glutamic Acid, %	4.96	**Energy (kcal/g)[3]**		**3.62**
Glycine, %	0.79	*From:*	*kcal*	*%*
Proline, %	1.83	Protein	0.84	23.1
Serine, %	1.25	Fat (ether extract)	0.315	8.7
Taurine, %	0	Carbohydrates	2.487	68.3
Minerals		**Vitamins**		
Calcium, %	0.8	Vitamin A, IU/g		1.7
Phosphorus, %	0.72	Vitamin 0-3 (added), IU/g		0.2
Phosphorus (available), %	0.4	Vitamin E, IU/kg		11
Potassium, %	0.27	Vitamin K (as menadione), ppm		0.52
Magnesium, %	0.04	Thiamin Hydrochloride, ppm		1
Sodium, %	0.3	Ribonavin, ppm		3.1
Chlorine, %	0.31	Niacin, ppm		13
Fluorine, ppm	0	Pantothenic Acid, ppm		9
Iron, ppm	82	Folic Acid, ppm		0.3
Zinc, ppm	84	Pyridoxine, ppm		1.7
Manganese, ppm	3	Biotin, ppm		0.1
Copper, ppm	4.9	Vitamin B-12, mcg/kg		15
Cobalt, ppm	0.1	Choline Chloride, ppm		410
Iodine, ppm	0.15	Ascorbic Acid, ppm		0
Chromium, ppm	0			
Molybdenum, ppm	0.01			
Selenium, ppm	0.26			

FOOTNOTES

[1] This special purified diet was originally developed for lead RBA studies.

[2] Based on the latest ingredient analysis information. Since nutrient composition of natural ingredients varies, analysis will differ accordingly. Nutrients expressed as percent of ration on an As Fed basis except where otherwise indicated.

[3] Energy (kcal/gm) - Sum of decimal fractions of protein, fat and carbohydrate x 4,9,4 kcal/gm respectively.

TABLE 2-3 ARSENIC CONCENTRATIONS IN FEED AND WATER SAMPLES

STUDY 1

Sample ID	Sample Type	Arsenic Concentration	Units
EP3-2-407	Feed	0.22	µg/g
EP3-2-408	Feed	<0.05	µg/g
EP3-2-409	Feed	<0.05	µg/g
EP3-2-410	Water	1	µg/L
EP3-2-411	Water	0.5	µg/L
EP3-2-412	Water	<0.6	µg/L
EP3-2-413	Water	1	µg/L
EP3-2-414	Water	<0.5	µg/L

STUDY 2

Sample ID	Sample Type	Arsenic Concentration	Units
MS-5-223	Feed	0.07	µg/g
MS-5-228	Water	<1	µg/L
MS-5-227	Water	<1	µg/L
MS-5-226	Water	<1	µg/L
MS-5-225	Water	<1	µg/L
MS-5-224	Water	<1	µg/L

STUDY 3

Sample ID	Sample Type	Arsenic Concentration	Units
BOrch-MS4&8-311	Feed	0.1	µg/g
BOrch-MS4&8-312	Water	<1	µg/L
BOrch-MS4&8-313	Water	<1	µg/L
BOrch-MS4&8-314	Water	<1	µg/L
BOrch-MS4&8-315	Water	<1	µg/L
BOrch-MS4&8-316	Water	<1	µg/L
BOrch-MS4&8-317	Water	<1	µg/L

TABLE 4-1 UEF ESTIMATES FOR EACH TEST MATERIAL AND CORRESPONDING REFERENCE MATERIAL

STUDY 1: MS-1 Data

Time Interval	Outliers Excluded	Slopes (UEF Estimates)	
		b_r	b_{t1}
Days 6/7	1	0.85	0.24
Days 9/10	1	0.79	0.25
Days 12/13	1	0.83	0.26
All Days	3	0.83	0.25

STUDY 2: MS-5 Data

Time Interval	Outliers Excluded	Slopes (UEF Estimates)	
		b_r	b_{t1}
Days 6/7	0	0.62	0.38
Days 9/10	1	0.80	0.31
Days 12/13	0	0.79	0.35
All Days	1	0.73	0.35

STUDY 3: MS-4 and MS-8 Data

Time Interval	Outliers Excluded	Slopes (UEF Estimates)		
		b_r	b_{t1}	b_{t2}
Days 6/7	0	0.67	0.29	0.36
Days 9/10	0	0.72	0.29	0.38
Days 12/13	0	0.70	0.28	0.37
All Days	0	0.70	0.28	0.37

Notes:

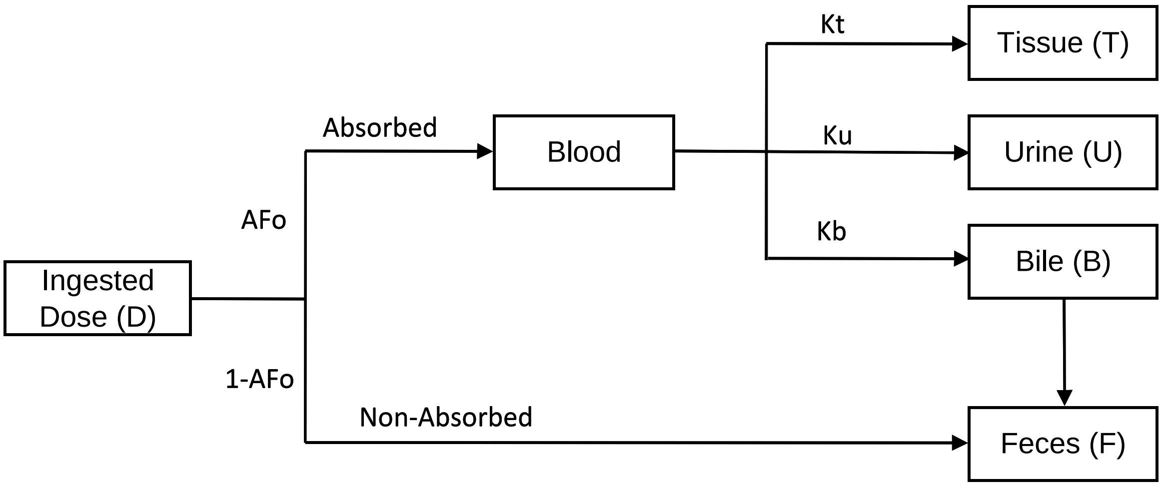
Slopes represent final fittings (outliers excluded).

b_r = slope term for the reference material data set

b_{t1} = slope term for the test material 1 data set

b_{t2} = slope term for the test material 2 data set

FIGURE 3-1. CONCEPTUAL MODEL FOR ARSENIC TOXICOKINETICS



where:

D = Ingested dose
AFo = Oral absorption fraction
Kt = Fraction of absorbed arsenic that is retained in tissues
Ku = Fraction of absorbed arsenic that is excreted in urine
Kb = Fraction of absorbed arsenic that is excreted in bile

Basic Equations

Amount absorbed	= D x AFo
Amount excreted in urine	= Amount absorbed x Ku = D x AFo x Ku
Urinary excretion fraction (UEF)	= Amount excreted / Amount ingested = D x AFo x Ku / D = AFo x Ku
Relative bioavailability (RBA)	= AFo(test) / AFo(reference) = AFo(test) x Ku / (AFo(reference) x Ku) = UEF(test) / UEF(reference)

FIGURE 3-2 URINARY ARSENIC VARIANCE MODEL

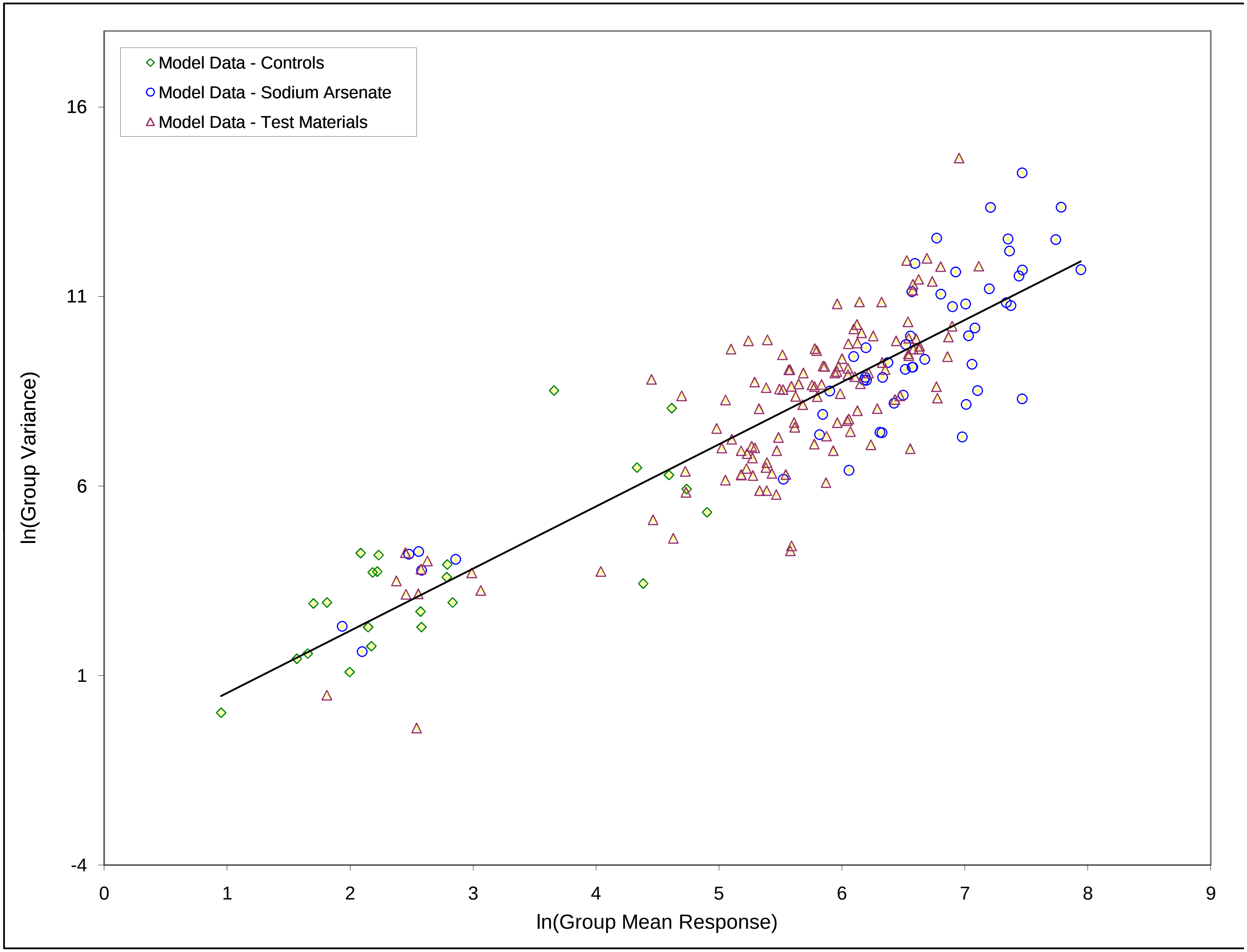
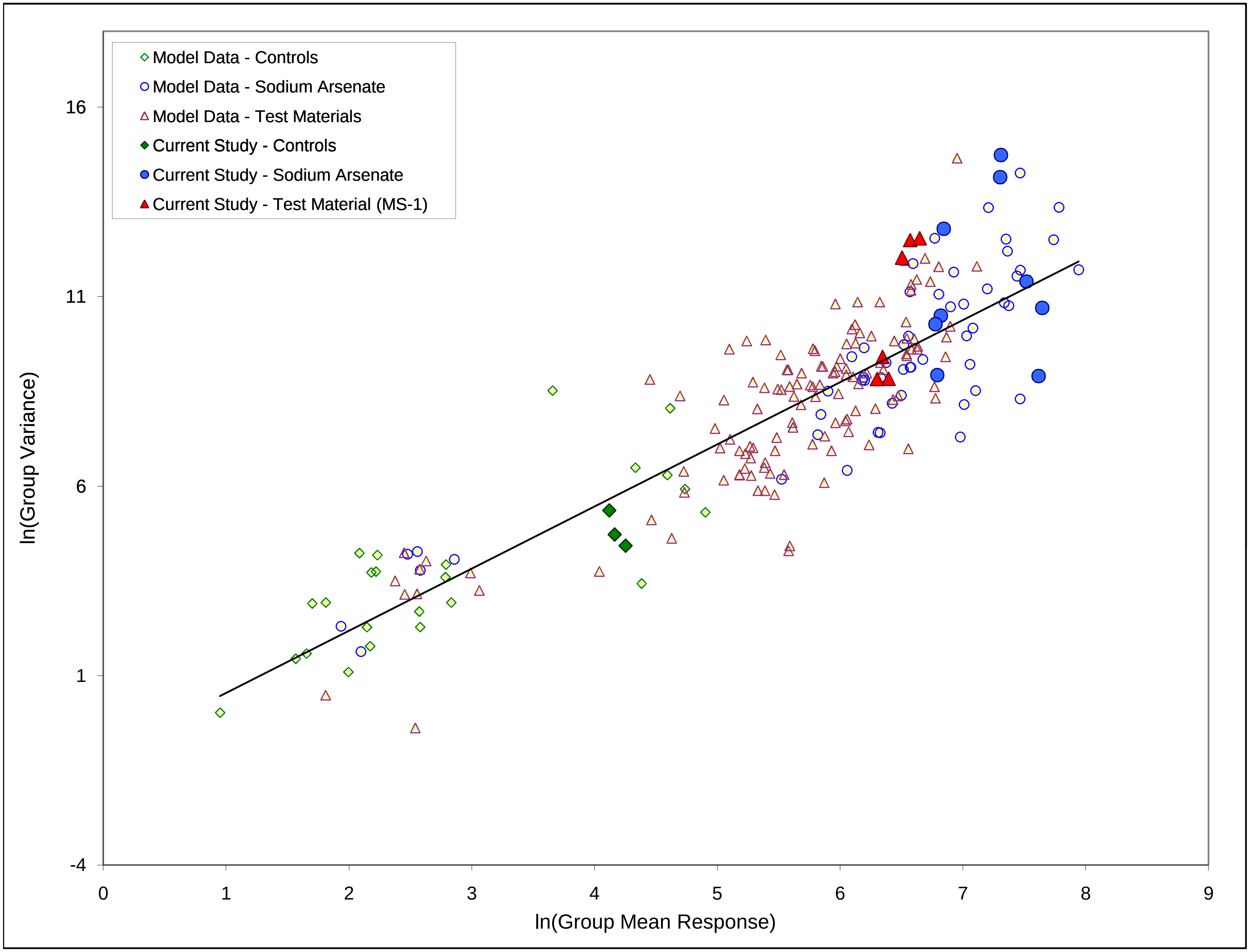


Figure 3-2 Barber Orchard.xls (Fig 4-1B)

FIGURE 4-1 STUDY 1 DATA COMPARED TO URINARY ARSENIC VARIANCE MODEL



\\DENVER2\Public\Swine Bioavailability\EPA3-2-ORCH Barber Orchard\Barber Orchard Report\Originals\Figure 4-1 MS-1 Barb Orch.xlsFig 4-1

FIGURE 4-2 STUDY 2 DATA COMPARED TO URINARY ARSENIC VARIANCE MODEL

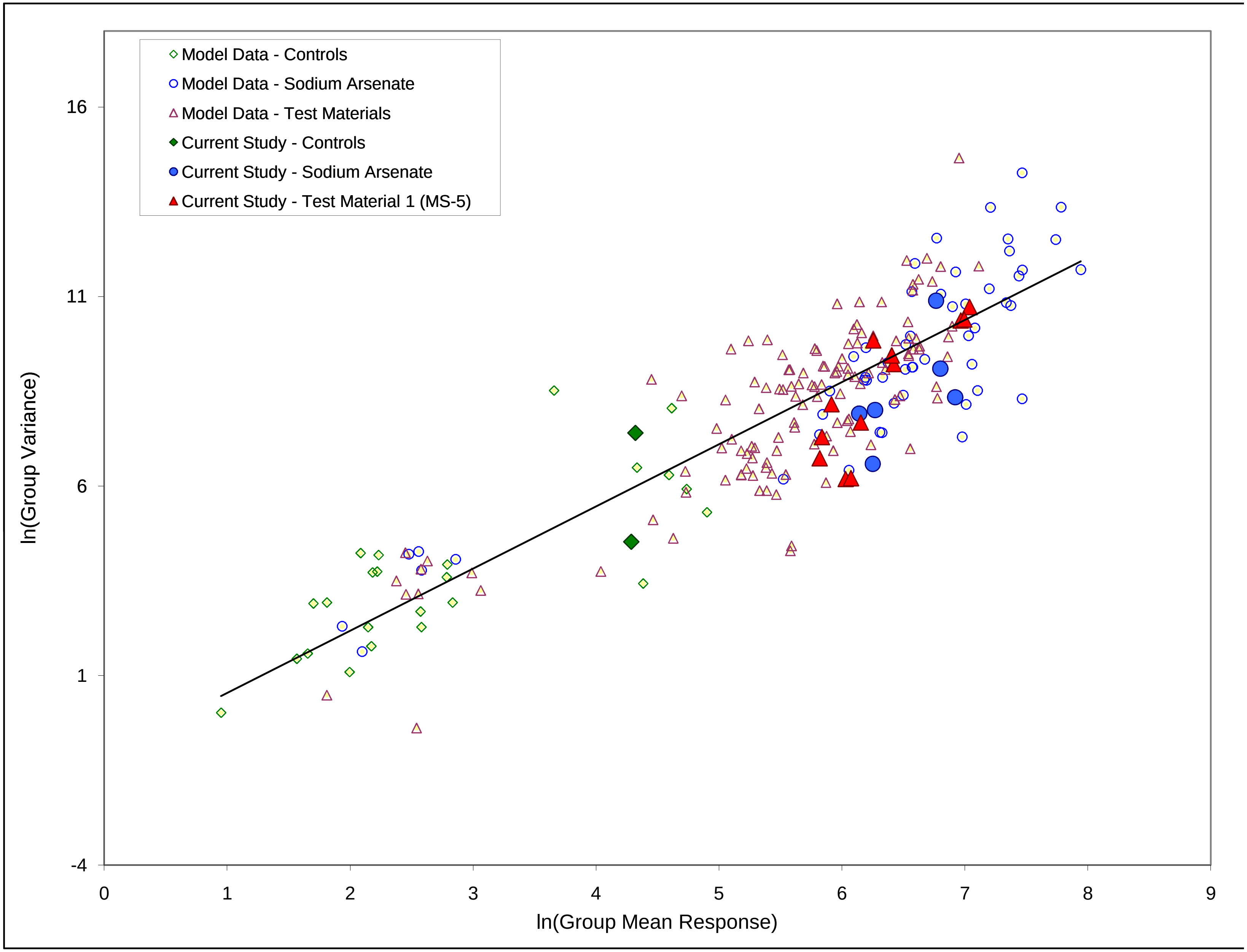


Figure 4-2 MS-5 Barb Orch.xls (Fig 4-1B)

FIGURE 4-3 STUDY 3 DATA COMPARED TO URINARY ARSENIC VARIANCE MODEL

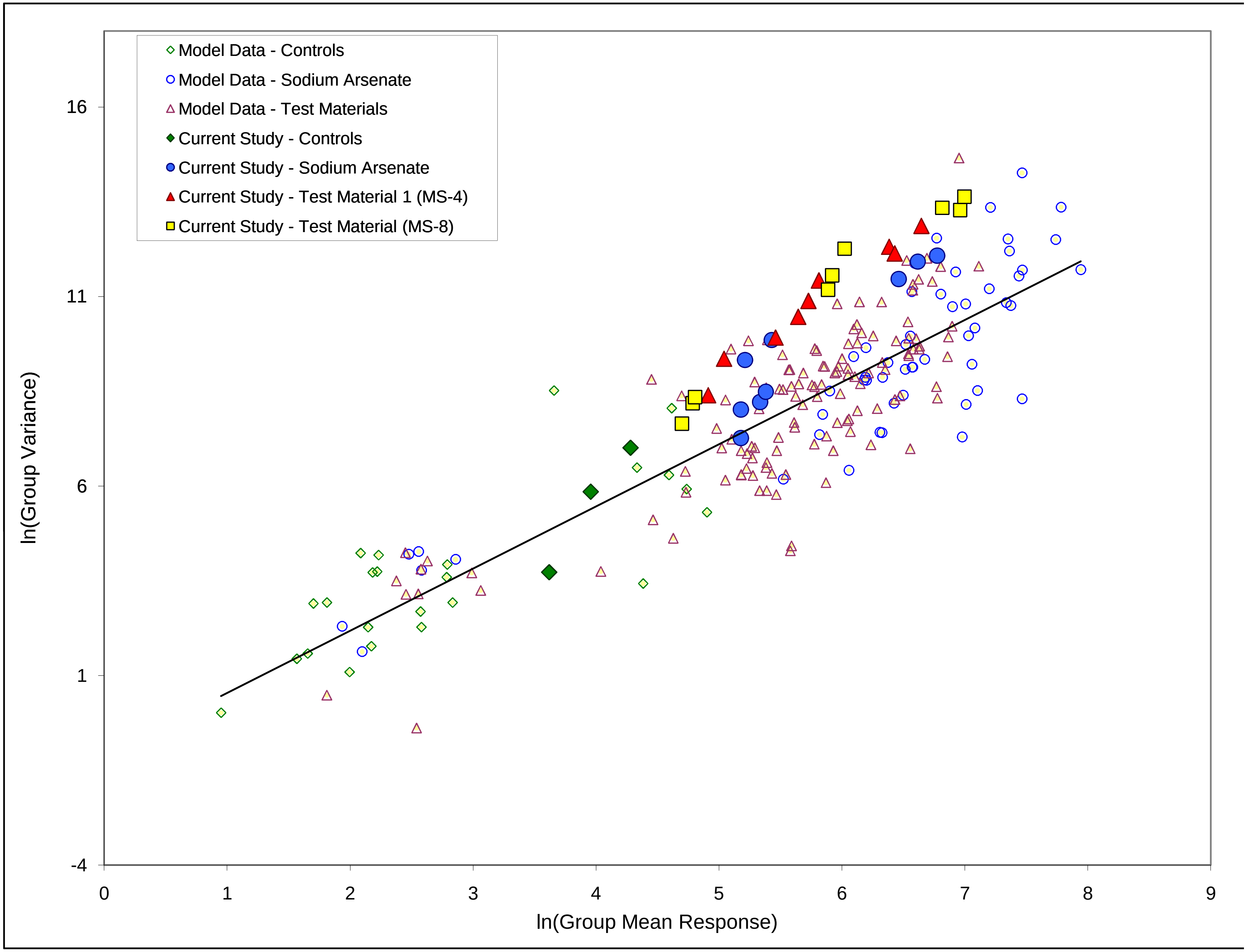
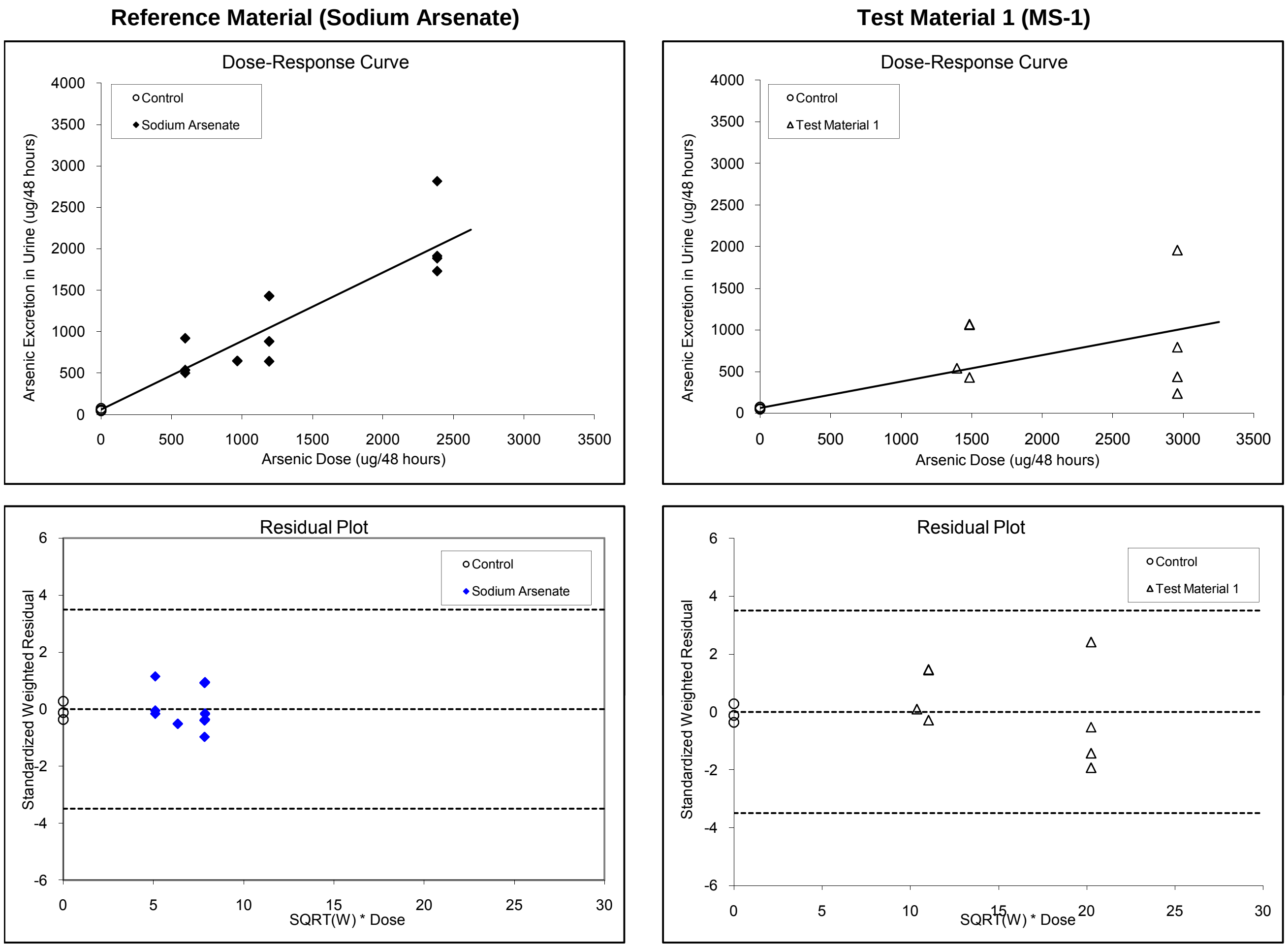


