CONTAMINATED SOILS FORUM

A stakeholder body advising the Florida Department of Environmental Protection

F I N A L

Recommendations for Update to Arsenic Soil CTL Computation

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Contaminated Soils Forum

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Introduction and Purpose

When the Florida Environmental Regulation Commission recommended that the Florida Department of Environmental Protection (FDEP) support the establishment of the standing stakeholder forum that became the Contaminated Soils Forum, one of the primary charges was that such an organization evaluate with a broad base of input emerging technical information that should be considered in the calculation of Cleanup Target Levels (CTLs) incorporated into the state's cleanup programs and make subsequent recommendations to the FDEP. In accordance with this charge, the Methodology Focus Group (MFG) of the Contaminated Soils Forum is pleased to present recommendations regarding a specific technical update to the soil CTLs for arsenic following the completion of an extensive evaluation of this topic.

The MFG has also produced a wide-ranging white paper, *Arsenic Bioavailability from Florida Soils: Uncertainty Evaluation of the University of Florida/Florida Department of Environmental Protection Study,* addressing various aspects of earth science, sources of arsenic in soil, and toxicology important to characterizing the uncertainties associated with soil arsenic bioavailability. Based on discussions at three one-day meetings focused primarily on this topic and consideration of the uncertainty evaluation, the MFG reached consensus recommendations on both using a revised bioavailability assumption and on specific numerical factors supported by the current scientific information. A brief overview will serve to explain the significance of such factors.

Significance of Soil Bioavailability Considerations

The calculation of risk-based CTLs requires an assumption regarding the proportion of a given chemical present within ingested soil that is actually absorbed by the body. The standard assumption is that the absorption from soil equals the absorption of the chemical in the form used in the study underlying CTL calculation for that chemical (100% relative bioavailability). For chemicals such as arsenic where toxicity has been characterized based on the ingestion of water and dissolved forms of the chemical, it is necessary to consider the validity of assuming 100% relative bioavailability in developing soil CTLs. For naturally occurring metals and metal-like elements, it is well accepted that absorption from solid materials like soil during digestive passage may be substantially lower than absorption from water. Absorption of soil arsenic into the body is readily observed to be less efficient than absorption of arsenic in water. In such cases, the assumption of 100% relative bioavailability significantly overestimates the potential risks from the metal in soil.

While it is observable, and even intuitively apparent, that many metals in solid materials like soil are not completely absorbed into the body after they are ingested, it is much more challenging to establish a scientifically based numerical representation of the relative proportion that is absorbed versus that which simply passes through the body. The factors controlling bioavailability are known to be diverse, depending on the particular metal in question, the form of the metal, the soil characteristics and conditions in the digestive tract. Consequently, bioavailability from soil is not readily or reliably predicted from straightforward chemical-physical properties of the metals, but must be determined based on direct measurements.

Further, studies to measure the bioavailability of a chemical after soil ingestion are complex and expensive.

Corresponding to the relative prominence of arsenic in environmental concerns, however, several studies of soil arsenic bioavailability have been carried out. The most recent results come from a study commissioned by the FDEP to address specifically Florida soils. Following up on the proactive efforts to better characterize soil arsenic bioavailability, the MFG undertook to 1) evaluate the scientific methods used in the FDEP-sponsored study, 2) characterize it in comparison to the other available studies, and 3) determine whether a numerical bioavailability factor could be appropriately recommended to replace the assumption of 100% bioavailability for soil arsenic used in calculating direct-contact soil CTLs. The outcomes of these three considerations are summarized below.

Charge 1 – Evaluation of Methodology in UF/FDEP Bioavailability Study

A research team from The Center for Environmental and Human Toxicology at the University of Florida headed by Professor Stephen Roberts was commissioned by the FDEP to complete a soil arsenic bioavailability study. Professor Roberts is a well regarded research scientist who has chaired national advisory panels, including for U.S. EPA, has had numerous research articles accepted by the top scientific journals in the field, and has interacted with the other principal U.S. research teams in the field of soil arsenic bioavailability for a number of years. Professor Roberts' team undertook to measure soil arsenic bioavailability from samples of Florida soils following their ingestion by cebus monkeys.

