Human Health Risk Evaluation of ACQ-Treated Wood

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ABSTRACT Alkaline copper quaternary (ACQ) Type D is one of several compounds currently being used as a chemical preservative to treat wood for prevention of rot and decay. As wood weathers naturally, human exposure to ACQ might occur through dermal contact or incidental ingestion of residues from the wood surface. To understand any potential for health risks from the use of ACQ- treated wood, a health-based evaluation was undertaken on the primary components of ACQ, which are copper, didecyl dimethyl ammonium carbonate, 2-methyl-4-isothiazolin-3-one, and 5-chloro-2- methyl-4-isothiazolin-3-one. For these components, there are no formalized toxicity values in USEPA's Integrated Risk Information System, although extensive toxicity data are available in the scientific literature. Therefore, health-based toxicity benchmarks were derived from a review of existing toxicity data. The exposure assessment was based on methods developed by the Consumer Product Safety Commission in their evaluation of the potential for children's exposure to arsenic from wood treated with chromated copper arsenate. This approach entailed wipe testing the surface of treated wood to determine the amount of chemical that might be removed from the wood, and estimating the amount of chemical that a child might contact via the dermal route or incidental ingestion through hand-to-mouth activities. All calculated exposure estimates were well below toxicity benchmarks.

Key Words: ACQ treated wood, children, DDAC, MI, MCI, risk assessment.

INTRODUCTION

Numerous chemicals have been used as preservatives to treat wood for prevention of rot and decay. These chemicals include creosote, pentachlorophenol (PCP), and chromated copper arsenate (CCA). Although all of these substances demonstrated efficacy for their intended purpose, each chemical preservative has raised concern about exposure to these substances from use in treated wood, and potential health effects, including cancer. The principal basis for these concerns has been the potential for long-term dermal exposure to, and incidental ingestion of, wood preservative chemicals resulting from children's contact with treated wood on decks and play structures.

Alkaline copper quaternary (ACQ) Type D is one of several pesticide replacements for CCA as a wood preservative. To understand any potential for health risks to consumers from the use of ACQ- treated wood, an extensive hazard evaluation and risk assessment was undertaken and is reported herein. The following topics are addressed:

* Identification of the components of ACQ.

* Review of the inherent toxicity associated with ACQ Type D and individual chemical components.

* Assessment of potential exposure to chemical components from ACQ-treated wood.

* Evaluation of the potential risk presented by human exposure to ACQ-treated wood.

The approach used in this evaluation follows the guidelines outlined by the National Academy of Sciences (1983) and the U.S. Environmental Protection Agency (USEPA 1989) for conducting risk assessments that may be used to inform risk management decisions. In this assessment of ACQ-treated wood, particular attention has been focused on potential exposures associated with the use of products by children, because certain behaviors generally specific to children (e.g., greater hand-to-mouth contact) may subject them to higher exposure levels.

IDENTICATION OF CHEMICALS OF INTEREST

The active ingredients in the ACQ used for this evaluation are copper oxide (CuO), combined with didecyl dimethyl ammonium carbonate (DDA Carbonate) dissolved in a water-based carrier (monoethanolamine). When used in wood treatment, both ingredients form stable complexes with various components of wood, including lignin, cellulose, and hemicellulose, thereby imparting their preservative properties (Brooks 2001). In addition, the ACQ Type D formulation contains a moldicide, consisting of two heterocyclic organic compounds, to inhibit the growth of mold (i.e., 2-methyl-4- isothiazolin-3-one [MI] and 5-chloro-2-methyl-4-isothiazolin-3-one [MCI]). Assuming use of an approximately 1% ACQ treating solution to achieve a 0.25-pounds-per-cubic-foot (pcf) above-ground retention in wood, the composition of ACQ Type D with moldicide is presented in Table 1.

TOXICITY ASSESSMENT

This section presents a summary of the acute toxicity of the neat constituents of ACQ Type D, prior to being applied to lumber, followed by a more detailed review of the acute and chronic toxicity of the constituent components of ACQ Type D, including regulatory levels or benchmark exposure levels for use in assessing potential risks. Because none of the constituents of ACQ Type D are associated with potential carcinogenic effects, the toxicity assessments focus only on non-cancer endpoints of toxicity (i.e., potential carcinogenicity or mutagenicity/genotoxicity are not considered). Subsequent sections of this report combine this toxicity information with estimates of exposure to the constituents of ACQ Type D to assess potential risks from contact with ACQ Type D treated wood.

Toxicity of ACQ Type D with Moldicide

The acute toxicity of ACQ Type D with moldicide was determined in a series of five studies following applicable guidelines from the USEPA Office of Prevention, Pesticides and Toxic Substances. The material evaluated in these tests was the formulated product prior to its application to wood. Once the product is applied to wood, the components are not as readily available for potential exposure (i.e., formation of complexes with the wood, degradation, or evaporation); however, the formulated product was the basis of these tests, to provide a comprehensive database on the product. The magnitude of potential exposures to each component from treated wood was also evaluated, and is discussed in a subsequent section.

The results of the acute toxicity studies of the complete ACQ Type D formulation are summarized in Table 2 and demonstrate that this formulation has low systemic toxicity following oral, dermal, or inhalation exposure. However, at 100% concentration, the neat solution of ACQ Type D is moderately irritating to the skin of rabbits and produces dermal sensitization in guinea pigs following initial exposure to a 25% solution. As discussed later in this review, it is likely that the observed sensitization is due to the MI/MCI component (Springborn Laboratories 2004a-e).

Toxicity Review of Individual Constituents of ACQ Type D Copper

Copper is an active ingredient of ACQ Type D and is also an essential nutrient in the human diet. This section describes why copper is an essential nutrient and includes various regulatory guidelines that have been established for this metal (e.g., Recommended Dietary Allowance [RDA]), along with available toxicological information.

Copper essentiality, typical intakes, dietary requirements, and regulatory levels

Copper is one of a relatively small group of metallic elements that are essential to maintaining human health. Consequently, the human diet must supply regular amounts of copper. A deficiency of copper in the diet can lead to a variety of abnormalities, including anemia, skeletal defects, degeneration of the nervous system (demyelination), reproductive failure, cardiovascular lesions, elevated blood cholesterol, impaired immunity, and defects in the pigmentation and structure of hair. Copper is involved in the process of iron incorporation into hemoglobin and also helps the crosslinking of collagen Fibers, thereby supporting the healing process (IPCS 1998).

Copper is found in many foods in small amounts, and beef/calf liver, shrimp, nuts, avocados, and beans are among the richest sources (Agency for Toxic Substances and Disease Registry [ATSDR] 2004). In the United States, the total daily intake of copper ranges between 0.9 and 2.2 mg for adults, and most studies suggest daily intakes at the lower end of that range. According to the Institute of Medicine (IOM), the median intake of copper from food in the United States is approximately 1.0 to 1.6 mg/day for adult men and women (IOM 2000). Although total daily oral intakes of copper from all sources are generally between 1 and 2 mg/day, they may occasionally exceed 5 mg/day (IPCS 1998). In Table 3 are summarized the established dietary requirements for copper (IOM 2000) and various regulatory criteria for copper (USEPA 2005; ATSDR 2004; ICPS 1998).