Figure 4-3 MS4+MS8 Barb Orch.xls (Fig 4-1B)

APPENDIX A

GROUP ASSIGNMENTS

FIGURE 4-4 STUDY 1 URINARY EXCRETION OF ARSENIC: Days 6/7 (Outlier Excluded)



Summary of Fitting[b]

Parameter	Estimate	Standard Error
a	61.2	26.5
b_r	0.83	0.12
b_{t1}	0.32	0.06
Covariance (b_r,b_{t1})	0.0292	--
Degrees of Freedom	20	--

[b] $y = a + b_r*x_r + b_{t1}*x_{t1}$

where r = Reference Material, t1 = Test Material 1

ANOVA

Source	MSE
Fit	277.66
Error	8.17
Total	33.84

Statistic	Estimate
F	33.966
p	< 0.001
Adjusted R^2	0.7584

RBA and Uncertainty

	Test Material 1
RBA	0.38
Lower bound[c]	0.24
Upper bound[c]	0.58
Standard Error[c]	0.094**

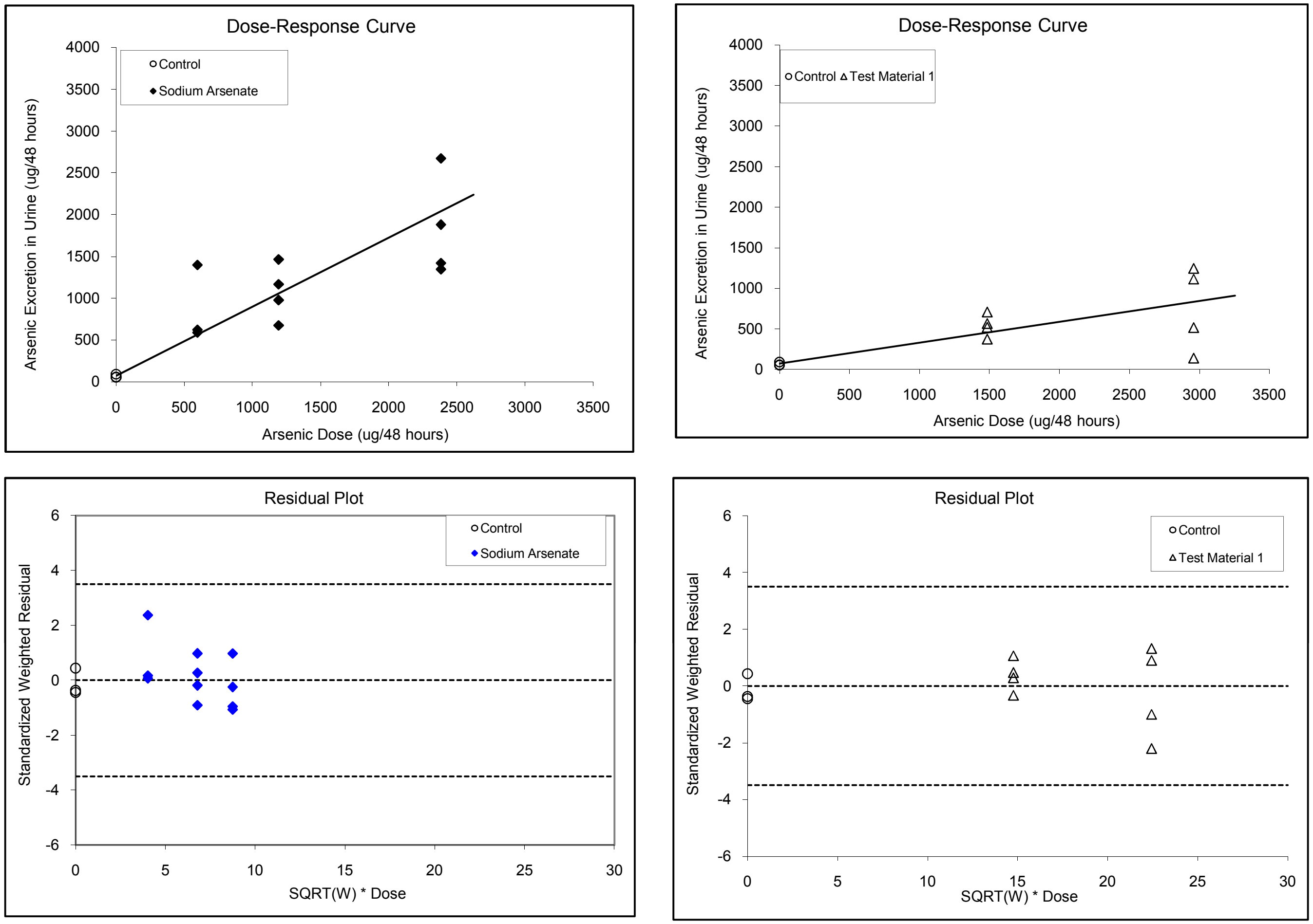
[c] 90% confidence interval calculated using Fieller's theorem

** g ≥ 0.05 (Feiller's SE is uncertain)

2_MS-1 As RBA Calcs all data 8-19-09 sieved no outlier v2.xls (Graph_1)

FIGURE 4-5 STUDY 1 URINARY EXCRETION OF ARSENIC: Days 9/10 (Outlier Excluded)

Reference Material (Sodium Arsenate) | **Test Material 1 (MS-1)**



Summary of Fitting[a]

Parameter	Estimate	SE
a	71.0	25.6
b_r	0.83	0.11
b_{t1}	0.26	0.05
Covariance (b_r,b_{t1})	0.0371	--
Degrees of Freedom	20	--

[a] $y = a + b_r*x_r + b_{t1}*x_{t1}$

where r = Reference Material, t1 = Test Material 1

ANOVA

Source	MSE
Fit	260.44
Error	6.29
Total	30.49

Statistic	Estimate
F	41.420
p	< 0.001
Adjusted R^2	0.7938

RBA and Uncertainty

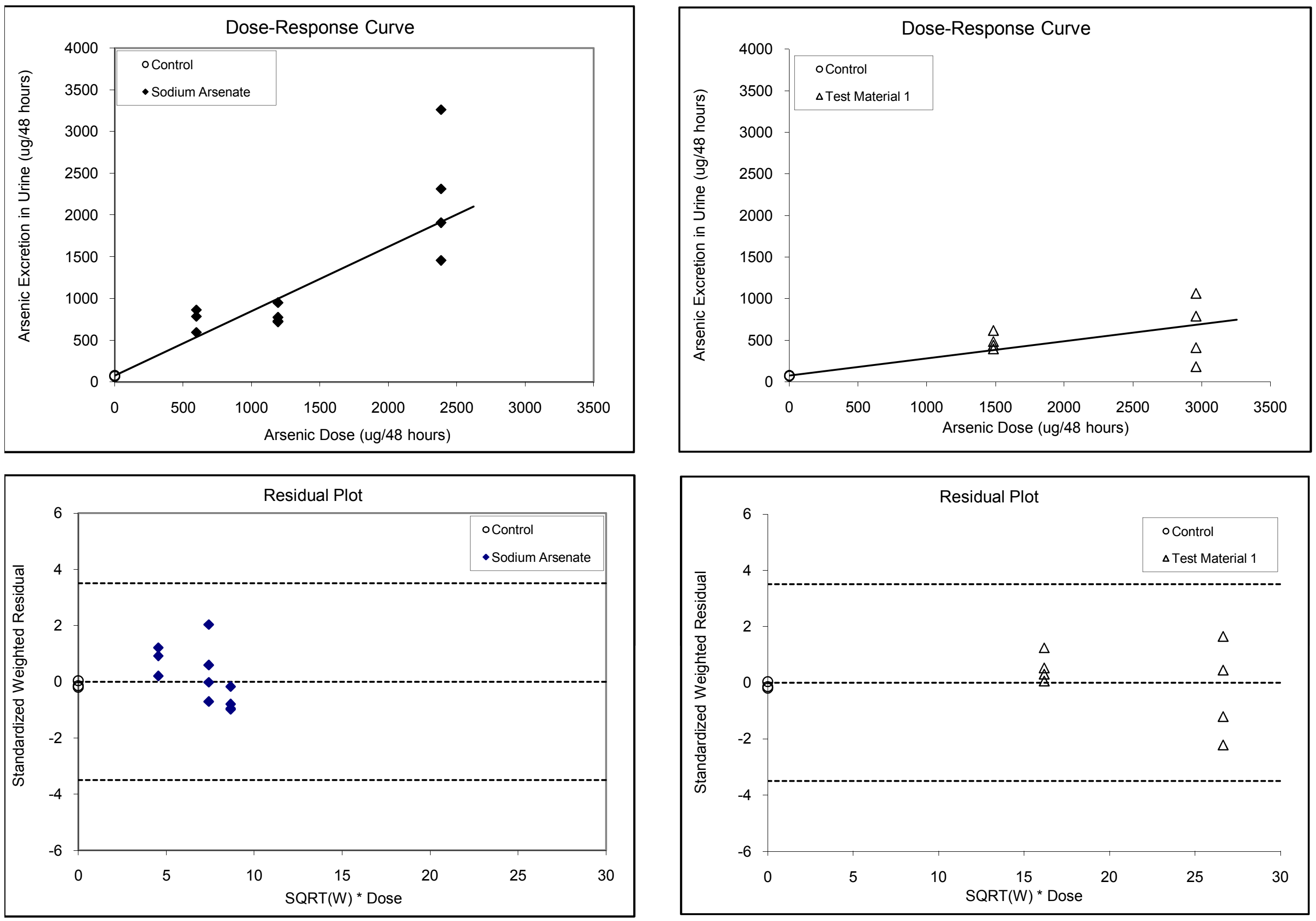
	Test Material 1
RBA	0.31
Lower bound[c]	0.20
Upper bound[c]	0.45
Standard Error[c]	0.070**

[c] 90% confidence interval calculated using Fieller's theorem

** g ≥ 0.05 (Feiller's SE is uncertain)

FIGURE 4-6 STUDY 1 URINARY EXCRETION OF ARSENIC: Days 12/13 (Outlier Excluded)

Reference Material (Sodium Arsenate) | **Test Material 1 (MS-1)**



Summary of Fitting[a]

Parameter	Estimate	SE
a	77.9	24.3
b_r	0.77	0.09
b_{t1}	0.21	0.04
Covariance (b_r,b_{t1})	0.0587	--
Degrees of Freedom	20	--

[a] $y = a + b_r*x_r + b_{t1}*x_{t1}$

where r = Reference Material, t1 = Test Material 1

ANOVA

Source	MSE
Fit	229.41
Error	4.69
Total	26.09

Statistic	Estimate
F	48.928
p	< 0.001
Adjusted R^2	0.8203

RBA and Uncertainty

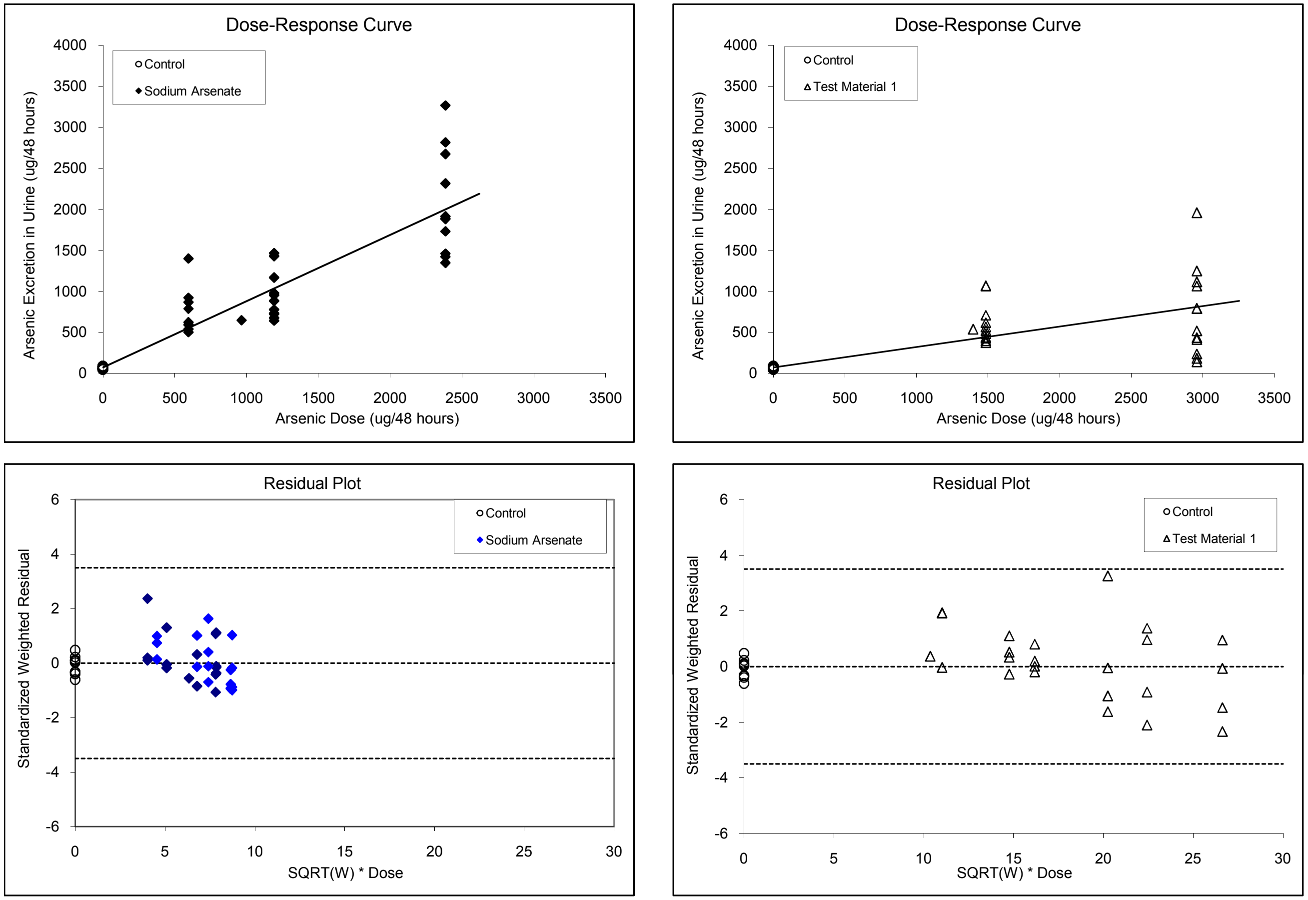
	Test Material 1
RBA	0.27
Lower bound[c]	0.18
Upper bound[c]	0.37
Standard Error[c]	0.055

[c] 90% confidence interval calculated using Fieller's theorem

2_MS-1 As RBA Calcs all data 8-19-09 sieved no outlier v2.xls (Graph_3)

FIGURE 4-7 STUDY 1 URINARY EXCRETION OF ARSENIC: All Days (Outliers Excluded)

Reference Material (Sodium Arsenate) | **Test Material 1 (MS-1)**



Summary of Fitting[b]

Parameter	Estimate	SE
a	68.9	14.4
b_r	0.81	0.06
b_{t1}	0.25	0.03
Covariance (b_r,b_{t1})	0.0404	--
Degrees of Freedom	64	--

[b] $y = a + b_r*x_r + b_{t1}*x_{t1}$

where r = Reference Material, t1 = Test Material 1

ANOVA

Source	MSE
Fit	763.36
Error	6.05
Total	29.35

Statistic	Estimate
F	126.105
p	< 0.001
Adjusted R^2	0.7938

RBA and Uncertainty

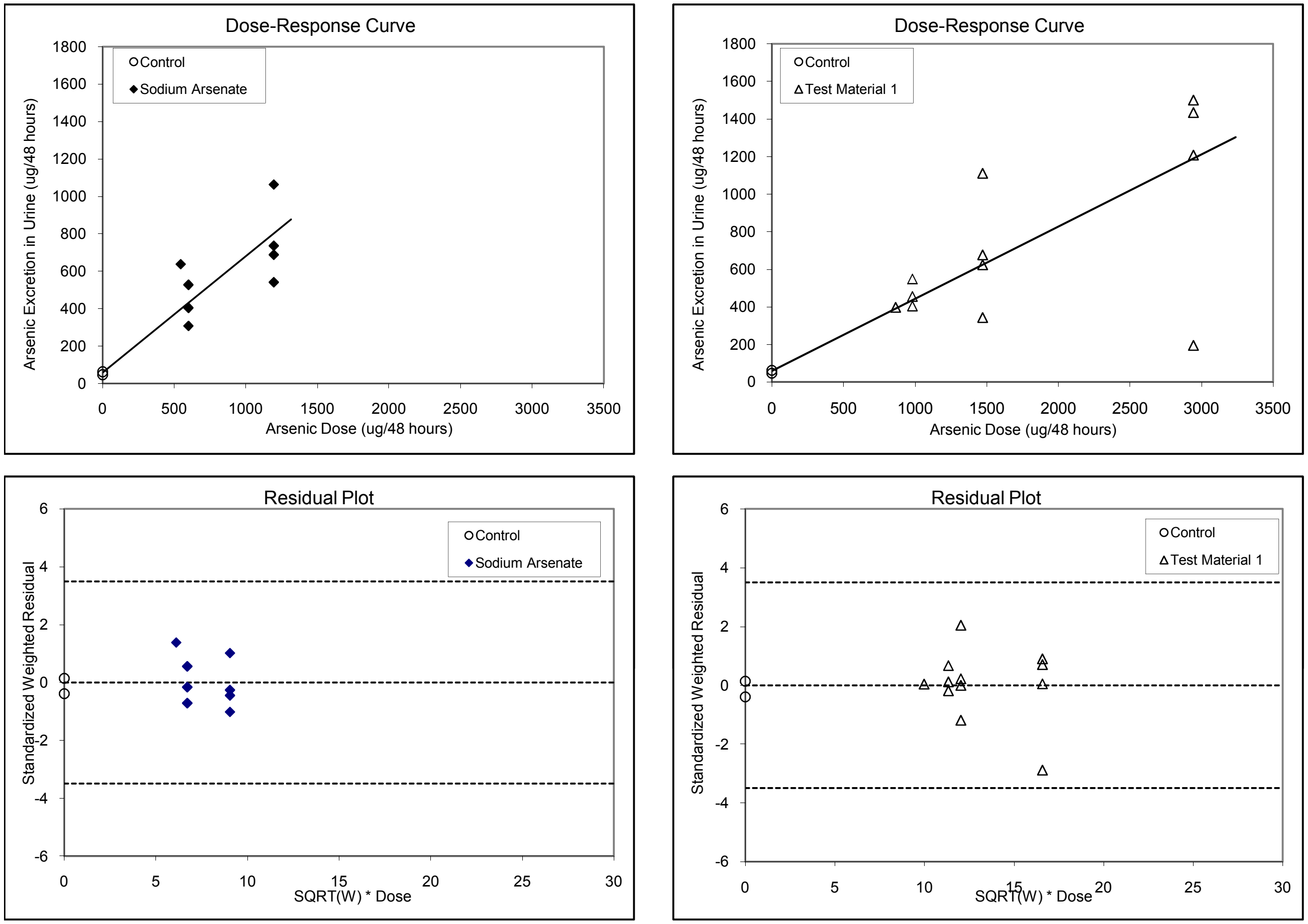
	Test Material 1
RBA	0.31
Lower bound[c]	0.25
Upper bound[c]	0.38
Standard Error[c]	0.040

[c] 90% confidence interval calculated using Fieller's theorem

2_MS-1 As RBA Calcs all data 8-19-09 sieved no outlier v2.xls (Graph_All)

FIGURE 4-8 STUDY 2 URINARY EXCRETION OF ARSENIC: Days 6/7 (Outlier Excluded)

Reference Material (Sodium Arsenate) | **Test Material 1 (MS-5)**



Summary of Fitting[b]

Parameter	Estimate	Standard Error
a	58.3	21.8
b_r	0.62	0.09
b_{t1}	0.38	0.05
Covariance (b_r,b_{t1})	0.0733	--
Degrees of Freedom	20	--

