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APPENDIX E-2

METHODOLOGY OF THE KRUSKAL-WALLIS TEST

APPENDIX E.2

METHODOLOGY OF THE KRUSKAL-WALLIS TEST

The Kruskal-Wallis test is a nonparametric analysis of variance (ANOVA) by ranks test. It is a generalization of the two-sample Mann-Whitney Test, and is similar to the parametric F test, with ranks replacing the original observations (Andrews, 1954).

The Kruskal-Wallis test is generally used to test for differences among more than two groups. When used to test for differences between two groups, the results are identical to those from the nonparametric two-group Mann-Whitney test. The test involves the calculation of a test statistic, and comparison of this statistic with a critical value for a specified significance level. If the test statistic exceeds the critical value, it can be concluded that the two groups are significantly different.

The test statistic, H, is calculated as:

$$H = \frac{12}{N(N+1)} \sum_{i=1}^{k} \frac{R_i^2}{n_i} - 3(N+1)$$

where n_i is the number of observations in group i, N is the total number of observations in all groups, and R_i is the sum of the ranks of the n_i observations in group i. If there are any ties (observations of equal value, and therefore equal rank), a corrected H is calculated by dividing the original H by the following correction factor (C):

$$C = 1 - \frac{\sum_{i=1}^{m} (t_i^3 - t_i)}{(N^3 - N}$$

where t_i is the number of ties in the ith group of ties and m is the number of groups of tied ranks.

The H distribution is similar to the Chi-Square distribution; the critical value is equal to the Chi-Square critical value, obtained from tables or calculated. For all of the comparisons, a significance level of 0.05 was used; the critical value for two groups (i.e., one degree of freedom) at this significance level is 3.841.

POWER

The power (efficiency) of a statistical test is its ability to detect differences between groups. Nonparametric tests may need larger sample sizes than parametric tests because: (1) these tests make fewer assumptions concerning the distribution of the data, and, (2) procedures based on ranks have a discrete distribution rather than the continuous distribution of the parametric tests (EPA, 1992).

The Kruskal-Wallis test is generally considered to be among the most powerful of the nonparametric tests for inter-group differences. It is at least 86 percent as efficient as the analogous parametric ANOVA. When used with normally distributed data, it is 3/p = 95 percent as efficient as a parametric ANOVA test. When the data are not normally distributed, and/or when the population variances of the groups are not homogeneous, the test is much more powerful than the parametric test (Zar, 1984). In these cases, additional samples are not needed to match the power of a parametric test; power similar to that of a parametric test can be obtained with fewer samples. Statistical methods are not available to calculate the exact power of a nonparametric test.

The Kruskal-Wallis tests were performed with the combined Phase I and II data sets using *The Monitor System* software. The accuracy of the Monitor System's *H* and Chi-Square calculations provided on the ANOVA reports was checked and found to be correct. The results generally matched those performed with the t-tests. Although no exact power calculations can be provided, it is reasonable to assume that the actual power values for the nonparametric tests performed with the current data are higher than those calculated with the t-tests for the Phase I data because:

1. The departures from normality which may have reduced the power of some of the Phase I t-tests do not affect the nonparametric tests because these tests do make any assumptions about underlying distributions;

2. The large variances observed in many of the parameter groups which reduced the power of the t-test to identify differences with the given number of samples do not affect the nonparametric tests which are based on ranks, not measurement values; and,

3. Additional samples were collected for both background and SWMU data sets, increasing the power of all performed tests.

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DATA DISTRIBUTION
FOR ALL DATES

COMPANY: Central Landfill

SITE: Central Landfill

PROGRAM: Sediment

PROGRAM TYPE:

DATA GROUP: Sediment Data

All Duplicates Used
Significance Level (1 - alpha): 95%

Non-Detects = Detection Limit/2

LOCATION ID	SAMPLE SIZE	% N-Ds	SHAPIRO-WILK DISTRIBUTION	CALCULATED W	TABULAR W	SKEWNESS	KURTOSIS	COEFFICIENT OF VARIATION
Import								
PARAMETER: Aluminum, total								UNIT: mg/kg
SED	40	0	Normal	0.9591	0.9400	0.08	1.84	0.47
PARAMETER: Arsenic, total								UNIT: mg/kg
SED	34	24	Non-Normal	0.8998	0.9330	0.86	2.64	0.98
PARAMETER: Beryllium, total								UNIT: mg/kg
SED	34	0	Lognormal	0.9332	0.9330	0.84	2.31	1.02
PARAMETER: Cadmium, total								UNIT: mg/kg
SED	34	32	Non-Normal	0.8548	0.9330	1.16	3.43	1.17
PARAMETER: Lead, total								UNIT: mg/kg
SED	40	3	Non-Normal	0.9263	0.9400	1.09	3.17	0.94

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DATA DISTRIBUTION FOR ALL DATES

LOCATION ID	SAMPLE SIZE	% N-Ds	SHAPIRO-WILK DISTRIBUTION	CALCULATED W	TABULAR W	SKEWNESS	KURTOSIS	COEFFICIENT OF VARIATION
PARAMETER: Manganese, total								UNIT: mg/kg
SED	40	0	Lognormal	0.9596	0.9400	3.15	11.99	2.21
PARAMETER: Vanadium, total								UNIT: mg/kg
SED	40	0	Non-Normal	0.9197	0.9400	0.93	3.47	0.67

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DATA DISTRIBUTION
FOR ALL DATES

COMPANY: Central Landfill

SITE: Central Landfill

PROGRAM: Sediment

PROGRAM TYPE:

DATA GROUP: Background Sediment

All Duplicates Used
Significance Level (1 - alpha): 95%

Non-Detects = Detection Limit/2

LOCATION ID	SAMPLE SIZE	% N-Ds	SHAPIRO-WILK DISTRIBUTION	CALCULATED W	TABULAR W	SKEWNESS	KURTOSIS	COEFFICIENT OF VARIATION
Import								
PARAMETER: Aluminum, total								UNIT: mg/kg
SED_BK	7	0	Normal	0.9248	0.8030	-0.03	1.19	0.54
PARAMETER: Arsenic, total								UNIT: mg/kg
SED_BK	7	29	Lognormal	0.8516	0.8030	0.22	0.87	0.91
PARAMETER: Beryllium, total								UNIT: mg/kg
SED_BK	7	0	Normal	0.8988	0.8030	0.02	1.06	0.57
PARAMETER: Cadmium, total								UNIT: mg/kg
SED_BK	7	14	Normal	0.8803	0.8030	0.48	1.57	1.01
PARAMETER: Lead, total								UNIT: mg/kg
SED_BK	7	14	Normal	0.8967	0.8030	0.19	1.16	0.81

(continues)

DATA DISTRIBUTION FOR ALL DATES

LOCATION ID	SAMPLE SIZE	% N-Ds	SHAPIRO-WILK DISTRIBUTION	CALCULATED W	TABULAR W	SKEWNESS	KURTOSIS	COEFFICIENT OF VARIATION
PARAMETER: Manganese, total								UNIT: mg/kg
SED_BK	7	0	Normal	0.8392	0.8030	0.86	2.17	1.10
PARAMETER: Vanadium, total								UNIT: mg/kg
SED_BK	7	0	Normal	0.8927	0.8030	0.48	1.35	0.84

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ANOVA (KRUSKAL-WALLIS/NONPARAMETRIC)
FOR ALL DATES

COMPANY: Central Landfill
SITE: Central Landfill
PROGRAM: Sediment
PROGRAM TYPE:
DATA GROUP: Sediment Kruskal

All Duplicates Used — Non-Detects = Detection Limit/2
Significance Level (1 - alpha): 95%

Import

PARAMETER: Arsenic, total — UNIT: mg/kg

Number of Ties > 0 Total Degrees Of Freedom: 1 Calculated H' Value: 0.043 Tabular H: 3.841

Since the calculated Kruskal-Wallis H' value is less than the tabular value of H, it can be concluded that a statistically significant difference does not exist among the selected locations.

PARAMETER: Beryllium, total — UNIT: mg/kg

Number of Ties > 0 Total Degrees Of Freedom: 1 Calculated H' Value: 0.203 Tabular H: 3.841

Since the calculated Kruskal-Wallis H' value is less than the tabular value of H, it can be concluded that a statistically significant difference does not exist among the selected locations.

PARAMETER: Cadmium, total — UNIT: mg/kg

Number of Ties > 0 Total Degrees Of Freedom: 1 Calculated H' Value: 0.188 Tabular H: 3.841

Since the calculated Kruskal-Wallis H' value is less than the tabular value of H, it can be concluded that a statistically significant difference does not exist among the selected locations.

PARAMETER: Lead, total — UNIT: mg/kg

Number of Ties > 0 Total Degrees Of Freedom: 1 Calculated H' Value: 1.032 Tabular H: 3.841

Since the calculated Kruskal-Wallis H' value is less than the tabular value of H, it can be concluded that a statistically significant difference does not exist among the selected locations.

(continues)

ANOVA (KRUSKAL-WALLIS/NONPARAMETRIC)
FOR ALL DATES

All Duplicates Used — Non-Detects = Detection Limit/2
Significance Level (1 - alpha): 95%

PARAMETER: Manganese, total — UNIT: mg/kg

Number of Ties = 0 Total Degrees Of Freedom: 1 Calculated H Value: 5.294 Tabular H: 3.841

Since the calculated Kruskal-Wallis H value exceeds the tabular value of H, it can be concluded that a statistically significant difference may exist among the selected locations.

Additionally, based on the Bonferroni t-test, the location comparisons below with asterisks are considered statistically significant since the calculated critical values are less than or equal to the difference of the average ranks for each location comparison.

BACKGROUND LOCATION / COMPLIANCE LOCATION	CRITICAL VALUE	DIFFERENCE OF RANKS	AVERAGE RANK
SED	N/A	N/A	25.925
SED_BK	9.240	-12.925	13.000

PARAMETER: Vanadium, total — UNIT: mg/kg

Number of Ties > 0 Total Degrees Of Freedom: 1 Calculated H' Value: 1.157 Tabular H: 3.841

Since the calculated Kruskal-Wallis H' value is less than the tabular value of H, it can be concluded that a statistically significant difference does not exist among the selected locations.

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T-TEST (CABF)
FOR ALL DATES

COMPANY: Central Landfill

SITE: Central Landfill

PROGRAM: Sediment

PROGRAM TYPE:

DATA GROUP: Sediment T-Test

All Duplicates Used — Non-Detects = Detection Limit/2

Monitor Location SED — Background Location SED_BK

PARAMETER	UNIT	BACK SAMPLE SIZE	MON SAMPLE SIZE	BACK T VALUE	MON T VALUE	t*	tc	SIGNIFICANT DIFFERENCE
Import								
Aluminum, total	mg/kg	7	40	1.943	1.697	0.903	1.904	No

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DATA DISTRIBUTION
FOR ALL DATES

COMPANY: Central Landfill

SITE: Central Landfill

PROGRAM: Surface Water

PROGRAM TYPE:

DATA GROUP: Surface Water Data

All Duplicates Used
Significance Level (1 - alpha): 95%

Non-Detects = Detection Limit/2

LOCATION ID	SAMPLE SIZE	% N-Ds	SHAPIRO-WILK DISTRIBUTION	CALCULATED W	TABULAR W	SKEWNESS	KURTOSIS	COEFFICIENT OF VARIATION
Import								
PARAMETER: Aldrin								UNIT: mg/l
SW	36	100	Non-Normal	0.2507	0.9350	3.72	15.18	0.00
PARAMETER: Arsenic, total								UNIT: mg/l
SW	38	55	Non-Normal	0.8245	0.9380	1.24	3.72	0.00
PARAMETER: Beryllium, total								UNIT: mg/l
SW	38	11	Lognormal	0.9779	0.9380	1.77	6.22	0.00
PARAMETER: Manganese, total								UNIT: mg/l
SW	38	3	Non-Normal	0.9085	0.9380	3.33	13.44	2.18
PARAMETER: Mercury, total								UNIT: mg/l
SW	38	61	Non-Normal	0.8064	0.9380	1.98	6.49	0.00

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DATA DISTRIBUTION
FOR ALL DATES

COMPANY: Central Landfill
SITE: Central Landfill
PROGRAM: Surface Water
PROGRAM TYPE:
DATA GROUP: Background

All Duplicates Used — Non-Detects = Detection Limit/2
Significance Level (1 - alpha): 95%

LOCATION ID	SAMPLE SIZE	% N-Ds	SHAPIRO-WILK DISTRIBUTION	CALCULATED W	TABULAR W	SKEWNESS	KURTOSIS	COEFFICIENT OF VARIATION
Import								
PARAMETER: Aldrin								UNIT: mg/l
SW_BK	7	100	Non-Normal	0.6008	0.8030	0.75	1.40	0.00
PARAMETER: Arsenic, total								UNIT: mg/l
SW_BK	8	50	Normal	0.8224	0.8180	0.29	1.17	0.00
PARAMETER: Beryllium, total								UNIT: mg/l
SW_BK	8	0	Normal	0.9194	0.8180	0.46	1.69	0.00
PARAMETER: Manganese, total								UNIT: mg/l
SW_BK	8	13	Normal	0.8266	0.8180	0.78	1.80	0.92
PARAMETER: Mercury, total								UNIT: mg/l
SW_BK	8	63	Lognormal	0.9060	0.8180	1.65	4.22	0.00

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ANOVA (KRUSKAL-WALLIS/NONPARAMETRIC)
FOR ALL DATES

COMPANY: Central Landfill

SITE: Central Landfill

PROGRAM: Surface Water

PROGRAM TYPE:

DATA GROUP: Surface Water Kruska

All Duplicates Used
Significance Level (1 - alpha): 95%

Non-Detects = Detection Limit/2

Import

PARAMETER: Beryllium, total — UNIT: mg/l

Number of Ties > 0 Total Degrees Of Freedom: 1 Calculated H' Value: 0.322 Tabular H: 3.841

Since the calculated Kruskal-Wallis H' value is less than the tabular value of H, it can be concluded that a statistically significant difference does not exist among the selected locations.

PARAMETER: Manganese, total — UNIT: mg/l

Number of Ties > 0 Total Degrees Of Freedom: 1 Calculated H' Value: 11.108 Tabular H: 3.841

Since the calculated Kruskal-Wallis H' value exceeds the tabular value of H, it can be concluded that a statistically significant difference may exist among the selected locations.

Additionally, based on the Bonferroni t-test, the location comparisons below with asterisks are considered statistically significant since the calculated critical values are less than or equal to the difference of the average ranks for each location comparison.