Review of Copper Toxicity

Humans

Copper (primarily as $CuSO_4$) is a well-studied chemical for which abundant animal toxicity data exist, as do a somewhat smaller body of human data. Acute copper poisoning in humans is a rare event, primarily restricted to suicide or the accidental drinking of solutions of copper nitrate or copper sulfate, which is used as a fungicide or algicide. Because these and organic copper salts are powerful emetics (vomit inducing) , inadvertent large doses are normally rejected by

vomiting. Chronic copper poisoning is also very rare, and the few reports have typically occurred in patients with existing liver disease. The capacity for healthy human livers to excrete copper is considerable, and it is primarily for this reason that so few cases of chronic copper poisoning have been reported (ATSDR 2004). However, there are a number of reports of acute gastrointestinal effects in humans after ingestion of large amounts of copper, mainly as copper sulfate (CuSO4). Doses between 250 mg and 500 mg can induce vomiting, whereas amounts greater than 25 mg/ L in drinking water can produce gastrointestinal effects (usually immediately after consumption) such as vomiting, diarrhea, and abdominal pain, as well as dizziness and respiratory difficulty. Prolonged consumption can produce hematuria, gastrointestinal bleeding, liver and kidney failure, and death (ATSDR 2004; IPCS 1998). Some of these symptoms have also been reported in individuals who consumed drinking water containing copper at approximately 7.8 mg/L for more than 1 year (Spitalny et al. 1984).

With respect to potential chronic toxicity, although the data are sparse, it appears that, unless doses are excessive, chronic effects following ingestion of copper are rare. For example, following a three-year exposure to copper supplements (30 mg/day for 2 years and 60 mg/day for 21 years), an adult developed jaundice and hepatomegaly (O'Donohue et al. 1993). In contrast, in a small study in seven adults receiving capsules containing 0.14 mg/kg/day of copper gluconate, there were no significant alterations in the activity of serum aspartate aminotransferase, alkaline phosphatase, serum gamma glutamyl transferase, or lactate dehydrogenase (Pratt et al. 1985). This value of 0.14 mg/kg/day (equivalent to 10 mg/day for a 70-kg adult) was selected by the Institute of Medicine as the basis for a tolerable upper intake level (IOM 2000). Similarly, a no-observed-adverse-effect level (NOAEL) for liver effects was identified in infants (3 months of age at study initiation) exposed to copper sulfate in drinking water at 0.315 mg/kg/day for 9 months (Olivares et al. 1998). No alterations were observed in total bilirubin levels or activities of serum alanine aminotranferase, aspartate aminotransferase, or gamma-glutamyl transferase.

Topical exposure to sufficient concentrations of copper or copper salts may induce allergic contact dermatitis in susceptible individuals, producing signs and symptoms that include itching, redness, swelling, and vesicle formation. Patch-testing to identify sensitive individuals generally involved covered, 24- to 48-h contact with 0.5%-5.0% copper sulfate in water or petrolatum. Topical exposure to copper can result from its use in pigments, ornaments, and jewelry. Although copper-containing algicides are used in the treatment of water in swimming pools, there are no reports of toxicity from this application. Although there are numerous reports on the allergic response to unintentional dermal exposure to copper or preparations containing copper, the exposure concentrations and conditions leading to any effect are poorly characterized in most cases (IPCS 1998). For example, routine patch testing of 1,190 eczema patients found that only 13 (1.1%) cross- reacted to 2% copper sulfate in petrolatum (Karlberg et al. 1983).

Rodents

In the rat, the acute oral LD^sub 50^^sup 1^ of copper oxide is 470 mg/kg. Somewhat lower lethal doses have been reported following unconventional routes of exposure such as intraperitoneal injection or intratracheal instillation. The principal target organs from oral exposure to copper are the liver and kidneys. In numerous acute and subchronic animal studies, large oral doses of copper (primarily CuSO^sub 4^) produced hepatotoxicity characterized by

centrilobular necrosis followed by regeneration. For this effect, the NOAEL is approximately 50 mg/kg/day (ATSDR 2004).

Oral exposure of rats via gavage to very large doses (e.g., 100 mg/kg/day as CuSO^sub 4^) in a subchronic (i.e., 90-day) animal study resulted in necrosis of the renal tubules. Even larger doses can cause more extensive degenerative changes in the proximal tubules. For these effects, the acute NOAEL is approximately 50 mg/ kg/day, whereas the lowest-observed-adverse-effect level (LOAEL) for longer-duration exposure is approximately 10 mg/kg/day. There is no evidence from either acute or subchronic animal studies, or from clinical reports in humans who have accidentally ingested copper, of adverse neurological, immune, or developmental effects (ATSDR 2004).

In a subchronic study, copper sulfate was administered for 90 days in the diet of rats and mice at levels up to 138 mg/kg/day in rats and up to 1,000 mg/kg/day in mice. Other than a dose-related reduction in growth, there were no overt signs of toxicity in either rats or mice. Microscopic examination showed hyperplasia and hyperkeratosis in the forestomach in both species, and liver and kidney effects in the rats only (i.e., inflammation of the liver and degeneration of the kidney tubule epithelium). In rats, iron levels were reduced in the spleen, and there were hematological changes indicative of microcytic anemia. The NOAEL was 17 mg/kg/day in rats, and 44 and 126 mg/kg/day in male and female mice, respectively (Hebert et al. 1993).

This assessment used the same NOAEL (0.14 mg/kg/day) that was used by the IOM in setting the tolerable upper intake level (UL). The IOM (2000) selected a target endpoint of liver damage, and based the UL on a NOAEL of 10 mg/day from the human study by Pratt et al. (1985), described earlier. When converted to a body-weight basis, using USEPA's standard body weight for adults of 70 kg (USEPA 1989), this NOAEL is equivalent to 0.14 mg/kg/day (i.e., 10 mg/day / 70 kg = 0.14 mg/kg/day). No uncertainty factor was applied to the toxicity benchmarks.

Review of Didecyl Dimethyl Ammonium Carbonate Toxicity

Didecyl dimethyl ammonium carbonate/bicarbonate (generically called DDA Carbonate; commercially produced as Carboquat(R); CAS Nos. 148788-550/148812651), is a quaternary ammonium compound that is structurally identical to didecyl dimethyl ammonium chloride (DDA Chloride), with a carbonate/bicarbonate anion replacing the chloride anion. DDA Chloride has a long history of use due to its germicidal, fungicidal, and algicidal activity and is formulated into numerous products, including wood preservatives, antiseptics, bactericides, and disinfectants for use in restaurants, dairies, food plants, laundries, and operating rooms. In the ACQ Type D formulation, DDA+ (as carbonate or chloride) functions as a co-biocide for preventing the growth of copper-tolerant fungus and mold. DDA Carbonate has recently been substituted for DDA Chloride to decrease the corrosive nature of the treatment solution to metals in chemical storage and wood treatment equipment that was resulting from the chloride anion in the formulation. In this document, unless specifically noted (i.e., DDA Carbonate), DDAC refers to the chloride. Although most of the available toxicity data are based on testing of the chloride formulation, any associated toxicity is expected to be similar for both compounds, because they similarly dissociate in water, with the cation (i.e., DDA) as the active moiety. DDAC is non-volatile and highly soluble in water, with an octanol/water partition coefficient of close to

zero. Because most of the available toxicity data on DDAC are proprietary in nature, unless otherwise noted, the extensive review by Henderson (1992) and/or a recent USEPA (2006a) document supporting the Re-Registration Eligibility Decision (RED) for DDAC serves as the principal basis for the following summaries of data.

