Draft Environmental Hazard Assessment for 1,2-Dichloroethane

Technical Support Document for the Draft Risk Evaluation

CASRN 107-06-2

November 2025

TABLE OF CONTENTS

25

26	ACKN	NOWLEDGEMENTS	5
27	SUMN	MARY	6
28	1	APPROACH AND METHODOLOGY	7
29	2	AQUATIC SPECIES HAZARD	8
30	3	TERRESTRIAL SPECIES HAZARD	17
31	4	ENVIRONMENTAL HAZARD THRESHOLDS	
32	4.1	Aquatic Species COCs	
33	4.2		26
34 35	5	WEIGHT OF SCIENTIFIC EVIDENCE CONCLUSIONS FOR ENVIRONMENTAL HAZARD	30
36	5.1	Quality of the Database; Consistency; Strength (Effect Magnitude) and Precision; and	
37		Biological Gradient (Dose-Response)	
38	5.2		
39	6	ENVIRONMENTAL HAZARD ASSESSMENT CONCLUSIONS	
40		RENCES	
41	APPE	NDICES	44
42	Apper	ndix A ANALOG SELECTION FOR ENVIRONMENTAL HAZARD	44
43	A.1	Structural Similarity	45
44	A.2	J , , , , ,	
45 46	A.3 A.4	· · · · · · · · · · · · · · · · · · ·	
46 47		C .	
47		ndix B ENVIRONMENTAL HAZARD DETAILS	
48		Hazard Identification	
49 50	Б	B.1.1 Aquatic Hazard Data	
51		B.1.1.2 Species Sensitivity Distribution (SSD)	
52		B.1.1.3 Dose-Response Curve Fit Methods	
53	В	3.1.2 Evidence Integration	67
54		B.1.2.1 Rubric for Weight of Scientific Evidence	68
55	TIO		
56		T OF TABLES	
57		2-1. Aquatic Species Environmental Hazard Studies for 1,2-Dichloroethane	
58 50		3-1. Terrestrial Organisms Environmental Hazard Studies Used for 1,2-Dichloroethane	
59 60		4-1. Environmental Hazard Thresholds for Aquatic Environmental Toxicity4-2. Environmental Hazard Thresholds for Terrestrial Environmental Toxicity	
61		5-1. 1,2-Dichloroethane Evidence Table Summarizing the Overall Confidence Derived from	49
62	1	Hazard Thresholds	31

	F FIGURES
	. TRV Flowchart
Figure 4-2	. Mammalian TRV Derivation for 1,2-Dichloroethane
	OF APPENDIX TABLES
	x A-1. Structure Program Filtering Criteria
Table_Apx	A A-2. Structural Similarity Between 1,2-Dichloroethane and Analog Candidates Which
	Met Filtering Criteria in at Least 3 Out of 4 Structure Programs
Table_Ap	A-3. Analog Candidates with Similar Log K _{OW} and Vapor Pressure Values to That of 1,2 Dichloroethane
Table_Apx	A-4. Comparison of 1,2-Dichloroethane and Analog Candidates 1,1-Dichloroethane, 1,2
_ _	Dichloropropane, and 1,1,2-Trichloroethane for Several Physical and Chemical and
	Environmental Fate Properties Relevant to Water, Sediment, and Soil
Table_Apx	A-5. Comparison of Measured 1,2-Dichloroethane and Analog Hazard Values in Aquation
•	Benthic, and Soil Invertebrates
Table_Apx	x B-1. Empirical Species Hazard Data and Web-ICE Predicted Species That Met Model
•	Selection Criteria
Table_Apx	x B-2. Considerations That Inform Evaluations of the Strength of the Evidence Within an
	Evidence Stream
LIST O	F APPENDIX FIGURES
Figure_Ap	x A-1. Framework for 1,2-Dichloroethane Environmental Hazard Analog Selection
Figure_Ap	x B-1. SSD Toolbox Interface Showing HC05s and P Values for Each Distribution Using
	Maximum Likelihood Fitting Method Using Acute Aquatic Hazard Data (Etterson,
	2020a)
Figure_Ap	x B-2. AICc for the Five Distribution Options in the SSD Toolbox for Acute Aquatic
	Hazard Data (Etterson, 2020a)
Figure_Ap	x B-3. Q-Q Plot of 1,2-Dichloroethane Acute Aquatic Hazard Data With the Logistic
	Distribution (Etterson, 2020a)
Figure_Ap	x B-4. SSD Distribution for 1,2-Dichloroethane Acute Hazard Data in μg/L (Etterson,
	2020a; Wickham, 2016)
Figure_Ap	x B-5. Log-Logistic Curve Fit to Hatching Percent Data From <i>Ophryotrocha labronica</i>
	Exposed to 1,2-Dichloroethane (Rosenberg et al., 1975)
KEY A	BBREVIATIONS AND ACRONYMS
AF	Assessment factor
ASF	Artificial seawater
BIC	Bayesian information criterion
CASRN	Chemical Abstracts Service Registry Number
ChV	Chronic value
COC	Concentration(s) of concern
EC50	Effect concentration at which 50 percent of test organisms exhibit an effect
EPA	Environmental Protection Agency (U.S.)
HC05	Hazard concentration that is protective of 95 percent of the species in the SSD
LC50	Lethal concentration at which 50 percent of test organisms die
LD50	Lethal dose at which 50 percent of test organisms die
LOAEC	Lowest-observed-adverse-effect concentration

112 113	LOAEL LOEC	Lowest-observed-adverse-effect level Lowest-observed-effect-concentration
114	LOEL	Lowest-observed-effect-level
115	NITE	National Institute of Technology and Evaluation
116	NOAEC	No-observed-adverse-effect concentration
117	NOAEL	No-observed-adverse-effect level
118	NOEC	No-observed-effect concentration
119	NOEL	No-observed-effect level
120	OCSPP	Office of Chemical Safety and Pollution Prevention (EPA)
121	OPPT	Office of Pollution Prevention and Toxics (EPA)
122	OQD	Overall Quality Determination
123	QSAR	Quantitative structure-activity relationship (model)
124	SSD	Species sensitivity distribution
125	TRV	Toxicity reference value
126	TSD	Technical support document
127	TSCA	Toxic Substances Control Act
128	U.S.	United States
129	Web-ICE	Web-based Interspecies Correlation Estimation

130	ACKNOWLEDGEMENTS
131	The Assessment Team gratefully acknowledges the participation, review, and input from U.S.
132	Environmental Protection Agency (EPA or the Agency) Office of Pollution Prevention and Toxics
133	(OPPT) and Office of Chemical Safety and Pollution Prevention (OCSPP) senior managers and science
134	advisors. The Agency is also grateful for assistance from the following EPA contractor for the
135	preparation of this draft technical support document (TSD): SRC, Inc. (Contract No.
136	68HERH19D0022).
137	
138	Docket
139	Supporting information can be found in the public docket, Docket ID <u>EPA-HQ-OPPT-2018-0427</u> .
140	
141	Disclaimer
142	Reference herein to any specific commercial products, process, or service by trade name, trademark,
143	manufacturer, or otherwise does not constitute or imply its endorsement, recommendation, or favoring
144	by the United States Government.
145	
146	Authors: Kelley Stanfield (TSD Lead), Albana Bega (Assessment Lead), Seema Schappelle (Branch
147	Supervisor), and Lauren Housley
148	
149	Contributors: Jennifer Brennan, James Bressette, and Janet Burris
150	
151	Technical Support: Mark Gibson and Hillary Hollinger

SUMMARY

This technical support document (TSD) accompanies the *Draft Risk Evaluation for 1,2-Dichloroethane* (U.S. EPA, 2025f). EPA evaluated the reasonably available information for environmental hazard endpoints for aquatic and terrestrial species following exposure to 1,2-dichloroethane or its analogs 1,1-dichloroethane, 1,2-dichloropropane, and 1,1,2-trichloroethane.

Aquatic Species Hazard

To estimate aquatic hazards (mortality or immobilization) from acute exposures, the Agency supplemented empirical data for 1,2-dichloroethane aquatic species and sediment-dwelling species for analogs 1,1-dichloroethane and 1,2-dichloropropane with hazard predictions from an EPA predictive tool, Web-based Interspecies Correlation Estimation (Web-ICE). These data, which included toxicity predictions for a total of 80 species, were used with the empirical aquatic invertebrate, fish, and amphibian data and empirical sediment-dwelling invertebrate data to create a species sensitivity distribution (SSD) and calculate a hazardous concentration threshold for 5 percent of species (HC05; *i.e.*, hazard concentration that is protective of 95 percent of the species in the SSD) of 17,860 µg/L. The concentration of concern (COC) of 11,909 µg/L for acute exposures of aquatic species was derived by using the lower 95th percentile of the HC05 to account for uncertainty, which is analogous to EPA's use of an adjustment factor (AF) for chronic and algal COCs.

EPA also calculated a COC of 0.48 mg/L (reproduction in *Daphnia magna*) for chronic exposures to aquatic species using empirical 1,2-dichloroethane hazard data. The Agency calculated COCs for chronic exposures in benthic pore water and sediment to sediment-dwelling species (based on growth and development of *Chironomus riparius*; 9.3 mg/L in benthic pore water and 2.9 mg/kg in sediment) using empirical sediment-dwelling invertebrate hazard data on analog 1,1,2-trichloroethane.

EPA also calculated an algal COC of 12.4 mg/L for exposures to aquatic plants using empirical 1,2-dichloroethane hazard data on algae (based on growth of *Raphidocelis subcapitata*).

Terrestrial Species Hazard

Terrestrial hazard data for 1,2-dichloroethane were available for mammals, birds, and plants. Empirical toxicity data for mice and rats were used to derive a chronic toxicity reference value (TRV) of 93 mg/kg-bw/day for terrestrial mammals (based on reproduction and growth). Based on empirical toxicity data for chickens (*Gallus gallus domesticus*) from a dietary study, the chronic hazard threshold for terrestrial birds is 16 mg/kg-bw/day based on reduced flock production. Based on empirical toxicity data for tobacco pollen exposed via gas injected into germination medium, the acute hazard threshold for terrestrial plants is 9.2 mg/L.

1 APPROACH AND METHODOLOGY

1,2-Dichloroethane is a colorless, oily liquid with a chloroform-like odor, and is primarily used to manufacture vinyl chloride (U.S. EPA, 2025f). EPA reviewed studies of the toxicity of 1,2-dichloroethane and analogs 1,1-dichloroethane, 1,2-dichloropropane, and 1,1,2-trichloroethane to aquatic and terrestrial organisms to determine environmental hazard thresholds for use in the *Draft Risk Evaluation for 1,2-Dichloroethane* (U.S. EPA, 2025f).

During scoping, EPA reviewed potential environmental hazards associated with 1,2-dichloroethane and identified sources of environmental hazard data shown in Figure 2-9 of *Final Scope of the Risk Evaluation for 1,2-Dichloroethane; CASRN 107-06-2* (also called the "final scope") (U.S. EPA, 2020b).

EPA completed the review of environmental hazard data during risk evaluation using the data quality review evaluation metrics and the rating criteria described in the *Draft Systematic Review Protocol Supporting TSCA Risk Evaluations for Chemical Substances Version 1.0: A Generic TSCA Systematic Review Protocol with Chemical-Specific Methodologies* (also called the "Draft Systematic Review Protocol") (U.S. EPA, 2021). Studies were assigned an overall quality of high, medium, low, or uninformative. Studies that received overall quality determinations (OQDs) of high or medium were used to set quantitative hazard thresholds.

EPA assigned OQDs of low or uninformative to 20 aquatic toxicity studies and 6 terrestrial toxicity studies and OQDs of high or medium to 18 aquatic toxicity studies and 3 terrestrial toxicity studies. One study was identified for 1,2-dichloroethane for sediment-dwelling invertebrates. Therefore, in addition to the single study of a benthic invertebrate exposed to 1,2-dichloroethane for 15 days in water, the Agency also used benthic hazard information for the analogy 1,1-dichloroethane, 1,2-dichloropropane, and 1,1,2-trichloroethane to supplement the 1,2-dichloroethane benthic hazard dataset. See Appendix A for the analog selection rationale. EPA identified three sources of benthic hazard data generated from 1,1-dichloroethane, 1,2-dichloropropane, and 1,1,2-trichloroethane test orders (Smithers, 2024a, b, 2023), to assess hazards to benthic species. The studies on the analogs were also reviewed and assigned overall quality determinations of high. For the aquatic studies, seven species had lethal concentration at which 50 percent of test organisms die (LC50) data from acute exposure durations, an appropriate endpoint for assessing acute hazards. The Web-ICE (Version 4.0) modeling approach can predict toxicity values for environmental species that are absent from a dataset and therefore provide a more robust dataset to estimate toxicity thresholds. EPA used predictions for 80 aquatic species from Web-ICE to supplement the acute aquatic empirical hazard data for 1,2-dichloroethane to model an aquatic SSD. Details outlining the Web-ICE and SSD methods are included in Appendix A.

In lieu of terrestrial mammalian wildlife studies, all mammal studies were from mice and rats used as human health model organisms. These mammal studies were used to calculate a mammalian TRV and a chronic dietary chicken study was used to calculate an avian hazard threshold. The TRV and hazard value are expressed as a dose in units of mg/kg-bw/day. Because body weight is normalized, the mammalian TRV and avian hazard threshold can be used with ecologically relevant wildlife species to evaluate chronic dietary exposure to 1,2-dichloroethane.

AQUATIC SPECIES HAZARD

Toxicity to Aquatic Organisms

230 231

232 233

234

235

236 237

238

239

240

241

242 243

244

245

246

247

248 249

250

251

252 253

254

255 256

257

258

259

260

261

262 263

264

265 266

267

268

269 270

271

272

273 274

275

276

277

EPA assigned OQDs of low or uninformative to 20 aquatic toxicity studies and high or medium to 15 aquatic toxicity studies for 1,2-dichloroethane, and high to three studies for analogs 1,1-dichloroethane, 1,2-dichloropropane, and 1,1,2-trichloroethane. All three analog studies were submitted under a TSCA section 4 test order. The Agency identified 17 high- or medium-rated aquatic toxicity studies, summarized in Table 2-1, as the most relevant for quantitative assessment. The remaining high-rated study was represented by a short-term exposure (1 hour) of a single, low-dose of 1,2-dichloroethane, testing for effects on ventilation frequency, ventilation amplitude, and swimming behavior in rainbow trout (Oncorhynchus mykiss (Kaiser K et al., 1995)); however, the data from this study were considered less relevant for establishing a hazard threshold due to the short exposure duration and transient nature of the endpoint.

The Web-ICE application was used to predict LC50 and EC50 (effect concentration at which 50% of test organisms exhibit an effect) toxicity values for 80 additional aquatic organisms (fish, amphibians, aquatic invertebrates, and benthic invertebrates) from empirical fathead minnow and rainbow trout 96hour LC50 data as well as daphnid 48-hour LC50 and EC50 data (Raimondo and Barron, 2010). The Web-ICE application did not allow for entry of hazard values from the following four additional test species as they are not currently included in Web-ICE as surrogate species: midge 48-hour EC50 (analogs 1,1-dichlorethane and 1,2-dichloropropane); brine shrimp 24-hour EC50; northwestern salamander 5.5-day LC50; and leopard frog 5-day LC50. However, these empirical data were used in the SSDs. The aquatic test species (n = 7) and predicted aquatic species (n = 80) toxicity data were then used to calculate the distribution of aquatic species sensitivity to acute 1,2-dichloroethane exposure. For additional details regarding Web-ICE predictions and the SSD analyses, see Appendices B.1.1.1 and B.1.1.2.

Aquatic Vertebrates

Amphibians: EPA assigned an OQD of high to one study containing 1,2-dichloroethane amphibian hazard data resulting from acute exposure (Table 2-1). In the embryo-larval test, northwestern salamanders (Ambystoma gracile) exposed to measured concentrations of 1,2-dichloroethane for 5.5 days under flow-through conditions led to an LC50 of 6.53 mg/L. Leopard frogs (*Lithobates pipiens*) exposed similarly for 5 days had an LC50 of 4.52 mg/L (Black et al., 1982).

Fish: EPA assigned OODs of high or medium to seven studies with 1,2-dichloroethane fish hazard data. Four of the studies contained fish hazard data resulting from acute exposures, one contained fish hazard data resulting from chronic exposures, and two contained fish hazard data for both acute and chronic exposures (Table 2-1). EPA assigned OQDs of low or uninformative to seven studies with 1,2dichloroethane fish hazard data. Six of the studies contained fish hazard data resulting from acute exposures and one contained fish hazard data for both acute and chronic exposures.

For toxicity following acute exposure in fish from high- and medium-rated studies, mortality was observed in fathead minnows (*Pimephales promelas*) and rainbow trout (*Oncorhynchus mykiss*) with 96hour LC50s ranging from 116 to 225 mg/L (Mayer and Ellersieck, 1986; Geiger et al., 1985; Walbridge et al., 1983). EPA used the fathead minnow 96-hour LC50 values to calculate a geometric mean of 126 mg/L. In a fathead minnow early life stage test, no effects were observed 4 to 5 days post-spawning on either hatchability or percent normal larvae at hatch up to the maximum measured concentration of 59 mg/L (Benoit et al., 1982). No mortality occurred in Japanese medaka (Oryzias latipes) after 7 days of exposure up to the maximum measured concentration in the study (77.2 mg/L; (CITI, 1996c)).

quantitative assessment, mortality was observed in bluegill (*Lepomis macrochirus*), sheepshead minnow (*Cyprinodon variegatus*), mud dab (*Limanda limanda*), largemouth bass (*Micropterus salmoides*), and rainbow trout with 96-hour LC50s ranging from 66 to 430 mg/L (<u>Dow Chemical, 1987</u>; <u>Buccafusco et al., 1981</u>; <u>Heitmuller et al., 1981</u>; <u>Dow Chemical, 1979</u>; <u>Pearson and McConnell, 1975</u>). Mortality was also observed in guppy (*Poecilia reticulata*) with a 7-day logLC50 of 3.03 µmol/L (<u>Könemann, 1981</u>) and eyed coho salmon eggs (*Oncorhynchus kisutch*) exposed to 100 percent 1,2-dichloroethane for 1 hour, which resulted in 100 percent mortality 8 hours after initial exposure (<u>Reid et al., 1982</u>). In general, the studies considered uninformative for quantitative use lack key reported details such as chemical information (Chemical Abstracts Service Registry Number [CASRN], source, purity, etc.), the use of a control, and/or the concentrations tested.

For toxicity following chronic exposure in fish from high- and medium-rated studies, in a prolonged toxicity test, Japanese medaka were exposed to measured concentrations of 1,2-dichloroethane under flow-through conditions for 21 days. The no-observed-effect concentration (NOEC) and lowestobserved-effect concentration (LOEC) for mortality were 41.3 and 78.9 mg/L, respectively. EPA calculated the 21-day mortality NOEC and LOEC geometric mean of 57.1 mg/L as the chronic value (ChV) for mortality (Table 2-1). In an embryo-larval test, after 27 days of chronic exposure to measured concentrations of 1,2-dichloroethane under flow-through conditions, rainbow trout survival was determined to be 52 percent at 34.4 mg/L 1,2-dichloroethane (Black et al., 1982). In a fish early life stage test, fathead minnow exposed to measured concentrations of 1,2-dichloroethane under flowthrough conditions for 32 to 33 days resulted in a NOEC and LOEC for decreased weight at 29 and 59 mg/L, respectively, and a NOEC for survival of greater than 59 mg/L (Benoit et al., 1982). EPA calculated the 32- to 33-day growth NOEC and LOEC geometric mean of 41 mg/L as the ChV for fathead minnow growth (Table 2-1). Additionally, for toxicity following chronic exposure in fish from studies considered uninformative for quantitative assessment, mortality and developmental effects were observed in eyed coho salmon eggs exposed to 1,2-dichloroethane concentrations ranging from 54 to 539 ppm for 21 days (Reid et al., 1982). This study was considered uninformative for quantitative use due to concentrations only being measured after the first 24 hours and lacking key reported details including chemical identity (CASRN and analytical verification of chemical identity) and allocation of test organisms to groups.

Aquatic Invertebrates

 EPA assigned OQDs of high or medium to seven studies with 1,2-dichloroethane aquatic invertebrate hazard data. Five of these studies contained hazard data for acute exposures of aquatic invertebrates to 1,2-dichloroethane, and two contained hazard data for both acute and chronic exposures of aquatic invertebrates to 1,2-dichloroethane. EPA assigned OQDs of low or uninformative to five studies with aquatic invertebrate hazard data for acute exposures to 1,2-dichloroethane.