BACKGROUND LOCATION COMPLIANCE LOCATION	CRITICAL VALUE	DIFFERENCE OF RANKS	AVERAGE RANK
SW_BK	N/A	N/A	9.125
* SW	8.589	17.401	26.526

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DATA DISTRIBUTION
FOR ALL DATES

COMPANY: Central Landfill

SITE: Central Landfill

PROGRAM: Groundwater

PROGRAM TYPE:

DATA GROUP: Groundwater Data

All Duplicates Used — Non-Detects = Detection Limit/2
Significance Level (1 - alpha): 95%

LOCATION ID	SAMPLE SIZE	% N-Ds	SHAPIRO-WILK DISTRIBUTION	CALCULATED W	TABULAR W	SKEWNESS	KURTOSIS	COEFFICIENT OF VARIATION
Import								
PARAMETER: Aluminum, total								UNIT: mg/l
GW	26	27	Lognormal	0.9648	0.9200	2.35	7.62	2.12
PARAMETER: Arsenic, total								UNIT: mg/l
GW	26	42	Non-Normal	0.8338	0.9200	2.73	9.95	0.90
PARAMETER: Barium, total								UNIT: mg/l
GW	26	8	Lognormal	0.9406	0.9200	1.99	7.15	1.15
PARAMETER: Beryllium, total								UNIT: mg/l
GW	26	15	Lognormal	0.9687	0.9200	2.52	9.25	0.00
PARAMETER: Cadmium, total								UNIT: mg/l
GW	26	65	Non-Normal	0.8164	0.9200	4.50	22.07	0.00

(continues)

DATA DISTRIBUTION
FOR ALL DATES

LOCATION ID	SAMPLE SIZE	% N-Ds	SHAPIRO-WILK DISTRIBUTION	CALCULATED W	TABULAR W	SKEWNESS	KURTOSIS	COEFFICIENT OF VARIATION
PARAMETER: Copper, total								UNIT: mg/l
GW	26	42	Lognormal	0.9516	0.9200	3.09	13.00	1.81
PARAMETER: Iron, total								UNIT: mg/l
GW	26	8	Lognormal	0.9484	0.9200	3.59	16.29	2.15
PARAMETER: Lead, total								UNIT: mg/l
GW	26	65	Non-Normal	0.9029	0.9200	2.32	7.39	1.44
PARAMETER: Manganese, total								UNIT: mg/l
GW	26	8	Lognormal	0.9751	0.9200	2.74	10.69	1.83
PARAMETER: Vanadium, total								UNIT: mg/l
GW	26	50	Lognormal	0.9431	0.9200	2.62	10.29	0.00

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DATA DISTRIBUTION
FOR ALL DATES

COMPANY: Central Landfill

SITE: Central Landfill

PROGRAM: Groundwater

PROGRAM TYPE:

DATA GROUP: Background

All Duplicates Used — Non-Detects = Detection Limit/2
Significance Level (1 - alpha): 95%

LOCATION ID	SAMPLE SIZE	% N-Ds	SHAPIRO-WILK DISTRIBUTION	CALCULATED W	TABULAR W	SKEWNESS	KURTOSIS	COEFFICIENT OF VARIATION
Import								
PARAMETER: Aluminum, total								UNIT: mg/l
GW BK	4	0	Normal	0.8271	0.7480	0.62	1.22	0.68
PARAMETER: Arsenic, total								UNIT: mg/l
GW BK	4	50	Normal	0.7913	0.7480	0.62	1.21	0.00
PARAMETER: Barium, total								UNIT: mg/l
GW BK	4	0	Normal	0.7947	0.7480	0.67	1.26	1.01
PARAMETER: Beryllium, total								UNIT: mg/l
GW BK	4	0	Normal	0.8087	0.7480	0.02	0.59	0.00
PARAMETER: Cadmium, total								UNIT: mg/l
GW BK	4	0	Normal	0.9210	0.7480	0.43	1.07	0.00

(continues)

DATA DISTRIBUTION
FOR ALL DATES

LOCATION ID	SAMPLE SIZE	% N-Ds	SHAPIRO-WILK DISTRIBUTION	CALCULATED W	TABULAR W	SKEWNESS	KURTOSIS	COEFFICIENT OF VARIATION
PARAMETER: Copper, total								UNIT: mg/l
GW BK	4	50	Normal	0.7545	0.7480	0.71	1.28	0.00
PARAMETER: Iron, total								UNIT: mg/l
GW BK	4	50	Lognormal	0.9497	0.7480	0.73	1.30	1.54
PARAMETER: Lead, total								UNIT: mg/l
GW BK	4	25	Normal	0.8874	0.7480	-0.03	0.65	0.45
PARAMETER: Manganese, total								UNIT: mg/l
GW BK	4	0	Normal	0.9661	0.7480	0.17	1.12	0.51
PARAMETER: Vanadium, total								UNIT: mg/l
GW BK	4	50	Normal	0.9861	0.7480	0.14	0.93	0.00

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ANOVA (KRUSKAL-WALLIS/NONPARAMETRIC)
FOR ALL DATES

COMPANY: Central Landfill

SITE: Central Landfill

PROGRAM: Groundwater

PROGRAM TYPE:

DATA GROUP: Groundwater Kruskal

All Duplicates Used
Significance Level (1 - alpha): 95%

Non-Detects = Detection Limit/2

Import

PARAMETER: Aluminum, total — UNIT: mg/l

Number of Ties = 0 Total Degrees Of Freedom: 1 Calculated H Value: 1.344 Tabular H: 3.841

Since the calculated Kruskal-Wallis H value is less than the tabular value of H, it can be concluded that a statistically significant difference does not exist among the selected locations.

PARAMETER: Barium, total — UNIT: mg/l

Number of Ties = 0 Total Degrees Of Freedom: 1 Calculated H Value: 3.130 Tabular H: 3.841

Since the calculated Kruskal-Wallis H value is less than the tabular value of H, it can be concluded that a statistically significant difference does not exist among the selected locations.

PARAMETER: Beryllium, total — UNIT: mg/l

Number of Ties > 0 Total Degrees Of Freedom: 1 Calculated H' Value: 0.411 Tabular H: 3.841

Since the calculated Kruskal-Wallis H' value is less than the tabular value of H, it can be concluded that a statistically significant difference does not exist among the selected locations.

PARAMETER: Copper, total — UNIT: mg/l

Number of Ties > 0 Total Degrees Of Freedom: 1 Calculated H' Value: 0.023 Tabular H: 3.841

Since the calculated Kruskal-Wallis H' value is less than the tabular value of H, it can be concluded that a statistically significant difference does not exist among the selected locations.

(continues)

ANOVA (KRUSKAL-WALLIS/NONPARAMETRIC)
FOR ALL DATES

All Duplicates Used
Significance Level (1 - alpha): 95%
Non-Detects = Detection Limit/2

PARAMETER: Manganese, total
UNIT: mg/l

Number of Ties = 0 Total Degrees Of Freedom: 1 Calculated H Value: 6.257 Tabular H: 3.841

Since the calculated Kruskal-Wallis H value exceeds the tabular value of H, it can be concluded that a statistically significant difference may exist among the selected locations.

Additionally, based on the Bonferroni t-test, the location comparisons below with asterisks are considered statistically significant since the calculated critical values are less than or equal to the difference of the average ranks for each location comparison.

BACKGROUND LOCATION COMPLIANCE LOCATION	CRITICAL VALUE	DIFFERENCE OF RANKS	AVERAGE RANK
GW BK	N/A	N/A	5.250
* GW	7.777	11.827	17.077

---------- End of Report ----------

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APPENDIX E-3

TOXICITY PROFILES

1,1,1-TRICHLOROETHANE

GENERAL BACKGROUND INFORMATION

1,1,1-Trichloroethane (also known as 1,1,1-TCA) is a colorless man-made chemical. It can be found in a liquid state, vapor, or dissolved in water or other chemicals. When found as a liquid, it evaporates rapidly and becomes a vapor in the air. 1,1,1-TCA has a sweet, sharp odor (ATSDR, 1990). 1,1,1-Trichloroethane is often used as a solvent to dissolve other substances such as glue or paint. Industrially, it is used to remove oil or grease from manufactured metal parts. Residentially, it is used for spot removal cleaners, aerosol sprays and glues. 1,1,1-Trichloroethane can be found in hazardous waste sites in the soil, water and in the air (ATSDR, 1990). It can be found in rivers, lakes, soil, drinking water, and drinking water from underground wells.

PHARMACOKINETICS

1,1,1-Trichloroethane is rapidly and completely absorbed by ingestion and inhalation (U.S. EPA, 1984). It distributes throughout the body and crosses the blood-brain barrier (U.S. EPA, 1984). If spilled topically, absorption via the skin would occur in small amounts because of quick evaporation into the air (U.S. EPA, 1984; ATSDR, 1990). Regardless of how 1,1,1-trichloroethane enters the body, most will quickly leave as exhalation occurs (ATSDR, 1990). What does not exit from expiration (metabolites) will be excreted through the urine and breath in a few days.

HUMAN TOXICOLOGICAL PROFILE

The toxic effects of 1,1,1-TCA are generally seen at concentrations well above those likely in an ambient environment. The most notable toxic effects of 1,1,1-TCA in humans are central nervous system depression, including anesthesia at very high concentrations, and impairment of coordination, equilibrium, and judgement at lower concentrations. Exposure to high concentrations may also result in cardiovascular effects, including premature ventricular contractions, decreased blood pressure and sensitization of the heart to epinephrine-induced arrhythmias, leading possibly to cardiac arrest (U.S. EPA, 1985; ATSDR, 1990). Acute exposure to minimal concentrations of 1,1,1-trichloroethane did not produce respiratory or lung volume effects (Dornette, 1960; Torkelson et al., 1958).

1,1,2-TRICHLOROETHANE

Summary

1,1,2-Trichloroethane induced liver tumors and pheochromocytomas in mice. It caused liver and kidney damage in dogs.

CAS Number: 79-00-5

Chemical Formula: $CH_2ClCHCl_2$

IUPAC Name: 1,1,2-Trichloroethane

Important Synonyms and Trade Names: Vinyl trichloride, ethane trichloride

Chemical and Physical Properties

Molecular Weight: 133.41

Boiling Point: 133.8°C

Melting Point: -36.5°C

Specific Gravity: 1.4397 at 20°C

Solubility in Water: 4,500 mg/liter at 20°C

Solubility in Organics: Soluble in alcohol, ether, and chloroform

Log Octanol/Water Partition Coefficient: 2.17

Vapor Pressure: 19 mm Hg at 20°C

Vapor Density: 4.63

Transport and Fate

Volatilization and subsequent photooxidation in the troposphere are probably the primary transport and fate processes for 1,1,2-trichloroethane. Some sorption, bioaccumulation, and biodegradation may occur, but these processes are probably not very important processes for trichloroethane transport or fate.

Risk	Concentration
10^{-5}	6.0 µg/liter
10^{-6}	0.6 µg/liter
10^{-7}	0.06 µg/liter

CAG Unit Risk (USEPA): 5.7×10^{-2} $(mg/kg/day)^{-1}$

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1,1-DICHLOROETHANE

GENERAL BACKGROUND INFORMATION

1,1-Dichloroethane (1,1-DCA) is a colorless, oily, lipophilic liquid which evaporates quickly at room temperature and has an ether-like odor. Its liquid and vapor forms ignite easily and may pose a fire hazard when handled improperly. It does not dissolve easily in water. 1,1-DCA is used primarily as an industrial solvent and as a dissolving agent for paint, varnish, finish removers and grease (ATSDR, 1990).

PHARMACOKINETICS

Little information exists quantitating the absorption of 1,1-DCA. However, based on its chemical and physical properties, it would be predicted to be readily absorbed via any route of exposure (ATSDR, 1990). Once absorbed, it should be readily distributed to bodily tissues, with highest concentrations achieved in tissues of greatest lipid content (Sato and Nakajima, 1987). A large percentage of an administered dose is exhaled unchanged (Mitoma et al., 1985). The remainded undergoes biotranformation mediated by the microsomal mixed function oxidase enzyme system to yield reactive acylchloride metabolite(s) which covalently bind to cellular macromolecules (Colacci et al., 1985). An alternative MFO-mediated pathway yields 2,2-dichloroethanol which undergoes subsequent oxidation to dichloroacetaldehyde and dichloroacetic acid (McCall et al., 1983). These metabolites are excreted through urine or further metabolized to CO_2 (Sato and Nakajima, 1987).

HUMAN TOXICOLOGICAL PROFILE

Relatively little information is available on the health effects of 1,1-dichloroethane in humans. It induces central nervous system depression and anesthesia upon inhalation. In fact, it was used as an inhalation anesthetic in the past. The use of 1,1-DCA as an inhalation anesthetic was discontinued when it was discovered that this compound induced cardiac arrhythmias in humans at anesthetic doses ((Reinhardt et al., 1971). No studies were located concerning threshold effects of exposure on any other organ system.

MAMMALIAN TOXICOLOGICAL PROFILE

Limited data indicate that 1,1-dichloroethane is less toxic than its isomer, 1,2-dichloroethane and most other chlorinated aliphatic solvents (Parker et al., 1979). Exposure of animals to 1,1-DCA results in central nervous system depression which may be fatal if exposure levels are high (Plaa and Larson, 1965). Nephrotoxicity has been observed in cats and mice

1,1-DICHLOROETHYLENE

GENERAL BACKGROUND INFORMATION

1,1-Dichloroethylene (1,1-DCE or vinylidene chloride) is a synthetic chemical used to make certain plastic products and flame retardant fabrics. It is released into the environment primarily as a result of air and water emissions coming from factories where 1,1-DCE is manufactured, hazardous waste sites where 1,1-DCE has been improperly disposed of, or as a result of accidental spills. 1,1-DCE is also found as a breakdown product of other chemicals present in the environment. Although high percentages of 1,1-DCE in soil and water quickly escape to the air, small concentrations remain and undergo biodegradation into other compounds. Once in the air, the compound rapidly decomposes through a variety of processes. It is estimated that 1,1-DCE released into the atmosphere persists for only about two days (ATSDR, 1988).

PHARMACOKINETICS

1,1-DCE is rapidly absorbed by the oral and inhalation routes. In animal studies, it was found to accumulate preferentially in the kidney, liver, and lung. 1,1-DCE undergoes complex biotransformation processes and numerous metabolites have been identified. The initial metabolic step is possibly the formation of an unstable reactive epoxide intermediate. Metabolites are ultimately conjugated with glutathione and excreted in urine (ATSDR, 1988).

