Attachment A

Relative Bioavailability of Inorganic Arsenic

This attachment provides more detailed information regarding the basis for assuming reduced relative bioavailability for arsenic derived from dislodgeable materials as recommended in these comments. Both the regulatory and technical bases for developing relative bioavailability adjustment (RBA) factors are discussed. Information is provided on studies of the relative bioavailability of dislodgeable arsenic, as well as other relevant media such as arsenic in soil originating from CCA-treated wood. Arsenic leaching studies that provide additional information regarding the likely bioavailability of arsenic from sources associated with wood treated with chromated copper arsenate (CCA) are also reviewed.

Overview

A critical factor determining the magnitude of potential exposures and risks associated with a chemical is its bioavailability, *i.e.*, the amount of the chemical that is actually absorbed into the body. A chemical's bioavailability is influenced by such factors as the species of the chemical, the matrix in which it is present, the amount of time that a chemical is in a matrix, and the route by which exposure occurs. When chemicals are ingested, bioavailability is determined by the amount of a chemical that is dissolved in gastrointestinal fluids and absorbed across the gastrointestinal tract into the bloodstream. An ingested chemical that is adsorbed to soil or some other solid medium like wood dust may be absorbed less completely than the same ingested dose of the chemical when dissolved in water (NEPI, 2000).

Another important factor to consider is the relative bioavailability of the chemical under the exposure conditions of interest when compared to the bioavailability of the chemical under the exposure conditions present in the study that forms the basis for the quantitative toxicity factor for the chemical (USEPA, 1989). Frequently, quantitative toxicity factors are calculated based on studies where the chemical was administered in food or water. By contrast, risk assessments for chemicals in the environment often require assessments of the exposures and risks associated with chemicals in soil or other solid media. Where the bioavailability of the chemical observed in the toxicity study is likely to differ from that under the exposure conditions of interest, a relative bioavailability adjustment (RBA) factor is derived. The RBA factor for a specific chemical reflects the absorption fraction from the exposure medium of interest in the risk analyses (*e.g.*, soil or wood dust) relative to the absorption fraction from the exposure medium used in the relevant toxicity study (*e.g.*, food or water).

It is widely recognized that the bioavailability of many metals and organic chemicals in soil or other solid media tends to be considerably lower than bioavailability from food or water (see, *e.g.*, Ruby *et al.*, 1999; Alexander, 2000). Bioavailability from soil and other solid media can be affected by a number of factors, including the form of the chemical, its solubility, the size distribution of the ingested particles, the type of soil or other medium, the degree of encapsulation of the chemical within an insoluble matrix, and the nutritional status of the exposed individual.

Guidance from the U.S. Environmental Protection Agency (EPA) recognizes the need to make adjustments for the reduced bioavailability of compounds in soil and other media. For example, EPA's *Risk Assessment Guidance for Superfund* (USEPA, 1989) notes:

> "If the medium of exposure in the site exposure assessment differs from the medium of exposure assumed by the toxicity value (*e.g.*, RfD values usually are based on or have been adjusted to reflect exposure *via* drinking water, while the site medium of concern may be soil), an absorption adjustment may, on occasion, be appropriate. For example, a substance might be more completely absorbed following exposure to contaminated drinking water than following exposure to contaminated food or soil (*e.g.*, if the substance does not desorb from soil in the gastrointestinal tract)."

EPA guidance also recommends the use of RBA factors "to adjust a food or soil ingestion exposure estimate to match an RfD or slope factor based on the assumption of drinking water ingestion " (USEPA, 1989).

The risk analyses conducted by the staff of the Consumer Product Safety Commission (CPSC) focus on potential exposures and risks associated with arsenic from dislodgeable materials on the surface of CCA-treated wood. To assess the potential bioavailability of arsenic from this source, data from bioavailability studies using wood dust and dislodgeable residue itself are of interest. For arsenic present in material directly contacted and dislodged from CCA-treated wood, data from two studies of dogs fed sawdust from CCA-treated wood suggest a relative bioavailability estimate of 47% (Peoples, 1976; Peoples and Parker, 1979). Initial results from a recent study in which hamsters were fed dislodgeable arsenic support reduced RBA estimates for dislodgeable arsenic and suggest that the RBA value may be in the range of 10-20% (Aposhian, 2001). Additional animal studies of the bioavailability of dislodgeable arsenic have been designed with input from EPA and other regulatory agencies and are currently underway. The results of these studies, as well as other factors indicating the reduced bioavailability of dislodgeable arsenic, should be incorporated into CPSC's risk analyses. Other factors supporting a reduced bioavailability of dislodgeable arsenic from CCA-treated wood include the chemistry of the

wood treatment process, which is designed to fix arsenic and the other metals within the wood matrix; the form of arsenic found on the wood surface; studies indicating that only a small proportion of dislodgeable arsenic is soluble; and toxicology and epidemiology studies indicating few adverse effects that are attributable to arsenic exposure from CCA-treated wood.

