APPENDIX W

TOXICOLOGICAL PROFILES FOR THE CONTAMINANTS OF CONCERN

Toxicological Evaluation

Toxicological profiles for the contaminants of concern are summarized in the following paragraphs.

Arsenic. Arsenic metal is used in various industrial processes from metallurgy and glass manufacturing to pesticides and wood preservatives. It has also been used for medicinal purposes. Soluble inorganic salts are absorbed through the gastrointestinal tract. As with other metals, it is not readily absorbed through the skin (EPA, 1985d). The systemic toxicity of arsenic is to the gastrointestinal tract and neurological system. It has been classified by the EPA Cancer Assessment Group (CAG) as a Class A carcinogen, indicating that sufficient evidence exists to link exposure and carcinogen effect in humans (EPA, 1986). Arsenic has also been shown to be teratogenic and mutagenic (EPA, 1985e).

As noted earlier, there is considerable uncertainty surrounding the subchronic health effects of arsenic. This in part stemmed from a carcinogenic potency factor developed by the CAG, which was based on a study whose link between exposure and health effect was weak. This CAG potency value subsequently was considered too conservative, and recently has been reduced by a factor of 10.

Benzene. Benzene is commonly used as a solvent and a feedstock for synthesizing other organic chemicals. The chemical was found in the air emissions. Benzene is acutely toxic at high doses; however, the principal toxicological factor for risk characterization is potential for carcinogenicity. Benzene has been found to cause cancer in humans and is categorized as a chemical sufficiently supported by evidence from epidemiologic studies to be considered a human carcinogen. The compound also has been shown to be mutagenic to humans and animals. An RMCL of 0 and a proposed MCL of 5.0 µg/L have been established for benzene under the Safe Drinking Water Act. Inhalation and ingestion, in general, are principal routes of exposure to benzene. Risk characterization considering these routes.

Human exposure to high concentrations of benzene (>20,000 ppm) in the air can cause central nervous system (CNS) depression, convulsions, and death via cardiovascular collapse. Less severe symptoms can be noted during exposures as low as 50 ppm (USEPA, 1983). When administered orally, a 2-ml dose of benzene can produce symptoms including vomiting and unconsciousness; a 10 ml-dose can cause death (Thienes, et. al., 1972). Although considered less significant than other routes, dermal absorption of benzene can cause blistering, redness, and dermatitis (USEPA, 1985A). During studies conducted with experimental animals, effects similar to those noted for humans have been shown. The oral LD_{50} for rats is 5.96 g/kg (USEPA, 1983).

Chronic human exposure to benzene can cause many hematopoietic effects including myelocytic anemia, thrombocytopenia, leukopenia, and eventually leukemia. Although a no-effect dose has not been determined for benzene, continuous exposure to low levels is likely to cause such hematopoietic effects. In a study of the rubber sheeting industry (Infante, et. al., 1977), long term exposure to <100 ppm benzene showed a correlation between the exposure and the incidence of death from leukemia. In experiments with laboratory animals, leukopenia is the most commonly observed effect of chronic benzene exposure.

As discussed previously, existing evidence shows that chronic exposure to benzene causes leukemia in humans. A study (Maltoni, et. al., 1979) conducted on laboratory rats showed that when benzene was administered orally, an increase in leukemia, Zymbal gland carcinomas, and mammary carcinomas was noted.

Because a causal relationship exists between benzene exposure and the incidence of leukemia, benzene is recognized by the IARC as a human carcinogen and is a level 1 in its weight of evidence ranking. The National Toxicology Program (NTP) has categorized benzene as providing sufficient evidence of carcinogenic activity, and the EPA weight-of-evidence system categorizes benzene in Group A. Group A compounds have shown sufficient evidence from epidemiologic studies to support a causal association between exposure and cancer (USEPA, 1985B).

Benzene has been found to be mutagenic in both humans and animals but not in microorganisms. Aberrations in the bone marrow and peripheral lymphocytes have been noted in humans when exposed to 100 ppm benzene (IARC, 1983). Similar observa tions were noted during laboratory experiments on rats (USEPA, 1983).

2-Butanone (Methyl Ethyl Ketone). The environmental fate of 2-butanone is unknown because little information is available on the physical and chemical characteristics of this compound. As a group, ketones are not expected to be persistent in the environment. 2-Butanone is of relatively low toxicity but, at high air concentrations (3,000 ppm), it has been shown to cause systemic disorders and irritation of the eyes, nose, and skin (EPA, 1985a). 2-Butanone can be absorbed across the skin, gastrointestinal tract, and respiratory tract (EPA, 1984a). No information concerning the carcinogenicity or mutagenicity of 2-butanone was found in the available literature (EPA, 1985a); however, 2-butanone is reported to be embryotoxic in rats (Clement, 1985). Despite its low toxicity, 2-butanone was chosen as a contaminant of concern because of its teratogenic potential and because of its high concentration in groundwater and frequency of occurrence in other media.