For toxicity following acute exposures in aquatic invertebrates from high- and medium-rated studies, immobilization was observed in brine shrimp (*Artemia salina*) with 24-hour EC50s ranging from 36.4 to 93.64 mg/L (Foster and Tullis, 1985; Foster and Tullis, 1984). The exposures occurred under static conditions in sealed containers ranging from 25 to 100 percent artificial seawater (ASW). Salinity was measured in both studies but only reported in one study (Foster and Tullis, 1984) as 3.2 percent salinity with 100 percent ASW. No immobilization was observed in control groups in either study, indicating that changes in salinity alone did not significantly contribute to immobilization. Immobilization EC50 values decreased with decreasing ASW, which suggests that osmotic stress at lower salinities can increase sensitivity of *A. salina* to toxicants. EPA calculated the 24-hour brine shrimp immobilization EC50 geometric mean of 64.8 mg/L (Table 2-1). *Daphnia magna* exposed to unmeasured concentrations of 1,2-dichloroethane for 48 hours in static conditions in closed test vessels had LC50s ranging from 220

to 270 mg/L, and an immobilization EC50 of 160 mg/L (Richter et al., 1983; Leblanc, 1980). *D. magna* exposed to measured concentrations of 1,2-dichloroethane in semi-static conditions (renewal after 24 hours) for 48 hours had an immobilization EC50 of 99.4 mg/L (CITI, 1996a). EPA acknowledges that the differences in reported EC50 values for *D. magna* between studies may be associated with reported nominal exposures vs. measured.

The Agency considered the immobilization EC50s and mortality LC50s as equivalent measures of acute toxicity and used both to calculate the *D. magna* 48-hour geometric mean of 175 mg/L based on definitive immobilization and mortality EC50s and LC50s (Table 2-1). During the first 4 days of a reproductive inhibition test, no mortality occurred at the highest concentration (86.8 mg/L) in D. magna exposed to measured concentrations of 1,2-dichloroethane, resulting in a 96-hour LC50 of greater than 86.8 mg/L (CITI, 1996d). Nominal concentrations were used by the study authors to set the LC50s as measured concentrations were within 20 percent of nominal concentrations. However, within this hazard assessment the reported time-weighted mean measured concentrations have been used instead of nominal concentrations for the LC50 values that were reported as greater than the highest tested concentration. Additionally, for toxicity following acute exposures in aquatic invertebrates from studies that were considered uninformative for quantitative assessment, mortality was observed in brine shrimp with 24-hour LC50 values ranging from 0.07 to 0.34 mmol/L (Sanchez-Fortun et al., 1997) and 320 mg/L (Price et al., 1974). Teratogenicity of 1,2-dichloroethane was observed in brine shrimp at concentrations ranging from 0.25 to 25 ppm, although the authors noted that "the impression from the limited data is that the system is not very sensitive" (Kerster and Schaeffer, 1983). Immobilization was observed in D. magna with 24-hour EC50 values ranging from 150 to 383 mg/L (Freitag et al., 1994; Kühn et al., 1989). In general, the studies considered uninformative for quantitative use lack key reported details such as chemical information (CASRN, source, purity, etc.), the use of a control, and/or the concentrations tested.

For toxicity following chronic exposures in water-column dwelling invertebrates, *D. magna* is the only species represented in the dataset. *D. magna* exposed to measured concentrations of 1,2-dichloroethane for 21 days in semi-static conditions (daily renewal) in sealed test vessels had a chronic 21-day NOEC of 0.934 mg/L and LOEC of 2.44 mg/L for reproductive inhibition, based on the number of offspring produced (CITI, 1996d). Nominal concentrations were used to set the NOEC and LOEC by the study authors as measured concentrations were within 20 percent of nominal. However, within this hazard assessment the reported time-weighted mean measured concentrations have been used instead of nominal concentrations for the reported NOECs and LOECs. Additionally, *D. magna* exposed to measured concentrations of 1,2-dichloroethane for 28 days in semi-static conditions (3 times weekly renewal) in covered test vessels had a chronic 28-day NOEC of 11 mg/L and LOEC of 21 mg/L for reproductive inhibition, respectively, based on the number of offspring produced (Richter et al., 1983). EPA calculated the chronic reproductive NOEC and LOEC geometric mean of 4.8 mg/L as the ChV for reproduction based on the 21- and 28-day NOECs and LOECs (Table 2-1).

Benthic Invertebrates

EPA assigned OQDs of high- or medium-rated to five studies with sediment-dwelling invertebrate hazard data for 1,2-dichloroethane or its analogs 1,1-dichloroethane, 1,2-dichloropropane, and 1,1,2-trichloroethane. One study contained hazard data for acute exposure to 1,2-dichloroethane, one contained hazard data for chronic exposure to 1,2-dichloroethane, one contained hazard data for acute exposure to the analog 1,1-dichloroethane, one contained hazard data for acute exposure to the analog 1,2-dichloropropane, and one contained hazard data for chronic exposure to the analog 1,1,2-trichloroethane. EPA assigned OQDs of low or uninformative to two studies with sediment-dwelling invertebrate hazard data for 1,2-dichloroethane. One study contained hazard data for acute exposure to

1,2-dichloroethane and one study contained hazard data for both acute and chronic exposure to 1,2-dichloroethane.

380 For h
381 matu
382 nymp
383 non-o
384 excee
385 insta
386 dichl
387 immo
388 EPA
389 immo
390 sedir

377

378

379

For hazard from acute exposure sediment-dwelling invertebrates from high- and medium-rated studies, mature scud (Gammarus fasciatus) and late instar (second year) stonefly (Pteronarcys californica) nymphs exposed to measured concentrations of 1,2-dichloroethane for 96 hours in static conditions had non-definitive LC50s (i.e., the highest concentration tested did not result in 50% or greater mortality) exceeding 100 mg/L, which cannot be used to set a hazard threshold (Mayer and Ellersieck, 1986). First instar midge (Chironomus riparius) larvae exposed to measured concentrations of the analogs 1.2dichloropropane and 1,1-dichloroethane for 48 hours in static or static-renewal conditions had immobilization and mortality EC50 values of 49 mg/L and 150 mg/L, respectively (Smithers, 2024a, b). EPA calculated the C. riparius 48-hour EC50 geometric mean of 86 mg/L based on definitive immobilization and mortality EC50s (Table 2-1). Additionally, for hazard from acute exposure to sediment-dwelling invertebrates from portions of studies considered uninformative for quantitative assessment, mortality was observed in Australian barnacles (Elminius modestus), the marine polychaete worm species Ophryotrocha labronica, and sand shrimp (Crangon crangon). The Australian barnacles had a 48-hour LC50 value of 186 mg/L (Failla et al., 1982), the O. labronica had two 96-hour LC50 values of 400 mg/L (shock exposure) and 900 mg/L (successive increase of concentration during the first hour), and sand shrimp had a 24-hour LC50 of 170 mg/L (Rosenberg et al., 1975). The study by Failla et al. (1982) was considered uninformative for quantitative assessment due to the lack of a control and the number of exposure groups and concentrations tested. The study by Rosenberg et al. (1975) was considered uninformative for quantitative assessment due to estimating a 96-hour LC50, despite reaching 50 percent mortality at 24-hours, in addition to the lack of reported details regarding chemical source, allocation of test organisms to study groups, and acclimation of test organisms.

401 402 403

404

405

406

407

408

409

410

411

412

413

414

415

416

391

392

393

394

395

396 397

398

399

400

For hazard from chronic exposures to sediment-dwelling invertebrates, O. labronica exposed to nominal concentrations of 1,2-dichloroethane in water for 15 days under semi-static renewal conditions had reduced hatching with a modeled EC10 of 309 mg/L and EC50 of 352 mg/L (Rosenberg et al., 1975). Derivation of the EC10 and EC50 is described in Appendix B.1.1.3. EPA also considered data from an analog, 1,1,2-trichloroethane, which was deemed suitable for targeted read-across of chronic benthic hazard to 1,2-dichloroethane as described in Appendix A. Larvae of the freshwater midge C. riparius exposed over two generations to measured concentrations of 1,1,2-trichloroethane in sediment had significantly decreased emergence in second-generation (F1) larvae exposed to the highest tested concentration of 1,1,2-trichloroethane (measured 44 mg/kg sediment dry weight, nominal 1,000 mg/kg), resulting in a chronic 28-day NOEC of 19 mg/kg and LOEC of 44 mg/kg. Using these values, EPA calculated a ChV of 29 mg/kg for growth and development (Table 2-1). The decrease in F1 larval emergence at the LOEC was approximately half of the control value ($42 \pm 24\%$ emergence in the 44 mg/kg treatment group compared to $77 \pm 8\%$ in the control group; values presented as average \pm standard deviation) (Smithers, 2023). The NOEC and LOEC for the same endpoint within this study were also expressed in measured pore water concentrations at 66 and 130 mg/L, from which EPA calculated a growth and development ChV of 93 mg/L in benthic pore water (Table 2-1).

417 418 419

420

421

422

423

424

425

None of the other measured endpoints for F1 midges or parent midges (F0) in the definitive study resulted in a definitive LOEC. However, it should be noted that percent emergence was significantly decreased in F0 larvae ($44 \pm 16\%$ compared to $81 \pm 8\%$ emergence in the controls) exposed to the second highest tested 1,1,2-trichloroethane concentration (measured 10 mg/kg), but not the highest tested 1,1,2-trichloroethane concentration (30 mg/kg). Therefore, an LOEC was not established for percent emergence in the F0 larval midges. In the preliminary range-finding study conducted to select nominal test concentrations for the definitive study, decreased emergence was also noted in F1 larval

Table 2-1. Aquatic Species Environmental Hazard Studies for 1,2-Dichloroethane

Study Type	Test Organism	Species	Endpoint	Hazard Values ^a (mg/L)	Geometric Mean ^b (mg/L)	Effect Endpoint(s)	Citation (Study Quality)
		Northwestern	5.5-day freshwater EC50	6.53			Black et al. (1982) (High)
		salamander (Ambystoma gracile)	9.5-day freshwater LC50	2.54			
	Amphibians		5-day freshwater EC50	4.52			
		Leopard frog (Lithobates pipiens)	9-day freshwater LC10	0.1832			
		(Limoducs pipiens)	9-day freshwater LC50	4.4			
		Rainbow trout (Oncorhynchus mykiss)	24-hour freshwater LC50	225		Mortality	Walbridge et al. (1983) (Medium); Mayer and Ellerrical (1986) (Medium)
		Fathead minnow		141			Ellersieck (1986) (Medium)
Acute	Fish	(Pimephales promelas)	48-hour freshwater LC50	118			Walbridge et al. (1983)
			72-hour freshwater LC50	116			(Medium)
		Fathead minnow (Pimephales promelas)	96-hour freshwater LC50	116; 136	126		Geiger et al. (1985) (High); Walbridge et al. (1983) (Medium)
		Rainbow trout (Oncorhynchus mykiss) 4-5-day freshwater NOEC Pathead minnow 96-hour freshwater LC50 225 225 4-5-day freshwater NOEC	96-hour freshwater LC50	225		Mortality	Mayer and Ellersieck (1986) (Medium)
					D 1 (1000) (W. 1)		
		(Pimephales promelas)	4–5-day freshwater NOEC	≥59		Development/Growth	Benoit et al. (1982) (High)
	Fish	Japanese medaka (Oryzias latipes)	7-day freshwater LC50	>77.2		Mortality	<u>CITI (1996c)</u> (High)
		Brine shrimp (Artemia salina)	24-hour saltwater EC50	36.4; 79.7; 93.64	64.8		Foster and Tullis (1985) (Medium); Foster and Tullis (1984) (Medium)
Acute	Aquatic		24-hour freshwater EC50	185		Immobilization	<u>CITI (1996a)</u> (High)
	invertebrates	Daphnia magna	24-hour freshwater NOEC/LOEC	93.3/174	127		
			24-hour freshwater LC50	>86.8; 250		Mortality	CITI (1996d) (High); <u>Leblanc</u> (1980) (Medium)

Study Type	Test Organism	Species	Endpoint	Hazard Values ^a (mg/L)	Geometric Mean ^b (mg/L)	Effect Endpoint(s)	Citation (Study Quality)
			48-hour freshwater LC50	>86.8; 220; 270	175		CITI (1996d) (High); Leblanc (1980) (Medium); Richter et al. (1983) (Medium)
			48-hour freshwater EC50	99.4; 160		Immobilization	CITI (1996a) (High); Richter et al. (1983) (Medium)
	Aquatic invertebrates	Daphnia magna	48-hour freshwater NOEC/LOEC	41.8/61.8	51	immodifization	<u>CITI (1996a)</u> (High)
Acute			48-hour freshwater NOEC	<68			Leblanc (1980) (Medium)
			96-hour freshwater LC50	>100; >86.8			Mayer and Ellersieck (1986) (Medium); CITI (1996d) (High)
	Benthic invertebrates	Stonefly (Pteronarcys californica); Scud (Gammarus fasciatus)	24-hour freshwater LC50	>100; >100		Mortality	Mayer and Ellersieck (1986) (Medium)
			96-hour freshwater LC50	>100; >100			Mayer and Ellersieck (1986) (Medium)
		Chironomus riparius	48-hour freshwater EC50	49 ^d ; 150 ^e	86		Smithers (2024a) (High); Smithers (2024b) (High)
		Japanese medaka	14-day freshwater LC50	>75.9			
		(Oryzias latipes)	21-day freshwater LC50	>78.9		Mortality	
			21-day freshwater NOEC/LOEC	41.3/78.9	57.1	Wiortanty	CITI (1996c) (High)
		Japanese medaka (Oryzias latipes)	21-day freshwater NOEC/LOEC	41.3/78.9		Behavioral	(ingii)
Chronic	Fish		21-day freshwater NOEC	≥78.9		Developmental/ Growth	
		Rainbow trout	23-day freshwater LC50	~34.4 ^c		Montolity	Plack et al. (1092) (High)
		(Oncorhynchus mykiss)	27-day freshwater LC50	~34.4 ^c		Mortality	Black et al. (1982) (High)
		Fathead minnow (Pimephales promelas)	32–33-day freshwater NOEC/LOEC	29/59	41	Development/ Growth (weight)	Benoit et al. (1982) (High)

Study Type	Test Organism	Species	Endpoint	Hazard Values ^a (mg/L)	Geometric Mean ^b (mg/L)	Effect Endpoint(s)	Citation (Study Quality)
			32–33-day freshwater NOEC	59		Mortality	
			7-day freshwater LC50	>86.8		Mortality	
Chronic			~8-day freshwater NOEC/LOEC	38.1/86.8		Reproductive/ Teratogenic (time to first brood)	
	Aquatic	Danhuia magna	14-day freshwater LC50	>86.8		Mortality	
	Invertebrates	Llanhuia maana	14-day freshwater EC50	2.19		Reproductive/ Teratogenic (offspring produced)	CITI (1996d) (High)
			21-day freshwater LC50	>86.8		Mortality	
			21-day freshwater NOEC	86.8		Mortality	
		rtebrates Daphnia magna	21-day freshwater EC50	3.58		Reproductive/ Teratogenic (offspring produced)	
	Aquatic		21-day freshwater NOEC/LOEC	0.934/2.44	4.0	Reproductive/	
	Invertebrates		28-day freshwater NOEC/LOEC	11/21	4.8	Teratogenic (offspring produced)	Richter et al. (1983) (High)
Chronic			28-day freshwater NOEC/LOEC	42/72	55	Development/ Growth (length)	Richter et al. (1983) (High)
	Benthic Invertebrates	Ophryotrocha labronica	15-day saltwater EC10	309		Reproductive/ Teratogenic (hatchability)	Rosenberg et al. (1975) (High)
		Chironomus riparius	2-generation freshwater NOEC/LOEC	66/130 ^f 19/44 ^{f g}	93 (ChV) 29 (ChV) ^g	Mortality/Growth/ Reproduction/ Development	Smithers (2023) (High)
Acute	Algae	Raphidocelis subcapitata	72-hour freshwater EC50	124		Development/ Growth	<u>CITI (1996b)</u> (High)

Study Type	Test Organism	Species	Endpoint	Hazard Values ^a (mg/L)	Geometric Mean ^b (mg/L)	Effect Endpoint(s)	Citation (Study Quality)
---------------	------------------	---------	----------	---	--	--------------------	-----------------------------

ChV = chronic value; EC = effect concentration; LC = lethal concentration; LOEC = lowest-observed-effect concentration; NOEC = no-observed-effect concentration

^a Hazard values presented as ranges represent the range of all the definitive values in the citations and are presented with the number of significant figures reported by the authors. Values in bold were used to derive hazard thresholds for aquatic species as described in Section 4 of this document.

^b Geometric mean of definitive values only (*i.e.*, >100 mg/L was not used in the calculation).

^c Study authors reported that 52% survival was observed at 34.4 mg/L.

^d Hazard values represented by analog 1,2-dichloropropane.

^e Hazard values represented by analog 1,1-dichloroethane.

^f Hazard values represented by analog 1,1,2-trichloroethane.

g Hazard values in mg/kg sediment.

midges exposed to the highest tested concentration of 1,1,2-trichloroethane ($14 \pm 6\%$ emergence of F1 larval midges exposed to nominal 1,000 mg/kg sediment dry weight compared to $90 \pm 11\%$ emergence in the control larval midges (Smithers, 2023)). Although the preliminary range-finding study did not report measured concentrations of 1,1,2-trichloroethane in the sediment and nominal concentrations are not expected to be representative of actual concentrations, the results supported decreased emergence in F1 larvae in the definitive study as reduced emergence was observed at the same nominal concentration in both studies (1,000 mg/kg sediment dry weight).

Aquatic Plants

EPA assigned OQDs of high to one study and low or uninformative to six studies with aquatic plant hazard data. Green algae species *Raphidocelis subcapitata* (formerly *Selenastrum capricornutum*) exposed to measured concentrations of 1,2-dichloroethane for 72 hours under static conditions in closed vessels had a growth inhibition EC50 value of 124 mg/L (CITI, 1996b) that was used for quantitative risk assessment. Additional aquatic plant hazard observed in studies considered uninformative for quantitative assessment included growth inhibition, effects on respiration, and decreased carbon uptake during photosynthesis. Growth inhibition EC50 values were observed for *R. subcapitata* (48-hour EC50s: 154.93–209.3 mg/L) (Tsai and Chen, 2007; Hsieh et al., 2006) and *Desmodesmus subspicatus* (72-hour EC50: 189 mg/L; 96-hour EC50s: 166–213 mg/L) (Behechti et al., 1995; Freitag et al., 1994). A reduction in dissolved oxygen production was observed in *R. subcapitata* with a 48-hour EC50 of 193.4 mg/L (Hsieh et al., 2006). A reduction in carbon uptake during photosynthesis was observed for the marine diatom *Phaeodactylum tricornutum* with an EC50 of 340 mg/L (Pearson and McConnell, 1975). These studies were generally considered uninformative for quantitative assessment due to limited reported study details (*e.g.*, use of a control was unclear, number and spacing of exposure groups was not reported, etc.).

3 TERRESTRIAL SPECIES HAZARD

EPA assigned OQDs of high or medium to seven acceptable terrestrial toxicity studies and OQDs of uninformative to six studies. The high- and medium-rated studies contained relevant 1,2-dichloroethane terrestrial toxicity data for three Norway rat (Rattus norvegicus) strains (Sprague-Dawley, F344/N, and an unidentified strain), one mouse (Mus musculus) strain (B6C3F1), the domesticated white leghorn chicken (Gallus gallus domesticus), and the terrestrial plant Nicotiana tabacum (tobacco). Because no hazard data for mammalian wildlife exposed to 1,2-dichloroethane were reasonably available, EPA used ecologically relevant hazard data from human health animal model laboratory rat and mouse studies to represent hazard for terrestrial mammals. Although the study methods are designed for use in determining human health hazard effects, some of the outcomes measured in these studies are ecologically relevant. An additional study assigned an overall quality rating of high was identified for the terrestrial soil invertebrate earthworm (Eisenia fetida); however, this study was not deemed suitable for quantitative assessment due to the exposure method. Earthworms were exposed for 48 hours in closed vials via contact with filter paper treated with target 1,2-dichloroethane and analog 1,1,2trichloroethane (Neuhauser et al., 1985). The filter paper contact test is not considered a relevant exposure pathway for soil invertebrates due to uncertainty in the amount of chemical absorbed by the earthworm via dermal contact. EPA identified the other nine high- or medium-rated terrestrial toxicity studies, displayed in Table 3-1, as relevant for quantitative assessment.