In addition to the animal studies available for deriving an estimate of oral bioavailability, other factors support an assumption of reduced bioavailability for dislodgeable arsenic. First, the chemical process that occurs during wood treatment is designed to bind the CCA in the wood so that the fixative will persist and prevent deterioration of the wood over a long period of time (Bull, 2001). Second, a study of the composition of dislodgeable materials suggests that a substantial proportion of the arsenic observed on the surface of CCA-treated wood is insoluble. Specifically, an analysis of dislodgeable surface materials collected from samples of CCA-treated wood found that arsenic comprised a maximum average value of 0.2% of the surface material on the treated wood and that approximately 94-100% of the surface arsenic was insoluble in water (Cui, 2001; Osmose, 2001). X-ray diffraction techniques have shown the form of arsenic on the surface of CCA-treated wood to be non-crystalline amorphous oxide complexes (Kamdem, 2001; Kamdem and Cui, 2001), which is consistent with the foregoing observations. Overall, these findings support the assumption that the bioavailability of arsenic present in dislodged materials is less than would be expected based on consideration of the total measured arsenic concentration.

Additional evidence of the reduced bioavailability of dislodgeable arsenic comes from the results of leaching studies. Data from leaching studies indicate that arsenic is not released from treated wood to any appreciable extent under normal outdoor conditions (*e.g.*, when exposed to rainwater) and is primarily mobilized from the wood through physical transport of dislodgeable particles (*e.g.*, wood particles). Based on a review of the leaching studies, two key observations support reduced RBA factors for dislodgeable arsenic. First, the duration of the leaching studies in acidic solutions ranged from 4 to 40 days. This duration is significantly longer than the period of time that food (or ingested dislodgeable arsenic) remains in the human stomach, *i.e.*, approximately 4 hours (Vander *et al*., 1994). Thus, the leaching studies are likely to overestimate arsenic leaching that would occur in the human gastrointestinal tract. Second, the reported amount of arsenic leached in these studies ranged from 17 to 44%. Together, these observations suggest that the RBA estimate of 47% for dislodgeable arsenic that is derived from the dog studies is likely to represent a conservative value. The lower RBA values suggested by the

preliminary results from the hamster studies (*i.e.*, 10-20%) are also consistent with the results of the leaching studies.

The reduced bioavailability of arsenic associated with dislodgeable materials is also consistent with extensive information in the scientific literature indicating the generally reduced relative bioavailability of arsenic from soil and other solid matrices, including soil from a CCA treatment site. Overall, based on rabbit, monkey, dog, and swine studies published in the peer-reviewed literature, relative bioavailability estimates for arsenic in soil range from near zero to approximately 50%. The corresponding oral bioavailability for soluble forms of arsenic (*i.e.,* the type of arsenic present in the epidemiological and animal studies upon which the standard toxicity factors are based) reported in published *in vivo* studies is as high as approximately 95%. Results from two studies of soil from CCA wood treatment sites revealed a similarly reduced relative bioavailability of arsenic. In particular, results from a study in which primates were fed soil collected at a CCA treatment site indicate an RBA value of 16.3% (Roberts *et al*., 2001).

The chemistry of arsenic in soil also suggests a reduced bioavailability. Arsenic is generally tightly bound to soils (Cooper, 1990; USDA, 1980). Arsenates, including chromium arsenate, are the form of arsenic in found in treated wood, released from treated wood as dislodgeable arsenic, and observed in soil in the vicinity of structures built of CCA-treated wood. Arsenates strongly bind to ferric hydroxides, which are abundant in soils. Arsenates can also form insoluble complexes with ferric iron, aluminum, or calcium, all of which are abundant in soil (Cooper, 1990). Unless there are unusual circumstances, arsenic will remain in the arsenate form. Reducing conditions can yield changes in the form of arsenic found in the environment; however, such conditions are rare in surface soils. In the arsenate form, arsenic is in its +5 oxidation state, which is a less soluble and less mobile form than arsenite (As^{+3}) (ATSDR, 2000; Masscheleyn *et al*., 1991 as cited in Townsend, *et al*., 2001). In fact, arsenite (As^{+3}) was looked for and not found in properly treated wood (Nygren and Nilsson, 1993). These observations, regarding the chemical species of arsenic in soil near treated wood structures, its strong binding to soil, and its reduced solubility and mobility, all support a reduced bioavailability of CCA-derived arsenic in soil.