HUMAN TOXICOLOGICAL PROFILE

Humans exposed to high concentrations of 1,1-DCE (approximately 4,000 ppm) show central nervous system depression which sometimes progresses to convulsions, spasm, and unconsciousness (Tierney et al., 1979). Repeated exposure to 1,1-DCE causes hepatotoxicity. Preliminary clinical findings on workers exposed to 1,1-DCE for up to 6 years in a polymerization plant in New Jersey revealed a high incidence of hepatotoxicity (U.S. EPA, 1985).

MAMMALIAN TOXICOLOGICAL PROFILE

Signs of central nervous system toxicity are the predominant effects observed in animals acutely exposed to high concentrations of 1,1-DCE via the inhalation route. The toxic signs consist primarily of central nervous system depression, lacrimation, dyspnea, tremor, convulsions, and narcosis, finally resulting in death (Klimisch and Freisberg, 1979a,b; Zeller et al., 1979). Rodents acutely exposed to high levels of 1,1-DCE (500 - 15,000 ppm) via inhalation show irritation of the mucous membranes and pulmonary edema, congestion and

active as a tumor-initiating agent (Van Duuren et al., 1979). U.S. EPA has classified 1,1-DCE as a Group C agent (possible human carcinogen) for which there is limited evidence of carcinogenicity in animals.

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1,2-DICHLOROETHYLENE

GENERAL BACKGROUND INFORMATION

There are two isomers of 1,2-dichloroethene (1,2-DCE), cis and trans. Neither of these isomers has developed wide industrial usage in the United States partly due to their flammability. The trans isomer is more widely used in industry than either the cis isomer or the 60:40 cis/trans mixture. It is used as either a low-temperature extraction solvent or as a direct solvent in materials such as dyes, perfume oils, waxes, resins and thermoplastics. It is also used as a chemical intermediate in the synthesis of polymers. 1,2-DCE is highly volatile, weakly adsorbed by soil and has no significant potential for bioaccumulation. It may volatilize from soil surfaces, but that portion not subject to volatilization is likely to be mobile in groundwater (IRP, 1985).

PHARMACOKINETICS

1,2-DCE is absorbed by all routes of exposure (see section on Relative Absorption Factors) (ATSDR, 1989). Distribution is expected to be rapid. Due to the lipophilic nature of 1,2-DCE, tissues of high lipid content would be expected to attain the highest levels. 1,2-DCE is metabolised via the mixed function oxidase enzyme system to chloroethylene epoxides which undergo rearrangement to dichloroacetaldehyde or chloroacetic acids (Henschler, 1977; Liebman and Ortiz, 1977). Excretion of 1,2-DCE and its metabolites has been largely uncharacterized (ATSDR, 1989).

HUMAN TOXICOLOGICAL PROFILE

1,2-DCE was once used as a general inhalation anesthetic in humans (Proctor and Hughes, 1978). Exposure to the trans isomer at a level of 2000 ppm causes burning of the eyes, vertigo and nausea (Proctor and Hughes, 1978). Within the limited industrial usage, only one toxic effect in humans was reported - a fatality due to very high vapor inhalation in a small enclosure (Rosenthal-Deussen, 1931). 1,2-DCE causes eye and skin irritation upon contact (Grant, 1974). There are no reports of long-term human exposure to 1,2-DCE isomers.

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DICHLOROBENZENE

Summary

Dichlorobenzene (DCB) is probably persistent in the natural environment. In rats, chronic oral exposure to dichlorobenzene caused liver and kidney damage and changes in the hematopoietic system. In humans, DCB is a skin and eye irritant; inhalation exposure causes nausea and irritates the membranes.

CAS Number: 1,2-Dichlorobenzene (1,2-DCB) 95-50-1
1,3-Dichlorobenzene (1,3-DCB) 541-73-1
1,4-Dichlorobenzene (1,4-DCB) 106-46-7

Chemical Formula: $C_6H_4Cl_2$

IUPAC Name: Dichlorobenzene

Important Synonyms and Trade Names: Dichlorobenzene, DCB

Chemical and Physical Properties

Molecular Weight: 147.01

Boiling Point: 1,2-DCB: 180.5°C
1,3-DCB and 1,4-DCB: 173°C

Melting Point: 1,2-DCB:-17.0°C
1,3-DCB:-24°C
1,4-DCB:-53°C

Specific Gravity: 1.3 at 20°C

Solubility in Water: 1,2-DCB: 145 mg/liter at 25°C
1,3-DCB: 123 mg/liter at 25°C
1,4-DCB: 80 mg/liter at 25°C

Solubility in Organics: Soluble in alcohol, ether, acetone, benzene, carbon tetrachloride, and ligroin

Log Octanol/Water Partition Coefficient: 3.38

Vapor Pressure: 1 mm Hg at 20°C

Vapor Density: 5.05

ACETONE

Summary

Acetone is a commonly used solvent, which probably is not very persistent in the environment. It is considered to have rather low toxicity, and no chronic health hazards have been associated with exposure to it. Acetone is not very toxic to aquatic organisms.

CAS Number: 67-64-1

Chemical Formula: CH_3-CO-CH_3

IUPAC Name: Propanone

Important Synonyms and Trade Names: Dimethyl ketone, 2-propanone

Chemical and Physical Properties

Molecular Weight: 58.08

Boiling Point: 56.2°C

Melting Point: -95°C

Specific Gravity: 0.7899 at 20°C

Solubility in Water: miscible

Solubility in Organics: Soluble in alcohol, ether, benzene, and chloroform

Log Octanol/Water Partition Coefficient: -0.24

Vapor Pressure: 190 mm Hg at 20°C

Vapor Density: 2.00

Flash Point: -16°C (closed cup)

Transport and Fate

Very limited information on the transport and fate of acetone was found in the literature reviewed. However, ketones in general are probably not very persistent. Acetone has a high vapor pressure and therefore would be expected to volatilize readily, but because of its high water solubility, volatilization is probably limited. Once in the atmosphere, it is apparently

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BENZENE

GENERAL BACKGROUND INFORMATION

Benzene is a clear, volatile, highly flammable, aromatic hydrocarbon which exists naturally and is produced by volcanoes and forest fires. Benzene is also a very common industrial solvent, produced from petroleum. It is used as a solvent for fats, inks, paints, plastics, rubber, in the extraction of oils from seeds and nuts, in photogravure printing, as a chemical intermediate and in the manufacture of detergents, explosives, pharmaceuticals and dyestuffs. It is also a component of gasoline and other petroleum-based fuels. Exposure to benzene can occur via inhalation, ingestion, especially of contaminated drinking water, and dermal contact (as in contact with liquid benzene found in gasoline.) (Sittig, 1981; ATSDR, 1989)

PHARMACOKINETICS

Benzene is readily absorbed through ingestion, moderately absorbed through inhalation and poorly absorbed through intact skin (see section on Relative Absorption Factors). Once in the bloodstream, benzene is distributed throughout the body, with the concentration in any one compartment dependent on the degree of perfusion of tissues by blood. Since benzene is lipid-soluble, it accumulates in fat, but the rate of accumulation is slow since fat is poorly perfused. The metabolites of benzene are responsible for its toxic effects. These include phenol (which is either formed via an unstable benzene oxide precursor or directly from benzene), catechol, hydroquinone and conjugated phenolic compounds. The primary site of benzene metabolism is the liver via the cytochrome P450 mixed function oxidase system. Some benzene metabolism may also occurs in the bone marrow via the same enzyme system. Benzene is excreted either unchanged from the lungs or as metabolites in the urine (ATSDR, 1989).

HUMAN TOXICOLOGICAL PROFILE

Benzene targets its effects on the hemopoietic, immune and nervous systems (ATSDR, 1989). Exposure to benzene has produced irritation of the skin, eyes and upper respiratory tract. Acute exposure has produced central nervous system depression, headache, dizziness, nausea, convulsions, coma and death at extremely high concentrations (Sittig, 1981). Health effects in humans have been reported starting as low as 50 ppm via inhalation. Twenty-five ppm for 6 hrs had no obvious effects though benzene was detected in blood (Sandmeyer, 1981). Early autopsy reports found benzene-induced hemorrhages of the brain, pericardium, urinary tract, mucous membranes and skin (Sittig, 1981). Chronic exposure to benzene produces blood changes involving an initial increase in levels of erythrocytes, leukocytes and

CARBON TETRACHLORIDE

GENERAL BACKGROUND INFORMATION

Carbon Tetrachloride is a clear, heavy aromatic liquid with a sweet odor. Although this compound does not occur naturally, it is distributed extensively in the earth's atmosphere due to its extensive anthropogenic production and use. Carbon tetrachloride is currently widely used as a refrigerant and a propellant. Carbon tetrachloride is also used a solvent for oil, fats, lacquers, varnishes, rubber, waxes and resins. Until the mid-1960s, carbon tetrachloride was used as an industrial degreaser, as a household spot remover, and as a fire-extinguishing agent. Until 1986, carbon tetrachloride was used to fumigate grain. Carbon tetrachloride is very stable in the atmosphere, with a half-life in air of about 30-100 years. Thus, it persists in the environment for many years (Sittig, 1981; ATSDR, 1989).

PHARMACOKINETICS

Carbon tetrachloride is readily absorbed through ingestion and inhalation and poorly absorbed through the skin (see section on Relative Absorption Factors). The metabolism of carbon tetrachloride occurs primarily in the liver, where a specific form of hepatic cytochrome P-450 initiates a reductive dehalogenation yielding a trichloromethyl free radical and a chloride ion. The trichloromethyl radical is then further reacted upon either anaerobically or aerobically. Anaerobically, either $CHCl_3$, Cl_3CCCl_3 or $CO^+/HCOO^-$ can be produced depending on which of several anaerobic reactions take place. Aerobically, the precursor, Cl_3CO_4 could be produced, leading to formation of phosgene ($COCl_2$). Hydrolytic cleavage of $COCl_2$ leads to formation of HCl. Although it is known that metabolism of carbon terachloride plays an important role in its toxicity, the specific mechanism relating the metabolites to toxicity has not yet been determined. Excretion of carbon tetrachloride from the body has been found to occur largely in the form of the parent compound. Exposure studies in animals have shown that about 30-40% of an inhaled dose of carbon tetrachloride is recovered in expired air and about 50-60% is recovered in feces. Via oral exposure, one rat study indicated that about 70-90% of an administered oral dose was recovered in expired air and lower amounts were recovered as CO_2 or $CHCl_3$ or as nonvolatile metabolites in feces or urine. Via dermal exposure, carbon tetrachloride excretion has also been found to occur rapidly through expired air, but this was not quantified (ATSDR, 1989).

HUMAN TOXICOLOGICAL PROFILE

Most of the human health data for carbon tetrachloride come from acute exposure case studies in individuals who have been exposed to large doses for short periods of time. Health effects of carbon tetrachloride include defatting of skin leading to a dry, fissured dermatitis

International Agency for Research on Cancer (IARC) that sufficient evidence exists to designate this compound carcinogenic in experimental animals (ATSDR, 1989).

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CHLOROBENZENE

GENERAL BACKGROUND INFORMATION

Chlorobenzene is a clear liquid with an almond-like odor. Although chlorobenzene does not occur naturally in the environment, it is used in industry as a solvent, in the manufacture of aniline, phenol and chloronitrobenzene, and as an intermediate in the manufacture of dyestuffs and pesticides (ATSDR, 1990; Sittig, 1981).

PHARMACOKINETICS

Chlorobenzene is assumed to be readily absorbed via ingestion, moderately absorbed through inhalation and poorly absorbed through the skin, based on its structural similarity to benzene (see section on Relative Absorption Factors). The major metabolites of chlorobenzene are p-chlorophenylmercapturic acid and 4-chlorocatechol. Excretion of chlorobenzene occurs via urine in the form of its two metabolites, with the excretion of p-chlorophenylmercapturic acid reported to be much lower than of 4-chlorocatechol. A portion of an absorbed dose is excreted as unchanged chlorobenzene through the lungs (ATSDR, 1990).

HUMAN TOXICOLOGICAL PROFILE

Acute exposure to chlorobenzene has produced the following health effects in workers exposed to high levels: irritation of the eyes and nose, skin irritation, central nervous system depression with symptoms such as drowsiness, incoherence, numbness, nausea and vomiting. However, these workers were simultaneously exposed to other solvents so it is not clear whether chlorobenzene is responsible for these effects (ATSDR, 1990; Sittig, 1989).

MAMMALIAN TOXICOLOGICAL PROFILE

Acute lethality via both inhalation and ingestion is relatively low in animals. One study produced 100% mortality in mice after 2 hrs of exposure to 4,300 ppm. In rats exposed to a single dose of 4000 mg/kg and mice exposed to a single dose of 1000 mg/kg via corn oil by gavage, death occurred in 2-3 days (ATSDR, 1990). Animal studies indicate that exposure to chlorobenzene via either inhalation or ingestion can produce severe kidney and liver damage. Typical signs of liver damage reported include increased serum enzymes, changes in liver weights, degeneration, necrosis and interference with porphyrin metabolism. Signs of kidney damage include degeneration or focal necrosis of proximal tubules and increased kidney weights. Animal evidence also exists that chlorobenzene is immunotoxic via ingestion with the potential of producing thymic necrosis and lymphoid or myeloid depletion of bone marrow, spleen or thymus. Neurological effects, manifested by miscellaneous spasms and

CHLOROFORM

GENERAL BACKGROUND INFORMATION

Chloroform is a clear, colorless, liquid with a characteristic odor, which exists both naturally and as a man-made compound. Chloroform was one of the earliest general anaesthetics but was later banned because of toxic effects. Chloroform is largely used in the production of fluorocarbon 22 (used as a coolant in air conditioners and to make fluoropolymers) (ATSDR, 1989). In addition, chloroform is used as a solvent, in the extraction and purification of pharmaceuticals, in the manufacture of pesticides and dyes and in various products including fire extinguishers, dry cleaning agents, artificial silk, plastics and floor polishes. Chloroform is also widely found in drinking water supplies as a byproduct of chlorination (ATSDR, 1989; Sittig, 1981).

PHARMACOKINETICS

Chloroform is readily absorbed via inhalation and ingestion and poorly absorbed through the skin, unless the dose is occluded, in which case it is very well absorbed (see section on Relative Absorption Factors). Chloroform is lipid-soluble and passes through cell membranes easily. Thus it will reach the central nervous system and cross the placental barrier. It has been found in fresh cow's milk and is thus expected to reach human milk too. Chloroform is metabolized via cytochrome P450 by oxidative dechlorination to form phosgene. The phosgene either reacts with glutathione to form diglutathionyl dithiocarbonate or causes cytotoxicity directly by reacting with other cellular constituents. Inorganic chloride ion and carbon monoxide are minor metabolites of chloroform metabolism. Although there are species differences as to relative amounts metabolized, chloroform is largely excreted unchanged through the lungs. Carbon dioxide is also a major endproduct of chloroform metabolism, most of which is excreted via the lungs but some of which is also incorporated into endogenous metabolites and excreted as bicarbonate, urea, methionine and other amino acids. Carbon monoxide is a minor metabolite also excreted through the lungs. In addition, inorganic chloride ions are excreted via the urine (ATSDR, 1989).

