SUMMARY REPORT

on the

U.S. EPA Region VIII

report titled:

BIOAVAILABILITY OF LEAD IN SOIL SAMPLES FROM THE NEW JERSEY ZINC NPL SITE PALMERTON, PENNSYLVANIA

Prepared by: Robert H. Hosking, Jr., Project Manager

With Assistance from:
Dr. Dale Bruns, Ph.D., Environmental Toxicologist

May 23, 1996

for:

The Palmerton Citizens For A Clean Environment

In Response to Task Schedule #16, Item #2

OVERVIEW

The following report has been prepared in response to Task Schedule #16, Item #2, which requests a written review of the results of the pig feeding study, titled: "Bioavailability of Lead in Soil Samples from the New Jersey Zinc NPL Site - Palmerton, Pennsylvania". Task Schedule #16, Item #1 requested that Robert H. Hosking Jr., and Dr. Dale Bruns, Ph.D., participate in the EPA/PETF teleconference scheduled for 10:00 A.M. Tuesday, April 23, 1996. The stated agenda for the above-referenced teleconference was to discuss the results of the pig study; however, it was reported that Dr. Chris Weis, Ph.D, DABT, was called out on an emergency response in Montana and was unable to participate. Consequently, the PETF and EPA discussed the "Final Draft Responsiveness Summary", dated March 5, 1996. The teleconference was scheduled to start at 10:00 A.M., but the actual discussion was delayed until at least 10:15 A.M. because of uncertainty regarding Dr. Weis's participation. Dr. Bruns maintained his participation until around 11:00 A.M. (for approximately an hour), and Robert H. Hosking Jr., maintained his participation for the duration of the teleconference (approximately 2 hours). Although the agenda had changed, participation was maintained in anticipation that Dr. Weis might phone in from a remote location, returning the teleconference to the original agenda. The following individuals participated in the Tuesday, April 23, 1996 teleconference:

John McAleese - an attorney with Morgan, Lewis and Brockius
Mark Mummert - with R.E. Wright
Chuck Campbell - with R.E. Wright
Carol Barbett
John Reed
Bruce Conrad - representing Horsehead
Art Larvey
Bob Endress
Barbara Forslund - Advanced GeoServices Corp.
Dolores Ziegenfus - PETF
Roger Danielson - PETF and Palmerton Borough
Roy Smith - EPA Region III Toxicologist
Fred Mac Millan - EPA Region III Remedial Project Manager
Jim LaVelle - EPA Region VIII
Dale Bruns - McTish, Kunkel & Associates
Bob Hosking - McTish, Kunkel & Associates

Fred Mac Millan proposed that the "Responsiveness Summary" discussion proceed page by page starting with page 2, the first page with comments and responses. Barbara Forslund and Bruce Conrad expressed their concurrence with this approach. Barbara Forslund initiated the discussion from page 1, by requesting that 2 specific PETF letters be included in the list of documents submitted for response. The first letter requested that the Uranium storage issue be addressed. Fred Mac Millan responded that EPA would see to it that the letter was listed. The second letter requested a qualification of the OU-3 vs. the OU-4 risk assessments. Ms. Forslund stated that she believed that the substance in these letters were covered in the "Responsiveness Summary", but that she was requesting that the specific correspondence from PETF be listed on the first page. Fred Mac Millan responded that he recalled receiving the second letter in January. Apparently the second letter of correspondence was submitted after the deadline date, but a request was being made that if it could be worked in, particularly with the process EPA and the PETF risk assessment subcommittee are currently working with, that the referenced correspondence was an important one. Fred Mac Millan replied that EPA would consider the request since it did not seem unreasonable. The discussion proceeded page by page from that point, until the teleconference adjourned.

The EPA/PETF discussion of the "Responsiveness Summary" was interesting at several points, but time constraints do not allow a complete review of the discussion at this time. At some future date, a recapitulation of my notes on the various discussions will be provided to the PCCE membership for their information. In general, a brief review of the "Responsiveness Summary" document did not appear to yield much substantial information about EPA's intentions regarding the risk assessment process, nor about potential health risks from the environmental contamination present in Palmerton. It is the opinion of this reviewer that many of the responses provided relevant to MKA reports were replies to individual comments taken out of context from the intent of the summary reports for which they were originally prepared. This opinion was communicated to EPA during the teleconference.