A detailed description of the specific research methodology was presented in person by Professor Roberts at two MFG meetings and contained in a manuscript that was provided to the MFG. The MFG considered the choice of soils, the choice of the animal model, the method by which the soil was ingested by the monkeys, and the manner in which bioavailability was measured. Professor Roberts was present and addressed MFG questions at all three of the principal meetings on this topic. The MFG white paper, *Arsenic Bioavailability from Florida Soils: Uncertainty Evaluation of the Florida Department of Environmental Protection Study*, provides a detailed discussion of potential uncertainties relating to the experimental design. In brief, the study was agreed by the MFG to have been methodologically up-to-date, well carried out, and particularly relevant for Florida based on the inclusion of samples from Florida representing a range of soil types characteristic to Florida.

Several key elements were identified in determining the UF/FDEP study to be scientifically appropriate for establishing a numerical bioavailability factor for soil arsenic. The five soils tested were agreed to be broadly representative of soils widely encountered in Florida. The animal system used for the study (cebus monkeys) is widely used for chemical absorption studies in U.S. FDA testing for pharmaceuticals due to the demonstrated similarities to humans in its digestive system and in chemical uptake through the digestive tract. The manner of calculating the bioavailability factors in this study made use of measurements of treatment and control responses from the same animal. And, important potential sources of uncertainty were considered in both the design and analysis, minimized to the extent reasonable, and pointed out by the authors. The study was reported in the form of a manuscript that was peer reviewed and

published in one of the top toxicology journals (Roberts S.M. et al.; *Toxicological Sciences* 67: 303-310; 2002).

Limitations due to methodological uncertainties in the UF/FDEP study and more generally associated with attempts to measure bioavailability from ingested soils were discussed at length by the MFG and are covered in detail in the MFG white paper. In brief, the representativeness of the five soil samples for generalizing to other Florida soils was one major question discussed. The relevance of the tested doses and duration of the dosing period in the study for extrapolating the bioavailability of the lower doses expected to be more typical for human exposures was also a major question. (For the sake of clarity, the animals were handled humanely in accordance with the university's institutional animal care and use requirements and the doses of arsenic that were used were low enough that no adverse or toxic effects occurred.) The general issue of whether bioavailability testing results are adequately reflective of what might occur in humans to be used in setting risk-based CTLs was also discussed. After considering these issues, preparing a draft of the white paper, and subsequently discussing the issues again, the overall conclusion of the MFG was that uncertainties could be expected to be reflected in the UF/FDEP study results, however, the numerical effect of the uncertainty was expected to be small relative to the measurements reported in the study. Further, the study was designed such that most uncertainty sources would be expected to bias the results such that the bioavailability estimates were calculated in a protective manner. In other words, properly and responsibly interpreted, the results were expected to be robust with the uncertainties essentially "lost in the rounding." After the various considerations and discussions, the MFG was posed the question of whether the UF/FDEP study was suitable for numerically determining soil arsenic bioavailability factors appropriate for use in the calculation of soil CTLs and returned a consensus finding that the study was appropriate for such use.

Charge 2 – Comparison of the UF/FDEP Bioavailability Study to Other Studies

This charge was considered in order to determine how the results from the UF/FDEP study should be prioritized relative to other reported soil arsenic bioavailability results. The numerical results from the UF/FDEP are discussed in conjunction with Charge 3, below.

The U.S. EPA conducted two studies using juvenile swine, released in 1996 and 2001, to assess the bioavailability of soils from areas impacted by mining wastes in the Rocky Mountain west. The U.S. EPA also conducted one soil arsenic bioavailability study with monkeys. Detailed comparisons among these primary studies, as well as other literature, sample size and study design were made in MFG discussions and are provided in the MFG white paper, *Arsenic Bioavailability from Florida Soils: Uncertainty Evaluation of the Florida Department of Environmental Protection Study*.

Briefly, the swine studies were characterized as useful context for interpreting the UF/FDEP study, but not usable for numerical determination of a soil arsenic bioavailability factor for Florida soils. Juvenile swine were originally developed as a test system due to similarities to humans in lead uptake. The unique aspects of lead uptake relevant to this model are not applicable for soil arsenic. The study design of the swine studies was also not as powerful as the UF/FDEP study. While the UF/FDEP study measured the response of each individual monkey

to control conditions and factored this into the calculation of bioavailability, the swine studies relied on separate groups of pigs receiving control versus arsenic impacted soil. Also, the mine slag impacted soils and soil types were considered to be less representative of Florida than the soils used in the UF/FDEP study. With regard to numerical interpretation, the initial swine study was subsequently determined to have failed to account thoroughly for the doses that were given. The more recent swine study corrected this and it is notable that these results were more consistent with the UF/FDEP study than were the initial swine study results. The 2001 U.S. EPA study reported bioavailability of 23% for a sample to which arsenic was added in the laboratory, and 31% for a sample obtained from an impacted site. Both of these swine studies were issued as internal reports of research done in conjunction with site investigation/characterization activities and were not published in the peer-reviewed scientific literature.