Following oral exposure, [^sup 14^C]-labeled DDAC is poorly absorbed from the gastrointestinal (GI) tract, as demonstrated by the appearance of 89%-99% of radioactivity in the feces, with <2.5% in the urine. In a study of the dermal and GI absorption of [3H]- labeled DDAI,2 the compound did not readily penetrate cell membranes and was poorly absorbed following both routes of exposure (Henderson 1992). The in vitro percutaneous absorption of [^sup 14^C]-labeled DDAC through human skin has also been determined. In this study, [^sup 14^C]-labeled DDAC in either water or a commercial wood preservative formulation was applied to skin membranes at a concentration of 1.85%, which corresponded to a target dose level of DDAC of 185 [mu]g/cm^sup 2^. Less than 0.1% of the [^sup 14^C]- labeled DDAC penetrated human skin when delivered in either water or the wood preservative formulation, whereas total skin absorption (i.e., the amount remaining in the dermis) was reported to be 2.92% and 6.79% of the applied [^sup 14^C]-labeled DDAC in water or the wood preservative formulation, respectively (Roper 2001).

There are a number of reports on both acute oral and dermal toxicity of DDAC. As reviewed by both Henderson (1992) and the USEPA (2006a), acute oral and dermal LD^sub 50^ values for DDAC range from approximately 85 to 400 mg/kg (rats) and 230 to >3,000 mg/kg (rabbits), respectively. One representative set of acute toxicity data is summarized in Table 4. In a primary skin irritation study to intact and abraded skin of rabbits, a single application of technical-grade (50%) DDAC at 0.1% (w/v) caused erythema and edema locally, and in skin around the abraded area after 24 and 72 h. No irritant dermal effects were observed in rabbits following direct skin application of technical-grade DDAC at a concentration of 0.01% (i.e., 0.005% DDAC) (Weeks et al. 1970). In one study in humans and two studies in guinea pigs, DDAC did not induce skin sensitization (Henderson 1992).

There are several subchronic as well as lifetime feeding studies with DDAC, all of which demonstrate low toxicity. In a 90-day subchronic feeding study in male and female mice at doses of 0, 100, 300, 600, 1,000, and 3,000 ppm (corresponding to approximately 20, 60, 120, and 200 mg/kg)^sup 3^ the NOAEL was 600 ppm (107-134 mg/kg/ day) (Henderson 1992). Effects reported at higher doses included decreased body weights, wasting, and gastrointestinal effects. In a 90-day study in male and female Sprague-Dawley rats at similar dose levels (i.e., 0, 100, 300, 600, 1,000, and 3,000 ppm), decreased serum glucose, protein, albumin, and globulin, and increased erythrocyte, hemoglobin, and hematocrit were observed, all in conjunction with general debilitation at the four highest doses; the NOAELs in this study were 61 and 74 mg/kg/day for male and female rats, respectively (Henderson 1992). DDAC was tested for potential toxicity and carcinogenicity in male and female Sprague-Dawley rats following dietary exposure at O, 300, 750, and 1,500 ppm for 104 weeks (equivalent to 13, 32, and 64 mg/kg/day for males and 16, 41, and 83 mg/kg/day for females). Other than body-weight effects, there were no treatment-related effects on clinical signs, survival, clinical pathology, organ weights, or gross anatomic pathology; the NOAELs for toxicity in both sexes were 750 ppm (i.e., 32 and 41 mg/ kg/day, for males and females, respectively) (Gill et al. 1991). The results of this study are

the basis for the Acceptable Daily Intake (ADI) of 0.32 mg/kg/day derived by the British Columbia Ministry of Environment. In another chronic study with male and female mice, DDAC was administered in the feed at doses of 0, 100, 500, or 1,000 ppm (equivalent to approximately 15, 76, and 155 mg/kg/day in males, and 19, 93, and 193 mg/kg/day for females) for 78 weeks. Other than body-weight effects at the highest dose, there were no treatment- related effects. The NOAELs were 76 and 93 mg/kg/day for males and females, respectively (Henderson 1992). DDAC was also tested in male and female Sprague-Dawley rats in a dermal toxicity study at doses of 2, 6, and 12 mg/kg/day for 6 h/day, 5 days/week for 13 weeks. There were no treatment-related effects on clinical signs, food consumption, body weight, hematology, clinical chemistry, and gross or histopathology. Toxicity was limited to dermal effects (i.e., erythema, edema, exfoliation, ulceration) in mid-dose females and the high dose in both sexes (USEPA 2006a). The dermal LOAEL was 6 mg/ kg/day, and the NOAEL was 2 mg/kg/day. In a 21-day rat dermal toxicity study 100% pure DDAC was applied directly to the skin of CD rats at doses of 100, 500, and 1000 mg/kg/day with occlusion. There were no skin irritation or treatment-related effects other than a reduction in hind-limb grip strength in females at 500 mg/kg/day; the systemic NOAEL in this study was 1000 mg/kg/day (USEPA 2006a).

A second 21-day rat dermal toxicity study with DDAC evaluated by the New York State Department of Environmental Conservation (NYSDEC 2003) reported a NOAEL of 1.3 mg/kg/day. It was noted by the NYSDEC that the experimental exposure conditions of these dermal toxicity tests (e.g., occlusion by bandages) are likely to be more intensive than the type of contact that would occur with products containing DDAC. In this dermal toxicity research using animals, dose was typically expressed in units of mass/time (i.e., mg/kg/day). For assessing the irritation or sensitization potential of DDAC, it is more appropriate to express dose in units of mass/skin surface area (i.e., [mu]g/cm^sup 2^). In order to do this, the NYSDEC made some assumptions to "convert" between these two expressions of dose, yielding a skin loading rate of 7.8 [mu]g/cm^sup 2^ associated with the NOAEL identified earlier. However, a more recent study provides data that require no assumptions for converting doses from mg/kg/ day to [mu]g/cm^sup 2^. Specifically, research with DDA Carbonate examined skin irritation in the rat following repeated cutaneous dosing over five days per week for three consecutive weeks. The dosing regimen was designed to evaluate skin irritation at dose rates based on a [mu]g/cm^sup 2^ of skin basis, rather than mg/kg/ day. This approach provides data for direct comparison to dislodgeable residue data for DDA Carbonate from treated wood. Rats were dermally dosed with DDA Carbonate at concentrations ranging from 0.1% to 0.5% at a dose rate of 10 [mu]L/cm^sup 2^ of skin. The NOAEL for this study was 10 [mu]g DDA Carbonate/cm^sup 2^ of skin (Van Miller 2006, pers. comm.). This NOAEL is consistent with the value of 7.8 [mu]g/cm^sup 2^ inferred by NYSDEC (2003).

Finally, DDAC was also tested in a one-year oral dosing study in male and female beagle dogs at doses of O, 3, 10, and 20 mg/kg/day. Other than significantly decreased cholesterol levels in females at 20 mg/kg/day, there were no other treatmentrelated effects; the NOAEL for both males and females was 10 mg/kg/day (NYSDEC 2003; USEPA 2006a). Using the NOAEL of 10 mg/kg/day from this study, the USEPA Office of Pesticide Programs established a reference dose (RfD) of 0.1 mg/kg/day (USEPA 2000, 2006b), although this RfD has not yet been included in USEPA's Integrated Risk Information System [IRIS].