HUMAN TOXICOLOGICAL PROFILE

Skin contact with chloroform can produce burns. Chloroform is a central nervous system depressant and was used in the past as an anaesthetic until it was determined that it caused liver and kidney toxicity. Specific central nervous system symptoms resulting from acute exposure include fatigue, dizziness, headache, digestive disturbance and mental dullness, as well as

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ETHYLBENZENE

GENERAL BACKGROUND INFORMATION

Ethylbenzene is a colorless liquid that smells like gasoline. It is volatile and flammable. Ethylbenzene occurs naturally in coal tar and petroleum, and is also manufactured for commercial uses in paints, inks, and insecticides (ATSDR, 1990). The two major uses of ethylbenzene are in the plastic and rubber industry, where it is used in the synthesis of styrene (U.S. EPA, 1980). Gasoline contains about 2% (by weight) ethylbenzene (ATSDR, 1990). Ethylbenzene has a wide environmental distribution due to its widespread use.

PHARMACOKINETICS

Ethylbenzene has been shown to be readily absorbed via inhalation, ingestion, and dermal exposure in humans as well as in laboratory animals (see section on Relative Absorption Factors). Following exposure, ethylbenzene is distributed throughout the body, with the highest levels detected in the kidney, lung, adipose tissue, digestive tract, and liver (Chin et al., 1980). There appears to be quantitative differences in metabolism of the chemical in humans and laboratory animals. However, in all species, ethylbenzene undergoes a variety of microsomally-mediated side-chain hydroxylations to yield the major metabolites, mandelic acid and phenylglyoxylic acid (Engstrom et al., 1984). The oxidation products are conjugated followed by urinary excretion which appears to be complete within 2 days of exposure (ATSDR, 1990).

HUMAN TOXICOLOGICAL PROFILE

Humans exposed to low levels of ethylbenzene in air for short periods of time experience eye and throat irritation. Exposure to higher levels may cause more severe effects such as central nervous system depression, decreased movement and dizziness, and more severe mucous membrane irritation. No studies have reported death in humans following exposure to ethylbenzene. No information was located to indicate that ethylbenzene produces toxicity in other organ systems upon short-term or prolonged exposure (ATSDR, 1990).

MAMMALIAN TOXICOLOGICAL PROFILE

Animal studies indicate that the primary symptoms resulting from acute exposure to ethylbenzene are manifested as neurological and respiratory depression. Other studies suggest that the liver, kidney and hematopoietic system may also be targets of ethylbenzene toxicity (ATSDR, 1990). Studies indicate that ethylbenzene exposure of pregnant rats can produce fetotoxic effects at doses that also induce maternal toxicity (Andrew et al., 1981).

METHYL ETHYL KETONE

GENERAL BACKGROUND INFORMATION

Methyl ethyl ketone (also known as MEK or 2-butanone) is a colorless liquid with an acetone-like odor, moderate water solubility and high volatility. The major uses of MEK are as a solvent for coatings, adhesives and printing inks, as a cleaning/degreasing agent and as a chemical intermediate in the production of synthetic leathers, transparent paper and aluminum foil. MEK is a highly flammable substance and may pose a fire hazard if handled improperly (ATSDR, 1990).

PHARMACOKINETICS

MEK is readily absorbed by all routes of exposure (see section on Relative Absorption Factors). It is readily soluble in blood and appears to distribute uniformly to all organs (Perbellini et al., 1984). MEK is metabolized by both oxidative and reductive pathways (DiVincenzo et al., 1976). It undergoes reduction to 2-butanol and oxidation to 3-hydroxy-2-butanone, which is further reduced to 2,3-butanediol. Small amounts of unmetabolized MEK can be excreted in urine or exhaled air. All metabolites are excreted in the urine as glucuronides or sulfate conjugates.

HUMAN TOXICOLOGICAL PROFILE

MEK can produce irritation to the eyes, respiratory tract and skin following high level exposure. Central nervous system effects have been reported, including headache, dizziness, nausea and fatigue (ATSDR, 1990). No studies were located regarding the possible consequences of exposure on the liver, kidney, reproductive organs or developing fetus. This ketone has been demonstrated to be very hazardous in combination with other solvents by potentiating the neurotoxicity of n-hexane, methyl-n-butyl ketone and ethyl-n-butyl ketone (Altenkirch et al., 1979).

MAMMALIAN TOXICOLOGICAL PROFILE

High level inhalation exposure to MEK results in upper respiratory tract and ocular irritation. Exposure to high level MEK by the inhalation or oral route resulted in liver congestion, increase liver weight and renal tubular necrosis (Patty, 1935; Cavender et al., 1983). Narcosis and incoordination, indicators of central nervous system effects, were also observed, with no signs of periphereal neuropathy. Inhalation exposure during gestation resulted in fetotoxic effects such as reduced fetal weight, skeletal variations and delayed

TETRACHLOROETHYLENE

GENERAL BACKGROUND INFORMATION

The major use for tetrachloroethylene (perchloroethylene, PCE) is in the dry-cleaning industry. Its popularity in this area is due to its nonflammability, ease of recovery for reuse and its compatibility with various fabrics. It is also used in cold cleaning and vapor degreasing of metals. Its remaining uses are as a chemical intermediate in the synthesis of fluorocarbons, various manufacturing and industrial processes as well as medicinal uses (IRP, 1985).

PHARMACOKINETICS

PCE is readily absorbed by humans through the lungs into the blood. Pulmonary uptake is proportional to ventilation rate, duration of exposure and (at lower concentrations of PCE) to the concentration of PCE in the inspired air (Hake and Stewart, 1977). PCE is also rapidly aborbed following oral administration, but is poorly absorbed following dermal exposure (see section on Relative Absorption Factors). Distribution occurs rapidly with the highest concentrations of PCE achieved in tissues of high fat content (ATSDR, 1990). Metabolism of PCE is believed to be mediated by the microsomal mixed function oxidase enzyme system involving the formation of an epoxide intermediate. Major metabolites of PCE are trichloroacetic acid and trichloroethanol. Unmetabolized PCE is excreted largely by exhalation with urinary excretion of metabolites representing a small percentage (ATSDR, 1990).

HUMAN TOXICOLOGICAL PROFILE

Stewart et al. (1977) found that exposure of 11 subjects to a mean PCE concentration of 101 ppm for 7 hours produced symptoms of headache, dizziness, difficulty in speaking, and sleepiness. Long-term exposed subjects are also reported to experience effects such as short-term memory defects, ataxia, irritability, disorientation, and sleep disturbances (USEPA, 1985). PCE causes hepatotoxicity in humans. A number of reports of liver damage after inhalation of PCE in acute or chronic exposure situations have been documented (Hake and Stewart, 1977). PCE ingestion in humans results in symptoms indicative of liver damage, including elevated SGOT and SGPT levels, hepatomegaly, and fatty degeneration of the liver cells (Koppel et al., 1985).

carcinogenicity in humans, the U.S. EPA places PCE in Group B2, meaning that is considered a probable human carcinogen.

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TOLUENE

GENERAL BACKGROUND INFORMATION

Toluene is a clear, colorless organic liquid with a sweet smell and a high degree of lipid solubility. It is used as an industrial solvent/degreaser, as an intermediate in the manufacture of chemicals and pharmaceuticals, and is present as a component of gasoline and other fuels, paints, lacquers, adhesives, rubber and printing ink. Toluene is a volatile molecule with relatively low water solubility. It is flammable and may pose a fire hazard if handled improperly (ATSDR, 1989).

PHARMACOKINETICS

Toluene is readily absorbed by all routes of exposure (see section on Relative Absorption Factors). Once absorbed, it is rapidly distributed to all organ systems, including fetal tissue, with highest concentrations occuring in organs with high lipid content such as adipose tissue, brain and bone marrow. Toluene undergoes primarily oxidative metabolism to benzyl alcohol mediated by the mixed function oxidase enzyme system. Benzyl alcohol is further oxidized by alcohol and aldehyde dehydrogenase to produce benzoic acid which is primarily conjugated with glycine or glucuronic acid and excreted in urine as hippuric acids or benzoyl glucuronide. Toluene may also be excreted unchanged in exhaled air. Metabolism and excretion occurs rapidly, with the major portion occurring within 12 hours of exposure (Fishbein, 1985).

HUMAN TOXICOLOGICAL PROFILE

In humans, the most profound effects of toluene are on the central nervous system. Acute exposure results in reversible depression of the central nervous system, neurological dysfunction, impaired performance and narcosis. Chronic exposure has been reported to result in permanent central nervous system effects such as ataxia, tremors and impaired speech, hearing and vision (ATSDR, 1989). Toluene vapors cause irritation of the upper respiratory tract, mucous membranes and eyes, and may produce cardiac arrhythmias upon chronic exposure (Anderson et al., 1982). Reports of effects on the hematological system, liver, kidney, immune system, reproductive organs and the developing fetus are confounded by exposure to multiple solvents (ATSDR, 1989).

MAMMALIAN TOXICOLOGICAL PROFILE

Toluene has been demonstrated to produce similar effects in humans and animals. The major target organ following acute or chronic exposure is the central nervous system. Signs

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TRICHLOROETHYLENE

GENERAL BACKGROUND INFORMATION

Trichloroethylene (TCE) is widely used as an industrial solvent, particularly in metal degreasing, which consumes about 90% of TCE produced annually in the U.S. TCE is also used for dry-cleaning, as a low-temperature heat exchange fluid, as a fumigant, as a diluent in paints and adhesives, in aerospace operations, and in textile processing. Previously, TCE was used as an extractant in food-processing. These uses were discontinued in 1975 due to evidence of possible carcinogenic activity. Its earlier use in anesthetics was also discontinued (IRP, 1985).

PHARMACOKINETICS

Absorption of TCE from the gastrointestinal and respiratory tracts is extensive. TCE is extensively metabolized in humans to trichloroethanol, trichloroethanol glucuronide, and trichloroacetic acid. Although the liver is the primary site of TCE metabolism, there is evidence for extrahepatic metabolism in the lungs and kidneys (ATSDR, 1988).

HUMAN TOXICOLOGICAL PROFILE

TCE is assumed to be responsible for the deaths of four men employed at degreasing operations using TCE as the solvent (Kleinfeld and Tabershaw, 1954). Toxicological analysis revealed TCE in varying concentrations in various tissues. Kleinfeld and Tabershaw (1954) reported that, despite treatment, a man died 11 days after he accidentally drank an unknown quantity of TCE. TCE has been shown to affect the central nervous system. Short-term exposure to high concentrations of TCE caused dizziness, headache, nausea, confusion, facial numbness, blurred vision, and, at very high levels, unconsciousness. Longer exposures cause ataxia, decreased appetite, sleep disturbances, and trigeminal neuropathy (U.S. EPA, 1985). Information regarding hepatotoxicity in humans is limited and derived from acute overexposures. U.S. EPA (1985) has concluded that it is unlikely that chronic exposure to trichloroethylene at concentrations found or expected in ambient air would result in liver damage.

MAMMALIAN TOXICOLOGICAL PROFILE

In laboratory animals, the acute toxicity of trichloroethylene is low. Oral LD_{50} values of 4920 mg/kg in the rat, 3200 mg/kg in the mouse and 2800 mg/kg in the dog have been reported. In a study by Baker (1958), several dogs died within 20 minutes of being exposed to TCE at 30,000 ppm. Rats exposed to 20,000 ppm for 5 hours died (Adams, 1951). A 2-year study

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VINYL CHLORIDE

GENERAL BACKGROUND INFORMATION

About 90% of the vinyl chloride produced in the U.S. is used to manufacture polyvinyl chloride (PVC) and other vinyl polymers. The remainder is used to synthesize 1,1,1-trichloroethane. The major uses of PVC are in the building and construction industries, in consumer goods, packaging and electrical wire insulation. PVC is also used in packaging, such as plasticized film, bottles and bottle-cap liners and gaskets (IRP, 1985).

PHARMACOKINETICS

Respiratory and gastrointestinal absorption of vinyl chloride is rapid and nearly complete. Distribution may be widespread with the highest concentration of the parent compound located in the fat. Metabolism and excretion occur rapidly. The highest levels of excretory products are located in the liver and kidney (ATSDR, 1989).

HUMAN TOXICOLOGICAL PROFILE

Several epidemiologic studies have associated occupational exposure with impaired liver function and biochemical or histological evidence of liver damage (U.S. EPA, 1985a,b). Symptoms and signs of liver disease associated with occupational exposure to vinyl chloride include pain or discomfort, hepatomegaly, portal hypertension, thrombocytopenia, esophageal varices (Lee et al., 1977). Acute toxicity at high levels has resulted in lethality among occupationally exposed workers. Death appeared to be due to narcosis (U.S. EPA, 1985a). Acute inhalation exposure to high levels of vinyl chloride leads to CNS effects. Exposures to 8,000 to 20,000 ppm have been associated with dizziness, giddiness, euphoria, ataxia, headache, and narcosis (Nicholson et al., 1975; Lester et al., 1963). Dinceva et al. (1985) reported electroencephalogram changes that they thought were indicative of early evidence of neurotoxicity in workers exposed to vinyl chloride along with other organic solvents. Vinyl chloride disease is the name given to the total clinical syndrome associated with occupational exposure. It includes a syndrome known as acroosteolysis or dissolution of the ends of the distal phalanges of the hands, circulatory disturbance in the extremities, Raynaud syndrome, scleroderma, hematologic effects, and lung and liver effects (ATSDR, 1989).

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XYLENES

GENERAL BACKGROUND INFORMATION

Xylenes are colorless liquid organic molecules with a sweet odor and a high degree of lipid solubility. There are three isomers of xylene: meta- ortho- and para-xylene (m-, o- and p-xylene, respectively). The term "total xylenes" is used to designate a mixture of the three possible isomers, in any proportions. They are commonly used as industrial solvents, as components of paints, varnishes, cleaners, degreasers and gasoline and as chemical intermediates in the manufacture of other chemicals, plastics and synthetic fibers. Xylenes are volatile molecules and therefore, evaporate quickly. They are also flammable and may pose a fire hazard if handled improperly (ATSDR, 1990).