The one other soil arsenic bioavailability study conducted with monkeys also looked at soil from a western area impacted by mining and smelting. One soil was tested using three cynomulgus macaques. The study design was similar to the UF/FDEP study in terms of using each animal as its own control and the results of this study were published in the peer-reviewed literature. Numerically, the results from this study were similar to the UF/FDEP study with a reported bioavailability of 20%.

The MFG concluded that the U.S. EPA monkey study represented a substantially stronger technical basis for characterizing bioavailability than the swine studies. However, several key advantages of the UF/FDEP study led to the further conclusion that it was the results from this study alone that should be discussed with regard to providing numerical recommendations for a revised bioavailability factor. The UF/FDEP study evaluated soil samples from Florida and provided the largest sample groups and number of samples tested, measuring bioavailability in each of five monkeys for each of five soils. Also, cebus monkeys as used in the UF/FDEP study are the species routinely used to test drug uptake. The MFG recognized that since the one value reported in the U.S. EPA monkey study (20%) was within the range of results found in the UF/FDEP study (see below), the range of values considered for numerical recommendations would not be changed by the U.S. EPA monkey study results.

In summary, the UF/FDEP study was considered to be the most comprehensive, most up-to-date, and most effective design for identifying a soil arsenic bioavailability factor for Florida soils. The primary rationales for this characterization were 1) Florida soils impacted by various sources of arsenic were tested, 2) the individually controlled monkey study design, 3) the larger number of observations, and 4) publication of the UF/FDEP report in one of the most respected and most cited toxicology journals following peer review. In addition, the general consistency with other results and finding that observations from the other studies were typically within the range of values reported in the UF/FDEP study reinforce its usefulness. The other studies were characterized as significant supplementary information, however, their numerical findings should not be given the same consideration as the UF/FDEP study with regard to determining a bioavailability factor for application in Florida. The MFG reached a consensus finding that the UF/FDEP study results were suitable as the sole numerical basis for making recommendations regarding soil arsenic bioavailability factors appropriate for use in the calculation of soil CTLs.

Charge 3 – Recommendations for Revised Bioavailability Assumptions

In discussing recommendations for revising soil arsenic bioavailability assumptions used in calculating soil CTLs, the MFG noted that its charge was to provide recommendations on the technical suitability of emerging information for use in Florida's cleanup programs, but not to provide guidance with regard to appropriate environmental policy.

In selecting the various factors used to quantitatively characterize potential human exposure in calculating CTLs, FDEP has followed U.S. EPA's long-standing approach of combining upper-bound and central tendency values. The goal is a set of specific factors to construct a "Reasonable Maximum Exposure" scenario such that corresponding risk-based CTLs are expected to be broadly protective. A scenario made up of only central tendency values would theoretically represent only the "average exposure," and a scenario made up of only upper-bound values is not useful since the compounding of unlikely occurrences does not reasonably reflect any individual's exposure potential. With regard to soil bioavailability specifically, there is no clear precedence for whether soil bioavailability should be selected as a central tendency or upper-bound value. Bioavailability adjustments have been made on a site-specific basis, but not generically as for default CTLs. Absent technical rationale for choosing between a central tendency and upper-bound value, the MFG determined that it should make the strongest possible technical recommendation for values in each of these categories. Choosing between an upper-bound or central tendency value for soil bioavailability is a matter of environmental policy.

Central Tendency Recommendation

Identifying a numerical representation of the central tendency recommendation was straightforward. While the central tendency refers to what is typically thought of as "average," for environmental decisions where protectiveness is a goal, this is usually characterized using the mean (average) plus a factor that captures the variability associated with the value. Like U.S. EPA and most other environmental agencies, the FDEP typically requests that central tendency estimates for human health risks be made using a statistic called the 95 percent upper confidence limit of the mean (95% UCL).