Potential teratogenicity and reproductive effects following exposure to DDAC have also been studied. In a developmental toxicity study in pregnant New Zealand white rabbits, DDAC was administered by gavage at doses of 0,1,3, and 10 mg/kg/day on gestational days (GDs) 6-18. Maternal toxicity was reported at the two highest doses, and fetal mortality and reduced body weight at the highest dose; no teratogenic effects were observed at any dose. The NOAELs for maternal toxicity and developmental toxicity were 1 mg/kg/day and 3 mg/kg/day, respectively (USEPA 2006a). In another developmental toxicity study with pregnant Sprague-Dawley rats, DDAC was administered by gavage on GDs 6-15 at doses of 0,1,10, or 20 mg/kg/ day. Maternal toxicity was evident at doses of 10 and 20 mg/kg/day, whereas developmental toxicity, in the form of increased incidence of skeletal variations, was observed at the highest dose level. The NOAELs for maternal toxicity and developmental toxicity were 1 mg/ kg/day and 10 mg/kg/day, respectively (USEPA 2006a). In a two- generation study with male and female Sprague-Dawley rats (FO), dietary levels of DDAC at O, 300, 750, and 1,500 ppm were administered for 10 weeks prior to mating. Continuous dietary exposure to DDAC for two generations resulted in no adverse reproductive effects. The only parental toxicity noted was decreased food consumption and resulting decreased body weight at 1,500 ppm (approximately 112 mg/kg/day). The same dose also reduced body weight in offspring. The NOAEL for both adults and offspring was 750 ppm (56 mg/kg/day), demonstrating no effects in the absence of overt adult toxicity (USEPA 2006a).

The totality of the data, including several long-term toxicity, and reproduction and developmental studies indicate that, depending on dose and route of administration, DDAC has low toxicity. Because it is poorly absorbed and rapidly excreted, the major endpoint of toxicity following exposure appears to be skin and eye irritation.

For oral exposures, this assessment used the same NOAEL-10 mg/kg/ day-that was selected by the USEPA Office of Pesticide Programs in establishing their RfD, as described earlier (USEPA 2000), as well as the NOAEL used in support of the chronic RfD for DDAC in the RED (USEPA 2006b). No uncertainty factor was applied to the toxicity benchmark. For dermal exposures, this assessment used the same value, 8 [mu]g/cm^sup 2^, as was selected in USEPA's draft risk assessment of DDAC (USEPA 2006b).

Review of 2-Methyl-4-isothiazolin-3-one and 5-Chloro-2-methji-4- isothiazolin-3-one Toxicity

MI/MCI has been evaluated extensively and critically by the Cosmetic Ingredient Review (CIR 1992) in the Final Report on the Safety Assessment of Methylisothiazolinone and Methylchloroisothiazolinone. In addition, the USEPA (1998) completed its reregistration eligibility review and decisions on methylisothiazolinone, which includes both MI and MCI. The Reregistration Eligibility Decision (RED) contains the Agency's evaluation of the database of these chemicals and its conclusions pertaining to potential human health risks of various product uses, including its use in treating wood. The following summary of relevant data is excerpted from the two aforementioned documents.

MI and MCI are broad-spectrum microbial biocides that are used as preservatives in cosmetics, moldicides for leather and fabric, antibiofoulants and slimicides for cooling towers and swimming pools, and preservatives for cutting fluids. The formulation most commonly used

contains MI/MCI at a 3:1 ratio and is also the formulation used in all toxicity studies (CIR 1992; USEPA 1998). FDA has also approved the use of MI/MCI as an antimicrobial agent for polymer latex emulsions in adhesives and in paper coatings that contact food, at a concentration not to exceed 50 ppm. MI/MCI is typically used in cosmetics at concentrations ranging from 0.02% to 0.1% (3-15 ppm [0.003%-0.0015% active ingredients]) (CIR 1992).

MI/MCI is well absorbed following oral administration to rats, with rapid elimination in the urine and feces. The majority (39%- 62%) of a single dermal dose of [^sup 14^C] MI/MCI was associated with the skin at the site of application 24 h following exposure. Elimination of the ^sup 14^C radioactivity from the site of application showed a half-life of 13.1 days, which was suggested as due to the normal desquamation of dermal epithelial cells. Following dermal application of 100 ppm of [^sup 14^C]-labeled MI/MCI for three consecutive days, no radioactivity was detected in the blood of rabbits (CIR 1992).

Acute toxicity studies demonstrated oral LD^sub 50^ values of 45- 64 mg/kg and 40-105 mg/kg in female and male rats, and 30 mg/kg in female rabbits. Following dermal exposure, LD^sub 50^ values ranged from 4.5 to 94 mg/kg in abraded skin, and 112 to 200 mg/kg in intact skin. MI/MCI was corrosive in a rabbit eye irritation test, was severely irritating in a rabbit dermal irritation study, and was a sensitizer in a guinea pig dermal sensitization study (USEPA 1998). One representative set of acute toxicity data is summarized in Table 5.

MI/MCI has been tested extensively for dermal irritation and sensitization potential in humans. For irritation, this endpoint is dose dependent, with 400-800 ppm strongly irritating, 200 ppm slightly irritating, and 100 ppm nonirritating. Numerous studies in human volunteers have investigated the sensitization potential of MI/ MCI (CIR 1992). Although there is general agreement that MI/MCI is a skin sensitizer, the concentrations in cosmetic products that produce this effect appear to vary depending on whether MI/MCI is formulated into "rinse-off" products (e.g., shampoos, skin- cleansing preparations) or "leave-on" products (e.g., body lotions, suntan preparations). It is currently recommended that MI/MCI can be used safely, with no risk of skin sensitization, at concentrations not to exceed 15 ppm and 7.5 ppm in "rinse-off" and "leave-on" products, respectively (CIR 1992). In a subacute toxicity study, after two weeks of oral exposure, no treatment-related effects were observed in rats at doses of MI/MCI up to 24 mg/kg/day. Similarly, subchronic dietary exposure of rats and dogs for three months revealed no treatmentrelated effects of MI/MCI at doses of 30 and 28 mg/kg/day, respectively.

In a subchronic study, Sprague-Dawley rats were exposed to MI/ MCI via drinking water at dose levels of 25,75, or 225 ppm (equivalent to 2.4,6.3, or 16.3 mg/kg/day in males and 4.1,10.8, or 24.7 mg/kg/day in females) for three months. Although there were some decreases in body weight, body-weight gain, and food consumption during the first few weeks, none of these effects were permanent. With respect to clinical chemistry, there was a significant decrease in total protein in males and serum glutamic oxaloacetic transaminase (SCOT) in females at the highest dose, whereas relative liver and kidney weights were also increased in both sexes at the highest dose. These changes were considered to be lexicologically insignificant (USEPA 1998).

