Remediation and
Redevelopment Division

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TOXICOLOGICAL ASSESSMENT
For Part 201Criteria//213 RBSL Development

para-Chlorobenzenesulfonic Acid
CAS #98-66-8

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para-Chlorobenzenesulfonic acid (p-CBSA) is a byproduct of the manufacture of DDT. This chemical has been found at sites of environmental contamination where DDT manufacturing occurred or where wastes associated with the manufacture of DDT have been disposed. Recently, it has been identified in municipal drinking water wells for the City of St. Louis, MI. The source is the Velsicol Superfund site in St. Louis. p-CBSA is extremely mobile in groundwater due to its high water solubility. In addition, it is resistant to both degradation in water and adsorption to soil or sediment particles.

Toxicity data for p-CBSA is very limited. A published toxicity endpoint does not exist. In 1985, EPA requested the development of toxicity studies for this chemical. The need was related to the RI/FS for the Stringfellow Superfund site in California. In 1985 and 1986, the following studies were commissioned by EPA. Brief summaries of the results of those studies are included.

Ames Salmonella Assay: This assay detects mutations in *Salmonella typhimurium* bacteria. p-CBSA was tested at 50, 167, 500, 1,667 and 5,000 mg/plate both with and without metabolic activation (Pharmakon Research International, Inc., 1985a). Test results were negative in all five strains tested both with and without metabolic activation.

L5178Y Mouse Lymphoma Assay: This assay measures the ability of a chemical to induce forward mutations at the thymidine kinase (TK) locus in L5178Y mouse lymphoma cells. p-CBSA was tested at five concentrations (50, 125, 250, 500, and 1,000 mcg/ml) with and without metabolic activation (Pharmakon Research International, Inc., 1985b). p-CBSA did not produce an increase in mutation frequency with or without metabolic activation at any of the doses administered.

***in vivo* Bone Marrow Cytogenetics Assay:** This assay measures the ability of a test substance to induce chromosomal aberrations in the bone marrow of treated rats. Male rats were administered a single dose of 2,000 mg/kg p-CBSA by oral gavage (Pharmakon Research International, Inc., 1985c). Groups were sacrificed at 6, 12, and 24 hours post-treatment. No significant increases in the incidence of aberrations or in the number of cells with aberrations were observed in any of the test animals.

Teratogenicity Screening Assay: This test evaluates the potential of chemicals to induce teratogenic effects (birth defects) in pregnant animals. Pregnant female rats were administered high doses of p-CBSA on days 7 to 16 of pregnancy (Chernoff and Rosen, 1985). The number of live births and the weight of newborn animals on days one and three post-birth are used as the screening effects for teratogenicity. p-CBSA did not produce any dose-related teratogenic effects.

28-Day Oral Toxicity Study in Rats: Groups of ten female and ten male rats were administered p-CBSA via oral gavage at doses of 0, 10, 50, 500, 1,000 or 2,000 mg/kg body weight for 28 days (American Biogenics Corp., 1985). Statistically significant reductions in the weights of the left adrenal gland were seen in the 500 mg/kg male dose group. Since this effect was not seen at the higher dose groups, it was not considered to be toxicologically significant. Noteworthy effects were seen in two of the high dose males which included slightly lower body weights and observations of salivation, gasping and irregular breathing. Since it is not certain that these effects were related to treatment (one animal appeared to have been injured during dosing), the NOAEL for males was determined to be 1,000 mg/kg. Since no effects were reported in females, the NOAEL for females is 2,000 mg/kg.

Structural Analog: A similar compound for which there are toxicity data is the 4-chlorophenyl ester of 4-chlorbenzenfulfonate (chlorfenson). In place of the hydrogen atom of the hydroxyl group, chlorfenson has an additional benzene ring with a single chlorine atom attached to it. Chlorfenson is a registered pesticide, specifically a miticide. The database for chlorfenson is more complete and gives no indication that it is a carcinogen. The oral rat LD50 is 2,000 mg/kg and a two year in-feed rat study reported a lowest observed effect level (LOEL; minimal effects) at 50 ppm (in feed; approximately equal to 3.5 mg/kg body weight). The no observed effect level (NOEL) was 25 ppm (approximately equal to 1.8 mg/kg body weight). These data suggest that the analog is significantly more toxic however, this is expected since it is less water soluble than p-CBSA.

Conclusions: Based on the limited toxicity data available for p-CBSA, it does not appear to be highly toxic. In addition, it is highly water soluble suggesting that it is not likely to be rapidly or extensively absorbed by the gastrointestinal tract; lipid soluble chemicals are typically absorbed to the greatest degree. p-CBSA is also likely to be readily excreted in urine due to its high water solubility. Although the animal bioassay was conducted for only 28 days, no clear treatment-related effects were observed. The teratogenicity screen was negative as were the three mutagenicity studies. Based on the negative mutagenicity studies, p-CBSA is not expected to be carcinogenic.

Chlorobenzene, a related chemical, was tested by the National Toxicology Program in a gavage study in rats and mice (a standard two-year cancer bioassay); no excess tumor incidence was found. The addition of a sulfate group to chlorobenzene (forming p-CBSA) would likely decrease its toxicity by increasing its solubility and thereby hastening its excretion from the body. Even the more toxic structural analog (chlorfenson) did not cause cancer in a two year rodent study (see previous section).

Although p-CBSA was tested in a 28-day study in lieu of a subchronic or chronic study, the uncertainty factor (UF) typically used for subchronic data was considered sufficient for this chemical. It is not expected that p-CBSA would cause any significantly different effects in a subchronic study than it did in the 28-day study due to its high solubility in

water and minimal accumulation in the body; p-CBSA is not expected to be absorbed by the gastrointestinal system to any significant degree and is expected to be readily excreted in urine. As a result, an UF of 1,000 is applied to the NOAEL to derive the reference dose (RfD) of 1 mg/kg-day. The UF includes a 10-fold factor for each of the following: interspecies variation; intraspecies variation; and extrapolation from a subchronic study to a chronic study.

Groundwater Criteria: The RfD noted above was incorporated into the generic drinking water criteria (DWC) algorithms for noncarcinogens to generate a residential DWC of 7,300 ppb and an industrial DWC of 21,000 ppb. Other groundwater criteria could not be developed due to insufficient data.

Soil Criteria: Soil criteria protective of residential and industrial/commercial drinking water are 1.5E+05 and 4.2E+5 ppb, respectively. The soil direct contact criterion (DCC) for residential land use is 2.3E+8 ppb. The industrial, commercial III, and commercial IV soil DCC are 7.3E+8, 1.0E+9, and 8.6E+8 ppb, respectively. Csat and the inhalation-based soil criteria could not be developed due to insufficient data for this hazardous substance.

Other agency standards: The California Environmental Protection Agency (Cal/EPA) and the United States Environmental Protection Agency (U.S. EPA) have derived acceptable daily intakes (ADI) for p-CBSA in drinking water. The ADI of 35,000 ppb derived by the Cal/EPA is based on the same RfD as the Part 201 DWC. The equation used to derive the Cal/EPA ADI includes the standard assumptions for human body weight and water ingestion but none of the others that are included in the Part 201 DWC equation. The primary difference between the Cal/EPA ADI and the MDEQ Part 201 DWC is due to the 20% relative source contribution factor (RSC) required by the Part 201 rules. The default RSC of 20% is required unless chemical-specific data are available which support a different value. The U.S. EPA developed an ADI of 25,000 ppb in 1986 based on the same 28-day rat study, however, EPA has not been able to provide details that would explain the difference between it and the Cal/EPA ADI.

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