To determine a central tendency recommendation for soil arsenic bioavailability, the MFG suggested that the 95% UCL of all the observations from the UF/FDEP study be used. This was undertaken and standard statistical requirements for determining that the 95% UCL was calculated appropriately were checked. The resulting value of 19% is a conservatively estimated "average" value for bioavailability of arsenic from soil in that it represents the mean plus an additional amount based on the variability among the observations. The statistical analysis presented in the published report of the UF/FDEP study does not clearly indicate that the observations are from one population that can be combined into a single statistical pool. While this could result in additional uncertainty in calculating a central tendency estimate, the distributional testing done in conjunction with the 95% UCL calculation and the inclusion of a variability-based factor in addition to the mean supports the conclusion that the calculated value of 19% is technically comparable to 95% UCL values typically used.

The MFG recommends that 19% be used as a central tendency value for soil arsenic bioavailability in Florida. While final computation of the corresponding soil CTL would be the responsibility of FDEP, the direct-contact CTLs for the FDEP standard residential and commercial/industrial scenarios can be approximated as follows if the bioavailability factor of 19% is incorporated into the ingestion portion of the direct-contact soil CTL equation.

Central Tendency Recommendation: *19% soil arsenic bioavailability*

Corresponding CTLs: *Residential –* *3.7 mg/kg*
Comm./Indus.- *21 mg/kg*

Upper-Bound Recommendation

Specifying the upper-bound value to represent soil arsenic bioavailability was less straightforward in that scientific rationale could be provided for three different values. The MFG determined that all three values should be presented as possible high-end recommendations along with a characterization of the specific scientific basis for each.

Highest Bioavailability Reported for a Florida Soil

Five soil samples were tested in the UF/FDEP study. The highest reported bioavailability factor for an individual soil reported in the study was 25%. This represents the mean of the observations from the 5 monkeys for this soil sample. The bioavailability factor from the "most bioavailable" of the Florida soils can be represented as an upper-bound of the expected bioavailability. The published report of the UF/FDEP study presents the results from the point of view of the bioavailability factor for each soil sample. Previous reports have also reported results grouping the observations by soil sample and this is technically sound since each soil being tested is typically the factor of interest for the study.

The MFG recommends that 25% be considered as an upper-bound bioavailability factor for soil arsenic in Florida on the basis that this represents the highest reported bioavailability for a Florida soil sample. Subject to final computation of the corresponding soil CTL by FDEP, the direct-contact CTLs for the FDEP standard residential and commercial/industrial scenarios can be approximated as follows if the bioavailability factor of 25% is incorporated into the ingestion portion of the direct-contact soil CTL equation.

Highest Florida Soil
Upper-Bound Recommendation: *25%*

Corresponding CTLs: *Residential –* *2.8 mg/kg*
Comm./Indus.- *16 mg/kg*

95th Percentile of All Observations from Florida Soil

Specifying the results from individual soil samples does not combine all of the observations from the UF/FDEP study into one statistical pool. As an additional approach to characterizing an upper-bound value from the study, the observations from all soils were combined and a statistical approach to finding an upper-bound for all of these observations was used. A common statistical approach for defining an upper-bound characterization of a set of values is to use the 95th percentile of the distribution of values. This is intended to statistically capture the value at which 95 percent of the overall results are expected to be lower. Upper-bound estimates used by U.S. EPA and FDEP in characterizing a "Reasonable Maximum Exposure" have been selected as the 95th percentile value where a sufficiently large set of observations is available. The scientific strength of this approach depends on the number and distribution of the observations. The statistical analysis presented in the published report of the UF/FDEP study does not clearly indicate that the observations are from one population that can be combined into a single statistical pool. However, the MFG determined that calculating a 95th percentile from all of the observations could provide an upper-bound value for consideration and the calculation yielded a value of 28%.

The MFG recommends that 28% be considered as an upper-bound bioavailability factor for soil arsenic in Florida based on the 95th percentile of all the observations in the UF/FDEP study. Subject to final computation of the corresponding soil CTL by FDEP, the direct-contact CTLs for the FDEP standard residential and commercial/industrial scenarios can be approximated as follows if the bioavailability factor of 28% is incorporated into the ingestion portion of the direct-contact soil CTL equation.

Statistical Upper-Bound Recommendation:		*28%*
Corresponding CTLs:	*Residential –*	*2.5 mg/kg*
	Comm./Indus.-	*15 mg/kg*

Maximum Observation for a Florida Soil

The single highest observed soil arsenic bioavailability among the five monkeys and five soil samples reported in the UF/FDEP was 32%. This value was recorded for a soil sample other than the soil that generated the highest overall soil bioavailability (noted above); in other words, the single highest experimental observation was recorded for a soil that was not the highest overall in terms of bioavailability. Also, the animal for which the highest bioavailability was observed did not produce the highest bioavailability recorded for each soil. In other words, this one animal did not represent consistently the "most sensitive" case. The MFG recognized that scientific characterizations of experimental studies are not often based on an observation from a single experimental animal and that regulatory applications do not routinely make use of observations from individual subjects, except for human case reports in some cases. However, the single highest observation from the UF/FDEP study could be characterized as an upper-bound value for bioavailability from Florida soils.