The NOAEL was 6.3 mg/kg/day for males and 10.8 mg/kg/day for females, whereas the LOAEL was 16.3 mg/kg/day in males and 24.7 mg/ kg/day in females, based on microscopic findings in

the stomach in both sexes. The corrosive properties of MI/MCI imposed limitations on the dose levels that could be tested for any duration (USEPA 1998). Similarly, subchronic dietary exposure of rats and dogs for three months revealed no treatment-related effects of MI/MCI at doses of 30 and 28 mg/kg/day, respectively (CIR 1992).

In a subchronic inhalation study, male and female Sprague-Dawley rats were exposed to MI/MCI at dose levels of 0.34,1.15, or 2.64 mg/ m^sup 3^ for 90 days. This resulted in decreased body weight in the high-dose males and decreased body-weight gains in both sexes at the high-dose level. There were no treatment-related deaths, and no treatment-related effects on hematology, clinical chemistry, ophthalmoscopic, or gross pathology parameters monitored. Treatment- related lesions in the nasal turbinate were observed at the mid- and high-dose levels, consisting of eosinophilic droplets in the respiratory mucosa at the highest dose and rhinitis in the lining of the nasal cavity at the mid-level and high doses. These findings were consistent with a normal physiological response to a respiratory irritant. The NOAEL was 0.34 mg/m^sup 3^ (i.e., 0.34 [mu]g/L), and the LOAEL was 1.15 [mu]g/L, based on microscopic lesions in the nasal mucosa (USEPA 1998).

Several teratogenicity and reproductive toxicity studies have been conducted on MI/MCI and are reviewed in CIR (1992) and the USEPA (1998). In pregnant Dutch belted rabbits exposed by gavage on GDs 6-18 to doses of O, 1.5, 4.4, and 13.3 mg/kg/day, MI/MCI was maternally toxic at all doses (i.e., 5/15, 12/15, and 14/15 deaths at the low, middle, and high doses, respectively). While maternal toxicity was also reflected in decreased numbers of live fetuses and increased resorptions and postimplantation losses, there was no indication of teratogenic effects at any dose level. In pregnant Sprague-Dawley rats exposed on GDs 5-15 to MI/MCI doses of 1.5, 4.5, and 15 mg/kg/day, there was also maternal toxicity, but no treatment- related effects on any reproductive parameters, including no teratogenic effects. Finally, in a drinking-water study, Charles River rats were exposed to MI/MCI doses of 0, 3, 8, and 20 mg/kg/ day for 15 weeks and then mated. No adverse effects on fertility, reproduction, fetal survival, or fetal health were noted (CIR 1992).

In a developmental toxicity study, pregnant New Zealand white rabbits were exposed via the diet to MI/MCI at dose levels of 0.5,2,8, or 20 mg/kg/day on GDs 7-19. All animals dosed at 20 mg/kg/ day died during the study; scant or no feces, diarrhea, and decreased body-weight gain were observed at the 8 mg/kg/day dose level. The numbers of implantations, live fetuses, resorptions, dead implants, and dead fetuses per dose were comparable among the groups, and fetal body weight was comparable among the groups. The maternal toxicity NOAEL was 2 mg/kg/day; the maternal toxicity LOAEL was 8 mg/kg/day, based on decreased body-weight gain, and scant or no feces and diarrhea. The developmental toxicity NOAEL was 2 mg/kg/ day, whereas the developmental toxicity LOAEL was 8 mg/kg/day, based on the slight increase in fetal alterations (USERA 1998).

In another study, pregnant Sprague-Dawley rats were exposed to MI/ MCI via gavage on GDs 6-15 at dose levels of 0,10,30, or 100 mg/kg/ day. There was a doserelated decrease in maternal body-weight gain during treatment, and a dose-related increase in maternal death. There were no effects on pregnancy rate, numbers of corpora lutea, implantations, resorptions, and/or live fetuses; pup weights, sex ratios, and crown-rump length were comparable among the groups. MI/

MCI was not fetotoxic, embryotoxic, or teratogenic in rats. The maternal toxicity NOAEL was 10 mg/kg/day; the maternal LOAEL was 30 mg/kg/day, based on decreased bodyweight gains; the NOAEL for developmental toxicity was 100 mg/kg/day, the highest dose tested (USEPA 1998).

For oral exposures to MI/MCI, this assessment selected a NOAEL of 2 mg/kg/day, which was the lowest NOAEL observed in any of the subchronic toxicity studies reviewed. This value was also the lowest reported NOAEL for both maternal and developmental toxicity in the USERA (1998) RED for MI/MCI. No uncertainty factors were applied to the toxicity benchmarks, as discussed in the risk assessment results section. For dermal exposures, the allowable limit for leave-on cosmetics of 7.5 ppm (CIR 1992) was used, which was converted to an allowable skin loading value based on the use of lotion at 2 mg lotion per cm^sup 2^ of skin, as specified by the FDA as the appropriate application rate in testing of skin creams (21 CFR Parts 310, 352, 700, and 740). This yields a benchmark value of 0.015 [mu]g/cm^sup 2^, based on the following equation:

Skin loading benchmark value ([mu]g/cm^sup 2^)

= 7.5 mg MI-MCI/kg lotion x 2 mg lotion/cm^sup 2^ skin x 10^sup -6^ kg/mg x 10^sup 3^ Mg/mg

USEPA Assessment of MI/MCI

USEPA reviewed the mammalian toxicology data and characterized MI/ MCI (at 14% active ingredients) as "highly to very highly toxic, especially corrosive, by acute routes of exposure" (USEPA 1998). They cited findings from subchronic oral and inhalation dosing studies in rats that the most significant lexicological effect was microscopic lesions in the nasal turbinates from inhalation exposure with a NOAEL of 0.34 [mu]g/L. This response is common in the presence of respiratory irritants. In the absence of frank maternal toxicity, no significant effects were noted in developmental studies (USEPA 1998). This report also stated that the most appropriate lexicological endpoint for assessing the risk associated with short- and intermediateterm occupational exposures to MI/MCI is the aforementioned respiratory effect, although the risks to most workers are negligible, and workplace precautions can mitigate any risk of corrosivity from short-term exposures. The report also concluded that potential risks associated with other exposure scenarios, such as secondary occupational, residential, and post- application (e.g., from use of MI/MCI in wood treatment applications, such as those evaluated herein) would be less than that of the primary occupational exposures evaluated, and therefore below any level of concern (USEPA 1998).

Based on the NOAEL of 0.00034 mg/L (0.049 mg/kg/day) from the 90- day inhalation study for MI/MCI, USEPA characterized the intermediate-term risks by a margin-of-exposure (MOE) approach (i.e., the ratio of the NOAEL to an exposure estimate). For the residential scenario, exposure was assumed to occur indoors associated with using one gallon of MI/MCI-containing paint per day, with 0.143 [mu]g/day of MI/MCI inhaled, for an actual daily exposure of 2 x 10^sup -6^ mg/kg/day, which resulted in an MOE of ~25,000. (Regulatory agencies generally assume that an MOE of 100 is adequate to ensure reasonable certainty that the toxic effect will

not occur in exposed populations.)

Because both MCI and MI are quite volatile (i.e., the vapor pressures of MCI and MI are 1.8 x 10^sup -2^ torr and 6.2 x 10^sup -4^ torr, respectively), the inhaled indoor air concentration associated with use in paint would overestimate potential concentrations from outdoor uses of MI/MCI and its presence on a product such as treated lumber, with the resulting MOE from exposure to treated lumber therefore being greater than 25,000.