Terrestrial Vertebrates

452

453 454

455

456

457

458 459

460

461

462 463

464

465

466

467

468

469

470 471

472

473

474

475

476

477 478

479

480

481

482

483

484 485

486

487 488

489

490

491 492

493

494

495

496

497

498

499

500

EPA did not identify any reasonably available terrestrial vertebrate studies with mammalian or avian wildlife species for either 1,2-dichloroethane or its analogs 1,1-dichloroethane and 1,1,2-trichloroethane. Six chronic toxicity studies for human health animal model laboratory rodents and the domesticated chicken with ecologically relevant effects (*e.g.*, behavior, reproduction, growth, survival) were identified for use in deriving hazard thresholds.

EPA has quantitatively evaluated the relative contribution of inhalation exposures for terrestrial mammals and birds in *U.S. EPA Guidance for Developing Ecological Soil Screening Levels* (Eco-SSLs) (<u>U.S. EPA, 2003a</u>, <u>b</u>). For terrestrial mammals and birds, relative contribution to total exposure associated with inhalation is minor in comparison to exposures by diet and indirect ingestion. Therefore, the Agency selected toxicity studies with oral exposure to 1,2-dichloroethane and not inhalation exposure to represent ecological hazard to terrestrial vertebrates.

Mammals: Ecologically relevant, population-level effects were observed in the mammalian studies (Table 3-1). Observed effects occurred below 500 mg/kg-bw/day in rats and mice. One study observed decreased feed consumption in rats exposed to 1,2-dichloroethane via gavage for 90 days (NOAEL: 75 mg/kg-bw/day; LOAEL: 150 mg/kg-bw/day) (Daniel et al., 1994). Tremors were observed by NTP (1991) in male and female rats exposed to 1,2-dichloroethane via gavage for 13 weeks (NOAEL range: 86–107 mg/kg-bw/day; LOAEL range: 171–214 mg/kg-bw/day). Increased testes weights were observed in one study in rats exposed to 1,2-dichloroethane via gavage for 90 days (NOAEL: 75 mg/kgbw/day; LOAEL: 150 mg/kg-bw/day) (Daniel et al., 1994). A significant decrease in maternal body weight was observed by Payan et al. (1995) in rats exposed to 1,2-dichloroethane via gavage for 15 days (NOAEL: 158 mg/kg-bw/day; LOAEL: 198 mg/kg-bw/day). Rats and female mice exhibited significant decreases in body weight following exposure to 1,2-dichloroethane via gavage over the course of 90 days to 78 weeks (NOAEL range: 75–106 mg/kg-bw/day; LOAEL range: 150–214 mg/kg-bw/day) (Daniel et al., 1994; NTP, 1978). Mortality occurred in both rats and mice exposed to 1,2-dichloroethane via gavage over the course of 10 days to 78 weeks (NOAEL range: 100–238 mg/kg-bw/day; LOAEL range: 238-300 mg/kg-bw/day) (Payan et al., 1995; Daniel et al., 1994; NTP, 1991, 1978). For additional details on these calculations, see Draft Mammalian TRV Calculator for 1,2-Dichloroethane

501 (<u>U.S. EPA, 2025e</u>).

Birds: EPA assigned an OQD of medium to one study containing 1,2-dichloroethane avian hazard data resulting from chronic exposure. In the dietary study, Alumot et al. (1976a) observed effects on feed intake and reproduction for white leghorn chickens (Gallus gallus domesticus) exposed to 1,2-dichloroethane. The feed intake rate from months 9 through 18 of egg laying at the highest treatment level was decreased compared to the control, which the authors indicated could be a result of decreased egg production. The author-reported NOAEL and LOAEL were 175 and 350 ppm, respectively, which EPA converted to a NOAEL and LOAEL of 8.8 mg/kg-bw/day and 18 mg/kg-bw/day. The Agency calculated the geometric mean of the feed intake rate NOAEL and LOAEL as 13 mg/kg-bw/day (Table 3-1). The flock production rate following 8.5 months of exposure to 1,2-dichloroethane was significantly decreased at the highest treatment level compared to the control, with the author-reported NOAEL and LOAEL of 175 ppm and 350 ppm. EPA converted those to a NOAEL and LOAEL of 11 mg/kg-bw/day and 22 mg/kg-bw/day, respectively. The Agency subsequently calculated the geometric mean of the flock production rate NOAEL and LOAEL as 16 mg/kg-bw/day (Table 3-1). For additional details on these calculations, see Draft Avian Hazard Value Calculator for 1,2-Dichloroethane (U.S. EPA, 2025a).

Terrestrial Invertebrates

One soil invertebrate hazard study for 1,2-dichloroethane was assigned an OQD of high, and six terrestrial invertebrate studies were assigned OQDs of uninformative. A 48-hour contact exposure of earthworms to 1,2-dichloroethane applied to filter paper reported a mortality LC50 of 60 µg/cm² (Neuhauser et al., 1985). However, because the filter paper contact test is not considered a relevant exposure pathway for soil invertebrates due to the absorbed amount of chemical to earthworm via dermal contact being uncertain, EPA did not establish a hazard threshold from the earthworm hazard data. A 14-day LC50 toxicity prediction of 195 mg/L 1,2-dichloroethane for earthworm was generated from the neutral organics category using U.S. EPA's Ecological Structure Activity Relationships (ECOSAR) Prediction Model (V2.2) (U.S. EPA, 2022). The relevant chemical category for 1,2-dichloroethane (neutral organics category) in ECOSAR includes data from several species of earthworm, including data from *Eisenia fetida* (U.S. EPA, 2022).

Additional hazard effects observed in terrestrial invertebrates from studies considered uninformative for quantitative assessment include mortality, genotoxicity, and oxidative stress. One study with the skin beetle (Trogoderma granarium), (Punj, 1970), reported 7-day LD50 values ranging from 43.85 mg/L to 142.00 mg/L in the skin beetle reared on 10 natural foods. In another study with T. granarium, Shivanandappa and Rajendran (1987) determined percent mortality 15 days after exposure durations of 1, 3, and 5 hours to the concentration 70.0 mg/L (1-hour: 0%; 3-hour: 17.7%; 5-hour: 24.0%). The study by Shivanandappa and Rajendran (1987) also noted reduced glutathione levels at 70.0 mg/L following 1-hour of exposure. However, glutathione levels were not significantly reduced after 3 and 5 hours of exposure. Mortality was observed in three mite species: grain mite (Acarus siro), long hairy mite (Glycyphagus destructor), and mite (Tyrophagus longior); however, the quantity of mortality observed was unclear (Bowley and Bell, 1981). Genotoxic effects were observed in fruit flies (Drosophila melanogaster) ranging from 50 to 200 mM (Rodriguez-Arnaiz, 1998; Ballering et al., 1994). These studies were generally considered uninformative for quantitative use due to issues such as low replication, unclear inclusion of a control group, limited details regarding statistical analysis or inappropriate statistical methods, and the lack of key reported details such as chemical information (CASRN, source, analytical verification, purity), allocation of test organisms to study groups, and analytical verification of test concentrations.

548 Terrestrial Plants

For terrestrial plant species, one medium-quality study was available for the tobacco plant (*Nicotiana tabacum*) and one study considered uninformative for quantitative use was available for the potato plant (*Solanum tuberosum*). Schubert et al. (1995) reported a 25 percent effect dose (ED25) value and an ED50 value for germination inhibition for a 2-hour exposure of tobacco pollen to 1,2-dichloroethane in germination medium (ED25 = 9.2 mg/L and ED50 = 17.1 mg/L, respectively; see Table 3-1). The study authors noted that the short exposure period was necessary to avoid stimulation of pollen germination in the closed test vessel due to an increase in CO₂ partial pressure (Schubert et al., 1995). This study was used for quantitative risk assessment. Rama and Narasimham (1982) tested the effect of 1,2-dichloroethane on changes to potato sprouting. 1,2-dichloroethane did not significantly impact early sprouting, the number of sprouts produced per tuber, sprout length. Sprout yield was significantly increased at 100 ppm compared to the control, but not at the other concentrations tested (10 and 1,000 ppm). This study was considered uninformative for quantitative assessment due to the lack of analytical verification of test concentrations and few reported details regarding test media preparation methods, chemical information (source, analytical verification, purity), allocation and acclimation of the test system, environmental conditions, statistical methods, and the outcome assessment methodology.

Table 3-1. Terrestrial Organisms Environmental Hazard Studies Used for 1,2-Dichloroethane

Study Duration (Type)	Exposure Route	Test Organism	Endpoint(s)	Hazard Values (mg/kg-bw/day) ^a	Geometric Mean (mg/kg- bw/day) ^a	Effect(s)	Citation (Data Evaluation Rating)					
	Terrestrial mammals											
10 days (short-term)	Oral gavage	Sprague-Dawley rat (Rattus norvegicus)	NOAEL	100		Behavior: feeding	Daniel et al. (1994) (High)					
90 days (subchronic)	Oral gavage	Sprague-Dawley rat (Rattus norvegicus)	NOAEL/LOAEL	75/150		Behavior: feeding	Daniel et al. (1994) (High)					
13 weeks (subchronic)	Oral gavage	F344/N rat (Rattus norvegicus)	NOAEL/LOAEL	86/171		Behavior: male tremors	NTP (1991) (High)					
13 weeks (subchronic)	Oral gavage	F344/N rat (Rattus norvegicus)	NOAEL/LOAEL	107/214		Behavior: female tremors	NTP (1991) (High)					
10 days (short-term)	Oral gavage	Sprague-Dawley rat (Rattus norvegicus)	NOAEL	100		Reproduction: testes weight	Daniel et al. (1994) (High)					
90 days (subchronic)	Oral gavage	Sprague-Dawley rat (Rattus norvegicus)	NOAEL/LOAEL	75/150		Reproduction: testes weight	Daniel et al. (1994) (High)					
13 weeks (subchronic)	Oral gavage	F344/N rat (Rattus norvegicus)	NOAEL	86	93 ^b	Reproduction: testes weight	NTP (1991) (High)					
10 days (short-term)	Oral gavage	Sprague-Dawley rat (Rattus norvegicus)	NOAEL	100		Reproduction: ovaries weight	Daniel et al. (1994) (High)					
90 days (subchronic)	Oral gavage	Sprague-Dawley rat (Rattus norvegicus)	NOAEL	150		Reproduction: ovaries weight	Daniel et al. (1994) (High)					
15 days (short-term)	Oral gavage	Sprague-Dawley rat (Rattus norvegicus)	NOAEL/LOAEL	158/198		Reproduction: maternal body weight	Payan et al. (1995) (High)					
5 weeks (subchronic)	Dietary	Rat (Rattus norvegicus)	NOAEL	16	93^b	Growth: female body weight	Alumot et al. (1976b) (Medium)					
13 weeks (subchronic)	Dietary	Rat (Rattus norvegicus)	NOAEL	26	73	Growth: male body weight	Alumot et al. (1976b) (Medium)					
10 days (short-term)	Oral gavage	Sprague-Dawley rat (Rattus norvegicus)	NOAEL	100		Growth: body weight	Daniel et al. (1994) (High)					

Study Duration (Type)	Exposure Route	Test Organism	Endpoint(s)	Hazard Values (mg/kg-bw/day) ^a	Geometric Mean (mg/kg- bw/day) ^a	Effect(s)	Citation (Data Evaluation Rating)
90 days (subchronic)	Oral gavage	Sprague-Dawley rat (Rattus norvegicus)	NOAEL/LOAEL	75/150		Growth: body weight	Daniel et al. (1994) (High)
78 weeks (chronic)	Oral gavage	B6C3F1 mouse (Mus musculus)	NOAEL/LOAEL	106/214		Growth: female body weight	NTP (1978) (Medium)
78 weeks (chronic)	Oral gavage	B6C3F1 mouse (Mus musculus)	NOAEL	139		Growth: male body weight	NTP (1978) (Medium)
13 weeks (subchronic)	Oral gavage	F344/N rat (Rattus norvegicus)	NOAEL	86		Growth: male body weight	NTP (1991) (High)
13 weeks (subchronic)	Oral gavage	F344/N rat (Rattus norvegicus)	NOAEL	107		Growth: female body weight	NTP (1991) (High)
10 days (short-term)	Oral gavage	Sprague-Dawley rat (Rattus norvegicus)	NOAEL/LOAEL	100/300		Mortality	Daniel et al. (1994) (High)
15 days (short-term)	Oral gavage	Sprague-Dawley rat (Rattus norvegicus)	NOAEL	238		Mortality	Payan et al. (1995) (High)
90 days (subchronic)	Oral gavage	Sprague-Dawley rat (Rattus norvegicus)	NOAEL	150		Mortality	Daniel et al. (1994) (High)
13 weeks (subchronic)	Oral gavage	F344/N rat (Rattus norvegicus)	NOAEL/LOAEL	86/171		Mortality: male	NTP (1991) (High)
13 weeks (subchronic)	Oral gavage	F344/N rat (Rattus norvegicus)	NOAEL/LOAEL	107/214		Mortality: female	NTP (1991) (High)
78 weeks (chronic)	Oral gavage	B6C3F1 mouse (Mus musculus)	NOAEL/ LOAEL	106/214		Mortality: female	NTP (1978) (High)
78 weeks (chronic)	Oral gavage	B6C3F1 mouse (Mus musculus)	NOAEL	139		Mortality: male	NTP (1978) (High)
			Te	errestrial birds			

Study Duration (Type)	Exposure Route	Test Organism	Endpoint(s)	Hazard Values (mg/kg-bw/day) ^a	Geometric Mean (mg/kg- bw/day) ^a	Effect(s)	Citation (Data Evaluation Rating)		
8 weeks (subchronic)			NOAEL	≥28		Behavior: feed efficiency			
13.5 months (chronic)	Distant		NOAEL/LOAEL	8.8/18	13	Behavior: feed intake			
7.5 months (chronic)	Dietary		LOAEL	≤9.8		Reproduction: egg weight			
8.5 months (chronic)			NOAEL/LOAEL	11/22	16	Reproduction: flock production rate			
2 years (chronic)			NOAEL	≥20		Reproduction: fertilization rate for treated cocks and hens			
2 years (chronic)		White leghorn chicken (Gallus gallus domesticus)	NOAEL	≥20		Reproduction: fertilization rate for control cocks and treated hens	Alumot et al. (1976a) (Medium)		
2 years (chronic)	Dietary		NOAEL	≥70		Reproduction: fertilization rate for treated cocks and control hens			
8 weeks (subchronic)			NOAEL	≥28		Growth: body weight			
4.5 months (chronic)			NOAEL	≥23		Growth: female body weight			
4.5 months (chronic)			NOAEL	≥70		Growth: male body weight			
	Terrestrial plants								
2 hours (acute)	Germination medium	Tobacco (Nicotiana tabacum)	ED25	9.2 mg/L		Reproductive/ Teratogenic	Schubert et al. (1995) (Medium)		

Study Duration (Type)	Exposure Route	Test Organism	Endpoint(s)	Hazard Values (mg/kg-bw/day) ^a	Geometric Mean (mg/kg- bw/day) ^a	Effect(s)	Citation (Data Evaluation Rating)
2 hours (acute)		Tobacco (Nicotiana tabacum)	ED50	17.1 mg/L			

^a Values in bold were used to derive hazard thresholds for terrestrial species as described in Section 4 of this draft TSD. All values are listed individually with study quality in <u>U.S. EPA (2025d)</u> and <u>U.S. EPA (2025c)</u>.

^b This geometric mean was calculated using the NOAEL values for reproduction and growth.

4 ENVIRONMENTAL HAZARD THRESHOLDS

EPA calculates hazard thresholds to identify hazard to aquatic and terrestrial species. For aquatic species, the hazard threshold is a COC, and for terrestrial species, the hazard threshold is called a hazard value or TRV. These terms (COC, TRV, and hazard value) describe how the values are derived and can encompass multiple taxa or ecologically relevant groups of taxa as the environmental risk characterization serves populations of organisms within a wide diversity of environments. After weighing the scientific evidence, the Agency selects the appropriate toxicity value from the integrated data to use for hazard thresholds. See Section 5 for more details on how EPA weighed the scientific evidence.

For aquatic species, EPA estimates hazard by calculating a COC. These hazard thresholds can be calculated using a deterministic method by dividing a toxicity value by an assessment factor (AF) according to EPA methods (U.S. EPA, 2016b, 2013, 2012). For 1,2-dichloroethane, an AF of 10 was applied to chronic and plant COCs as data were available from all three taxonomic groups (invertebrates, vertebrates, and plants).

Equation 4-1.

 $COC = toxicity\ value\ \div AF$

COCs can also be calculated using probabilistic methods. For example, an SSD can be used to calculate a hazardous concentration for 5 percent of species (HC05). The HC05 estimates the concentration of 1,2-dichloroethane that is expected to be protective for 95 percent of species. The lower-bound of the 95 percent confidence interval (CI) of the HC05 can be used to account for uncertainty and is thus assigned as the COC rather than dividing by a fixed AF. EPA has more confidence in the probabilistic approach when enough data are available because an HC05 is representative of a larger portion of species in the environment. The use of the lower 95 percent CI instead of a fixed AF of 5 also increases confidence as it is a more data-driven way of accounting for uncertainty (see EPA-HQ-OPPT-2023-0265).

For terrestrial mammals and birds, EPA estimates hazard by calculating a TRV when the minimum dataset requirement is met. When the minimum dataset requirement is not met for a given taxon, the relevant hazard value is assigned as the corresponding hazard threshold. Similarly for terrestrial plants and soil invertebrates, the relevant hazard value is assigned as the hazard threshold. When the minimum TRV dataset requirement (3 results [NOAEL or LOAEL values] for reproduction, growth, or mortality for at least 2 mammalian or avian species) is met, EPA prefers to derive the TRV by calculating the geometric mean of the NOAELs across sensitive endpoints (growth and reproduction), rather than using a single endpoint. The TRV method is preferred because the geometric mean of NOAELs across studies, species, and endpoints provides greater representation of environmental hazard to terrestrial mammals and/or birds. However, when the criteria for using the geometric mean of the NOAELs as the TRV are not met (according to methodology described in Section 4.2), the TRV is derived using a single hazard endpoint.

4.1 Aquatic Species COCs

EPA derived an acute COC, three chronic COCs, and an aquatic plant COC using a combination of probabilistic and deterministic approaches with 1,2-dichloroethane hazard data supplemented with read-across from 1,1-dichloroethane, 1,2-dichloropropane, and 1,1,2-trichloroethane. Algae were assessed separately and not incorporated into acute or chronic aquatic COCs, because durations normally considered acute for other species (*e.g.*, up to 96 hours) can encompass several generations of algae. See Appendix A for additional information on methods used to derive COCs. Table 4-1 summarizes the

aquatic hazard thresholds.

Acute Aquatic and Benthic Threshold

Due to little reasonably available acute toxicity data for aquatic organisms exposed to 1,2-dichloroethane, for the acute aquatic and benthic COC, EPA used the 48-hour EC50 toxicity data from *D. magna* and 96-hour LC50 toxicity data from fathead minnow and rainbow trout (Table 2-1) as surrogate species to predict LC50 toxicity values for 80 additional aquatic organisms (including fish, amphibians, and invertebrates) using the Web-ICE application as described in Appendix B.1.1.1 (Raimondo and Barron, 2010). Empirical acute toxicity data were also available for midges (analog 1,1-dichloroethane and 1,2-dichloropropane), brine shrimp, northwestern salamander, and leopard frog, but those species are not available as surrogates in Web-ICE; therefore, data from these three species were used in the SSD but not in generating Web-ICE toxicity predictions. Toxicity data from the test species (n = 7) and predicted species (n = 80) were then used to calculate the distribution of species sensitivity to 1,2-dichloroethane exposure through the SSD Toolbox as shown in Appendix B.1.1.2 (Etterson, 2020a). The calculated HC05 was 17.86 mg/L (95% CI = 11.909–26.445 mg/L; Figure_Apx B-4). The lower 95 percent CI of the HC05 (11.909 mg/L) was selected as the acute COC to represent hazard to aquatic invertebrates and vertebrates.