PHARMACOKINETICS

Xylenes are readily absorbed by all routes of exposure (see section on Relative Absorption Factors). Xylenes are very soluble in blood and therefore are absorbed easily into the systemic circulation during exposure (Astrand, 1982). Following absorption, distribution occurs rapidly to all organs, including fetal tissue, with greatest distribution occuring to organs having a high lipid content, such as adipose tissue, bone marrow and brain (Astrand, 1982; Engstron and Bjurstrom, 1978; Riihimaki et al., 1979). In humans, xylenes are primarily metabolized by the mixed function oxidase enzyme system to methylbenzyl alcohols which are further oxidized by alcohol and aldehyde dehydrogenase to yield methyl benzoic acids. The acids are readily conjugated and excreted in urine (Fishbein, 1985). In addition, a small percentage (3-6%) is exhaled unchanged due to the volatile nature of these compounds.

HUMAN TOXICOLOGICAL PROFILE

Human data suggests that the three xylene isomers all produce qualitatively similar effects, although the individual isomers are not necessarily equal in potency with regard to a given effect (ATSDR, 1990). Exposure, by any route, results in primarily central nervous system effects that may include headaches, nausea, mental confusion, narcosis, impaired learning and memory, dizziness, tremors, unconscienceness and coma, depending on dose and length of exposure. High doses may result in death. The respiratory system may also be a target of xylene toxicity in humans, producing respiratory tract irritation, pulmonary edema and inflammation after inhalation. Ocular irritation may result following exposure to xylene vapors. Skin irritation, dryness and scaling may result following dermal exposure. Limited data are available concerning effects of exposure on the hepatic, renal, cardiovascular,

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2,4-DICHLOROPHENOL

Summary

2,4-Dichlorophenol (2,4-DCP) is not very persistent in the environment. There is equivocal evidence suggesting that it may act as a tumor promoter. Subcutaneous administration of 2,4-dichlorophenol to pregnant mice induced minor teratogenic effects. Chronic exposure caused nonspecific liver changes in mice.

CAS Number: 120-83-2

Chemical Formula: $C_6H_3Cl_2OH$

IUPAC Name: 2,4-Dichlorophenol

Important Synonyms and Trade Names: 2,4-DCP

Chemical and Physical Properties

Molecular Weight: 163.0

Boiling Point: 210°C

Melting Point: 45°C

Specific Gravity: 1.383 at 25°C

Solubility in Water: 4,500 mg/liter

Solubility in Organics: Soluble in benzene, alcohol, ether, and chloroform

Log Octanol/Water Partition Coefficient: 2.75

Vapor Pressure: 0.12 mm Hg at 20°C (calculated)

Vapor Density: 5.62

pKa: 7.48

Flash Point: 114°C

Toxicity to Wildlife and Domestic Animals

Species mean acute values reported for the freshwater species *Daphnia magna*, fathead minnow, and bluegill are 2,605, 8,230, and 2,020 µg/liter, respectively. A chronic value of 365 µg/liter and an acute-chronic ratio of 23 are reported for the fathead minnow. The only information available concerning saltwater species indicates that the mountain bass *Kuhlia sandvicensis* exhibits a moderate reaction in response to 20 mg/liter 2,4-DCP. Complete destruction of chlorophyll and 56.4% reduction of photosynthetic oxygen production are observed after exposure of the freshwater alga *Chlorella pyrenoidosa* to 100 and 50 mg/liter, respectively. The weighted average bioconcentration factor for 2,4-DCP and the edible portion of all freshwater and estuarine organisms consumed by Americans is calculated to be 40.7.

2,4-DCP residues have been detected in the liver and kidneys of cattle and chickens, and in chicken eggs. Concentrations of 2,4-DCP in animal tissues are reported to diminish rapidly after withdrawal of the 2,4-DCP precursor, 2,4-dichlorophenoxyacetic acid (2,4-D). No information concerning toxicity of 2,4-DCP to domestic animals is available.

Regulations and Standards

Ambient Water Quality Criteria (USEPA):

Aquatic Life

The available data are not adequate for establishing criteria.

Human Health

Health criterion: 3.09 mg/liter
Organoleptic criterion: 0.3 µg/liter

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4-METHYLPHENOL

I. CHEMICAL AND PHYSICAL INFORMATION

A. Synonyms: p-cresol; 1-hydroxy-4-methylbenzene; 4-hydroxytoluene
B. CAS No. : 106-44-5
C. Molecular Formula: C_7H_8O
D. Molecular Weight: 108.13
E. Chemical and physical properties:

1. Physical State: Crystalline solid
2. Odor/Odor Threshold: Phenolic; sweet and tarry; 0.0005 ppm
3. Melting point: 34.8°C
4. Boiling point: 201.9°C at 760 mmHg
5. Vapor pressure: 0.13 mmHg at 25°C
6. Specific gravity:
7. Vapor density: 3.72
8. Refractive index:
9. Solubility in water: 22.6 g/l at 40°C
10. Solubility in organic solvents:
11. Log octanol/water partition coefficient: 1.94
12. Henry's Law Constant: 9.6×10^{-7} atm-m^3/mol.

F. Uses:

II. TRANSPORT AND FATE

When released to the atmosphere, 4-methylphenol will react with photochemically produced hydroxyl radicals during the day (half-life of 10 hours) and react with nitrate radicals at night (half-life of 4 minutes). It will also be scavenged by rain and oxidized by metal cations in rain water and fogwater. Biodegradation is expected to be the dominant loss mechanism when 4-methylphenol is released into water. Volatilization, bioconcentration in fish, and adsorption to sediment will be unimportant and photolysis is only expected to be significant in surface waters of oligiotrophic lakes.

III. TOXICITY

A. Human: Toxic properties from short-term exposure of 4-methylphonal are similar to those of phenol. 4-methylphenol may be absorbed through the skin and this is a major route of exposure. Contact with skin may cause inflammation, blistering and scarring. Respiratory hazard is low because of its low volatility. However, exposure to high vapor concentrations may cause irritation to the respiratory tract. Ingestion has caused pneumonia, irritation, kidney and nervous system damage.

BENZO[a]ANTHRACENE

GENERAL BACKGROUND INFORMATION

Benzo[a]anthracene (BaA) is a member of the polycyclic aromatic hydrocarbons (PAH). PAHs are a class of non-polar compounds that contain two or more aromatic rings. They are ubiquitous in nature and are both naturally occurring and man-made. The overall database for benzo[a]anthracene is limited. Human exposures to BaA can come from the oral, inhalation or dermal routes. BaA is produced when gasoline or other organic material is burned. It is also found in cigarette smoke and cooked food. People most at risk from exposure to BaA are those in the coal tar and asphalt production industries, cooking plants, coal gasification plants, smoke houses and industrial plants that burn wood, trash, coal or oil.

PHARMACOKINETICS

BaA is absorbed by the dermal and oral routes. There is no information on absorption by inhalation. Biotransformation to reactive intermediates is necessary for toxicity (ATSDR, 1990). BaA accumulates in adipose tissue. The metabolism of BaA is similar to the metabolism of benzo[a]pyrene (Cooper et al., 1983). In brief, the aromatic ring is oxidized by arene oxides to form reactive intermediates. The reactive intermediates are subsequently hydrolyzed to diols (Sims and Grover, 1974). The diols are conjugated with glutathione and excreted.

HUMAN TOXICOLOGICAL PROFILE

There are no reports directly correlating human exposure to BaA with the development of excess tumors.

MAMMALIAN TOXICOLOGICAL PROFILE

The only toxicity endpoint that has been adequately studied for BaA is dermal carcinogenicity. There is some evidence that benz[a]anthracene is carcinogenic in laboratory animals by the oral route (Klein, 1963; Bock and King, 1959) and also by subcutaneous injection (IARC, 1973). BaA has been shown to cause skin tumors after dermal application (Bingham and Falk, 1969). Tumorigenicity of the diol epoxide metabolite has been shown (Levin et al., 1978) as well as the mutagenicity of the diol epoxide (Wood et al., 1977).

BENZO[a]PYRENE

GENERAL BACKGROUND INFORMATION

Benzo[a]pyrene (BaP) is a member of the class of compounds generally referred to as polyaromatic hydrocarbons (PAH).
PAHs contain two or more aromatic rings. They are ubiquitous in nature and are both naturally occurring and man-made. BaP is a component of fossil fuels and is produced from the incomplete combustion of organic compounds. BaP and other PAHs are found in coal tar, creosote oils and pitches formed from the distillation of coal tars (ATSDR, 1990).

PHARMACOKINETICS

BaP is readily absorbed by dermal, inhalation and oral routes (see section on Relative Absorption Factors). Distribution of BaP is rapid among several tissues. Following inhalation exposure to ^{3}H labeled BaP, maximum levels of radioactivity were found in the liver, esophagus, small intestine and blood after 30 minutes. After 12 hours, maximum levels were found in the cecum, stomach and large intestine (Sun et al., 1982). This and other studies provide evidence for the enterohepatic circulation of BaP metabolites.

Mammalian metabolism of BaP follows the mechanism established for smaller aromatic compounds (Williams, 1959). There is an initial oxidation of a double bond on one of the rings to an arene oxide. The oxide is then hydrolyzed to the diol. Oxidations may occur at multiple sites on the BaP molecule. Phase II metabolism is considered the detoxication pathway and involves the conjugation of the activated Phase I metabolites with easily eliminated substrates such as glutathione, glucuronide or sulfate (Cooper et al., 1983). In addition to being conjugated, the diol intermediate can undergo (1) further oxidation to several uncharacterized metabolites via the P-450 monooxygenase system, (2) spontaneous rearrangement to the phenol or (3) hydration to the trans-diols through a reaction catalyzed by epoxide hydrolase (Cooper et al., 1983). BaP 7,8-diol-9,10-epoxide has been established as an ultimate carcinogen (ATSDR, 1990). The primary route of excretion of BaP is through the feces. BaP undergoes first-pass metabolism and is reabsorbed via enterohepatic circulation (Chipman et al., 1982). Rats exposed by gavage to ^{14}C labeled BaP in peanut oil excreted up to 85% in the feces. Excretion in the urine was 1 to 3% of the administered dose (Hecht et al., 1979).

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BENZO[b]FLUORANTHENE

GENERAL BACKGROUND INFORMATION

Benzo[b]fluoranthene (BbF) is a member of the class of compounds referred to as polycyclic aromatic hydrocarbons (PAHs). PAHs contain two or more aromatic rings. PAHs are ubiquitous in nature and are both naturally occurring and man-made. Exposure to BbF can come from air, water, or soil. As a PAH, BbF is present in the emissions from industrial plants that produce coal tar, cooking plants, asphalt production plants, and home heating with wood and coal. BbF is also present in charcoal-broiled foods and cigarette smoke (ATSDR, 1990).

PHARMACOKINETICS

No data on the absorption, distribution or excretion of BbF were identified. BbF is metabolized under *in vitro* incubation conditions to phenol and dihydrodiol metabolites (Amin et al., 1982). The general metabolic pathways elucidated for benzo(a)pyrene are also active on BbF (Cooper et al., 1983; Levin et al., 1982; Grover et al., 1986). The reactive metabolites associated with the tumorigenic effects of BbF may not be the diol epoxides (Amin et al., 1982; Amin et al., 1985). As for the other PAHs, the material excreted is expected to consist primarily of dihydrodiol and phenol conjugates (Grover et al., 1986).

HUMAN TOXICOLOGICAL PROFILE

The database for human toxicity is very limited. There are no studies correlating exposure to BbF and cancer or systemic toxicity. The only data implicating BbF as a carcinogen come from carcinogenicity studies using a mixture of PAHs.

MAMMALIAN TOXICOLOGICAL PROFILE

The database on the toxicity of BbF is limited. Intratracheal administration of BbF to rats resulted in an increase in respiratory tract tumors (Deutsch-Wenzel et al., 1983). BbF has caused skin tumors in mice following dermal application (Wynder and Hoffman, 1959). The skin tumor initiating ability of BbF has been demonstrated in mice using a standard initiation/promotion protocol with either croton oil or phorbol myristate acetate as a tumor promotor (Amin et al., 1985; LaVoie et al., 1979, 1982).

BENZO[g,h,i]PERYLENE

GENERAL BACKGROUND INFORMATION

Benzo[g,h,i]perylene is a member of the polyaromatic hydrocarbons (PAH). PAHs constitute a class of non-polar compounds that contain two or more aromatic rings. They are ubiquitous in nature and are both naturally occurring and man-made. The data regarding benzo[g,h,i]perylene are limited. As a PAH, it is found in food (charcoal broiled meats), vegetables, tobacco smoke and soot (U.S. EPA, 1980). Exposure occurs by inhalation, ingestion and by dermal contact.

PHARMACOKINETICS

No data were found regarding the pharmacokinetics of benzo[g,h,i]perylene.

HUMAN TOXICOLOGICAL PROFILE

No data were found regarding the human toxicology of benzo[g,h,i]perylene.

MAMMALIAN TOXICOLOGICAL PROFILE

No data were found regarding the mammalian toxicity of benzo[g,h,i]perylene.

GENOTOXICITY

No data were found regarding the genotoxicity of benzo[g,h,i]perylene.

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BIS(2-ETHYLHEXYL)PHTHALATE

GENERAL BACKGROUND INFORMATION

Bis(2-ethylhexyl)phthalate, often referred to as Di(2-ethylhexyl)phthalate (DEHP), exists as a colorless, oily liquid at room temperature. It is used industrially as a plasticizer for resins, to make plastic materials more flexible. DEHP is contained in many plastic products such as imitation leather, rainwear, footwear and toys. It is used in the manufacture of tubing and containers used for blood transfusions and kidney dialysis. DEHP is also used in the manufacture of organic pump fluids in electrical capacitors. DEHP may migrate into the environment under improper use/disposal conditions. As a result, exposure could occur via air, water and food. Patients receiving blood transfusions or kidney dialysis can also be exposed to DEHP (ATSDR, 1989; Sittig, 1981).

PHARMACOKINETICS

DEHP is readily absorbed through ingestion and inhalation and poorly absorbed through the skin (see section on Relative Absorption Factors). DEHP is largely metabolized prior to intestinal absorption, via hydrolysis, to its corresponding monoester metabolite (MEHP), with the release of 2-ethylhexanol. Once absorbed, DEHP and its metabolites are distributed throughout the body, with most of the compounds initially going to the liver. In general, DEHP and its metabolites are converted to more polar derivatives and are then excreted. DEHP is rapidly cleared from the body, with little potential for accumulation. There are differences in the way DEHP is metabolized among species. Although phase I reactions are essentially the same across species except for quantitative differences, phase II reactions differ among species as to the ability to glucuronidate DEHP and its metabolites. The relationship between pharmacokinetics and toxicity is not known due to gaps in knowledge regarding mechanisms of toxic action (ATSDR, 1989).

