Comments on Selected Sections

of the February 2003 CPSC Briefing Package

re: *Petition to Ban Chromated Copper Arsenate (CCA) - Treated Wood in Playground Equipment* (Petition HP 01-3)

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1 Overview

On behalf of the Wood Preservative Science Council (WPSC), Gradient Corporation has prepared these comments on selected sections of the Briefing Package regarding the *Petition to Ban Chromated Copper Arsenate (CCA)-Treated Wood in Playground Equipment* (Petition HP 01-3), which was prepared by the staff of the U.S. Consumer Product Safety Commission (CPSC; CPSC, 2003). The risk assessment conducted by CPSC staff examines the potential risks posed to young children by exposures to arsenic associated with contacts with playground equipment built of CCA-treated wood. As summarized in Table 1-1, these comments focus on certain elements of the risk assessment prepared by the CPSC staff, including data from research programs conducted by CPSC and other analyses conducted by CPSC staff to support assumptions used in the risk analyses. These comments also address selected issues regarding the potential toxicity of ingested inorganic arsenic that were raised in the March 17, 2003 public hearing addressing the Briefing Package. These issues are also indicated in Table 1-1.

Table 1-1
Summary of Issues Addressed in Comments

Section of Comments	Issue	Section of CPSC Staff Briefing Package
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All of the issues addressed in these comments are also discussed in the summary report of the Briefing Package.

The risk assessment approach applied in the Briefing Package incorporates a number of appropriate elements, *e.g.*, the use of an empirical approach (rather than a mechanistic approach) to assess incidental ingestion of dislodgeable materials from the treated wood surfaces and the use of a focused sensitivity analysis (rather than a probabilistic risk analysis) to evaluate the potential influence of sources of variability and uncertainty on the risk assessment results. A number of specific assumptions regarding exposure parameters and arsenic toxicity that are used in the risk analyses (including assumptions applied in the sensitivity analysis), however, do not accurately reflect currently available scientific information and are likely to overestimate potential exposures and risks associated with young children's arsenic exposures from playground equipment built of CCA-treated wood.

Moreover, additional studies of several critical factors for assessing the potential risks associated with CCA-treated wood have been designed with input from the U.S. Environmental Protection Agency (EPA) and other regulatory agencies and are currently underway. These research programs include animal studies of the bioavailability of arsenic in dislodgeable residue (and arsenic in soil affected by CCA-treated wood) and hand and wipe studies of the potential removal of dislodgeable residue from treated wood surfaces. In light of these ongoing, relevant studies, the release of the CPSC staff risk assessment is premature. Instead, the CPSC staff risk analyses should be revised to reflect the results of these studies when they become available. The bioavailability study results and the pilot results from the hand and wipe studies are anticipated to be available during the spring of 2003, while the results from the full hand and wipe studies are expected to be available during the late spring of 2003

Specific elements of the risk analyses that inaccurately reflect currently available data or represent overly conservative assumptions include the following:

- The carcinogenic slope factor (CSF) for ingested arsenic. The risk assessment conducted by the CPSC staff applies a range of potential values for this parameter ranging from 0.41 $(mg/kg\text{-}day)^{-1}$ to 23 $(mg/kg\text{-}day)^{-1}$. All of the values included in this range include conservative elements that are likely to overestimate potential carcinogenic risks for U.S. populations exposed to low levels of ingested arsenic. The high-end estimate in this range, however, is implausible, inconsistent with the results of well-designed epidemiological studies in U.S. populations, and inconsistent with toxicity assessment methodologies applied by other regulatory agencies. This high-end value should be eliminated from the risk assessment calculations. Based on the analyses presented by the CPSC staff, eliminating this high-end CSF value would leave a more reasonable, yet still

highly health-protective, range of potential CSF values from 0.41 $(mg/kg\text{-}day)^{-1}$ to 3.7 $(mg/kg\text{-}day)^{-1}$ for use in the risk analyses. It should be noted, however, that the upper end of this range appears to reflect a miscalculation of the CSF by CPSC staff based on the underlying data. Correction of this apparent error would yield an alternative upper end CSF that is approximately 2-fold lower than the value presented by CPSC staff, resulting in a range of CSF values from 0.41 $(mg/kg\text{-}day)^{-1}$ to 1.9 $(mg/kg\text{-}day)^{-1}$.

- The relative bioavailability adjustment (RBA) factor for ingested dislodgeable arsenic. The risk assessment conducted by the CPSC staff assumes that the relative bioavailability of arsenic in dislodgeable residue is the same as that of arsenic dissolved in drinking water. This assumption ignores substantial available data indicating that dislodgeable residue is not highly soluble and is likely to have reduced bioavailability. These data include the reduced bioavailability observed in animal studies of dislodgeable residue and sawdust from CCA-treated wood; information regarding the chemistry of the wood treatment process; studies of the composition, solubility, and leaching of dislodgeable materials; toxicology and epidemiology studies indicating few adverse health effects attributable to arsenic exposure from CCA-treated wood; and data indicating reduced bioavailability of arsenic (including arsenic originating from CCA treatment solutions) from other solid matrices, such as soil. Based on these data, risk analyses of dislodgeable residue should assume that the relative bioavailability of arsenic from this material is no more than 50%, and may be as low as 10%.

- Incorporation of exposure time in exposure calculations. The risk assessment acknowledges that young children are likely to visit a playground only a few days per week and, on those days, will likely spend only a small fraction of their time at the playground, *i.e.*, approximately 1 hour. While the risk calculations quantitatively account for the limited exposure frequency (*i.e.*, the number of days per week when visits occur), the risk calculations do not quantitatively account for the limited exposure time. Instead, the risk calculations inherently assume that a child who contacts a play structure built of CCA-treated wood for a short amount of time (*e.g.*, on the order of minutes) will have equal exposure potential as a child who contacts such a play structure for a longer period of time (*e.g.*, on the order of hours). To better account for this factor, a fractional intake parameter should be applied in the risk calculations. This factor estimates the contribution of a specific exposure source (*e.g.*, the play structure) to overall exposures based on the proportion of the child's waking hours that are spent in contact with the source. In this case, inclusion of such a factor would reduce the exposure and risk estimates presented in the risk assessment by a factor of approximately 4 to 12.

The combined impact of these and other conservative elements is that the risk assessment developed by the CPSC staff provides a misleading perspective regarding the range and significance of the risks associated with the exposure scenario examined in the risk analyses. In particular, if more scientifically sound assumptions are applied for the parameters discussed above, the modified risk estimates and resulting conclusions drawn based on those results are completely changed. Specifically, instead of suggesting that a risk estimate of 2×10^{-6} is likely to represent the low-end of the calculated risk range (as indicated in the CPSC staff report), the modified risk estimates indicate that this value more plausibly represents the high end of the risk range. In addition, if the calculation error in the CSF noted

above were corrected, this high-end estimate would decrease by another factor of two to 1×10^{-6}, the benchmark risk level of interest identified in the CPSC staff report. Moreover, the plausible low end of the risk range is reduced by more than two orders of magnitude to 2×10^{-8}. Even with these modifications, numerous conservative elements remain in this calculation. As a result, risk estimates for this scenario are likely to be less than those suggested by the modified calculations. Thus, instead of suggesting that the risk estimates associated with this exposure scenario almost certainly exceed a risk level of 1×10^{-6} (as indicated in the CPSC staff report), more scientifically-sound risk calculations indicate that the risk estimates for this exposure scenario are highly unlikely to exceed 1×10^{-6}.

Other specific elements of the risk assessment also present concerns. For example, a number of the assumptions applied in the sensitivity analysis inaccurately portray the range of plausible values for the input parameters, yielding misleading results and conclusions drawn based on these results. These inaccurate assumptions include the implausible high-end value assumed for the hand-transfer efficiency (HTE) factor, the elevated values assumed for the high and low end RBA values, and the elevated value assumed for the estimate of the concentration of dislodgeable arsenic on the hands. In addition, the risk assessment documentation fails to place the estimated exposures and risks in context. In particular, the risk assessment neglects to mention that the estimated potential intake of ingested arsenic from treated wood would contribute only modestly to total exposures to arsenic, particularly when lifetime exposures are considered. Moreover, the estimated intake of arsenic from treated wood is less than what is permitted by other regulatory standards established to protect public health, *e.g.*, intake of arsenic from drinking water. Such comparisons are critical to accurately communicate the significance of the staff report's exposure and risk estimates to risk managers and to the public.

Additional detail regarding these comments is provided in the following sections of this document and the associated attachments. Comments regarding exposure assessment issues are presented in Section 2, comments regarding toxicity assessment issues are presented in Section 3, and comments regarding risk characterization issues are presented in Section 4.

2 Comments on Exposure Assessment Issues

This section includes comments on issues discussed in Tabs G, H, and I.

2.1 Validity of Assumed Exposure Scenario

The risk assessment prepared by CPSC staff addresses potential exposures and risks associated with children's contacts with playground structures built of CCA-treated wood. It should be noted that such consumer uses of CCA-treated wood are being voluntarily ended and will be cancelled by the end of 2003. As a result, the average age of the playground structures built of CCA-treated wood to which future exposures may occur will increase over time as, no new structures will be built. As discussed below, available data suggest that the amount of dislodgeable arsenic released *via* direct contact with the surfaces of CCA-treated wood may decrease with age and weathering (Solomon and Warner, 1989; Stilwell, 1998; SCS, 1998, 2001). Thus, the risk estimates derived in the CPSC risk assessment may increasingly overestimate potential future risks as time elapses after consumer uses are cancelled.

The risk assessment prepared by CPSC staff should also provide more detailed information describing the nature of the potentially exposed population examined in the risk assessment and how the scenario evaluated in the risk assessment may overestimate risks for certain segments of the potentially exposed population. For example, as discussed below, the exposure frequency assumed in the risk assessment (*i.e.*, 3 days/week for 52 weeks/year) is likely to overestimate potential exposures and risks in those parts of the country where colder or more inclement weather (*i.e.*, rain or snow) may be prevalent for several months of the year.

2.2 Selection of Specific Exposure Parameters

2.2.1 Bioavailability of Dislodgeable Arsenic

In the risk assessment calculations, CPSC staff assume that arsenic associated with dislodgeable material from CCA-treated wood is as available as arsenic dissolved in water. This assumption fails to recognize substantial evidence indicating that the bioavailability of ingested arsenic from soil or other solid matrices is generally considerably less than bioavailability from food or water (see, *e.g.*, Ruby *et al*., 1999 and Alexander, 2000). Moreover, this approach fails to reflect available bioavailability information

that is specific for dislodgeable arsenic. Because the available toxicity factors for arsenic ingestion are based on exposure to soluble arsenic in water, it is important to accurately determine the relative bioavailability of ingested arsenic in other media to enhance the accuracy of calculated exposures and risks. The critical role of the relative bioavailability adjustment (RBA) factor in risk evaluations has been acknowledged in regulatory guidance issued by EPA and state agencies (*e.g.*, U.S. EPA, 1989; WA Ecology, 1991, 1996; and WVDEP, 1998) and in numerous site-specific analyses.