[b] $y = a + b_r{*}x_r + b_{t1}{*}x_{t1}$

where r = Reference Material, t1 = Test Material 1

ANOVA

Source	MSE
Fit	221.77
Error	4.18
Total	24.91

Statistic	Estimate
F	53.014
p	< 0.001
Adjusted R^2	0.8320

RBA and Uncertainty

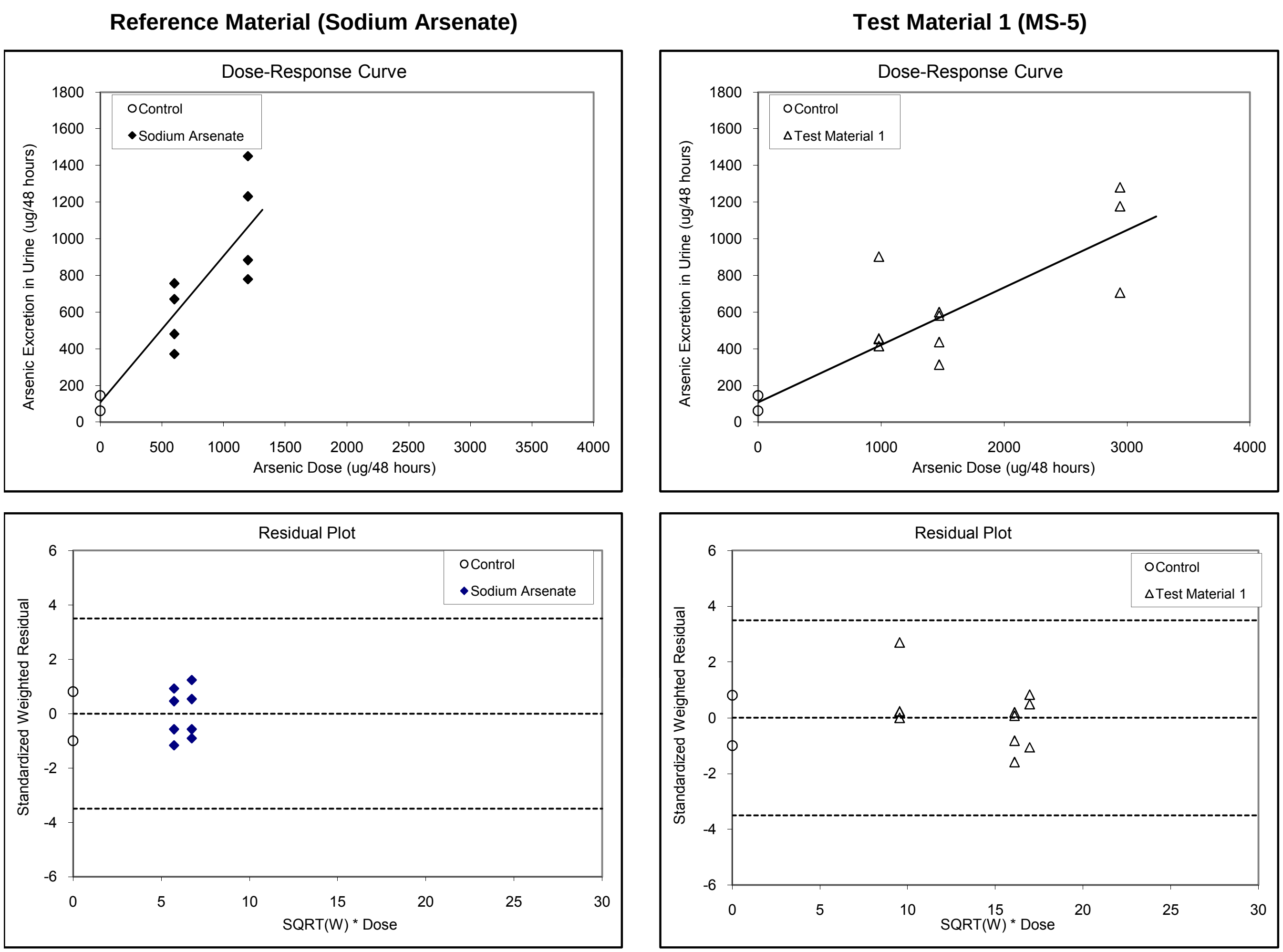
	Test Material 1
RBA	0.62
Lower bound[c]	0.45
Upper bound[c]	0.87
Standard Error[c]	0.115**

[c] 90% confidence interval calculated using Fieller's theorem

** g ≥ 0.05 (Feiller's SE is uncertain)

2_MS-5 As RBA Calcs all data 8-19-09 no outlier.xls (Graph_1)

FIGURE 4-9 STUDY 2 URINARY EXCRETION OF ARSENIC: Days 9/10 (Outlier Excluded)



Summary of Fitting[a]

Parameter	Estimate	SE
a	108.0	33.0
b_r	0.80	0.11
b_{t1}	0.31	0.04
Covariance (b_r,b_{t1})	0.1592	--
Degrees of Freedom	19	--

[a] $y = a + b_r{*}x_r + b_{t1}{*}x_{t1}$

where r = Reference Material, t1 = Test Material 1

ANOVA

Source	MSE
Fit	150.99
Error	3.44
Total	18.19

Statistic	Estimate
F	43.920
p	< 0.001
Adjusted R^2	0.8110

RBA and Uncertainty

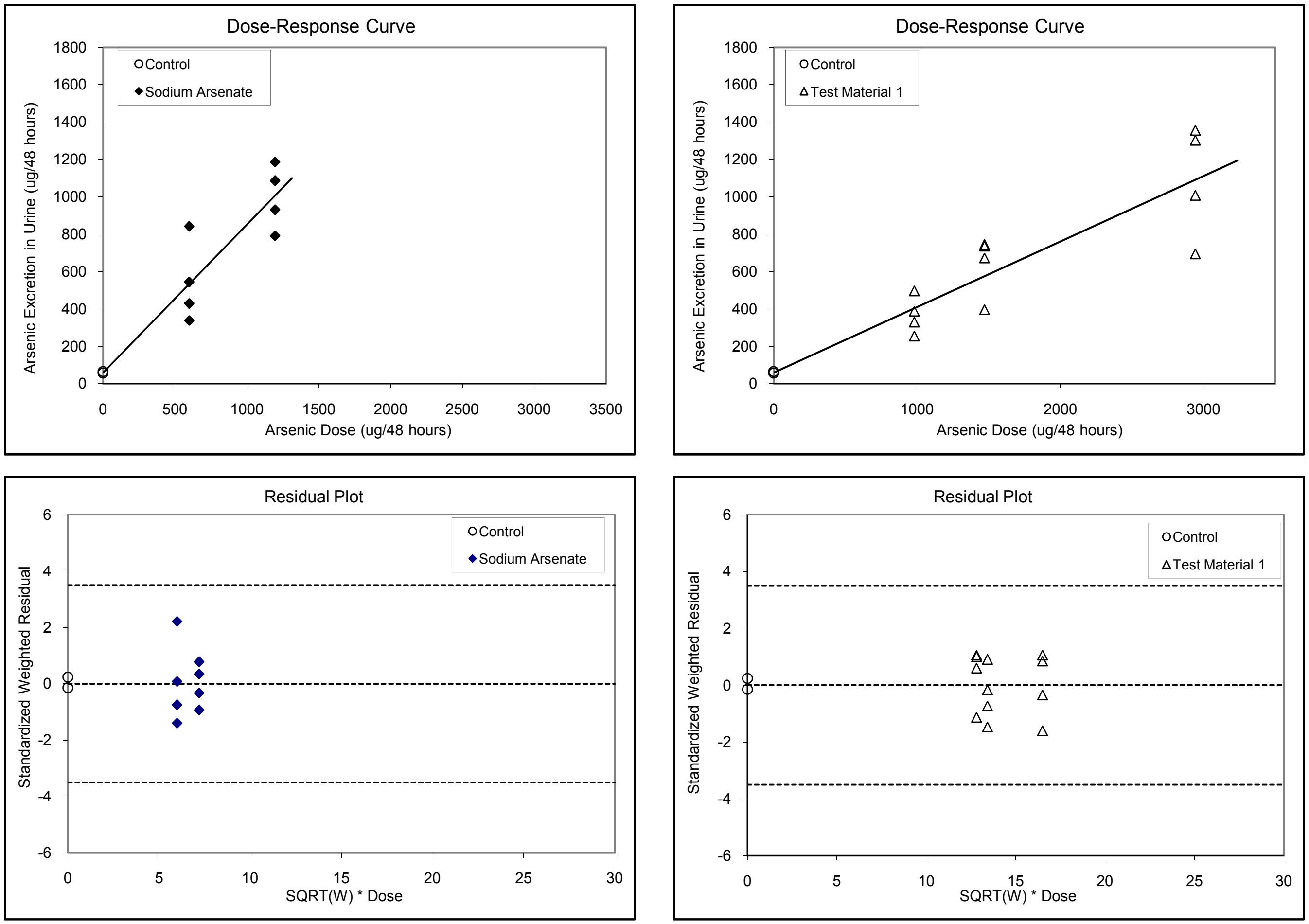
	Test Material 1
RBA	0.39
Lower bound[c]	0.28
Upper bound[c]	0.54
Lower bound[c]	0.071**

[c] 90% confidence interval calculated using Fieller's theorem

** g ≥ 0.05 (Feiller's SE is uncertain)

FIGURE 4-10 STUDY 2 URINARY EXCRETION OF ARSENIC: Days 12/13 (Outlier Excluded)

Reference Material (Sodium Arsenate) | **Test Material 1 (MS-5)**



Summary of Fitting[a]

Parameter	Estimate	SE
a	60.3	17.1
b_r	0.79	0.08
b_{t1}	0.35	0.03
Covariance (b_r,b_{t1})	0.0858	--
Degrees of Freedom	20	--

[a] $y = a + b_r*x_r + b_{t1}*x_{t1}$

where r = Reference Material, t1 = Test Material 1

ANOVA

Source	MSE
Fit	217.93
Error	2.14
Total	22.69

Statistic	Estimate
F	101.741
p	< 0.001
Adjusted R^2	0.9056

RBA and Uncertainty

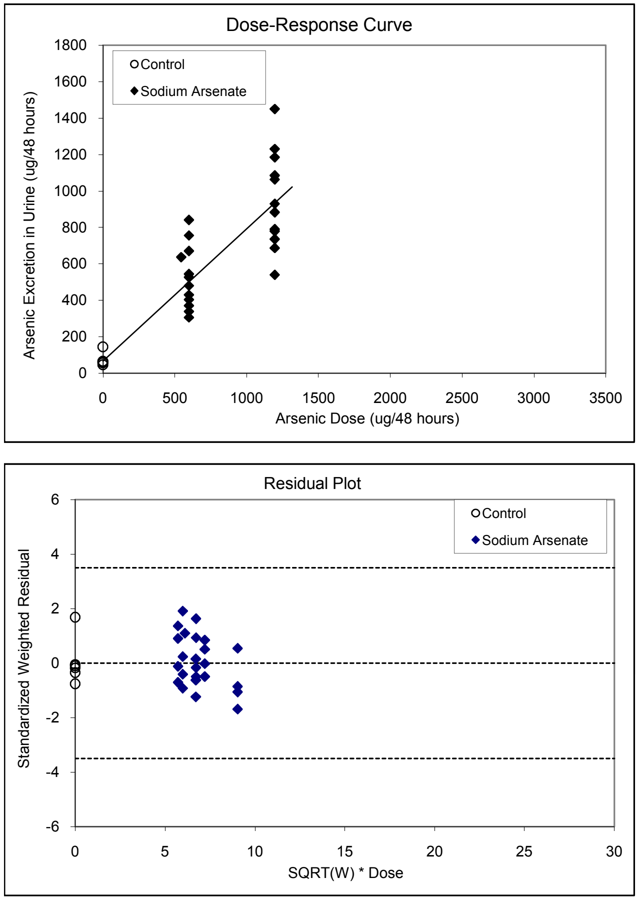
	Test Material 1
RBA	0.44
Lower bound[c]	0.35
Upper bound[c]	0.56
Lower bound[c]	0.058

[c] 90% confidence interval calculated using Fieller's theorem

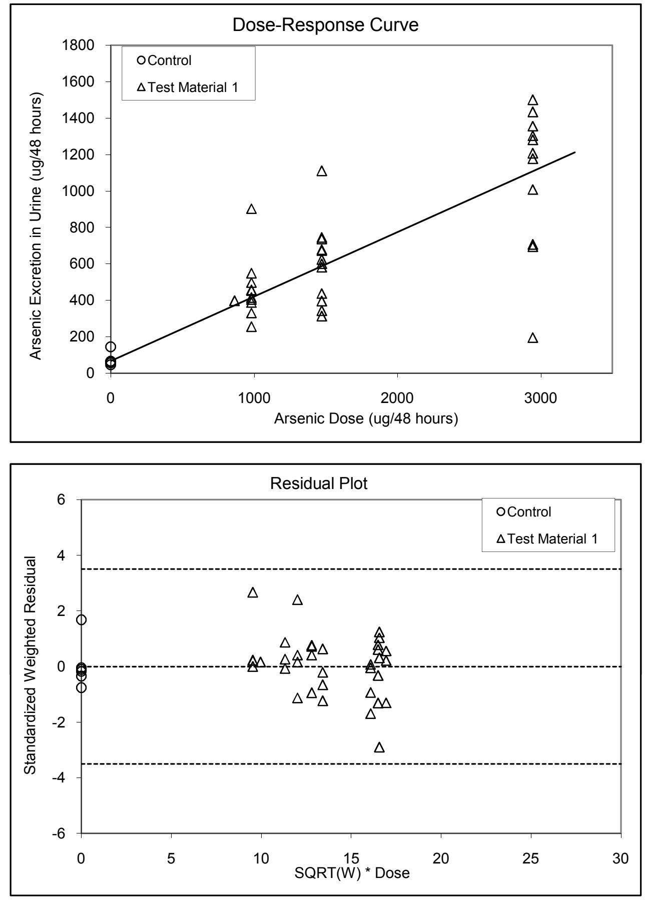
2_MS-5 As RBA Calcs all data 8-19-09 no outlier.xls (Graph_3)

FIGURE 4-11 STUDY 2 URINARY EXCRETION OF ARSENIC: All Days (Outlier Excluded)

Reference Material (Sodium Arsenate)



Test Material 1 (MS-5)



Summary of Fitting[b]

Parameter	Estimate	SE
a	67.3	13.0
b_r	0.73	0.06
b_{t1}	0.35	0.02
Covariance (b_r,b_{t1})	0.0939	--
Degrees of Freedom	63	--

[b] $y = a + b_r*x_r + b_{t1}*x_{t1}$

where r = Reference Material, t1 = Test Material 1

ANOVA

Source	MSE
Fit	607.89
Error	3.27
Total	22.16

Statistic	Estimate
F	185.930
p	< 0.001
Adjusted R^2	0.8525

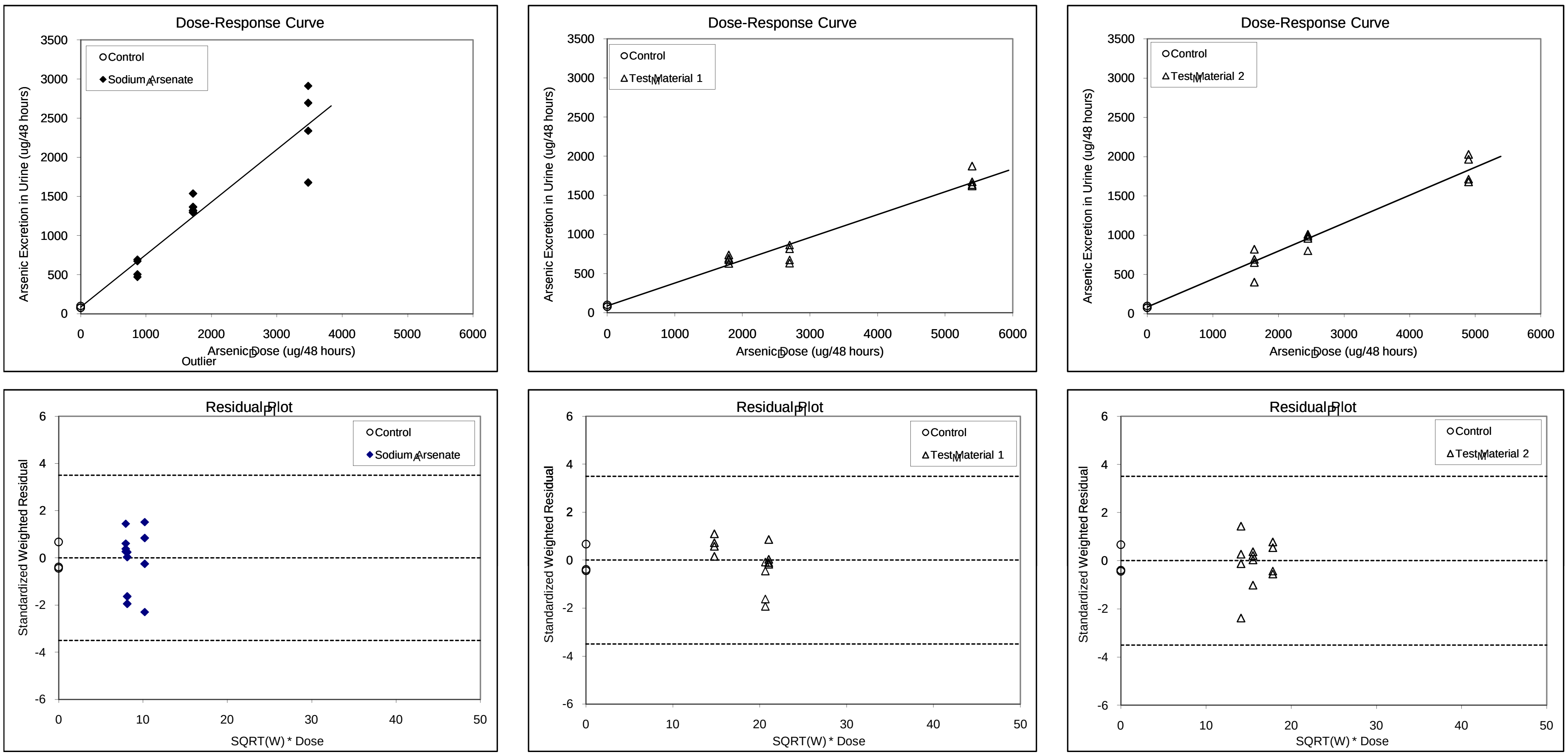
RBA and Uncertainty

	Test Material 1
RBA	0.49
Lower bound[c]	0.42
Upper bound[c]	0.57
Standard Error[c]	0.047

[c] 90% confidence interval calculated using Fieller's theorem

FIGURE 4-12 STUDY 3 URINARY EXCRETION OF ARSENIC: Days 6/7

Reference Material (Sodium Arsenate) | **Test Material 1 (MS-4)** | **Test Material 2 (MS-8)**



Summary of Fitting[a]

Parameter	Estimate	Standard Error
a	85.1	30.0
b_r	0.67	0.03
b_{t1}	0.29	0.02
b_{t2}	0.36	0.02
Covariance (b_r,b_{t1})	0.2916	--
Covariance (b_r,b_{t2})	0.2356	--
Degrees of Freedom	36	--

[a] $y = a + b_r*x_r + b_{t1}*x_{t1} + b_{t2}*x_{t2}$

where r = Reference Material, t1 = Test Material 1, and t2 = Test Material 2

ANOVA

Source	SSE	DF	MSE
Fit	987.75	3	329.25
Error	34.45	35	0.98
Total	1022.19	38	26.90

Statistic	Estimate
F	334.537
p	< 0.001
Adjusted R^2	0.9634

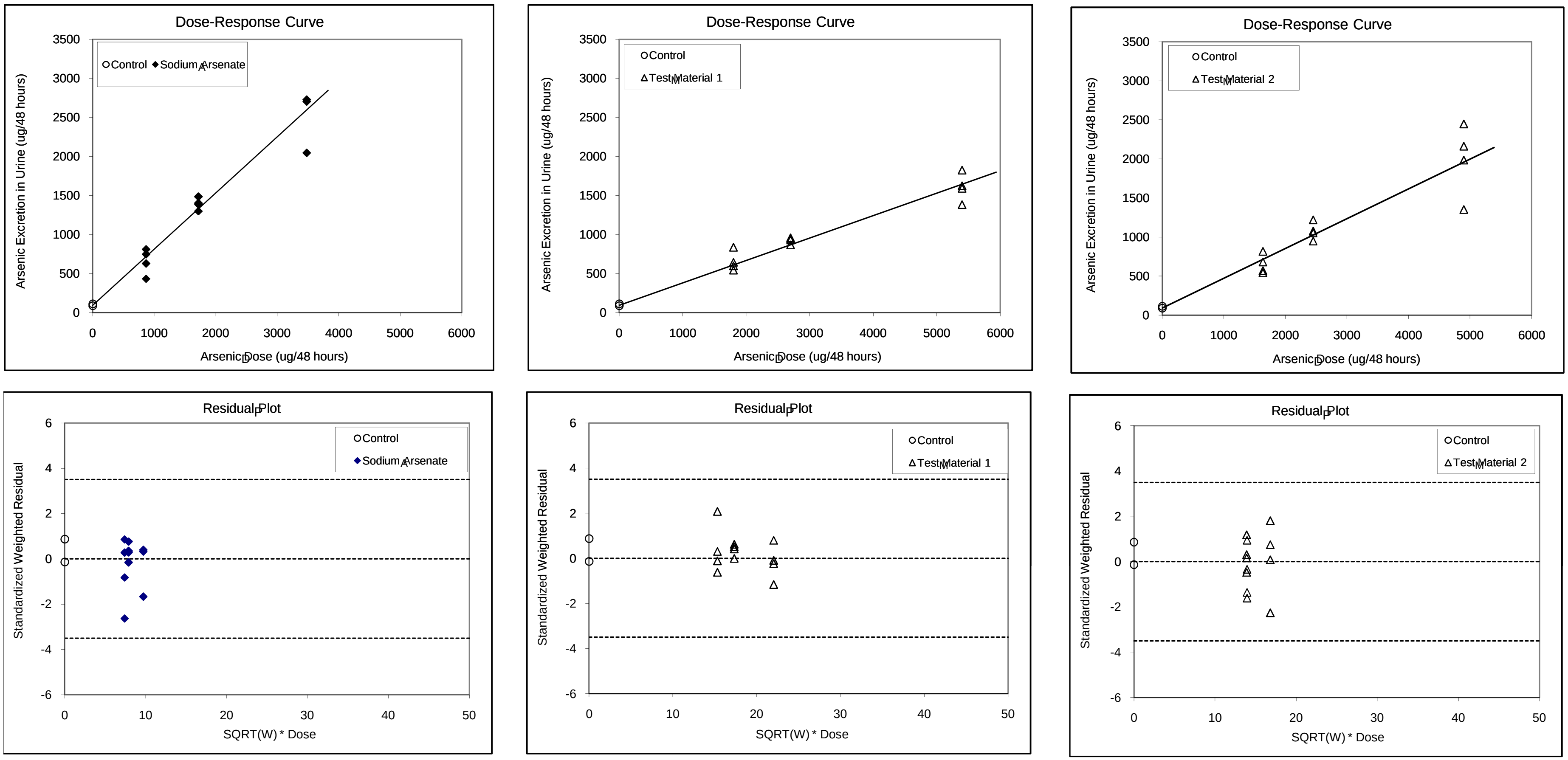
RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.43	0.53
Lower bound[c]	0.39	0.48
Upper bound[c]	0.48	0.59
Standard Error[c]	0.026	0.033

[c] 90% confidence interval as calculated using Fieller's theorem

FIGURE 4-13 STUDY 3 URINARY EXCRETION OF ARSENIC: Days 9/10

Reference Material (Sodium Arsenate) | **Test Material 1 (MS-4)** | **Test Material 2 (MS-8)**



Summary of Fitting[a]

Parameter	Estimate	SE
a	93.5	43.5
b_r	0.72	0.04
b_{t1}	0.29	0.02
b_{t2}	0.38	0.02
Covariance (b_r,b_{t1})	0.3871	--
Covariance (b_r,b_{t2})	0.3359	--
Degrees of Freedom	35	--