HUMAN TOXICOLOGICAL PROFILE

Acute toxicity from DEHP is relatively low by both inhalation and ingestion. A 1-hr exposure to 23,670 mg/m^3 DEHP did not result in any deaths. The oral LD50 for DEHP ranges from 26,000 to 49,000 mg/kg (ATSDR, 1989). Exposure to DEHP has produced irritation of the eyes, and mucous membranes, nausea and diarrhea (Sittig, 1981). Liver biopsies from dialysis patients showed liver abnormalities (peroxisome proliferation) (ATSDR, 1989). Most of the toxicity data for DEHP originate from animal studies.

CHRYSENE

GENERAL BACKGROUND INFORMATION

Chrysene is one of the polycyclic aromatic hydrocarbon (PAH) compounds which are formed during the combustion of organic material. Chrysene often exists in particulate form, adsorbing to existing particulate material in air. Human exposure can occur in the workplace (coal and asphalt production plants, cooking plants, smoke houses) or in the environment due to chrysene contamination of air, food, soil and water (ATSDR, 1990).

PHARMACOKINETICS

Chrysene can be absorbed by all routes of exposure (see section on Relative Absorption Factors). Its absorption is believed to be qualitatively similar to benzo[a]pyrene (ATSDR, 1990). Following absorption, chrysene distributes to all organs, reaching the highest concentration in tissues with large fat content (adipose tissue, mammary tissue, brain) (Modica et al., 1983). Chrysene undergoes metabolic biotransformation mediated by the mixed function oxidase enzyme system to form reactive intermediates hypothesized to be responsible for its toxicity. The major metabolites include trans-dihydrodiols, phenols, diol epoxides and triol epoxides (Thakker et al., 1985). The reactive metabolites are conjugated and excreted primarily in feces (Schlede et al., 1970).

HUMAN TOXICOLOGICAL PROFILE

There is no information available on threshold toxic effects of chrysene in humans. Since it is structurally similar to benzo[a]pyrene, it would be expected to produce effects similar to B[a]P following acute or chronic exposure (see Toxicity Profile on Benzo[a]pyrene).

MAMMALIAN TOXICOLOGICAL PROFILE

There is no information available on threshold toxic effects of chrysene in animals. Since it is structurally similar to benzo[a]pyrene, it would be expected to produce effects similar to B[a]P following acute or chronic exposure (see Toxicity Profile for Benzo[a]pyrene).

DI-N-BUTYL PHTHALATE

SUMMARY

Dibutyl phthalate is used extensively as a plasticizer, as a solvent in the lacquer industry and as an insect repellent on clothing. Industrially, the material has proven relatively innocuous except for cases of accidental human ingestion where symptoms have been reported.

CAS Number: 84-74-2
Chemical Formula: C_6-H_{22}-O_4
Important Synonyms and Trade Names: DBP; Phthalic Acid, Dibutyl Ester; O-Benzene dicarboxylic Acid.

CHEMICAL AND PHYSICAL PROPERTIES

Molecular Weight: 278.4
Boiling Point: 644°F (340°C)
Melting Point: -31°F (-35°C)
Specific Gravity: 1.0
Solubility in Water: 13 mg/l
Solubility in Solvents: Alcohol, Ether, Benzene
Log Octanol/Water Partition Coefficient: 5.60
Vapor Pressure: 1.00E-05 mm Hg at 20° to 30°C
Flash Point: 315°F (157°C)

TRANSPORT AND FATE

Very little specific information on the fate and transport of di-n-butyl phthalate is available. The fate of this compound is to a large extent inferred from data for phthalate esters as a group (see bis(2-ethylhexyl) phthalate).

HEALTH EFFECTS

Delayed symptoms resulting from ingestion include nausea, vomiting, and dizziness, followed later by headache, pain, and irritation in the eyes, lacrimation, photophobia, and conjunctivitis. Slight, temporary renal effects may also occur. Animal experiments have shown that the material has generally low acute and chronic toxicity.

TOXICITY TO WILDLIFE AND DOMESTIC ANIMALS

See bis(2-ethylhexyl) phthalate

NAPHTHALENE

GENERAL BACKGROUND INFORMATION

Naphthalene is a white solid substance at room temperature. It has a distinct odor of mothballs or tar. Humidity and sunshine cause evaporation into the air within a few hours. When placed in water or soil, bacteria will destroy naphthalene, or will render it airborne within a few hours (ATSDR, 1990). Tobacco smoke is known to release 3 ug of naphthalene per cigarette (U.S. EPA, 1982). The compound is used in the production of dyes, solvents, lubricants, motor fuels (U.S. EPA, 1980) and is a major component of many moth ball preparations.

PHARMACOKINETICS

Humans can absorb naphthalene by dermal, inhalation and oral routes (see section on Relative Absorption Factors). Metabolism occurs via the P450 mixed function oxidase enzyme system to yield multiple intermediates which are then conjugated. Key metabolites are responsible for each toxicity endpoint following intraperitoneal administration: 2-naphthoquinones --> hemolysis; 1,2-naphthoquinones --> cataracts; 3-GSH adducts --> pulmonary toxicity (Buckpitt et al., 1984). Excretion of metabolites occurs via urine and feces (ATSDR, 1990).

HUMAN TOXICOLOGICAL PROFILE

Adults and children exposed to airborne naphthalene experience vomiting, abdominal pain and anemia (ATSDR, 1990). Most of the data is for inhalation of naphthalene from mothballs. The primary site of toxicity is the erythrocyte resulting in hemolytic crisis (hemolytic anemia). Jaundice is seen upon dermal, inhalation, and oral exposures, as are kidney effects (ATSDR, 1990). Near-blindness resulted in male and female subjects with 5 gram ingestion (ATSDR, 1990).

MAMMALIAN TOXICOLOGY PROFILE

Oral doses in rats have hepatic effects. Dogs (1800 mg/kg) for 5 days of exposure showed signs of lethargy and ataxia, and decreased hemoglobin levels (ATSDR, 1990)

GENOTOXICITY

No studies of genotoxic effects in humans or laboratory animals were located. No human epidemiological evidence for cancer.

PHENANTHRENE

GENERAL BACKGROUND INFORMATION

Phenanthrene is a member of the polyaromatic hydrocarbons (PAH). PAHs constitute a class of non-polar compounds that contain two or more aromatic rings. They are ubiquitous in nature and are both naturally occurring and man-made. The database on the potential health effects of phenanthrene is limited.

PHARMACOKINETICS

Little data are available regarding the pharmacokinetics of phenanthrene. The intestinal absorption of phenanthrene is less dependent on the presence of bile in the stomach than is the absorption of the larger PAHs (such as benzo(a)pyrene) (Rahman et al, 1986).

HUMAN TOXICOLOGICAL PROFILE

Phenanthrene has been shown to be a skin photosensitizer in humans (Sax, 1984).

MAMMALIAN TOXICOLOGICAL PROFILE

Phenanthrene has a reported LD 50 of 700 mg/kg in mice (Simmon et al., 1979). Rats injected intraperitoneally evidenced liver effects (Yoshikawa et al, 1987).

There is equivocal evidence for cancer from dermal application of phenanthrene in rats (IARC, 1983). Phenanthrene is not a complete skin carcinogen (ATSDR, 1990). It is neither an initiator (LaVoie et al, 1981; Roe, 1962) nor a promoter (Roe and Grant, 1964). Higgins and Yang (1962) reported no tumor production within two months after the ingestion of 200 mg of phenanthrene by rats.

GENOTOXICITY

There are limited data that suggest that phenanthrene is mutagenic (Wood et al., 1979). However, the majority of tests are negative (ATSDR, 1990).

POLYCHLORINATED BIPHENYLS (PCBs)

GENERAL BACKGROUND INFORMATION

The thermal stability, nonflammability, and dielectric capability of PCBs resulted in their use in electrical capacitors and transformers (NIOSH, 1986). The manufacturing, processing, distribution in commerce, and use of PCBs after January 1, 1978 was prohibited under Section 6(e) of the Toxic Substances Control Act. PCBs can be released to the environment during fires involving electrical equipment containing these compounds. PCBs are strongly adsorbed on solid surfaces, including glass and metal surfaces in laboratory apparatus, and onto soils, sediments, and particulates in the environment.

PHARMACOKINETICS

Gastrointestinal absorption of most PCB isomers is large. PCBs can also be absorbed by the inhalation and dermal routes but limited data are available (see section on Relative Absorption Factors). Distribution of PCBs follows a biphasic pattern. Initially, PCBs distribute to liver and muscle tissue. They are then redistributed to the fat, skin, and other fat-containing organs (ATSDR, 1989). PCBs are poorly metabolized in humans with major metabolites being 3- or 4-hydroxy compounds. Metabolism may proceed through formation of arene oxide intermediates (U.S. EPA, 1988). The slow metabolism of PCB congeners to more polar compounds is responsible for long biological half-lives of PCBs. Excretion occurs primarily through the feces (Goto et al., 1974).

HUMAN TOXICOLOGICAL PROFILE

Dermatologic signs are the most persistent indicator of PCB toxicity. Skin manifestations have been observed also in newborn infants of mothers exposed to high levels of PCBs and related compounds. Cases of severe chloracne were reported in a work environment in which PCB air levels were found to be between 5.2 and 6.8 mg/m^3. The workers developing chloracne had been exposed for 2 to 4 years. Other analyses revealed worker complaints of dry sore throat, skin rash, gastrointestinal disturbances, eye irritation, and headache at work area concentrations of 0.013 to 0.15 mg PCB/m^3. Higher blood PCB levels are associated with higher serum triglyceride and/or cholesterol levels, as well as high blood pressure. Air PCB concentrations as low as 0.1 mg/m^3 can produce toxic effects, and exposure to levels producing no overt toxicity can affect liver function. Recovery after termination of exposure occurs but is slow and depends upon the amount of PCBs stored in adipose tissue (Clayton and Clayton, 1981). Human exposures to PCBs resulting in toxic effects have almost all resulted from the ingestion of rice oil contaminated with "Kanechlor 400" in Japan (resulting in Yusho or rice oil disease) or from industrial exposure. Clinical symptoms of poisoning

Immunological effects (decreased IgM, IgG induction) were noted in monkeys following a 27 month exposure at a dose of 0.005 mg/kg/day (Tryphonos et al., 1989).

GENOTOXICITY

Most genotoxicity assays of PCBs have been negative. The majority of microbial assays of PCB mixtures and various congeners show no evidence of mutagenic effects (U.S. EPA, 1980). The carcinogenic effects of PCBs have been studied in rats and mice. In a study conducted by Kimbrough et al. (1975) rats were exposed via the diet to 100 ppm Aroclor 1260 for 21 months. Hepatocellular carcinomas were observed in 26 of the 184 treated rats but only in one of the 173 controls. Neoplastic nodules were not found in controls but occurred in 144/184 of treated rats. The National Cancer Institute (NCI, 1978) reported a high incidence of hepatocellular proliferative lesions in male and female Fischer 344 rats fed three dose levels of Aroclor 1254 for 104-105 weeks, but, in part due to the small number of animals tested, carcinogenicity was not statistically demonstrable. Norback and Weltman (1985) fed a diet containing relatively high concentrations Aroclor 1260 (100 ppm for 16 months followed by 50 ppm for an additional 8 months) to Sprague-Dawley rats. In the PCB-exposed group, neoplastic nodules were observed at 12 months followed by trabecular carcinoma at 15 months and adenocarcinoma at 24 months (52/93). In the control rats, the incidence of hepatocellular neoplasms was low (1/81). Metastases to distant organs was not observed and mortality in the PCB exposed animals was not increased. The incidence of these slow-growing hepatocellular neoplasms was strikingly higher in female rats than in male rats.

PCBs (Clophen C) have also been shown to be cocarcinogenic. When PCBs were mixed with diethylnitrosamine (DENA), twice as many tumors were observed as were observed in animals treated with DENA alone (Brunn, 1987).

Based on the positive evidence for carcinogenicity of Aroclor 1254, Aroclor 1260, Kaneclor 500, and Clophen A-30 and A-60 in animals, along with adequate evidence in humans, the U.S. EPA has placed these PCBs in categroy B2 - probable human carcinogen (U.S. EPA, 1988).

Overmann, S.R., Kostas, J., Wilson, L.R., Shain, W. and Bush, B. (1987) *Neurobehavioral and somatic effects of perinatal PCB exposure in rats*. **Environ. Res.** 44:56-70.

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ALDRIN/DIELDRIN

Summary

Aldrin degrades to dieldrin, which is very persistent in the environment. Both pesticides are carcinogenic in rats and mice and are teratogenic and reproductive toxicants. Aldrin and dieldrin cause liver toxicity and central nervous system abnormalities following chronic exposure. Both are also acutely toxic, with oral LD_{50} values of about 50 mg/kg. Both pesticides are very toxic to aquatic organisms and have been associated with large-scale kills of terrestrial wildlife in treated areas.

Background Information

Dieldrin is the 6,7-epoxide of aldrin and is readily obtained from aldrin under normal environmental conditions and by metabolism in animals.

CAS Number: Aldrin: 309-00-2
Dieldrin: 60-57-1

Chemical Formula: Aldrin: $C_{12}H_8Cl_6$
Dieldrin: $C_{12}H_8Cl_6O$

IUPAC Name: Aldrin: 1,2,3,4,10,10-hexachloro-1,4,4a,5,8,8a-hexahydro-1,4:5,8-exo-dimethanonaphthalene

Dieldrin: 1,2,3,4,10,10-hexachloro-6,7-epoxy-1,4,4a,5,6,7,8,8a-octahydro-endo,exo-1,4:5,8-dimethanonaphthalene

Chemical and Physical Properties

Molecular Weight: Aldrin: 365
Dieldrin: 381

Melting Point: Aldrin: 104°C
Dieldrin: 176°C

webbed foot, and skeletal anomalies. Chronic effects attributed to aldrin and dieldrin include liver toxicity and central nervous system abnormalities. Both chemicals are acutely toxic; the oral LD_{50} is around 50 mg/kg, and the dermal LD_{50} is about 100 mg/kg.

Toxicity to Wildlife and Domestic Animals

Aldrin and dieldrin are both acutely toxic to freshwater species at low concentrations. Tests in fish showed that the two chemicals had similar toxicities, with LC_{50} values ranging from 1 to 46 µg/liter for different species. Final acute values for freshwater species were determined to be 2.5 µg/liter for dieldrin and 3.0 µg/liter for aldrin. Saltwater species were also quite sensitive to aldrin and dieldrin. The range of LC_{50} values was similar to that for freshwater species: 2 to 100 µg/liter for aldrin and 1 to 34 µg/liter for dieldrin. The saltwater Final Acute Values were 1.3 µg/liter for aldrin and 0.71 µg/liter for dieldrin.