On Friday May 10, 1996, at the request of the PCCE, Dr. Dale Bruns, Ph.D., and Robert H. Hosking Jr., participated in a second EPA/PETF teleconference. Once again, the stated agenda for the above-referenced teleconference was to discuss the results of the pig study, titled: "Bioavailability of Lead in Soil Samples from the New Jersey Zinc NPL Site - Palmerton, Pennsylvania". The following individuals participated in the Friday, May 10, 1996 teleconference:

John McAleese - an attorney with Morgan, Lewis and Brockius
Chuck Campbell - with R.E. Wright
Carol Barbett
John Reed
Bruce Conrad - representing Horsehead
Barbara Forslund - Advanced GeoServices Corp.
Dolores Ziegenfus - PETF
Roger Danielson - PETF and Palmerton Borough
Roy Smith - EPA Region III Toxicologist
Fred Mac Millan - EPA Region III Remedial Project Manager
Chris Weis - EPA Region VIII
Dale Bruns - McTish, Kunkel & Associates
Bob Hosking - McTish, Kunkel & Associates

It was noted that Jim LaVelle had been invited to participate, but was in Chicago, so he could not join the discussion. Dr. Chris Weis initiated the discussion by providing some general background information on the pig-lead bioavailability study. He expressed dismay at Dr. Jim LaVelle's absence, since Dr. LaVelle was part of the early history of the project. The content of the general background discussion is as follows: In 1989, when Dr. Weis first joined EPA, the regulated industry (a PRP) questioned whether lead sulfide is absorbable at all across the gastro-intestinal tract, and into the blood. EPA knew that the solubility of lead sulfide was very low, and was aggressively regulating an industry in the Salt Lake Valley for lead sulfide contamination. Environmental Managers in Denver (presumably EPA managers) wanted to know if EPA was over regulating the site because of the low bioavailability that the PRP's claimed. Dr. Weis responded that the question of low bioavailability was a plausible argument that could be made, but that the literature was not replete with information that would allow EPA to answer the question unequivocally. Dr. Weis was somewhat uncomfortable with the default estimates that were being used at that site in light of the extremely low solubility of lead sulfide. Dr. Weis, having actively conducted research at the University of Virginia a short-time prior to joining EPA Region VIII, believed that the question was testable, and that the implementation of a study to test the question was not all that complex. Given the potential cost of the regulation, Dr. Weis believed that conducting a study to test lead bioavailability was cost effective.

Dr. Weis and Dr. LaVelle initially designed a quick pilot study to answer the yes or no question: Is lead sulfide absorbed or is it not absorbed? This question was asked because the PRP was claiming that lead sulfide was not absorbed, and that no regulation was necessary. In cooperation and collaboration with Michigan State University, in East Lansing Michigan, Dr. LaVelle and Dr. Weis designed a simple pilot study to answer the yes or no question. They were surprised to discover that the results of the test indicated that lead sulfide, while absorbed to a lesser degree than presumed by the standard EPA default, was absorbed to a relatively significant degree, somewhere between 20% to 25% (quantification of percent absorption was not part of the simple yes or no study design). Professional judgement was applied by EPA, resulting in an adjustment of the assessment of risk to reflect the lower lead bioavailability at that site.

Because there are many large lead contaminated sites throughout EPA Region VIII, several other PRP's, as well as EPA Region VIII Remedial Project Managers immediately asked if the results of the pilot project could be extrapolated to the 10 or 15 other sites in the Region where there is residential exposure to lead. Dr. Weis stated that he was very uncomfortable with the notion of extrapolating the results of the pilot study to other sites since the study was very quickly implemented, it was not comprehensive, and it was still considered by EPA to be somewhat of a pilot study. Other factors considered are that the pilot study was relatively short term, as is typical of an acute study, and provided no information about chronic or longer term exposure (weeks or months vs. the hours examined in the pilot study). There were other technical problems that the investigators were uncomfortable with in general terms, for extrapolating the data from the pilot study to other sites in the Region.

Aware that the problem of lead bioavailability was not going to go away, EPA Region VIII began developing a comprehensive approach to solving the problem. Dr. Weis stated that the lead bioavailability issue "certainly has lots to do with the problem of uncertainty in risk assessment". This resulted in the development of a two phase program of applied investigation.

