Appendix E
Technical Memorandum—pCBSA

December 2, 2004

MEMORANDUM

SUBJECT: Transfer of information related to p-Chlorobenzene Sulfonic Acid. (Velsicol Superfund Site, 01-R05-002)

FROM: Randall R. Ross, Ph.D., Hydrologist
Applied Research & Technical Support Branch

TO: Stephanie Linebaugh, RPM
U.S. EPA, Region 5

The following information related to p-Chlorobenzene Sulfonic Acid (pCBSA) is provided for your consideration per your request for continued technical assistance at the Velsicol Superfund Site, St. Louis, Michigan. Most of this information was extracted from materials related to the Montrose Superfund Site in Region 9 provided by Jeff Dhont. If you have any questions or would like to discuss these comments further, please do not hesitate to contact me at your convenience (580-436-8611).

Regulatory Standards

Currently, there are no promulgated health-based standards or accepted toxicological values (slope factor, risk reference dose (RfD), dose-response relationships, etc.) for pCBSA. There are also no acceptable surrogate compounds upon which to base toxicological values for pCBSA. The few short-term acute toxicity studies provide no indication of mutaginic or teratogenic health effects. However, limitations of the studies may require additional short-term studies to confirm their results. Additionally, no chronic (long-term) studies have been conducted on this compound.

Based on the available data, the State of California established a non-promulgated and provisional No Observed Adverse Effect Level (NOEL) of 1 mg/Kg/day for pCBSA, that would approximately translate to a provisional drinking water standard of 25,000 ug/l. Similarly, the State of California holds that 25,000 ug/l can be considered a provisional health standard for pCBSA with respect to ground water injection at the Montrose Chemical and Del Amo Superfund Sites (U.S. EPA, 1999).

The American Conference of Governmental Industrial Hygienists (ACGIH) and the Occupational Safety and Health Administration (OSHA) have not set either a threshold limit value time weighted average (TLV-TWA) or permissible exposure limit (PEL) for pCBSA.

Toxicity Studies

The U.S. EPA commissioned a series of toxicology assays in 1985 and 1986 to investigate the potential toxicity of pCBSA. The studies did not demonstrate any significant toxicity of pCBSA in three mutagenicity assays, a teratology screening test, and a short-term oral toxicity study, described below. However, the U.S. EPA determined that additional studies would be required if toxicity values were to be established.

- Ames Salmonella assay did not indicate an increase in mutation rates in bacterial cell lines at pCBSA concentrations ranging from 0 to 5,000 mg/plate (Pharmakon Research International, 1985a),
- L5178Y Mouse Lymphoma assay did not induce forward mutations at the thymidine kinase (TK) locus at pCBSA concentrations of 0 to 1,000 mg/l (Pharmakon Research International, 1985b),
- *In Vivo* Bone Marrow Cytogenetics Assay did not indicate an increase in the number of observed aberrations nor the number of cells with aberrations in bone marrow smears prepared from individual groups of rats sacrificed at 6, 12 and 24 hours after a single dose of pCBSA of 2,000 mg/kg body weight by oral gavage (Pharmakon Research International, 1985c),
- Chernoff and Rosen (1985) concluded that there were no teratogenic effects on the offspring of rats treated with 0, 1,000, and 2,000 mg/kg body weight of pCBSA-Na on days 7 through 16 of pregnancy.
- Twenty-eight day oral toxicity study indicated no opthalmalogic or histopathologic effects related to administration of pCBSA by oral gavage to rats at levels of 0, 10, 50, 500, 1,000 or 2,000 mg/kg body weight (American Biogenics Corporation, 1985). Statistically significant differences were observed in lower left adrenal gland weights and left adrenal/body weight ratios from the 500 mg/kg dose male group. However, researchers did not consider this to be of toxicological importance. Based on this study, U.S. EPA determined the no observed effect level (NOEL) was equal to or greater than 1,000 mg/kg body weight and 2,000 mg/kg body weight for male and female rats, respectively.

Carcinogenicity Studies and Classifications

The National Toxicology Program conducted a gavage study in rats and mice with chlorobenzene and found no excess tumor incidence in a standard two-year cancer bioassay (National Toxicology Program, 1987). It is noted that the addition of a sulfate group to chlorobenzene (forming pCBSA) would likely decrease its toxicity by increasing its solubility and thereby hasten its excretion from the body.

pCBSA has not been classified as a potential carcinogen by either the International Agency for Research on Cancer (IARC) or the U.S. EPA. The U.S. EPA has assigned Chlorobenezene a “D” classification for carcinogenicity (i.e., not classifiable as to human

carcinogenicity) based on a lack of human data, inadequate animal data and predominately negative genetic toxicity data in bacterial, yeast, and mouse lymphoma cells.

