# MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY
# WATER BUREAU
# HUMAN & WILDLIFE TOXICITY SUMMARY

| | | | |
|---|---|---|---|
| Chemical Name: | 1,1-Dichloroethylene | CAS No.: | 75-35-4 |
| Derived By: | A. Perbeck | Literature Review Date: | 07/26/07 |
| Reviewed By: | D. Bush | Verification Date: | 9/11/07 |

| | Drinking Water | Nondrinking Water |
|---|---|---|
| **Surface Water** | | |
| **HNV (Tier 1 )** | 1200 ug/L | 33000 ug/L |
| **HCV (Tier __ )** | NA | NA |
| **Screening Level** | | |
| **Ground Water** | | |
| **GW Noncancer** | | |
| **GW Cancer** | | |

HUMAN HEALTH INTERMEDIATE VALUES:

| | |
|---|---|
| **RfD** | 0.046 mg/kg/d |
| **POTENCY** | NA |
| **HH-BAF-$TL_3$** | 3.4 L/kg |
| **HH-BAF-$TL_4$** | 5. L/kg |

| | |
|---|---|
| **WV** | |
| **WV-BAF-$TL_3$** | |
| **WV-BAF-$TL_4$** | |

Comments:

A literature search conducted in July 2007 revealed no new studies for use in criteria development.

D. Bush
September 13, 2002

HNV Justification
1,1-Dichloroethylene
(vinylidene chloride; VDC)
CAS No. 75-35-4

A review of the available literature revealed two oral lifetime-exposure rodent studies which are suitable for the derivation of a Human Noncancer Value (HNV). A brief summary of the potential for VDC to cause cancer in laboratory animals is also included below since these two studies were also cancer bioassays. Other studies available in the literature were either inhalation studies or oral studies that did not approximate the lifespan of the test animal.

Noncancer Effects:

The National Toxicology Program (NTP) (1982) administered 1 or 5 mg VDC/kg/d to F344/N rats via gavage for 5 days/week for 104 weeks. Mean body weights of both male and female rats were comparable to control animals throughout most of the study. The only statistically significant effect noted in rats was an increased incidence of renal inflammation in high-dose male rats. According to EPA (2002), since this lesion commonly occurs in male rats, it is not considered biologically significant in this study. The NOAEL for both male and female rats is 5 mg/kg/d. NTP (1982) also administered VDC to groups of male and female mice at 2 or 10 mg/kg/d for 104 weeks. The only noncancer effect observed was necrosis of the liver. However, the incidence was not statistically significant (EPA, 2002) so the dose of 10 mg/kg/d was considered a NOAEL.

Quast et al. (1983) conducted a two-year study in which Sprague-Dawley rats were administered VDC in the drinking water at concentrations of 0, 50, 100, and 200 ppm (7, 10, and 20 mg/kg/d, respectively, for males and 9, 14, and 30 mg/kg/d, respectively, for females). The only dose-related pathological changes involved the liver, including a minimal amount of midzonal hepatocellular fatty change and hepatocellular swelling in both male and female rats. The high-dose males showed a statistically significant increased incidence of fatty change and cellular swelling while the 100 ppm male group showed a trend towards an increased incidence of hepatic changes. There were no exposure-related changes seen in the low-dose males. Hepatocellular swelling was detected in females at all dose levels, whereas, hepatocellular fatty change was significant only at 100 and 200 ppm. The NOAEL for female and male rats based on liver toxicity was 9 and 10 mg/kg/d, respectively. This is consistent with the approach used by EPA (2002) in IRIS.

The critical effect used for risk assessment was liver toxicity in rats. EPA (2002) derived a benchmark dose of 4.6 mg/kg/d based on the midzonal fatty change in female rats used in the Quast et al. (1983) study. The benchmark dose was divided by 10x for each intraspecies and interspecies extrapolation.