EXPOSURE ASSESSMENT

An exposure assessment includes identifying human populations that could potentially come into contact with the chemicals of interest, and the magnitude, frequency, duration, and routes of potential exposure. This section includes a description of the exposure scenarios and pathways, calculation of exposure-point concentrations, and determination of input parameters for the quantitative calculation of exposure.

The methods used in this exposure assessment are based on those developed by the U.S. Consumer Products Safety Commission (CPSC) in their evaluation of the potential for children's exposure to arsenic from CCA-treated wood (CPSC 2003). Conceptually, the approach used by the CPSC is to conduct wipe testing of the surface of treated wood to determine the amount of chemical that might be removed from the wood. The mass removed from wood is then converted into a skin loading onto hands, and the associated ingestion that might occur from subsequent hand-to-mouth activity. This approach was selected because it specifically assesses the potential exposures that might be incurred from a similar product (e.g., treated wood) and to the same target population of interest (i.e., children). The methodology developed by the CPSC focuses specifically on assessing potential exposures incurred by children. This population was targeted because of the likelihood of possible contact during play on structures constructed of treated wood, and because of behaviors (e.g., increased hand-to-mouth contact) that potentially result in elevated exposures of children, compared to those experienced by adults under normal use of treated wood. As part of their efforts, CPSC staff conducted numerous scientific studies to measure removal of residues from wood onto wipes or hands, and characterized exposure parameters to assess children's exposure from treated wood products. This approach incorporates several conservative assumptions that may result in calculated estimates of exposure that are higher than actual exposures, as discussed in the following section. However, the CPSC approach provides a useful documented framework for exposure evaluation for preserved-wood products.

Exposure Scenario and Pathways

Children might be exposed to ACQ from treated wood in residential decks and playsets as dislodgeable wood residues dirough incidental ingestion or dermal contact (Figure 1). Exposures via inhalation are expected to be insignificant because of the outdoor nature of product use and the low potential for long-term volatilization of components from wood. Intake via incidental ingestion could occur if a child's hand is "loaded" with chemicals from dislodgeable residues on treated wood, and the child ingests some of this residue through typical hand-to-mouth behavior. Exposure via the dermal route could potentially occur through direct skin contact with residues

from a treated wood surface.

Chemical-specific information, such as physical properties and endpoints of toxicity, are also considered, to determine which exposure pathways are relevant for each of these chemicals. For all chemical components of ACQ-treated wood that are evaluated in this assessment, potential ingestion exposures are calculated, because this is the predominant exposure pathway dictated by the CPSC paradigm for pressure-treated wood. In addition to ingestion exposures, the potential for dermal effects is also evaluated for DDA Carbonate and MI/MCI because of the relevance of these toxicity endpoints, as described earlier in the discussion of toxicity. For copper, however, exposures via dermal absorption were not quantified in this evaluation because of the low dermal penetration rate for this chemical. Specifically, the guidance regarding dermal absorption of chemicals (USEPA 2004), provides a comparison of default residential exposures (for copper in water), which shows that copper exposures via dermal absorption would be < 1 % of exposures via the oral route. The guidance determined that the dermal route would be insignificant and could be eliminated from consideration, because it would not be expected to contribute at least 10% of the exposures derived from the oral pathway. Thus, this assessment eliminated dermal exposures to copper from further consideration and focused on oral exposures associated with inadvertent ingestion.

Exposure Concentrations

Wood wipe sampling

To determine the amounts of chemicals that might be present in dislodgeable residues, wipe samples were collected from the surface of ACQ-treated wood in two separate studies. In the first study, the wood samples were provided by Georgia-Pacific (GP), and came directly from a GP facility where they had been treated with ACQ Type D with MI/MCI moldicide to a standard retention of 0.25 lb/ ft3. No sealants were applied, and wipe samples were taken 12 days after the wood had been treated. The sampling procedures followed the CPSC approach for surface testing.

In general, this procedure involves placing a dry polyester wipe on an 8- x 8-cm steel block weighing 1.1 kg, and pulling the block back and forth across a 40-cm length of board for a total of 20 passes. During the 20 passes, the block is slowly steered within a 12.5- x 40-cm rectangle, yielding a total sampling area of approximately 480 cm^sup 2^. All wipe testing was conducted at the Centre for Toxicology at the University of Guelph, Ontario. Analyses of wipes for DDA Carbonate and MI/MCI were conducted at the Centre for Toxicology at Guelph. For copper, the wipes were sent to Columbia Analytical Services, in Kelso, Washington, USA, for analysis. Results are presented in Table 6. Two boards were each sampled in four locations (top-right, top-left, bottom-right, and bottom-left) in this evaluation. Additionally, for comparison, two samples were taken from a board that had not been treated with any preservative. The amounts of chemical present on the surface of the wood samples (expressed as micrograms [[mu]g] of chemical per wipe) are summarized in Table 6.

A second study was designed to determine how dislodgeable residues of DDA Carbonate would change during a period of approximately one month under ambient, outdoor conditions (Hall

2006, pers. comm.; Cushing et al. 2006). Freshly treated wood was tested via wipe sampling (treatment rates and procedures were similar to those described earlier), starting approximately 8 days after treatment. The wood was then wipe tested at four additional time periods (days 14,21,28, and 35). Results show that DDA Carbonate dislodgeable residue concentrations declined during the period studied (Table 7 and Figure 2).

For this evaluation, a 95% upper confidence limit (UCL) on the mean was calculated to use as the exposure-point concentration term for detected chemicals, as recommended by USEPA guidance (USEPA 1989, 2002a). Details of the equations used are presented by chemical.

Copper. For copper, the UCL was determined by using the copper wipe concentration data for treated wood from Table 6 in USEPA's ProUCL software (version 3.00.02). The model output indicated that the data best fit a normal distribution, and the recommended method for calculating the UCL was the student's t-UCL, resulting in a value of 425 [mu]g/wipe.

DDA Carbonate. For DDA Carbonate, the UCL was determined by combining results from the two available data sets (i.e., results from the GP product residues measured 12 days after the wood was treated, and results from the second monthlong study, Figure 2). As can be seen in Figure 2, there is a clear and consistent decline in DDA Carbonate concentration over time, with concentrations ranging from 252 [mu]g/wipe to 3,052 [mu]g/wipe at 8 days after treatment, and then falling to the range of 98 [mu]g/wipe to 241 [mu]g/wipe at 35 days after treatment. Because of the decline in concentration with time, the exposure-point concentration was estimated in a three- step process. The first step was to estimate the declining trend using a standard linear regression of log-transformed concentrations, resulting in the following equation (Systat, version 11).

CONC = 992.6 x 10^sup -00241*DAY^

The second step was to calculate a 95% UCL on the fitted regression line for wipe concentrations taken through 35 days post- treatment, resulting in the following equation.