Additional support for the recommended assumptions regarding the reduced bioavailability of arsenic associated with CCA-treated wood is provided below.

Bioavailability of Dislodgeable Arsenic

Several studies have assessed the bioavailability of arsenic associated with CCA-treated wood. These studies have examined the bioavailability and toxicity of arsenic in sawdust from CCA-treated wood and provide a useful basis for estimating the relative bioavailability of dislodgeable arsenic. They are also the most relevant studies currently available. In these studies, dogs were fed sawdust from CCA-treated wood (Peoples, 1976; Peoples and Parker, 1979). In the first of these studies, two dogs were fed sawdust from CCA-treated wood (equal to an arsenic dose of 39 mg/day) for a period of 5 days (Peoples, 1976). Urine and feces samples were collected from these animals on the days when the sawdust was administered as well as for several days before and after this treatment period. Arsenic absorption was then assessed by comparing the amounts of arsenic excreted in urine with the total ingested arsenic dose. This comparison yielded an estimate of absolute arsenic absorption of 26% based on data from one animal and 29% based on data from the other.

A test group using ingested soluble arsenic was not included in the study; therefore, relative bioavailability cannot be calculated from the study results. Data presented in Hollins *et al*. (1979), however, indicate that absorption of soluble arsenic is similar in dogs and monkeys. As a result, RBA estimates were derived by comparing the absolute arsenic bioavailability measured in this study with the soluble arsenic bioavailability estimate for monkeys (68%) observed in a study by Freeman *et al*. (1995). This calculation yields RBAs of 38% and 43% for the two animals in this study.

In a second study, a dog was fed sawdust from CCA-treated wood (equal to an arsenic dose of 6 mg/day) for a period of 8 days (Peoples and Parker, 1979). Chemical analyses indicated that the dog received an additional 0.135 mg/day of arsenic through dietary sources. Comparison of the total arsenic intake during the feeding period with the amount of arsenic excreted in the urine indicated that approximately 40% of the ingested arsenic was absorbed. Using the same approach as noted above, an RBA estimate of 59% was derived. The absorption estimates derived in these two studies are relatively similar to each other and are consistent with the range of bioavailability estimates observed for arsenic in soil, as described below. Thus, these data support use of an RBA value of 47% for estimating the relative bioavailability of dislodgeable arsenic from CCA-treated wood.

Another recently conducted bioavailability study has administered dislodgeable arsenic to hamsters *via* oral gavage (Aposhian, 2001). Initial results from this study support reduced bioavailability

estimates for dislodgeable arsenic and suggest that the RBA value for dislodgeable arsenic may be in the range of 10-20%. Moreover, additional animal studies of the bioavailability of dislodgeable arsenic have been designed with input from EPA and other regulatory agencies. These data should be used to derive a refined estimate of the bioavailability of dislodgeable arsenic.

A single study of dermal absorption of arsenic from CCA-treated sawdust also observed reduced bioavailability of this material. Specifically, no significant change in urinary arsenic excretion was observed in a single dog exposed to a test patch of the sawdust for 2 days (Peoples, 1979).

Finally, while only a few studies have been undertaken to directly evaluate the toxicity of arsenic in sawdust from CCA-treated wood, the available data do not indicate substantial uptake and adverse health effects associated with this material. For example, the researchers who conducted the two bioavailability studies of CCA-treated sawdust reported that no signs of toxicity were observed in the dogs used in the studies (Peoples, 1976; Peoples and Parker, 1979). Similarly, a teratogenicity study saw no significant adverse maternal or fetal toxicity (Hood, 1979). In this study, mice were exposed to CCA-treated sawdust *via* dermal contact or ingestion in the diet. In a study of mice exposed to treated sawdust administered in the diet or *via* oral gavage, no chromosomal damage or apparent adverse hematological effects were observed (Graham, 1979). In a retrospective epidemiology study of carpenters in Hawaii, the patterns of cancer mortality in this group were compared with cancer mortality in the general population (Budy and Rashad, 1976). In particular, the mortality rates were examined before and after the use of arsenic-treated wood in Hawaii, including CCA-treated wood. This study observed no adverse health effects related to the use of arsenic-treated wood. Thus, although these studies do not conclusively demonstrate an absence of effects from these materials, they also have not observed any significant adverse health impacts associated with exposure to these materials.