Chronic Aquatic Threshold

The chronic aquatic COC was derived from the 1,2-dichloroethane ChV of the 21- and 28-day LOECs/NOECs of 4.8 mg/L for the aquatic invertebrate *Daphnia magna* with the application of an AF of 10. The ChV for *D. magna* was the most sensitive chronic endpoint represented (see Table 2-1) for aquatic vertebrates and invertebrates, representing effects of reproductive inhibition of adult *D. magna* (CITI, 1996d; Richter et al., 1983).

Chronic Benthic Thresholds

Due to limited reasonably available chronic toxicity data for benthic organisms exposed to 1,2-dichloroethane, the chronic benthic COCs were derived from the 1,1,2-trichloroethane ChV of the 2-generation LOECs/NOECs for *C. riparius*. The ChV of 93 mg/L with the application of an AF of 10 was selected for comparison to benthic pore water concentrations. The ChV of 29 mg/kg with the application of an AF of 10 was selected for comparison to sediment concentrations. The benthic pore water ChV for *C. riparius* was the most sensitive benthic pore water value for benthic species and the sediment ChV for *C. riparius* was the single sediment hazard value for benthic species. The ChVs represent growth and development effects for second generation larvae (Smithers, 2023).

Aquatic Plant Threshold

- For the algal COC of 1,2-dichloroethane, EPA used the 72-hour 1,2-dichloroethane EC50 toxicity data
- 650 for growth/development from the *R. subcapitata* study (Table 2-1). An AF of 10 was applied to the
- hazard value of 124 mg/L.

Table 4-1. Environmental Hazard Thresholds for Aquatic Environmental Toxicity

Environmental Aquatic Toxicity	Analog	Hazard Value (ppm)	Assessment Factor (AF)	COC (ppm)	Assessment Medium
Acute aquatic exposure: Lower 95% CI of HC05 from SSD	N/A	11.909	N/A ^a	11.909	Water column
Acute benthic exposure: Lower 95% CI of HC05 from SSD	N/A	11.909	N/A ^a	11.909	Benthic pore water
Chronic aquatic exposure: daphnid ChV	N/A	4.8	10	0.48	Water column
Chronic benthic exposure: midge ChV	1,1,2- Trichloroethane	93	10	9.3	Benthic pore water
Chronic benthic exposure: midge ChV	1,1,2- Trichloroethane	29 ^b	10	2.9^{b}	Sediment
Aquatic plant exposure: algae EC50	N/A	124	10	12.4	Water column

ChV = chronic value; CI = confidence interval; COC = concentration of concern; EC = effect concentration; HC05 = hazard concentration that is protective of 95% of the species in the SSD; SSD = species sensitivity distribution ^a EPA used the lower 95% CI of the HC05 to account for uncertainties rather than an AF. ^b Values in mg/kg, otherwise, hazard values in mg/L.

4.2 Terrestrial Species Hazard Values

Terrestrial Vertebrate Threshold

For terrestrial species exposed to 1,2-dichloroethane, EPA estimated hazard using a deterministic approach for plants and birds or by calculating a TRV for mammals (Figure 4-2). For terrestrial mammals, the TRV is expressed as doses in units of mg/kg-bw/day. Although the TRV for 1,2-dichloroethane is derived from laboratory mouse and rat studies, body weight is normalized, therefore the TRV can be used with ecologically relevant wildlife species to evaluate chronic dietary exposure to 1,2-dichloroethane. The flowchart in Figure 4-1 was used to select the data to calculate the TRV with NOAEL and/or LOAEL data (U.S. EPA, 2007). The movement through the flowchart used to calculate the TRV for 1,2-dichloroethane is described below and illustrated in Figure 4-1. EPA used Eco-SSL methods as a starting point in order to establish a TRV-derivation process for use in risk evaluations of chemicals evaluated under TSCA, starting with the chlorinated solvents 1,1-dichloroethane and 1,2-dichloroethane. EPA may not establish TRVs for volatile chemicals in future risk evaluations.

Step 1: The minimum dataset required to derive a TRV consists of three results (NOAEL or LOAEL values) for reproduction, growth, or mortality for at least two mammalian or avian species.

- There are 25 results across 2 species: rats (*Rattus norvegicus*) and mice (*Mus musculus*), which were identified as suitable for use. Endpoints included 10-day, 15-day, 90-day, 5-week, 13-week, and 78-week NOAELs/LOAELs in both male and female rodents. These results are summarized in Table 3-1.
- **Step 2:** Calculation of a geometric mean requires at least three NOAEL results from the reproduction or growth effect groups.
 - Fourteen of the above-referenced results report a NOAEL in the reproduction or growth effect groups.
- Move from Step 2 to Step 4: Calculate a geometric mean of the NOAELs for reproduction and growth.

 Is this number lower than the lowest bounded LOAEL for reproduction, growth, and mortality? Is the mechanism of toxicity addressed?

• The geometric mean of the NOAELs for reproduction and growth is 93 mg/kg-bw/day. This is lower than 150 mg/kg-bw/day, which is the lowest bounded LOAEL for reproduction, growth, and mortality. The primary target organs for 1,2-dichloroethane oral intermediate exposure are the kidney and liver (ATSDR, 2022). Effects on reproduction, growth, and survival are observed at similar concentrations. Therefore, the mechanism of toxicity is addressed.

Therefore, the TRV equals the geometric mean for reproduction and growth.

• The mammalian wildlife TRV for 1,2-dichloroethane is 93 mg/kg-bw/day.

The TRV is representative of various exposure durations (*e.g.*, chronic, subchronic, short-term) but does not encompass acute exposure durations (*e.g.*, <3 days). The TRV is used to assess dietary exposure by trophic transfer from conditions of use (COUs) with releases to surface water and daily maximum deposition, and/or annual land application of 1,2-dichloroethane to soil.

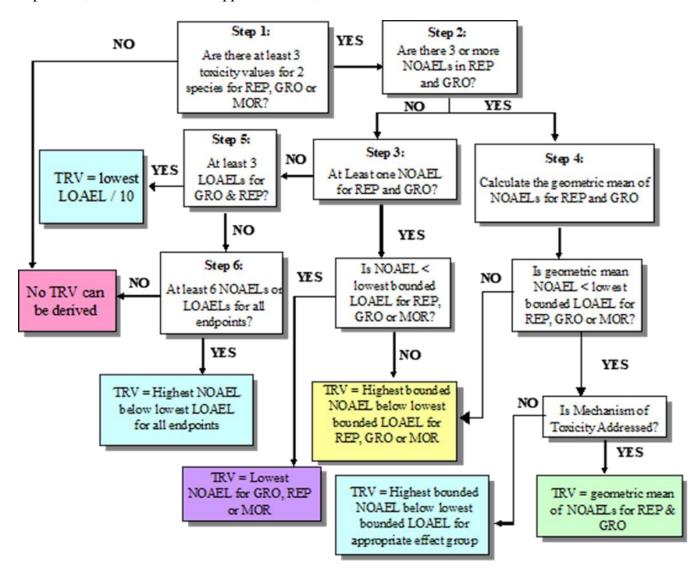
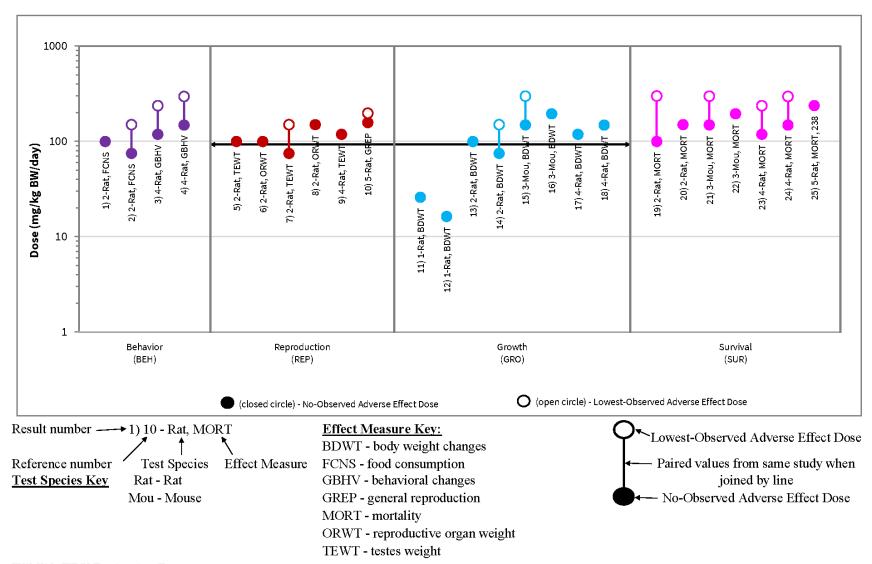


Figure 4-1. TRV Flowchart



Wildlife TRV Derivation Process

- 1) There are at least three results available for two test species within the growth, reproduction, and survival effect groups. There are enough data to derive a TRV.
- 2) There are at least three NOAEL results available in the growth and reproduction effect groups for calculation of a geometric mean.
- 3) The geometric mean of the NOAEL values for growth and reproductive effects equals 92.7 mg 1,2-dichloroethane/kg BW/day, which is lower than the lowest bounded LOAEL of 150 mg 1,2-dichloroethane/kg BW/day for reproduction, growth or survival.

Figure 4-2. Mammalian TRV Derivation for 1,2-Dichloroethane

Avian Threshold

The avian hazard threshold of 16 mg/kg-bw/day was derived from the 1,2-dichloroethane geometric mean of the 8.5-month NOAEL/LOAEL for reduced flock production in the white leghorn chicken. The reproductive endpoint for flock production rate is representative of reproductive success and is the most sensitive and population level-relevant endpoint represented in Table 3-1 for birds (<u>Alumot et al.</u>, <u>1976a</u>).

Terrestrial Plant Threshold

The terrestrial plant hazard threshold was derived from the 1,2-dichloroethane 2-hour ED25 of 9.2 mg/L for tobacco. The ED25 (effective dose of a test material that reduces tissue viability by 25% in toxicity testing) for tobacco was the most sensitive hazard value in the single terrestrial plant reference representing germination effects for pollen (Schubert et al., 1995) (see also Table 4-2).

Table 4-2. Environmental Hazard Thresholds for Terrestrial Environmental Toxicity

Environmental Terrestrial Toxicity	Hazard Value or TRV	Assessment Medium				
Mammal: TRV	93 mg/kg-bw/day	Dietary (trophic transfer)				
Avian (Gallus gallus domesticus): ChV	16 mg/kg-bw/day	Dietary (trophic transfer)				
Soil invertebrate	No data	No data				
Terrestrial plant (Nicotiana tabacum): ED25	9.2 mg/L	Soil pore water				
ChV = chronic value; ED = effective dose; TRV = toxicity reference value						

711 5 WEIGHT OF SCIENTIFIC EVIDENCE CONCLUSIONS FOR 712 ENVIRONMENTAL HAZARD

- After calculating the hazard thresholds that will be carried forward to characterize risk in the *Draft Risk*
- 714 Evaluation for 1,2-Dichloroethane (U.S. EPA, 2025f), a table describing the weight of scientific
- evidence and uncertainties was created to support EPA's decisions (see Table 5-1). See Appendix
- 716 B.1.2.1 for more information on the method the Agency used to weigh the scientific evidence.

Table 5-1. 1,2-Dichloroethane Evidence Table Summarizing the Overall Confidence Derived from Hazard Thresholds

Types of Evidence	Quality of the Database	Consistency	Strength and Precision	Biological Gradient/ Dose-Response	Relevance ^a	Hazard Confidence				
Aquatic										
Acute aquatic assessment	+++	+++	+++	+++	+++	Robust				
Acute benthic assessment	++	+++	++	+++	++	Moderate				
Chronic aquatic assessment	+++	+++	+++	+++	+++	Robust				
Chronic benthic assessment	++	++	+++	+++	+	Moderate				
Algal assessment	+	++	+++	+++	++	Moderate				
Terrestrial										
Chronic mammalian assessment	++	++	++	+++	++	Moderate				
Chronic avian assessment	+	+	++	+++	++	Moderate				
Soil invertebrate assessment	N/A ^b	N/A	N/A	N/A	N/A	Indeterminate ^c				
Terrestrial plant assessment	+	+	++	+++	+	Slight				

^a Relevance includes biological, physical/chemical (including use of analogs), and environmental relevance.

⁺⁺⁺ Robust confidence suggests thorough understanding of the scientific evidence and uncertainties. The supporting weight of scientific evidence outweighs the uncertainties to the point where it is unlikely that the uncertainties could have a significant effect on the hazard estimate.

⁺⁺ Moderate confidence suggests some understanding of the scientific evidence and uncertainties. The supporting scientific evidence weighed against the uncertainties is reasonably adequate to characterize hazard estimates.

⁺ Slight confidence is assigned when the weight of scientific evidence may not be adequate to characterize the scenario, and when the assessor is making the best scientific assessment possible in the absence of complete information. There are additional uncertainties that may need to be considered.

^b N/A indicates that a slight, moderate, or robust confidence cannot be assigned due to the lack of reasonably available data.

^c Indeterminate is noted when a hazard confidence cannot be assigned to an assessment.

5.1 Quality of the Database; Consistency; Strength (Effect Magnitude) and Precision; and Biological Gradient (Dose-Response)

For the acute aquatic assessment, the database consisted of 13 studies with OQDs of high or medium with both aquatic invertebrates and vertebrates represented. Data from six of these studies were supplemented by using Web-ICE version 4.0 (accessed October 8, 2025) to obtain additional estimated acute toxicity values and generate a subsequent SSD output, therefore a robust confidence was assigned to quality of the database. Outcomes in the empirical and predicted data were generally consistent with most toxicity values falling within two log scales of each other. 1,2-Dichloroethane had similar effects on the same species across multiple studies, within one order of magnitude. For example, daphnid 48hour LC50 values ranged from 220 to 270 mg/L across two independent studies, daphnid 48-hour immobilization EC50 values ranged from 99.4 to 160 mg/L across two independent studies, and fathead minnow 96-hour LC50 values ranged from 116 to 136 mg/L across two independent studies. Because toxicity values were comparable among independent studies conducted in well-characterized test organisms, a robust confidence was assigned to consistency of the acute aquatic assessment. The effects observed in the 1,2-dichloroethane empirical dataset for acute aquatic assessment were immobilization, mortality, and development/growth. EC50 (D. magna and A. salina) and LC50 (D. magna, fathead minnow, rainbow trout, northwestern salamander, and leopard frog) values were reported in the six species utilized in the SSD analysis with additional predicted EC50 and LC50 values reported from Web-ICE. Therefore, a robust confidence was assigned to the strength and precision consideration. Dose-response is a prerequisite of obtaining reliable LC50 values and was observed in the empirical studies that were used in the SSD. Effects generally increased with time and increasing chemical concentration. Because dose-response was observed in the empirical studies, a robust confidence was assigned to the dose-response consideration. (Table 5-1).

For the acute benthic assessment, the database consisted of two *C. riparius* studies for the analogs 1,1-dichloroethane and 1,2-dichloropropane with OQDs of high and 96-hour LC50 toxicity predictions for 28 benthic invertebrates based on empirical fish, amphibian, and aquatic invertebrate data for 1,2-dichloroethane (Table_Apx B-1), resulting in a moderate confidence in quality of the database. Outcomes in the empirical and predicted data were generally consistent with most toxicity values falling within 1-log scale (Figure_Apx B-4); therefore, a robust confidence was assigned to consistency of the acute benthic assessment. Empirical analog and predicted data indicate mortality in 29 benthic species; however, there are a lack of reasonably available empirical data on the target chemical to confirm acute hazard in sediment-dwelling organisms. The Web-ICE obtained predictions are based on regressions to a database of empirical toxicity data. Therefore, a moderate confidence was assigned to the strength and precision consideration. A robust confidence was assigned to the dose-response consideration as mortality and immobilization increased with increasing concentration in the empirical study (Table 5-1).

For the chronic aquatic assessment, the database consisted of five studies with OQDs of high with both aquatic invertebrates and vertebrates represented, resulting in robust confidence for quality of the database. The effects observed in the 1,2-dichloroethane empirical dataset for chronic aquatic assessment were mortality, abnormal behavior, growth inhibition, and reproductive inhibition. 1,2-Dichloroethane had chronic effects on daphnid reproduction which were well within two orders of magnitude, with 21 or 28-day NOEC/LOEC pairs ranging from 0.934/2.44 to 11/21 mg/L across two independent studies. Chronic effects observed for multiple fish species across endpoints were similar, with 21-day ChVs of 57.1 in *O. latipes* for both behavioral and mortality effects, and a 21-day NOEC of 78.9 mg/L in *O. latipes* and a 32 to 33-day NOEC/LOEC pair of 29/59 mg/L in *P. promelas* for growth effects. Thus, a robust confidence was assigned to the consistency consideration. Reproductive inhibition was considered the most sensitive endpoint and presented a clear dose-response, with the

LOEC resulting in approximately 80 percent inhibition compared to control and 100 percent in the high dose. Therefore, a robust confidence was assigned to the strength and precision consideration and the dose-response consideration for the chronic aquatic assessment (Table 5-1).

For the chronic benthic assessment, the database consisted of two studies with OODs of high based on target and analog hazard data. One of the studies is a TSCA section 4(a)(2) test order report conducted according to OECD Guideline for the Testing of Chemicals, Guideline 233 ("Sediment-Water Chironomid Life-Cycle Toxicity Test Using Spiked Water or Spiked Sediment") with C. riparius; the second study was an exposure of O. labronica in water, resulting in moderate confidence for quality of the database. Similar adverse reproductive outcomes were observed in offspring of both studies (either % emerged in C. riparius or % hatched in O. labronica); therefore, a moderate confidence was assigned to the consistency consideration. Percent of O. labronica eggs hatched decreased to 0 percent at the highest 1,2-dichloroethane concentration, and emergence in the second-generation (F1) larvae in the 1,1,2-trichloroethane test order report was approximately 50 percent of the control treatment emergence. Additionally, the definitive chironomid emergence result is qualitatively supported by similar findings in the preliminary two-generation screening study in the same study report where percent emergence at the high dose was less than 20 percent that of the control treatment. Therefore, the strength and precision consideration was assigned robust confidence. Because decreases in percent eggs hatched and secondgeneration larval emergence were observed as chemical concentrations increased, a robust confidence was assigned to the dose-response consideration (Table 5-1).

For the algal assessment, the database consisted of one study with an OQD of high containing 1,2-dichloroethane hazard data for one species (*R. subcapitata*). Additionally, the database contains one study with an OQD of low for a second species (*D. subspicatus*), which was not deemed suitable for use in quantitative risk assessment, resulting in a low confidence for quality of the database. Outcomes were consistent between the two algal species, with growth inhibition EC50 values of 124 and 189 mg/L from the high- and low-rated study, respectively. Therefore, a moderate confidence was assigned to the consistency consideration. The empirical value used to set the hazard threshold has a relatively narrow 95 percent confidence interval (106–144 mg/L) with a clear dose-response, with little growth observed at the highest concentration. Therefore, a robust confidence was assigned to the strength and precision consideration and to the dose-response consideration for the algal assessment (Table 5-1).

For the terrestrial mammal assessment, no wildlife studies were available from systematic review; however, five studies with OQDs of high or medium representing two species (mice and rats), were used from human health animal model studies. A TRV derived from the mammal studies was used to calculate the hazard threshold in mg/kg-bw/day. Effects were generally consistent with most of the NOAELs and LOAELs falling within a log-scale of each other, and no apparent differing trends between species. Regarding strength of the effect, mortality was substantial in the datum (ranging from 52–100 percent reduction in survival compared to the relevant study control) whereas growth and reproductive effects, although significant, were generally smaller in magnitude (ranging from 11–57% effects compared to the relevant study control). Moderate confidence was assigned to quality of the database, consistency, and strength and precision for the terrestrial mammalian assessment. Effects were generally noted at higher 1,2-dichloroethane concentrations and increased with increasing study duration; therefore, robust confidence was assigned to the dose-response consideration (Table 5-1).

For the terrestrial bird assessment, a single study with an OQD of medium was available for the chicken resulting in slight confidence for the quality of the database. The terrestrial bird study measured behavioral, reproductive, and growth effects. The single terrestrial bird study was insufficient to characterize consistency in the outcome resulting in slight confidence for consistency. For strength of

effect in the terrestrial bird assessment, the flock production rate at the highest treatment level was consistently statistically significantly reduced compared to the control over the course of the study, with the effect magnitude varying by week and ranging from 10 to 62 percent. Therefore, moderate confidence was assigned to this consideration. Effects observed in the study increased with increasing chemical concentration, therefore robust confidence was assigned to the dose-response consideration (Table 5-1).