Substantial available information indicates that the oral absorption of arsenic from material dislodged from CCA-treated wood (dislodgeable arsenic) is reduced relative to the absorption of soluble arsenic. Specifically, the results of two studies of dogs fed sawdust from CCA-treated wood support an RBA value for ingested dislodgeable arsenic of 47% (Peoples, 1976; Peoples and Parker, 1979). Initial results from a more recent study in which hamsters were fed dislodgeable arsenic also 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 (and arsenic in soil affected by CCA-treated wood) have been designed with input from EPA 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.

For example, studies of dislodgeable residue collected from the surface of CCA-treated wood indicate that arsenic comprises only a small fraction of the surface residue, and that the form of arsenic in dislodgeable residue is insoluble in water. On average, arsenic comprised at most 0.2% of dislodgeable residue and approximately 94-100% of the arsenic in this material was insoluble in water (Cui, 2001; Osmose, 2001). Other factors supporting reduced bioavailability of dislodgeable arsenic from CCA-treated wood include the chemistry of the wood treatment process, which is designed to chemically bond arsenic and the other metals within the wood matrix, and toxicology and epidemiology studies indicating few adverse effects that are attributable to arsenic exposure from CCA-treated wood. Additional information regarding these findings is provided in Attachment A.

The reduced bioavailability of arsenic associated with dislodgeable materials is consistent with the results of numerous studies indicating the reduced relative bioavailability of arsenic from a number of solid matrices. Rabbit, monkey, dog, and swine studies published in the peer-reviewed literature have yielded relative bioavailability estimates for arsenic in soil and other matrices ranging from near zero to approximately 50%. Results from two studies of soil from CCA wood treatment sites revealed a similarly reduced relative bioavailability of arsenic. In particular, in a study in which primates were fed soil

collected at a CCA treatment site (Roberts *et al*., 2001), an RBA factor of 16.3% was observed. A study of rats exposed to soil from a CCA-treatment site also indicated a reduced bioavailability of arsenic (Ng and Moore, 1996). By contrast, the oral bioavailability for soluble forms of arsenic reported in *in vivo* studies (*e.g.*, arsenic dissolved in water) is as high as 95%. These factors indicate the need to account for reduced bioavailability when assessing exposures and risks for arsenic associated with CCA-treated wood.

Thus, the available data indicate that the relative bioavailability of dislodgeable arsenic is no more than 50% and may range as low as 10%. CPSC staff should modify their risk calculations to include these more technically-sound assumptions. Additional information regarding these observations and the bioavailability study results discussed above is provided in Attachment A.

2.2.2 Hand-Transfer Efficiency Factor

One of the most important, and least well characterized, aspects of assessing children's potential exposures to arsenic from CCA-treated wood is the exposure pathway whereby dislodgeable residue is removed from on wood surfaces by hand-to-wood contact and is incidentally ingested when the hand contacts the mouth. To quantify potential arsenic intake *via* this exposure pathway, CPSC staff have applied an empirical approach. Most importantly, this type of approach estimates incidental ingestion of dislodgeable material by extrapolating from available data regarding children's incidental ingestion of soil, skin surface areas, and adherence of soil to skin. Thus, intake estimates based on this approach can readily be benchmarked against empirical data, enhancing the likelihood that such estimates are plausible. In addition, in contrast to alternative mechanistic approaches, the empirical approach minimizes the number of poorly characterized parameter estimates that are required to estimate intake *via* this exposure pathway, a factor that also reduces uncertainty in the results obtained using this approach.

While the HTE parameter estimate used in the main risk calculations (0.43) represents a reasonable interpretation of the available data, the range of estimates applied in the sensitivity analysis is not plausible. Specifically, as recognized by CPSC staff in the risk assessment documentation, the high-end estimate of seven for this parameter is highly unlikely. A value this high suggests that a child could incidentally ingest an amount of soil equal to the seven times the total amount on the hand surfaces. CPSC staff suggest that this value could occur for "children who transfer large amounts of soil from their relatively clean hands." The occurrence of this combination of conditions is unlikely. Moreover, when combined with more typical adherence values for dislodgeable materials, such a parameter estimate is

likely to yield highly inflated exposure estimates. In addition, such extensive removal and subsequent complete re-loading of hand surfaces with dislodgeable material is highly unlikely to occur during the more limited periods of time that a child will actually be in contact with the playground structure built of CCA-treated wood. Similarly, available data regarding children's hand-to-mouth contact frequencies suggest that such contacts are more limited when children are engaged in active play outdoors (Freeman *et al*., 2001), the typical type of activity that would be expected during contacts with playground equipment built of treated wood. As a result, an HTE value of this magnitude is highly unlikely to occur and should be eliminated from the sensitivity analysis.

A detailed evaluation of the plausible range of values for this factor was undertaken in another risk assessment of children's potential exposures to arsenic from CCA-treated wood (Gradient, 2001b). This analysis examined the variability and uncertainty inherent in the component parameters used to calculate the HTE factor. Based on this analysis, a reasonable high-end estimate for the HTE was determined to be 1. This value should be used instead of 7 as the high-end estimate in the sensitivity analysis.

2.2.3 Time Spent at Playgrounds

The magnitude of a child's exposures to substances associated with playground structures depends on amount of time during which the child could potentially encounter such structures. One component of the time element influencing exposure is the frequency of the child's visits to a playground. The other critical component is the amount of time that the child spends at the playground in contact with the play structure built of treated wood. The role of time in determining the magnitude of exposures is particularly important when estimating exposures associated with discrete exposure sources, such as structures built of treated wood. Because the area potentially affected by the exposure source (*i.e.*, the treated wood) is relatively localized, the time spent in the vicinity of those localized sources must be correctly accounted for.

For the frequency of visits to a playground, the risk assessment prepared by CPSC staff correctly recognizes that children are unlikely to visit a playground 365 days/year. Instead, based primarily on professional judgment, the CPSC risk analysis assumes that children visit a playground 3 days per week for 52 weeks per year (Midgett, 2003b). This assumption is reasonable for certain parts of the U.S. The analysis also notes that this exposure frequency is likely to range from 2-4 times per week. While the assumption used by CPSC staff is reasonable for this age group, it may overestimate potential exposures

for children residing in northern climates. In such areas, cold or inclement weather is likely to prevent children from visiting playgrounds at a frequency of three days/week for several months of the year.

While the risk assessment prepared by CPSC staff discusses the amount of time that children may spend at playgrounds, the CPSC staff elected to not incorporate this factor quantitatively into the risk calculations. By omitting this factor from the calculations, the risk estimates generated by CPSC staff may overestimate potential exposures and risks by a factor of approximately 4- to 12-fold. Specifically, the CPSC staff documentation notes that the 50th percentile for hours per day spent at a playground for 5 to 11 year olds is 1 hour/day (Midgett, 2003a). Time-activity pattern data indicate that the 90th percentile for time spent at playgrounds for young children is 2.9 hours/day (U.S. EPA, 1997b). As noted above, the primary exposures to the substances associated with treated wood are likely to occur while the child is in the vicinity of the treated wood structures. As a result, it is reasonable to assume that the amount of potential exposure to substances associated with treated wood structures will increase as the amount of time spent in contact with such structures increases (*e.g.*, a child who spends 3 hours playing on a play set constructed of treated wood is likely to have greater exposures than a child who spends 0.5 hours playing on a play set.)

Moreover, the hand-transfer efficiency factor reflects underlying data based on exposures occurring during an entire day (*e.g.*, soil ingestion rates). As a result, when applying such data to estimate exposures associated with localized exposure sources, the magnitude of the potential intake should be adjusted to reflect the likely proportion of the total exposure that is likely to be derived from the localized source of interest. A reasonable approach for estimating the fraction of total intake that may be derived from the localized source is to base the proportion on the relative fraction of time spent in the vicinity of the localized source and at other locations. In this case, the CPSC staff risk assessment should use a fractional intake value that is calculated by dividing the assumed number of hours potentially spent in the vicinity of the localized source by the total number of waking hours. Assuming the 50th percentile value for time spent outdoors at a playground and assuming that children have 12 waking hours per day, a fractional intake value of 0.08 can be calculated (*i.e.*, 1 hour/day divided by 12 hours/day). Using the 90th percentile value for time spent outdoors at a playground, a fractional intake value of 0.25 is calculated (2.9 hours/day divided by 12 hours/day).

Although calculating fractional intake based on relative time spent in various locations may not completely reflect the mechanics of incidental ingestion of dislodgeable material from treated wood structures (*i.e.*, incidental ingestion of material adhering to hands may not occur at a completely

unvarying pace throughout the day), this approach is likely to yield conservative (*i.e.*, health-protective) exposure estimates. In particular, the estimates of time spent in contact with treated wood play sets at a playground are actually based on data reflecting the total amount of time spent at playgrounds by young children. In reality, children at a playground are likely to spend their time at a variety of locations and may spend only a fraction of their total time outdoors actually in contact with a play structure built of treated wood. Thus, this factor would tend to overestimate actual exposures.

In addition, it has been suggested that incidental ingestion of materials adhering to the hands may continue after the child has left the vicinity of the treated wood structure. While this may occur, it is critical to note that once the child has left the vicinity of the treated wood structure, additional re-loading of materials onto the hands will not occur. It has been suggested that clothing which has contacted dislodgeable materials or other subsequently contacted surfaces (*e.g.*, furniture) may serve as repositories for re-loading of hands after a child has left the vicinity of the treated play set. Transfers from such surfaces (particularly textured surfaces such as cloth) are likely to be substantially different and less than those that would occur during contacts with wood surfaces. As a result, such contacts would likely play a negligible role in overall intake. Thus, after leaving the vicinity of the treated wood structure, the amount of material potentially available for incidental ingestion will only decrease over time. Such decreases could occur *via* deliberate removal of materials from hand surfaces (*e.g.*, through hand washing) or incidental removal of materials (*e.g.*, through brushing hands against clothes or other surfaces). These factors would tend to reduce the potential contributions to total exposures of incidental ingestion occurring after the child has left the vicinity of the localized source.

2.2.4 Impact of Aging of Wood on Exposure Concentrations

Due to variability and inconsistencies in the results of the hand loading and wipe studies, CPSC staff have concluded that these data are insufficient to draw conclusions regarding the influence of wood aging on the amount of dislodgeable residue that is potentially available for contact. In particular, CPSC staff have concluded that the data are insufficient to make inferences or to calculate an exposure adjustment factor to estimate the relative concentrations of dislodgeable materials on new *versus* weathered wood. A number of factors support this conclusion including: the small number of structures tested in the study, differences among the structures in age and post-commercial consumer applications, and variability in the amount of dislodgeable arsenic removed from a single structure (in different sample collection events) and from structures of similar age. In addition, all of the studied structures were

located in the Washington, DC area, which represents another limitation when attempting to extrapolate the results of the CPSC study to evaluate potential exposures in other parts of the U.S.

The hand loading and adjusted wipe data used in the risk assessment were collected from eight decks and twelve play structures built of CCA-treated wood. These structures were not built specifically for the study (*i.e.*, the structures were existing prior to the initiation of the study) and most of the structures were in-service at the time of the study. These treated wood structures were mostly uncoated or had been coated 1-2 years prior to the sampling. On average, the tested structures were approximately 7 years old. Thus, the structures that are the source of the data used in the risk assessment prepared by CPSC staff are largely representative of aged wood.