Evaluation of Physical and Chemical Characteristics Influencing the Bioavailability of Dislodgeable Arsenic

Other factors also support an assumption of reduced bioavailability for dislodgeable arsenic. First, the chemical process that occurs during wood treatment is designed to bind the CCA in the wood so that the fixative will persist and prevent deterioration of the wood over a long period of time (Bull, 2001). As discussed below, data from leaching studies indicate that arsenic is not released from treated wood to any appreciable extent under normal outdoor conditions (*e.g.*, when exposed to rainwater) (Ziobro, 2000)

and is primarily mobilized from the wood through physical transport of dislodged particles. Moreover, a study of the composition of dislodgeable materials suggests that a substantial proportion of the arsenic observed on the surface of CCA-treated wood is insoluble. Specifically, an analysis of dislodgeable surface materials from CCA-treated wood found that arsenic comprised a maximum average value of 0.2% of the surface material on the treated wood and that approximately 94-100% of the surface arsenic was insoluble in water (Cui, 2001; Osmose, 2001). This finding supports the assumption that the bioavailability of arsenic present in dislodged materials is less than would be expected based on consideration of the total measured arsenic concentration.

Studies evaluating the leachability of arsenic from small sized wood particles (*e.g.*, sawdust and chipped wood) used in some of the leaching studies can provide insights regarding the leachability and potential bioavailability of dislodgeable arsenic from a CCA-treated structure. To assess the bioavailability of ingested dislodgeable arsenic, the leaching studies conducted at or near the pH of the human stomach (pH 1.0-3.5) are more relevant than those conducted at a neutral pH range (pH 5.0-7.5). These studies are described briefly here.

Murphy and Dickinson (1990) found no change in the arsenic content of CCA type C wood subjected to simulated rain at pH 3.0 and pH 5.6. Similarly, Ziobro (2000) found no change in the amount of fixed arsenic in CCA-treated lumber in a deck exposed for 7 years in Florida. Cooper (1991) observed that only 2.9 to 6.9% of the arsenic was leached from small CCA-treated wood specimens (with dimensions of 1 cm × 1 cm × 4 cm) exposed to acidic solutions (at pH values of 3.5, 4.5, and 5.5) for 13 days. In another study, Warner and Solomon (1990) subjected small blocks of treated wood for 40 days to a citric acid buffered solution at pH 3.5, and to a sulfuric acid solution at pH 2.5. The citric acid buffer reportedly leached 68% of the arsenic from the blocks. Following up on these results, Cooper (1991) conducted a similar experiment and determined that the citric acid buffer, not the pH of the solution, caused the release of arsenic. Warner and Solomon (1990) also reported that sulfuric acid at pH 2.5 released 39.7% of the arsenic after 40 days of digestion. Sulfuric acid is an oxidizing acid and may have deteriorated the wood itself, enhancing the leaching power of the acidic solution. By contrast, stomach acid consists of hydrochloric acid, which is not an oxidizing acid. CPSC (1990) performed a number of experiments to evaluate the leaching of arsenic from treated wood under acidic conditions. In one set of experiments, 4 days of leaching in HCl at pH 1.0 released 44% of the arsenic from a small piece (32 mg) of treated wood. Similarly, a nitric acid solution at pH 1.0 leached 43% of the arsenic from a 34 mg piece of wood in 4 days. In another series of experiments, 17-19% of the arsenic was leached by HCl at pH 1.0

in 18 days, and 18-31% of the arsenic was released in a nitric acid solution at pH 1.0 after 17 days (CPSC, 1990).

Based on the results of the preceding leaching studies, two key observations support reduced bioavailability estimates for dislodgeable arsenic. First, the duration of the leaching studies in acidic solutions ranged from 4 to 40 days. This duration is significantly longer than the period of time that food or ingested dislodgeable arsenic would be in the human stomach (*i.e.*, approximately 4 hours; Vander *et al*., 1994). Therefore, the results of the leaching studies would be expected to overestimate the amount of leaching that would occur during passage through the stomach. Second, the reported amount of leached arsenic in all of these studies ranged from 17 to 44% (with the exception of the experiment performed in citric acid solution). These observations support the 47% bioavailability estimate for dislodgeable arsenic recommended in these comments.

Bioavailability of Arsenic in Soil and Other Solid Matrices

As noted above, the reduced bioavailability of dislodgeable arsenic is also supported by data indicating reduced bioavailability of arsenic from soil and other solid matrices. Recognition of the importance of this factor in assessing potential exposures and risks associated with arsenic is reflected in generic regulatory guidance (*e.g.*, MIDEQ, 2000; WVDEP, 1998; WA Ecology, 1991, 1996; USEPA, 1989) as well as regulatory decisions reached at specific sites (*e.g.*, Gradient, 2000; USEPA, Region 3, 1998; USEPA, Region 8 and MDEQ, 1996; MIDEQ, 1995; ODEQ, 1994). Typically, the selected RBA values for arsenic in soil have been less than 50% at both the state and federal level.