Chronic studies have been conducted on the effects of dieldrin on freshwater and saltwater species. For freshwater organisms, chronic values as low as 0.2 µg/liter were obtained. The Final Acute Chronic Ratio was determined to be 3.5, and the calculated Freshwater Final Chronic Value was 0.29 µg/liter. Only one chronic study was done on saltwater species. Therefore, the saltwater Final Chronic Value of 0.084 µg/liter was determined by dividing the Final Acute Value by the acute-chronic ratio. No chronic studies were performed on aldrin, but because its acute toxicity is comparable to that of dieldrin and because it is readily converted to dieldrin in animals and in the environment, it probably has similar chronic toxicity.

Both pesticides, and especially dieldrin, have been associated with large-scale bird and mammal kills in treated areas. Experimental feeding studies have shown that the chemicals are quite toxic to terrestrial wildlife and domestic animals at low levels.

Regulations and Standards

Ambient Water Quality Criteria (USEPA):

Aquatic Life

Freshwater

Acute toxicity: Aldrin: 3.0 µg/liter
Dieldrin: 2.5 µg/liter

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA). 1980. Ambient Water Quality Criteria for Aldrin/Dieldrin. Office of Water Regulations and Standards, Criteria and Standards Division, Washington, D.C. October 1980. EPA 440/5-80-019

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ARSENIC

GENERAL BACKGROUND INFORMATION

The toxicity of arsenic depends upon its chemical form along with the route, dose, and duration of exposure. In general, arsenites (As^{+3}) are potentially more toxic than arsenates, soluble arsenic compounds are potentially more toxic than insoluble compounds, and inorganic arsenic compounds are potentially more toxic than organic derivatives (U.S. EPA, 1985).

PHARMACOKINETICS

Absorption from the gastrointestinal tract is dependent upon the solubility of the specific arsenic compound and the dose. Absorption from the respiratory tract is also dependent upon the specific arsenic compound, along with particle size (see section on Relative Absorption Factors).

HUMAN TOXICOLOGICAL PROFILE

Depending upon dose and exposure route, arsenic is an irritant of the skin, mucous membranes, and the gastrointestinal tract. Acute toxicity from the ingestion of higher doses of arsenic may result in vomiting, diarrhea, convulsions, a severe drop in blood pressure, and cardiovascular effects. The lethal dose for humans is reported to be 1.0 to 2.6 mg/kg-bw (Vallee et al., 1960). Acute toxicity from inhalation exposure to arsenic adsorbed to particulate matter may result in conjunctivitis and pharyngitis. Subchronic effects included hyperpigmentation (melanosis), multiple arsenical keratoses, sensory-motor polyneuropathy, persistent chronic headache, lethargy, gastroenteritis, and mild iron deficiency anemia. Inhaled arsenic compounds have been reported to be associated with skin lesions, cardiovascular and respiratory effects, and peripheral neuropathy (Stokinger, 1981; IARC, 1980). Chronic oral exposure of humans to inorganic arsenic compounds has been reported to cause skin lesions, peripheral vascular disease, and peripheral neuropathy (Silver and Wainman, 1952). The incidence of blackfoot disease, a peripheral circulatory disease characterized by gangrene of the extremities, has reportedly been related to the presence of arsenic in the drinking water of residents of the southwest of Taiwan (Tseng, 1977). The symptoms of chronic inhalation exposure to arsenic compounds are similar to those associated with chronic oral toxicity.

BARIUM

Summary

In its pure form, barium is an extremely reactive metal that decomposes in water. In natural waters it forms insoluble carbonate or sulfate salts and is usually present at concentrations of less than 1 mg/liter. Insoluble forms of barium are not very toxic; but soluble barium salts are highly toxic after acute exposure, and they have a prolonged stimulant effect on muscles. A benign pneumoconiosis, baritosis, can result from inhaling barium dusts. The EPA Interim Primary Drinking Water Standard is 1 mg/liter.

CAS Number: 7440-39-3

Chemical Formula: Ba

IUPAC Name: Barium

Chemical and Physical Properties

Atomic Weight: 137.3

Boiling Point: 1,640°C

Melting Point: 725°C

Specific Gravity: 3.5

Solubility in Water: Decomposes; combines with sulfate present in natural waters to form $BaSO_4$, which has a solubility of 1.6 mg/liter at 20°C

Solubility in Organics: Soluble in alcohol; insoluble in benzene

Transport and Fate

Barium is extremely reactive, decomposes in water, and readily forms insoluble carbonate and sulfate salts. Barium is generally present in solution in surface or groundwater only in trace amounts. Large amounts will not dissolve because natural waters usually contain sulfate, and the solubility of barium sulfate is generally low. Barium is not soluble at more than a few parts per million in water that contains sulfate at more than a few parts per million. However, barium sulfate may become considerably more soluble in the presence

Regulations and Standards

Interim Primary Drinking Water Standard: 1 mg/liter

OSHA Standard: 0.5 mg/m^3 (soluble compounds, as Ba)

ACGIH Threshold Limit Value: 0.5 mg/m^3 (soluble compounds, as Ba)

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Although little information concerning adsorption of beryllium is available, based on its geochemical similarity to aluminum it is expected to be adsorbed onto clay mineral surfaces at low pH and to be complexed into some insoluble compounds at high pH. In most natural environments, beryllium is likely to be present in sorbed or precipitated, rather than dissolved, form.

Beryllium may be accumulated to a slight extent by aquatic organisms. Although it has a low solubility in water, it is possible that benthos could accumulate beryllium from sediment and thereby transfer the metal to higher organisms via the food chain. However, there is no evidence for food chain magnification. Airborne transport of beryllium, generally in the form of particulates, may also occur.

Health Effects

The results of some epidemiological studies of workers occupationally exposed to beryllium indicate that beryllium may cause lung cancer in humans. Although this evidence is equivocal, beryllium and many of its compounds are known to be carcinogenic in several animal species. Inhalation exposure to beryllium has resulted in the development of lung or bone cancer in animals, and exposure by injection has produced bone cancer. Although beryllium compounds may impair DNA polymerization, there is no other evidence of mutagenic or clastogenic activity. However, the number of compounds tested and the types of tests conducted have been limited. There is little information concerning the possible teratogenic effects of beryllium. It is reported to inhibit embryonic development of the snail and regeneration of the limbs of the salamander.

Acute respiratory effects due to beryllium exposure include rhinitis, pharyngitis, tracheobronchitis, and acute pneumonitis. Dermal exposure to soluble beryllium compounds can cause contact dermatitis. Ocular effects include inflammation of the conjunctiva from splash burns or in association with contact dermatitis. The most common clinical symptoms caused by chronic beryllium exposure are granulomatous lung inflammation, with accompanying cough, chest pain, and general weakness. Systemic effects include right heart enlargement with accompanying cardiac failure, liver and spleen enlargement, cyanosis, digital clubbing, and kidney stone development.

Toxicity to Wildlife and Domestic Animals

Data for several freshwater fish species indicate that the acute toxicity of beryllium decreases by about two orders of magnitude with an increase in hardness from about 20 to

Risk	Concentration
10^{-5}	37 ng/liter
10^{-6}	3.7 ng/liter
10^{-7}	0.37 ng/liter

CAG Unit Risk (USEPA): 2.6 $(mg/kg/day)^{-1}$

OSHA Standards (air): 2 $\mu g/m^3$ TWA
5 $\mu g/m^3$ Ceiling Level
25 $\mu g/m^3$/30 min Peak Concentration

ACGIH Threshold Limit Value: Suspected human carcinogen
2 $\mu g/m^3$

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CADMIUM

GENERAL BACKGROUND INFORMATION

Cadmium typically exists in the environment as a salt of the +2 valence state or as a metal. It forms no stable organic compounds. Cadmium releases are generally associated with mining, smelting, manufacturing operations, and from the disposal of alkaline batteries containing cadmium (Doull, 1980; U.S. EPA, 1981).

PHARMACOKINETICS

Cadmium is absorbed by all routes of exposure (see section on Relative Absorption Factors). Absorption through the gastrointestinal tract is low, respiratory absorption more efficient and dermal absorption relatively insignificant (ATSDR, 1989). Absorbed cadmium is widely distributed throughout the body, with the major portion of the body burden located in liver and kidney (Sumino et al., 1975). The distribution of cadmium is linked to the distribution of metallothionein, a low-moleculer-weight protein, rich in cadmium-binding sites. Cadmium is not known to undergo any direct metabolic conversions in vivo. The principle excretory route for absorbed cadmium is urinary. Excretion is slow, accounting for the long half-life of cadmium in the body (17-38 years) (ATSDR, 1989).

HUMAN TOXICOLOGICAL PROFILE

Cadmium is a local respiratory tract irritant. Systemic symptoms occur in a few hours after an acute exposure to cadmium dust or fumes. Upper respiratory tract irritation is followed by coughing, chest pain, sweating, and chills. These symptoms resemble nonspecific upper respiratory infection (Sittig, 1985). Within 24 hours severe pulmonary irritation may develop, with progressively increasing pain in the chest, dyspnea, pulmonary edema, cough, and generalized weakness. Chronic exposure to cadmium fumes may result in emphysema-like lung damage (Sittig, 1984). Renal dysfunction may ensue (Friberg, 1950). Bernard and Lauwerys (1984) observed that the gastrointestinal tract is adversely affected by acute oral exposure with such symptoms as nausea, vomiting, salivation, abdominal pain, cramps, and diarrhea. The principal effects of chronic cadmium exposure are osteomalacia and osteoporosis (Itai Itai disease) secondary to glomerular and tubular necrosis in the kidney. The Itai Itai ("ouch-ouch") disease is endemic areas in Japan, which have been contaminated with mining wastes containing cadmium. Victims display the osteomalacia and osteoporosis as primary symptoms, as well as protein, sugar and amino acids not normally found in the urine. Other chronic effects include immunosuppression and decreases in measures of respiratory fitness (ventilation capacity, vital capacity, forced expiratory volume, etc.) (U.S. EPA, 1981).

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COPPER

Summary

Copper is among the more mobile metals in the environment. It is toxic to humans at high levels; it causes irritation following acute exposure and anemia following chronic exposure. Sheep are very susceptible to copper toxicosis, as are many aquatic organisms.

Background Information

Copper exists in a valence state of +1 or +2. It is a lustrous, reddish metal. The physical properties of copper include ductility and conductivity of heat and electricity. Copper is found in nature as sulfide, oxide, or carbonate ore.

CAS Number: 7440-50-8

Chemical Formula: Cu

IUPAC Name: Copper

Chemical and Physical Properties

Atomic Weight: 63.546

Boiling Point: 2,567°C

Melting Point: 1,083°C

Specific Gravity: 8.92

Solubility in Water: Most copper salts are insoluble, with the exception of $CuSO_4$, $Cu(NO_3)_2$, and $CuCl_2$ (the more common copper salts). The metal is insoluble in water.

Vapor Pressure: 1 mm Hg at 1,628°C

Transport and Fate

Copper has two oxidation states, +1 (cuprous) and +2 (cupric Cuprous copper is unstable in aerated water over the pH range of most natural waters (6 to 8) and oxidizes to the cupric state. Several processes determine the fate of copper in the aquatic environment: formation of complexes, especially with humic substances; sorption to hydrous metal oxides, clays, and organic materials; and bioaccumulation. In waters polluted

Clement Associates

respiratory tract irritation, a metallic or sweet taste, nausea, metal fume fever, and sometimes discoloration of skin and hair. Individuals exposed to dusts and mists of copper salts may exhibit congestion of nasal mucous membranes, sometimes of the pharynx, and occasionally ulceration with perforation of the nasal septum.

If sufficient concentrations of copper salts reach the gastrointestinal tract, they act as irritants and can produce salivation, nausea, vomiting, gastritis, and diarrhea. Elimination of ingested ionic copper by vomiting and diarrhea generally protects the patient from more serious systemic toxic effects, which can include hemolysis, hepatic necrosis, gastrointestinal bleeding, oliguria, azotemia, hemoglobinuria, hematuria, proteinuria, hypotension, tachycardia, convulsions, and death. Chronic exposure may result in anemia.

Copper salts act as skin irritants producing an itching eczema. Conjunctivitis or even ulceration and turbidity of the cornea may result from direct contact of ionic copper with the eye.

Toxicity to Wildlife and Domestic Animals

Mean acute toxicity values for a large number of freshwater animals range from 7.2 µg/liter for *Daphnia pulicaria* to 10,200 µg/liter for the bluegill. Toxicity tends to decrease as hardness, alkalinity, and total organic carbon increase. Chronic values for a variety of freshwater species range from 3.9 µg/liter for brook trout to 60.4 µg/liter for northern pike. Hardness does not appear to affect chronic toxicity. The acute-chronic ratios for different species range from 3 to 156. The more sensitive species tend to have lower ratios than the less sensitive species. In addition, the ratio seems to increase with hardness. Acute toxicity values for saltwater organisms range from 17 µg/liter for a calanoid copepod to 600 µg/liter for the shore crab. A chronic value of 54 µg/liter and an acute-chronic ratio of 3.4 is reported for the mysid shrimp. Long-term exposure to 5 µg/liter is fatal to the bay scallop.

Bioconcentration factors in freshwater species range from zero for the bluegill to 2,000 for the alga *Chlorella regularis*. Among saltwater species, the highest bioaccumulation factors are those for the bivalve molluscs. Oysters can bioaccumulate copper up to 28,200 times without any significant mortality.

Sheep are very susceptible to copper toxicosis, and poisoning may be acute or chronic. Acute poisoning is caused by direct action of copper salts on the gastrointestinal tract, resulting in gastroenteritis, shock, and death. The toxic dose is about 200 mg/kg and is usually obtained through an

IRON

Summary

There is some evidence that high concentrations of certain soluble iron salts may be teratogenic. The ingestion of excess amounts of iron can irritate the gastrointestinal tract. Inhaling some iron-containing dusts and fumes can cause siderosis, a type of benign pneumoconiosis.

Background Information

Iron is the fourth most abundant element in the earth's crust. The pure metal is very reactive chemically. It corrodes readily in the presence of oxygen and moisture, forming iron (III) hydroxide [$Fe(OH)_3$].