Cancer Risk Assessment:

EPA (2002) has reviewed eleven inhalation and five oral cancer bioassays that are available for VDC. EPA considers VDC to exhibit suggestive evidence of carcinogenicity based on tumors observed in one mouse strain after inhalation exposure and limited evidence of genotoxicity. None of the oral cancer bioassays found a significant increase in tumors.

The only well-conducted study which has found a statistically significant increase in tumors following exposure to VDC is an inhalation study by Maltoni et al. (1977, 1985). In this study, male and female Swiss mice were exposed via inhalation to 0, 10, or 25 ppm VDC for 12 months. The incidence of kidney adenocarcinomas in male mice resulted in the highest potency using the linear multistage model. These tumors appeared in control, 10 ppm, and 25 ppm groups at rates of 0/126, 0/25, and 28/119, respectively.

A study by NTP (1982) exposed male and female F344/N rats to vinylidene chloride via gavage for 104 weeks. This study found the following incidence of adrenal tumors in male rats: controls, low-dose and high-dose males had 6/50, 5/48, and 13/47 adrenal tumors, respectively. The significant ($p=0.045$) difference between high-dose and control groups in the Fisher exact test was very insignificant ($p=0.422$) after life table analyses of primary tumor incidence were carried out by NTP (1982). This procedure adjusts for early mortalities and thus minimizes the influence of animals dying before the onset of late-appearing tumors (control and low dose groups experienced earlier mortality than the high-dose group in this bioassay). The NTP (1982) concluded that VDC was not carcinogenic for mice or rats of either sex, but noted that the maximum tolerated dose (MTD) was not used in the study.

Quast et al. (1983) exposed Sprague-Dawley rats to concentrations of 50, 100, or 200 ppm VDC in drinking water for two years. These exposures resulted in VDC doses of 7, 10, or 20 mg/kg/d (males) or 9, 14, or 30 mg/kg/d (females). There was no biologically significant increase in tumors in this study. An increase in female rat mammary gland fibroadenomas/adenofibromas occurred at 50 ppm, but this increase was not dose-related and was within the normal range of the historical control data. The authors stated that the highest dose level was below the level which would exceed the capacity of the primary detoxification pathway.

According to EPA (2002), the data for VDC are "inadequate for an assessment of human carcinogenic potential via the oral route based on an absence of statistically or biologically significant tumors in limited bioassays in rats and mice balanced against the suggestive evidence in mice in a single bioassay by inhalation and limited evidence of genotoxicity." Based on this assessment, an HCV was not derived for VDC.

References:

Maltoni, C. et al. 1977. Carcinogenicity Bioassays of Vinylidene Chloride. Research Plan and Early Results. La Medicina del Lavaro. 68(4):241-262.

Maltoni, C. et al. 1985. Experimental Research on Vinylidene Chloride Carcinogenesis. In: Maltoni, C. and Mehlman, M.A., Eds. Archives of Research on Industrial Carcinogenesis. V.3. Princeton, N.J.: Princeton Scientific Publishers.

NTP. 1982. Carcinogenesis Bioassay of Vinylidene Chloride in F344 Rats and B6C3F1 Mice (gavage study). U.S. DHHS. NTP TR No. 228.

Quast et al. 1983. A chronic toxicity and oncogenicity study in rats and subchronic toxicity study in dogs on ingested vinylidene chloride. Fund. Appl. Toxicol. 3:55-62.

U.S. EPA. 2002. Integrated Risk and Information Retrieval System (IRIS database). Chemical file for vinylidene chloride (CAS No. 75-35-4). Last revised 8/13/2002.

# HUMAN NONCANCER VALUE WORKSHEET

Chemical Name: 1,1-Dichloroethylene CAS No. 75-35-4

Developed By: D. Bush

Reviewed By: S. Briggs Verification Date: 9/20/02

Key Study: The HNV is based on a benchmark dose of 4.6 mg/kg/d based on midzonal fatty change in female rats used in the Quast et al. (1983) study. The benchmark dose was divided by 10x for each intraspecies and interspecies extrapolation.