These regulatory actions have been based on studies of the oral bioavailability of soil-bound arsenic. Several reviews of these studies have been prepared (*e.g.*, Valberg *et al*., 1997; Ruby *et al*., 1999; NEPI, 2000). The results from the available published arsenic bioavailability studies are summarized in Table A-1. In all of these studies, soil-bound arsenic has been found to be less bioavailable than soluble arsenic compounds. Specifically, all of the reported relative bioavailability estimates for soil-bound arsenic from the peer-reviewed literature are less than 50%.

Table A-1
Estimates of Oral Bioavailability of Arsenic in Solid Matrices

Site	Sample Type[a]	Test Species	As Conc. in mg/kg	Mean Relative Bioavailability (%)	Source
Anaconda, MT	Residential soil	Rabbit	3,900	47	1
Anaconda, MT	Residential soil (9)	Monkey	410	20[b]	2
	Residential house dust (4)		170	28[b]	2
Mining/Smelter Sites	Soil, sediment, smelter slag, and mill tailings (13)	Pig	233 to 17,500	3 to 43	3
Butte, MT	Soil[c]	Rat	626	37.8[d]	4
Villa de la Paz, Mexico	Mining waste	Rat	9,647	12	5
Gelderland, Netherlands	Bog ore soil	Dog	339	12[e]	6

Sources:
(1) Freeman et al., 1993
(2) Freeman et al., 1995
(3) Rodriguez et al., 1999
(4) Ellickson et al. 2001
(5) Rodriguez et al., 1998
(6) Groen et al., 1994

Notes:
a = Number in parentheses indicates number of samples.
b = Mean relative bioavailability based on urinanalysis.
c = National Institute of Standards and Technology (NIST) standard reference soil.
d = Absolute bioavailability estimate.
e = Relative bioavailability estimate derived based on absolute bioavailability estimate for soil from cited study (0.08) and bioavailability estimate for soluble arsenic (0.68) from Freeman et al., 1995.

As indicated by the studies reviewed above, most of the available data suggest that the bioavailability of ingested arsenic in soil is less than 50%, which is significantly less than that for ingested arsenic dissolved in water. In one study conducted by EPA that has not been published in the peer-reviewed literature, an RBA estimate of 78% was derived for ingested arsenic in soil (USEPA, Region 10, 1996). In this study, immature swine were fed soil, as well as other metals-containing materials, collected in the vicinity of a smelter site in Tacoma, Washington. Treated animals were given a single dose of arsenic, with doses from soil ranging from 0.04 to 0.24 mg of arsenic per kg of body weight. Arsenic bioavailability was assessed based on arsenic analyses of blood samples and regression analyses using these results. Although the results of this study suggest that the relative bioavailability of arsenic in soil can be greater than 50% under some conditions, several limitations in this study weaken confidence in the results. In particular, because the regression analyses were based on only three data points, uncertainty exists in the quantitative significance of these results. In addition, the first blood sample was not collected from the animals until 15 minutes after the arsenic doses were administered. Because arsenic is rapidly cleared from the blood, the blood arsenic concentration was likely underestimated for animals dosed with arsenic intravenously. As a result, the relative bioavailability

values calculated using the intravenous data from this study are likely to overestimate the actual bioavailability of the soil-bound arsenic.

The evidence for reduced bioavailability of soil arsenic from *in vivo* and *in vitro* laboratory studies is supported by a study of arsenic exposures in children living in the vicinity of a former copper smelter. Based on urinary arsenic measurements, actual arsenic exposures from soil were less than those predicted using standard risk assessment assumptions (Walker and Griffin, 1998; Cohen *et al*., 1998). The relative bioavailability of arsenic in site soils was estimated to be about 20% based on Freeman *et al*. (1995). When site-specific relative bioavailability estimates were incorporated into the exposure calculations, predicted exposures more closely matched observed exposures (Walker and Griffin, 1998; Cohen *et al*. 1998).

A few studies are available that have specifically examined the bioavailability of soil arsenic associated with CCA-treated wood. The results observed in these studies are consistent with the general results observed in other studies of soil containing arsenic from various sources, *i.e.*, these results suggest that the bioavailability of CCA-related arsenic from soil or dislodgeable materials is reduced relative to the bioavailability of dissolved arsenic. Two animal studies have used soil obtained from CCA treatment sites. In the first study, soil from nine samples collected at a wood treatment site that used CCA was mixed with water and administered to rats *via* gavage (Ng and Moore, 1996). The researchers selected rats for use in these studies because they accumulate arsenic in their blood to a greater extent than other species, and thus, can serve as a sensitive indicator of arsenic uptake. Results from the test animals were compared with results from rats administered an equivalent dose of arsenic in an aqueous solution containing sodium arsenite or sodium arsenate, or in wheat flour spiked with calcium arsenite. Blood arsenic concentrations were measured 96 hours after the arsenic dosing (*i.e.*, the time at which the researchers state that maximum blood arsenic concentrations would be attained). Relative bioavailability was then estimated by comparing the blood arsenic concentrations observed in the soil group with the concentrations observed in the other three groups. These calculations yielded relative bioavailability estimates of 13.4% (relative to sodium arsenite), 32.2% (relative to calcium arsenite), and 38.0% (relative to sodium arsenate). These results are well within the range of RBA estimates observed in the soil studies discussed above.