[a] $y = a + b_r*x_r + b_{t1}*x_{t1} + b_{t2}*x_{t2}$

where r = Reference Material, t1 = Test Material 1, and t2 = Test Material 2

ANOVA

Source	SSE	DF	MSE
Fit	874.36	3	291.45
Error	31.48	34	0.93
Total	905.84	37	24.48

Statistic	Estimate
F	314.800
p	< 0.001
Adjusted R^2	0.9622

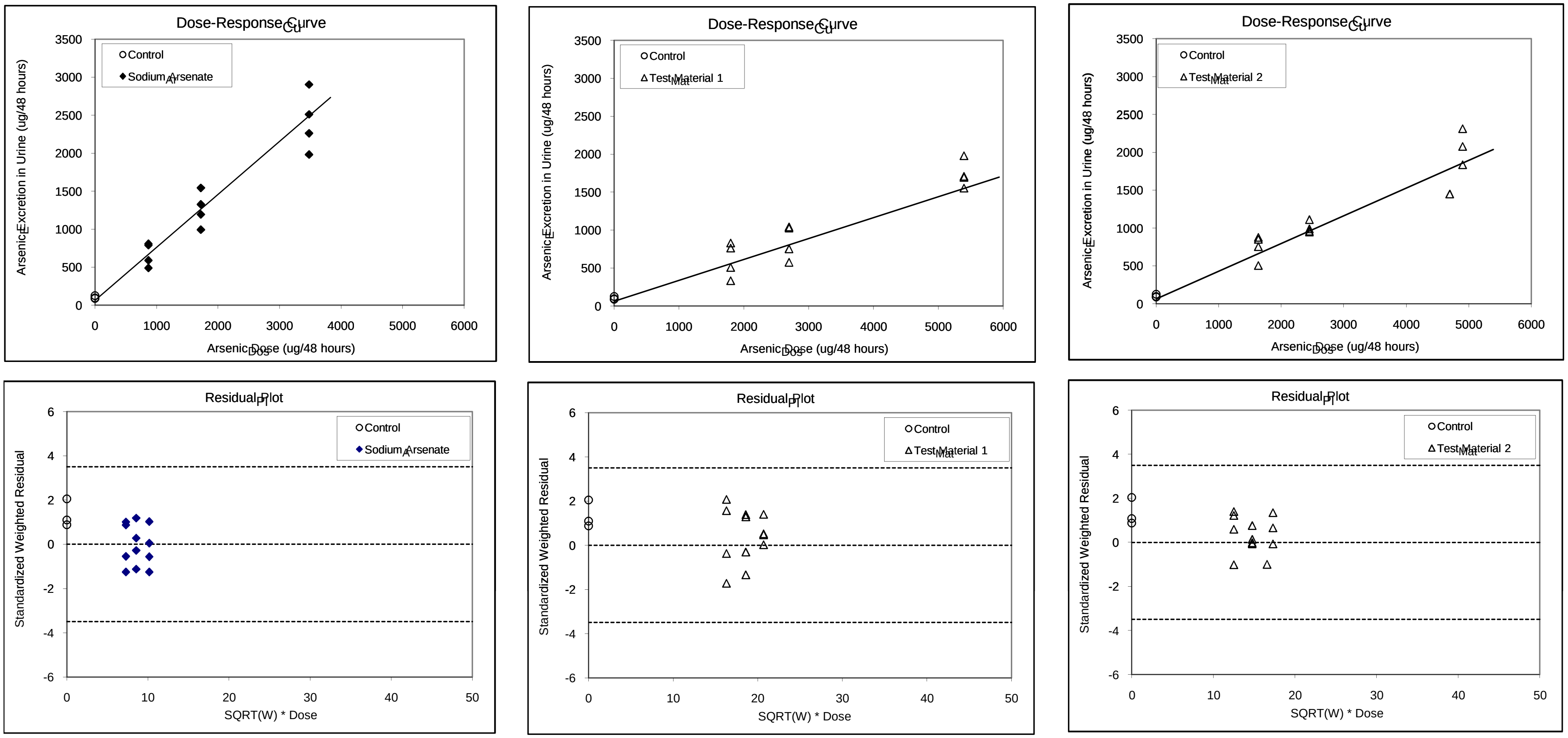
RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.40	0.53
Lower bound[c]	0.36	0.47
Upper bound[c]	0.45	0.59
Standard Error[c]	0.027	0.034

[c] 90% confidence interval as calculated using Fieller's theorem

FIGURE 4-14 STUDY 3 URINARY EXCRETION OF ARSENIC: Days 12/13

Reference Material (Sodium Arsenate) | **Test Material 1 (MS-4)** | **Test Material 2 (MS-8)**



Summary of Fitting[a]

Parameter	Estimate	SE
a	62.0	39.6
b_r	0.70	0.05
b_{t1}	0.28	0.02
b_{t2}	0.37	0.03
Covariance (b_r,b_{t1})	0.2097	--
Covariance (b_r,b_{t2})	0.1477	--
Degrees of Freedom	36	--

[a] $y = a + b_r*x_r + b_{t1}*x_{t1} + b_{t2}*x_{t2}$

where r = Reference Material, t1 = Test Material 1, and t2 = Test Material 2

ANOVA

Source	SSE	DF	MSE
Fit	918.67	3	306.22
Error	58.88	35	1.68
Total	977.55	38	25.73

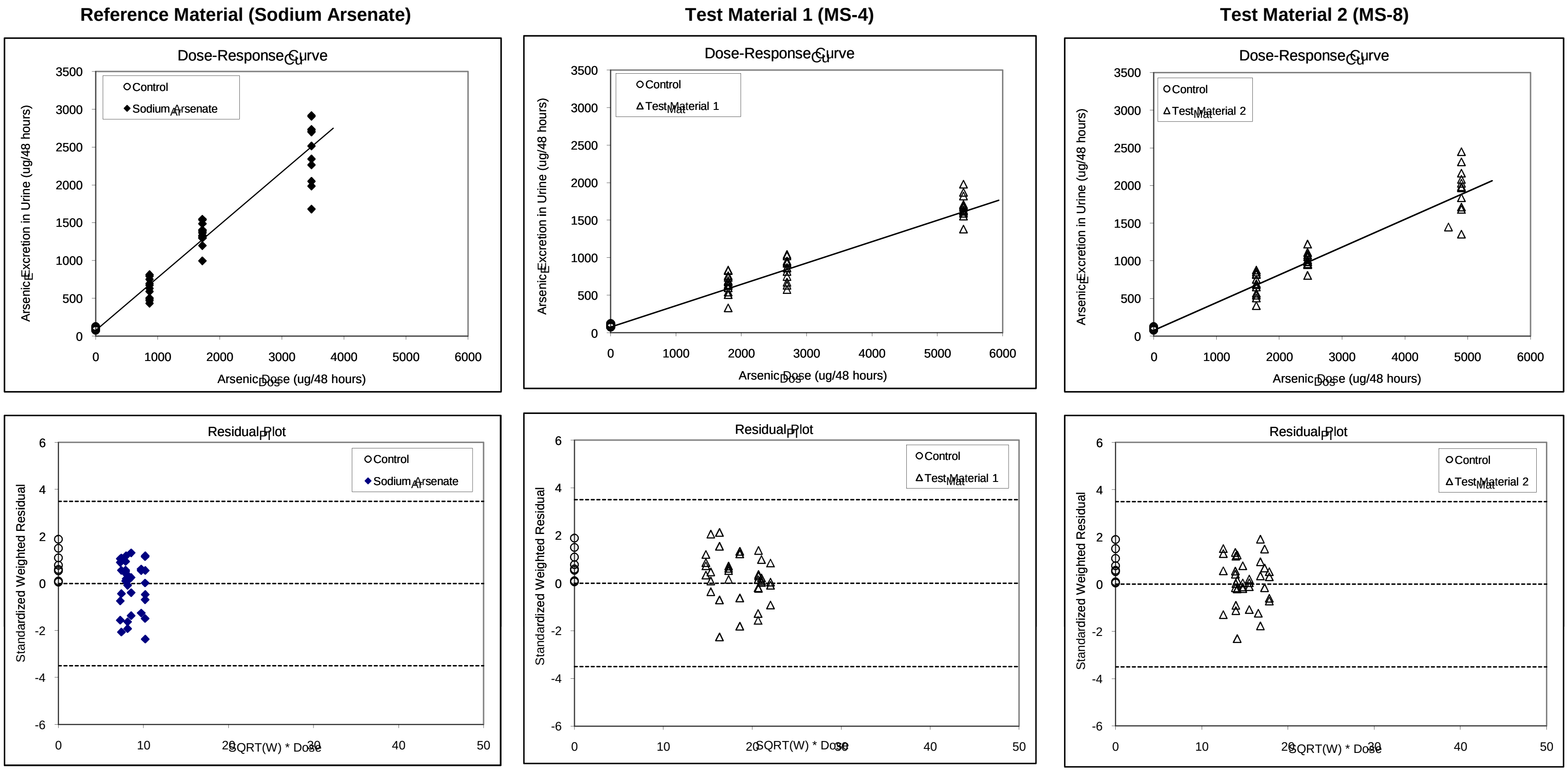
Statistic	Estimate
F	182.013
p	< 0.001
Adjusted R^2	0.9346

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.39	0.53
Lower bound[c]	0.33	0.45
Upper bound[c]	0.46	0.62
Standard Error[c]	0.038	0.049

[c] 90% confidence interval as calculated using Fieller's theorem

FIGURE 4-15 STUDY 3 URINARY EXCRETION OF ARSENIC: All Days



Summary of Fitting[a]

Parameter	Estimate	SE
a	74.6	21.3
b_r	0.70	0.02
b_{t1}	0.28	0.01
b_{t2}	0.37	0.01
Covariance (b_r,b_{t1})	0.2729	--
Covariance (b_r,b_{t2})	0.2135	--
Degrees of Freedom	113	--

[a] $y = a + b_r*x_r + b_{t1}*x_{t1} + b_{t2}*x_{t2}$

where r = Reference Material, t1 = Test Material 1, and t2 = Test Material 2

ANOVA

Source	SSE	DF	MSE
Fit	2815.63	3	938.54
Error	122.72	112	1.10
Total	2938.34	115	25.55

Statistic	Estimate
F	856.575
p	< 0.001
Adjusted R^2	0.9571

RBA and Uncertainty

	Test Material 1	Test Material 2
RBA	0.41	0.53
Lower bound[c]	0.38	0.49
Upper bound[c]	0.44	0.57
Standard Error[c]	0.018	0.023

[c] 90% confidence interval as calculated using Fieller's theorem

APPENDIX A GROUP ASSIGNMENTS

STUDY 1 (MS-1 MATERIAL)

Pig Number	Group	Dosing Material	Target Arsenic Dose (μg/kg-day)
353	1	Control	0
359			
373			
368	2	NaAs	25
374			
367			
370			
351	3	NaAs	50
356			
361			
372			
358	4	NaAs	100
365			
366			
371			
360	5	TM1	60
363			
369			
375			
352	6	TM1	120
364			
354			
362			

STUDY 2 (MS-5 MATERIAL)

Pig Number	Group	Dosing Material	Target Arsenic Dose (μg/kg-day)
463 465 474 475	1	NaAs	25
448 451 454 483	2	NaAs	50
450 466 468 481	3	TM1	40
445 452 470 482	4	TM1	60
250 449 455 464	5	TM1	120
249 446 453 467	6	TM2	40
469 473	7	Control	0

<u>Notes:</u>
MS-1 material was used for the TM2 group but RBA was not evaluated for TM2.

STUDY 3 (MS-4 and MS-8 MATERIALS)

Pig Number	Group	Dosing Material	Target Arsenic Dose (μg/kg-day)
503	1	NaAs	25
511			
529			
543			
502	2	NaAs	50
505			
506			
527			
501	3	NaAs	100
516			
521			
531			
530	4	TM1	40
535			
538			
541			
513	5	TM1	60
525			
526			
537			
507	6	TM1	120
514			
515			
533			
504	7	TM2	40
508			
519			
534			
509	8	TM2	60
532			
536			
540			
510	9	TM2	120
517			
518			
520			
512	10	Control	0
522			
539			

APPENDIX B

BODY WEIGHTS

APPENDIX B BODY WEIGHTS

Body weights were measured on days -1, 2, 5, 8, 11, and 14. Weights for other days are estimated, based on linear interpolation between measured values.

STUDY 1

Group	Pig #	Day -1	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14	Days 0-14
		BW (kg)	BW (kg)	BW (kg)	BW (kg)	BW (kg)	BW (kg)	BW (kg)	BW (kg)	BW (kg)	BW (kg)	BW (kg)	BW (kg)	BW (kg)	BW (kg)	BW (kg)	BW (kg)	Mean Daily BW Gain
1	503	14.8	15.1	15.3	15.6	15.9	16.2	16.5	16.8	17.2	17.5	17.9	18.3	18.7	19.0	19.2	19.5	0.32
1	511	11.7	11.9	12.2	12.4	12.8	13.1	13.5	13.8	14.1	14.4	14.7	15.0	15.3	15.8	16.2	16.7	0.34
1	529	13.4	13.7	14.1	14.4	14.7	15.1	15.4	15.7	16.0	16.3	16.7	17.1	17.5	17.9	18.3	18.7	0.35
1	543	15.1	15.4	15.7	16.0	16.4	16.7	17.1	17.3	17.5	17.7	18.2	18.8	19.3	19.7	20.1	20.5	0.36
2	502	12.8	13.0	13.2	13.4	13.7	14.0	14.3	14.7	15.0	15.4	15.8	16.2	16.6	16.9	17.3	17.6	0.33
2	505	12.0	12.3	12.6	12.9	13.2	13.6	13.9	14.4	14.8	15.3	15.7	16.1	16.5	16.9	17.2	17.6	0.38
2	506	12.5	12.8	13.1	13.4	13.7	13.9	14.2	14.5	14.9	15.2	15.6	16.0	16.4	16.7	17.1	17.4	0.33
2	527	13.4	13.7	14.1	14.4	14.6	14.8	15.0	15.4	15.7	16.1	16.3	16.5	16.7	17.1	17.6	18.0	0.30
3	501	11.7	12.0	12.3	12.6	12.9	13.3	13.6	13.9	14.2	14.5	14.9	15.2	15.6	15.9	16.3	16.6	0.33
3	516	15.2	15.5	15.9	16.2	16.5	16.7	17.0	17.3	17.7	18.0	18.4	18.8	19.2	19.5	19.9	20.2	0.33
3	521	12.0	12.4	12.7	13.1	13.4	13.6	13.9	14.3	14.8	15.2	15.5	15.8	16.1	16.4	16.8	17.1	0.34
3	531	13.9	14.2	14.5	14.8	15.2	15.5	15.9	16.2	16.6	16.9	17.3	17.8	18.2	18.6	18.9	19.3	0.36
4	530	14.2	14.5	14.9	15.2	15.6	16.0	16.4	16.8	17.2	17.6	17.9	18.2	18.5	18.9	19.3	19.7	0.37
4	535	13.0	13.3	13.6	13.9	14.0	14.1	14.2	14.6	15.1	15.5	15.8	16.1	16.4	16.7	17.1	17.4	0.29
4	538	14.3	14.6	15.0	15.3	15.7	16.1	16.5	16.8	17.1	17.4	17.8	18.2	18.6	19.1	19.5	20.0	0.38
4	541	13.1	13.4	13.6	13.9	14.1	14.4	14.6	15.0	15.3	15.7	16.0	16.4	16.7	17.1	17.4	17.8	0.32
5	513	14.3	14.6	14.8	15.1	15.5	15.8	16.2	16.5	16.8	17.1	17.5	17.9	18.3	18.6	18.9	19.2	0.33
5	525	13.6	13.8	14.1	14.3	14.6	14.9	15.2	15.6	16.0	16.4	16.8	17.3	17.7	18.2	18.7	19.2	0.38
5	526	15.9	16.1	16.4	16.6	16.9	17.2	17.5	17.9	18.4	18.8	19.2	19.6	20.0	20.4	20.9	21.3	0.37
5	537	12.1	12.4	12.8	13.1	13.5	13.9	14.3	14.6	14.9	15.2	15.6	16.0	16.4	16.7	17.0	17.3	0.35
6	507	14.4	14.8	15.1	15.5	15.6	15.8	15.9	16.3	16.8	17.2	17.6	17.9	18.3	18.7	19.0	19.4	0.33
6	514	15.3	15.7	16.2	16.6	16.9	17.3	17.6	18.0	18.3	18.7	19.1	19.6	20.0	20.3	20.6	20.9	0.37
6	515	14.8	15.2	15.6	16.0	16.4	16.7	17.1	17.4	17.8	18.1	18.6	19.0	19.5	19.9	20.3	20.7	0.39
6	533	14.6	15.0	15.4	15.8	16.0	16.2	16.4	16.8	17.3	17.7	18.3	18.8	19.4	19.7	20.0	20.3	0.38
7	504	16.2	16.7	17.1	17.6	17.8	18.0	18.2	18.5	18.8	19.1	19.5	20.0	20.4	20.7	21.1	21.4	0.34
7	508	15.0	15.4	15.7	16.1	16.3	16.6	16.8	17.0	17.3	17.5	17.9	18.4	18.8	19.1	19.4	19.7	0.31

STUDY 2

Group	Pig #	Day -1 BW (kg)	Day 0 BW (kg)	Day 1 BW (kg)	Day 2 BW (kg)	Day 3 BW (kg)	Day 4 BW (kg)	Day 5 BW (kg)	Day 6 BW (kg)	Day 7 BW (kg)	Day 8 BW (kg)	Day 9 BW (kg)	Day 10 BW (kg)	Day 11 BW (kg)	Day 12 BW (kg)	Day 13 BW (kg)	Day 14 BW (kg)	Days 0-14 Mean Daily BW Gain
1	463	9.0	9.2	9.4	9.6	9.7	9.9	10.0	10.3	10.6	10.9	11.1	11.3	11.5	11.7	12.0	12.2	0.21
1	465	7.2	7.4	7.6	7.8	8.0	8.3	8.5	8.7	9.0	9.2	9.4	9.6	9.8	10.2	10.5	10.9	0.25
1	474	7.6	7.9	8.1	8.4	8.6	8.7	8.9	9.1	9.3	9.5	9.8	10.0	10.3	10.7	11.0	11.4	0.25
1	475	7.5	7.6	7.6	7.7	7.9	8.2	8.4	8.7	8.9	9.2	9.4	9.7	9.9	10.2	10.5	10.8	0.23
2	448	8.2	8.4	8.6	8.8	9.0	9.3	9.5	9.7	10.0	10.2	10.5	10.7	11.0	11.2	11.5	11.7	0.24
2	451	8.7	8.8	8.9	9.0	9.2	9.4	9.6	9.8	10.1	10.3	10.5	10.8	11.0	11.3	11.5	11.8	0.21
2	454	9.1	9.3	9.4	9.6	9.7	9.9	10.0	10.3	10.5	10.8	11.1	11.3	11.6	11.9	12.1	12.4	0.22
2	483	7.2	7.4	7.6	7.8	8.1	8.3	8.6	8.8	9.0	9.2	9.4	9.7	9.9	10.2	10.5	10.8	0.24
3	450	7.7	7.9	8.0	8.2	8.4	8.7	8.9	9.1	9.4	9.6	9.9	10.1	10.4	10.6	10.9	11.1	0.23
3	466	7.9	8.1	8.2	8.4	8.6	8.8	9.0	9.2	9.5	9.7	10.0	10.2	10.5	10.8	11.1	11.4	0.24
3	468	9.1	9.1	9.2	9.2	9.4	9.6	9.8	10.0	10.3	10.5	10.8	11.1	11.4	11.7	12.0	12.3	0.23
3	481	8.8	8.9	9.0	9.1	9.4	9.6	9.9	10.1	10.3	10.5	10.8	11.1	11.4	11.6	11.9	12.1	0.23
4	445	7.9	8.1	8.3	8.5	8.7	9.0	9.2	9.4	9.7	9.9	10.2	10.4	10.7	11.0	11.2	11.5	0.24
4	452	7.7	7.9	8.1	8.3	8.5	8.8	9.0	9.2	9.4	9.6	9.9	10.1	10.4	10.7	11.0	11.3	0.24
4	470	8.5	8.8	9.0	9.3	9.6	9.9	10.2	10.4	10.7	10.9	11.1	11.3	11.5	11.8	12.0	12.3	0.25
4	482	7.9	8.1	8.3	8.5	8.7	8.8	9.0	9.3	9.5	9.8	10.0	10.2	10.4	10.7	11.0	11.3	0.23
5	250	7.2	7.3	7.4	7.5	7.8	8.2	8.5	8.7	8.8	9.0	9.3	9.5	9.8	10.1	10.4	10.7	0.24
5	449	8.6	8.8	8.9	9.1	9.3	9.6	9.8	10.0	10.2	10.4	10.7	11.1	11.4	11.7	12.1	12.4	0.26
5	455	9.2	9.4	9.6	9.8	10.0	10.3	10.5	10.7	10.9	11.1	11.3	11.6	11.8	12.1	12.4	12.7	0.24
5	464	8.8	8.9	9.1	9.2	9.3	9.5	9.6	9.9	10.1	10.4	10.6	10.9	11.1	11.4	11.7	12.0	0.22
6	249	8.7	8.7	8.7	8.7	8.9	9.0	9.2	9.6	9.9	10.3	10.5	10.8	11.0	11.3	11.7	12.0	0.24
6	446	8.0	8.1	8.1	8.2	8.4	8.6	8.8	9.1	9.3	9.6	9.9	10.1	10.4	10.7	11.0	11.3	0.23
6	453	8.5	8.6	8.7	8.8	8.9	9.1	9.2	9.3	9.4	9.5	9.8	10.0	10.3	10.6	10.8	11.1	0.18
6	467	8.0	8.1	8.1	8.2	8.5	8.7	9.0	9.2	9.3	9.5	9.8	10.1	10.4	10.6	10.9	11.1	0.22
6	469	8.8	9.0	9.2	9.4	9.6	9.7	9.9	10.2	10.4	10.7	11.0	11.2	11.5	11.8	12.0	12.3	0.24
6	473	8.1	8.0	8.0	7.9	8.1	8.2	8.4	8.6	8.8	9.0	9.1	9.3	9.4	9.5	9.7	9.8	0.13