For the terrestrial plant assessment, a single study with an OQD of medium was available for tobacco resulting in slight confidence for the quality of the database. The terrestrial plant study measured germination inhibition. The single terrestrial plant study was insufficient to characterize consistency in the outcome resulting in slight confidence for consistency. For strength of effect, germination inhibition was substantial (50% inhibition achieved); therefore, moderate confidence was assigned to this consideration. Germination inhibition sharply increased with increasing dose; therefore, robust confidence was assigned to the dose-response consideration (Table 5-1).

5.2 Relevance (Biological; Physical/Chemical; Environmental)

For the acute aquatic assessment, immobilization and mortality were observed in the empirical data for freshwater and saltwater aquatic invertebrates, freshwater fish, and freshwater amphibians, and mortality was predicted in additional species. Three of the six species with empirical data are considered representative test species, and all six species are ecologically relevant. Although modeled approaches such as Web-ICE can have more uncertainty than empirical data when determining the hazard, the use of the SSD probabilistic approach within this risk evaluation increases confidence compared to a deterministic approach and the use of the lower 95 percent CI instead of a fixed AF also increases confidence, as it is a more data-driven way of accounting for uncertainty. The empirical hazard data for the acute aquatic assessment resulted from exposure to the target chemical, 1,2-dichloroethane. Therefore, a robust confidence was assigned to the relevance consideration for the acute aquatic assessment (Table 5-1).

For the acute benthic assessment, immobilization and mortality were observed in the empirical data for one freshwater invertebrate species, *C. riparius*, which is an ecologically relevant representative test species. Additionally, EC50 and LC50 predictions were observed in 27 benthic invertebrates. As stated above, the use of the lower 95 percent CI of a probabilistically derived hazard value instead of a fixed AF is a more data-driven way of accounting for uncertainty and increases confidence. The predictions were based on empirical 1,2-dichloroethane aquatic species data, whereas the empirical benthic study was based on exposure to analogs 1,1-dichloroethane and 1,2-dichloropropane. Therefore, a moderate confidence was assigned to the relevance consideration for the acute benthic assessment (Table 5-1).

For the chronic aquatic assessment, ecologically relevant population level effects (reproductive, growth, mortality) were observed in four species (*D. magna*, fathead minnow, Japanese medaka, and rainbow trout), all of which are considered representative test species for aquatic toxicity tests. Although *the D. magna* studies utilized semi-static renewal, chemical measurements were obtained and confirmed that actual concentrations remained within 20 percent of nominal concentrations, and the fish studies utilized flow-through conditions, which is environmentally relevant for chronic exposure. Exposure in each study was to 1,2-dichloroethane. Therefore, robust confidence was assigned to the relevance consideration for the chronic aquatic assessment (Table 5-1).

For the chronic benthic assessment, an ecologically relevant population level effect (emergence) was observed in a representative test species (*C. riparius*) for benthic toxicity tests, whereas *O. labronica*, a marine annelid, is less represented in the literature as a test species. Regarding physical and chemical

relevance, the study used to set the hazard threshold was the *C. riparius* study, which tested exposure to 1,1,2-trichloroethane rather than 1,2-dichloroethane. Regarding environmental relevance, in the study exposing *C. riparius*, the test was conducted with sediment present in the system that is environmentally relevant for benthic exposure. However, the chemical exposure was administered at the beginning of each sediment exposure phase with 1,1,2-trichloroethane concentrations in sediment and benthic pore water significantly decreasing over the duration of the exposure phase (so not truly representative of chronic exposure in the benthic environment). The second study exposed *O. labronica* to 1,2-dichloroethane in aqueous conditions without sediment present in the system. Therefore, slight confidence was assigned to relevance.

For the algal assessment, similar effects were observed in two different species of green algae (*D. subspicatus* and *R. subcapitata*). Of these two species, *R. subcapitata* is considered a representative test species for algal toxicity tests and the testing likely encompassed several generations of algae. However, a definitive approach was utilized with an AF of 10 applied to the EC50 from the *R. subcapitata* test to account for uncertainty when applying results from one green algae species to all algal species. The algal testing took place in aqueous growth medium, which is considered environmentally relevant, and was conducted with 1,2-dichloroethane. Therefore, a moderate confidence was assigned to the relevance consideration for the algal assessment (Table 5-1).

For the terrestrial mammalian assessment, the studies tested the target chemical, 1,2-dichloroethane. The TRV was established using the geometric mean of the NOAELs for reproduction and growth, from a dataset including behavior, growth, reproduction, and survival effects in mice and rats, which are considered ecologically relevant apical effects in mammalian receptors, although laboratory mice and rats are not typical ecologically relevant test species. It should be noted that four of the studies utilized gavage administration, which could be considered less environmentally relevant than other methods of administration such as via the diet. Nevertheless, moderate confidence was assigned to the relevance consideration for the terrestrial mammal assessment (Table 5-1).

For the terrestrial avian assessment, ecologically relevant population-level effects observed included effects on behavior, growth, and reproduction. The hazard threshold was set based on reproductive success in chickens (*Gallus gallus domesticus*), which is not a standard representative test species for wildlife toxicity testing. However, that species is a member of the same order (*Galliformes*) as representative upland gamebird test species, such as the northern bobwhite (*Colinus virginianus*). Regarding physical/chemical and environmental relevance, the study tested exposure via the diet to the target chemical, 1,2-dichloroethane. Therefore, a moderate confidence was assigned to the relevance consideration for the terrestrial avian assessment (Table 5-1).

For the terrestrial plant assessment, the observed effect of germination inhibition is an ecologically relevant apical effect and the testing was performed with 1,2-dichloroethane. However, testing was performed in a single agricultural species in growth medium, which could be considered less environmentally relevant than tests conducted in soil. Therefore, a slight confidence was assigned to the relevance consideration for the terrestrial plant assessment (Table 5-1).

6 ENVIRONMENTAL HAZARD ASSESSMENT CONCLUSIONS

EPA considered all reasonably available information identified through the systematic review process under TSCA to characterize environmental hazard endpoints for 1,2-dichloroethane. The following summarizes the hazard values and overall hazard confidence:

• Aquatic species:

- o LC50 and EC50 values from eight exposures to 1,2-dichloroethane in aquatic invertebrates, amphibians, and fish and immobilization EC50 values from exposure to the analogs 1,1-dichloroethane and 1,2-dichloropropane in a benthic invertebrate species were used alongside Web-ICE derived hazard estimates to develop an aquatic and benthic SSD. The lower confidence interval of the HC05 was used as the COC and indicated that acute aquatic toxicity occurs at 11.9 mg/L. EPA has robust confidence that this hazard value represents the level of acute 1,2-dichloroethane exposure at which ecologically relevant effects will occur in aquatic invertebrates and vertebrates.
- O Chronic aquatic effects were observed in aquatic invertebrates and fish. Twenty-one (21-) and 28-day exposures in *D. magna* to 1,2-dichloroethane resulted in reproductive inhibition. The COC based on these studies indicated that chronic toxicity to aquatic species occurs at 0.48 mg/L. EPA has robust confidence that this hazard value represents the level of chronic 1,2-dichloroethane exposure at which ecologically relevant effects will occur in aquatic species.
- o A 72-hour exposure to 1,2-dichloroethane in the green algae *Raphidocelis subcapitata* found a significant reduction in population growth. The COC based on this study indicated that toxicity in algae occurs at 12.4 mg/L. EPA has moderate confidence that this hazard value represents the level of 1,2-dichloroethane at which ecologically relevant effects will occur in algae, because only one high-rated study testing one species was available in the database.

Benthic species:

- An acute benthic COC of 11.9 mg/L was selected based on an aquatic and benthic SSD developed as described above. EPA has moderate confidence that this hazard value represents the level of acute benthic 1,2-dichloroethane exposure at which ecologically relevant effects will occur in benthic invertebrates.
- O A two-generation study in the freshwater midge *C. riparius* exposed to the analog 1,1,2-trichloroethane resulted in significantly decreased emergence in second-generation larvae. The two COCs set based on this study indicated that chronic toxicity occurs at 2.9 mg/kg in benthic invertebrates exposed via sediment and at 9.3 mg/L in benthic invertebrates exposed via benthic pore water. EPA has moderate confidence that these hazard values represent the level of 1,2-dichloroethane exposure at which ecologically relevant effects will occur in benthic invertebrates, because hazard information for only two species was identified, and one of the studies was based on exposure to an analog rather than the target chemical.

Terrestrial species:

O Subchronic and chronic exposure to 1,2-dichloroethane resulted in behavior, growth, reproduction, and mortality effects in rats and mice. The TRV derived from the dataset was ultimately set based on the geometric mean of the NOAELs for reproduction and growth, which was 93 mg/kg-bw/day. EPA has moderate confidence that this hazard value represents the level of 1,2-dichloroethane exposure at which ecologically relevant effects will occur in terrestrial vertebrates, because no wildlife mammalian studies were

available and exposure for the studies used to set the TRV was primarily via gavage,
 which is considered a less environmentally relevant form of exposure.
 Chronic exposure to 1,2-dichloroethane resulted in effects on feed consumption and

- O Chronic exposure to 1,2-dichloroethane resulted in effects on feed consumption and reproduction in chickens. The hazard value derived from this study indicated that chronic toxicity in terrestrial birds occurs at 16 mg/kg-bw/day. EPA has moderate confidence that this hazard value represents the level of 1,2-dichloroethane exposure at which ecologically relevant effects will occur in terrestrial birds, because only a single study in a non-wildlife species was available in the database.
- O Acute exposure to 1,2-dichloroethane resulted in inhibition of germination in tobacco pollen. The hazard value derived from this study indicated that acute toxicity in terrestrial plants occurs at 9.2 mg/L. EPA has slight confidence that this hazard value represents the level of acute 1,2-dichloroethane exposure at which ecologically relevant effects will occur in terrestrial plants, because only one study in an agricultural crop species was represented in the database and the exposure route was via growth medium, which could be considered less environmentally relevant than tests conducted in soil.

For aquatic species, EPA has sufficient hazard data to assess acute and chronic risk to aquatic and sediment-dwelling species, as well as risk to algae from exposure to 1,2-dichloroethane. For terrestrial species, the Agency has sufficient hazard data to assess risk to plants from direct exposure to soil pore water, as well as risk to mammals and birds from dietary exposure to 1,2-dichloroethane.

REFERENCES

972

979

980

981

982

983

984 985

986

987

988

989

990 991

994

1001

1002

1003 1004

1005

1006

- 973 <u>3M Environmental Lab.</u> (1984). [Redacted] Data summary report on the tests for acute & chronic 974 toxicity of fluorochemicals to Daphnia magna (water flea). (Lab Request No. 81098). St. Paul, 975 MN: 3M.
- 976 Alumot, E; Meidler, M; Holstein, P; Herzberg, M. (1976a). Tolerance and acceptable daily intake of ethylene dichloride in the chicken diet. Food Cosmet Toxicol 14: 111-114. 978 http://dx.doi.org/10.1016/S0015-6264(76)80253-2
 - <u>Alumot, E; Nachtomi, E; Mandel, E; Holstein, P.</u> (1976b). Tolerance and acceptable daily intake of chlorinated fumigants in the rat diet. Food Cosmet Toxicol 14: 105-111. http://dx.doi.org/10.1016/S0015-6264(76)80252-0
 - <u>ASTM.</u> (2014). Standard guide for conducting acute toxicity tests on test materials with fishes, macroinvertebrates, and amphibians. (E 29-96(2014)). West Conshohocken, PA. https://compass.astm.org/document/?contentCode=ASTM%7CE0729-96R14%7Cen-US
 - ATSDR. (2022). Toxicological profile for 1,2-dichloroethane: Draft for public comment [ATSDR Tox Profile]. Atlanta, GA. https://wwwn.cdc.gov/TSP/ToxProfiles/ToxProfiles.aspx?id=592&tid=110
 - Ballering, LA; Nivard, MJ; Vogel, EW. (1994). Mutation spectra of 1,2-dibromoethane, 1,2-dichloroethane and 1-bromo-2-chloroethane in excision repair proficient and repair deficient strains of Drosophila melanogaster. Carcinogenesis 15: 869-875. http://dx.doi.org/10.1093/carcin/15.5.869
- 992 <u>Behechti, A; Ballhorn, L; Kettrup, A.</u> (1995). Toxicity of chlorinated alkanes on the alga Scenedesmus 993 subspicatus in a closed test vessel. Fresen Environ Bull 4: 148-153.
 - Belford, B. (2023). Cheminformatics
- 6.2: Similarity coefficients [Encyclopedia]. Davis, CA: LibreTexts.
 https://chem.libretexts.org/Courses/Intercollegiate Courses/Cheminformatics/06%3A Molecular
 Similarity/6.02%3A Similarity Coefficients
- 998 Benoit, DA; Puglisi, FA; Olson, DL. (1982). A fathead minnow Pimephales promelas early life stage 999 toxicity test method evaluation and exposure to four organic chemicals. Environ Pollut Ser A 28: 1000 189-197. http://dx.doi.org/10.1016/0143-1471(82)90075-7
 - Black, JA; Birge, WJ; McDonnell, WE; Westerman, AG; Ramey, BA; Bruser, DM. (1982). The aquatic toxicity of organic compounds to embryo-larval stages of fish and amphibians (pp. 61). (KWRRI Research Report No. 133). Lexington, KY: University of Kentucky. Kentucky Water Resources Research Institute. http://dx.doi.org/10.13023/kwrri.rr.133
 - Bowley, CR; Bell, CH. (1981). The toxicity of twelve fumigants to three species of mites infesting grain. Journal of Stored Products Research 17: 83-87. http://dx.doi.org/10.1016/0022-474X(81)90021-7
- Buccafusco, RJ; Ells, SJ; Leblanc, GA. (1981). Acute toxicity of priority pollutants to bluegill (Lepomis macrochirus). Bull Environ Contam Toxicol 26: 446-452. http://dx.doi.org/10.1007/BF01622118
- 1010 <u>CITI.</u> (1996a). Acute immobilization test on Daphnia magna exposed to 1,2-dichloroethane (translation). 1011 (Test No. 91502). Tokyo, Japan: Ministry of the Environment.
- 1012 <u>CITI.</u> (1996b). Algal growth inhibition test of Selenastrum capricornurum exposed to 1,2-dichloroethane (translation). (Test No. 91501). Tokyo, Japan: Ministry of the Environment.
- 1014 <u>CITI.</u> (1996c). Prolonged toxicity test (21 days) on medaka (Oryzias latipes) exposed to 1,2dichloroethane (translation). (Test No. 91505). Tokyo, Japan: Ministry of the Environment.
- 1016 <u>CITI.</u> (1996d). Reproductive inhibition test on Daphnia magna exposed to 1,2-dichloroethane (translation). (Test No. 91503). Tokyo, Japan: Ministry of the Environment.
- Daniel, FB; Robinson, M; Olson, GR; York, RG; Condie, LW. (1994). Ten and ninety-day toxicity studies of 1,2-dichloroethane in Sprague-Dawley rats. Drug Chem Toxicol 17: 463-477. http://dx.doi.org/10.3109/01480549409014312

- Dow Chemical. (1979). Toxicity of ethylene dichloride to rainbow trout [TSCA Submission]. (ES-288. OTS0517174. 86-870002085. TSCATS/309922).
- https://ntrl.ntis.gov/NTRL/dashboard/searchResults/titleDetail/OTS0517174.xhtml
- 1024 <u>Dow Chemical.</u> (1987). Fish toxicity studies [TSCA Submission]. (OTS0517186. 86-870002097. 1025 TSCATS/309946).
- $\underline{https://ntrl.ntis.gov/NTRL/dashboard/searchResults/titleDetail/OTS0517186.xhtml}$

1030 1031

1032

1033 1034

1035

1039

1040 1041

1042

1043

1044

1045

1046 1047

1048

1049 1050

10511052

1053

1054

1055

1056

- 1027 <u>Dow Chemical.</u> (1988). Letter from Dow Chem Co to U.S. EPA regarding submission of final study 1028 reports for 1,2-dichloropropane with attachments. (EPA/OTS Doc #40-8867156). Midland, MI. 1029 <u>https://ntrl.ntis.gov/NTRL/dashboard/searchResults/titleDetail/OTS0527733.xhtml</u>
 - Etterson, M. (2020b). Technical Manual: SSD Toolbox Version 1.0. (EPA/600/R-19/104). Duluth, MN: U.S. Environmental Protection Agency. https://www.epa.gov/sciencematters/species-sensitivity-distribution-toolbox-new-tool-identify-and-protect-vulnerable
 - Failla, ML; van de Veerdonk, M; Morgan, WT; Smith, JC, Jr. (1982). Characterization of zinc-binding proteins of plasma in familial hyperzincemia. Transl Res 100: 943-952. http://dx.doi.org/10.5555/uri:pii:0022214382904048
- Foster, G; Tullis, RE. (1984). A quantitative structure-activity relationship between partition coefficients and the acute toxicity of naphthalene derivatives in Artemia salina nauplii. Aquat Toxicol AMST: 245-254. http://dx.doi.org/10.1016/0166-445X(84)90023-7
 - Foster, GD; Tullis, RE. (1985). Quantitative structure-toxicity relationships with osmotically stressed Artemia salina nauplii. Environ Pollut Ser A 38: 273-281. http://dx.doi.org/10.1016/0143-1471(85)90132-1
 - Freitag, D; Ballhorn, L; Behechti, A; Fischer, K; Thumm, W. (1994). Structural configuration and toxicity of chlorinated alkanes. Chemosphere 28: 253-259. http://dx.doi.org/10.1016/0045-6535(94)90122-8
 - Geiger, DL; Northcott, CE; Call, DJ; Brooke, LT. (1985). Acute toxicities of organic chemicals to fathead minnows (Pimephales promelas): Volume II. Superior, WI: Center for Lake Superior Environmental Studies, University of Wisconsin-Superior.
 - Heitmuller, PT; Hollister, TA; Parrish, PR. (1981). Acute toxicity of 54 industrial chemicals to sheepshead minnows (Cyprinodon variegatus). Bull Environ Contam Toxicol 27: 596-604. http://dx.doi.org/10.1007/BF01611069
 - Hsieh, SH; Hsu, CH; Tsai, D; Chen, CY. (2006). Quantitative structure-activity relationships for toxicity of nonpolar narcotic chemicals to Pseudokirchneriella subcapitata. Environ Toxicol Chem 25: 2920-2926. http://dx.doi.org/10.1897/06-127R.1
 - <u>Kaiser K, LE; McKinnon, MB; Stendahl, DH; Pett, WB.</u> (1995). Response threshold levels of selected organic compounds for rainbow trout (Oncorhynchus mykiss). Environ Toxicol Chem 14: 2107-2113. http://dx.doi.org/10.1002/etc.5620141214
 - Kerster, HW; Schaeffer, DJ. (1983). Brine shrimp (Artemia salina) nauplii as a teratogen test system. Ecotoxicol Environ Saf 7: 342-349. http://dx.doi.org/10.1016/0147-6513(83)90079-9
- Könemann, H. (1981). Quantitative structure-activity relationships in fish toxicity studies. Part 1:
 Relationship for 50 industrial pollutants. Toxicology 19: 209-221.
 http://dx.doi.org/10.1016/0300-483X(81)90130-X
- 1062 Kühn, R; Pattard, M; Pernak, KD; Winter, A. (1989). Results of the harmful effects of selected water pollutants (anilines, phenols, aliphatic compounds) to Daphnia magna. Water Res 23: 495-499. http://dx.doi.org/10.1016/0043-1354(89)90141-3
- Leblanc, GA. (1980). Acute toxicity of priority pollutants to water flea (Daphnia magna). Bull Environ Contam Toxicol 24: 684-691. http://dx.doi.org/10.1007/BF01608174
- Mayer, FL, Jr.; Ellersieck, MR. (1986). Manual of acute toxicity: Interpretation and data base for 410 chemicals and 66 species of freshwater animals. (PB86239878). Columbia, MO: U.S.
 Department of the Interior, Fish and Wildlife Service.