The first phase was intended to characterize the animal model. This was accomplished through the following methods:

1. Test the time dependence of absorption. EPA chose a 25 day time frame, during which animals were dosed every day, to characterize absorption across that time frame.

2. Characterization of the dose dependence of absorption. That is, give different test animals differing doses to characterize the influence of dose on the absorption characteristics.

The second phase of the program was intended to make the model more efficient based upon what was learned from the first phase, by developing a skeleton or trimmed down bioassay, which included only the essential components derived from phase I, to shorten the time frame and the number of doses which could then be employed on a variety of soils with varying characteristics across Region VIII and other Regions if they wanted to participate. A more complete review of the phase II study protocol was provided in response to PCCE Task Schedule 13 #2.

Dr. Weis stated that the phase II part of the program is not yet complete, but should probably be completed by late fall 1996. EPA has completed phase I and is now in the process of finalizing the analysis of several bioassays that have been conducted as part of phase II. EPA has tested approximately 20+ soils to date. These soils have been characterized in terms of their geochemistry and geophysical nature, and applied to a scaled down bioassay, using the swine model as a surrogate for young children.

The work conducted on soils from the Palmerton site is one of the 20 or so bioassays that have been conducted. The intention of the study authors is for the reports of the 20 or so sites to be very similar, except for those components that are site specific. Consequently, some of the language in the report refers to the larger body of work that has been done. Dr. Weis stated that the "Bioavailability of Lead in Soil Samples from the New Jersey Zinc NPL Site - Palmerton, Pennsylvania" report is just one of many reports that will be available for review very soon.

As with the discussion on the "Responsiveness Summary", a comprehensive point by point review of the EPA/PETF teleconference on the pig-lead bioavailability study will be provided at some future date, but there are more important issues regarding the "Bioavailability of Lead in Soil Samples from the New Jersey Zinc NPL Site - Palmerton, Pennsylvania" document that need to be addressed within the limited time-frame available.

Task Schedule #16, Item #2 requested that Robert H. Hosking Jr., and Dr. Dale Bruns, Ph.D., review the Lead Bioavailability Report (Pig Feeding Study), and provide a written review and comments.

COMMENTS

The study design section is very thorough in that it cites the required GLP's (Good Laboratory Practices) and SOP's (Standard Operating Procedures), but the basis and technical justification for using only two samples from Palmerton is lacking. In the context of a site specific risk assessment study, the small sample population of 2 could be viewed as a serious flaw. However, in the context of a Region-wide, or a Nation-wide study, the sample population (as Dr. Weis pointed out) is much larger, allowing for a much more robust statistical analyses of the data. It would appear that the study design, allowing for only a sample population of 2 from the Palmerton site, was intended to make an intersite comparison of lead bioavailability from a Regional or National perspective. The context and objective of a national study is not apparent from reviewing the text and data provided in the Palmerton report.

The Palmerton Lead Bioavailability report should explicitly state the primary goal of the study, and the extent to which the sample size for soils was dictated by the intent of conducting a Regional or National study. There is no site-specific context from which to judge the relevancy of the bioavailability data calculated for the two samples studied from Palmerton regardless of whether the primary goal of the study was to examine Regional/National patterns, or to define local conditions. It is centrally important to the study that the following questions be addressed:

1. To what extent do the Palmerton soil samples used in the study represent conditions on a site specific basis?

2. Is one soil sample more typical of conditions in Palmerton than the other?

3. To what extent do these two soil samples reflect a bias (as suggested in several comments made during the teleconference) toward high lead concentration soils, and/or toward high or low zinc to lead ratios.

4. How variable are Palmerton soil samples, relative to metal concentrations, and given this variability, do even "average" soil metal concentrations reflect typical conditions?

5. How close are the two soil samples used in the study to these "average" conditions in the context of site-specific variability in metals concentrations? More specifically, what percentage of Palmerton soil samples have lead and zinc concentrations and lead to zinc ratios greater than or less than those values found in the composite samples used in the bioavailability study?

6. Will potential future use of these bioavailability data from the two composite soil samples result in "appropriately conservative" (i.e., providing additional protection because of the variability and uncertainty of the data) risk assessment estimates, or just the opposite?