STUDY 3

Group	Pig #	Day -1	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14	Days 0-14
		BW (kg)	BW (kg)	BW (kg)	BW (kg)	BW (kg)	BW (kg)	BW (kg)	BW (kg)	BW (kg)	BW (kg)	BW (kg)	BW (kg)	BW (kg)	BW (kg)	BW (kg)	BW (kg)	Mean Daily BW Gain
1	503	14.8	15.1	15.3	15.6	15.9	16.2	16.5	16.8	17.2	17.5	17.9	18.3	18.7	19.0	19.2	19.5	0.32
1	511	11.7	11.9	12.2	12.4	12.8	13.1	13.5	13.8	14.1	14.4	14.7	15.0	15.3	15.8	16.2	16.7	0.34
1	529	13.4	13.7	14.1	14.4	14.7	15.1	15.4	15.7	16.0	16.3	16.7	17.1	17.5	17.9	18.3	18.7	0.35
1	543	15.1	15.4	15.7	16.0	16.4	16.7	17.1	17.3	17.5	17.7	18.2	18.8	19.3	19.7	20.1	20.5	0.36
2	502	12.8	13.0	13.2	13.4	13.7	14.0	14.3	14.7	15.0	15.4	15.8	16.2	16.6	16.9	17.3	17.6	0.33
2	505	12.0	12.3	12.6	12.9	13.2	13.6	13.9	14.4	14.8	15.3	15.7	16.1	16.5	16.9	17.2	17.6	0.38
2	506	12.5	12.8	13.1	13.4	13.7	13.9	14.2	14.5	14.9	15.2	15.6	16.0	16.4	16.7	17.1	17.4	0.33
2	527	13.4	13.7	14.1	14.4	14.6	14.8	15.0	15.4	15.7	16.1	16.3	16.5	16.7	17.1	17.6	18.0	0.30
3	501	11.7	12.0	12.3	12.6	12.9	13.3	13.6	13.9	14.2	14.5	14.9	15.2	15.6	15.9	16.3	16.6	0.33
3	516	15.2	15.5	15.9	16.2	16.5	16.7	17.0	17.3	17.7	18.0	18.4	18.8	19.2	19.5	19.9	20.2	0.33
3	521	12.0	12.4	12.7	13.1	13.4	13.6	13.9	14.3	14.8	15.2	15.5	15.8	16.1	16.4	16.8	17.1	0.34
3	531	13.9	14.2	14.5	14.8	15.2	15.5	15.9	16.2	16.6	16.9	17.3	17.8	18.2	18.6	18.9	19.3	0.36
4	530	14.2	14.5	14.9	15.2	15.6	16.0	16.4	16.8	17.2	17.6	17.9	18.2	18.5	18.9	19.3	19.7	0.37
4	535	13.0	13.3	13.6	13.9	14.0	14.1	14.2	14.6	15.1	15.5	15.8	16.1	16.4	16.7	17.1	17.4	0.29
4	538	14.3	14.6	15.0	15.3	15.7	16.1	16.5	16.8	17.1	17.4	17.8	18.2	18.6	19.1	19.5	20.0	0.38
4	541	13.1	13.4	13.6	13.9	14.1	14.4	14.6	15.0	15.3	15.7	16.0	16.4	16.7	17.1	17.4	17.8	0.32
5	513	14.3	14.6	14.8	15.1	15.5	15.8	16.2	16.5	16.8	17.1	17.5	17.9	18.3	18.6	18.9	19.2	0.33
5	525	13.6	13.8	14.1	14.3	14.6	14.9	15.2	15.6	16.0	16.4	16.8	17.3	17.7	18.2	18.7	19.2	0.38
5	526	15.9	16.1	16.4	16.6	16.9	17.2	17.5	17.9	18.4	18.8	19.2	19.6	20.0	20.4	20.9	21.3	0.37
5	537	12.1	12.4	12.8	13.1	13.5	13.9	14.3	14.6	14.9	15.2	15.6	16.0	16.4	16.7	17.0	17.3	0.35
6	507	14.4	14.8	15.1	15.5	15.6	15.8	15.9	16.3	16.8	17.2	17.6	17.9	18.3	18.7	19.0	19.4	0.33
6	514	15.3	15.7	16.2	16.6	16.9	17.3	17.6	18.0	18.3	18.7	19.1	19.6	20.0	20.3	20.6	20.9	0.37
6	515	14.8	15.2	15.6	16.0	16.4	16.7	17.1	17.4	17.8	18.1	18.6	19.0	19.5	19.9	20.3	20.7	0.39
6	533	14.6	15.0	15.4	15.8	16.0	16.2	16.4	16.8	17.3	17.7	18.3	18.8	19.4	19.7	20.0	20.3	0.38
7	504	16.2	16.7	17.1	17.6	17.8	18.0	18.2	18.5	18.8	19.1	19.5	20.0	20.4	20.7	21.1	21.4	0.34
7	508	15.0	15.4	15.7	16.1	16.3	16.6	16.8	17.0	17.3	17.5	17.9	18.4	18.8	19.1	19.4	19.7	0.31
7	519	12	12.77	13.13	13.5	13.8	14.1	14.4	14.7	15	15.3	15.8	16.3	16.8	17.17	17.53	17.9	0.37
7	534	15	15.367	15.733	16.1	16.467	16.833	17.2	17.567	17.933	18.3	18.667	19.033	19.4	19.7	20	20.3	0.35
8	509	13	13.367	13.633	13.9	14.1	14.3	14.5	14.833	15.167	15.5	15.9	16.3	16.7	17	17.3	17.6	0.30
8	532	14	14.5	14.8	15.1	15.5	15.9	16.3	16.767	17.233	17.7	17.867	18.033	18.2	18.533	18.867	19.2	0.34
8	536	13	13.633	13.967	14.3	14.667	15.033	15.4	15.5	15.6	15.7	16.5	17.3	18.1	18.333	18.567	18.8	0.37
8	540	13	13.667	13.933	14.2	14.467	14.733	15	15.567	16.133	16.7	17.033	17.367	17.7	18	18.3	18.6	0.35
9	510	11	11.6	12.1	12.6	13.133	13.667	14.2	14.433	14.667	14.9	15.4	15.9	16.4	16.8	17.2	17.6	0.43
9	517	12	11.7	11.6	11.5	11.933	12.367	12.8	13.167	13.533	13.9	14.067	14.233	14.4	14.767	15.133	15.5	0.27
9	518	13	13.367	13.733	14.1	14.5	14.9	15.3	15.6	15.9	16.2	16.633	17.067	17.5	17.767	18.033	18.3	0.35
9	520	14	14.067	14.333	14.6	14.933	15.267	15.6	15.867	16.133	16.4	16.733	17.067	17.4	17.633	17.867	18.1	0.29
10	512	13	13.333	13.767	14.2	14.533	14.867	15.2	15.4	15.6	15.8	16.333	16.867	17.4	17.5	17.6	17.7	0.31
10	522	14	14.333	14.567	14.8	15.167	15.533	15.9	16.133	16.367	16.6	17	17.4	17.8	18.1	18.4	18.7	0.31
10	539	15	14.767	15.033	15.3	15.667	16.033	16.4	16.8	17.2	17.6	17.933	18.267	18.6	18.9	19.2	19.5	0.34

APPENDIX C

MISSED AND LATE DOSE CONSUMPTION

APPENDIX C MISSED AND LATE DOSE CONSUMPTION

STUDY 1

Day	Pig No.	Note
0	360	Day 0 - Pig 360 at only 1/2 of his dose in the AM and the PM. Dose adjusted to 50%.
0	368	Day 0 - Pig 368 slow to eat AM dose but did finish it by PM dose time.
1	360	Day 1 - Pig 360 slow to eat AM dose but did eat it all by 3 PM.
2	372	Day 2 - Pig 372 did not eat his dose in the AM or PM.
2	360	Day 2 - Pig 360 slow to eat AM dose but did eat it all by 3 PM.
3	372	Day 3 - Pig 372 at only 1/2 of his dose in the AM. AM dose adjusted to 50%.

STUDY 2

Day	Pig No.	Note
0	468	Day 0 - Pig 468 did not consume PM dose.
0	445	Day 0 - Pig 445 lost 10% of dose.
1	468	Day 1 - Pig 468 did not consume AM dose.
2	474	Day 2 - Pig 474 lose 5% of PM dose.
3	474	Day 3 - Pig 474 ate 70% of AM dose and 90% of PM dose.
4	474	Day 4 - Pig 474 ate 30% of AM dose.
4	453	Day 4 - Pig 453 lost 10% of PM dose
9	469	Day 9 - Pig 469 did not eat AM dose
10	469	Day 10 - Pig 469 did not eat AM dose
11	469	Day 11 - Pig 469 did not eat AM dose

STUDY 3

Day	Pig No.	Note
0 - 14	510	Throughout dosing period pig 510 was slow to consume doses.
11	518	Day 11 - Pig 518 dropped doughball on cage floor and lost 25% of dose.

APPENDIX D

URINE VOLUMES

APPENDIX D URINE VOLUMES

STUDY 1

Group	Pig Number	Urine Collection (mL) U-1 Days 6-7	U-2 Days 9-10	U-3 Days 12-13
1	353	3240	9790	8290
	359	4710	4000	5400
	373	6120	5030	6123
2	368	3540	3420	4660
	374	20130	42300	37980
	367	7730	8520	7680
	370	4075	4140	5030
3	351	3890	3530	3660
	356	2920	2700	3860
	361	5890	6220	7520
	372	2870	1900	1940
4	358	2390	2000	3350
	365	12560	16320	10360
	366	3260	2370	2480
	371	2660	2137	2420
5	360	2560	5260	5660
	363	1780	2950	2102
	369	1980	3930	3140
	375	5960	9220	8840
6	352	6960	6480	4830
	364	7180	6560	12230
	354	2560	3380	4040
	362	9960	9840	11410

STUDY 2

Group	Pig ID	Urine Collection (mL)		
		U-1 Days 6-7	**U-2** Days 9-10	**U-3** Days 12-13
1	463	3740	5380	6780
	465	1720	1180	2370
	474	3200	3460	4250
	475	6940	9680	6640
2	448	1040	1020	1980
	451	2280	1500	1990
	454	3800	10280	13100
	483	11160	7560	5430
3	450	3000	2080	4220
	466	6220	10200	20520
	468	3780	3460	2760
	481	2280	1660	2400
4	445	4700	5260	4540
	452	2800	5850	8200
	470	440	520	520
	482	10590	8280	7600
5	250	7600	10010	9040
	449	2480	3020	3260
	455	6040	5430	5340
	464	5020	1220	560
6	249	1860	2250	2000
	446	5620	4640	3560
	453	500	760	1060
	467	1860	2170	1790
7	469	3680	3350	4680
	473	5700	4240	3880

STUDY 3

Group	Pig Number	Urine Collection (mL)		
		U-1 Days 6-7	**U-2** Days 9-10	**U-3** Days 12-13
1	503	3350	5240	5900
	511	3200	3120	4160
	529	3360	3400	4260
	543	3300	1880	2130
2	502	3160	5120	4680
	505	14340	9920	9960
	506	9610	7220	10570
	527	5460	5390	6990
3	501	4085	5680	5460
	516	4700	4260	4130
	521	2330	3740	4350
	531	1560	2080	2640
4	530	3700	5490	5440
	535	2460	2320	2070
	538	880	980	1080
	541	7020	4020	3810
5	513	7850	5460	6130
	525	4300	3420	6460
	526	3540	2300	3420
	537	11740	10720	12520
6	507	13640	9360	7430
	514	1740	1160	1650
	515	1620	1520	2320
	533	4680	4460	7400
7	504	4040	3800	4200
	508	3660	3400	5000
	519	16800	10360	11250
	534	4660	9040	10600
8	509	1130	1250	860
	532	5740	6100	6380
	536	4400	4310	5840
	540	3660	4580	4700
9	510	7310	5100	2460
	517	3500	4240	6300
	518	840	820	680
	520	2460	1410	2240
10	512	1070	not measured	2380
	522	1980	1920	2960
	539	2170	1900	1540

APPENDIX E

URINARY ARSENIC ANALYTICAL RESULTS FOR STUDY SAMPLES

APPENDIX E URINARY ARSENIC ANALYTICAL RESULTS FOR STUDY SAMPLES

STUDY 1

sample number	tag number	Pig#	Group	Material	Urine Collection Day(s)	Arsenic Dose (ug As/48 hrs)	Q	Urine As Concentration (ug/L)	Urine Volume (mL/48 hrs)	Total As Excreted (ug As/48 hrs)
EP3-2-353-U1	EP3-2-127	353	1	Control	6/7	0		14	3240	45.36
EP3-2-359-U1	EP3-2-123	359	1	Control	6/7	0		14	4000	56
EP3-2-373-U1	EP3-2-105	373	1	Control	6/7	0		12	6123	73.476
EP3-2-354-U1	EP3-2-108	354	6	TM1	6/7	2958		170	2560	435.2
EP3-2-362-U1	EP3-2-126	362	6	TM1	6/7	2958		24	9840	236.16
EP3-2-367-U1	EP3-2-118	367	2	NaAs	6/7	596		70	7680	537.6
EP3-2-370-U1	EP3-2-113	370	2	NaAs	6/7	596		123	4075	501.225
EP3-2-351-U1	EP3-2-130	351	3	NaAs	6/7	1192		250	3530	882.5
EP3-2-356-U1	EP3-2-124	356	3	NaAs	6/7	1192		370	3860	1428.2
EP3-2-361-U1	EP3-2-129	361	3	NaAs	6/7	1192		109	5890	642.01
EP3-2-372-U1	EP3-2-122	372	3	NaAs	6/7	965.52		340	1900	646
EP3-2-358-U1	EP3-2-107	358	4	NaAs	6/7	2384		840	3350	2814
EP3-2-365-U1	EP3-2-128	365	4	NaAs	6/7	2384		150	12560	1884
EP3-2-366-U1	EP3-2-109	366	4	NaAs	6/7	2384		730	2370	1730.1
EP3-2-371-U1	EP3-2-120	371	4	NaAs	6/7	2384		790	2420	1911.8
EP3-2-360-U1	EP3-2-131	360	5	TM1	6/7	1395.712		210	2560	537.6
EP3-2-363-U1	EP3-2-115	363	5	TM1	6/7	1484.8		360	2950	1062
EP3-2-369-U1	EP3-2-110	369	5	TM1	6/7	1484.8		340	3140	1067.6
EP3-2-375-U1	EP3-2-125	375	5	TM1	6/7	1484.8		72	5960	429.12
EP3-2-352-U1	EP3-2-114	352	6	TM1	6/7	2958		122	6480	790.56
EP3-2-364-U1	EP3-2-103	364	6	TM1	6/7	2958		160	12230	1956.8
EP3-2-368-U1	EP3-2-111	368	2	NaAs	6/7	596		260	3540	920.4
EP3-2-374-U1	EP3-2-101	374	2	NaAs	6/7	596		89	42300	3764.7
EP3-2-353-U2	EP3-2-133	353	1	Control	9/10	0		6.3	8290	52.227
EP3-2-359-U2	EP3-2-158	359	1	Control	9/10	0		19	4710	89.49
EP3-2-373-U2	EP3-2-150	373	1	Control	9/10	0		11	5030	55.33
EP3-2-354-U2	EP3-2-144	354	6	TM1	9/10	2958		128	4040	517.12
EP3-2-362-U2	EP3-2-142	362	6	TM1	9/10	2958		14	9960	139.44
EP3-2-367-U2	EP3-2-145	367	2	NaAs	9/10	596		73	8520	621.96
EP3-2-370-U2	EP3-2-137	370	2	NaAs	9/10	596		117	5030	588.51
EP3-2-351-U2	EP3-2-153	351	3	NaAs	9/10	1192		300	3890	1167
EP3-2-356-U2	EP3-2-161	356	3	NaAs	9/10	1192		250	2700	675
EP3-2-361-U2	EP3-2-140	361	3	NaAs	9/10	1192		130	7520	977.6
EP3-2-372-U2	EP3-2-139	372	3	NaAs	9/10	1192		510	2870	1463.7
EP3-2-358-U2	EP3-2-135	358	4	NaAs	9/10	2384		710	2000	1420
EP3-2-365-U2	EP3-2-157	365	4	NaAs	9/10	2384		130	10360	1346.8
EP3-2-366-U2	EP3-2-132	366	4	NaAs	9/10	2384		820	3260	2673.2
EP3-2-371-U2	EP3-2-156	371	4	NaAs	9/10	2384		880	2137	1880.56
EP3-2-360-U2	EP3-2-154	360	5	TM1	9/10	1484.8		100	5660	566
EP3-2-363-U2	EP3-2-138	363	5	TM1	9/10	1484.8		210	1780	373.8
EP3-2-369-U2	EP3-2-141	369	5	TM1	9/10	1484.8		180	3930	707.4
EP3-2-375-U2	EP3-2-147	375	5	TM1	9/10	1484.8		59	8840	521.56
EP3-2-352-U2	EP3-2-149	352	6	TM1	9/10	2958		160	6960	1113.6
EP3-2-364-U2	EP3-2-146	364	6	TM1	9/10	2958		190	6560	1246.4
EP3-2-368-U2	EP3-2-160	368	2	NaAs	9/10	596		300	4660	1398
EP3-2-374-U2	EP3-2-136	374	2	NaAs	9/10	596		91	20130	1831.83
EP3-2-353-U3	EP3-2-178	353	1	Control	12/13	0		7.4	9790	72.446
EP3-2-359-U3	EP3-2-182	359	1	Control	12/13	0		13	5400	70.2
EP3-2-373-U3	EP3-2-173	373	1	Control	12/13	0		13	6120	79.56
EP3-2-354-U3	EP3-2-185	354	6	TM1	12/13	2958		122	3380	412.36
EP3-2-362-U3	EP3-2-181	362	6	TM1	12/13	2958		16	11410	182.56
EP3-2-367-U3	EP3-2-174	367	2	NaAs	12/13	596		77	7730	595.21
EP3-2-370-U3	EP3-2-186	370	2	NaAs	12/13	596		209	4140	865.26
EP3-2-351-U3	EP3-2-189	351	3	NaAs	12/13	1192		260	3660	951.6
EP3-2-356-U3	EP3-2-184	356	3	NaAs	12/13	1192		250	2920	730
EP3-2-361-U3	EP3-2-168	361	3	NaAs	12/13	1192		116	6220	721.52
EP3-2-372-U3	EP3-2-169	372	3	NaAs	12/13	1192		400	1940	776
EP3-2-358-U3	EP3-2-188	358	4	NaAs	12/13	2384		610	2390	1457.9
EP3-2-365-U3	EP3-2-187	365	4	NaAs	12/13	2384		200	16320	3264
EP3-2-366-U3	EP3-2-183	366	4	NaAs	12/13	2384		770	2480	1909.6
EP3-2-371-U3	EP3-2-175	371	4	NaAs	12/13	2384		870	2660	2314.2
EP3-2-360-U3	EP3-2-167	360	5	TM1	12/13	1484.8		92	5260	483.92
EP3-2-363-U3	EP3-2-172	363	5	TM1	12/13	1484.8		210	2102	441.42
EP3-2-369-U3	EP3-2-180	369	5	TM1	12/13	1484.8		200	1980	396
EP3-2-375-U3	EP3-2-177	375	5	TM1	12/13	1484.8		67	9220	617.74
EP3-2-352-U3	EP3-2-176	352	6	TM1	12/13	2958		220	4830	1062.6
EP3-2-364-U3	EP3-2-166	364	6	TM1	12/13	2958		110	7180	789.8
EP3-2-368-U3	EP3-2-171	368	2	NaAs	12/13	596		230	3420	786.6
EP3-2-374-U3	EP3-2-170	374	2	NaAs	12/13	596		85	37980	3228.3

STUDY 2

sample number	tag number	Pig#	Group	Material	Urine Collection Day(s)	Arsenic Dose	Q	Urine As Concentration (ug/L)	Urine Volume (mL/48 hrs)	Total As Excreted (ug As/48 hrs)
MS-5-463-U1	MS-5-126	463	1	NaAs	6/7	599		108	3740	403.92
MS-5-465-U1	MS-5-120	465	1	NaAs	6/7	599		260	1180	306.8
MS-5-474-U1	MS-5-119	474	1	NaAs	6/7	545		150	4250	637.5
MS-5-475-U1	MS-5-130	475	1	NaAs	6/7	599		76	6940	527.44
MS-5-448-U1	MS-5-118	448	2	NaAs	6/7	1196		530	1020	540.6
MS-5-451-U1	MS-5-128	451	2	NaAs	6/7	1196		370	1990	736.3
MS-5-454-U1	MS-5-110	454	2	NaAs	6/7	1196		280	3800	1064
MS-5-483-U1	MS-5-121	483	2	NaAs	6/7	1196		91	7560	687.96
MS-5-450-U1	MS-5-103	450	3	TM1	6/7	981		130	4220	548.6
MS-5-466-U1	MS-5-102	466	3	TM1	6/7	981		65	6220	404.3
MS-5-468-U1	MS-5-112	468	3	TM1	6/7	864		115	3460	397.9
MS-5-481-U1	MS-5-108	481	3	TM1	6/7	981		190	2400	456
MS-5-445-U1	MS-5-114	445	4	TM1	6/7	1472		73	4700	343.1
MS-5-452-U1	MS-5-101	452	4	TM1	6/7	1472		190	5850	1111.5
MS-5-470-U1	MS-5-109	470	4	TM1	6/7	1472		1200	520	624
MS-5-482-U1	MS-5-122	482	4	TM1	6/7	1472		64	10590	677.76
MS-5-250-U1	MS-5-116	250	5	TM1	6/7	2944		150	10010	1501.5
MS-5-449-U1	MS-5-123	449	5	TM1	6/7	2944		440	3260	1434.4
MS-5-455-U1	MS-5-133	455	5	TM1	6/7	2944		200	6040	1208
MS-5-464-U1	MS-5-105	464	5	TM1	6/7	2944		160	1220	195.2
MS-5-249-U1	MS-5-124	249	6	TM2	6/7	968		200	2000	400
MS-5-446-U1	MS-5-131	446	6	TM2	6/7	968		62	5620	348.44
MS-5-453-U1	MS-5-106	453	6	TM2	6/7	968		620	760	471.2
MS-5-467-U1	MS-5-134	467	6	TM2	6/7	968		170	1790	304.3
MS-5-469-U1	MS-5-115	469	7	Control	6/7	0		17	3680	62.56
MS-5-473-U1	MS-5-127	473	7	Control	6/7	0		11	4240	46.64
MS-5-463-U2	MS-5-144	463	1	NaAs	9/10	599		99	6780	671.22
MS-5-465-U2	MS-5-167	465	1	NaAs	9/10	599		440	1720	756.8
MS-5-474-U2	MS-5-161	474	1	NaAs	9/10	599		139	3460	480.94
MS-5-475-U2	MS-5-136	475	1	NaAs	9/10	599		56	6640	371.84
MS-5-448-U2	MS-5-150	448	2	NaAs	9/10	1196		850	1040	884
MS-5-451-U2	MS-5-142	451	2	NaAs	9/10	1196		520	1500	780
MS-5-454-U2	MS-5-158	454	2	NaAs	9/10	1196		94	13100	1231.4
MS-5-483-U2	MS-5-163	483	2	NaAs	9/10	1196		130	11160	1450.8
MS-5-450-U2	MS-5-164	450	3	TM1	9/10	981		220	2080	457.6
MS-5-466-U2	MS-5-154	466	3	TM1	9/10	981		44	20520	902.88
MS-5-468-U2	MS-5-145	468	3	TM1	9/10	981		120	3780	453.6
MS-5-481-U2	MS-5-143	481	3	TM1	9/10	981		250	1660	415
MS-5-445-U2	MS-5-153	445	4	TM1	9/10	1472		128	4540	581.12
MS-5-452-U2	MS-5-165	452	4	TM1	9/10	1472		112	2800	313.6
MS-5-470-U2	MS-5-159	470	4	TM1	9/10	1472		840	520	436.8
MS-5-482-U2	MS-5-162	482	4	TM1	9/10	1472		79	7600	600.4
MS-5-250-U2	MS-5-155	250	5	TM1	9/10	2944		93	7600	706.8
MS-5-449-U2	MS-5-139	449	5	TM1	9/10	2944		390	3020	1177.8
MS-5-455-U2	MS-5-135	455	5	TM1	9/10	2944		240	5340	1281.6
MS-5-464-U2	MS-5-160	464	5	TM1	9/10	2944		780	5020	3915.6
MS-5-249-U2	MS-5-140	249	6	TM2	9/10	968		150	2250	337.5
MS-5-446-U2	MS-5-138	446	6	TM2	9/10	968		84	3560	299.04
MS-5-453-U2	MS-5-149	453	6	TM2	9/10	968		390	500	195
MS-5-467-U2	MS-5-141	467	6	TM2	9/10	968		160	2170	347.2
MS-5-469-U2	MS-5-146	469	7	Control	9/10	0		31	4680	145.08
MS-5-473-U2	MS-5-156	473	7	Control	9/10	0		11	5700	62.7
MS-5-463-U3	MS-5-172	463	1	NaAs	12/13	599		80	5380	430.4
MS-5-465-U3	MS-5-173	465	1	NaAs	12/13	599		230	2370	545.1
MS-5-474-U3	MS-5-201	474	1	NaAs	12/13	599		106	3200	339.2
MS-5-475-U3	MS-5-182	475	1	NaAs	12/13	599		87	9680	842.16
MS-5-448-U3	MS-5-169	448	2	NaAs	12/13	1196		470	1980	930.6
MS-5-451-U3	MS-5-184	451	2	NaAs	12/13	1196		520	2280	1185.6
MS-5-454-U3	MS-5-192	454	2	NaAs	12/13	1196		77	10280	791.56