UCL= 10^sup (2.964-0.024141 x DAY+1.675 x SEprediction)^ x 1.0793

The third step was to use day-specific values from the 95% UCL line to calculate a time-weighted UCL over the entire 5-year exposure duration (i.e., ages 2-6 yrs, equivalent to 1,825 days). The UCLs for the first 35 days were taken directly from the equation derived earlier. For example, the value on the 95% UCL line at day 0 (1,362 [mu]g/wipe) was assumed to represent the concentration from day 0 to day 1, and the value on the 95% UCL line at day 1 (1,272 jug/wipe) was assumed to represent the concentration from day 1 to day 2, and so forth. The trend line clearly shows that all DDA Carbonate concentrations beyond 35 days post-treatment are expected to be equal to or less than the value observed at day 35. Thus, it was assumed that the concentration for exposures beyond the first month (i.e., day 35 to day 1,825) were equal to the UCL at day 35 (185 [mu]g/wipe). The values were combined in the following equation.

The resulting exposure-point concentration is 192 [mu]g/wipe.

MI/MCI. For MI and MCI, toxicity benchmarks are available for the combination of these two compounds, rather than each individual compound. Therefore, the concentrations for these two chemicals were summed. Additionally, because all results for MI were below the limit of quantitation (2.5 [mu]g/wipe) and results for MCI were below the limit of detection (0.75 [mu]g/wipe), one-half of the maximum summed value was used as the exposure-point concentration (i.e., one-half of 3.25 or 1.63 [mu]g/wipe).

Ingestion

Exposure-point concentrations of the chemicals of interest were combined with input parameters representing human contact rates, to estimate exposures from direct contact with treated wood structures (i.e., deck or playset) and subsequent incidental ingestion from hand-to-mouth activity. Intakes were calculated for each chemical- the average daily intake (an estimate of the long-term average concentration, averaged over the entire 5-year exposure duration) and the daily intake for a single day. Calculation of both long- term and single-day intakes allows for characterization of both long- term and shorter-term exposures. The exposure parameters and equations are presented in Table 8, and selected parameters are described in what follows. Conversion from wipes to hands (CFl). To estimate potential human exposures, experimental results from wipes, such as those described earlier, need to be correlated to the mass of chemical that would be expected to be transferred to a child's hand when contacting the same wood. The CPSC conducted several experiments to derive such a correlation. Their experiments established a good correlation for arsenic between data from dry wipes and loading onto hands (correlation coefficient = 0.91), and indicated that a single adult hand removed approximately 20% of the mass removed by a dry polyester wipe. In other words, if a dry polyester wipe removes 100 [mu]g from a wood surface, then a hand rubbed across the same surface would be expected to remove 20 /Ltg (CPSC 2003). Thus, a conversion factor of 0.20 was used in the calculations to convert the mass of chemical found on dry laboratory wipes to an estimated mass of chemical that would be expected to be loaded onto a hand during contact with treated wood. The CPSC also found a correlation between wet wipes and hands, but determined that the correlation between dry wipes and hands was a better statistical fit. There is some uncertainly with regard to the accuracy of this correlation for assessing exposures to other chemicals, such as the constituents of ACQ-treated wood. However, research targeted at assessing the relation has consistently indicated that the loading from wood onto test wipes is higher than loading onto hands in contact with the same surface (CPSC 2003; USEPA 2003; RTI 2003; SCS 1998; Shalat et al. 2006; Hall 2006, pers. comm.). Based on this body of research, the potential magnitude of error from incorporating the value reported by the CPSC is expected to be low, and is consistent with the broader CPSC methodology adopted for this assessment.

The CPSC recommendation for the relation between loading onto wipes versus loading onto hands following contact with treated wood is higher than other recommendations regarding the transfer of pesticides from surfaces to hands. USEPA's Office of Pesticide Programs recommends "the use of a 5% transferability value" based on data showing that removal of residues by the hands from surfaces such as vinyl range from 0.04% to 4% (USEPA 1997). In tests by the Midwest Research Institute (MRI 1994), pesticide transfer from surfaces to hands or fabric was evaluated. Results from this study indicate that, for a porous surface such as wallboard, the amount transferred directly onto skin was 0.6% to 8.1% of that transferred to

fabric. Even for a less porous surface such as vinyl flooring, direct skin contact resulted in only 3% to 9% of the loading achieved with fabric wipes. The 20% transfer rate found by the CPSC is higher than the range from these studies. Additionally, a recent study of arsenic loading onto the hands of children following play on CCA structures by Kwon et al. (2004, as revised in Wang et al. 2005 in response to comments) demonstrated loading rates much lower than those reported by the CPSC for loading under test conditions. The CPSC reported a mean arsenic loading onto hands of 7.7 [mu]g (with a maximum of 116 [mu]g for new wood and 64 [mu]g for an older deck), whereas Kwon et al. and Wang et al. measured a mean arsenic loading of 0.93 [mu]g, with a maximum of 4.7 [mu]g. These hand loading levels found during actual play on treated structures reported by Kwon and Wang are similar to more recent data from a study by Shalat et al. (2006), who report loading of arsenic onto the hands of children following play on CCA-treated structures, with a mean loading of 0.93 [mu]g, and a maximum of 1.9 [mu]g. These consistent results suggest that the CPSC method may overestimate mean loading onto children's hands by nearly an order of magnitude.

The experiment described earlier was done using a single hand from each adult volunteer. However, the CPSC also determined, through tracing, that the palm area (including fingers) of one adult hand (141 cm^sup 2^) was roughly equivalent to the palm area (including fingers) of two hands for children aged 2-6 years (129 cm^sup 2^) (CPSC 2003). Therefore, it is appropriate, and likely conservative, to use the conversion factor discussed earlier (i.e., 20%) to convert the mass of chemical on a wipe to the mass that might be transferred to both hands of a child.

Hand-to-mouth transfer (HT). This evaluation assumes that hand- to-mouth contact results in 0.43 handloads of wood residue being transferred to the mouth each day, as described by the CPSC (2003). The approach used by the CPSC for estimating exposures through hand- to-moudi transfer is based on empirical databases on soil adherence and soil ingestion rates, combined with the surface area of a child's hand that might contribute exposures from hand-to-mouth contact. This information can be combined to understand the magnitude of exposure contributed from hand-tomoudi activity.

Dermal

For DDA Carbonate, the endpoint of interest is dermal irritation. For MI/MCI, a potentially important endpoint is elicitation of an allergic skin reaction in individuals who are sensitized to these chemicals. Therefore, the input parameters for dermal exposure were derived to correspond to these toxicity endpoints and are presented in Table 9. For dermal exposure, chemical concentrations on wipes were combined with two parameters to derive an estimate of the skin loading that might occur following contact with treated wood. Specifically, a conversion factor of 0.20 was used to convert the mass of chemical found on laboratory wipes to an estimated mass of chemical that would be expected to be loaded onto hands during contact with treated wood, along with a surface area of 129 cm^sup 2^, representing the palms of two hands of a child aged 2-6 years. The input parameters and equations are presented in Table 9.

RISKASSESSMENT RESULTS

As described earlier, none of the constituents in ACQ-treated wood are known to be associated with carcinogenicity. Therefore, the focus of this evaluation is the potential risks from non-cancer endpoints. Consequently, for this assessment, calculated intakes are divided by reference values or toxicity benchmarks. For the chemicals included in this evaluation, no standard toxicity values are available such as those provided by USEPA in the IRIS database. Instead, the potential toxicity associated with the use of ACQ- treated wood is assessed by comparing the calculated exposure levels against the health-based criteria or toxicity benchmarks presented in Tables 8 and 9. The potential for risk is evaluated by calculating a "risk ratio" that is defined as the ratio of exposure from ACQ-treated wood to each toxicity benchmark.