References

American Biogenics Corporation, 1985. Final Report for American Biogenics Corporation Study 410-2298. Twenty-eight Day Oral (gavage) Toxicity Study in Albino Rats using A-100.

Chernoff, N. and Rosen, M., 1985. Study of Teratogenic Potential of Na Parachlorobenzene Sulfonic Acid. Health Effects Research Laboratory Developmental Biology Division. Research Triangle Park, N.C.

National Toxicology Program, 1987. Toxicology and carcinogenesis studies of 1,4-dichlorobenzene (CAS No. 106-46-7) in R344/N rats and B6C3F1 mice (gavage studies). NTP TR 319. NIH Bubl. No. 86-2575.

Pharmakon Research International, Inc., 1985a. Ames Samlonella/Microsome Plate Test (EPA/OECD). PH 301-EPA-001-85, 4-chlorobenzene sulfonic acid. Lot E-2663. Waverly, PA.

Pharmakon Research International, Inc., 1985b. L5178Y Mouse Lymphoma Cell TK +/- Forward Mutation Assay. PH 313-EPA-001-85, 4-chlorobenzene sulfonic acid. Lot E-2663. Waverly, PA.

Pharmakon Research International, Inc., 1985c. In Vivo Bone Marrow Cytogenetics Rat Metaphase Analysis. PH 315S-EPA-001-85, 4-chlorobenzene sulfonic acid. Lot E-2663. Waverly, PA.

U.S. Environmental Protection Agency, 1999. Record of Decision, Dual Site Groundwater Operable Unit, Montrose Chemical and Del Amo Superfund Sites, March 1999.

cc: Rich Steimle (5102G)
Rafael Gonzalez (5204G)
Luanne Vanderpool, Region 5
David Wilson, Region 5,

Current Understanding of p-Cholorobenzenesulfonic acid (pCBSA) for Groundwater Studies

PREPARED FOR: Theo von Wallmenich/LSG

PREPARED BY: Jim Hartley

COPIES: Jeff Dhont/USEPA Region IX

PROJECT NUMBER: 184199.CV.05

DATE: November 30, 2004

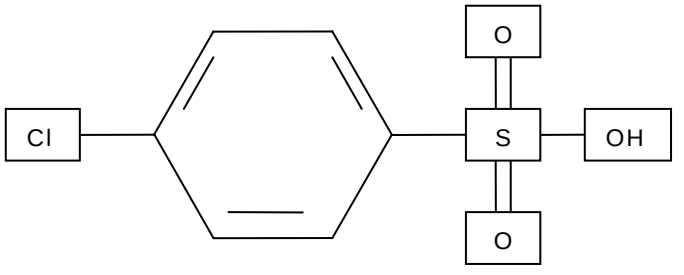
p-Chlorobenzenesulfonic acid (pCBSA) is a byproduct of the manufacture of DDT. It has been found at Superfund sites that are near former DDT manufacturing areas, or in areas that have received wastes associated with DDT manufacture.

Although several sites have some reference to pCBSA, only two seem to have extensive public documentation regarding its migration, fate, and toxicity: Stringfellow Acid Pits, in Glen Avon, California, and Montrose Chemical/Del Amo Superfund Site, Southern California.

This memorandum summarizes knowledge about this chemical as an environmental contaminant. Like others that have been brought to public attention, this compound is extremely mobile due to its aqueous solubility, and not substantially researched as far as toxicity. In pCBSA's case, however, the only toxicity studies that can be found suggest that its risk to human health or the environment is not great; moreover, this preliminary finding seems to have suppressed the priority for further research, so that information from 5 years ago may still be the most up to date.

Chemical Structure and Properties

pCBSA can be represented as follows:



p-Cholorobenzenesulfonic Acid (pCBSA)

pCBSA is highly soluble in water, especially when compared to other contaminants such as chlorobenzene and benzene. pCBSA has been found to disperse more widely than its associated discharge compounds.

Environmental Fate and Toxicity

At the Montrose Chemical/Del Amo Superfund site, pCBSA seems to have dispersed more broadly than the original benzene plume, with no apparent attenuation other than dispersion. At the Stringfellow hazardous waste disposal site, pCBSA is found originally in the discharged waste stream of the treatment plant, together with other hydrophobic and hydrophilic acid and neutral compounds. In the groundwater, pCBSA (as a transphilic acid) appears to progressively fractionate to other hydrophobic and hydrophilic compounds in the presence of naturally occurring fulvic acid. This fractionation (conversion into alternate compounds), promoted by an intervening organic acid, represents the only non-dispersive attenuation process suggested for pCBSA in the environment.