STUDY 2

sample number	tag number	Pig#	Group	Material	Urine Collection Day(s)	Arsenic Dose	Q	Urine As Concentration (ug/L)	Urine Volume (mL/48 hrs)	Total As Excreted (ug As/48 hrs)
MS-5-483-U3	MS-5-189	483	2	NaAs	12/13	1196		200	5430	1086
MS-5-450-U3	MS-5-197	450	3	TM1	12/13	981		110	3000	330
MS-5-466-U3	MS-5-177	466	3	TM1	12/13	981		25	10200	255
MS-5-468-U3	MS-5-185	468	3	TM1	12/13	981		180	2760	496.8
MS-5-481-U3	MS-5-187	481	3	TM1	12/13	981		170	2280	387.6
MS-5-445-U3	MS-5-168	445	4	TM1	12/13	1472		140	5260	736.4
MS-5-452-U3	MS-5-190	452	4	TM1	12/13	1472		82	8200	672.4
MS-5-470-U3	MS-5-181	470	4	TM1	12/13	1472		900	440	396
MS-5-482-U3	MS-5-174	482	4	TM1	12/13	1472		90	8280	745.2
MS-5-250-U3	MS-5-198	250	5	TM1	12/13	2944		150	9040	1356
MS-5-449-U3	MS-5-176	449	5	TM1	12/13	2944		280	2480	694.4
MS-5-455-U3	MS-5-178	455	5	TM1	12/13	2944		240	5430	1303.2
MS-5-464-U3	MS-5-194	464	5	TM1	12/13	2944		1800	560	1008
MS-5-249-U3	MS-5-175	249	6	TM2	12/13	968		170	1860	316.2
MS-5-446-U3	MS-5-196	446	6	TM2	12/13	968		122	4640	566.08
MS-5-453-U3	MS-5-200	453	6	TM2	12/13	968		380	1060	402.8
MS-5-467-U3	MS-5-183	467	6	TM2	12/13	968		170	1860	316.2
MS-5-469-U3	MS-5-199	469	7	Control	12/13	0		17	3350	56.95
MS-5-473-U3	MS-5-170	473	7	Control	12/13	0		17	3880	65.96

STUDY 3

sample number	tag number	Pig#	Group	Material	Urine Collection Day(s)	Arsenic Dose	Q	Urine As Concentration (ug/L)	Urine Volume (mL/48 hrs)	Total As Excreted (ug As/48 hrs)
BOrch-MS4&8-503-U1	BOrch-MS4&8-123	503	1	NaAs	6/7	868		150	3350	504
BOrch-MS4&8-511-U1	BOrch-MS4&8-105	511	1	NaAs	6/7	868		210	3200	693
BOrch-MS4&8-529-U1	BOrch-MS4&8-122	529	1	NaAs	6/7	868		140	3360	442.4
BOrch-MS4&8-543-U1	BOrch-MS4&8-106	543	1	NaAs	6/7	868		210	3300	3011.4
BOrch-MS4&8-502-U1	BOrch-MS4&8-102	502	2	NaAs	6/7	1720		410	3160	3940.1
BOrch-MS4&8-505-U1	BOrch-MS4&8-119	505	2	NaAs	6/7	1720		92	14340	502.32
BOrch-MS4&8-506-U1	BOrch-MS4&8-110	506	2	NaAs	6/7	1720		160	9610	653.6
BOrch-MS4&8-527-U1	BOrch-MS4&8-103	527	2	NaAs	6/7	1720		250	5460	1175
BOrch-MS4&8-501-U1	BOrch-MS4&8-101	501	3	NaAs	6/7	3480		660	4085	1537.8
BOrch-MS4&8-516-U1	BOrch-MS4&8-120	516	3	NaAs	6/7	3480		620	4700	967.2
BOrch-MS4&8-521-U1	BOrch-MS4&8-121	521	3	NaAs	6/7	3480		720	2330	2664
BOrch-MS4&8-531-U1	BOrch-MS4&8-129	531	3	NaAs	6/7	3480		1500	1560	3690
BOrch-MS4&8-530-U1	BOrch-MS4&8-117	530	4	TM1	6/7	1799		170	3700	149.6
BOrch-MS4&8-535-U1	BOrch-MS4&8-118	535	4	TM1	6/7	1799		300	2460	2106
BOrch-MS4&8-538-U1	BOrch-MS4&8-124	538	4	TM1	6/7	1799		770	880	6044.5
BOrch-MS4&8-541-U1	BOrch-MS4&8-113	541	4	TM1	6/7	1799		99	7020	425.7
BOrch-MS4&8-513-U1	BOrch-MS4&8-128	513	5	TM1	6/7	2699		110	7850	389.4
BOrch-MS4&8-525-U1	BOrch-MS4&8-116	525	5	TM1	6/7	2699		190	4300	2230.6
BOrch-MS4&8-526-U1	BOrch-MS4&8-107	526	5	TM1	6/7	2699		190	3540	2591.6
BOrch-MS4&8-537-U1	BOrch-MS4&8-125	537	5	TM1	6/7	2699		54	11740	93.96
BOrch-MS4&8-507-U1	BOrch-MS4&8-126	507	6	TM1	6/7	5397		120	13640	194.4
BOrch-MS4&8-514-U1	BOrch-MS4&8-127	514	6	TM1	6/7	5397		960	1740	4492.8
BOrch-MS4&8-515-U1	BOrch-MS4&8-112	515	6	TM1	6/7	5397		1000	1620	4040
BOrch-MS4&8-533-U1	BOrch-MS4&8-218	533	6	TM1	6/7	5397		400	4680	1464
BOrch-MS4&8-504-U1	BOrch-MS4&8-221	504	7	TM2	6/7	1633		100	4040	1680
BOrch-MS4&8-508-U1	BOrch-MS4&8-217	508	7	TM2	6/7	1633		190	3660	885.4
BOrch-MS4&8-519-U1	BOrch-MS4&8-212	519	7	TM2	6/7	1633		49	16800	55.37
BOrch-MS4&8-534-U1	BOrch-MS4&8-220	534	7	TM2	6/7	1633		140	4660	803.6
BOrch-MS4&8-509-U1	BOrch-MS4&8-215	509	8	TM2	6/7	2450		850	1130	3740
BOrch-MS4&8-532-U1	BOrch-MS4&8-216	532	8	TM2	6/7	2450		140	5740	512.4
BOrch-MS4&8-536-U1	BOrch-MS4&8-219	536	8	TM2	6/7	2450		230	4400	1681.3
BOrch-MS4&8-540-U1	BOrch-MS4&8-225	540	8	TM2	6/7	2450		270	3660	945
BOrch-MS4&8-510-U1	BOrch-MS4&8-222	510	9	TM2	6/7	4900		230	7310	193.2
BOrch-MS4&8-517-U1	BOrch-MS4&8-224	517	9	TM2	6/7	4900		580	3500	1426.8
BOrch-MS4&8-518-U1	BOrch-MS4&8-213	518	9	TM2	6/7	4900		2040	840	2182.8
BOrch-MS4&8-520-U1	BOrch-MS4&8-211	520	9	TM2	6/7	4900		800	2460	1584
BOrch-MS4&8-512-U1	BOrch-MS4&8-226	512	10	Control	6/7	0		72	1070	156.24
BOrch-MS4&8-522-U1	BOrch-MS4&8-223	522	10	Control	6/7	0		50	1980	262
BOrch-MS4&8-539-U1	BOrch-MS4&8-214	539	10	Control	6/7	0		35	2170	109.2
BOrch-MS4&8-503-U2	BOrch-MS4&8-148	503	1	NaAs	9/10	868		120	5240	408
BOrch-MS4&8-511-U2	BOrch-MS4&8-146	511	1	NaAs	9/10	868		260	3120	488.8
BOrch-MS4&8-529-U2	BOrch-MS4&8-152	529	1	NaAs	9/10	868		220	3400	1126.4
BOrch-MS4&8-543-U2	BOrch-MS4&8-143	543	1	NaAs	9/10	868		230	1880	2281.6
BOrch-MS4&8-502-U2	BOrch-MS4&8-158	502	2	NaAs	9/10	1720		290	5120	2093.8
BOrch-MS4&8-505-U2	BOrch-MS4&8-135	505	2	NaAs	9/10	1720		140	9920	754.6
BOrch-MS4&8-506-U2	BOrch-MS4&8-144	506	2	NaAs	9/10	1720		180	7220	1022.4
BOrch-MS4&8-527-U2	BOrch-MS4&8-155	527	2	NaAs	9/10	1720		260	5390	1107.6
BOrch-MS4&8-501-U2	BOrch-MS4&8-134	501	3	NaAs	9/10	3480		480	5680	1795.2
BOrch-MS4&8-516-U2	BOrch-MS4&8-132	516	3	NaAs	9/10	3480		480	4260	998.4
BOrch-MS4&8-521-U2	BOrch-MS4&8-154	521	3	NaAs	9/10	3480		730	3740	4007.7
BOrch-MS4&8-531-U2	BOrch-MS4&8-136	531	3	NaAs	9/10	3480		1300	2080	3016
BOrch-MS4&8-530-U2	BOrch-MS4&8-150	530	4	TM1	9/10	1799		99	5490	97.02
BOrch-MS4&8-535-U2	BOrch-MS4&8-160	535	4	TM1	9/10	1799		360	2320	1447.2
BOrch-MS4&8-538-U2	BOrch-MS4&8-159	538	4	TM1	9/10	1799		610	980	3330.6
BOrch-MS4&8-541-U2	BOrch-MS4&8-133	541	4	TM1	9/10	1799		160	4020	547.2
BOrch-MS4&8-513-U2	BOrch-MS4&8-140	513	5	TM1	9/10	2699		170	5460	391
BOrch-MS4&8-525-U2	BOrch-MS4&8-141	525	5	TM1	9/10	2699		280	3420	3001.6
BOrch-MS4&8-526-U2	BOrch-MS4&8-139	526	5	TM1	9/10	2699		410	2300	3837.6
BOrch-MS4&8-537-U2	BOrch-MS4&8-161	537	5	TM1	9/10	2699		81	10720	93.96
BOrch-MS4&8-507-U2	BOrch-MS4&8-157	507	6	TM1	9/10	5397		170	9360	258.4
BOrch-MS4&8-514-U2	BOrch-MS4&8-142	514	6	TM1	9/10	5397		1400	1160	6244
BOrch-MS4&8-515-U2	BOrch-MS4&8-137	515	6	TM1	9/10	5397		1200	1520	4560
BOrch-MS4&8-533-U2	BOrch-MS4&8-236	533	6	TM1	9/10	5397		310	4460	1054
BOrch-MS4&8-504-U2	BOrch-MS4&8-234	504	7	TM2	9/10	1633		150	3800	1554
BOrch-MS4&8-508-U2	BOrch-MS4&8-235	508	7	TM2	9/10	1633		200	3400	1808
BOrch-MS4&8-519-U2	BOrch-MS4&8-240	519	7	TM2	9/10	1633		79	10360	98.75
BOrch-MS4&8-534-U2	BOrch-MS4&8-228	534	7	TM2	9/10	1633		60	9040	366
BOrch-MS4&8-509-U2	BOrch-MS4&8-231	509	8	TM2	9/10	2450		760	1250	3275.6
BOrch-MS4&8-532-U2	BOrch-MS4&8-238	532	8	TM2	9/10	2450		200	6100	916
BOrch-MS4&8-536-U2	BOrch-MS4&8-232	536	8	TM2	9/10	2450		250	4310	1275

STUDY 3

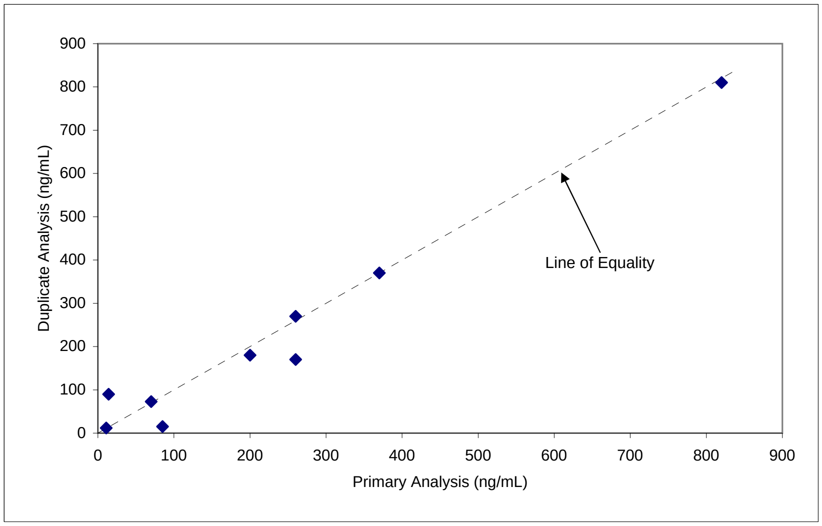
sample number	tag number	Pig#	Group	Material	Urine Collection Day(s)	Arsenic Dose	Q	Urine As Concentration (ug/L)	Urine Volume (mL/48 hrs)	Total As Excreted (ug As/48 hrs)
BOrch-MS4&8-540-U2	BOrch-MS4&8-241	540	8	TM2	9/10	2450		230	4580	975.2
BOrch-MS4&8-510-U2	BOrch-MS4&8-239	510	9	TM2	9/10	4900		480	5100	393.6
BOrch-MS4&8-517-U2	BOrch-MS4&8-233	517	9	TM2	9/10	4900		510	4240	719.1
BOrch-MS4&8-518-U2	BOrch-MS4&8-237	518	9	TM2	9/10	4900		2420	820	0
BOrch-MS4&8-520-U2	BOrch-MS4&8-230	520	9	TM2	9/10	4900		960	1410	1843.2
BOrch-MS4&8-512-U2	BOrch-MS4&8-229	512	10	Control	9/10	0		110		209
BOrch-MS4&8-522-U2	BOrch-MS4&8-227	522	10	Control	9/10	0		47	1920	277.3
BOrch-MS4&8-522-U2	BOrch-MS4&8-309	539	10	Control	9/10	0		60	1900	249.6
BOrch-MS4&8-503-U3	BOrch-MS4&8-183	503	1	NaAs	12/13	868		100	5900	426
BOrch-MS4&8-511-U3	BOrch-MS4&8-171	511	1	NaAs	12/13	868		190	4160	404.7
BOrch-MS4&8-529-U3	BOrch-MS4&8-177	529	1	NaAs	12/13	868		190	4260	889.2
BOrch-MS4&8-543-U3	BOrch-MS4&8-192	543	1	NaAs	12/13	868		230	2130	2290.8
BOrch-MS4&8-502-U3	BOrch-MS4&8-182	502	2	NaAs	12/13	1720		330	4680	3488.1
BOrch-MS4&8-505-U3	BOrch-MS4&8-185	505	2	NaAs	12/13	1720		120	9960	838.8
BOrch-MS4&8-506-U3	BOrch-MS4&8-180	506	2	NaAs	12/13	1720		94	10570	513.24
BOrch-MS4&8-527-U3	BOrch-MS4&8-166	527	2	NaAs	12/13	1720		190	6990	784.7
BOrch-MS4&8-501-U3	BOrch-MS4&8-189	501	3	NaAs	12/13	3480		460	5460	2001
BOrch-MS4&8-516-U3	BOrch-MS4&8-181	516	3	NaAs	12/13	3480		480	4130	1267.2
BOrch-MS4&8-521-U3	BOrch-MS4&8-178	521	3	NaAs	12/13	3480		520	4350	2828.8
BOrch-MS4&8-531-U3	BOrch-MS4&8-162	531	3	NaAs	12/13	3480		1100	2640	2277
BOrch-MS4&8-530-U3	BOrch-MS4&8-184	530	4	TM1	12/13	1799		61	5440	65.88
BOrch-MS4&8-535-U3	BOrch-MS4&8-172	535	4	TM1	12/13	1799		400	2070	1524
BOrch-MS4&8-538-U3	BOrch-MS4&8-191	538	4	TM1	12/13	1799		470	1080	2881.1
BOrch-MS4&8-541-U3	BOrch-MS4&8-173	541	4	TM1	12/13	1799		200	3810	1292
BOrch-MS4&8-513-U3	BOrch-MS4&8-167	513	5	TM1	12/13	2699		170	6130	581.4
BOrch-MS4&8-525-U3	BOrch-MS4&8-174	525	5	TM1	12/13	2699		89	6460	1114.28
BOrch-MS4&8-526-U3	BOrch-MS4&8-163	526	5	TM1	12/13	2699		300	3420	2229
BOrch-MS4&8-537-U3	BOrch-MS4&8-186	537	5	TM1	12/13	2699		60	12520	99
BOrch-MS4&8-507-U3	BOrch-MS4&8-170	507	6	TM1	12/13	5397		230	7430	533.6
BOrch-MS4&8-514-U3	BOrch-MS4&8-188	514	6	TM1	12/13	5397		1200	1650	8880
BOrch-MS4&8-515-U3	BOrch-MS4&8-165	515	6	TM1	12/13	5397		730	2320	3066
BOrch-MS4&8-533-U3	BOrch-MS4&8-244	533	6	TM1	12/13	5397		210	7400	1050
BOrch-MS4&8-504-U3	BOrch-MS4&8-246	504	7	TM2	12/13	1633		120	4200	1350
BOrch-MS4&8-508-U3	BOrch-MS4&8-256	508	7	TM2	12/13	1633		170	5000	1802
BOrch-MS4&8-519-U3	BOrch-MS4&8-245	519	7	TM2	12/13	1633		78	11250	67.08
BOrch-MS4&8-534-U3	BOrch-MS4&8-252	534	7	TM2	12/13	1633		71	10600	452.98
BOrch-MS4&8-509-U3	BOrch-MS4&8-249	509	8	TM2	12/13	2450		1100	860	6424
BOrch-MS4&8-532-U3	BOrch-MS4&8-250	532	8	TM2	12/13	2450		150	6380	705
BOrch-MS4&8-536-U3	BOrch-MS4&8-247	536	8	TM2	12/13	2450		190	5840	467.4
BOrch-MS4&8-540-U3	BOrch-MS4&8-248	540	8	TM2	12/13	2450		210	4700	1323
BOrch-MS4&8-510-U3	BOrch-MS4&8-255	510	9	TM2	12/13	4900		940	2460	639.2
BOrch-MS4&8-517-U3	BOrch-MS4&8-242	517	9	TM2	12/13	4900		330	6300	739.2
BOrch-MS4&8-518-U3	BOrch-MS4&8-253	518	9	TM2	12/13	4694		2130	680	5069.4
BOrch-MS4&8-520-U3	BOrch-MS4&8-243	520	9	TM2	12/13	4900		820	2240	2427.2
BOrch-MS4&8-512-U3	BOrch-MS4&8-254	512	10	Control	12/13	0		40	2380	61.6
BOrch-MS4&8-522-U3	BOrch-MS4&8-251	522	10	Control	12/13	0		30	2960	88.8
BOrch-MS4&8-522-U3	BOrch-MS4&8-310	539	10	Control	12/13	0		42	1540	64.68

APPENDIX F

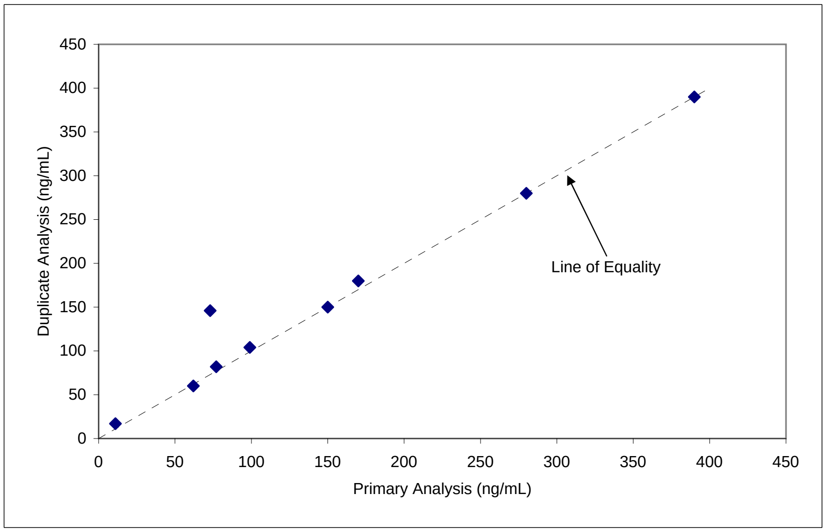
ARSENIC ANALYTICAL RESULTS FOR QUALITY CONTROL SAMPLES

FIGURE F-1 URINARY ARSENIC BLIND DUPLICATES

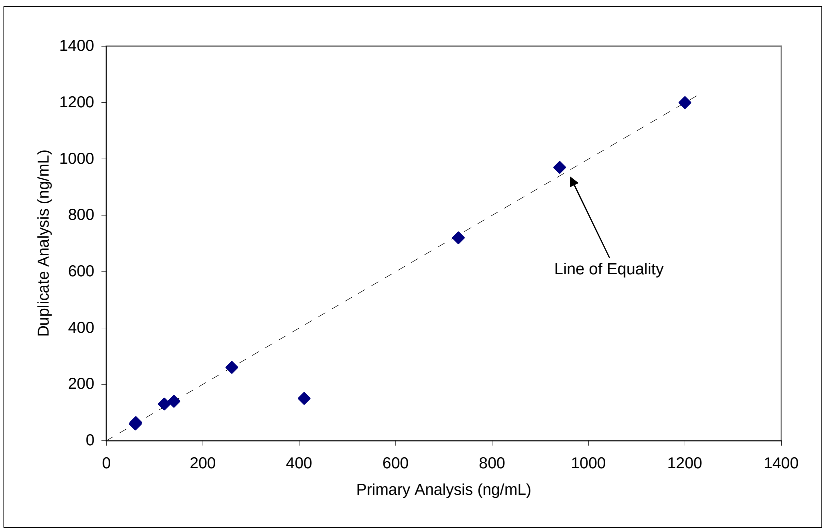
STUDY 1



STUDY 2



STUDY 3



APPENDIX F ARSENIC ANALYTICAL RESULTS FOR QUALITY CONTROL SAMPLES

TABLE F-1 BLIND DUPLICATE SAMPLES

STUDY 1

Blind Duplicate Sample ID	Sample type	Pig Number	Urine Collection Days	Duplicate concentration (ppb)	Sample Concentration (ppb)	RPD
EP3-2-119	Urine	367	U1	73	70	4%
EP3-2-121	Urine	356	U1	370	370	0%
EP3-2-112	Urine	368	U1	170	260	42%
EP3-2-148	Urine	373	U2	12	11	9%
EP3-2-151	Urine	362	U2	90	14	146%
EP3-2-159	Urine	366	U2	810	820	1%
EP3-2-179	Urine	351	U3	270	260	4%
EP3-2-164	Urine	369	U3	180	200	11%
EP3-2-162	Urine	374	U3	15	85	140%

STUDY 2

Blind Duplicate Sample ID	Sample type	Pig Number	Urine Collection Days	Duplicate concentration (ppb)	Sample Concentration (ppb)	RPD
MS-5-113	Urine	445	U1	146	73	67%
MS-5-125	Urine	446	U1	60	62	3%
MS-5-132	Urine	474	U1	150	280	60%
MS-5-166	Urine	453	U2	390	390	0%
MS-5-151	Urine	463	U2	104	77	30%
MS-5-152	Urine	473	U2	17	99	141%
MS-5-179	Urine	449	U3	280	11	185%
MS-5-191	Urine	454	U3	82	150	59%
MS-5-171	Urine	481	U3	180	170	6%

STUDY 3

Blind Duplicate Sample ID	Sample type	Pig Number	Urine Collection Days	Duplicate concentration (ppb)	Sample Concentration (ppb)	RPD
BOrch-MS4&8-104	Urine	502	U1	150	410	93%
BOrch-MS4&8-114	Urine	507	U1	130	120	8%
BOrch-MS4&8-109	Urine	532	U1	140	140	0%
BOrch-MS4&8-145	Urine	511	U2	260	260	0%
BOrch-MS4&8-147	Urine	521	U2	720	730	1%
BOrch-MS4&8-153	Urine	539	U2	59	60	2%
BOrch-MS4&8-168	Urine	510	U3	970	940	3%
BOrch-MS4&8-164	Urine	514	U3	1200	1200	0%
BOrch-MS4&8-190	Urine	530	U3	64	61	5%