The MFG recommends that 32% be considered as an upper-bound bioavailability factor for soil arsenic in Florida based on the highest single observation in the UF/FDEP study. The MFG also notes that this is the highest value supportable based on reported results of the UF/FDEP study. Subject to final computation of the corresponding soil CTL by FDEP, the direct-contact CTLs for the FDEP standard residential and commercial/industrial scenarios can be approximated as follows if the bioavailability factor of 32% is incorporated into the ingestion portion of the direct-contact soil CTL equation.

Maximum Observation
Upper-Bound Recommendation: *32%*

Corresponding CTLs: *Residential –* *2.2 mg/kg*
Comm./Indus.- *13 mg/kg*

While the MFG reached consensus that there was a technical basis for recommending each of the above percentages as an upper-bound bioavailability factor for arsenic in ingested soil, the discussions also indicated that a prioritization of the relative technical basis for each recommendation could be provided.

The technical basis for the recommendation of 25% bioavailability as an upper-bound value was the least subject to debate and this recommendation is prioritized on that basis as having the strongest technical basis. The most important factor noted was the direct reporting of 25%, specifically, 24.7%, as the highest bioavailability for a Florida soil in a peer reviewed study agreed to represent the highest quality study designed to date.

The statistical appropriateness of the technical basis for the recommendation of 28% bioavailability as an upper-bound value was discussed at length by the MFG. While there was broad agreement that the underlying concept of using a 95th percentile value is well founded, the lack of specific analyses from the UF/FDEP study demonstrating that the reported observations could be treated as one population was expected to result in a moderate, but not clearly quantifiable degree of uncertainty in the calculation of the 95th percentile value. Correspondingly, the technical basis for this recommendation was given a secondary prioritization.

The technical basis for the recommendation of 32% is accorded the lowest prioritization because of its reliance on the uncommon practice of selecting an observation from the unanalyzed information in a study, specifically one reported observation from one experimental animal. Findings in experimental studies are typically reported on the basis of the results for groups of experimental animals. While the technical basis for using a maximum-reported value in the literature as an upper-bound value is clear, characterizing an individual animal observation from within an experimental group as indicative of the highest bioavailability for a soil sample is not a common approach.

The range and breadth of the MFG discussions about the technical strength of the various upper-bound recommendations resulted in the prioritization discussed above being reached based on

general or majority agreement among the members. The MFG did not reach consensus that there was a single upper-bound value supported on a technical basis and individual members expressed differing opinions about whether the factors identified in prioritizing the upper-bound recommendations should preclude any of them from being applicable for use by FDEP. The primary reason for not choosing just one value was that the MFG felt that selection between the technically derived values would involve judgment about the desired level of protectiveness in any value ultimately used for chemical-specific adjustment of the soil arsenic CTLs. This judgment was recognized to be beyond the charge of the MFG to provide technical advice, and the members indicated the need to defer to the Forum, FDEP, and other interested stakeholders for such policy-related input. The MFG noted, however, that the values identified as upper-bound technical candidate values all fell within a relatively narrow range (25-32%).

Conclusions

In conclusion, the MFG has considered the issue of arsenic soil bioavailability and determined that scientific information that has become available since the prior promulgation of direct-contact CTLs for arsenic is technically suitable for inclusion in revised calculations. The release of a peer-reviewed report on bioavailability of arsenic from Florida soils provides a demonstrably useful database for revising the default assumption of 100% relative bioavailability with chemical-specific information. The lack of a scientific basis for assuming complete absorption of naturally occurring metals and metal-like elements, including arsenic, has long been clear. However the assumption of 100% relative bioavailability has been used due to the absence of quantitative information on most chemicals. The general research interest in soil arsenic and the in-depth study sponsored by FDEP to measure the bioavailability of arsenic from Florida soils has produced such technically reliable chemical-specific information. The MFG determined that this information is suitable for inclusion in the calculation of risk-based CTLs, recommended specific bioavailability factors that could be incorporated into the ingestion portion of the direct-contact soil CTL computation, and prioritized the technical basis for the recommendations.

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