1070 https://ntrl.ntis.gov/NTRL/dashboard/searchResults/titleDetail/PB86239878.xhtml

1078

10791080

1081

1082

1083

1084

1085 1086

1087

1088

1100 1101

1102

1103

1104 1105

- Mellor, CL; Marchese Robinson, RL; Benigni, R; Ebbrell, D; Enoch, SJ; Firman, JW; Madden, JC;
 Pawar, G; Yang, C; Cronin, MTD. (2019). Molecular fingerprint-derived similarity measures for toxicological read-across: Recommendations for optimal use. Regul Toxicol Pharmacol 101: 121-134. http://dx.doi.org/10.1016/j.yrtph.2018.11.002
- 1075 <u>Mitsubishi Chemical Medience Corporation.</u> (2009a). Acute immobilization test on Daphnia magna 1076 exposed to 1,1-dichloroethane (translation). (A090026). Tokyo, Japan: Ministry of the 1077 Environment (Japan).
 - Mitsubishi Chemical Medience Corporation. (2009b). Reproduction test on Daphnia magna exposed to 1,1-dichloroethane (translation). (A090028). Tokyo, Japan: Ministry of the Environment (Japan).
 - Neuhauser, EF; Durkin, PR; Malecki, MR; Anatra, M. (1986). Comparative toxicity of ten organic chemicals to four earthworm species. Comp Biochem Physiol C Comp Pharmacol Toxicol 83: 197-200. http://dx.doi.org/10.1016/0742-8413(86)90036-8
 - Neuhauser, EF; Loehr, RC; Malecki, MR; Milligan, DL; Durkin, PR. (1985). The toxicity of selected organic chemicals to the earthworm Eisenia fetida. J Environ Qual 14: 383-388. http://dx.doi.org/10.2134/jeq1985.00472425001400030015x
 - NITE. (1995a). J-Check data: Acute immobilization test of 1,2-dichloropropane to Daphnia magna [Website]. https://www.nite.go.jp/chem/jcheck/template.action?ano=28173&mno=2-0081&cno=78-87-5&request_locale=en
- 1089 NITE. (1995b). J-Check Data: Reproduction inhibition test of 1,2-dichloropropane to Daphnia magna 1090 [Website]. https://www.nite.go.jp/chem/jcheck/template.action?ano=28174&mno=2-0081&cno=78-87-5&request_locale=en
- NTP. (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity [NTP]. (TR 55). Bethesda,
 Maryland: U.S. Department of Health and Human Services, National Institutes of Health,
 National Cancer Institute.
 https://ntp.niehs.nih.gov/sites/default/files/ntp/htdocs/lt_rpts/tr055.pdf?vvv
- NTP. (1991). Toxicity studies of 1,2-dichloroethane (ethylene bichloride) (CAS No. 107-06-2) in F344/N rats, Sprague Dawley rats, Osborne-Mendel rats, and B6C3F1 mice (drinking water and gavage studies). In Toxicity Report Series, vol 4. (NTP TOX 4; NIH Publication No. 91-3123). Research Triangle Park, NC. https://ntp.niehs.nih.gov/publications/reports/tox/000s/tox004
 - OECD. (2010). OECD 233: Sediment-water chironomid life-cycle toxicity test using spiked water or spiked sediment. Paris, France.
 - OECD. (2011). OECD 235: Chironomus sp., Acute immobilisation test. Paris, France.
 - Payan, JP; Saillenfait, AM; Bonnet, P; Fabry, JP; Langonne, I; Sabate, JP. (1995). Assessment of the developmental toxicity and placental transfer of 1,2-dichloroethane in rats. Toxicol Sci 28: 187-198. http://dx.doi.org/10.1006/faat.1995.1159
 - Pearson, CR; McConnell, G. (1975). Chlorinated C1 and C2 hydrocarbons in the marine environment. Proc Biol Sci 189: 305-332. http://dx.doi.org/10.1098/rspb.1975.0059
- 1108 Pestana, CB; Firman, JW; Cronin, MTD. (2021). Incorporating lines of evidence from New Approach
 1109 Methodologies (NAMs) to reduce uncertainties in a category based read-across: A case study for
 1110 repeated dose toxicity. Regul Toxicol Pharmacol 120: 104855.
 1111 http://dx.doi.org/10.1016/j.yrtph.2020.104855
- Price, KS; Waggy, GT; Conway, RA. (1974). Brine shrimp bioassay and seawater BOD of petrochemicals. Water Environment and Technology 46: 63-77.
- Punj, GK. (1970). The effect of nutrition on the susceptibility of larvae of Trogoderma granarium Everts (Coleoptera, Dermestidae) to certain fumigants. Journal of Stored Products Research 6: 181-185. http://dx.doi.org/10.1016/0022-474X(70)90007-X
- Raimondo, SDNV; Barron, MG. (2010). Web-Based Interspecies Correlation Estimation (Web-ICE) for Acute Toxicity: User Manual Version 3.1. (600R10004). Raimondo, S., D.N. Vivian, and M.G.

Barron. http://nepis.epa.gov/exe/ZyPURL.cgi?Dockey=P10068ND.txt

1130

1131

1132

1133

1144 1145

1146

1147 1148

1149 1150

1151

1152

11531154

- Rama, MV; Narasimham, P. (1982). A comparative study on the effect of gibberellic acid, Ethrel and Ethylene Chloride on potato (Solanum tuberosum Linn.) sprouting. J Food Sci Tech 19: 144-147.
- Reid, BJ; Morgan, JD; Whelen, MA. (1982). A preliminary examination of the effects of ethylene dichloride on the hatchability of Coho salmon eggs (Oncorhynchus kisutch). Canadian Tech Rep Fish Aquat Sci 1163: 145-153.
- Richter, JE; Peterson, SF; Kleiner, CF. (1983). Acute and chronic toxicity of some chlorinated benzenes, chlorinated ethanes, and tetrachloroethylene to Daphnia magna. Arch Environ Contam Toxicol 12: 679-684. http://dx.doi.org/10.1007/BF01060751
- Ritz, C; Baty, F; Streibig, JC; Gerhard, D. (2015). Dose-Response Analysis Using R. PLoS ONE 10: e0146021. http://dx.doi.org/10.1371/journal.pone.0146021
 - Rodriguez-Arnaiz, R. (1998). Biotransformation of several structurally related 2B compounds to reactive metabolites in the somatic w/w+ assay of Drosophila melanogaster. Environ Mol Mutagen 31: 390-401. http://dx.doi.org/10.1002/(SICI)1098-2280(1998)31:4http://dx.doi.org/10.1002/(SICI)1098-2280(1998)31:4http://dx.doi.org/10.1002/(SICI)1098-2280(1998)31:4http://dx.doi.org/10.1002/(SICI)1098-2280(1998)31:4https://dx.doi.org/10.1002/(SICI)1098-2280(1998)31:4https://dx.doi.org/10.1002/(SICI)1098-2280(1998)31:4https://dx.doi.org/10.1002/(SICI)1098-2280(1998)31:4https://dx.doi.org/10.1002/(SICI)1098-2280(1998)31:4<a href="https://dx.doi.org/10.1002/(SICI)1098-2280(1998)31:4<a href="https://dx.doi.org/10.1002/(SICI)1098-2280
- Rosenberg, R; Grahn, O; Johansson, L. (1975). Toxic effects of aliphatic chlorinated by-products from vinyl chloride production on marine animals. Water Res 9: 607-612. http://dx.doi.org/10.1016/0043-1354(75)90164-5
- Sanchez-Fortun, S; Sanz, F; Santa-Maria, A; Ros, JM; De Vicente, ML; Encinas, MT; Vinagre, E;
 Barahona, MV. (1997). Acute sensitivity of three age classes of Artemia salina larvae to seven chlorinated solvents. Bull Environ Contam Toxicol 59: 445-451.
 http://dx.doi.org/10.1007/s001289900498
- Schubert, U; Wisanowsky, L; Kull, U. (1995). Determination of phytotoxicity of several volatile organic compounds by investigating the germination pattern of tobacco pollen. J Plant Physiol 145: 514-518. http://dx.doi.org/10.1016/S0176-1617(11)81780-3
 - Shivanandappa, T; Rajendran, S. (1987). Induction of glutathione S-transterase by fumigants in larvae of the Khapra beetle, Trogoderma granarium (E.). Pestic Biochem Physiol 28: 121-126. http://dx.doi.org/10.1016/0048-3575(87)90120-9
 - Smithers. (2023). 1,1,2-Trichloroethane Sediment-water chironomid (Chironomus riparius) life-cycle toxicity test using spiked sediment, following OECD Guideline 233. (Smithers Study No. 14331.6105). Pittsburgh, PA: Stantec ChemRisk.
 - Smithers. (2024a). [14C]1,2-Dichloropropane Acute toxicity to midges (Chironomus riparius) under static conditions. (Smithers Study No. 14339.6107). Washington, DC: PDC Consortium.
 - Smithers. (2024b). Acute toxicity to midges (Chironomus riparius) under static-renewal conditions. (Smithers Study No. 14331.6102). Pittsburgh, PA: Stantec ChemRisk, The Vinyl Institute 1,1-Dichloroethane Consortia.
 - <u>Tsai, KP; Chen, CY.</u> (2007). An algal toxicity database of organic toxicants derived by a closed-system technique. Environ Toxicol Chem 26: 1931-1939. http://dx.doi.org/10.1897/06-612R.1
- U.S. EPA. (1998). Guidelines for ecological risk assessment [EPA Report]. (EPA/630/R-95/002F).
 Washington, DC: U.S. Environmental Protection Agency, Risk Assessment Forum.
 https://www.epa.gov/risk/guidelines-ecological-risk-assessment
- U.S. EPA. (2003a). Attachment 1-3 Guidance for Developing Ecological Soil Screening Levels (Eco-SSLs): Evaluation of Dermal Contact and Inhalation Exposure Pathways for the Purpose of Setting Eco-SSLs. (OSWER9285755E). Washington, DC: .S. Environmental Protection Agency, Office of Solid Waste and Emergency Response.
- https://www.epa.gov/sites/production/files/2015-09/documents/ecossl_attachment_1-3.pdf
- U.S. EPA. (2003b). Attachment 1-4. Guidance for developing ecological soil screening levels (Eco SSLs): Review of background concentration for metals. (OSWER Directive 92857-55).
 Washington, DC. https://www.epa.gov/sites/default/files/2015-

1168 09/documents/ecossl_attachment_1-4.pdf

1170

1196

1197

1198

1199

1169 <u>U.S. EPA.</u> (2005). Guidelines for carcinogen risk assessment [EPA Report]. (EPA630P03001F).

Washington, DC. https://www.epa.gov/sites/production/files/2013-

- 1171 09/documents/cancer_guidelines_final_3-25-05.pdf
- U.S. EPA. (2007). Attachment 4-3 Guidance for Developing Ecological Soil Screening Levels (Eco SSLs) Eco-SSL Standard Operating Procedure (SOP) #4: Wildlife Toxicity Reference Value
 Literature Review, Data Extraction and Coding. (OSWER9285755F).
 http://nepis.epa.gov/exe/ZyPURL.cgi?Dockey=P100CDHC.txt
- 1176 <u>U.S. EPA.</u> (2012). Benchmark dose technical guidance [EPA Report]. (EPA100R12001). Washington,
 1177 DC: U.S. Environmental Protection Agency, Risk Assessment Forum.
 1178 https://www.epa.gov/risk/benchmark-dose-technical-guidance
- 1179 <u>U.S. EPA.</u> (2013). Updating CEB's method for screening-level estimates of dermal exposure. Chemical Engineering Branch.
- U.S. EPA. (2016a). Ecological effects test guidelines: OCSPP 850.1075: Freshwater and saltwater fish acute toxicity test [EPA Report]. (EPA 712-C-16-007; EPA-HQ-OPPT-2009-0154-0035).
 Washington, DC: U.S. Environmental Protection Agency, Office of Chemical Safety and Pollution Prevention. https://www.regulations.gov/document/EPA-HQ-OPPT-2009-0154-0035
- 1185 <u>U.S. EPA.</u> (2016b). Weight of evidence in ecological assessment [EPA Report]. (EPA/100/R-16/001).
 1186 Washington, DC: Office of the Science Advisor.
 1187 https://nepis.epa.gov/Exe/ZyPURL.cgi?Dockey=P100SFXR.txt
- U.S. EPA. (2020a). Final Scope of the Risk Evaluation for 1,1,2-Trichloroethane. (EPA-740-R-20-003).
 Washington, DC: U.S. Environmental Protection Agency, Office of Chemical Safety and
 Pollution Prevention. https://www.epa.gov/sites/default/files/2020-09/documents/casrn_79-00-5_112-trichloroethane_finalscope.pdf
- U.S. EPA. (2020b). Final scope of the risk evaluation for 1,2-dichloroethane; CASRN 107-06-2. (EPA 740-R-20-005). Washington, DC: Office of Chemical Safety and Pollution Prevention.
 https://www.epa.gov/sites/default/files/2020-09/documents/casrn 107-06-2 12-dichloroethane final scope.pdf
 - <u>U.S. EPA.</u> (2020c). Final Scope of the Risk Evaluation for 1,2-Dichloropropane. (EPA-740-R-20-006). Washington, DC: U.S. Environmental Protection Agency, Office of Chemical Safety and Pollution Prevention. https://www.epa.gov/sites/default/files/2020-09/documents/casrn_78-87-5_12-dichloropropane_finalscope.pdf
- U.S. EPA. (2021). Draft systematic review protocol supporting TSCA risk evaluations for chemical substances, Version 1.0: A generic TSCA systematic review protocol with chemical-specific methodologies. (EPA Document #EPA-D-20-031). Washington, DC: Office of Chemical Safety and Pollution Prevention. https://www.regulations.gov/document/EPA-HQ-OPPT-2021-0414-0005
- 1205 <u>U.S. EPA.</u> (2024a). Environmental Hazard Assessment for Diisodecyl Phthalate (DIDP). Washington,
 1206 DC: Office of Pollution Prevention and Toxics. https://www.regulations.gov/document/EPA-HQ-OPPT-2024-0073
- U.S. EPA. (2024b). Web-based Interspecies Correlation Estimation (Web-ICE) for Acute Toxicity: User
 Manual, Version 4.0. (EPA/600/B-24/158). Gulf Breeze, FL: Office of Research and
 Development, Gulf Ecosystem Measurement and Modeling Division.
 https://www3.epa.gov/webice/iceManual.html
- 1212 <u>U.S. EPA.</u> (2025a). Draft Avian Hazard Value Calculator for 1,2-Dichloroethane. Washington, DC:
 1213 Office of Pollution Prevention and Toxics, Office of Chemical Safety and Pollution Prevention.
- 1214 <u>U.S. EPA.</u> (2025b). Draft Chemistry and Fate and Transport Assessment for 1,2-Dichloroethane.
- Washington, DC: Office of Pollution Prevention and Toxics, Office of Chemical Safety and Pollution Prevention.

1217 U.S. EPA. (2025c). Draft Data Extraction Information for Environmental Hazard and Human Health 1218 Hazard Animal Toxicology and Epidemiology for 1,2-Dichloroethane. Washington, DC: Office 1219 of Pollution Prevention and Toxics, Office of Chemical Safety and Pollution Prevention. 1220 U.S. EPA. (2025d). Draft Data Quality Evaluation Information for Human Health Hazard Animal Toxicology for 1,2-Dichloroethane. Washington, DC: Office of Pollution Prevention and Toxics, 1221 1222 Office of Chemical Safety and Pollution Prevention. 1223 U.S. EPA. (2025e), Draft Mammalian TRV Calculator for 1,2-Dichloroethane. Washington, DC: Office 1224 of Pollution Prevention and Toxics, Office of Chemical Safety and Pollution Prevention. U.S. EPA. (2025f). Draft Risk Evaluation for 1.2-Dichloroethane. Washington, DC: Office of Pollution 1225 Prevention and Toxics, Office of Chemical Safety and Pollution Prevention. 1226 1227 U.S. EPA. (2025g). Risk Evaluation for 1,1-Dichloroethane. Washington, DC: Office of Pollution 1228 Prevention and Toxics, Office of Chemical Safety and Pollution Prevention. 1229 https://www.regulations.gov/docket/EPA-HO-OPPT-2024-0114 Walbridge, CT; Fiandt, JT; Phipps, GL; Holcombe, GW. (1983). Acute toxicity of ten chlorinated 1230 1231 aliphatic hydrocarbons to the fathead minnow (Pimephales promelas). Arch Environ Contam 1232 Toxicol 12: 661-666. http://dx.doi.org/10.1007/BF01060748 1233 Wickham, H. (2016). ggplot2: Elegant graphics for data analysis. In Use R! New York, NY: Springer-

Verlag. http://dx.doi.org/10.1007/978-3-319-24277-4

APPENDICES

123512361237

12381239

1240

1241

1242

1243

1244

1245 1246

1247

1248

1249

1250

1251

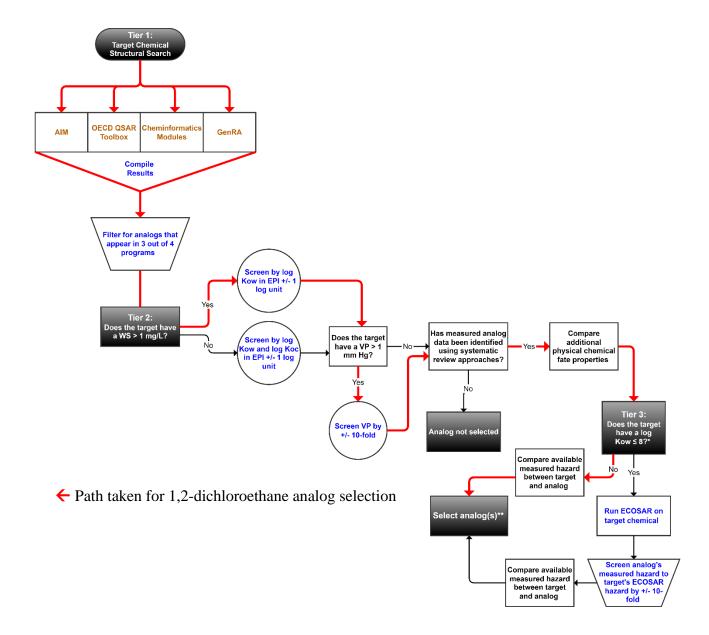
1252

1253

1254

Appendix A ANALOG SELECTION FOR ENVIRONMENTAL HAZARD

Few data were identified for 1,2-dichloroethane for sediment-dwelling invertebrates exposed under chronic durations in sediment or exposed under acute conditions in water, the standard accepted methods to expose sediment-dwelling invertebrates to a chemical (OECD, 2011, 2010). Using a tiered approach with multiple lines of evidence (structural similarity, physical chemical, environmental fate and transport similarity, and ecotoxicological similarity), analog selection was performed to identify appropriate analogs to read-across to 1,2-dichloroethane (Figure_Apx A-1). 1,1-Dichloroethane, 1,2dichloropropane, and 1,1,2-trichloroethane were selected as analogs for read-across of benthic environmental hazard data to supplement the 1,2-dichloroethane benthic environmental hazard based on structural similarity, physical and chemical similarity, environmental fate and transport similarity in water and sediment, and similar ecotoxicological behavior demonstrated in available benthic invertebrate hazard data as well as in hazard data and predictions for relevant taxa (aquatic invertebrates and earthworms) (Figure Apx A-1). The 1,1-dichloroethane and 1,2-dichloropropane acute benthic hazard data and the 1,1,2-trichloroethane chronic benthic hazard data to be used as analog data for 1,2dichloroethane received overall quality determinations (OQDs) of high and are described in Section 2. The similarities between 1,2-dichloroethane and analogs 1,1-dichloroethane, 1,2-dichloropropane, and 1,1,2-trichloroethane are described in detail below.



Figure_Apx A-1. Framework for 1,2-Dichloroethane Environmental Hazard Analog Selection

- * Target chemicals without aquatic hazard data gaps may also bypass the ECOSAR toxicity comparisons.
- ** Weight of scientific evidence and professional judgement involved in finalizing selection.