In terms of suggested toxicity, there are a limited number of studies which, if relied upon, would indicate a low toxicity for pCBSA. In these studies, indicator tests performed did not give indications of mutagenicity (causing mutations) or teratogenicity (causing birth defects) in laboratory animals. In another study, there was an indication that another chemical was converted into pCBSA by the body in order to excrete it: pCBSA has a high water solubility. This may mean that pCBSA residence time in the human body is short compared to other chemicals.

There are no promulgated health-based standards for pCBSA, and no accepted toxicological values for formal risk evaluation. This is due to the absence of any chronic studies and only a small number of limited acute studies of the toxicity of pCBSA in animals. This conclusion of the state of knowledge of the toxicity of pCBSA was first published in 1999; a conversation in 2004 with the USEPA Region IX specialist involved in this work reported that no new chronic studies had been performed in the intervening 5 years to add to the knowledge of its toxicity.

One non-promulgated and provisional standard for pCBSA was established by the state of California, as a No Observed Adverse Effect (NOEL) standard of 1 milligram per kilogram per day (mg/kg/day), which would approximately translate to a provisional drinking water standard of 25,000 part(s) per billion (ppb), based on one sub-chronic non-cancer study.

References

Compound data courtesy of WCAS Laboratories, Santa Fe Springs, California; http://www.wcaslab.com/tech/PCBSA.htm

Record of Decision, Dual Site Groundwater Operable Unit, Montrose Chemical and Del Amo Superfund Sites, Decision Summary: Section 8.4 (Risk Status of pCBSA), March 1999.

Record of Decision, Dual Site Groundwater Operable Unit, Montrose Chemical and Del Amo Superfund Sites, Response Summary: Section 2 (Responses to Short Written Comments), March 1999.

Leenheer, Jerry A., John Hsu, and L.B. Barber, "Transport and Fate of Organic Wastes in Groundwater at the Stringfellow Hazardous Waste Disposal Site, Southern California." *Journal of Contaminant Hydrology* 51 (2001), pp. 163-178.

Telephone conversation, Jeff Dhont, USEPA Region IX, November 18, 2004.

OK. Trying again — let me know if you get full pages this time —

K

From: <Theo.VonWallmenich@CH2M.com>
To: <KKlein@dtsc.ca.gov>
Date: 9/19/2005 9:26:35 AM
Subject: RE: pcbsa

Hi Kimi. Thanks for the quick help on faxing the memos. Unfortunately, the pages seem to have overlapped when going through the fax machine (I've got half pages covered by other half pages). Could you please try to re-send the fax?

Thanks,
Theo

-----Original Message-----
From: Kimi Klein [mailto:KKlein@dtsc.ca.gov]
Sent: Monday, September 19, 2005 11:51 AM
To: Von Wallmenich, Theo/LSG
Subject: Re: pcbsa

hello Theo,
I have found several memos that I shall be faxing to you supporting a human health risk-based groundwater concentration of 35 mg pCBSA/liter water. I do not have in my file a letter that actually documents the adoption of that concentration as the reinjection standard. if you need that official thing, I think Jeff will have to look for it in the EPA file.

regards,
k

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>>> <Theo.VonWallmenich@CH2M.com> 9/19/2005 8:09:49 AM >>>
Here is my contact info per our discussion earlier today.

Thanks!

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Cal/EPA

Department of Toxic Substances Control

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MEMORANDUM

Pete Wilson Governor

Peter M. Rooney Secretary for Environmental Protection

TO: Bonnie Wolstoncroft
Legal Office
400 P Street, 4th Floor
Sacramento, CA 95812-0806

FROM: A. Kimiko Klein, Ph.D.
Staff Toxicologist
Human and Ecological Risk Division (HERD)

DATE: November 20, 1997 CONFIDENTIAL - ATTORNEY/CLIENT PRIVILEGE

SUBJECT: MONTROSE/DEL AMO, TORRANCE CA
PCA: 14125 SITE: 400100-66

Background

The Montrose property consists of 13 acres and was the site of a DDT manufacturing plant for 35 years before closing down in 1982. The adjacent and much larger Del Amo property occupies 240 acres and was the former location of a synthetic rubber manufacturing plant for 30 years before closing down in 1972. The Del Amo site consists of a former styrene plant, butadiene plant, copolymer plant, and waste pit area. The lead regulatory agency for this site is the US Environmental Protection Agency (US EPA) Region IX. The Human and Ecological Risk Division (HERD) has been requested to provide toxicological support for both properties for the Department of Toxic Substances Control (DTSC).