In the second study, five *Cebus apella* monkeys received oral doses of arsenic in soil collected at four types of sites, including a CCA wood treatment site (Roberts *et al*., 2001). Because primates are

more similar physiologically to humans than rats, and because the primate study design was stronger and more comprehensive than the rat study, the data from this study provide a stronger basis for assessing the relative bioavailability of soil arsenic associated with CCA-treated wood. To estimate the relative bioavailability of the soil arsenic, urinary excretion of arsenic following dosing with soil was compared to that observed following an oral dose of an aqueous solution of sodium arsenate. The researchers found that the pharmacokinetic behavior of the arsenic, including the proportions of arsenic excreted in urine and feces, was similar to observations made in humans. In this test system, the relative bioavailability of arsenic in the CCA treatment site soils was estimated to be 16.3%. Arsenic in soil from the other three types of sites evaluated in this experiment (*i.e.*, an electrical substation, a pesticide application site, and a cattle dip vat site) also showed reduced bioavailability. Specifically, the relative bioavailability of arsenic in the soil from the other sites ranged from 10.7 to 24.7%. Again, these results are well within the range of estimates observed for other studies of arsenic in soil and support the likelihood of reduced bioavailability of arsenic associated with CCA-treated wood.

References

Agency for Toxic Substances and Disease Registry (ATSDR). 2000. "Toxicological Profile for Arsenic." Prepared for the U.S. Department of Health and Human Services. September.

Alexander, M. 2000. Aging, bioavailability, and overestimation of risk from environmental pollutants. *Environmental Science and Technology* 34(20):4259-4265.

Aposhian, H.V. 2001. "Bioavailability of Dislodgeable CCA." Unpublished report to FDA.

Budy, A.M. and M.N. Rashad. 1976. Cancer mortality among carpenters in Hawaii. In *Prevention and Detection of Cancer: Proceedings of the Third International Symposium on Detection and Prevention of Cancer: Volume I - Etiology, April 26 to May 1, 1976, New York* (Ed: H.E. Nieburgs), Marcel Dekker, Inc., New York. pp. 901-907.

Bull, D.C. 2001. The chemistry of chromated copper arsenate. II. Preservative-wood interactions. *Wood Science and Technology* 34:459-466.

Cohen, J.T., B.D. Beck, T.S. Bowers, R.L. Bornschein, and E.J. Calabrese. 1998. An arsenic exposure model: Probabilistic validation using empirical data. *Human Ecol. Risk Assess.* 4(2):341-377.

Consumer Product Safety Commission (CPSC). 1990. "U.S. Consumer Product Safety Commission Project Report: Playground Equipment – Transmittal of Estimate of Risk of Skin Cancer from Dislodgeable Arsenic on Pressure Treated Wood Playground Equipment." Provided by Hickson Corporation, Atlanta, GA.

Cooper, P.A. 1990. Leaching of CCA from treated wood. In *Proceedings of the Canadian Wood Preservers Association, Volume II*, pp. 144-169.

Cooper, P.A. 1991. Leaching of CCA from treated wood: pH effects. *Forest Products Journal* 41(1): 30-32. January.

Cui, W. 2001. "Surface Arsenic Analysis of Commercial CCA Treated Southern Pine."

Ellickson, K.M., R.J. Meeker, M.A. Gallo, B.T. Buckley, and P.J. Lioy. 2001. Oral bioavailability of lead and arsenic from a NIST standard reference soil material. *Arch. Environ. Contam. Toxicol.* 40(1):128-135.

Freeman, G.B., J.D. Johnson, J.M. Killinger, S.C. Liao, A.O. Davis, M.V. Ruby, R.L. Chaney, S.C. Lovre, and P.D. Bergstrom. 1993. Bioavailability of arsenic in soil impacted by smelter activities following oral administration in rabbits. *Fund. Appl. Toxicol.* 21:83-88.