A.1 Structural Similarity

Structural similarity between 1,2-dichloroethane and candidate analogs 1,1-dichloroethane, 1,2-dichloropropane, and 1,1,2-trichloroethane was assessed using two TSCA NAMs (the Analog Identification Methodology (AIM) program and the Organisation of Economic Cooperative Development Quantitative Structure Activity Relationship [OECD QSAR] Toolbox) and two EPA Office of Research and Development products (Generalized Read-Across [GenRA] and the Search Module within the Cheminformatics Modules, both accessed October 8, 2025) as shown in Table_Apx A-1 and Figure_Apx A-1. These four programs provide complementary methods of assessing structural similarity. There are several different methods for determining structural similarity. A fragment-based

approach (e.g., as implemented by AIM) searches for compounds with similar structural moieties or functional groups. EPA's TSCA New Chemicals Program utilizes the Confidential Business Information (CBI) version of AIM to identify analogs with data (including analogs with CBI; however, no analogs with CBI were included in the environmental hazard analog selection for 1,2-dichloroethane). Analogs with CBI are not found in the public-facing version of AIM in order to protect business confidentiality, and CBI-AIM has undergone updates not found in the public-facing version of AIM. Therefore CBI-AIM can provide a more robust list of analogs, including analogs without CBI. A structural identifier approach (e.g., the Tanimoto coefficient) calculates a similarity coefficient based on molecular fingerprinting (Belford, 2023). Molecular fingerprinting approaches assess similarity in atomic pathway radius between the analog and target chemical substance (e.g., Morgan fingerprint in GenRA that calculates a Jaccard similarity index). Some fingerprints might be better suited for certain characteristics and chemical classes. For example, substructure fingerprints such as PubChem fingerprints perform best for small molecules like drugs, while atom-pair fingerprints—which assigns values for each atom within a molecule and thus computes atom pairs based on these values—are preferable for large molecules. Some tools (e.g., OECD OSAR Toolbox, HCD, GenRA) implement multiple methods for determining similarity. Regarding programs that generate indices, it has been noted that because the similarity value is dependent on the method applied these values should form a line of evidence rather than be utilized definitively (Pestana et al., 2021; Mellor et al., 2019).

Analogs identified via AIM analysis were described as 1st or 2nd pass, with 1st pass using more stringent search criteria than 2nd pass (only analogs not considered CBI are included in Table_Apx A-2). Tanimoto-based PubChem fingerprints were obtained in the OECD QSAR Toolbox (v4.4.1, 2020) using the "Structure Similarity" option. Chemical Morgan Fingerprint scores were obtained in GenRA (v3.1) (limit of 100 analogs, no ToxRef filter). Tanimoto scores were obtained in the Cheminformatics Search Module using Similar analysis. AIM 1st and 2nd pass analogs were compiled with the top 100 analogs with indices greater than 0.5 generated from the OECD QSAR Toolbox and the Cheminformatics Search Module and indices greater than 0.1 generated from GenRA. These filtering criteria are displayed in Table_Apx A-1. Analogs that appeared in three out of four programs were identified as potential analog candidates (Figure_Apx A-1). Using these parameters, 19 analogs were identified as potentially suitable analog candidates for 1,2-dichloroethane based on structural similarity (Table_Apx A-2). The results for structural comparison of 1,2-dichloroethane to 1,1-dichloroethane (CASRN 75-34-3), 1,2-dichloropropane (CASRN 78-87-5), and 1,1,2-trichloroethane (CASRN 79-00-5) are further described below due to those analog candidates having completed data evaluation and extraction.

1,1-Dichloroethane, 1,2-dichloropropane, and 1,1,2-trichloroethane were indicated as structurally similar to 1,2-dichloroethane in AIM (2nd pass), OECD QSAR Toolbox (PubChem features = 0.7–0.9), and the Cheminformatics Search Module (Tanimoto coefficient = 0.60–0.67) (Table_Apx A-2). The structural similarity of 1,2-dichloroethane to its analogs indicated in these tools supported the read-across to 1,2-dichloroethane benthic environmental hazard. 1,1-Dichloroethane, 1,2-dichloropropane, and 1,1,2-trichloroethane were ultimately selected for read-across of benthic hazard to 1,2-dichloroethane based on the additional lines of evidence (physical, chemical, and environmental fate and transport similarity and ecotoxicological similarity).

1314 Table_Apx A-1. Structure Program Filtering Criteria

Program	Index	Filtering Parameters
Analog Identification Methodology (AIM)	Fragment-based	1st or 2nd pass
OECD QSAR Toolbox	Tanimoto-based PubChem fingerprints	Top 100 analogs ≥ 0.5
Cheminformatics Search Module	Similarity-type: Tanimoto	Top 100 analogs with index ≥ 0.5
GenRA	Morgan Fingerprints	Top 100 analogs with index \geq 0.1 (ToxRef data filter off)

Table_Apx A-2. Structural Similarity Between 1,2-Dichloroethane and Analog Candidates Which

Met Filtering Criteria in at Least 3 Out of 4 Structure Programs

			OECD		l e e e e e e e e e e e e e e e e e e e	
Chlorinated Solvent	CASRN	AIM	QSAR	Cheminformatics	GenRA	Count
			Toolbox			
1,2-Dichloroethane	107-06-2	Exact	1.00	1.00	1.00	4
(target)		Match				
1,3-Dichloropropane	142-28-9	1st pass	0.7–0.8	0.56	0.50	4
1,4-Dichlorobutane	110-56-5	1st pass	0.6-0.7	0.50	0.44	4
1,5-dichloropentane	628-76-2	1st pass	0.6-0.7	_	0.36	3
1,1,2-Trichloroethane ^a	79-00-5	2nd pass	0.8-0.9	0.67	_	3
1,2-Dichloropropane ^a	78-87-5	2nd pass	0.8-0.9	0.60	_	3
1,2,3-Trichloropropane	96-18-4	2nd pass	0.8-0.9	0.55	_	3
Chloroethane	75-00-3	2nd pass	0.7–0.8	0.83	0.38	4
1,1,2,2-Tetrachloroethane	79-34-5	2nd pass	0.7-0.8	0.67	_	3
1,1-Dichloroethane ^a	75-34-3	2nd pass	0.7–0.8	0.63	_	3
2-Chloropropane	75-29-6	2nd pass	0.7-0.8	0.63	_	3
1,1,1,2-Tetrachloroethane	630-20-6	2nd pass	0.7–0.8	0.55	_	3
Pentachloroethane	76-01-7	2nd pass	0.7-0.8	0.55	_	3
2,3-Dichlorobutane	7581-97-7	2nd pass	0.7–0.8	0.50	_	3
1-Chloropropane	540-54-5	2nd pass	0.6-0.7	0.63	0.44	4
Hexachloroethane	67-72-1	2nd pass	0.5-0.6	0.55	_	3
1-Chlorobutane	109-69-3	2nd pass	0.5-0.6	0.50	0.33	4
Propane, 1-chloro-2-methyl-	513-36-0	2nd pass	0.5-0.6	0.50	_	3
1,1,1-Trichloroethane	71-55-6	2nd pass	0.5-0.6	0.50	_	3
1-Chloro-2-bromoethane	107-04-0	_	0.6-0.7	0.50	0.44	3

^a Analogs that have completed data evaluation and extraction are bolded.

1315 1316 1317

Dashes indicate structural similarity scores were not available for those analogs using the filtering parameters described in Table_Apx A-1.

A.2 Physical, Chemical, and Environmental Fate and Transport Similarity

1,2-Dichloroethane analog candidates from the structural similarity analysis were preliminarily screened based on similarity in log octanol-water partition coefficient (log K_{OW}) and vapor pressure obtained using EPI SuiteTM (Figure Apx A-1). Measured values were used when available for screening. For this screening step, 1,2-dichloroethane values and those of its candidate analogs 1,1-dichloroethane, 1,2dichloropropane, and 1,1,2-trichloroethane were obtained from U.S. EPA (2025b), the *Draft Risk* Evaluation for 1,1-Dichloroethane (U.S. EPA, 2025g), the Final Scope of the Risk Evaluation for 1,2-Dichloropropane; CASRN 78-87-5 (U.S. EPA, 2020c), and the Final Scope of the Risk Evaluation for 1,1,2-Trichloroethane; CASRN 79-00-5 (U.S. EPA, 2020a). Analog candidates with log K_{OW} and vapor pressure within one log unit relative to 1,2-dichloroethane were considered potentially suitable analog candidates for 1,2-dichloroethane (Figure Apx A-1). This preliminary screening analysis narrowed the analog candidate list from 19 candidate analogs to 8 candidate analogs (Table Apx A-3). Three of the 8 candidate analogs represented 1,1-dichloroethane, 1,2-dichloropropane, and 1,1,2-trichloroethane. Because these three solvents had benthic hazard data with completed data evaluation and extraction, a more expansive analysis of physical, chemical, environmental fate and transport similarities between 1,2-dichloroethane and candidate analogs 1,1-dichloroethane, 1,2-dichloropropane, and 1,1,2trichloroethane was conducted (see Figure Apx A-1 and Table Apx A-4).

1336 1337 1338

13201321

1322

1323 1324

1325

1326

1327

1328

1329 1330

1331 1332

1333

1334

1335

1339

Table_Apx A-3. Analog Candidates with Similar Log Kow and Vapor Pressure Values to That of 1,2-Dichloroethane

Chemical	CASRN	Log Kow	Vapor Pressure (mm Hg)
1,2-Dichloroethane (target)	107-06-2	1.48	78.9
1,3-Dichloropropane	142-28-9	2.00	18.2
1,1,2-Trichloroethane ^a	79-00-5	1.89	23.0
1,2-Dichloropropane ^a	78-87-5	1.98	53.3
1,1,2,2-Tetrachloroethane	79-34-5	2.39	13.3
1,1-Dichloroethane ^a	75-34-3	1.79	227
2-Chloropropane	75-29-6	1.90	515.0
1-Chloropropane	540-54-5	1.92^{b}	345

^a Values predicted using EPI SuiteTM

1340 1341

13421343

1344

1345

1346

1347

1348

1349

1350

Because the candidate analog benthic hazard data consisted of exposures in water and in sediment, physical, chemical, and environmental fate and transport similarities between 1,2-dichloroethane and its analog candidates 1,1-dichloroethane, 1,2-dichloropropane, and 1,1,2-trichloroethane were assessed based on additional properties relevant to the aquatic and benthic compartments (Table_Apx A-4). These properties were selected based on their general importance in determining similar exposure potential in the aquatic and benthic compartments. Physical, chemical, and environmental fate and transport values for 1,2-dichloroethane, 1,1-dichloroethane, 1,2-dichloropropane, and 1,1,2-trichloroethane are specified in the *Draft Risk Evaluation for 1,2-Dichloroethane: Chemistry and Fate Technical Support Document* (U.S. EPA, 2025b), the *Draft Risk Evaluation for 1,1-Dichloroethane* (U.S. EPA, 2025g), the *Final Scope of the Risk Evaluation for 1,2-Dichloropropane; CASRN 78-87-5*

1351 (U.S. EPA, 2020c), and the Final Scope of the Risk Evaluation for 1,1,2-Trichloroethane; CASRN 79-

^b Analogs which have completed data evaluation and extraction are bolded.

00-5 (U.S. EPA, 2020a). Similar values are observed for 1,2-dichloroethane and its candidate analogs 1,1-dichloroethane, 1,2-dichloropropane, and 1,1,2-trichloroethane for water solubility (2,800–8,600 mg/L), log K_{OW} (1.48–1.99), and log K_{OC} (1.3–2.32)—indicating all four solvents are highly water soluble with low affinity for sediment (Table_Apx A-4). All four chlorinated solvents also have relatively low bioconcentration factors (BCF, 0.5–7) and bioaccumulation factors (BAF, 3.78–7.1), indicating low bioaccumulation potential in aquatic and terrestrial environments. Although hydrolysis half-lives are relatively long for all four solvents—particularly for 1,2-dichloroethane and analog candidates 1,1-dichloroethane and 1,2-dichloropropane—other properties indicate that these chemicals will likely volatilize before hydrolyzing in aqueous environments.

All four chlorinated solvents are highly volatile (Henry's Law constants 8.24×10^{-4} to 5.62×10^{-3} atm-m3/mol and vapor pressures 23-227 mm Hg), indicating volatilization from water will occur. The vapor pressures indicate some difference in volatility between the four chlorinated solvents—particularly for 1,1-dichloroethane that has a higher vapor pressure at 227 mm Hg, suggesting it is more readily volatile than 1,2-dichloroethane with vapor pressure 79 mm Hg. However, potential impacts of volatility differences on read-across to 1,2-dichloroethane for environmental hazard can be addressed by factoring in experimental design considerations in the analog benthic hazard dataset such as chemical measurement of the substance in the test medium, regular renewal with chemical solution, capping of test vessels, and/or use of flow-through/dilutor systems. 1,2-Dichloroethane and candidate analogs 1,1-dichloroethane, 1,2-dichloropropane, and 1,1,2-trichloroethane exist as a colorless liquid at room temperature and have similar low molecular weights (Table_Apx A-4). In summary, the similarity of the physical, chemical, fate, and environmental transport behavior of 1,2-dichloroethane and its candidate analogs 1,1-dichloroethane, 1,2-dichloropropane, and 1,1,2-trichloroethane in aquatic and benthic environments supports the ability to read-across benthic hazard to 1,2-dichloroethane.

 Table_Apx A-4. Comparison of 1,2-Dichloroethane and Analog Candidates 1,1-Dichloroethane, 1,2-Dichloropropane, and 1,1,2-Trichloroethane for Several Physical and Chemical and Environmental Fate Properties Relevant to Water, Sediment, and Soil

Environmental Fate Pi	operties Reievant t	o water, Sediment	, and Son	
Property	1,2-Dichloroethane (Target)	1,1-Dichloroethane	1,2- Dichloropropane	1,1,2- Trichloroethane
Water solubility	8,600 mg/L	5,040 mg/L	2,800 mg/L	4,590 mg/L
Log K _{OW}	1.48	1.79	1.99	1.89
Log K _{OC}	1.3–1.77	1.48	1.67	1.9–2.05, 2.2–2.32
BCF	2–4.4	7	0.5-6.9	0.7–6.7
BAF	3.78	6.8	7.1	6.9
Hydrolysis t½	6.1–72 years	61.3 years	15.8 years	85 days
Henry's Law constant (atm-m³/mol)	1.54E-03	5.62E-03	2.82E-03	8.24E-04
Vapor pressure (mmHg)	78.9	227	40	23
Molecular weight	98.95 g/mol	98.95 g/mol	112.99 g/mol	133.41 g/mol
Physical state of the chemical	Colorless liquid	Colorless Liquid	Colorless liquid	Colorless Liquid

A.3 Ecotoxicological Similarity

Similarity in empirical hazard evidence for benthic and aquatic invertebrates exposed in water and soil invertebrates exposed on filter paper to 1,2-dichloroethane and its analogs was assessed to determine suitability of using analog sediment invertebrate hazard data to read-across to 1,2-dichloroethane

(Figure Apx A-1). A single study for aqueous exposure in a marine benthic invertebrate, *Ophryotrocha* labronica, was available with which to compare ecotoxicological similarity between 1,2-dichloroethane and 1,1,2-trichloroethane in benthic invertebrates (Rosenberg et al., 1975). Because ECOSAR does not encompass benthic invertebrates in its ability to predict toxicity, ecotoxicological similarity between 1,2-dichloroethane and its candidate analogs 1,1-dichloroethane, 1,2-dichloropropane, and 1,1,2-trichloroethane was assessed based on empirical hazard data in relevant taxa, aquatic invertebrates and soil invertebrates (earthworms), in order to determine suitability of a benthic hazard read-across. Data used in the following comparisons were from studies with OQDs of high and medium unless otherwise noted.

Ecotoxicological similarity for a sediment invertebrate chronic hazard read-across is inferred by the aquatic, benthic, and soil invertebrate toxicity comparisons made between 1,2-dichloroethane and its analogs (Table_Apx A-5), similar to the environmental hazard read-across approach used for phthalates (U.S. EPA, 2024a U.S. EPA, 2025, 11799662). The comparison of 1,2-dichloroethane's measured hazard in *Ophryotrocha labronica* (15-day EC10), *Daphnia magna* (48-hour EC50 and LC50, 21-day ChV, 28-day ChV), and *Eisenia fetida* (48-hour LC50) indicated that all three analogs were within 10-fold of 1,2-dichloroethane's toxicity and would be suitable to use for read-across of benthic hazard. Average ratios of empirical 1,1-dichloroethane, 1,2-dichloropropane, and 1,1,2-trichloroethane hazard values are 0.37 ± 0.20, 1.28 ± 0.69, and 0.82 ± 0.39 (standard error), respectively (Table_Apx A-5). Therefore, due to 1,1-dichloroethane's, 1,2-dichloropropane's, and 1,1,2-trichloroethane's similarity to 1,2-dichloroethane using multiple lines of evidence (structure, physical chemical, and ecotoxicological) and analog availability of benthic hazard data, 1,1-dichloroethane, 1,2-dichloropropane, and 1,1,2-trichloroethane are appropriate analogs for benthic hazard read-across to 1,2-dichloroethane.

Table Apx A-5. Comparison of Measured 1,2-Dichloroethane and Analog Hazard Values in Aquatic, Benthic, and Soil Invertebrates

Sun anti-ar	End-		1,2- Dichloroethane (Target)	1,1-Dio	1,1-Dichloroethane		1,2-Dichloropropane		1,1,2-Trichloroethane		
Species	Outcome	Point	Measured Hazard (mg/L)	Measured Hazard (mg/L)	Ratio to 1,2- Dichloroethane Toxicity	Measured Hazard (mg/L)	Ratio to 1,2- Dichloroethane Toxicity	Measured Hazard (mg/L)	Ratio to 1,2- Dichloroethane Toxicity		
Daphnia magna	Mortality and Immobilization	EC50, LC50	194.7 ^a	34 ^e	0.17	39.2 ^j	0.20	80.8 h	0.41		
Eisenia fetida	Mortality	LC50	60 ^b	_	_	64°	1.07	42 ^b	0.70		
Chironomus riparius	Mortality and Immobilization	EC50	Read-across	150 ^f	_	49 ^k	_	_	_		
Daphnia magna	Reproduction	ChV	1.62 ^c	0.93 g	0.57	4.16 1	2.57	3.17 ⁱ	1.96		
Ophryotrocha labronica	Reproduction	EC10	309 ^d	_	_	_	_	68 ^d	0.22		
Chironomus riparius	Growth/ Development	ChV	Read-across	_	-	_	_	29 ^{m n} , 93 ^m	-		
Average fold has	zard analog:1,2-di	chloroeth	ane		0.37 ± 0.20		1.28 ± 0.69		0.82 ± 0.39		

^a Value for 1,2-dichloroethane represents a geometric mean of *Daphnia magna* EC50 and LC50 data (220 [160–280] mg/L; 320 [270–410] mg/L; 270 [250–290] mg/L; 160 [140–190] mg/L; 180 [150–230] mg/L; 99.4 [88.3–115] mg/L) (CITI, 1996a; Richter et al., 1983; Leblanc, 1980). Exposure was 48 hours.

^b Data for 1,2-dichloroethane and 1,1,2-trichloroethane are from Neuhauser et al. (1985) and have CI [54–68] μg/cm² and [35–49] μg/cm², respectively. Exposure and study duration were 48 hours.

^c Value for 1,2-dichloroethane represents a geometric mean of *Daphnia magna* NOEC/LOEC pair for reproduction endpoints (1.02/2.56 mg/L) from <u>CITI (1996d)</u>. Exposure and study durations were 21 days.

^d Data are from Rosenberg et al. (1975). Exposure and study duration were 15 days.

^e Data are from Mitsubishi Chemical Medience Corporation (2009a) and have CI [30.0–39.1] mg/L. Exposure was 48 hours.

^f Data are from Smithers (2024b) and have CI [130–180] mg/L. Exposure was 48 hours.

^g Value for 1,1-dichloroethane represents a geometric mean of *Daphnia magna* NOEC/LOEC pair for reproduction endpoints (1.64/0.525 mg/L) from <u>Mitsubishi</u> Chemical Medience Corporation (2009b). Exposure and study durations were 21 days.

^h Value for 1,1,2-trichloroethane represents a geometric mean of *Daphnia magna* EC50 and LC50 data (81 [58–97] mg/L; 18 [11–32] mg/L; 190 [160–210] mg/L; 170 [150–200] mg/L; 81 [58–110] mg/L; 78 [57–110] mg/L) (3M Environmental Lab, 1984; Richter et al., 1983; Leblanc, 1980). Exposure was 48 hours.

ⁱ Value for 1,1,2-trichloroethane represents a geometric mean of *Daphnia magna* NOEC/LOEC pair for reproduction endpoints (2.4/4.2 mg/L) from <u>3M</u> Environmental Lab (1984). Exposure and study durations were 21 days.

^j Value for 1,2-dichloropropane represents a geometric mean of *Daphnia magna* EC50 and LC50 data (29.5 [26.5–32.8] mg/L and 52 [42–68] mg/L) (<u>NITE, 1995a;</u> <u>Leblanc, 1980</u>). Data from <u>NITE (1995a)</u> are unrated for data quality. Exposure was 48 hours.