As can be seen from Table 8, the risk ratios for ingestion indicate that exposures from ACQ-treated wood fall at least two orders of magnitude below the selected toxicity benchmarks for copper, DDA Carbonate, and MI/MCI. These results indicate that neither short- nor long-term exposures are expected to be associated with any adverse health effects.

For dermal exposures, risk ratios are 4 x 10^sup -2^ and 2 x 10^sup -1^ for DDA Carbonate and MI/MCI, respectively (Table 9). For interpreting the risk ratio for MI/MCI, it is important to note that the benchmark value selected was based on a level that has been identified by the FDA as an acceptable loading of this chemical onto skin in leave-on cosmetics, rather than a NOAEL; that is, the calculated exposure is well below the amount of MI/MCI that FDA has determined can be left on the skin indefinitely. Additionally, all residue concentrations for MI were below the limit of quantitation, and all residue concentrations for MCI were below the limit of detection, and thus, the calculated exposures likely overestimate actual exposures.

SUMMARY AND DISCUSSION

The totality of data on the acute toxicity of ACQ Type D with moldicide (i.e., ACQ) as a complete mixture (i.e., copper, DDA Carbonate, and MI/MCI) demonstrates that it is essentially non- toxic following oral exposure. The acute toxicity data on ACQ demonstrate that dermal exposures to sufficient concentrations (i.e., the neat product prior to dilution and use for wood treatment) can produce both dermal irritation and delayed sensitization. This is likely due to the DDA Carbonate and/or MI/ MCI, both of which are dermal irritants, while MI/MCI is also a skin sensitizer. However, exposures to ACQ-treated wood do not result in concentrations high enough to be associated with acute effects. With the exception of these skin effects resulting from exposure to the concentrate, both DDAC and MI/MCI have a low level of toxicity to mammalian systems. This is consistent with the long history of safe use of both DDAC and MI/MCI in consumer products (including preserved wood) with ample opportunity for human exposure.

Copper is well recognized as an essential nutrient, for which an RDA has been established. While exposure to high amounts of copper can produce a variety of adverse effects, primarily gastrointestinal effects, the health-effects literature demonstrates more concerns about effects associated with low exposure and resulting nutritional deficiency, rather than toxicity from overexposure. The essentiality of copper for optimum health permits a determination of levels that are either too low or too high.

The exposure assessment presented in this document was based on the methods developed by the

CPSC in their evaluation of the potential for children's exposure to arsenic from CCA-treated wood (CPSC 2003). Conceptually, the approach used by the CPSC is to conduct wipe testing of the surface of treated wood to determine the amount of chemical that might be removed from the wood. The mass removed from the wood is then converted into a skin loading onto hands, and the associated ingestion that might occur from subsequent hand-to-mouth activity. Children form the basis of this (and the CPSC's) evaluation because of associated behaviors that might result in higher contact with wood products, and greater intake following contact (e.g., higher rates of hand-to-mouth activity among children). In addition to the ingestion exposures estimated under the CPSC approach, dermal exposures were evaluated for the chemical constituents of ACQ-treated wood that are associated with dermal endpoints of toxicity. Two wood wipe studies were conducted on ACQ- treated wood. For both studies, sampling was conducted at the Centre for Toxicology at the University of Guelph, Ontario, following procedures based on those developed by the CPSC. In the first study, wood samples provided by GP were sampled 12 days after the wood had been treated. In the second study, wood wipe sampling for DDA Carbonate was conducted at five different time points to measure trends in residue concentrations over approximately one month. For this evaluation, the UCL concentration for the two detected chemicals was used as the exposure-point concentration term. The calculated UCL concentrations were 425 [mu]g/wipe for copper (from study 1) and 192 [mu]g/wipe for DDA Carbonate (from both studies). MCI was never detected, and MI was detected at only trace levels (below the level of quantitation). The assumed exposure-point concentration for MI/MCI used in the exposure assessment was 1.63 [mu]g/wipe, as described in Table 8.

The exposure assessment evaluated potential exposures from the following pathways:

* Copper: ingestion

* DDA Carbonate: ingestion and dermal contact irritation

* MI/MCI: ingestion and sensitization associated with dermal exposures.

This assessment of ACQ-treated wood was conducted by calculating a "risk ratio," defined as the ratio of calculated exposures to the available health-based criteria or toxicity levels. If the risk ratio is less than one, it indicates that exposures that occur from contact with ACQ-treated wood are below the toxicity benchmarks.

Calculated exposures via ingestion were all less than one-tenth of the healthbased criterion. In other words, the calculated exposures were more than an order of magnitude below any level that would likely be associated with adverse effects. Risk ratios for ingestion of copper were 6 x 10^sup -3^ and 1 x 10^sup -2^ for average and single-day exposures, respectively. Risk ratios for ingestion of DDA Carbonate were 4 x 10^sup -5^ and 9 x 10^sup - 5^ for average and single-day exposures, respectively. Risk ratios for ingestion of MCI/MCI were 2 x 10^sup -6^ and 4 x 10^sup -6^ for average and single-day exposures, respectively (Table 8).

For dermal exposures to DDA Carbonate, the risk ratio was 4 x 10^sup -2^, indicating that exposures to DDA Carbonate via dermal contact fall more than an order of magnitude below the NOAEL. For dermal exposures to MI/MCI, the risk ratio was 2 x 10^sup -1^, indicating that

exposures fall nearly an order of magnitude below the level that has been identified by the FDA as acceptable loading of this chemical onto skin from consumer products (Table 9). Generally, the risk ratios indicate that exposures from ACQ-treated wood fall well below (orders of magnitude) selected toxicity thresholds, thereby providing adequate margins of safety to accommodate any uncertainties about whether a toxic threshold may have been crossed. The one exception is the risk ratio for dermal exposures to MI/MCI, which is less than one order of magnitude. However, this specific risk ratio is based on the accepted exposure level (not on a toxicity threshold); therefore, the risk ratio for this compound indicates that exposures from wood are even lower than values already deemed to be acceptable for contact by the general public.

This risk evaluation included all chemical components of ACQ Type D that might be present on the surface of ACQ-treated wood. Overall, the results demonstrate that exposure to copper, DDA Carbonate, and MI/MCI from ACQ Type D from the surface of treated wood are not expected to be associated with any adverse effects to adults or children who might come into contact with this product.

ACKNOWLEDGMENTS

The authors gratefully acknowledge Dr. Jim Bestari at the University of Guelph, Centre for Toxicology, for his efforts in developing and implementing methods to assess the concentrations of MI and MCI in the residues collected from the surface of treated wood. The authors thank Melanie Edwards for statistical support. Georgia Pacific provided the funding to evaluate the potential for health risks associated with this product. To ensure humane treatment of animals used in testing, all of the animal testing of ACQ Type D with moldicide was conducted in compliance with the Good Laboratory Practice Standards as described by the USEPA (40 CFR Parts 160 and 792) and the OECD (ENV/MC/CHEM998 17).

1 Experimental dose that is lethal to 50% of the test animals in a study.

2 Identical to DDAC except that an iodide ion replaces the chloride ion.

3 High mortality at 3,000 ppm prohibited calculation of daily intakes.

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