Freeman, G.B., R.A. Schoof, M.V. Ruby, A.O. Davis, J.A. Dill, S.C. Liao, C.A. Lapin, and P.D. Bergstrom. 1995. Bioavailability of arsenic in soil and house dust impacted by smelter activities following oral administration in cynomolgus monkeys. *Fund. Appl. Toxicol.* 28:215-222.

Gradient Corporation (Gradient). 2000. "Human Health Risk Assessment (HHRA), Hurley Soils Investigation Unit, Volume I-III." Prepared for the State of New Mexico Environment Department (NMED). February 22.

Graham, B.Y. 1979. "*In Vivo* Cytogenetic Studies of Chromated Copper Arsenate Treated Sawdust in Mouse Bone Marrow." University of Alabama, Dept. of Chemistry. April 30.

Groen, K., H.A.M.G. Vaessen, J.J.G Kliest, J.L.M. de Boer, T. van Ooik, A. Timmerman, and R.F. Vlug. 1994. Bioavailability of inorganic arsenic from bog ore-containing soil in the dog. *Environ. Health Perspect*. 102(2):182-184.

Hollins, J.G., S.M. Charbonneau, F. Bryce, J.M. Ridgeway, G.K.H. Tam, and R.E. Willes. 1979. Whole body retention and excretion of [^{74}As] arsenic acid in the adult beagle dog. *Toxicol. Lett.* 4:7-13.

Hood, R.D. 1979. "Evaluation of Chromated Copper Arsenate (CCA) Impregnated in Sawdust for Teratogenicity and Maternal Toxicity in Mice and Rabbits." 14 p.

Kamdem, D.P. 2001. "ESEM of CCA Type C Treated Southern Pine." Michigan State University, Department of Forestry.

Kamdem, D.P. and W. Cui. 2001. "X-Ray Diffraction of CCA Treated Wood Surface." Michigan State University, Department of Forestry.

Masscheleyn, P.H., R.D. Delaune, and W.H. Patrick, Jr.. 1991. A hydride generation atomic absorption technique for arsenic speciation. *Journal of Environmental Quality* 20:96-100. (As cited in Townsend *et al*., 2001)

Michigan Department of Environmental Quality (MIDEQ). 1995. Interoffice Communication from L.D. Larson (Toxicologist) to B. Crowles (Environmental Quality Analyst) re: the Ralph Crego Park Site in Lansing, MI. Michigan Department of Natural Resources, Lansing, MI. February 24.

Michigan Department of Environmental Quality (MIDEQ). 2000. Environmental Response Division Operational Memorandum #18. www.deq.state.mi.us/erd/opmemos/opmemo18/opmemo18.html.

Murphy, R.J. and D.J. Dickinson. 1990. The effect of acid rain on CCA treated timber. In *Proceedings of the Wood Presentation Symposium*, Cannes, France, Feb. 19-20. IRG/WF/3600.

National Environmental Policy Institute (NEPI). 2000. Assessing the Bioavailability of Metals in Soil for Use in Human Health Risk Assessments. Bioavailability Policy Project Phase II, Metals Task Force Report. Summer. Downloaded from http://www.nepi.org/pubs/metals-bio%20final.pdf on June 27, 2001.

Ng, J.C. and M.R. Moore. 1996. Bioavailability of arsenic in soils form contaminated sites using a 96 hour rat blood model. In *The Health Risk Assessment and Management of Contaminated Sites: Proceedings of the Third National Workshop on the Health Risk Assessment and Management of Contaminated Sites, South Australian Health Commission, Adelaide* (A. Langley, B. Markey, and H. Hill, Eds.).

Nygren, O. and C.A. Nilsson. 1993. Determination and speciation of chromium, copper and arsenic in wood and dust from CCA-impregnated timber. *Analysis* 21:83-89.

Oklahoma Department of Environmental Quality (ODEQ). 1994. "Record of Decision for Operable Unit One of the National Zinc Site, Bartlesville, Oklahoma." ODEQ, Tulsa, OK.

Osmose. 2001. "Surface Chemical Analysis of CCA Treated Southern Pine Lumber." Research Document 33-258. June 4.

Peoples, S.A. 1976. "The Amount and Valence of Arsenic Excreted in the Urine of Dogs Fed CCA-C in Their Diet." University of California, Davis, CA.

Peoples, S.A. 1979. "The Dermal Absorption of Arsenic in Dogs from Sawdust from Wood Treated with ACA and CCA-C." University of California, School of Veterinary Medicine, Department of Physiological Science, Davis, CA. July.

Peoples, S.A and H.R. Parker. 1979. "The Absorption and Excretion of Arsenic from the Ingestion of Sawdust of Arsenical Treated Wood by Dogs." University of California, School of Veterinary Medicine, Davis, CA. July.