The results of several other hand/wipe studies (*i.e.*, Solomon and Warner, 1989; Stilwell, 1998; SCS 1998, 2001) indicate that the amount of dislodgeable arsenic released *via* direct contact with a CCA-treated wood surface may decrease with age and weathering. These findings suggest, therefore, that the exposure data used by CPSC staff to estimate potential risks to children from dermal contact with existing CCA-treated play structures (and decks) likely represent near high-end exposure levels that may decrease over time as the structures age naturally and the average age of the structures in service increases due to the cessation of new construction.

2.3 Interpretation of Exposure Assessment Study Results

As noted above (and acknowledged by CPSC staff), the exposure assessment study conducted by CPSC has a number of limitations which limit the applicability of the data for risk analyses at this time. Specifically, the CPSC study examined a limited sample of in-service decks and play structures located in the Washington, DC area. The decks varied in age and post-construction treatments that they had received. As a result, the degree to which the data derived from these structures may be representative of exposures in other parts of the country is unknown and it is premature to draw conclusions based on this study. Moreover, as presented in the Briefing Package, the documentation of the quality assurance and quality control procedures applied in developing the study results is incomplete. As a result, a complete evaluation of the validity of the study results is not possible. In addition, a more comprehensive hand and wipe sample study for CCA-treated wood has been designed with input from EPA and other regulatory agencies and is ongoing. When available, the results of this ongoing study should be incorporated into CPSC's risk analyses.

Despite these limitations, however, several results from this study are consistent with results observed in other similar studies. These results include the observation that a conversion factor is necessary to extrapolate hand loadings based on data obtained using wipes to collect dislodgeable material. The magnitude of this factor indicated by the CPSC staff report (*i.e.*, that hand loadings are approximately 5-fold less than the amount of material removed using wipes) is consistent with data from other studies that support examination of this factor. For example, data developed in a side-by-side comparison of hand and wipe results indicate that the amount of arsenic removed by wipes is 3 to 20 times greater than that removed by hands for the same sampled surface (SCS, 1998, 2001). The results from the SCS studies are similar to those observed in pesticide removal studies where removal of surface materials was observed to be 3- to 10-fold greater when a drag-sled or wipe sampling technique is used than when a hand sampling technique is used (Lu and Fenske, 1999; Camann *et al*., 1995; Fenske *et al*., 1990; and Vacarro, 1990, as reported in U.S. EPA, 1999; Gradient, 2001a). In another example of consistent results, the CPSC data suggest that the amount of dislodgeable arsenic removed from a treated wood surface reaches equilibrium with the amount on the wood surface.

Another important observation that CPSC staff made regarding exposure to CCA-treated wood is that the amount of dislodgeable arsenic removed from the wood surface reaches equilibrium with the amount on the wood surface. This observation is consistent with results in an exposure study conducted by the Maine Department of Human Services where it was noted that arsenic loadings on an adult hand did not appear to accumulate to a significant degree with longer durations of rubbing or with rubbing larger surface areas of wood (MEDHS, 1998).

3 Comments on Toxicity Assessment Issues

This section includes comments on issues discussed in Tabs F and I, as well as additional toxicity assessment issues raised during the March 17, 2003 public hearing addressing the CPSC staff briefing package.

3.1 Validity of CSF Estimates for Arsenic Ingestion

The risk assessment prepared by CPSC staff uses a range of carcinogenic slope factors (CSFs) for quantifying the potential risks associated with ingestion of arsenic. The range of values reflects different methodologies used to interpret the available epidemiological data regarding the carcinogenicity of arsenic ingestion. Specific methodological differences include the carcinogenic endpoints considered, the model used to extrapolate results observed at relatively high exposures to predict risks associated with low level exposures, and approaches used to account for background risk levels and arsenic intake from other sources such as food. The numerical CSF values considered by CPSC staff range from 0.41 to 23 $(mg/kg\text{-}day)^{-1}$, spanning almost two orders of magnitude. This considerable numerical range of values reflects the substantial uncertainty inherent in efforts to quantify the carcinogenic risks associated with ingested arsenic and the impacts of alternative modeling approaches on quantitative potency estimates. As discussed below and in Attachment B, however, available data indicate that the high-end CSF used by CPSC staff in their risk calculations (23 $[mg/kg\text{-}day]^{-1}$) is implausible and the remaining range of CSF values considered by CPSC staff represent conservative carcinogenic potency estimates, particularly when applied to evaluate potential risks in U.S. populations with low level arsenic exposures. Based on these evaluations, the high-end CSF of 23 $(mg/kg\text{-}day)^{-1}$ should be eliminated from the risk calculations. Moreover, an apparent error should be corrected in the calculations used to derive other CSF values considered in the CPSC staff analyses. In addition, the conservative elements of the remaining range of CSF values applied in the CPSC staff risk calculations should be acknowledged when interpreting the risk assessment results and making risk management decisions based on those results.

3.1.1 Conservative Elements of Slope Factor Calculations Based on EPA and NRC Analyses

The specific CSF values used by CPSC staff in the risk assessment were derived based on analyses of arsenic toxicity and carcinogenicity conducted by the U.S. Environmental Protection Agency (U.S. EPA, 2001) and the National Research Council (NRC, 1999, 2001) as part of their evaluations of an

appropriate maximum contaminant level (MCL) for arsenic in U.S. drinking water. While neither EPA nor the NRC explicitly published alternative CSF values for arsenic as part of these evaluations, CSF values can be calculated based on risk estimates presented in their reports, *i.e.*, risk summaries presented in the EPA report and maximum likelihood estimates of cancer-related deaths presented in the NRC report. It should be noted, however, that the NRC subcommittee never explicitly endorsed the use of the arsenic unit risk value reflected in its risk analyses. Instead, the subcommittee notes that, in accordance with its charge, it did not conduct a full-scale risk assessment and risk characterization for ingested arsenic. Instead, it provided an evaluation of the potential potency of arsenic intended for use in a "public-health context." The CSF values calculated based on the EPA assessment range between 0.4 and 3.7 $(mg/kg\text{-}day)^{-1}$, while the CSF value calculated based on the NRC report is 23 $(mg/kg\text{-}day)^{-1}$. As noted above, however, review of the CPSC staff calculations suggests that the upper-bound CSF value derived by CPSC staff based on the EPA risk analyses may reflect a calculation error. Correction of this apparent error yields a CSF estimate that is approximately 2-fold lower, *i.e.*, 1.9 $(mg/kg\text{-}day)^{-1}$. This error is discussed in more detail in Attachment B.

Although CPSC staff treat this full range of possible values as equally plausible in their risk analyses, CPSC staff also note "the shortcomings of the available data" when addressing these values (CPSC, 2003). As discussed below and Attachment B, these "shortcomings" in the available data result in substantial uncertainties in all of the CSF values that have been derived for ingested arsenic. Moreover, numerous factors suggest that the available CSFs are likely to overestimate actual risks associated with arsenic ingestion at the low levels typically associated with exposure settings such as contact with arsenic from CCA-treated wood. The high-end CSF derived based on the NRC analysis is particularly uncertain and is inconsistent with available epidemiological evidence.

The primary study used by EPA and the NRC to quantitatively assess cancer risks associated with arsenic ingestion in their evaluations of the MCL is a large-scale study conducted in Southwestern Taiwan in individuals exposed to arsenic in drinking water at levels that ranged from 10–1,752 μg/L (Chen *et al*., 1985; Chen *et al*., 1992; Wu *et al*., 1989). This study, which has been re-analyzed several different times, showed significant associations between arsenic exposure and cancer mortality from lung and bladder cancer, and weaker associations with cancer mortality from liver and kidney tumors. The NRC also used this study to derive a unit risk value for arsenic-induced cancer (*i.e.*, a value indicating the number of excess cases of bladder or lung cancer associated with intake of 1 μg/L of arsenic in drinking water over a 70-year lifetime). The NRC also took into consideration a study by Ferreccio *et al*. (2000). This study examined a South American population exposed to arsenic in drinking water (at concentrations

ranging between 1 and 860 μg/L) and established an association between arsenic exposure and lung cancer.

In general, it is problematic to use these epidemiological studies directly to predict risks posed by arsenic to U.S. populations (Brown *et al*., 1997; Chappell *et al*., 1997; Guo *et al*., 1998). For example, as discussed in more detail in Attachment B, substantial problems exist in identifying the specific arsenic doses that the study participants experienced (Brown *et al*., 1997). Other areas of concern involve defining an appropriate dose-response relationship, assessing the relevance and applicability of studies conducted in the poor agrarian society of the Southwestern Taiwanese for assessing risks to U.S. populations, and uncertainties regarding the shape of the dose-response curve at low doses (Abernathy *et al*., 1999). Moreover, the types of risk levels observed in the Taiwanese and South American study populations have not been observed in comparable studies conducted in U.S. populations. Similarly, no reliable available data indicate potential carcinogenic risks or other diseases associated with the negligible arsenic exposure levels from contacts with structures built of CCA-treated wood (*e.g.*, FPAW, 2002) or with the higher exposures experienced by various worker populations contacting CCA-treated wood (*e.g.*, Budy and Rashad, 1976; Decker *et al*., 2002). If these factors are not considered carefully, extrapolating risks for U.S. populations based on data from current epidemiological studies conducted in Taiwan and South American could overestimate risks for U.S. populations. Such extrapolations are particularly likely to overestimate potential risks associated with arsenic for populations exposed to structures built of CCA-treated wood.

While EPA and the NRC differ significantly in their methodologies for deriving a dose-response relationship for arsenic, certain features that are common to both analyses incorporate conservative assumptions and uncertainties into the evaluation. These conservative elements include the dose-response model assumed to extrapolate carcinogenic risks associated with low level arsenic exposures based on the higher exposure levels experienced in the epidemiological studies used to derive the cancer risk estimates. Specifically, both EPA and the NRC assumed a linear dose-response relationship for arsenic even at low doses (*i.e.*, they assumed that no dose of arsenic is without risk), and excluded non-linear models from their quantitative evaluations of potential CSF values. In fact, significant evidence exists from both genotoxicity and epidemiological studies suggesting that arsenic may contribute to carcinogenesis *via* a threshold mechanism of action and that a sub-linear or non-linear dose-response model may be appropriate for assessing potential risks associated with low dose exposures (U.S. EPA, 1997a; Clewall *et al*., 1999). In addition, there is evidence that low levels of arsenic may have a protective or anti-carcinogenic effect (Snow *et al*., 1999; Romach *et al*., 2000; Pott *et al*., 2001).

In addition, both EPA and the NRC only considered the results of the Taiwanese epidemiological studies when quantifying potential arsenic risks and discounted the results of analyses conducted in arsenic-exposed populations in the U.S. Exposure levels encountered in this study population differ significantly from those that would be expected in U.S. populations. Because toxicological and epidemiological data suggest that the dose-response curve for arsenic carcinogenicity is non-linear, the differences between the exposure levels of the Taiwanese and U.S. populations require particular attention when attempting to extrapolate potential risks for U.S. populations based on the Taiwanese data. Similarly, the EPA and NRC analyses failed to account for the poor nutritional status of the Taiwanese study population in a quantitative fashion and to address how this factor might increase their sensitivity to arsenic toxicity. For example, studies of arsenic-exposed populations in Taiwan and India provide evidence that nutritional deficiencies enhance responsiveness to arsenic (Mazumder *et al*., 1997a; Mazumder *et al*., 1998; Hsueh *et al*., 1997). The effects of these conservative elements mischaracterize the actual potency of arsenic. Moreover, these conservatively derived toxicity values are likely to overestimate risks for U.S. populations where arsenic exposures (*e.g.*, from water and CCA-treated wood) are significantly lower and nutritional status is better. These conservative assumptions are each discussed in more depth in Attachment B.