TABLE F-2. LABORATORY SPIKES

STUDY 1

Sample ID	Sample Type	Nominal Arsenic (ppb)	Spiked Concentration (ppb)	Sample concentration (ppb)	Recovered Spike (ppb)	% Recovery
EP3-2-129	Urine	200	320	109	211	106%
EP3-2-114	Urine	200	340	122	218	109%
EP3-2-144	Urine	200	330	128	202	101%
EP3-2-132	Urine	200	1000	820	180	90%
EP3-2-148	Urine	200	210	12	198	99%
EP3-2-189	Urine	200	460	260	200	100%
EP3-2-180	Urine	200	390	200	190	95%
EP3-2-162	Urine	200	220	15	205	103%
EP3-2-409	Feed	9880	10000	<50	10000	101%
EP3-2-414	Water	100	100	<0.5	100	100%

STUDY 2

Sample ID	Sample Type	Nominal Arsenic (ppb)	Spiked Concentration (ppb)	Sample concentration (ppb)	Recovered Spike (ppb)	% Recovery
MS-5-113	Urine	200	340	146	194	97%
MS-5-124	Urine	200	406	200	206	103%
MS-5-135	Urine	200	453	240	213	107%
MS-5-146	Urine	200	220	31	189	95%
MS-5-159	Urine	200	1100	840	260	130%
MS-5-169	Urine	294	800	470	330	112%
MS-5-179	Urine	200	510	280	230	115%
MS-5-192	Urine	200	290	77	213	107%
MS-5-200	Urine	200	556	380	176	88%
MS-5-223	Feed	9940	9600	70	9530	96%
MS-5-225	Water	111	110	<1	110	99%

STUDY 3

Sample ID	Sample Type	Nominal Arsenic (ppb)	Spiked Concentration (ppb)	Sample concentration (ppb)	Recovered Spike (ppb)	% Recovery
BOrch-MS4&8-110	Urine	200	360	160	200	100%
BOrch-MS4&8-121	Urine	1000	1700	720	980	98%
BOrch-MS4&8-131	Urine	200	260	55	205	103%
BOrch-MS4&8-135	Urine	200	350	140	210	105%
BOrch-MS4&8-145	Urine	200	480	260	220	110%
BOrch-MS4&8-155	Urine	200	460	260	200	100%
BOrch-MS4&8-169	Urine	200	240	38	202	101%
BOrch-MS4&8-179	Urine	200	260	55	205	103%
BOrch-MS4&8-189	Urine	1000	1400	460	940	94%
BOrch-MS4&8-220	Urine	200	350	140	210	105%
BOrch-MS4&8-230	Urine	200	1130	960	170	85%
BOrch-MS4&8-240	Urine	200	280	79	201	101%
BOrch-MS4&8-248	Urine	200	426	210	216	108%
BOrch-MS4&8-311	Feed	9980	10000	0.1	9999.9	100%
BOrch-MS4&8-312	Water	100	97	<1	97	97%
BOrch-MS4&8-316	Water	100	99	<1	99	99%

TABLE F-3 LABORATORY DUPLICATES

STUDY 1

Sample ID	Sample Type	Duplicate Concentration	Sample Concentration	Units	RPD
EP3-2-120	Urine	790	790	ug/L	0%
EP3-2-121	Urine	380	370	ug/L	3%
EP3-2-126	Urine	23	24	ug/L	4%
EP3-2-147	Urine	58	59	ug/L	2%
EP3-2-161	Urine	260	250	ug/L	4%
EP3-2-170	Urine	85	85	ug/L	0%
EP3-2-173	Urine	13	13	ug/L	0%
EP3-2-187	Urine	220	200	ug/L	10%
EP3-2-407	Feed	150	220	ng/g	38%
EP3-2-410	Water	0.7	1	ug/L	35%

STUDY 2

Sample ID	Sample Type	Duplicate Concentration	Sample Concentration	Units	RPD
MS-5-106	Urine	600	620	ug/L	3%
MS-5-119	Urine	140	150	ug/L	7%
MS-5-130	Urine	76	76	ug/L	0%
MS-5-141	Urine	160	160	ug/L	0%
MS-5-153	Urine	129	128	ug/L	1%
MS-5-164	Urine	220	220	ug/L	0%
MS-5-174	Urine	89	90	ug/L	1%
MS-5-185	Urine	180	180	ug/L	0%
MS-5-197	Urine	117	110	ug/L	6%
MS-5-227	Water	<1	<1	ug/L	0%
MS-5-223	Feed	100	70	ng/g	35%

STUDY 3

Sample ID	Sample Type	Duplicate Concentration	Sample Concentration	Units	RPD
BOrch-MS4&8-105	Urine	210	210	ug/L	0%
BOrch-MS4&8-116	Urine	200	190	ug/L	5%
BOrch-MS4&8-126	Urine	120	120	ug/L	0%
BOrch-MS4&8-140	Urine	170	170	ug/L	0%
BOrch-MS4&8-150	Urine	99	99	ug/L	0%
BOrch-MS4&8-160	Urine	370	360	ug/L	3%
BOrch-MS4&8-164	Urine	1200	1200	ug/L	0%
BOrch-MS4&8-174	Urine	94	89	ug/L	5%
BOrch-MS4&8-184	Urine	60	61	ug/L	2%
BOrch-MS4&8-215	Urine	850	850	ug/L	0%
BOrch-MS4&8-225	Urine	270	270	ug/L	0%
BOrch-MS4&8-235	Urine	190	200	ug/L	5%
BOrch-MS4&8-243	Urine	840	820	ug/L	2%
BOrch-MS4&8-253	Urine	2230	2130	ug/L	5%
BOrch-MS4&8-311	Feed	0.2	0.1	ug/g	67%
BOrch-MS4&8-314	Water	<1	<1	ug/L	0%

TABLE F-4 LABORATORY QUALITY CONTROL STANDARDS

STUDY 1

Tag Number	Arsenic Concentration	DL	Units	SRMID	Certified Mean
QC-1	<3	3	ug/L	NIST 2670a-L	3
QC-2	230	5	ug/L	NIST 2670a-H	220 ± 10
QC-3	<3	3	ug/L	NIST 2670a-L	3
QC-4	220	5	ug/L	NIST 2670a-H	220 ± 10
QC-5	28	1	ug/L	NIST 1640	26.7 ± 0.41
QC-6	21000	500	ng/g	NRCC TORT-2	21,600 ± 1,800

STUDY 2

Tag Number	Arsenic Concentration	DL	Units	SRMID	Certified Mean
QC-1	4	2	ug/L	NIST 2670a-L	3
QC-2	220	4	ug/L	NIST 2670a-H	220 ± 10
QC-3	<3	3	ug/L	NIST 2670a-L	3
QC-4	230	4	ug/L	NIST 2670a-H	220 ± 10
QC-5	220	4	ug/L	NIST 2670a-H	220 ± 10
QC-6	55	1	ug/L	NIST 1643e	60.5
QC-7	7.1	200	ug/g	NIST 1566b	7.65 +/-0.65

STUDY 3

Tag Number	Arsenic Concentration	DL	Units	SRMID	Certified Mean
QC-1	6	2	ug/L	NIST 2670a-L	3
QC-2	210	9	ug/L	NIST 2670a-H	220 ± 10
QC-3	230	9	ug/L	NIST 2670a-H	220 ± 10
QC-4	230	9	ug/L	NIST 2670a-H	220 ± 10
QC-5	3	2	ug/L	NIST 2670a-L	3
QC-6	220	9	ug/L	NIST 2670a-H	220 ± 10
QC-7	220	9	ug/L	NIST 2670a-H	220 ± 10
QC-8	57	1	ug/L	NIST 1643e	60.5
QC-9	7.2	0.2	ug/g	NIST 1566b	7.65 +/-0.65

TABLE F-5 BLANKS

STUDY 1

Tag Number	Arsenic Concentration	DL	Units
Blank-1	<1	1	ug/L
Blank-2	<1	1	ug/L
Blank-3	<1	1	ug/L
Blank-4	<1	1	ug/L
Blank-5	<0.5	0.5	ug/L
Blank-6	<50	50	ng/g

STUDY 2

Tag Number	Arsenic Concentration	DL	Units
Blank-1	<1	1	ug/L
Blank-2	<1	1	ug/L
Blank-3	<1	1	ug/L
Blank-4	<1	1	ug/L
Blank-5	<1	1	ug/L
Blank-6	<1	1	ug/L
Blank-7	<50	50	ng/g

STUDY 3

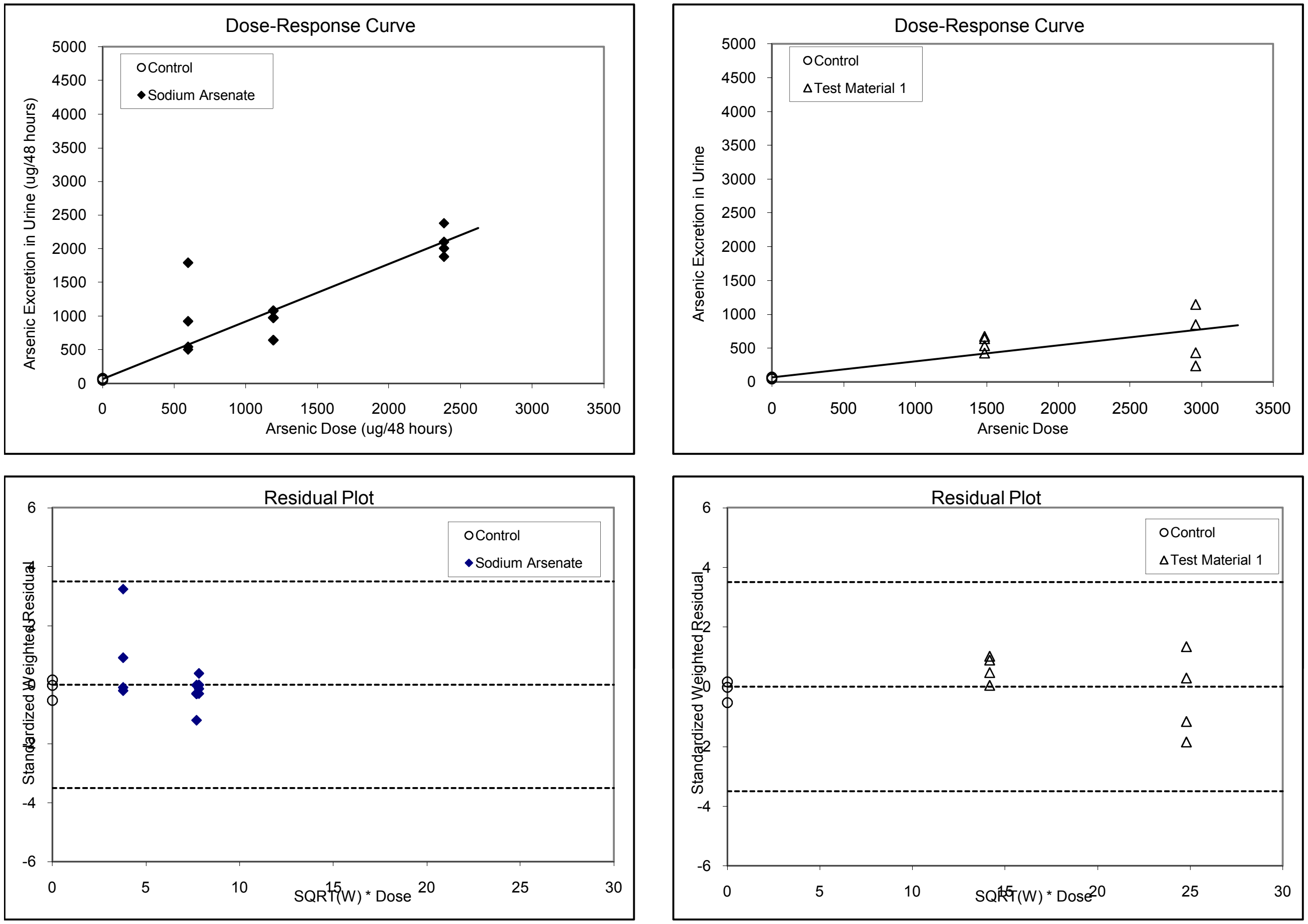
Tag Number	Arsenic Concentration	DL	Units
Blank-1	<1	1	ug/L
Blank-2	<1	1	ug/L
Blank-3	<1	1	ug/L
Blank-4	<1	1	ug/L
Blank-5	<1	1	ug/L
Blank-6	<1	1	ug/L
Blank-7	<1	1	ug/L
Blank-8	<1	1	ug/L
Blank-9	<0.1	0.1	ug/g

APPENDIX G

INITIAL ARSENIC DOSE-RESPONSE MODELING FOR STUDY 1 AND STUDY 2

FIGURE G-1 STUDY 1 URINARY EXCRETION OF ARSENIC: Days 6/7 (All Data)

Reference Material (Sodium Arsenate) | **Test Material 1 (MS-1)**



[a] Note that the data from this figure were refitted with the outlier excluded (see Figure 4-6); this outlier was excluded from the final evaluation for arsenic R

Summary of Fitting[b]

Parameter	Estimate	Standard Error
a	67.0	24.4
b_r	0.85	0.11
b_{t1}	0.24	0.05
Covariance (b_r,b_{t1})	0.0371	--
Degrees of Freedom	21	--

[b] $y = a + b_r{*}x_r + b_{t1}{*}x_{t1}$

where r = Reference Material, t1 = Test Material 1

ANOVA

Source	MSE
Fit	269.24
Error	6.33
Total	30.23

Statistic	Estimate
F	42.524
p	< 0.001
Adjusted R^2	0.7906

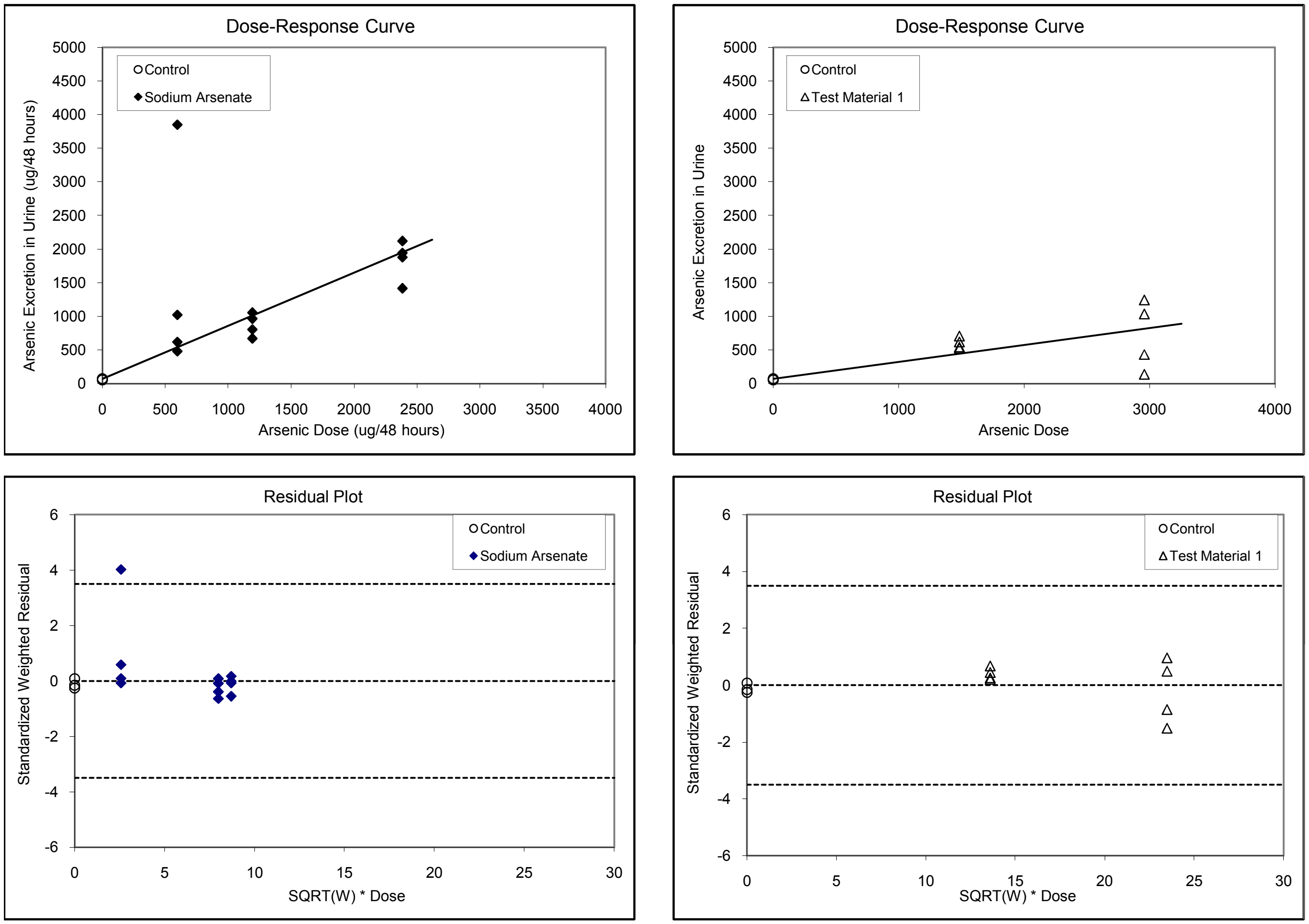
RBA and Uncertainty

	Test Material 1
RBA	0.28
Lower bound[c]	0.18
Upper bound[c]	0.40
Standard Error[c]	0.063

[c] 90% confidence intervals calculated using Fieller's theorem

FIGURE G-2 STUDY 1 URINARY EXCRETION OF ARSENIC: Days 9/10 (All Data)

Reference Material (Sodium Arsenate) | **Test Material 1 (MS-1)**



Summary of Fitting[a]

Parameter	Estimate	SE
a	71.2	37.9
b_r	0.79	0.16
b_{t1}	0.25	0.07
Covariance (b_r,b_{t1})	0.0355	--
Degrees of Freedom	21	--

[a] $y = a + b_r*x_r + b_{t1}*x_{t1}$

where r = Reference Material, t1 = Test Material 1

ANOVA

Source	MSE
Fit	257.39
Error	14.24
Total	36.34

Statistic	Estimate
F	18.078
p	< 0.001
Adjusted R^2	0.6082

RBA and Uncertainty

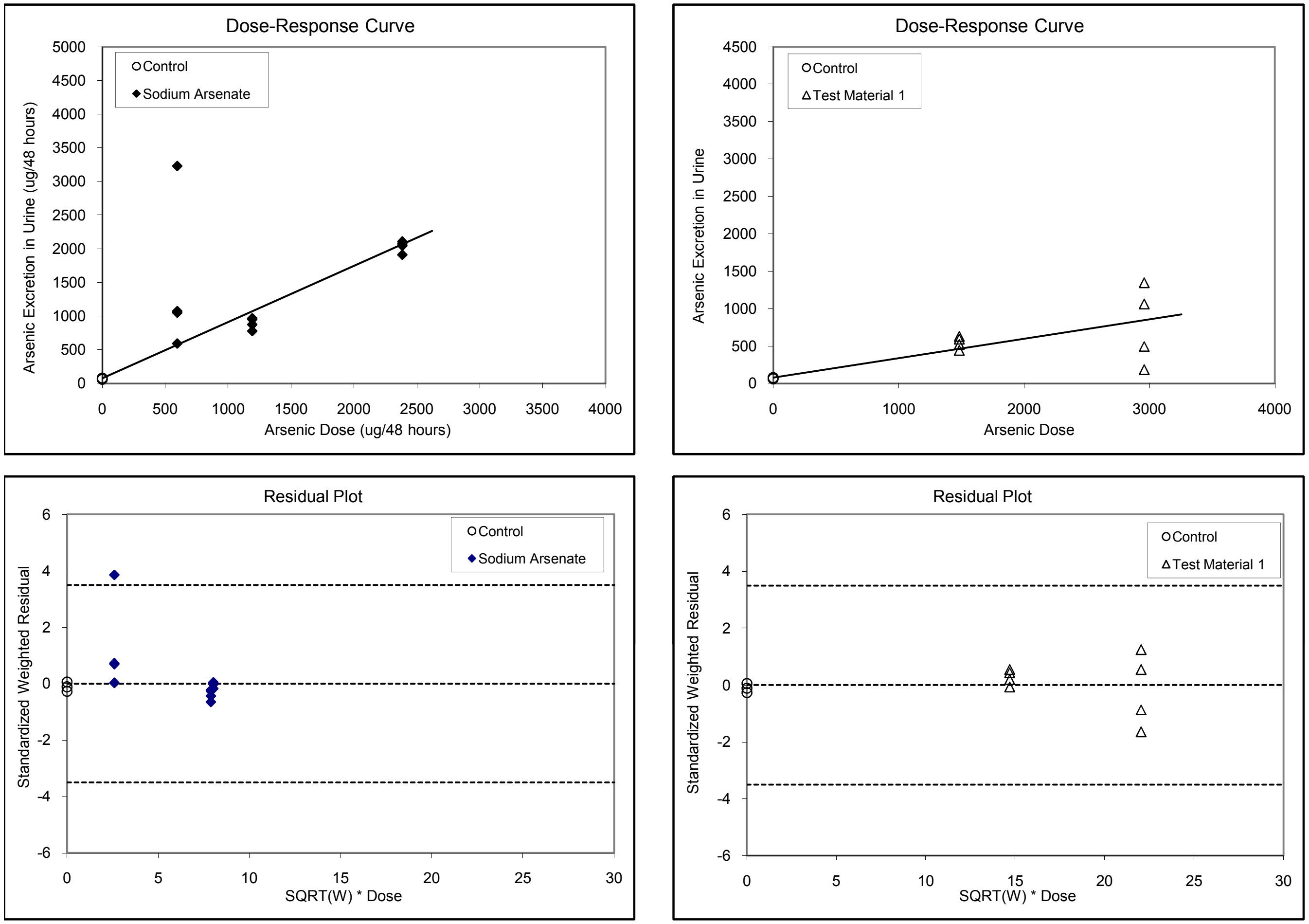
	Test Material 1
RBA	0.32
Lower bound[c]	0.16
Upper bound[c]	0.56
Standard Error[c]	0.109**

[c] 90% confidence intervals calculated using Fieller's theorem

** g ≥ 0.05 (Feiller's SE is uncertain)

FIGURE G-3 STUDY 1 URINARY EXCRETION OF ARSENIC: Days 12/13 (All Data)

Reference Material (Sodium Arsenate) | **Test Material 1 (MS-1)**



Summary of Fitting[a]

Parameter	Estimate	SE
a	76.6	34.4
b_r	0.83	0.14
b_{t1}	0.26	0.06
Covariance (b_r,b_{t1})	0.0409	--
Degrees of Freedom	21	--