Roberts, S.M., W.R. Weimar, J.R. Vinson, J.W. Munson, and R.J. Bergeron. 2001. Measurement of arsenic bioavailability from soils using a primate model. Abstract presented at the Annual Society of Toxicology Meeting. March.

Rodriguez, V.M., L. Dufour, L. Carrizales, F. Diaz-Barriga, and M.E. Jiménez-Capdeville. 1998. Effects of oral exposure to mining waste on *in vivo* dopamine release from rat striatum. *Environ. Health Perspect*. 106(8):487-491. August.

Rodriguez, R.R., N.T. Basta, S.W. Casteel, and L.W. Pace. 1999. An *in vitro* gastrointestinal method to estimate bioavailable arsenic in contaminated soils and solid media. *Environ. Sci. Technol.* 33(4):642-649.

Ruby, M.V., R. Schoof, W. Brattin, M. Goldade, G. Post, M. Harnois, D.E. Mosby, S.W. Casteel, W. Berti, M. Carpenter, D. Edwards, D. Cragin, and W. Chappell. 1999. Advances in evaluating the oral bioavailability of inorganics in soil for use in human health risk assessment. *Environmental Science & Technology* 33(21):3697-3705.

Townsend, T., K. Stook, T. Tolaymat, J.K. Song, H. Solo-Gabriele, N. Hosein, and B. Khan. 2001. "New Lines of CCA-Treated Wood Research: In-Service and Disposal Issues." Report #00-12. March 19.

U.S. Department of Agriculture (USDA). 1980. "The Biologic and Economic Assessment of Pentachlorophenol, Inorganic Arsenicals, Creosote. Volume I: Wood Preservatives." Cooperative Impact Assessment Report. Technical Bulletin Number 1658-1. November 4.

U.S. Environmental Protection Agency (USEPA). 1989. "Risk Assessment Guidance for Superfund (RAGS), Vol. I, Human Health Evaluation Manual (Part A)." Office of Emergency and Remedial Response, Washington, D.C. OSWER Directive 9285.7-01A. EPA-540/1-89-002. December.

U.S. Environmental Protection Agency, Region 3 (USEPA, Region 3). 1998. "Final Risk Assessment Report for the Palmerton Zinc Site." U.S. EPA, Region 3, Philadelphia, PA.

U.S. Environmental Protection Agency, Region 10 (USEPA, Region 10). 1996. "Bioavailability of Arsenic and Lead in Environmental Substrates. 1. Results of an Oral Dosing Study of Immature Swine." U.S. EPA, Region 10, Superfund/Office of Environmental Assessment, Seattle, WA. EPA 910/R-96-002. February.

U.S. Environmental Protection Agency, Region 8 and Montana Department of Environmental Quality (USEPA, Region 8 and MDEQ). 1996. "Record of Decision. Community Soils Operable Unit. Anaconda Smelter NPL Site, Anaconda, Montana." U.S. EPA, Region 8, Helena, MT and MDEQ, Helena, MT.

Valberg, P.A., B.D. Beck, T.S. Bowers, J.L. Keating, P.D. Bergstrom, and P.D. Boardman. 1997. Issues in setting health-based cleanup levels for arsenic in soil. *Regul. Toxicol. Pharmacol.* 26:219-229.

Vander, A.J., J.H. Sherman, and D.S. Luciano. 1994. Chapter 18: Regulation of organic metabolism, growth and energy balance. In *Human Physiology* (K.M. Prancan and J.W. Bradley, Eds.), Mc-Graw Hill, p. 602.

Walker, S. and S. Griffin. 1998. Site-specific data confirm arsenic exposure predicted by the U.S. Environmental Protection Agency. *Environ. Health Perspect*. 106(3):133-139.

Warner, J.E. and K.R. Solomon. 1990. Acidity as a factor in leaching of copper, chromium and arsenic from CCA-treated dimension lumber. *Environmental Toxicology and Chemistry* 9:1331-1337.

Washington State Department of Ecology (WA Ecology). 1991. Memo from Lon Kissinger to Marian Abbett re: Gastrointestinal Absorption of Arsenic from Arsenic Contaminated Soil. Washington State Department of Ecology, Olympia, WA. September 12.

Washington State Department of Ecology (WA Ecology). 1996. "Model Toxics Control Act Cleanup Levels and Risk Calculations (CLARC II) Update." Pub. #94-145. Washington State Department of Ecology. February.

West Virginia Department of Environmental Protection (WVDEP). 1998. "West Virginia Voluntary Remediation and Redevelopment Act Guidance Manual." Charleston, WV.

Ziobro, R.J. 2000. "CCA Retention Analysis of an Above Ground Depletion Deck Exposed at the Gainesville Test Plot." Research Document 33-184. April 12.