This conclusion is further supported by results in a number of epidemiology studies in which associations between arsenic exposure and carcinogenic effects were only observed at the higher exposure levels present in the study population. In these studies of Taiwanese, Mongolian, and U.S. populations, the minimum concentrations at which effects were observed ranged from 100-400 μg/L (Chiou *et al*., 2001; Morales *et al*., 2000; Lewis *et al*., 1999; Tucker *et al*., 2001). A fifth study of a Chilean population (Ferreccio *et al*., 2000) alleges effects at arsenic concentrations in drinking water that are less than the MCL for drinking water (10 μg/L); however, as discussed in more detail in Attachment B, this study has serious limitations that preclude its use for quantifying risks, *e.g.*, changing exposure group categories in different analyses. Although the NRC 2001 report acknowledges the limitations of this study, the NRC nevertheless used the study to quantify estimates for the Chilean study population, and to justify performing similar extrapolations based on the Southwestern Taiwanese data. Again, this approach ignores important available data and is likely to lead to overestimates of potential risks associated with low-level arsenic exposures.

As noted above, the EPA and NRC analyses also failed to reflect the results from studies in U.S. populations which suggest that the incidence of cancer in these groups is less than would be predicted

based on the Taiwanese or South American studies (*e.g.*, Lewis *et al*., 1999; Moore *et al*., 2002; Tollestrup *et al*., 2002; Valberg *et al*., 1998; Bates *et al*., 1995; Engel and Smith, 1994; Morton *et al*., 1976). The results from these studies thus present the possibility that no diseases associated with arsenic exposure have occurred at exposure levels typical of U.S. exposures. This finding suggests that the number of cancer cases reduced in the U.S. as the result of reducing any already low level arsenic exposures (*e.g.*, *via* arsenic in drinking water or associated with contacts with CCA-treated wood structures) may be unrecognizably small or nonexistent. The results of this and other studies of U.S. populations are discussed in more detail in Attachment B.

The advantage of analyzing arsenic-induced cancer effects in U.S. populations is apparent. Using results obtained from more relevant study populations avoids the many confounding factors that distort extrapolation of results observed in populations residing in areas of the world that differ significantly from U.S. populations in characteristics such as their nutritional status and other aspects of their lifestyle. Using study populations that have similar diets, a higher standard of living, and are exposed to levels of arsenic that are of current concern in the U.S. will generate a more realistic picture of anticipated risks for U.S. populations. These factors should be considered when selecting a CSF for estimating potential cancer risks and when interpreting the risk estimates derived from using specific CSF values.

3.1.2 Deficiencies in Procedures Used in EPA and NRC Risk Analyses

EPA and the NRC used some of the same information and considerations when estimating the carcinogenic potency of low-level arsenic exposures. In particular, based on policy considerations rather than scientific data, both EPA and NRC limited their quantitative evaluations of potential CSF values to models assuming linear dose-response relationships. As discussed above, however, substantial scientific evidence exists indicating that the dose-response relationship for carcinogenicity of ingested arsenic is non-linear and that use of such models would yield lower risk estimates than generated by linear models. At a minimum, because of the uncertainty regarding the comparison populations, the instability of the model fits, and the relative equivalence in various proposed models fitting the data, the NRC and EPA reports should have considered multiple plausible model forms simultaneously to establish a range of valid dose-response relationships and, therefore, a more comprehensive range of potential doses of concern. Instead, EPA's and NRC's characterization of the range of valid dose-response relationships has been distorted by their focus on thoroughly describing a single functional form, *i.e.*, a linear dose-response relationship.

Other elements of the EPA and NRC analyses differed, with the NRC consistently selecting conservative approaches that yielded the unreasonable inflated estimated of the carcinogenic potency of ingested arsenic of 23 $(mg/kg\text{-}day)^{-1}$. Most importantly, the NRC chose to use an external comparison population (rather than an internal comparison population) for determining likely baseline cancer rates in the study population. This approach distorted calculations of excess cancer risks associated with arsenic exposure. When combined with the linear constraint imposed on the dose-response model, this approach greatly enhanced the steepness of the apparent dose-response relationship between arsenic and cancer mortality. NRC also assumed a lower drinking water intake and a lower intake of arsenic from dietary sources, factors that would decrease estimated arsenic doses and consequently increase the estimated carcinogenic potency of ingested arsenic. These differences indicate that, while the CSF values resulting from the EPA analyses reflect many conservative elements, by comparison with the NRC evaluations the EPA values reflect a more reasonable and scientifically-sound approach than the NRC approach for estimating the carcinogenic potency of ingested arsenic.

Overall, the range of CSFs derived from the analyses of EPA and the NRC differed by a factor of almost 60-fold. This discrepancy is not simply a reflection of any variability or sensitivity in the analysis, but instead represents important and incompatible differences in scientific and mathematical methodologies. CPSC staff expressly state that their rationale for electing to use both analyses is that " both quantitative assessments by the EPA (2001) and the NRC (2001) are reasonable and appropriate." In fact, in light of the substantial uncertainties that exist in quantifying the carcinogenic potency of ingested arsenic, both assessments are likely to overestimate the potential carcinogenic risks associated with low-dose arsenic exposures in the U.S. Moreover, the CPSC staff analysis of the NRC risk evaluation yields a quantitative CSF value that is implausible and reflects numerous flawed assumptions, which should preclude its use in quantifying potential risks associated with typical U.S. exposures to ingested arsenic.

3.1.3 Lack of Evidence of Elevated Cancer Risk in U.S. Epidemiological Studies

Several well-designed epidemiological studies have been conducted in U.S. populations with elevated arsenic exposures; however, in contrast to the Taiwanese studies, results from these studies have been mostly negative (*e.g.*, Lewis *et al.*, 1999). These studies include several recent epidemiological studies of cohorts of U.S. children with elevated childhood arsenic exposures, which also do not show elevated incidence of mortality from bladder or lung cancer or leukemia (Tollestrup *et al.*, 2002; Moore *et al.*, 2002). Table 3-1 summarizes findings from the best available epidemiological studies of U.S. populations with elevated arsenic exposures. Additional information regarding these studies is provided in Attachment B.

Despite the existence of elevated arsenic exposures in these populations, these studies do not show evidence of increased excess bladder, lung, or skin cancer risk associated with arsenic exposures in U.S. populations. These studies provide evidence that ingestion of arsenic in drinking water - at the levels found in the U.S - is unlikely to cause cancer. Concentrations that are considered to be elevated arsenic exposures among U.S. populations are substantially less than those of the Taiwanese and South American populations where excess lifetime bladder, lung, and skin cancer risks have been observed. As a result, these U.S. epidemiological studies support the non-linearity of the arsenic dose-response relationship and are suggestive of a possible threshold for arsenic carcinogenicity. Furthermore, as briefly discussed below and reviewed in more detail in Attachment B, findings from these studies indicate that the use of a CSF based on studies of cancer occurrence (*i.e.*, bladder, lung, and skin) in highly exposed Taiwanese populations is likely to overestimate arsenic-related cancer incidence in the United States.

Table 3-1
Summary of Epidemiological Studies of Cancer Risks in U.S. Populations with Elevated Arsenic Exposures

Study Type	Study Location	Study Population(s)	As Drinking Water Levels (μg/L)	Estimated Daily As Intakes (μg/kg-day)	Key Findings on Cancer Health Effects	Reference
Lifetime/Adult Exposures						
Retrospective Cohort	Millard County, UT	4,058 Adults	Medians ranging from 14 to 166	0.3 to 3.3 (based on median water levels, 1.4 L/day ingestion rate, and 70 kg body weight)	No elevated death rates from bladder or lung cancers have been observed for those who died through November 1996, and death rates show no association with exposure level. For bladder and lung cancers together, the authors observed 39 deaths when 63.5 were expected ($p<0.05$).	Lewis *et al*., 1999
Meta-analysis	Utilized studies of Fallon, NV (Vig *et al*., 1984), Fairbanks, AK (Harrington *et al*., 1978), and Millard County, UT (Southwick *et al*., 1983)	105 for Fallon, 79 for Fairbanks, and 145 for Millard County	100 for Fallon, 76-401 for Fairbanks, and 208 for Millard County	2.9 for Fallon, 1.5-4.6 for Fairbanks, and 6.0 for Millard County	No skin cancers were found in the exposed populations in each study location. This study further examined whether an absence of risk in U.S. populations or random variability from a predicted risk was the more likely explanation for the study findings. Likelihood ratio analysis showed that no effect of arsenic on skin cancer prevalence is about 2.2 times more likely than an effect of arsenic exposure on skin cancer prevalence as predicted by EPA's current arsenic cancer potency factor of 1.5 $(mg/kg/day)^{-1}$.	Valberg *et al*., 1998
Case-control	88 towns in Utah	117 cases, 266 population-based controls	Range of 0.5 to 160, with a mean of 5 (81 out of 88 towns <10 μg/L; 1 town >50 μg/L)	0.01 to 3.2 (based on range of water levels, 1.4 L/day ingestion rate, and 70 kg body weight)	No association found between bladder cancer risk and arsenic exposure for two exposure metrics- total cumulative exposure (<19 up to >53 mg) and intake concentration. Analyses indicated increased bladder cancer risks for smokers, although authors could not rule out possible bias in data.	Bates *et al*., 1995

Study Type	Study Location	Study Population(s)	As Drinking Water Levels (μg/L)	Estimated Daily As Intakes (μg/kg-day)	Key Findings on Cancer Health Effects	Reference
Ecologic	30 U.S. counties with population-weighted mean arsenic levels 5 μg/L or greater	Residents of 30 U.S. counties between 1968-1984	Range of means of 5.4 to 91.5, with 5 counties with mean greater than 20	0.1 to 2 (based on range of water levels, 1.4 L/day ingestion rate, and 70 kg body weight)	The standardized mortality ratios (SMRs) for both all cancers and lung cancers were 1.0 for counties with drinking water levels of 5-10 μg/L, while the SMRs were nearly all less than 1.0 for those with higher drinking water levels (10-91.5 μg/L)	Engel and Smith, 1994
Ecologic	Lane County, Oregon	190,871 total study population	Averages of 16.5 and 4.8 in all rural and urban regions, respectively, with a maximum recorded conc. of 33	Averages of 0.3 and 0.1 for rural and urban regions, respectively (based on average water levels, 1.4 L/day ingestion rate, and 70 kg body weight)	Did not detect any excess risk of skin cancer associated with arsenic exposures up to 33 μg/L (note 19,063 people were exposed at this maximum concentration). Among the 3,237 skin-cancer cases identified in the study, only three had evidence of arsenic keratosis. Based on results, authors concluded that "it seems safe to conclude that our data showed no evidence of water arsenic influence on skin cancer incidence in Lane County over this 14-year period."	Morton *et al.*, 1976
Childhood Exposures						
Ecologic Study	Entire State of Nevada, including Churchill County and Fallon, Nevada, where a recent leukemia cluster has been reported	327,947 children between 0-19 years of age	0-7.8 in low-exposure group, 10-24.6 in medium-exposure group, 35.9-91.5 in high-exposure group	0.9 to 2.4 in high-exposure group (based on 1 L/day ingestion rate, and 38 kg body weight)	No evidence of excess childhood leukemia incidence for even elevated arsenic exposures (~90 μg/L with over 5,500 children at this exposure level). In fact, only 2 cases of leukemia were observed during the study period (1979-1999).	Moore *et al.*, 2002