Of particular concern to the DTSC is the presence of para-chlorobenzene sulfonic acid (pCBSA) in the groundwater underlying this site. On April 21, 1994, Dr. Judith Parker, a HERD toxicologist, provided a review of available toxicology data for para-chlorobenzene sulfonic acid (pCBSA). On January 31, 1997, the Office of Environmental Health Hazard Assessment (OEHHA) also reviewed the available toxicity studies and agreed with conclusions made by Dr. Parker and her calculations of a reference dose (RfD) of 1 mg/kg/day and an allowable daily intake (ADI) of 35 mg/l water for pCBSA.

On October 21, 1997, I participated in a conference call with staff from the DTSC and the Los Angeles Regional Water Quality Control Board in which we discussed the establishment of a California Applicable or Relevant and Appropriate Requirement (ARAR) for pCBSA. As part of the supporting documentation for the ARAR, information on ecological effects could be of value.

In regard to environmental pollution, pCBSA exhibits chemical properties that could adversely affect the environment - it is highly water soluble and resistant to both degradation in water and adsorption to soil or sediment particles. Therefore, once pCBSA reaches water, it is persistent and moves with the water. The HERD did a cursory search of available ecological toxicity data bases, and I summarize the results of our search in this memorandum.

Data Bases Reviewed

ECOTOX ECOlogical TOXicity Database, maintained by the U.S. Environmental Protection Agency (USEPA) National Health and Environmental Effects Research Laboratory, Mid-Continent Ecology Division and Western Ecology Division.

ASTER ECOTOXICITY PROFILE, maintained by the USEPA Office of Research and Development, National Health and Environmental Effects Research laboratory, Mid-Continent Ecology Division.

Results and Discussion

The toxicity of the sodium salt of 2,5-dichlorobenzenesulfonic acid (pCBSA) on aquatic organisms was reported in two studies listed in the ECOTOX database: 1) Dowden, B.F. and H.J. Bennett, 1965. Toxicity of selected chemicals to certain animals. J. Water Pollut. Control Fed. 37(9):1308-1316. 2) Freeman, L., 1953. Toxicity thresholds of certain sodium sulfonates for Daphnia magna Straus. Sewage Ind. Wastes 25(11):1331-1335. In these studies, the most sensitive species tested was Daphnia magna, the water flea: the LC50 (concentration lethal to fifty percent of the test organisms) for the sodium salt of pCBSA ranged from 4,931,000 ug/l for a one-day exposure to 1,468,000 ug/l for a four-day exposure.

In the ASTER ECOTOXICITY PROFILE database, quantitative structure activity relationship (QSAR) analysis can be performed to estimate ecotoxicological hazards of specific chemicals. This is done by using information about chemical structure to deduce uptake and effects on biota. For pCBSA, the most sensitive calculated acute LC50 is 3,809,036 ug/l for a two-day exposure by Daphnia magna. The calculated chronic maximum allowable toxic concentration is 1,036,254 ug/l for the fathead minnow over 32 days. The QSAR system indicates that pCBSA would not bioconcentrate in animal tissue (calculated bioconcentration factor = 1).

Calculations

Using the LC50 of 1,468,00 ug/l for a four-day exposure by Daphnia magna, a No Observed Adverse Effect Level (NOAEL) may be estimated by dividing the LC50 by an uncertainty factor of 500, as recommended in the DTSC Guidance for Ecological Risk Assessment at Hazardous Waste Sites and Permitted Facilities, Part A: Overview (July 1996). This calculation results in a concentration of 3 mg/l water (2,936 ug/l) representing a very conservative estimate of a level protective for aquatic ecological receptors in surface waters.

Though not directly applicable to groundwater (since aquatic organisms do not exist in groundwater), the HERD uses an ecologically-safe surface water concentration as a screening level for groundwater. If groundwater concentrations exceed this screening level, the next step is to apply a site-specific attenuation/dilution factor to the safe surface water concentration in order to back-calculate a safe level in a groundwater aquifer. This site-specific factor must account for the attenuation of pCBSA as it passes through soil from groundwater and its dilution after reaching a surface water body.

Conclusions

From a cursory search of these two data bases, there appear to be extremely limited toxicity data on pCBSA for ecological receptors. Similar to the previous review of mammalian toxicity data by Dr. Parker, available data indicate that pCBSA is not highly toxic to aquatic receptors. A level of 3 mg/l groundwater represents a conservative estimate of a concentration not likely to adversely affect aquatic receptors.