Carbon Tetrachloride. Carbon tetrachloride is a nonpolar compound. It is an industrial solvent which was primarily used in

the production of chlorofluorcarbons. It is highly volatile and is persistent in the atmosphere. Humans are commonly exposed to carbon tetrachloride in air, food, and water. It is readily absorbed via the lungs and GI track. Acute exposures have been shown to cause cirrhosis of the liver from inhalation exposure. Subchronic and chronic studies on animals have exhibited damage to liver, kidney, and occasionally the central nervous system. Humans have shown similar effects following exposure to carbon tetrachloride (U.S. EPA, 1987). Carbon tetrachloride has found to produce carcinogenic responses in the liver (U.S. EPA, 1987). It is classified as B2 by the U.S. EPA having adequate evidence of carcinogenicity in animals. Mutagenicity tests have been negative (U.S. EPA, 1987).

Chloroform. Chloroform is a highly volatile compound which has many sources of release into the environment. The primary route of exposure is inhalation, with the lungs absorbing up to 77 percent of the inhaled dose (U.S. EPA, 1984g). Almost 100 percent is absorbed through the GI tract (U.S. EPA, 1984g). Subchronic epidemiological studies have shown that depression, gastrointestinal disturbances and headaches are common symptoms of exposure. Chronic exposure has resulted in central nervous system effects in humans according to a NIOSH study (U.S. EPA, 1984g). Chloroform has not been unequivocally proven to be carcinogenic in humans, but has been shown to cause liver cancer in rodents (U.S. EPA, 1984g). Epidemiological studies have shown some association between exposure and increased risk of bladder, colon, and rectal cancer. It is classified as a B2 carcinogen. Chloroform has not been mutagenic in several different strains (U.S. EPA, 1984g).

1,1-Dichloroethane. 1,1-Dichloroethane is a common industrial solvent. In surface water and soil it will evaporate readily; in subsurface soils it will leach into the groundwater. No studies on rates of absorption in the lungs or gastrointestinal tract were located; however, based on structural similarities to 1,2-dichloroethane, it will be absorbed via both routes (EPA, 1984). No information was available on dermal absorption. It has been recently classified by EPA as a carcinogen. 1,1-Dichloroethane has been shown to produce tumors of the liver and mammary systems of rats. Due to its effect on the CNS, it was used at one time as an anesthetic (EPA, 1984).

1,1-Dichloroethene. 1,1-Dichloroethene (1,1-DCE) is used as a feed stock in the production of polymers. It is highly volatile but does not have a long half life in air or water. 1,1-DCE is readily absorbed via both the lungs and the GI tract (U.S. EPA, 1985h). Acute exposures in rates via oral administration have produced liver damage, especially fatty tissue infiltration (U.S. EPA, 1985h). Chronic exposures produce similar effects. In humans, the occupational literature indicates effects include central nervous system depression. One chronic inhalation study has shown 1,1-DCE to cause kidney adenocarcinomas in mice (U.S.

EPA, 1984h). EPA uses that data to classify 1,1-DCE as a B2 carcinogen. 1,1-DCE was mutagenic in several bacterial system (U.S. EPA, 1985h).

1,2-Dichloroethane. 1,2-dichloroethane is primarily used in the manufacture of other chlorinated compounds, but it has been also used as a solvent and metal cleaner. It will volatilize from water readily and can be released directly to the air from industrial operations. It decays slowly in the atmosphere. In humans, 1,2-dichloroethane is absorbed via the lungs and the GI tract, however, the primary route of exposure is inhalation. Acute exposure causes central nervous depression, extreme weakness and dizziness (U.S. EPA, 1985g). Subchronic studies where 1,2-dichloroethane was given via the diet showed some effect on the liver (U.S. EPA, 1985g), but methodological problems limit the usefulness of this study. 1,2-Dichloroethane has been shown to be carcinogenic in animals, causing squamous cell carcinomas (U.S. EPA, 1985g). It has also been shown to be mutagenic. U.S. EPA has classified it as a B2 carcinogen.

Trans-1,2-dichloroethene. There is little information on the fate of trans-1,2-dichloroethene in the environment. The cis-isomer has been identified as a degradation product of trichloroethylene and tetrachloethylene in groundwater (EPA, 1985c). It can be absorbed via all routes of exposure due to its low molecular weight and high lipid solubility. The toxic effect (at high concentrations) in humans is CNS depression. It has not been shown to be mutagenic or carcinogenic. Information on reproductive effects was not available.