Study Type	Study Location	Study Population(s)	As Drinking Water Levels (μg/L)	Estimated Daily As Intakes (μg/kg-day)	Key Findings on Cancer Health Effects	Reference
Retrospective Cohort	Ruston, Washington in vicinity of American Smelting and Refining Company (ASARCO) copper smelter	3,132 children residing near smelter between 1907-1932	Not reported in study (note that ambient air exposures are considered to be the primary exposure source)	Not known during 1907-1932 exposure period, although elevated urine As levels observed in 1970s following improvements in smelter processes	Despite extremely elevated childhood As exposures, no elevated incidence of bladder or lung cancer mortality observed in 1,075 deceased members of cohort as of 12/31/90.	Tollestrup *et al.*, 2002

3.1.4 Implausibility of High-end CSF and Inconsistency with Epidemiological Data

The high-end CSF of 23 $(mg/kg\text{-}day)^{-1}$ used by CPSC staff in their risk analyses was not explicitly calculated by NRC (2001) in its analysis of excess lifetime risk of lung and bladder cancer for the U.S. population. CPSC staff estimated this value, however, based on U.S. lung and bladder cancer risks for males and females combined, using the data available in the NRC (2001) report. This value is implausible and inconsistent with the best available epidemiological evidence from U.S. populations.

Most importantly, the results of Lewis *et al*. (1999) and other studies of highly-exposed U.S. populations clearly do not support the presence of an arsenic-induced epidemic in the United States, even among populations with elevated arsenic levels in drinking water. Areas with elevated arsenic exposure levels do not have death rates that stand out from other areas and demand public health concern. If cancer risks associated with arsenic were as high as those predicted using the CPSC staff high-end CSF of 23 $(mg/kg/day)^{-1}$, such risks would have been apparent in a study as well-designed and as large as the Lewis *et al*. (1999) Utah cohort study. Several lines of evidence support this conclusion.

First, a recent peer-reviewed sample size calculation indicates that studies such as the Lewis study of Millard County, Utah, have sufficient power to detect the postulated health risks associated with arsenic exposures if they are indeed as high as those predicted based on observations in the Taiwanese study populations (Frost *et al*., 2002). Specifically, for an arsenic concentration in drinking water of 100 μg/L, Frost *et al*. (2002) demonstrated that a sample size of approximately 1,400 would be sufficient to detect elevated bladder cancer incidence, if the excess risk of bladder cancer was as high as estimated by Morales *et al*. (2000) in their re-analysis of the Taiwanese data that are the basis of the CPSC staff high-end CSF.

Second, the Lewis *et al*., (1999) Utah study cannot be directly compared to the CSF derived by CPSC staff, in part because the CSF is based on data regarding tumor incidence whereas the Lewis study examined tumor mortality. By adjusting the excess tumor rates based on survivorship patterns seen both in Utah and in the total United States, however, the CSF may be transformed into a slope factor reflecting cancer mortality. The lifetime excess cancer mortality risks in the Lewis study may then be evaluated based on this adjusted factor.

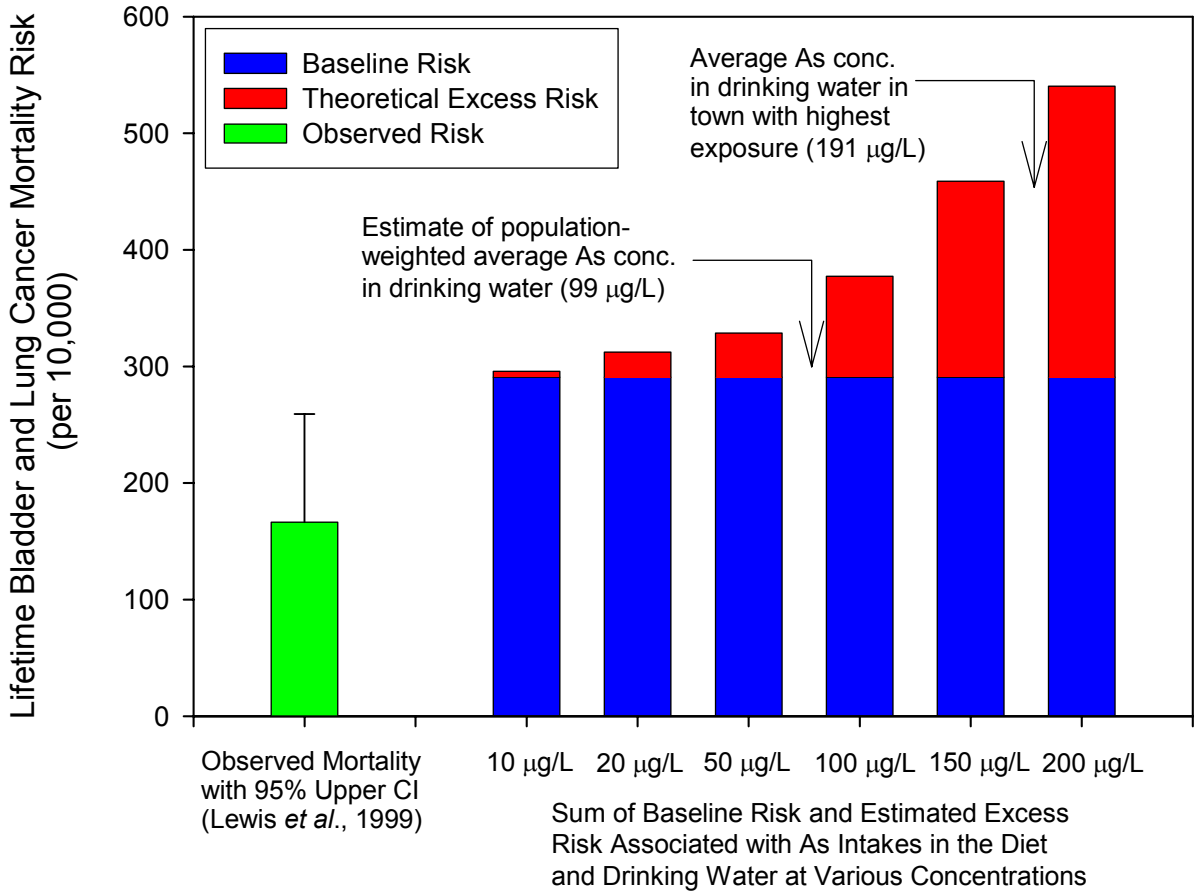
A CSF consistent with the cancer incidence data can be derived by examining the combined excess mortality from both lung and bladder cancer, for both genders. Based on data from U.S. tumor

registries (NCI, 2002), a reasonable estimate of the proportion of all tumors that are fatal is 20% for bladder cancer and 80% for lung cancer. By applying these adjustments to the data in Figure 3-1, an estimate of the slope factor reflecting cancer mortality can be derived (11.3 [mg/kg-day]-1). Additional information regarding the basis for this factor is provided in Attachment B.

This factor can then be used to estimate the excess mortality rates attributable to exposure to arsenic in combination with the baseline lifetime cancer mortality rates. In Utah during the period 1995-1999, these rates were 0.37% for bladder cancer and 2.54% for lung cancer, with a sum of 2.91% (NCI, 2002). This rate is the baseline risk for this combined endpoint in the absence of arsenic exposures.

Figure 3-1 clearly shows that observed bladder and lung cancer mortality risks in the Lewis *et al*. study are significantly less than those predicted by the high-end CSF derived by CPSC staff. The Lewis *et al*. (1999) Utah study followed a cohort of 4,058 individuals exposed to median drinking water arsenic levels that ranged from 14 to 166 μg/L (with average levels ranging from 18 to 191 μg/L). Nearly 1,200 of these individuals resided in the community with the highest median drinking water arsenic level of 166 μg/L. Despite these elevated arsenic concentrations in drinking water, no elevated death rates from bladder or lung cancers were observed for those who died through November 1996 (2,203 cohort members). Moreover, death rates were not elevated among the cohort members with the highest concentrations of arsenic in their drinking water. Both of these findings are inconsistent with the large excess cancer risks that would be predicted using the high-end CSF developed by CPSC staff.

Figure 3-1
Comparison of Observed Bladder and Lung Cancer Mortality Risk with Combined Baseline and Excess Lifetime Mortality Risks Predicted Based on CPSC High-end CSF



The observed mortality risk for combined lung and bladder cancer, averaged across males and females in the cohort, and the two-sided 95% upper confidence limit on this risk estimate (calculated according to the Poisson distribution) are displayed in Figure 3-1. Estimated excess lifetime mortality risks defined by a comparison population of Utah (1995-1999) are presented for a range of water concentrations that span the average concentrations measured in the seven towns included in the Lewis *et al*. study. Arrows indicate relevant exposure levels for the population as a whole (*i.e.*, 99 μg/L, which is an estimate of the population-weighted mean drinking water level) and for the most exposed members of the population (*i.e.*, 191 μg/L, which is the average measured drinking water concentration in the town of Deseret).

For an arsenic concentration in drinking water of 100 μg/L (which is just slightly greater than the estimate of the population-weighted mean drinking water level), the baseline and theoretical predicted excess lifetime bladder cancer mortality risk greatly exceeds the observed mortality rates. This disparity between the observed and estimated cancer mortality risks is even larger for greater exposures to arsenic. Specifically, for an arsenic concentration of 100 μg/L, the predicted cancer mortality risk is approximately 380 deaths per 10,000, more than two times greater than the observed death rate of approximately 170 per 10,000. For an arsenic concentration of 200 μg/L, which is slightly greater than the highest average drinking water concentration measured in the seven towns included in the study (191 μg/L), the predicted cancer mortality risks were more than three times greater than the observed cancer mortality risk based on the Lewis *et al*. findings.

In summary, as demonstrated in Figure 3-1, findings from the Lewis *et al*. study of a Utah cohort are clearly inconsistent with the CPSC staff high-end CSF of 23 $(mg/kg/day)^{-1}$. This high-end CSF is based on studies of a heavily-exposed Taiwanese population where arsenic exposure levels were substantially greater than those of exposed U.S. populations. The observed cancer mortality risks in the Lewis *et al*. study are not only substantially less than those that are predicted using the CPSC staff high-end CSF for the cohort exposures, but they are also less than the baseline cancer mortality risks predicted for the general population of Utah. This finding is observed even with arsenic drinking water concentrations that, on average, were as high as 191 μg/L, and at times exceeded 600 μg/L. These findings indicate the implausibility of such a high CSF for U.S. populations, where even exposures considered to be highly elevated are far less than those of the Taiwanese population that is the basis for the CPSC staff high-end CSF.