Reviewed by: James Polisini, Ph.D. D. Oudiz for J. Polisini
Staff Toxicologist
Human and Ecological Risk Division

cc: Deborah Oudiz
Senior Toxicologist
Human and Ecological Risk Division

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MEMORANDUM

Pete Wilson Governor

James M. Strock Secretary for Environmental Protection

TO: File

FROM: A. Kimiko Klein, Ph.D.
Staff Toxicologist
Human and Ecological Risk Division (HERD)

DATE: July 16, 1997

SUBJECT: MONTROSE/DEL AMO, TORRANCE CA
PCA: 14125 SITE: 400100-66

Background

On April 21, 1994, Judy Parker completed her review of available toxicology data for para-chlorobenzene sulfonic acid (pCBSA). pCBSA is found in groundwater under the Montrose Chemical site. It is also present at the Stringfellow site and is said to be quite difficult to remove using "normal" remediation technology. Judy calculated a provisional reference dose (RfD) of 1 mg/kg/day and derived a "safe" level of 25 mg pCBSA/l water for drinking water. The safe level is based on a single exposure pathway of ingestion of water. This review was itself reviewed by David Ting of the Office of Environmental Health Hazard Assessment (OEHHA) in a memorandum dated January 31, 1997. David agreed with Judy's findings in all aspects. On July 8, 1997, I went to a meeting in Region 4 with the US EPA, the Los Angeles Water Quality Control Board, and DTSC staff to discuss how the presence of pCBSA in groundwater may be addressed by the US EPA in their Record of Decision (ROD). The following are my notes of this meeting and a chronology of related events after the meeting.

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Summary of July 8, 1997 Meeting

Peter Garcia, Gloria Conti, Kim Christmann and I (DTSC), Jeff Dhont (US EPA), Hugh Marley and Jim Ross (LAWQCB) were present. The purpose of the meeting was to agree in principle to monitor for pCBSA in groundwater and include this as part of the remedy in the ROD. We agreed that the lack of toxicity data and feasible treatment technology posed significant limitations to our ability to regulate pCBSA under a responsible party cleanup scenario. All of the proposed alternatives for treatment of the other contaminants involve reinjection of the treated groundwater; therefore, any alternative chosen will both dilute and spread the pCBSA groundwater plume. We discussed the following possible remedies for pCBSA.

1. Define and monitor the vertical and horizontal boundaries of the plume at some frequency and focus on the impact the moving plume may have on nearby production wells. The LAWQCB thought that their state statutes could enforce this requirement.
2. Establish a reinjection standard of less than 25 mg/l pCBSA. The LAWQCB would support this standard. However, the question of whether and how this could be supported became a primary issue of this meeting. Is this an anti-degradation standard? (The LAWQCB does not really support anti-degradation anymore.) If this is a health-based standard, will it stand up as an ARAR?
3. Establish 25 mg/l as a trigger concentration. Use it to establish a containment zone. If groundwater concentrations exceed this level, some revision of the remedy would be considered, some contingent action would occur. This is another ARAR issue. Can the provisional RfD stand as an ARAR?
4. Do further toxicity studies. It was agreed that this is the most important possible remedy and was discussed at length, but, in fact, it is unlikely that this will occur any time soon.
5. Establish institutional controls. The US EPA said that this is going to occur anyway.
6. Modify the extraction/reinjection remedy.
7. Somehow contain the plume.
8. Consider some sort of attenuation strategy.

Numbers 6, 7, 8 were not discussed in depth. The US EPA asked for some assistance in determining the legal strength of the provisional RfD as an ARAR to support alternatives 1 through 3 above.

Follow-up on July 8, 1997 Meeting

I spoke to David Ting regarding the statutory authority allowing us to use the provisional RfD as an ARAR. He spoke with Lauren Zeiss and Bill Soo Hoo. Lauren said the OEHHA has general authority. Bill said the DTSC has general authority. I passed this information on to Peter Garcia, who passed it on to Bonnie Wolstoncroft. She is now working with the legal counsel at the LaWQCB to formulate a strategy.

Cal/EPA

California Environmental Protection Agency

Office of Environmental Health Hazard Assessment

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Governor

James M. Strock
Secretary for Environmental Protection

MEMORANDUM

TO: Deborah Oudiz, Ph.D.
Human and Ecological Risk Division
Department of Toxic Substances Control
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VIA: David M Siegel, Ph.D., Chief
Hazardous Waste Toxicology Section

FROM: David Ting, Ph.D.
Staff Toxicologist
Hazardous Waste Toxicology Section

DATE: January 31, 1997

SUBJECT: Review of Toxicology Data for Montrose Chemical
PCA Code: 14125 Site Code: 400100-66

Background

In response to your request of December 20, 1996, I have reviewed the memorandum from Dr. Judith Parker, Office of Scientific Affairs to Gloria Conti, Site Mitigation Branch, Region 4, dated April 21,1994, (Attachment 1) and the five toxicity studies, listed in the attachment to Dr. Parker's memorandum, on para-chlorobenzene sulfonic acid and its sodium salt (pCBSA) commissioned by U.S. EPA.