Lead. Lead is a highly toxic metal that accumulates in the body, (primarily in bone), and is only slowly removed. The major routes of lead absorption are through the gastrointestinal and respiratory tracts; dermal absorption of lead is significantly less (EPA, 1986). The overall absorption rate for the respiratory tract is 20 to 40 percent (EPA, 1984b). Numerous dietary factors influence the absorption of lead from the gastrointestinal tract (e.g., low dietary calcium and iron, high dietary fat, and high or low dietary protein). Lead is excreted mainly in the bile and urine.

Many organs and systems are adversely affected by lead exposure. The major target organs/systems of lead toxicity are the CNS, the peripheral nervous system, the kidneys, and the hematopoietic system. The CNS is the critical target for low-level lead effects. Repeated exposures to small amounts of lead over many months may produce elevated levels in the blood; blood lead levels are commonly used as an index of exposure. Lead is particularly hazardous to children.

Methylene Chloride. Methylene chloride (dichloromethane, DCM) is commonly used as a stripping and degreasing solvent and as solvent

extractant in the food processing industry. DCM was found in all media except surface water at the site. Methylene chloride is toxic by the inhalation and direct contact routes and has been categorized as a probable human carcinogen by the EPA. Inhalation and ingestion, in general, are principal routes of exposure to DCM.

Exposure to high levels of methylene chloride adversely affects the central and peripheral nervous systems and the heart (USEPA, 1985A). Inhalation exposure of 300 to 750 ppm DCM for three to four hours has been shown to result in decreased performance of psychomotor skills (Winneke, et. al., 1982). Industrial exposure to DCM has produced signs of eye, lung, and respiratory tract irritation and, in one case, produced death (Moskowitz, et. al., 1952). Deaths caused by acute methylene chloride poisoning are results of cardiac injury and heart failure. Direct contact with DCM produces eye, respiratory tract, and skin irritation. An oral LD_{50} value of 2,136 mg/kg and inhalation LC_{50} value of 88,000 mg/m^3 for 30 minutes are reported for rats (USEPA, 1985A).

Chronic toxic effects produced as a result of DCM inhalation include somnolence, lassitude, numbness, and tingling of the limbs, anorexia, and lightheadedness (USEPA, 1985A). In laboratory animals, long-term exposure to methylene chloride can cause adverse effects to the liver and central nervous system.

The carcinogenic effects of DCM exposure to humans have not been studied. However, in a National Toxicology Program study, inhalation exposure to DCM was shown to produce an increased incidence of lung and liver tumors in mice and mammary tumors in rats (NTP, 1984). The EPA weight-of-evidence system categorizes DCM as a Group B2 compound. B2 compounds show sufficient evidence of carcinogenicity in animals but insufficient evidence in humans.

Methylene chloride has been shown to be mutagenic in bacterial test systems and a rat embryo cell trans formation test (USEPA, 1985A).

1,1,2,2-Tetrachloroethane. 1,1,2,2-Tetrachloroethane is less volatile than the other chlorinated solvents found at this site and it is relatively soluble. Many of the toxicological studies have been based on inhalation exposures. Subchronic animal studies have shown that alterations in blood chemistry occurs, e.g., decreased hematocrit and decreased hemoglobin content (U.S. EPA, 1984i). Information for chronic exposers to 1,1,2,2-tetrachlorethane is based on the occupational experience. The most dose-related effect was hand tremors, but other symptoms such as headaches, numbness, and excessive perspiration have been reported (U.S. EPA, 1984i). 1,1,2,2-Tetrachloroethane was carcinogenic in one strain of mice, causing liver carcinoma (U.S. EPA, 1984i). However, other test species have not exhibited the

same response. It was mutagneic in several bacterial systems. EPA classifies this compound as a group C carcinogen.

Toluene. Toluene is a common solvent and is frequently found in various environmental media. It is biodegraded in surface water. Toluene is absorbed readily through the lungs, the gastrointestinal tract, and the skin (EPA, 1985b). Within the human body, it is excreted via the lungs (in expired air) or metabolized and excreted in the urine. It is more toxic via inhalation, causing central nervous system (CNS) toxicity and liver damage. Acute doses for eight hours (200 ppm) produced fatigue, headache, nausea, muscular weakness, and confusion (EPA, 1985c). Toluene has been shown to have some reproductive effects but has not been shown to be mutagenic or carcinogenic (EPA, 1984b).