Similar conclusions regarding the low likelihood of the CPSC staff high-end CSF can be drawn based on review of available data indicating trends in the incidence of lung and bladder cancer. Specifically, review of such data for the time period 1973-1999 shows no increases in the incidence of these cancer types in males or females under the age of 40 years old (NCI, 2002). During this time period, CCA-treated wood was in use for a variety of purposes (including construction of play structures) and individuals within this age range potentially could have experienced exposures to such structures as children. Instead of observing increases in the incidence rate of these cancers (as might have been expected if arsenic from CCA-treated wood was acting as a significant contributor to such risks), incidence rates for these cancers have been relatively stable or (in the case of lung cancer in males) decreasing over this time period.

These studies indicate that the use of the CPSC staff high-end CSF of 23 $(mg/kg/day)^{-1}$ in arsenic health risk assessments will significantly overestimate cancer risks in U.S. populations, even where elevated arsenic concentrations are present in drinking water supplies. Even under worst-case conditions, children's arsenic exposures associated with contacts with playground structures built of CCA-treated wood will be less than those for populations with elevated arsenic concentrations in their drinking water. Thus, the CPSC staff high-end CSF is also likely to overestimate cancer risks for this population. In summary, the best available scientific evidence does not support the widespread application of the CPSC staff high-end CSF to estimate potential cancer risks for U.S. populations exposed to arsenic *via* ingestion. Moreover, available evidence regarding the non-linearity of the dose-response relationship for carcinogenicity of ingested arsenic indicates that use of the CSF values applied by CPSC staff in their risk analyses is likely to overestimate potential carcinogenic risks for U.S. populations exposed to low levels of arsenic (*e.g.*, such as the levels estimated by CPSC staff to be associated with contacts with structures built of CCA-treated wood).

3.2 Relationship between Arsenic Exposure and Leukemia

At the March 17 public hearing, questions were raised regarding a potential association between arsenic exposures and childhood leukemia. In particular, questions were expressed regarding the potential enhanced susceptibility to arsenic-induced childhood leukemia in children with Down's syndrome and other special needs. No scientific studies to date have specifically addressed this issue; however, some studies have examined the relationship between high dose arsenic exposure and childhood leukemia in children without special needs. Nearly all of these studies have concluded that no association exists between elevated arsenic intake and childhood leukemia. In the following section, available data regarding the potential relationship between arsenic and leukemia are reviewed. Section 3.3 discusses how these results may be relevant for children with Down's syndrome.

Epidemiology studies have not provided credible evidence of an association between arsenic and leukemia. Studies in the Taiwanese study population failed to find a connection between arsenic exposure and leukemia. For example, Chen *et al*. (1985) did not find a significant association between arsenic exposure and leukemia in either males (SMR 142; 95% CI: 100 – 184) or females (SMR 90; 95% CI 53 – 127). In contrast, Chen *et al*. did establish a link between arsenic and cancer of the bladder, kidney, skin, lung, liver and colon. Other investigations of the same population found no dose-response for arsenic levels in drinking water and leukemia (Chen and Wang, 1990; Wu *et al*., 1989). Only one

study of the southwestern Taiwanese population showed a positive association, and that is just barely significant (SMR of 1.34, 95% CI 1.04 – 1.70) (Tsai *et al*., 1999). This study only showed a statistical association for adult males. As a result, the results of this study are of limited, if any, relevance to the question of whether arsenic exposure is associated with childhood leukemia. In additional, Cuzick *et al*. (1992) found no association between arsenic exposure and leukemia in a cohort of 478 patients in England who had been treated with Fowler's solution (potassium arsenite) for up to 12 years (Cuzick *et al*., 1992).

Most recently, Moore *et al*. (2002) investigated the relationship between childhood cancer incidence and arsenic exposure in drinking water in Nevada. The study was prompted by recent concern regarding a leukemia cluster in Churchill County, Nevada, where high arsenic concentrations were found in drinking water. As described above, the study population included all children within the state of Nevada. Key findings included no evidence of excess childhood leukemia incidence for even elevated arsenic exposures (~90 μg/L). In fact, only two cases of leukemia were observed during the study period (1979-1999). The authors concluded that leukemia risks were not increased at the concentrations of arsenic in water found in this study.

Only one study was located that specifically investigated arsenic exposure in association with childhood leukemia. Infante-Rivard *et al*. (2001) reported increased leukemia risk associated with post-natal arsenic exposure (OR 1.39; 95% CI 0.70 – 2.76). This association is not statistically significant, however, because the lower end of the 95% confidence interval is less than one (*i.e.*, the confidence interval included the possibility that arsenic exposure was not associated or was negatively associated with leukemia risk). (It should be noted that the study authors did not report significance levels.) Indeed, the study authors concluded, "Despite some strengths, this study had limited ability to establish clear associations between exposure parameters and leukemia."

In summary, there is no credible evidence that arsenic exposure is a causative factor for leukemia, including childhood leukemia. Most studies found no association between arsenic exposure and leukemia. Only one large-scale epidemiology study demonstrated a statistically significant association between arsenic exposure and leukemia in adults (not children), but this association was weak and of questionable biological significance.

Interestingly, the FDA has recently approved arsenic (in the form of arsenic trioxide) for use in treating acute promyelocytic leukemia (APL). This new drug was remarkably successful during clinical

trials, allowing for a 70% remission rate in previously non-curable APL patients. Due to its effectiveness, the FDA approved it in record time. Potential uses of the drug in treating other types of cancer are also being explored.

3.3 Potential Existence of Subpopulations with Special Susceptibility to Arsenic Toxicity

As noted above, in submittals presented at the March 17 hearing, the question was raised whether arsenic exposure through contact with CCA-treated wood might pose an unreasonable risk to children with special needs, in particular those with Down's Syndrome (DS). DS children are born with genetic alterations that make them susceptible to a multitude of medical conditions, including gastro-intestinal difficulties, diabetes, hypothyroidism, congenital heart difficulties, and leukemia. Throughout their lifetimes, DS patients are especially sensitive to bacterial and viral infections due to an immunosuppressive condition (NIH, 2002). DS children may also be susceptible to endogenous sources in the environment that generate oxidative damage, which can include anything from heavy metals, pesticides, and radiation exposures to certain foods in the diet (Caratelli *et al*., 2001; Jovanovic *et al*., 1998). Increased susceptibility to environmental factors is the result of disruption of normal homeostasis and internal defense mechanisms in DS patients.

As noted above, childhood leukemia (particularly acute lymphoblastic leukemia or ALL) develops in Down's Syndrome children at a higher than normal rate. Approximately 2% of DS children will contract childhood leukemia. This rate is 10-30 times more common than in children without DS (NIH, 2002). ALL is the most common childhood leukemia. Over the past 30 years, incidence rates have averaged about 3 in 100,000/year (NCI, 1999). A significant portion of the diagnosed children will have DS. The relationship between DS and increased susceptibility to ALL is unclear. As with ALL in all children, however, it is thought to stem from a combination of genetic factors and environmental influences (Krajinovic *et al*., 2001).

Post-ionizing radiation and certain types of chemotherapeutic drugs are known environmental agents that will contribute to ALL incidences. Other unconfirmed risk factors that have been suggested include exposure to electromagnetic fields, postnatal infections, and exposure to radon (NCI, 2002; Axelson *et al*., 2002). The associations with any of these agents are tenuous at best, and most studies have been inconclusive. Recent attention has focused on the possibility that maternal exposures to

chemicals during pregnancy will result in the development of ALL during early childhood. In particular, maternal exposure to paternal cigarette smoke results in an increased risk of approximately 1.5-fold (NCI, 2002). No citations have been located in the peer-reviewed literature, however, suggesting an association between ALL and arsenic exposure.

Despite hypothetical assumptions that may be made regarding arsenic exposure and increased risk of leukemia in DS children, as discussed above, epidemiological studies do not support an association. Large epidemiological studies conducted in Taiwan and Argentina show that exposure to arsenic in very high concentrations can result in lung, bladder and skin cancer, but do not indicate any increased incidence of leukemia in children or adults (Chen *et al*., 1985; Ferreccio *et al*., 2000). Moreover, ALL cancer clusters in children in Nevada could not be correlated to increased arsenic intake form drinking water (Moore *et al*., 2002). In all of these studies, arsenic intake was far greater than what would be expected from contact with CCA-treated wood. Thus, there is no credible evidence indicating that susceptibility to ALL in DS children is enhanced by potential exposure to arsenic from CCA-treated wood.

3.4 Evaluation of Potential Enhanced Susceptibility of Children to Arsenic Toxicity

At the March 17, 2003, hearing questions were raised regarding whether children have enhanced sensitivity to potential adverse health effects associated with arsenic exposure. Questions have also been raised regarding whether existing quantitative toxicity values for arsenic are adequately protective for children. EPA's draft *Supplemental Guidance for Assessing Cancer Susceptibility from Early-Life Exposure to Carcinogens* specifically mandates that if chemical-specific information exists indicating that individuals may have enhanced sensitivity to a chemical during early life exposures or that a chemical is mutagenic, this information must be incorporated into risk calculations (U.S. EPA, 2003). As discussed in more detail below, no evidence exists indicating that children are especially sensitive to the health effects associated with arsenic. In addition, arsenic is not a direct-acting mutagen. As a result, special adjustments to standard risk assessment procedures are not required to separately address childhood risks for arsenic. Similarly, no changes are required to the toxicity assessment procedures applied in the CPSC staff risk analyses to address EPA's recently issued draft cancer risk assessment guidance (U.S. EPA, 2003).

At the March 17 hearing, representatives of the Environmental Working Group (EWG) alleged that the results of a recent study in mice (Waalkes *et al*., 2003) indicates that children are more sensitive to the carcinogenic effects of arsenic than was previously thought (Houlihan, 2003). In this study, these researchers exposed pregnant mice to high doses of arsenic in drinking water and then observed the incidence of cancer in the offspring over their lifetime. The offspring were not exposed to any additional arsenic. In fact, EWG's allegation mischaracterizes and distorts the information presented in the Waalkes paper. Moreover, the results of this research are not relevant for assessing early childhood exposures to arsenic associated with playsets built of CCA-treated wood. Specifically, this research does not assess early childhood exposures to arsenic, but instead examines the relationship between transplacental arsenic exposure in mice and delayed tumor incidence during adulthood for the offspring that were exposed *in utero*. While this study has many interesting elements, it is not useful for projecting the possible arsenic-related health effects associated with early childhood exposures. In particular, arsenic-induced changes that may occur in the uterine environment are not relevant for assessing the potential risks associated with childhood exposure scenarios on a playground or on a wood deck.

Several other factors preclude the Waalkes study from being relevant for evaluating the potential health effects associated with childhood exposures to arsenic from CCA-treated wood. First, the arsenic concentrations used in the study are extremely high (*i.e.*, 42.5 mg/L and 85 mg/L). The authors state that the doses used in this study are "50- to 100-fold higher than those thought to potentially pose a significant health risk to humans." In fact, these dose levels are between 4,000 and 8,000 times greater than the current MCL for arsenic in drinking water. Moreover, if a person were to consume 1 L/day of drinking water containing the study dose concentrations, the resulting arsenic intakes (42.5 mg/day and 85 mg/day) would be 30,000-60,000 times greater than the average daily arsenic intake CPSC staff conservatively estimate for children's exposures to arsenic from playsets built of CCA-treated wood (1.4 μg/day). Thus, the dose levels of arsenic used in this study are not indicative of potential exposures that children or pregnant women might experience due to contacts with play structures built of CCA-treated wood.