Document Reviewed

In the memorandum, Dr. Parker indicated that she conducted a literature search on pCBSA in April 1994 and found only one study in J. Agric. Food Chem., (1977) that contains useful information. I searched the U.S. EPA Integrated Risk Information System (IRIS), Toxline, and Registry of Toxic Effects of Chemical Substances (RTECS) for the period between 1994 and 1997 and did not find any additional toxicity data. As a result, both Dr. Parker and I relied on the five unpublished studies done under U.S. EPA contract for evaluating the toxicity of pCBSA.

Recycled Paper

Comments on the Toxicity Data

Three of the studies commissioned by U.S. EPA were short-term mutagenicity tests; they are designed to detect both chromosomal alterations and gene mutations. The dosage used in the studies seems appropriate, tests were conducted with and without metabolic activation, and they all complied with current testing protocols. These three studies were negative indicating that pCBSA is not expected to cause damage to genetic material. However, additional tests are needed to conclude that pCBSA is not a carcinogen.

The fourth study was a short-term oral toxicity study in rats. The compound was evaluated for systemic toxicity by dosing male and female albino rats by gavage for 28 consecutive days. The dose range was 0, 10, 50, 500, 1000, or 2,000 mg/kg/day. The highest dose was chosen because it represents the solubility limit of the compound in water at ambient temperature. Two of the ten males at 2,000 mg/kg/day showed some abnormal behavior which may or may not be related to the test compound. The females showed no signs of toxicity in all the parameters measured. I agree with Dr. Parker's analysis that based on the information in this study, 1,000 mg/kg/day could be identified as the no observed effect level (NOEL).

The fifth study commissioned by U.S. EPA is to evaluate the potential of pCBSA to induce teratogenic effects. It was a screening study and used high doses (1,000 or 2,000 mg/kg/day) and measured the number of live births and the weight of newborn animals on days one and three after birth. The underlying hypothesis for this method is that most prenatal insults will manifest themselves postnatally as reduced viability or impaired growth. No difference was observed between controls and the two treatment groups. I agree with Dr. Parker's analysis that based on the information in this study, the NOEL was >2,000 mg/kg/day.

Comments on the Calculation of Reference Dose

Dr. Parker calculated a reference dose (RfD) of 1 mg/kg/day for pCBSA by using a NOEL of 1,000 mg/kg/day and an uncertainty factor of 1,000. The NOEL was taken from the short-term oral toxicity study in rats and an uncertainty factor of 1,000 was used to extrapolate from short-term exposure to long-term exposure (10X), to extrapolate from animal data to humans (10X), and to account for sensitive human populations (10X). It is my opinion that the approach and extrapolation factors used in the calculation are appropriate.

Comments on the Calculation of Allowable Daily Intake

As described in the memorandum, Dr. Parker also calculated an allowable daily intake (ADI) of 35 mg/L for pCBSA by assuming drinking water is the only relevant exposure route and using default values for daily water consumption rate (2 L) and body weight (70 kg). The derivation of the ADI used a standard approach and standard default assumptions.

Conclusion

The available toxicity information is very limited for pCBSA. Based on this sparse data set, Dr. Parker used standard and appropriate methods to develop an RfD and an ADI. However, these criteria should be viewed as interim and subject to change when and if additional toxicity data becomes available. The three genotoxicity studies provide some assurance that pCBSA is not carcinogenic, but only additional studies, including an oncogenicity study, will allow a definitive conclusion on pCBSA's carcinogenic potential. Likewise, potential reproductive and developmental effects, as well as other potential effects from long-term exposure, need to be better studied. Until additional information is available, the uncertainty associated with these criteria is moderately high.

Unfortunately, there is an immediate need for toxicity criteria on pCBSA and there is no reason to believe additional toxicity information will be available in the near future. Therefore, I agree that the RfD and ADI developed by Dr. Parker are the most appropriate to use at this time.

If we can be of further assistance, please call me at (916) 324-9092.

Attachments

STATE OF CALIFORNIA—ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF TOXIC SUBSTANCES CONTROL
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M E M O R A N D U M

TO: Gloria Conti
Site Mitigation Branch, Region 4
245 West Broadway, Suite 425
Long Beach, CA 90802-4444

FROM: Judith A. Parker, Ph.D., DABT
Office of Scientific Affairs (OSA)
Human and Ecological Risk Section (HERS)

DATE: April 21, 1994

SUBJECT: Review of Toxicology Data for Montrose Chemical
PCA Code:14125: Site Code:400100: Work Phase:60

BACKGROUND

Region 4 requested on March 17, 1994, an OSA review of toxicology data generated for para-chlorobenzensulfonic acid (pCBSA), which is found in groundwater under the Montrose Chemical Site. This chemical was reported by the project manager to have also been found at the Stringfellow site and to be difficult to remove using "normal" remediation technology. The United States Environmental Protection Agency (USEPA) is the lead agency for the Montrose Chemical site.