**ADE = 0.046 mg/kg/d**

$$ADE = \frac{4.6\ mg/kg/d}{100}$$

Where UF = 10x for each interspecies and intraspecies extrapolation.

drinking water

$$HNV = \frac{0.046\ mg/kg/d \quad (70\ kg) \quad (0.8)}{(2\ L/d) + (0.0036\ kg/d * 3.4\ L/kg) + (0.0114\ kg/d * 5.0\ L/kg)} = 1.24\ mg/L$$

**Human Noncancer Value for drinking water = 1,200 ug/L**

non-drinking water

$$HNV = \frac{0.046\ mg/kg/d \quad (70\ kg) \quad (0.8)}{(0.01\ L/d) + (0.0036\ kg/d * 3.4\ L/kg) + (0.0114\ kg/d * 5.0\ L/kg)} = 32.5\ mg/L$$

**Human Noncancer Value for non-drinking water = 33,000 ug/L**

# BIOACCUMULATION FACTOR WORKSHEET

Chemical Name: 1,1-Dichloroethylene CAS No. 75-35-4
BAF Derived By: D. Bush Literature Review Date: 07/30/02
BAF Reviewed By: S. Briggs Verification Date: 9/20/02

**HH-BAF-TL.3:** 3.4 L/kg **WL-BAF-TL.3:**
**HH-BAF-TL.4:** 5.0 L/kg **WL-BAF-TL.4:**

## I. FIELD BAFs, BSAFs, or LABORATORY BCFs

| Ref # | BAF, BSAF, or BCF | Value | Species | Exposure Duration days | Tissue Type | Tissue Lipid (%) | Steady State Tissue Conc. | Water or Sed. (BSAF) Conc. |
|---|---|---|---|---|---|---|---|---|
| .) | | | | | | | | |
| .) | | | | | | | | |
| .) | | | | | | | | |
| .) | | | | | | | | |
| .) | | | | | | | | |
| .) | | | | | | | | |
| .) | | | | | | | | |

**Final BAF, BSAF, or BCF:**
**Justification:**

## II. LOG Kow VALUES

| Ref # | Meas./Calc. Log Kow | Method | Value | Meas./Calc. Log Kow | Method | Value |
|---|---|---|---|---|---|---|
| 1 | calc | clogp | 2.11 | | | |
| | | | | | | |
| | | | | | | |
| | | | | | | |

**Final Log Kow:**
**Justification:** The final log Kow value

**Food Chain Multipliers**
**FCM-TL.3:** 1.0061
**FCM-TL.4:** 1.00044

# BIOACCUMULATION FACTOR WORKSHEET

Assessment/Calculations: Final log Kow 2.11

$$f_{fd\ ambient} = 1 / [1 + (2.4 \times 10^{-7})(10^{\log Kow})]$$

$f_{fd}$ 0.99999976

Baseline $BAF_{TLn} = FCM_{TLn} * (Kow)$

Baseline $BAF_{TL3}$ = $FCM_{TL3}$ * Kow
Baseline $BAF_{TL3}$ = 1.0061 * 128.82496
Baseline $BAF_{TL3}$ = 129.6108

Baseline $BAF_{TL4}$ = $FCM_{TL4}$ * Kow
Baseline $BAF_{TL4}$ = 1.00044 * 128.82496
Baseline $BAF_{TL4}$ = 128.8816

**HH $BAF_{TL3}$ = [(Baseline $BAF_{TL3}$)(0.0182) + 1] ($f_{fd\ ambient}$)**
**HH $BAF_{TL3}$ =** ( 129.6108 * 0.0182 + 1) * 0.99999976
**HH $BAF_{TL3}$ =** 3.358916 **= L/kg**

**HH $BAF_{TL4}$ = [(Baseline $BAF_{TL4}$)(0.0310) + 1] ($f_{fd\ ambient}$)**
**HH $BAF_{TL4}$ =** ( 128.8816 * 0.031 + 1) * 0.99999976
**HH $BAF_{TL4}$ =** 4.99533 **= L/kg**

**References:**

1 EPA. 1997. Aster Ecotoxicity Profile. On-line database.