Second, the types of health effects observed in the study also limit its relevance for assessing potential health effects associated with children's exposures to arsenic from CCA-treated wood. The main findings of the study include dose-related increases in liver and adrenal tumors in male offspring and increased lung and ovarian tumors in female offspring after reaching adulthood. These results are certainly worthy of further exploration and provide an interesting setting for examining the general effects of *in utero* exposures on subsequent offspring health. The fact that bladder and skin tumors were not among the target organs, however, argues against a direct role for arsenic, which has been documented to

increase lung, bladder, and skin tumors (Chen *et al*., 1992). In addition, available data indicate only a very weak association between arsenic exposures and hepatocellar carcinoma (Ferreccio *et al*., 2000; Chen *et al*., 1992). Non-specific tumor incidence may be more indicative of general issues of compromised maternal health and altered homeostasis during pregnancy, especially since such high doses of arsenic were used. Moreover, it should be noted that liver, lung, and, adrenal are lesions that often occur spontaneously in mice bioassays (Eaton and Klaassen, 1996).

While the Waalkes study does not specifically assess relevant arsenic exposure scenarios or doses for children, other studies have addressed these issues. Investigations into this subject indicate that children may, in some circumstances, ingest relatively more arsenic than adults. Once arsenic is ingested, however, arsenic metabolism and distribution does not appear to differ between adults and children.

For example, Kalman *et al*. (1990) saw no age-related differences in urinary arsenic speciation in a U.S. population living in arsenic-contaminated area. Similarly, when Buchet *et al*. (1980) measured arsenic speciation in the urine of children in Belgium, he found that it did not differ from adult levels reported in other studies. Finally, Concha *et al*. (1998) reported mixed results when arsenic metabolites were measured in adults and children in two areas of Argentina with elevated arsenic concentrations in drinking water (*i.e.*, concentrations of approximately 200 μg/L in each village). In one village, with a largely Caucasian population, urinary arsenic speciation did not significantly differ between children and adults. In another similarly exposed village, however, a decreased methylation capacity in children was observed. Inhabitants of this village were indigenous to the area. Thus, age-related differences in arsenic metabolism may be influenced by ethnicity and may be limited to high dose arsenic exposures. Since arsenic toxicokinetics are not significantly different in children and adults in lower dose exposure scenarios, toxic effects (assuming the same dose) would also not be expected to differ. In fact, incidence of skin lesions in several arsenic exposed populations was slightly less in children than adults (Rahman *et al*., 2001; Smith *et al*., 2000) despite higher body burdens in children.

In most risk assessments that have been conducted examining potential exposures to structures built of CCA-treated wood, exposure factors that reflect the sensitivity and special characteristics of children are considered and calculated. Some of these special considerations include reduced body weight, and other factors reflecting differences in children's physical or behavioral characteristics. Also, many of the toxicity factors for arsenic used in such analyses, such as the CSF, are based on studies in which individuals were exposed to arsenic over a lifetime. Thus, this value reflects arsenic exposure during prenatal, childhood, and adult periods. In particular, the studies in Taiwan are an example where

both children and adults were exposed to extremely high levels of arsenic but no increases in leukemia were noted (Chen *et al*., 1985; Chen *et al*., 1992). Although the number of studies that explicitly compare the toxicity of arsenic in adults and children is limited, existing data and analyses of lifetime cancer risk do not indicate a need for additional toxicity uncertainly factors to address child-specific sensitivity.

4 Comments on Risk Characterization Issues

This section includes comments on issues discussed in Tab I.

4.1 Validity of Sensitivity Analysis

In the risk assessment conducted by CPSC staff a deterministic approach was used, in which a single value was selected for each input parameter and was used to generate risk assessment results. To assess the potential influence of various sources of uncertainty and variability in input parameters on the risk assessment results, CPSC staff conducted a focused sensitivity analysis, applying alternative low-end and high-end parameter estimates in the risk algorithms and examining the impacts of the alternative values on the risk assessment results.

CPSC staff correctly determined that currently available data are insufficient to support a meaningful probabilistic risk assessment approach. Instead, the approach selected by CPSC staff for evaluating the influence of variability and uncertainty on the risk assessment results (*i.e.*, a deterministic risk assessment coupled with a focused sensitivity analysis) makes better use of available data. In addition, such an approach provides clearer and more readily interpreted analyses exploring the influence of various sources of uncertainty on the risk assessment results.

Although CPSC staff selected an appropriate framework for evaluating the range of plausible risk assessment results, several deficiencies exist in the way in which their evaluations were documented, implemented, and interpreted. For example, the documentation of the basis for selecting the input parameters applied in the sensitivity analysis is limited in many cases. This documentation should be expanded to provide more detail regarding the basis for the selected range of parameter values and, where available, should provide quantitative information presenting the segment of the underlying complete range of possible values that the selected range is intended to represent (*e.g.*, which percentiles of the complete range that the range applied in the sensitivity analysis corresponds to).

Some of the specific ranges applied in the sensitivity analysis also are implausible or inappropriate. As discussed above, the RBA value applied in the risk assessment conducted by CPSC staff to estimate the relative bioavailability of ingested dislodgeable arsenic (1.0) is overly conservative and fails to reflect substantial available data indicating that absorption of dislodgeable arsenic is likely to

be significantly less than absorption of arsenic dissolved in water. Similarly, the range of potential RBA values applied in the sensitivity analysis (0.2 to 1) is inappropriate. Based on available data, a more reasonable range of values is 0.1 to 0.7 (Gradient, 2001b). As discussed above, the high-end estimate of the hand transfer efficiency factor used in the sensitivity analyses (7) is also implausible and should be replaced by a more reasonable high-end value of 1. Finally, the high-end value for the concentration of dislodgeable arsenic on hands (300 μg/handload) is not supported by the available data. Instead, a high-end value for this parameter of approximately 3-fold less is more plausible and better supported by available data.

By using parameter estimates in the sensitivity analyses that overstate the plausible range of values for the input parameters, the sensitivity analysis approach applied by CPSC staff provides misleading perspectives on the results of the risk assessment. Specifically, when input parameter ranges that are unrealistically high are applied in the sensitivity analysis, the resulting risk estimates are skewed towards unrealistically high values. When compared to the results of the baseline risk assessment, these skewed high-end estimates then suggest that risk estimates could be substantially higher than is likely in light of more careful consideration of available scientific data. This bias is compounded if the relative degree of uncertainty reflected in the ranges selected for the various input parameters is not adequately accounted for when presenting the results of the sensitivity analyses. For example, the CPSC staff analysis notes that behavior corresponding to the high-end HTE (7) is "less likely" and that "CPSC staff has less confidence in the estimate based on the high value of soil ingestion." This lower degree of confidence needs to be retained in discussions of the sensitivity analysis and risk assessment results. By contrast, the presentation of the sensitivity analysis results (e.g., on p. A-4) presents all the results as if they have equal validity. The text and accompanying table should reflect the relative plausibility and likelihood of the various alternative risk estimates that were derived.

4.2 Modifications to Risk Assessment Results

As reflected in these comments, use of more technically sound exposure assumptions and consideration of additional context for carcinogenic risk estimates (including controversies surrounding procedures for quantifying carcinogenic risks associated with ingested arsenic and typical risk levels associated with natural or regulated exposures to arsenic) would substantially alter the perspective on potential adverse health risks presented in the risk analyses prepared by CPSC staff. The risk analyses conducted by CPSC staff suggest that potential risks associated with children's exposures to arsenic

through contact with playground equipment built with CCA-treated wood range from 2×10^{-6} to 1×10^{-4}. This risk assessment presents a misleading perception of likely actual risks for a number of reasons.

First, the high end of this range is largely driven by the unreasonable high-end CSF of 23 $(mg/kg\text{-}day)^{-1}$, which, as demonstrated in detail in these comments, is implausible and inconsistent with available epidemiological evidence in U.S. populations. Simply by eliminating this technically unsupported value from the CPSC staff risk estimates, the high end of the range of risk estimates presented by CPSC staff would be reduced by at least a factor of 6, to 2×10^{-5}. As noted, correction of an apparent error in the CSF calculations conducted by CPSC staff would reduce this estimate by an additional factor of 2, to 1×10^{-5}. Thus, it is clear that this single highly uncertain toxicity value is a primary factor contributing to the misimpression of elevated risks associated with this arsenic exposure source.

Second, these comments have identified numerous highly conservative assumptions that were applied in the CPSC staff risk analyses and have, in many cases, recommended more scientifically-supported modifications to the risk assessment approaches, many of which would alter the quantitative results of the risk analyses. As discussed in more detail in the following section, additional contextual issues also exist which should be considered in conducting the CPSC staff risk analyses and which would influence interpretation of the results. Consideration of these factors would substantially alter the perspective on potential health risks posed by the exposure scenarios addressed in these comments.

Specific modifications to the risk calculations recommended in these comments include adjusting the assumption regarding relative bioavailability of arsenic from ingested dislodgeable residue and by incorporating consideration of the influence of exposure time on exposure estimates. Specifically, the RBA assumption used in the CPSC staff risk analyses (100%) ignores the substantial body of evidence indicating that absorption of ingested arsenic in a variety of solid matrices, including dislodgeable residue from treated wood, is likely to be significantly less than absorption of dissolved arsenic in water. As reviewed in these comments, a more scientifically sound estimate of the relative bioavailability of arsenic from dislodgeable residue is unlikely to exceed 50% and may be as low as 10%. Similarly, the failure of the CPSC staff risk analyses to consider the influence of exposure time on exposures associated with a localized source such as a structure built of treated wood also leads to erroneously elevated exposure and risk estimates. As described in these comments, use of a fractional intake estimate to reflect this factor would reduce exposure estimates by a factor of 4-12 as a conservative estimate. Specifically, a fractional intake estimate of 0.25 reflects the assumption that children spend 2.9 hours/day playing outdoors (the

90th percentile value from a national survey) and that all of this time includes contact with a structure built of treated wood. Using mean data, a fractional intake estimate of 0.08 would reflect the assumption that children spend 1 hour/day playing outdoors in contact with a structure built of treated wood. Modified risk estimates reflecting these three specific quantitative recommendations (*i.e.*, eliminating the unsustainable high-end CSF and modifying the assumptions for the RBA and fractional intake) are summarized in Table 4-1.