DOCUMENT REVIEWED

The data reviewed consisted of photocopies supplied by USEPA of the available data on pCBSA. USEPA did a thorough literature search and reported these data as the only information available. The document consists of unpublished studies done under USEPA contract. A list of studies reviewed is included in the attachment. Articles describing analytical procedures used in the determination of pCBSA are also included; these were not reviewed. Perhaps a chemical engineer could use these to evaluate how pCBSA in groundwater could be remediated.

GENERAL COMMENTS

I searched the following data bases in April, 1994:

- Hazardous Substances Data Base (HSDB)
- USEPA Integrated Risk Information System (IRIS)
- Health Effects Summary Tables (HEAST)
- Registry of Toxic Effects of Chemicals (RTECS).

The only information available was an LD50 value of >500 mg/kg (rat, oral) in J. Agric. Food Chem., 25:501 (1977). Therefore, all conclusions will have to be based on the data that USEPA has generated.

Carl Hake, Ph.D., DABT, acted as consultant to the USEPA and recommended a series of tests to define the toxicology of pCBSA. The tests that he recommended were conducted and the reports submitted to DTSC for review.

Dr Peter Voytek, Director of the USEPA Reproductive Effects Assessment Group, recommended a battery of tests to define the toxicity of pCBSA. These tests were similar to those recommended by Dr. Hake.

SPECIFIC COMMENTS

Three mutagenicity tests were conducted that would detect both chromosomal alterations and point mutations. These studies were conducted by a reputable laboratory, complied with current testing protocols and followed the FDA Good Laboratory Practice Regulations. These three studies were negative; pCBSA did not cause genetic damage. Since a major mechanism of carcinogenesis is thought to be damage to the genetic material, the implication is that pCBSA would not be expected to be a carcinogen, at least not a genotoxic carcinogen.

A 28-day toxicity study was conducted with rats given daily doses of pCBSA by gavage (oral) at dose levels of 0 (vehicle, water), 10, 50, 500, 1000 or 2000 mg/kg/day. This is the longest study duration for tests using pCBSA. Two of ten males at the highest dose had symptoms that may have been related to pCBSA, although I think these were related to improper dosing. The females showed no signs of toxicity in any parameter measured (body weight, food consumption, clinical signs, hematologic values, or necropsy findings) at any dose level. The conservative estimate of a no observed effect level (NOEL) would be 1000 mg/kg/day. This study has a few weak points, but it provides useful information.

Reproductive and developmental toxicity was evaluated in a screening teratology test system developed by Kavlock and Chernoff. This study evaluated the effects of pCBSA administration (oral gavage) to pregnant female rats during days 7 through 16 of gestation at dose levels of 0 (vehicle, water), 1000 or 2000 mg/kg/day. There were no effects noted at any dose level in maternal weight gain, average litter size, pup survival or pup weight gain. The NOEL was >2000 mg/kg/day.

In a letter from Lawrence Valcovic, Acting Director of the USEPA Reproductive Effects Assessment Group to Gene Lucero, Director of the Office of Waste Programs Enforcement, it is stated that pCBSA has not produced any toxic effects and that long term study is not indicated. I concur with this opinion; the initial screening does not warrant further studies.

Toxicity data of structural analogs appears to be limited to the 4-chlorophenyl ester of 4-chlorobenezensulfonate (chlorfenson), which was registered as a pesticide (miticide). Its data base, which is more complete than that for pCBSA, gives no indication that carcinogenic effects would be expected. The oral LD50 of chlorfenson in rats was about 2000 mg/kg and a 2-year study in rats found only minimal effects at 50 ppm; the NOEL was 25 ppm (Handbook of Pesticide Toxicology, 1991, Academic Press, Inc. C. O. Knowles, pages 1471 -1473).