7. What percentage of Palmerton sites, areas, or soil samples are more similar to the Location 2 soil sample, what percentage is more similar to the Location 4 soil sample, and what proportion is not represented by either soil sample?

Without the overall statistical context of metals concentrations and the distribution and composition of various toxic heavy metal compounds in Palmerton soils, these questions cannot be addressed; yet they are essential in terms of how these bioavailability data may be used by EPA at a later date, especially for risk assessment.

A more geographically comprehensive soil sample data set, based on metals concentrations, and subjected to the appropriate level of statistical analysis, needs to be incorporated into the bioavailability study so that the questions asked in the previous paragraphs can be addressed. These are available, as compiled in several studies conducted by the National Enforcement Investigations Center (which also conducted geophysical and geochemical analyses of soil samples), as well as numerous other agencies, basic researchers and consultants, (including but not limited to the sampling and analysis conducted by CDM Federal as part of the ATSDR Biological Indicators study). Failure by EPA to verify the representativeness of the two composite samples, in-light of the large body of other peer-reviewed soil data reports available, adds to the questionable credibility of the use of the study for risk assessment.

Another crucial issue that needs to be addressed more explicitly is the concern about data variability - or the lack of quantified data variability in the study report. The investigators do point out at several places in the text that the issue of data variability (and related data uncertainty) is important, and that such variability can influence calculations and have an effect on how data are interpreted and used (e.g., at the bottom of page ES-3, in comments regarding low-dose and high dose uncertainty on the bottom of page 16, and in section 4.5 on page 30). Information about data variability is provided by Figures 4-2 through 4-5, and Figures A-5 through A-16, which show data variability either as SEMs (presumably Standard Error of the Means) or 95% confidence intervals, and all raw data and calculations are provided in an extensive appendix. However, the issue is that Figure 4-6 and the Tables on pages 29-30, which all deal with the "end product" bioavailability data (RBA or Relative Bioavailability, and ABA or Absolute Bioavailability as defined in this study), do not reflect nor quantify any aspect of data variability even though the investigators are very aware of its significance. At the bottom of page 29, the authors state that "there is no standard statistical procedure to estimate the confidence interval around these estimates of RBA". It is strongly recommended that some method or suite of indices be applied to these data - with some caveats - to at least provide some quantitative measure of variability in RBA's to managers and those charged with using such data for later risk assessment.

There are also several other specific issues of data variability that need to be addressed. As the investigators indicate, there is considerable data variability at the lower range of doses (e.g., as indicated in Figures A-5 through A-7). For example, Figure A-7 indicates that the 95% confidence interval for AUC (area under the curve) blood lead values is plus or minus about 75% of the mean at a dose of 25 ug Pb/kg-day vs. about 36% and 22% of the means respectively for doses of 100 and 200 ug Pb/kg-day. Once again, the authors do state the general concerns about data variability at various places in the text (and SEMs or 95% confidence intervals are shown on some figures), but there is no reporting in the text relative to the magnitude of some of this variability.

Another example is provided by the data represented by Figure 4-1, where group means for blood lead are shown by day but no measure of data variability are shown or discussed. Calculation of AUC from Figure 4-1 probably is not a significant issue in this regard, and showing the data variability directly on the figure would probably "clutter" the presentation. However, some mention and quantitative citation of data variability in the text would be useful. In general it appears that the investigators have tried to keep data presentation and discussion focused on "average" parameters (perhaps to make the data less complicated for use by managers). Nevertheless, data variability is crucial to the level of uncertainty in these measures, and is directly relevant to questions of risk assessment and risk management. In short, there should be more explicit citation and discussion of some of this data variability in the text - again, for the benefit of managers and those charged with using such data for later risk assessments.