Table 4-1
Summary of Modified Risk Estimates

	Unmodified CPSC Staff Risk Estimates	Modified Risk Estimates
Low End[a]	2×10^{-6}	2×10^{-8} to 3×10^{-7}
High End[b]	1×10^{-4}	2×10^{-7} to 2×10^{-6}

Notes:

(a) Low-end CPSC staff estimates assume a CSF of 0.41 (mg/kg-day)$^{-1}$, an RBA of 100%, and no fractional intake factor. Low-end modified risk estimates assume a CSF of 0.41 (mg/kg-day)$^{-1}$, an RBA of 10% or 50%, and a fractional intake factor of 0.08 or 0.25

(b) High-end CPSC staff estimates use a CSF of 23 (mg/kg-day)$^{-1}$, an RBA of 100%, and no fractional intake factor. High-end modified risk estimates assume a CSF of 3.7 (mg/kg-day)$^{-1}$, an RBA of 10% or 50%, and a fractional intake factor of 0.08 or 0.25

As shown in Table 4-1, incorporating only these three recommendations substantially changes the perspective on the range of risks associated with the exposure scenario examined in the risk analyses conducted by CPSC staff. Specifically, instead of suggesting that a risk estimate of 2×10^{-6} is likely to represent the low-end of the calculated risk range, the modified risk estimates indicate that this value more plausibly represents the high end of the risk range. If the apparent CSF calculation error noted above were corrected (*i.e.*, if a CSF value of 1.9 [mg/kg-day]$^{-1}$ were used), this value would be reduced by an additional factor of 2, to 1×10^{-6}. Moreover, the plausible low end of the risk range is reduced by two orders of magnitude to 2×10^{-8}. Even with these modifications, numerous conservative elements remain in this calculation. For example, as discussed above, all of the CSF values for ingested arsenic are likely to overestimate risks for U.S. populations exposed to low levels of arsenic. Similarly, the exposure times used to estimate the fractional intake factor are likely to represent a conservative estimate of the typical amount of time that children spend playing on playground equipment built of treated wood. As a result, risk estimates for this scenario are likely to be less than those suggested by the modified calculations. Thus, instead of suggesting that the risk estimates associated with this exposure scenario

almost certainly exceed a risk level of 1×10^{-6}, more scientifically-sound risk calculations indicate that the risk estimates for this exposure scenario are highly unlikely to exceed 1×10^{-6}.

4.3 Context for Risk Assessment Results

Because arsenic is ubiquitous in the environment from a variety of natural sources, an important part of any risk assessment for arsenic exposures is consideration of the studied exposures in the context of exposures resulting from natural sources (*e.g.*, dietary sources) as well as other regulated sources (*e.g.*, drinking water). As discussed below, consideration of these factors indicates that, even if the arsenic intake estimates generated by CPSC staff are not adjusted to reflect more scientifically-sound assumptions, intake of arsenic associated with children's contact with play sets built of CCA-treated wood is relatively small compared with other exposure sources. As a result, reductions in this exposure source will not significantly influence the magnitude of children's potential overall exposures to arsenic or any associated health risks.

Several studies have estimated the dietary intake of inorganic arsenic by children and adults. In one study, Yost *et al*. (1998) quantified the adult dietary intake of inorganic arsenic using data from the U.S. Food and Drug Administration's (FDA) Total Diet Study (conducted in 1982 to 1990), which surveyed more than 5,000 food types from 100 locations across the U.S. to estimate the typical U.S. diet and total arsenic concentrations in food. These data were combined with data from a 1986 study by the Ontario Ministry of the Environment that measured the percentage of total arsenic consisting of inorganic arsenic in 14 types of food. Based on these data, the typical dietary intake of inorganic arsenic intake was estimated to be 8.3 μg/day for infants, 9.4 μg/day for toddlers, and 14.0 μg/day for adults, respectively.

A later study by Schoof *et al*. (1999a) quantified the adult dietary intake of inorganic arsenic using two other datasets. Data from the U.S. Department of Agriculture's (USDA) Continuing Survey of Food Intake by Individuals (CSFII) for 1989-1992 were used to estimate the type and quantities of foods consumed in the U.S. Arsenic concentration data were obtained from a market basket survey by Schoof *et al*. (1999b), in which 40 food commodities purchased in 4 locations were analyzed for their inorganic and total arsenic content. The food types included in this survey were selected to represent those food sources thought to contribute more than 90% of total dietary arsenic intake. As a result, this survey provided a more extensive characterization of arsenic concentrations in potential dietary sources than the OME survey. Based on these data, the mean dietary inorganic arsenic exposure for an adult was

estimated as 3.2 μg/day, with a median of 2.4 and a 90th percentile of exposure of 6.7 μg/day (Schoof *et al*., 1999a).

The arsenic data generated in the Schoof *et al*. (1999b) market basket study were subsequently applied to estimate children's dietary intake of inorganic arsenic (Yost *et al*., 2002). Combining the market basket data with the FDA estimates of total arsenic intake, the dietary intake of inorganic arsenic was estimated to range from 3.4 to 8.5 μg/day for children and 3.9 to 7.2 μg/day for toddlers. Using a dietary analysis software package, the USDA CSFII data regarding food consumption patterns, and arsenic data from the Schoof market basket survey, dietary inorganic arsenic intake for young children was estimated to have a mean value of 3.2 μg/day and a high-end (99th percentile) value of 9.4 μg/day.

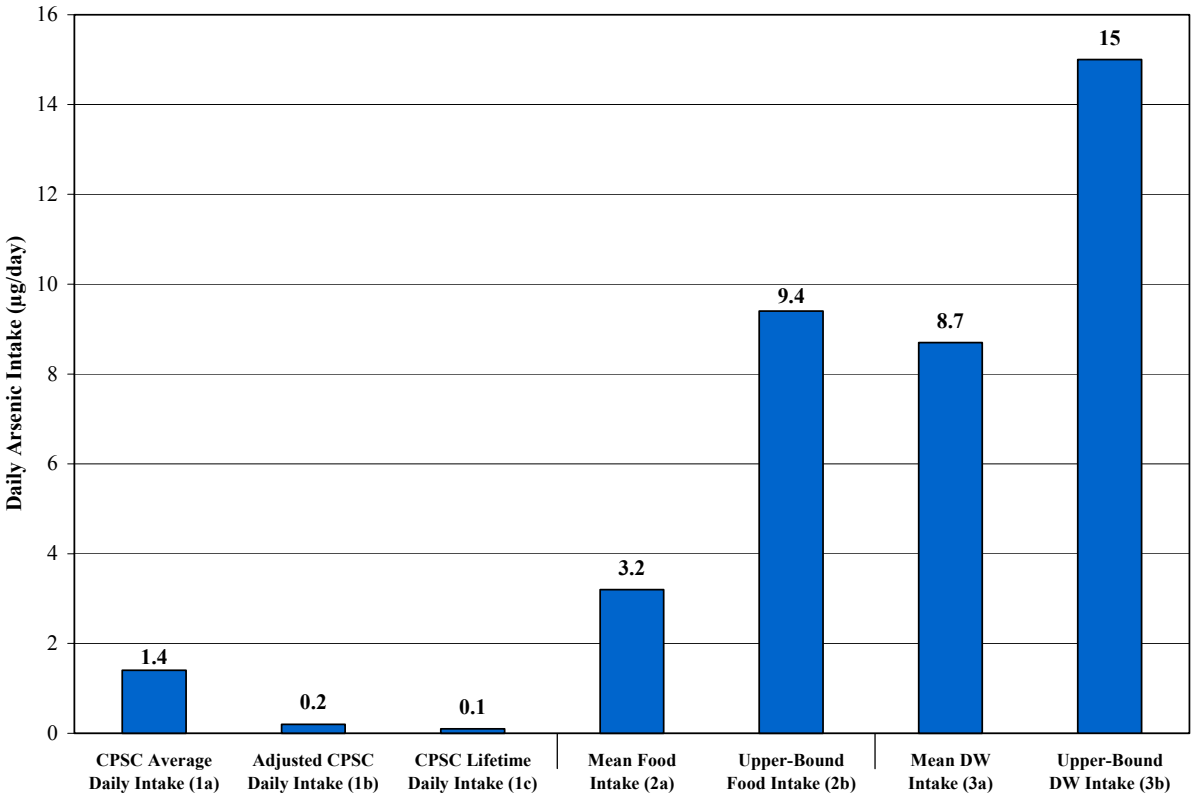
As noted above, another important natural source of exposure to inorganic arsenic is through drinking water. The current MCL for arsenic in drinking water is 10 μg/L, a value established by EPA as protective of public health. Assuming a mean drinking water consumption rate for young children of 0.87 L/day, the arsenic intake for a child consuming water containing arsenic concentrations equal to the allowable MCL concentration would be 8.7 μg/day. Using an RME estimate of drinking water consumption for a young child, the arsenic intake from this source would be 15 μg/day. Although a child's actual arsenic intake will vary depending on the arsenic concentrations present in his water supply, these estimates reflect the arsenic intakes that correspond to the health protective drinking water standard set by EPA.

Figure 4-1 compares the inorganic arsenic intake estimated by CPSC staff for children's exposures to play sets built of treated wood with a modified intake estimate (reflecting conservative application of several recommended changes described in these comment), intake estimates from dietary sources, and intake estimates corresponding to EPA's drinking water standard. As can be seen, inorganic arsenic intake associated with food and water is greater than that estimated by CPSC staff for children's exposures to treated wood. This difference is even more striking if average lifetime exposures are considered, the typical exposure estimate of primary concern when assessing potential carcinogenic health risks. For arsenic intake from dietary sources or drinking water, such intakes will likely continue throughout an individual's lifetime and intake is likely to increase. By contrast, the types of exposures estimated by CPSC staff for small children on treated wood play sets are likely to persist at that level for only a short period of time (approximately 5 years out of a 70-year lifetime). Thus, the lifetime-averaged intake of inorganic arsenic from this source (0.1 μg/day) will be an order of magnitude less than the

annual-average daily intake (1.4 μg/day) and will be approximately a factor of 30 to 100 less than corresponding estimates of intake from food or drinking water. As noted above, the intake estimates calculated by CPSC staff are likely to overestimate children's potential exposures to arsenic from play sets built of treated wood. As a result, these considerations further support the conclusion that arsenic exposures associated with children's contacts with play sets built of treated wood are likely to contribute negligibly to children's overall arsenic exposures. Moreover, these considerations indicate that reductions in children's arsenic exposures from this source are unlikely to substantially influence their overall inorganic arsenic exposures or consequent health risks.

Figure 4-1

Comparison of Daily Intakes of Inorganic Arsenic



Notes:

(1a) CPSC staff average daily intake is calculated by averaging the daily intake (3.3 µg/day) over a one-year period (i.e., daily intake times 156 days/year of exposure divided by 365 days/year).

(1b) Adjusted CPSC staff daily intake reflects application of several of the modifications recommended in these comments (i.e., application of an RBA of 50% and a fractional intake factor of 0.25).

(1c) CPSC staff lifetime daily intake is calculated by averaging the CPSC staff daily intake (3.3 µg/day) over a 70-year lifetime.

(2a) Mean food intake is based on mean dietary intake for a child ages 2-5 years (Yost et al., 2002).

(2b) Upper-bound food intake is based on 99th percentile intake for a child ages 2-5 years (Yost et al., 2002).

(3a) Mean drinking water (DW) intake is based on mean intake estimated for a child ages 3-5 years old (USEPA, 1997b) consuming drinking water containing arsenic concentrations equal to the arsenic MCL of 10µg/L.

(3b) Upper-bound DW intake is based on 90th percentile intake estimated for a child 3-5 years old (USEPA, 1997b) consuming drinking water containing arsenic concentrations equal to the arsenic MCL of 10µg/L.

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