SPECIFIC TOXICITY COMMENTS

Neither a reference dose (RfD) nor a cancer slope factor for pCBSA have been generated by USEPA or Cal/EPA. These factors are usually based on interpretation of long term toxicity studies. Although such studies have not been conducted with pCBSA, we can still calculate an allowable daily intake (ADI) using provisional factors. The limited data available give no indication that pCBSA is carcinogenic, so no slope factor can be calculated. Using the 28-day study, with a NOEL of 1000 mg/kg/day, we can estimate a RfD by applying an uncertainty factor of 1000: (10X for extrapolation from short term exposure to long term exposure; 10X extrapolation from animal data to humans and 10X to account for sensitive human populations). In a letter dated January 31, 1986, addressed to Mr. Michael Green, Dr. Hake concluded that the consumption of 25 mg pCBSA/liter of water for 7 years would not be expected to produced toxicity in humans. My calculations support this finding. Assuming a daily consumption of 2 liters of water per day, a body weight of 70 kg and an RfD of 1 mg/kg/day, the concentration of pCBSA in water that would yield a hazard index of 1 or less would be 35 mg/L. This assumes exposure only by the ingestion of water, not inhalation of volatilized pCBSA or dermal absorption of pCBSA in water. It does not include any contribution from pCBSA contaminated soil.

CONCLUSION

Available toxicity data to review, the available data and comparison to an analogue does not indicate that pCBSA is likely to be highly toxic. A concentration of 25-35 mg/L water could be consumed by humans with no likely adverse effects. If we can be of

further assistance, please contact us.

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Senior Toxicologist

Reviewer: John P. Christopher, Ph. D., DABT
Staff Toxicologist

Attachment

ATTACHMENT

1. TOXICITY DATA ON pCBSA

The following studies performed for USEPA have been reviewed by OSA:

1. Study of the Teratogenic Potential of NaParachlorobenzene Sulfonic Acid N. Chernoff and M. Rosen. 10-22-85. Health Effects Research Laboratory, Research Triangle Park.

   pCBSA was administered by gavage to groups of 25 pregnant Sprague-Dawley rats at 0 (distilled water), 1000 or 2000 mg/kg/day on days 7 - 16 of gestation. No effects were seen on maternal weight gain, average litter size, pup survival or pup weight gain. NOEL > 2000 mg/kg/day.

2. L5178Y Mouse Lymphoma Cell Tk +/- Forward Mutation Assay. 1-20-86. Pharmakon Research International, Waverly, Pennsylvania.

   4-Chlorobenzenesulfonic acid was tested at 50, 125, 250, 500 or 1000 µg/L with and without rat liver homogenate. No increase in mutation frequency was noted at any dose level. These dose levels are not to be compared to anticipated human dose levels.

3. Ames Salmonella/Microsome Plate Test with 4-Chlorobenzenesulfonic acid. 12-29-85. Pharmakon Research International, Waverly, Pennsylvania.

   4-Chlorobenzenesulfonic acid was tested to 5000 µg/plate on strains TA 1535, 1537, 1538, 98 and 100, with and without rat liver homogenate. No increase in mutation frequency was noted at any dose level. These dose levels are not to be compared to anticipated human dose levels.

4. In vivo Bone Marrow Cytogenetics Rat Metaphase Analysis with 4-Chlorobenzenesulfonic Acid. 11-85. Pharmakon Research International, Waverly, Pennsylvania.

   Groups of six male Sprague Dawley were administered 2000 mg/kg of 4-chlorobenzenesulfonic acid in deionized water. Groups were killed 6, 12 or 24 hours later and 50 cells/animal analyzed. No increases in chromosomal aberrations were observed. This dose level is not to be compared to anticipated human dose levels.

5. Twenty-eight day oral (gavage) toxicity study in albino rats using A-100 (4-Chlorobenzenesulfonic Acid). 12-3-85. American Biogenics Corporation, Decatur, IL

Groups of 10 male and 10 female Sprague Dawley rats received A-100 by gavage at dose levels of 0 (distilled water), 10, 50, 500, 1000 or 2000 mg/kg/day for 28 days. No differences were noted in body weight gain, food consumption, clinical chemistry, hematologic values, or necropsy findings. Two males at the high dose exhibited signs of toxicity which may be related to misdoing. The NOEL for males was 1000 mg/kg/day (based on the findings in these 2 males) and for females was >2000 mg/kg/day. Several deficiencies in this study were noted: dose solutions were analyzed by USEPA but the results were not presented; body weights at study initiation covered a wide range; the report states lengths of dosing from 28 to 31 days. However, the study is still useful for the toxicity assessment of pCBSA.

2. CALCULATION OF TOXICITY VALUES

RfD = NOEL/Uncertainty factor = 1000 mg/kg/day / 1000 = 1 mg/kg/day

Hazard Index (HI) = RfD / daily intake

Daily intake of pCBSA = 2 L/day x concentration pCBSA (mg/L) x 1/70 kg bodyweight

Allowable daily intake (ADI) corresponds to RfD, i.e. HI = 1

ADI = 35 mg/L = 35 ppm