Trichloroethylene. Trichloroethylene (TCE) is a common industrial solvent and degreaser which was found as a contaminant of all environmental media at the site. TCE is acutely toxic at high doses; however, the principal toxicological factor for risk characterization is potential for carcinogenicity. TCE has been found to cause cancer in mice and was mutagenic when tested using microbial assay systems. TCE has been classified by EPA as a probable human carcinogen. An RMCL of 0 and an MCL of 0.005 mg/L has been promulgated for TCE under the Safe Drinking Water Act. Inhalation and ingestion, in general, are principal routes of exposure to TCE.

Exposure to TCE at high concentrations can cause CNS depression, kidney and liver damage, painful breathing, and cardiac arrhythmia. Single oral doses of 7.6 to 35g can cause acute effect in humans (USEPA, 1985A).

The most important routes of exposure to TCE are inhalation and ingestion. Trichloroethylene is readily absorbed both orally and in the lungs. In mice and rats, 95% and 98% (respectively) of an orally administered dose of TCE was absorbed from the gastro intestinal tract within 72 hours (Dekart, et. al., 1984). Human data concerning TCE absorption has been obtained using the inhalation route of exposure. Stewart, et. al. (1962) reported TCE concentrations of 4.5 to 7 mg/L in blood within two hours of exposure to a time-weighted average concentration of 1,420 mg/m^3. Estimates of retention in the lung have ranged from 28% to 24%. Dermal absorption is also rapid but, in most cases, the opportunity for exposure by this route is insignificant.

The effects caused by chronic exposure to TCE are primarily neurological and neurophsychiatic symptoms including headaches, dizziness, tremors, fatigue, nausea, and vomiting. However, after the subject is removed from the exposure sources, the effects subside. Exposure over a 2.5-year period of up to 50 ppm in air had no effect on humans (USEPA, 1985A).

TCE has been found to cause cancer in mice after oral administration, producing hepatocellular carcinomas (NCI, 1976; NTP, 1982). Based on EPA proposed guidelines for carcinogen risk assessment (EPA, 1984B), the strength of the evidence for carcinogenicity of TCE is sufficient for establishing carcinogenicity in animals but inadequate evidence for humans. TCE has been classified by EPA as Group B2, probably a human carcinogen. Because of the relatively slight acute toxicity of TCE but potential for carcinogenicity, the most critical factor for toxicological evaluation and risk characterization for TCE is carcinogenic potential.

1,1,1-Trichloroethane. 1,1,1-trichloroethane (TCA) is commonly used as a solvent and as an intermediate in the manufacture of vinylidene chloride. At the Bridgewater site, the compound was found in soil and groundwater. Exposure to 1,1,1-TCA can produce both acute and chronic toxic effects and has been ranked by the NTP as showing clear evidence of carcinogenicity in laboratory animals. A proposed MCL and a final RMCL of 0.2 mg/L have been promulgated for 1,1,1-TCA under the Safe Drinking Water Act. Inhalation and ingestion, in general, are principal routes of exposure to the chlorinated ethane.

When 1,1,1-trichloroethane is inhaled by humans, acute toxic effects including CNS depression, cardio vascular effects, and adverse effects on the lungs, liver, and kidneys are produced (USEPA, 1985A).

Effects due to chronic exposure of 1,1,1-TCA are expected to be similar to those due to acute exposure (USEPA, 1985E). However, in two studies of industrial exposure to 1,1,1-TCA vapors ranging in concentration from 1 to 250 ppm and from 100 to 1,000 ppm for up to six years, no adverse effects were noted (Kramer, et. al., 1978; Maroni, et. al., 1977). Also, animals exposed to 500 ppm for 7 hours/day, 5 days/week for 130 exposures showed no adverse effects (Torkelson, et. al., 1958).

In a 1977 test by the National Cancer Institute (NCI, 1977), data was rendered inadequate for assessing carcinogenicity of 1,1,1-TCA due to early lethality. The National Toxicology Program conducted a retest in 1979 (NTP, 1979). 1,1,1-TCA was shown to be carcino genic in female mice. Therefore, 1,1,1-TCA is classified as showing clear evidence of carcinogenicity by the NTP, however the IARC and the EPA have not classified 1,1,1-TCA.

1,1,1-TCA was shown to be weakly mutagenic to Salmonella (Tu, et. al., 1985). The compound gave negative results in a study in which mice were given daily doses as high as 8,500 mg/kg (Clayton, et. al., 1981).

Zinc. Zinc is an essential trace element in human and animal nutrition. In the aquatic environment, it may partition between

soluble forms and adsorption to minerals or organic matter. It can be absorbed through the gastrointestinal tract, but the rate is dependent on a variety of dietary and physiological factors. Inhalation of zinc fumes can produce flu-like symptoms often referred to as metal fume fever. Like the other metals, it is not expected to be absorbed efficiently through the skin. Zinc has not been shown to be mutagenic or carcinogenic.