[a] $y = a + b_r*x_r + b_{t1}*x_{t1}$

where r = Reference Material, t1 = Test Material 1

ANOVA

Source	MSE
Fit	259.41
Error	10.13
Total	32.79

Statistic	Estimate
F	25.602
p	< 0.001
Adjusted R^2	0.6910

RBA and Uncertainty

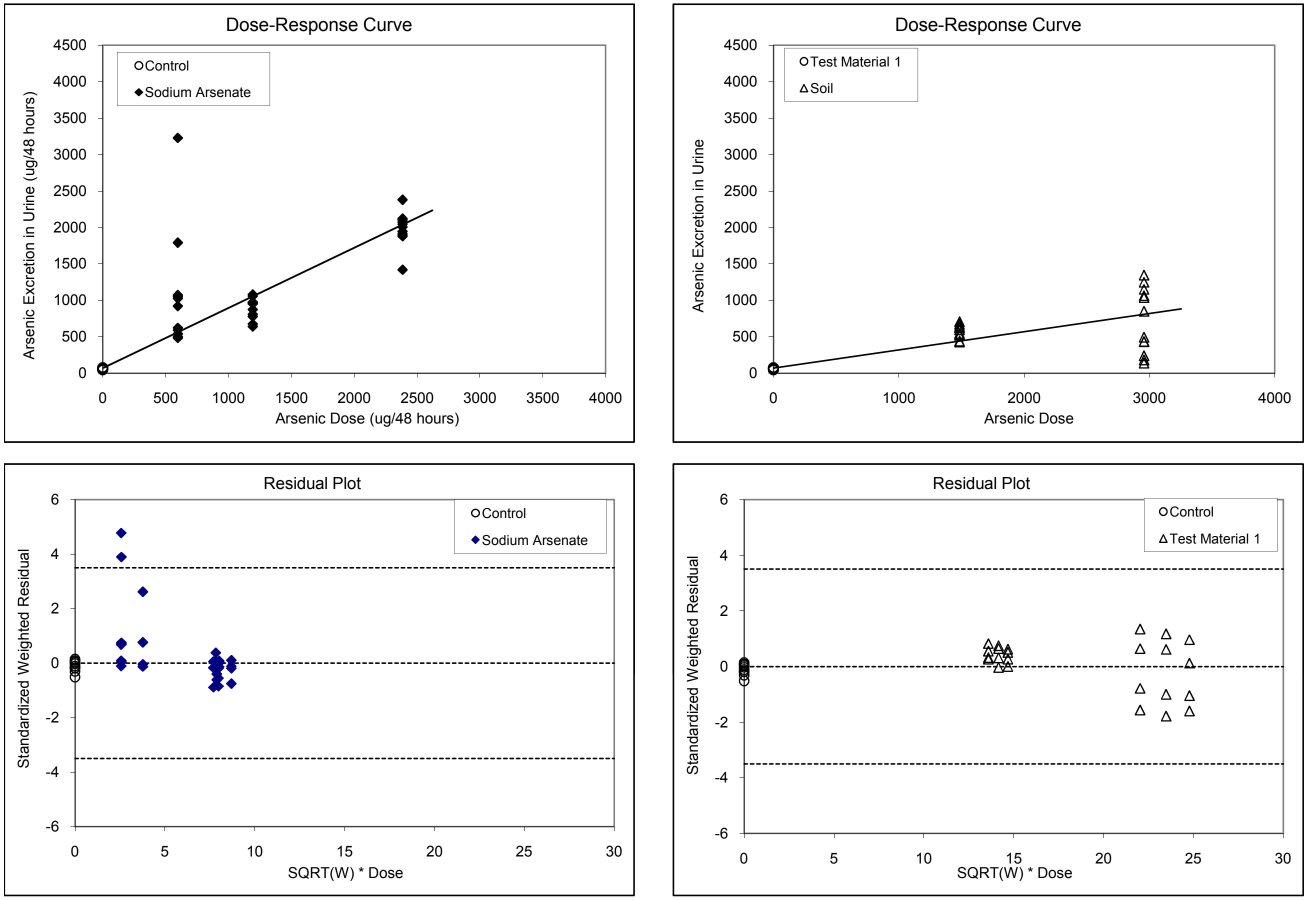
	Test Material 1
RBA	0.31
Lower bound[c]	0.18
Upper bound[c]	0.50
Standard Error[c]	0.089**

[c] 90% confidence intervals calculated using Fieller's theorem

** g ≥ 0.05 (Feiller's SE is uncertain)

FIGURE G-4 STUDY 1 URINARY EXCRETION OF ARSENIC: All Days (All Data)

Reference Material (Sodium Arsenate) | **Test Material 1 (MS-1)**



[a] Note that the data from this figure were refitted with the outlier excluded (see Figure 4-7); this outlier was excluded from the final evaluation for arsenic RBA.

Summary of Fitting[b]

Parameter	Estimate	SE
a	71.3	17.9
b_r	0.83	0.08
b_{t1}	0.25	0.03
Covariance (b_r,b_{t1})	0.0376	--
Degrees of Freedom	67	--

[b] $y = a + b_r * x_r + b_{t1} * x_{t1}$

where r = Reference Material, t1 = Test Material 1

ANOVA

Source	MSE
Fit	785.57
Error	9.35
Total	32.18

Statistic	Estimate
F	84.050
p	< 0.001
Adjusted R^2	0.7095

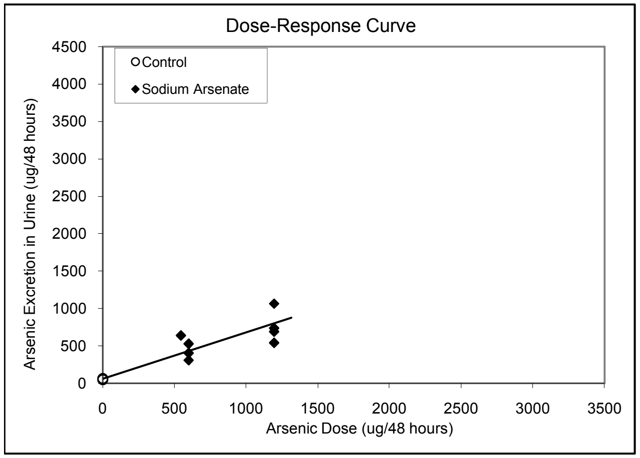
RBA and Uncertainty

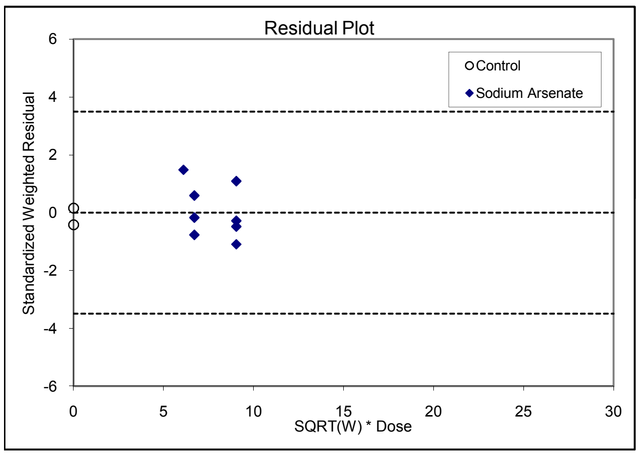
	Test Material 1
RBA	0.30
Lower bound[c]	0.23
Upper bound[c]	0.39
Standard Error[c]	0.048

[c] 90% confidence intervals calculated using Fieller's theorem

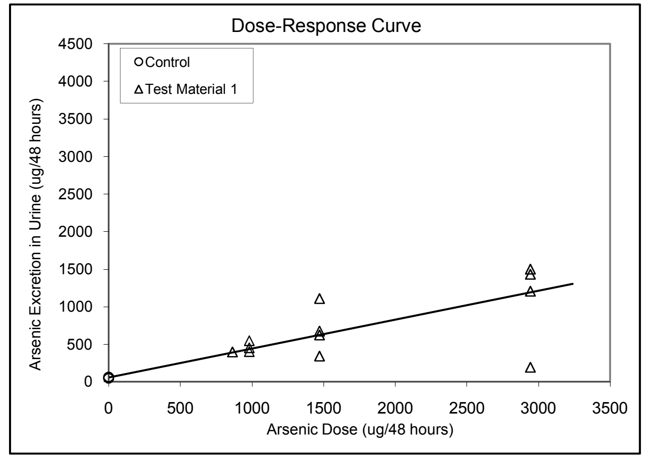
FIGURE G-5 STUDY 2 URINARY EXCRETION OF ARSENIC: Days 6/7 (All Data)

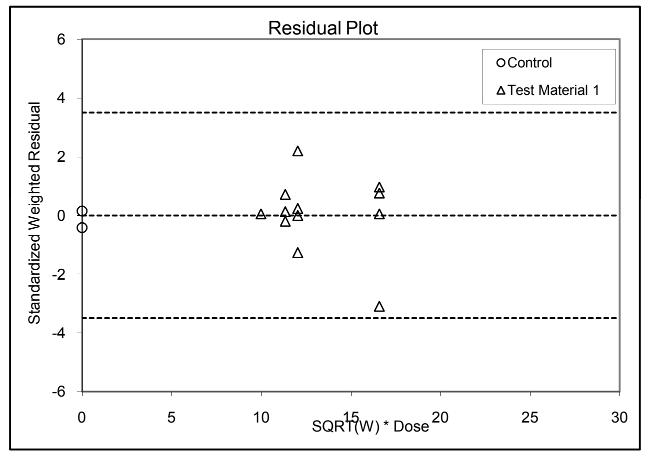
Reference Material (Sodium Arsenate)





Test Material 1 (MS-5)





Summary of Fitting[b]

Parameter	Estimate	Standard Error
a	58.3	20.6
b_r	0.62	0.09
b_{t1}	0.38	0.04
Covariance (b_r,b_{t1})	0.0733	--
Degrees of Freedom	23	--

[b] $y = a + b_r * x_r + b_{t1} * x_{t1}$

where r = Reference Material, t1 = Test Material 1

ANOVA

Source	MSE
Fit	160.52
Error	3.74
Total	22.55

Statistic	Estimate
F	42.958
p	< 0.001
Adjusted R^2	0.8343

RBA and Uncertainty

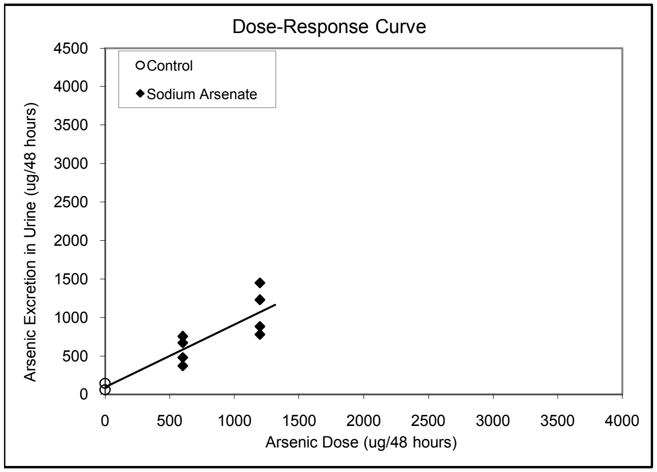
	Test Material 1
RBA	0.62
Lower bound[c]	0.46
Upper bound[c]	0.85
Standard Error[c]	0.109**

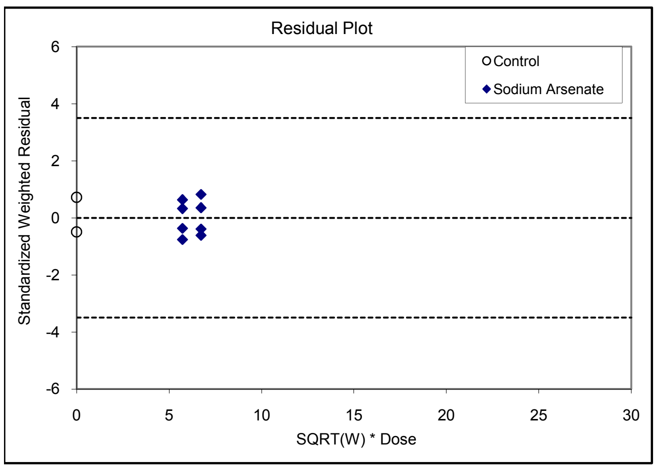
[c] 90% Confidence limit calculated using Fieller's theorem

** g ≥ 0.05 (Feiller's SE is uncertain)

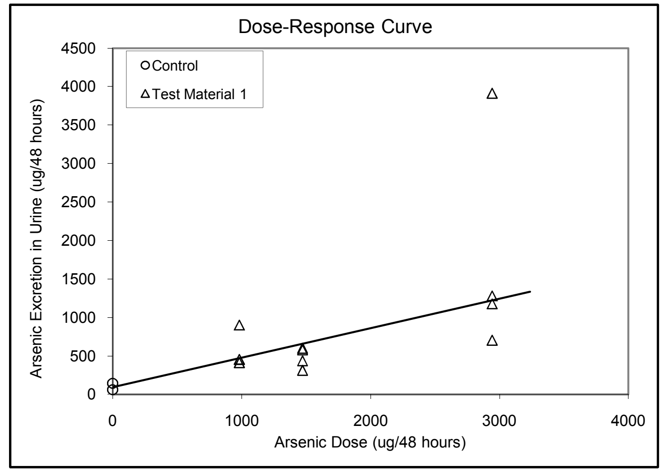
FIGURE G-6 STUDY 2 URINARY EXCRETION OF ARSENIC: Days 9/10 (All Data)

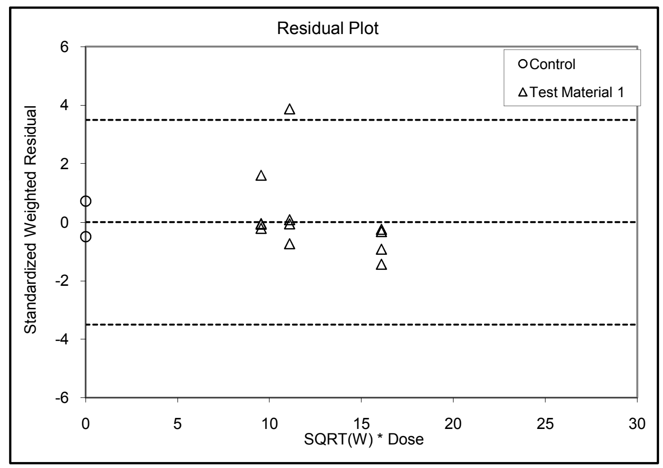
Reference Material (Sodium Arsenate)





Test Material 1 (MS-5)





Summary of Fitting[a]

Parameter	Estimate	SE
a	96.3	50.2
b_r	0.81	0.17
b_{t1}	0.38	0.07
Covariance (b_r,b_{t1})	0.1596	--
Degrees of Freedom	23	--

[a] $y = a + b_r*x_r + b_{t1}*x_{t1}$

where r = Reference Material, t1 = Test Material 1

ANOVA

Source	MSE
Fit	115.10
Error	7.86
Total	20.73

Statistic	Estimate
F	14.646
p	< 0.001
Adjusted R^2	0.6209

RBA and Uncertainty

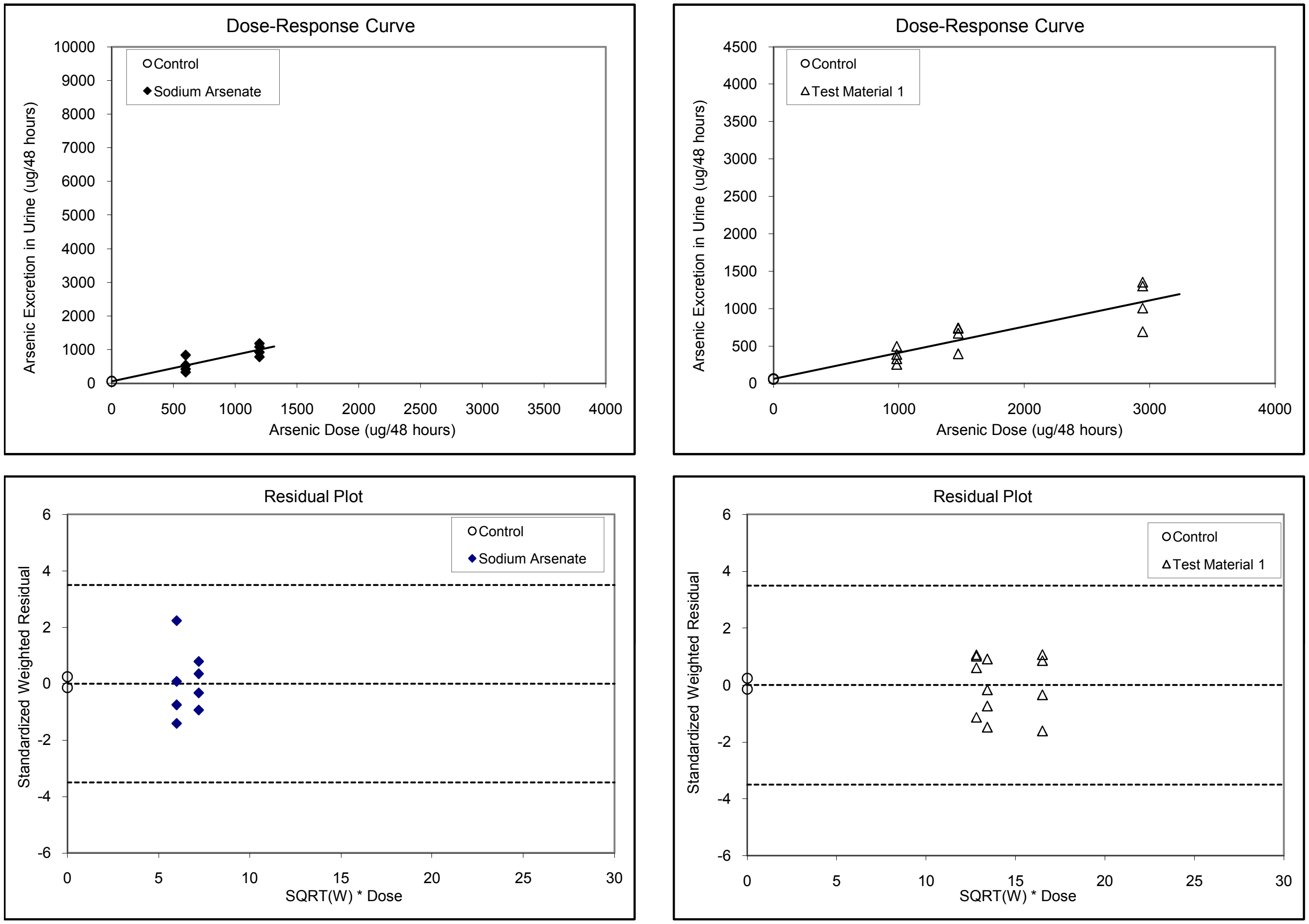
	Test Material 1
RBA	0.47
Lower bound[c]	0.30
Upper bound[c]	0.76
Standard Error[c]	0.122**

[c] 90% Confidence limit calculated using Fieller's theorem

** g ≥ 0.05 (Feiller's SE is uncertain)

FIGURE G-7 STUDY 2 URINARY EXCRETION OF ARSENIC: Days 12/13 (All Data)

Reference Material (Sodium Arsenate) | **Test Material 1 (MS-5)**



Summary of Fitting[a]

Parameter	Estimate	SE
a	60.3	17.2
b_r	0.79	0.08
b_{t1}	0.35	0.03
Covariance (b_r,b_{t1})	0.0858	--
Degrees of Freedom	23	--

[a] $y = a + b_r*x_r + b_{t1}*x_{t1}$

where r = Reference Material, t1 = Test Material 1

ANOVA

Source	MSE
Fit	156.97
Error	2.16
Total	20.74

Statistic	Estimate
F	72.750
p	< 0.001
Adjusted R^2	0.8959

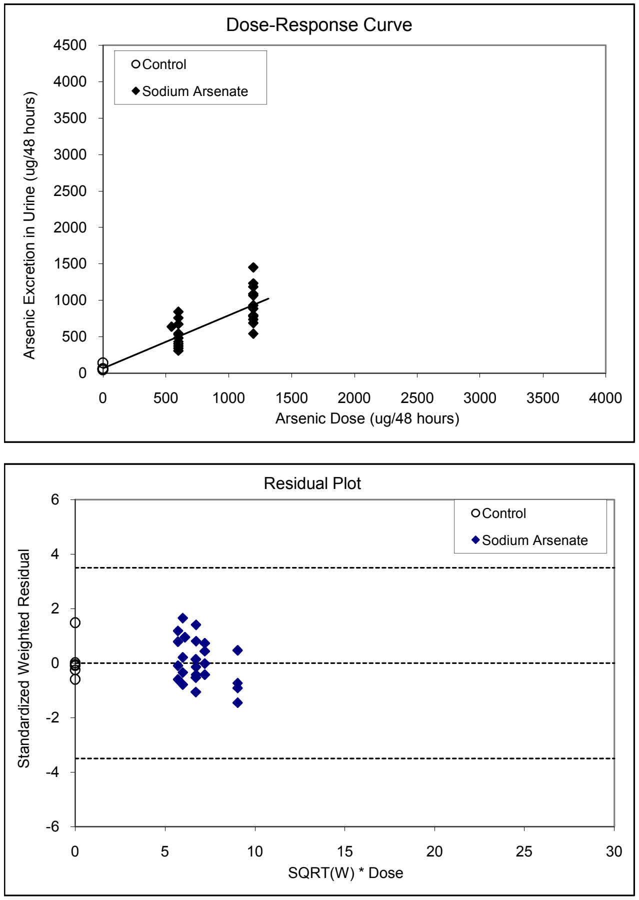
RBA and Uncertainty

	Test Material 1
RBA	0.44
Lower bound[c]	0.35
Upper bound[c]	0.56
Standard Error[c]	0.058

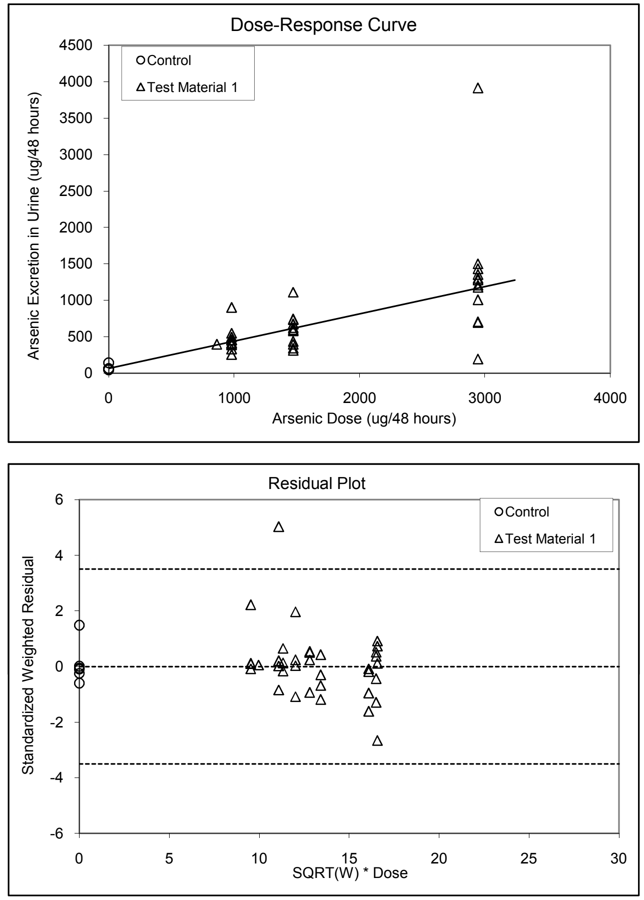
[c] 90% Confidence limit calculated using Fieller's theorem

FIGURE G-8 STUDY 2 URINARY EXCRETION OF ARSENIC: All Days (All Data)

Reference Material (Sodium Arsenate)



Test Material 1 (MS-5)



Summary of Fitting[b]

Parameter	Estimate	SE
a	65.4	15.2
b_r	0.73	0.06
b_{t1}	0.37	0.03
Covariance (b_r,b_{t1})	0.0938	--
Degrees of Freedom	75	--

[b] $y = a + b_r*x_r + b_{t1}*x_{t1}$

where r = Reference Material, t1 = Test Material 1

ANOVA

Source	MSE
Fit	442.90
Error	4.42
Total	21.51

Statistic	Estimate
F	100.115
p	< 0.001
Adjusted R^2	0.7943

RBA and Uncertainty

	Test Material 1
RBA	0.51
Lower bound[c]	0.43
Upper bound[c]	0.62
Standard Error[c]	0.056

[c] 90% Confidence limit calculated using Fieller's theorem

2_MS-5 As RBA Calcs all data 8-19-09.xls (Graph_All)