CAS Number: 7439-89-6

Chemical Formula: Fe

Chemical and Physical Properties

Atomic Weight: 55.847

Boiling Point: 2,750°C

Melting Point: 1,535°C

Specific Gravity: 7.86

Solubility in Water: Insoluble

Solubility in Organics: Soluble in alcohol and ether

Transport and Fate

Elemental iron and many iron compounds, including $Fe(OH)_3$ and the iron oxides, are insoluble in water. Iron also tends to chelate with organic and inorganic matter. Consequently, much of the iron present in aquatic systems tends to partition into the bottom sediments. Iron has relatively low mobility in soil. Atmospheric transport of iron can occur.

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LEAD

GENERAL BACKGROUND INFORMATION

Lead is used extensively in the manufacture of storage batteries and was used in gasoline and paint. Lead is also a natural constituent of many soils, for which concentrations normally range from 10 to 30 mg lead per kilogram of soil (U.S. EPA, 1980).

PHARMACOKINETICS

Lead can be absorbed by the oral, inhalation or dermal exposure routes (see section on Relative Absorption Factors). Gastrointestinal absorption of lead varies considerably depending upon chemical form, dietary intake, and age (Forbes and Reina, 1974; Barltrop and Meek, 1975). The deposition and absorption of inhaled lead depends upon particle size, chemical form and the rate and depth of breathing (Randall et al., 1975; Nozaki, 1966; Chamberlain et al., 1975). Once absorbed, lead is distributed to the various organs of the body, with most distribution occurring into mineralized tissues (ATSDR, 1990). Placental transfer to the developing fetus is possible (Bellinger et al., 1987). Inorganic lead is not known to be biotransformed within the body. Absorbed lead is excreted via the urinary or fecal routes (ATSDR, 1990)

HUMAN TOXICOLOGICAL PROFILE

Cases of acute lead poisoning in humans are not common and have not been studied in experimental animals as thoroughly as chronic lead poisoning. Symptoms of acute lead poisoning from deliberate ingestion by humans may include vomiting, abdominal pain, hemolysis, liver damage, and reversible tubular necrosis (U.S. EPA, 1984). Subacute exposures in humans reportedly may produce a variety of neurological effects including dullness, restlessness, irritability, poor attention span, headaches, muscular tremor, hallucinations, and loss of memory. Nortier et al., (1980) report encephalopathy and renal damage to be the most serious complications of chronic toxicity in man and the hematopoietic system to be the most sensitive. For this reason, most data on the effects of lead exposure in humans are based upon blood lead levels. The effects of lead on the formation of hemoglobin and other hemoproteins, causing decreased levels, are reportedly detectable at lower levels of lead exposure than in any other organ system (Betts et al., 1973). Peripheral nerve dysfunction is observed in adults at levels of 30 to 50 μg/dL-blood. Children's nervous systems are reported to be affected at levels of 15 μg/dL-blood and higher (Benignus et al., 1981). In high doses, lead compounds may potentially cause abortions, premature delivery, and early membrane rupture (Rom, 1976).

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MANGANESE

Summary

Manganese chloride produced lymphomas and manganese sulfate, tumors after injestion into mice. In humans, chronic exposure to manganese causes degenerative changes in the central nervous system in the form of a Parkinson-like disease; liver changes also occur. Acute exposure causes manganese pneumonitis.

CAS Number: 7439-96-5

Chemical Formula: Mn

IUPAC Name: Manganese

Chemical and Physical Properties

Atomic Weight: 54.938

Boiling Point: 1962°C

Melting Point: 1244°C

Specific Gravity: 7.20

Solubility in Water: Decomposes; some compounds are soluble

Transport and Fate

Manganese occurs most commonly in the +2 and +4 oxidation states in aquatic systems. Its solubility depends to a great extent on pH, dissolved oxygen, and presence of complexing agents. In saltwater, it is estimated that 85% or more of the manganese present exists in a soluble form. In freshwater, manganese can occur as the soluble ion, in complex organic ions, or in colloidal suspensions. Manganese often occurs at higher concentrations near the bottom of stratified lakes because it can be released from sediments, as the manganous ion, under reducing conditions.

In the soil, the concentration and chemical form in which manganese occur can be affected by pH, cation exchange capacity, drainage, organic matter content, and other factors. The solubility of manganese is increased at low pH and under reducing conditions. The presence of high concentrations of chlorides, nitrates, or sulfates may also increase solubility. Under these conditions, manganese is more easily taken up by plants

A 48-hour LC_{50} value of 16 mg/liter of manganese is reported for embryos of the oyster Crassostrea virginica. For the softshell clam Mya arenaria a 168-hour LC_{50} value of 300 mg/liter is reported.

Regulations and Standards

OSHA Standard: 5 mg/m^3 Ceiling Level

ACGIH Threshold Limit Values:

1 mg/m^3 TWA (fume)
3 mg/m^3 STEL (fume)
5 mg/m^3 Ceiling Level (dust and compounds)

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MERCURY

GENERAL BACKGROUND INFORMATION

Mercury has been used in the past for medicinal purposes (Gosselin et al., 1984). There are a number of occupations associated with mercury exposure, particularly through inhalation. These include mining, smelting, chloralkali production, and the manufacture of mercury-containing products such as batteries, measuring devices (thermometers) and paints. Mercury has also been used agriculturally as a seed and cereal protectant and as a fungicide.

PHARMACOKINETICS

The pharmacokinetics and pharmacodynamics of mercury depend largely on its chemical form, organic, inorganic or elemental. Absorption efficiencies vary depending on route of exposure and chemical form (see section on Relative Absorption Factors). Distribution, metabolism and excretion depend largely on the lipid solubility, ionization state and molecular size of the specific chemical form (ATSDR, 1989).

HUMAN TOXICOLOGICAL PROFILE

Exposure to most forms of mercury is associated with a high degree of toxicity. Elemental (metallic) mercury causes behavioral effects and other nervous system damage. Inorganic mercury salts do not generally reach the brain, but will produce kidney damage. Divalent (mercuric) mercury is substantially more toxic in this regard than the monovalent (mercurous) form. Organic mercury compounds are also toxic. Symptoms of chronic mercury poisoning can be both neurological and psychological in nature as the central nervous system is the primary target organ. Hand and finger tremors, slurred or scanning speech patterns, and drunken, stupor-like (ataxic) gait are some motor-control impairments that have been observed in chronic mercurial toxicity. Visual disturbances may also occur, and the peripheral nervous system may be affected. A psychological syndrome known as erethism is know to occur. It is characterized by changes in behavior and personality including depression, fearfulness, restlessness, irritability, irascibility, timidity, indecision, and early embarrassment. Advanced cases may also experience memory loss, hallucination, and mental deterioration.

MAMMALIAN TOXICOLOGICAL PROFILE

In a study by Mitsumori et al. (1981), male and female mice were fed methyl mercury chloride in their diet for up to 78 weeks. Most of the high dose group died from neurotoxicity before the 26th week. Renal tumors developed in 13 of 16 males in the

NICKEL

GENERAL BACKGROUND INFORMATION

Nickel in the ambient atmosphere typically exists as a constituent of suspended particulate matter (U.S. EPA, 1985). The greatest volume of nickel emitted into the atmosphere is the result of fossil fuel combustion. Other sources of nickel emissions are primary production, incinerators, metallurgy, chemical manufacturing, cement manufacturing, coke ovens, nickel recovery, asbestos mining/milling and cooling towers.

PHARMACOKINETICS

Studies of nickel absorption have shown that it is absorbed by all routes of exposure to varying degrees, primarily dependent on the chemical form (see section on Relative Absorption Factors). Absorbed nickel is bound to serum components and distributed to body organs, reaching highest concentrations in kidney and lung tissue (Whanger, 1973). Nickel is not known to be biotransformed. Excretion of absorbed nickel is primarily through urine, with minor excretory routes through hair and sweat (ATSDR, 1988).

HUMAN TOXICOLOGICAL PROFILE

Nickel carbonyl $Ni(CO)_4$ is a particularly toxic form of nickel upon inhalation and causes chest pain, dry coughing, hyperpnea, cyanosis, occasional gastrointestinal symptoms, sweating, visual disturbances and severe weakness. This is often followed by pulmonary hemorrhage, edema and cellular derangement. Survivors may be left with pulmonary fibrosis. In the workplace, nickel dermatitis may result at high nickel concentrations. At lower concentrations some susceptible individuals develop eczema-like lesions. The threshold for these health effects is much greater than exposures which occur in the ambient environment. The major adverse effects of nickel in man are dermatitis, chemical pneumonitis, and lung and nasal cancers.

MAMMALIAN TOXICOLOGICAL PROFILE

Deaths occurred in rats and mice at concentrations greater than 3.3 and 1.7 mg/m^3 nickel, respectively, upon extended inhalation exposure to $NiSO_4$ (Dunnick et al., 1987). Mice exposed to Ni_3S_2 died due to necrotizing pneumonia at 7.3 mg/m^3 nickel (Benson et al., 1987). Prolonged exposure of hamsters to nickel oxide at 41.7 mg/m^3 resulted in decreased survival due to emphysema (Wehner et al., 1975). Oral LD_{50}s in rats vary depending upon the nickel-containing compound to which the rats were exposed. These range from 355 mg compound/kg (118 mg Ni/kg) for nickel acetate (Haro, 1968) to greater than 5000 mg

THALLIUM

GENERAL BACKGROUND INFORMATION

Pure thallium is a soft bluish-white metal that is widely distributed in trace amount in the earth's crust. It is used in the manufacture of electronic devices, switches, and closures. It is also used to a limited extent in the manufacture of special glasses and for medical procedures that evaluate heart disease. Up until 1972, thallium was also used as a rat poison (ATSDR, 1991).

PHARMACOKINETICS

Thallium appears to be nearly completely absorbed from the gastrointestinal tract. No information was located on absorption following inhalation or dermal exposure. However, animal studies following intratracheal administration suggested that uptake through respiratory epithelium was rapid and complete. There is little information on the distribution of thallium in humans. Analysis of human tissues indicates that thallium is distributed throughout the body. The highest levels were found in the scalp hair, kidney, heart, bone, and spleen. In animals, the highest levels are found in the kidneys and liver. Excretion of thallium occurs by both the urinary and fecal routes (ATSDR, 1991).

HUMAN TOXICOLOGICAL PROFILE

Thallium is acutely lethal to humans following oral exposure at doses of 54-110 mg thallium/kg of body weight as thallium sulfate (Davis et al., 1981). The estimated lethal dose is approximately 14-15 mg/kg (Gosselin et al., 1984). Thallium compounds can affect the respiratory, cardiovascular, and gastrointestinal systems, the liver, kidneys and the male reproductive system. Alopecia (hair loss) and changes in the nervous system are characteristic of thallium exposure. A retrospective study was conducted which compared the incidence of congenital abnormalities in children born to mothers who had been exposed to thallium during pregnancy (Dolgner et al., 1983). The number of anomalies in the exposed group did not exceed the number of expected birth defects in the general population.

MAMMALIAN TOXICOLOGICAL PROFILE

In animals, the lowest doses showing lethality for a brief exposure period ranged from 5 to 30 mg/kg body weight for several species (Downs et al., 1960). Exposure to low doses (1.4 mg thallium as thallium sulfate/kg body weight/day) for longer durations (40-240 days) also cause death (Manzo et al., 1983). Electromyographic abnormalities without changes in

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VANADIUM

Summary

Occupational exposure to airborne vanadium has been shown to irritate the skin, eyes, and respiratory tract and to cause bronchitis, bronchospasms, and chest pain. Oral exposure has been associated with gastrointestinal disturbances and discoloration of the oral mucosa. Chronic exposure to vanadium may have an adverse effect on various enzyme systems.

Background Information

Vanadium can exist in the 0, +2, +3, +4, and +5 oxidation states. Elemental vanadium is insoluble in water. Vanadium usually occurs in some oxidized form, and soluble and insoluble vanadium compounds can occur. Vanadium can bind covalently to organic molecules to yield organometallic compounds.

CAS Number: 7440-62-2

Chemical Formula: V

IUPAC Name: Vanadium

Chemical and Physical Properties

Atomic Weight: 50.9

Boiling Point: 3,380°C

Melting Point: 1,890°C

Specific Gravity: 5.96

Solubility in Water: Insoluble

Transport and Fate

The extent to which vanadium is transported in aqueous media is largely determined by the chemical species present and by environmental factors determining its solubility and binding to organic materials. Some vanadium compounds are volatile, and atmospheric transport of fumes as well as particulates can occur. Some bioaccumulation of vanadium occurs. However, in mammals, it appears that excess vanadium can be rapidly excreted in the urine. In humans, it is excreted as sodium metavanadate or ammonium vanadyl tartiate.

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ZINC

GENERAL BACKGROUND INFORMATION

Zinc is used most commonly as a protective coating for other metals and in alloys such as bronze and brass. Zinc is emitted to the atmosphere during mining and refining, manufacturing processes, and combustion of zinc-containing materials. Zinc is an essential trace element in nutrition and is found in many foods (ATSDR, 1989).

PHARMACOKINETICS

It has been reported that about 20 to 30 percent of ingested zinc is absorbed and the mechanism may be homeostatically controlled and carrier-mediated. When zinc levels in the body are sufficient to sustain normal physiological functions, zinc absorption decreases. Absorption occurs by the inhalation and dermal routes as well. Once absorbed, zinc is distributed throughout the body where it is used as an essential cofactor in many enzyme systems. Excretion occurs primarily through the feces (ATSDR, 1989).

HUMAN TOXICOLOGICAL PROFILE

Zinc compounds are of relatively low toxicity by ingestion. In humans, exposure to 2 g or more of zinc produces symptoms of fever, nausea, vomiting, stomach cramps, and diarrhea 3-12 hours after ingestion. Zinc chloride is a primary component of smoke bombs, and pathologic changes in humans due to acute inhalation exposure to ZnCl include laryngeal, tracheal, and bronchial mucosal edema and ulceration, interstitial edema, interstitial fibrosis, alveolar obliteration and bronchiolitis obliterans. Severe acute injury is associated with a high mortality (Matarese and Matthews, 1986). Metal fume fever results from occupational inhalation of freshly formed fumes of zinc oxides. It is characterized by transient chills and fever, profuse sweating, and weakness some hours after exposure. The fumes usually consist of extremely fine particles containing other metals in addition to zinc. The very small size (submicronic) of the fume particles with their potential for alveolar deposition is thought to be an important aspect of this phenomenon. It has generally been estimated that fume fever does not occur at zinc oxide levels less than 15 mg/m^3 although some occurrence of fume fever has been reported at levels as low as 5 mg/m^3. This occupational hazard is not considered to be a general public health problem (U.S. EPA, 1987a; U.S. EPA, 1987b).
Poorly ionized zinc compounds have low dermal toxicity and have been used therapeutically and cosmetically for many years as mild astringents, antiseptics and perspirants (Gilman et al., 1985).

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