In the course of preparing this summary report, an attempt was made by Dr. Bruns to duplicate some of the RBA calculations as presented in the paper. Since the study did not address RBA calculations below blood lead doses of 20.91 ug Pb/kg-day (because of high data variability; see pages 16-17, section 3.4 on Low-Dose and High Dose Uncertainty, and see the raw data in Tables A-9 and A-10), we wanted to see what RBA values might result at lower doses based on assumptions and data used in this study. To check his calculations, Dr. Bruns first tried to duplicate the ABA and RBA calculations reported in the text. He used the bioavailability definitions and data example given on page 1 of the report in order to make these calculations. The example on page 1 calculates ABA and RBA based on differing biological responses (i.e., blood lead levels due to a dose of dissolved lead vs. blood lead levels due to a dose of lead in soil) at the same dose (i.e., 100 ug Pb in the page 1 example). Following this approach, Dr. Bruns was unable to duplicate RBA values as reported in the study. However, he performed the calculations again, based on the same biological response (i.e., same blood lead level) at differing doses of dissolved lead and soil lead. This method is different than the example presented on page 1, but is the same one documented on page A-5, in section 4.0 of the Appendix. Using the ratio of the dose of lead acetate (dissolved lead) to the dose of test material (soil lead), which resulted in the same blood lead level, Dr. Bruns was able to completely document and duplicate all blood lead RBAs as reported in Tables A-9 and A-10 of the report.

For the purpose of the following discussion, RBA values as reported in Tables A-9 and A-10 will be referred to as "differing dose" RBAs, and RBA values calculated by Dr. Bruns, following the formula provided on page 1 of the report will be referred to as "same dose" RBAs. During the process of attempting to duplicate the reported values through calculation, Dr. Bruns observed that "same dose" RBA values are more variable than "differing dose" RBA values, and that the magnitude of the variability is greater with low concentration samples than with high concentration samples. The difference in these RBA values resulting from these two methods of calculation are due to the non-linear nature of the dose-response curves (refer to Figure 4-2). If the lines were linear and parallel, then both methods would produce identical RBAs. Having observed these differences, Dr. Bruns first reviewed the pig study protocol, and then attempted to contact Dr. Chris Weis by telephone for more technical information.

As discussed on page 5 of the original study protocol, the method of calculating "different dose" RBAs is referred to and defined as the Relative Bioaccessability Factor (RBAF). An analogous approach to calculating "same dose" bioavailability, assuming a linear dose-response function, is provided in the protocol on page 7, but this equation specifically addresses oral vs. systemic doses for absolute bioavailability, and is not specifically defined as an RBA. Since the protocol added an additional question regarding RBAF values and did not resolve the question as to why one method was preferred over the other, Dr. Bruns attempted to contact Dr. Weis by telephone. Dr Weis was not available, as he is out on a weeks vacation, so Dr. Bruns was referred to Dr. Gerry Henningsen, also a co-author of the report.

Dr. Bruns reported that Dr. Henningsen was very helpful in answering several technical questions in regard to the above-referenced points. It was apparent to Dr. Bruns that the EPA technical team had given a considerable amount of previous thinking and technical evaluation , including development of the protocol, to most of the questions he addressed to Dr. Henningsen. The EPA team was very much aware of both approaches to calculating RBA values, and considered both in the early design phase of the project. However "same dose" RBAs typically vary more as a function of dose and EPA preferred a method that gave a more consistent finding over a range of doses to which people will be exposed to a specific site, and also comparisons between sites would be complicated by RBAs that vary with dose. Thus EPA decided to go with the "differing dose" approach to calculating RBAs. EPA also considered that a more consistent, less variable measure of RBA would be better defended and more readily employed by managers.

Dr. Henningsen also indicated why RBAs were not calculated at the lower doses (i.e., below 20.91 ug Pb/kg-day. His explanation was that the determination of blood lead in control animals was often below the limits of detection based on the methods used for this study. Dr. Bruns expressed that he is very much aware of this problem, and there is generally no easy solution or common approach on how to handle "zero" values below the limits of detection. EPA assumed a value of one-half the detection limit for their approach, and "forced" all dose-response curves through the same Y-intercept value. This is evident in their figures, and Dr. Bruns was aware of this, but not with the reason why; although the problem with detection limits was noted elsewhere in the report. This approach and the assumptions on which it is based prevents any "unreal" situations where lead in soils is more bioavailable than lead acetate - a statistical situation that could result due to data variability and curve fits not forced through a common Y-intercept. These conditions and assumptions preclude calculating valid RBAs at very low doses and the 20.91 dose at the lower end for RBA estimates was viewed by EPA as a reasonable limit.

In summary, there are two methods for calculating RBAs and the study design does not allow for good RBA estimates at very low doses. One could argue, point by point, about different approaches to these questions or problems, and the inherent tradeoffs of the different methods. It should be noted that there does not appear to be any standard references or peer-reviewed articles that would support one approach or the other at this time. However, I think it is more compelling to address the bigger picture and the general aspects of the study and study design while keeping in mind all the detail, issues and problems identified and discussed above. The following is intended as a synopsis and recommendations based on the discussion provided above.

In general, it appears that there are three major issues that need to be addressed in the study.

1. The first is the representativeness of the two samples. Details and specific questions on this are provided in the previous paragraphs, and do not need to be repeated here.

2. For various reasons, the study attempts to "simplify" or downplay inherent data variability. The discussion of this in the preceding paragraphs provides some suggestions for quantifying at least some of this variability and discussing it relative to questions of uncertainty, which need to be addressed if the study is applied to the risk assessment process.

3. The issue of data variability and the method of calculation is especially crucial to estimates of RBAs and uncertainty for risk assessments.

In general, given the methodology employed, and the data obtained, there is no scientific justification for concluding that the bioavailability of lead from Palmerton soils is less than that assumed by the standard IEUBK default parameters. In fact given the appropriate level of conservativism, necessary to protect human health and the environment, it can be inferred from the data that the IEUBK default parameter should be adjusted up, assuming greater bioavailability than is generally used with the model. Further, even at the lowest doses given to the pigs, the blood lead levels after 15 days were greater than the 10 ug/dL level of concern recommended by the Center for Disease Control. In this context, the following additional observations and recommendations are provided below.

1. The decision by the study authors to place greater emphasis on blood lead data (as opposed to other biological endpoints such as bone or muscle) seems reasonable, but there should be more explicit discussion on how this is considered in determining the suggested RBAs. In light of the levels of data variability and uncertainty, it is reasonable to use the higher values of blood lead RBA, unadjusted for the lower RBA values measured for other tissues. This would yield RBAs of 0.8 and 0.6 for Location 2 and Location 4 soils respectively. Note that the standard IEUBK default value is 0.30.

2. Both methods of calculating blood lead RBAs should be addressed in the report, even if only selected values are provided for the "same dose" RBA calculation. It is imperative that the public and EPA's Remedial Project Managers are aware of the differences in the calculations and the tradeoffs involved with both approaches. EPA should be more explicit in documenting their rational for the method that is chosen and risk managers should be aware of this when the RBAs are selected for risk management.

3. Given the levels of data variability and uncertainty as noted in the EPA report and discussed above in some detail, the use of blood lead RBAs for the risk assessment based on "same dose" calculations would be more conservative and protective of human health. It is recommended that this option be addressed, and if not the approach chosen by EPA, a more detailed rational should be provided for the one that is used. For example, at a dose of 20.91 ug Pb/kg-day, the "differing dose" method for calculating RBAs would yield values of 0.84 and 0.57, respectively for Location 2 and Location 4 soils. In contrast, using the "same dose" method of calculation, the RBAs at 20.91 ug Pb/kg-day are 0.90 and 0.72 for Location 2 and Location 4 respectively.

4. Recent EPA updates and guidance on the IEUBK model (EPA 1994, EPA/540/R-93/081; see also Renner, June 1995, ES&T, page 257) recommends a focus on "small-scale" risk assessment. The new guidance states that the "home and its surrounding yard is the basic unit for risk analysis because lead exposure for pre-school children commonly occurs within this domain". It would seem that bioavailability values used in risk assessment also should reflect this small scale approach, and if RBAs vary with dose as discussed above, then perhaps this part of data variability is real and should be incorporated as such into the risk assessment.

5. Regardless of which approach is finally selected for risk assessment, it is strongly recommended (most likely as part of the risk assessment itself, since this would seem beyond the scope of the current EPA study) that a sensitivity study be conducted to determine the relative importance of dose vs. bioavailability in determining risk. A range of RBAs should be addressed in such a sensitivity study, including those on the "conservative" range that would protect health in the context of undefined uncertainty. This would include a "same dose" RBA for blood lead at a dose of 20.91 ug Pb/kg-day. For this to be carried out in the risk assessment, it is crucial that these RBA and variability issues be reported and addressed in the current EPA report.