^k Data are from Smithers (2024a) and have CI [43–56] mg/L. Exposure was 48 hours.

Species Outcom	Outcome	End-	1,2- Dichloroethane (Target)	1,1-Dichloroethane		1,2-Dichloropropane		1,1,2-Trichloroethane		
Species	Outcome	Point	Measured Hazard (mg/L)	Measured Hazard (mg/L)	Ratio to 1,2- Dichloroethane Toxicity	Measured Hazard (mg/L)	Ratio to 1,2- Dichloroethane Toxicity	Measured Hazard (mg/L)	Ratio to 1,2- Dichloroethane Toxicity	

¹ Value for 1,2-dichloropropane represents a geometric mean of *Daphnia magna* NOEC/LOEC pairs for reproduction endpoints (8.3/15.8 mg/L and 0.96/2.40 mg/L) (NITE, 1995b; Dow Chemical, 1988). Data from NITE (1995b) are unrated for data quality. Exposure and study durations were 21 days.

^m Value for 1,1,2-trichloroethane represents a geometric mean of *Chironomus riparius* NOEC/LOEC pair for growth development endpoints (66/130 mg/L and 19/44 mg/kg) from <u>Smithers (2023)</u>. Exposure and study duration was carried out over 2 generations.

ⁿ Hazard value in mg/kg.

^o Data are from Neuhauser et al. (1986) and have CI [59-70] μg/cm², respectively. Data were rated uninformative. Exposure and study duration were 48 hours.

A.4 Read-Across Weight of Scientific Evidence and Conclusions

14101411

14121413

1414

1415

1416

1417

1418

1419

1420 1421

1422

1423

1424

1425 1426

1427

1428

1429

1430

1431

1432

1433

1434

1435

1436

1437 1438

1439

1440

1441

1442

1443

1444

1,2-Dichloroethane presented with minimal benthic hazard data. Analog selection was carried out to supplement the benthic hazard dataset for 1,2-dichloroethane. Several chlorinated solvents of interest (1,1-dichloroethane, 1,2-dichloropropane, and 1,1,2-trichloroethane) were indicated as structurally similar to 1,2-dichloroethane. A screening by log K_{OW} values and further comparison of additional physical, chemical, and environmental fate and transport properties indicated that all three analog candidates were similar to 1,2-dichloroethane with some differences in volatility for the analog 1,1-dichloroethane. To determine if any of the three candidate analogs would be suitable for sediment invertebrate read-across, a toxicity comparison was made in benthic invertebrate *Chironomus riparius* and aquatic invertebrate *Daphnia magna* exposed in water to either 1,2-dichloroethane or the three solvent analogs for 48 hours (*C. riparius* or *D. magna*) or 21 days (*D. magna*). Hazard data for the soil invertebrate *Eisenia fetida* exposed on filter paper for 48 hours to 1,2-dichloroethane and its analogs were also included in this comparison. The comparisons indicated that 1,1-dichloroethane, 1,2-dichloropropane, and 1,1,2-trichloroethane benthic hazard data were suitable for read-across to 1,2-dichloroethane.

Because ECOSAR hazard predictions do not encompass benthic invertebrates and 1,1,2-trichloroethane lacked acute hazard data for C. riparius with which to compare to that of 1,2-dichloroethane (Table Apx A-5), there is also some uncertainty in the chronic benthic hazard read-across from 1,1,2trichloroethane to 1,2-dichloroethane. However, the structural agreement and similar chemical behavior in sediment inferred from the physical, chemical, environmental fate and transport properties as well as the similar aquatic toxicity of 1,1,2-trichloroethane and 1,2-dichloroethane support the ability to readacross for benthic hazard. Another uncertainty in the analog selection for 1,2-dichloroethane is that the relatively small chemical structures of 1,2-dichloroethane and its analogs could result in lower structural similarity scores. However, looking for concordance across multiple structure programs increases the confidence that structurally similar analogs were identified for 1,2-dichloroethane in Table_Apx A-2. Regarding uncertainty in the physical, chemical, environmental fate and transport line of evidence used in the analog selection, higher vapor pressure of analog candidate 1,1-dichloroethane relative to 1,2dichloroethane (though still within 10-fold) could result in volatility differences between target and analog. However, by considering the experimental design in the analog's empirical hazard data used in the read-across (chemical measurement, chemical renewal, capping test vessels, use of flow-through, and so on), confidence is increased that the volatility differences do not impact the strength of the readacross. Looking across the multiple lines of evidence (structural, physical/chemical, ecotoxicological), 1,1-dichloroethane, 1,2-dichloropropane, and 1,1,2-trichloroethane are appropriate analogs with highquality benthic hazard data to be used in a read-across to 1,2-dichloroethane.

Appendix B ENVIRONMENTAL HAZARD DETAILS

B.1 Hazard Identification

B.1.1 Aquatic Hazard Data

B.1.1.1 Web-Based Interspecies Correlation Estimation (Web-ICE)

Results from the systematic review process assigned an overall quality level high or medium to 15 aquatic toxicity studies for 1,2-dichloroethane, high to one study for analog 1,1-dichloroethane and one study for analog 1,2-dichloropropane, and high to one study for analog 1,1,2-trichloroethane submitted under TSCA section 4 test orders. EPA identified 17 aquatic toxicity studies, displayed in Table 2-1, as the most relevant for quantitative assessment. For further details on these studies, see Section 2. To supplement the empirical data, EPA used a modeling approach, Web-ICE. Web-ICE predicts toxicity values for environmental species that are absent from a dataset and can provide a more robust dataset to estimate toxicity thresholds. Specifically, EPA used Web-ICE to quantitatively supplement empirical data for aquatic organisms for acute exposure durations.

The Web-ICE application was developed by the U.S. EPA and collaborators to provide interspecies extrapolation models for acute toxicity (Raimondo and Barron, 2010). Web-ICE models estimate the acute toxicity (EC50/LC50) of a chemical to a species, genus, or family with no test data (the predicted taxon) from the known toxicity of the chemical to a species with test data (the commonly tested surrogate species).

Web-ICE models are log-linear least square regressions of the relationship between surrogate and predicted taxon based on a database of acute toxicity values. It returns median effect or lethal water concentrations for aquatic species (EC50/LC50). Separate acute toxicity databases are maintained for aquatic animals (vertebrates and invertebrates), aquatic plants (algae), and wildlife (birds and mammals), with 2,286 models for aquatic animals, 58 models for algae, and 560 models for terrestrial wildlife taxa in Web-ICE v4.0 (U.S. EPA, 2024b). Open-ended toxicity values (*i.e.*, >100 mg/kg or <100 mg/kg) and duplicate records among multiple sources are not included in any of the databases.

The aquatic animal database within Web-ICE is composed of 48 or 96-hour EC50/LC50 values based on immobility or mortality. This database is described in detail in the Aquatic Database Documentation found on the <u>Download Model Data</u> page of Web-ICE and describes the data sources, normalization, and quality and standardization criteria (*e.g.*, data filters) for data used in the models. Data used in model development adhered to standard acute toxicity test condition requirements of the ASTM International (<u>ASTM</u>, 2014) and EPA's Office of Chemical Safety and Pollution Prevention (OCSPP) (<u>U.S. EPA</u>, 2016a).

EPA used 1,2-dichloroethane 48-hour LC50 and EC50 data for *Daphnia magna* and 96-hour LC50 data for fathead minnow (*Pimephales promelas*) and rainbow trout (*Oncorhynchus mykiss*; see Table 2-1) as surrogate species to predict LC50 toxicity values using the Web-ICE application (<u>Raimondo and Barron</u>, 2010). The Web-ICE model estimated toxicity values for 137 species. These toxicity predictions were then screened by the following quality standards to ensure confidence in the model predictions. If a predicted species did not meet all the quality criteria below, the species was eliminated from the dataset (U.S. EPA, 2024b).

o The proportion of the data variance that is explained by the model. The closer the R²

value is to one, the more robust the model is in describing the relationship between the

• High $R^2 (\geq 0.6)$

Appendix B.1.1.2.

predicted and surrogate taxa.

Low mean square error (MSE; ≤ 0.95)

1488

1489

1490

1491

1492 1493

1504

1494	 High slope (≥0.6)
1495	o The regression coefficient represents the change in log10 value of the predicted taxon
1496	toxicity for every change in log10 value of the surrogate species toxicity.
1497	• No more than two orders of magnitude of difference between the upper- and lower-bounds of the
1498	confidence interval of the predicted toxicity.
1499	After screening, the acute toxicity values for 79 additional aquatic organisms (fish, amphibians, and
1500	aquatic invertebrates) were added to the empirical data summarized in Table_Apx B-1. Including both
1501	empirical and predicted toxicity values with a confidence interval difference of two or less, there were
1502	126 data points across 85 species. This dataset was then used to calculate the distribution of species
1503	sensitivity through the SSD Toolbox (Etterson, 2020a) as shown in Table_Apx B-1 and described in

o An unbiased estimator of the variance of the regression line.

1505 Table_Apx B-1. Empirical Species Hazard Data and Web-ICE Predicted Species That Met Model Selection Criteria

Common Name	Genus	Species	Surrogate Species	LC50 or EC50 (µg/L)	95% CI	CI Diff	\mathbb{R}^2	MSE	Slope
			Measured d	ata					
Northern leopard frog	Lithobates	pipiens		4,520					
Northwestern salamander	Ambystoma	gracile		6,530					
Brine shrimp	Artemia	salina		36,400					
Brine shrimp	Artemia	salina		79,700					
Brine shrimp	Artemia	salina		93,640					
Fathead minnow	Pimephales	promelas		116,000					
Fathead minnow	Pimephales	promelas		136,000					
Cladocera	Daphnia	magna		220,000					
Cladocera	Daphnia	magna		160,000					
Cladocera	Daphnia	magna		270,000					
Cladocera	Daphnia	magna		99,400					
Rainbow trout	Oncorhynchus	mykiss		225,000					
Midge	Chironomus	riparius		150,000					
Midge	Chironomus	riparius		49,000					
			Modeled da	ata			ı		
Copepod	Acartia	clausi	Fathead minnow (Pimephales promelas)	13,076.68	1989.89–85935.44	1	0.8	0.23	0.88
Shortnose sturgeon	Acipenser	brevirostrum	Rainbow trout (Oncorhynchus mykiss)	441,249.83	68,448.48– 2,844,495.69	2	0.98	0.06	1.16
Amphipod	Allorchestes	compressa	Fathead minnow (Pimephales promelas)	29,524.84	8,275.63–105,336.7	2	0.96	0.02	0.84
Threeridge	Amblema	plicata	Daphnid (Daphnia magna)	35,118.96	112,66.51–109,470.83	1	0.97	0.13	0.94
Threeridge	Amblema	plicata	Fathead minnow (Pimephales promelas)	7,044.29	1,987.1–24,972.59	1	0.97	0.12	1.3
Black bullhead	Ameiurus	melas	Fathead minnow (Pimephales promelas)	228,726.92	18,488.26– 2,829,736.02	2	0.96	0.16	1.07

Common Name	Genus	Species	Surrogate Species	LC50 or EC50 (µg/L)	95% CI	CI Diff	\mathbb{R}^2	MSE	Slope
Mysid	Americamysis	bahia	Daphnid (Daphnia magna)	36,670.61	22,894.56–58,736.56	0	0.72	0.82	0.89
Mysid	Americamysis	bigelowi	Fathead minnow (Pimephales promelas)	15,524.55	1,487.94–161,979.12	2	0.89	0.05	1
Isopod	Asellus	aquaticus	Daphnid (Daphnia magna)	2,356,445.65	351268.93– 15,808,088.21	2	0.91	0.31	0.85
Silver perch	Bidyanus	bidyanus	Rainbow trout (Oncorhynchus mykiss)	607,483.52	199,347.99– 1,851,216.18	1	0.99	0	1.08
Vernal pool fairy shrimp	Branchinecta	lynchi	Daphnid (Daphnia magna)	115,482.92	53,946.01–247,218.45	1	0.98	0.07	0.94
Isopod	Caecidotea	brevicauda	Rainbow trout (Oncorhynchus mykiss)	37,223.52	5,566.52–248,914.84	2	0.69	0.52	0.77
Isopod	Caecidotea	brevicauda	Fathead minnow (Pimephales promelas)	6,916.48	721.64–66,290.87	2	0.72	0.49	0.76
Goldfish	Carassius	auratus	Rainbow trout (Oncorhynchus mykiss)	305,657.57	129,955.26–718,913.19	0	0.82	0.48	0.81
Goldfish	Carassius	auratus	Fathead minnow (Pimephales promelas)	148,568.9	92,261.81–239,243.76	1	0.94	0.14	0.97
White sucker	Catostomus	commersonii	Fathead minnow (Pimephales promelas)	308,348.67	39,613.81– 2,400,189.14	2	0.92	0.2	1.14
Daphnid	Ceriodaphnia	dubia	Fathead minnow (Pimephales promelas)	14,337.25	4,438.64–46,310.73	1	0.68	1.75	1.25
Bigscale mullet	Chelon	macrolepis	Daphnid (Daphnia magna)	6,964,776.15	1,922,799.21– 25,228,117.74	1	0.99	0	0.9
Water flea	Chydorus	sphaericus	Daphnid (Daphnia magna)	60,262.55	37,444.65–96,986.19	0	0.98	0.05	0.94
Mrigal carp	Cirrhinus	mrigala	Fathead minnow (Pimephales promelas)	114,821.46	29,054.48–453,775.07	1	0.98	0.01	1.1
Eastern oyster	Crassostrea	virginica	Fathead minnow (Pimephales promelas)	29,110.75	9,456.99–89,610.61	1	0.66	0.48	0.84
Sheepshead minnow	Cyprinodon	variegatus	Rainbow trout (Oncorhynchus mykiss)	15,0216.33	848,52.09–265,932.69	1	0.77	0.29	0.8
Sheepshead minnow	Cyprinodon	variegatus	Fathead minnow (Pimephales promelas)	40,026.97	18,838.7–85,047.14	0	0.72	0.33	0.75
Common carp	Cyprinus	carpio	Rainbow trout (Oncorhynchus mykiss)	171,196.39	62,616.18–468,061.17	1	0.74	0.51	0.8

Common Name	Genus	Species	Surrogate Species	LC50 or EC50 (µg/L)	95% CI	CI Diff	\mathbb{R}^2	MSE	Slope
Common carp	Cyprinus	carpio	Fathead minnow (Pimephales promelas)	129,619.75	51,958.96–323,361.84	1	0.84	0.2	0.99
Zebrafish	Danio	rerio	Daphnid (Daphnia magna)	182,940.78	22,226.21– 1,505,772.26	2	0.71	0.61	0.77
Zebrafish	Danio	rerio	Rainbow trout (Oncorhynchus mykiss)	72,876.04	20,860.95–254,586.51	1	0.95	0.13	0.72
Zebrafish	Danio	rerio	Fathead minnow (Pimephales promelas)	88,928.7	33136.47–238,662.35	1	0.97	0.04	0.9
Zebrafish	Danio	rerio	Daphnid (Daphnia magna)	148476.13	63,865.47–345,183.78	1	0.66	0.86	0.65
Zebrafish	Danio	rerio	Rainbow trout (Oncorhynchus mykiss)	131773.18	52,551.94–330,419.17	1	0.79	0.36	0.68
Zebrafish	Danio	rerio	Fathead minnow (Pimephales promelas)	133927.84	94,758.76–189,290.5	1	0.93	0.2	0.93
Daphnid	Daphnia	galeata	Daphnid (Daphnia magna)	120,074.97	11,918.65– 1,209,713.23	2	0.96	0.08	0.91
Daphnid	Daphnia	pulex	Daphnid (Daphnia magna)	137,785.3	80,960.92–234,495.94	1	0.95	0.14	1.01
Daphnid	Daphnia	pulicaria	Daphnid (Daphnia magna)	183,161.26	33,174.19– 1,011,281.86	2	0.94	0.23	1.06
Mosquitofish	Gambusia	affinis	Rainbow trout (Oncorhynchus mykiss)	278,492.21	11,886.88– 6,524,662.51	2	0.91	0.79	0.86
Mosquitofish	Gambusia	affinis	Fathead minnow (Pimephales promelas)	70,409.18	10,883.64-455,502.39	1	0.98	0.12	0.94
Amphipod	Gammarus	fasciatus	Daphnid (Daphnia magna)	54,218.53	18,288.95–160,735.09	1	0.75	0.75	0.81
Amphipod	Gammarus	minus	Fathead minnow (Pimephales promelas)	163,655.58	34,493.24–776,484.18	1	0.95	0.04	0.72
Amphipod	Gammarus	pseudolimnae us	Daphnid (Daphnia magna)	111,489.47	21,370.45–581,645.74	1	0.74	0.75	0.91
Catla	Gibelion	catla	Fathead minnow (Pimephales promelas)	165,045.95	11,926.95– 2,283,956.03	2	0.96	0.02	1.09
Bonytail	Gila	elegans	Rainbow trout (Oncorhynchus mykiss)	441,130.33	43,526.13– 4,470,784.96	2	0.89	0.21	0.92
Channel catfish	Ictalurus	punctatus	Rainbow trout (Oncorhynchus mykiss)	155,231.66	84,942.1–283,685.8	1	0.75	0.49	0.81

Common Name	Genus	Species	Surrogate Species	LC50 or EC50 (µg/L)	95% CI	CI Diff	\mathbb{R}^2	MSE	Slope
Channel catfish	Ictalurus	punctatus	Fathead minnow (Pimephales promelas)	111,171.66	65,539.36–188,578.74	1	0.87	0.3	0.97
Flagfish	Jordanella	floridae	Fathead minnow (Pimephales promelas)	54,292.45	8,138.62–362,188.13	2	0.83	0.46	0.9
Wavyrayed lampmussel	Lampsilis	fasciola	Daphnid (Daphnia magna)	82,982.04	7,687.69–895,732.27	2	0.99	0	1.18
Neosho mucket	Lampsilis	rafinesqueana	Daphnid (Daphnia magna)	82,226.61	20,159.41–335,390.85	1	0.99	0.02	0.89
Neosho mucket	Lampsilis	rafinesqueana	Fathead minnow (Pimephales promelas)	67,100.74	6,555.63–686,832.16	2	0.98	0.05	1.58
Fatmucket	Lampsilis	siliquoidea	Daphnid (Daphnia magna)	93,894.61	50,792.97–173,573.01	1	0.94	0.18	0.9
Fatmucket	Lampsilis	siliquoidea	Fathead minnow (Pimephales promelas)	24,526.21	4,444.87–135,334.34	2	0.64	0.93	0.93
Green floater	Lasmigona	subviridis	Daphnid (Daphnia magna)	27,579.07	1,857.31–409,521.47	2	0.96	0.07	0.66
Peppered loach	Lepidocephali chthys	guntea	Fathead minnow (Pimephales promelas)	50,416.35	10,570.84–240,457.64	1	0.99	0	0.78
Green sunfish	Lepomis	cyanellus	Rainbow trout (Oncorhynchus mykiss)	266,048.43	93,376.69–758,023.91	1	0.94	0.13	0.9
Bluegill	Lepomis	macrochirus	Daphnid (Daphnia magna)	84,665.38	5,4059.35–132,600.26	1	0.65	0.84	0.71
Bluegill	Lepomis	macrochirus	Rainbow trout (Oncorhynchus mykiss)	205,775.73	162,292.07–260,910.15	0	0.89	0.22	0.93
Bluegill	Lepomis	macrochirus	Fathead minnow (Pimephales promelas)	57,813.85	36,604.08–91,314.73	0	0.81	0.43	0.93
Oligochaete	Limnodrilus	hoffmeisteri	Daphnid (Daphnia magna)	305,026.07	62,525.8–1,488,052.06	2	0.8	0.35	0.7
Bullfrog	Lithobates	catesbeianus	Rainbow trout (Oncorhynchus mykiss)	324,051.67	116,001.16–905,245.1	0	0.95	0.3	0.87
Bullfrog	Lithobates	catesbeianus	Fathead minnow (Pimephales promelas)	125,878.36	64,366.95–246,176.13	1	0.98	0.09	0.97
Northern leopard frog	Lithobates	pipiens	Rainbow trout (Oncorhynchus mykiss)	259,958.24	120,608.89–560,309.32	0	0.99	0	0.71
Southern leopard frog	Lithobates	sphenocephal us	Rainbow trout (Oncorhynchus mykiss)	3772,971.93	665,705.69– 21,383,799.58	2	0.97	0.04	1.27

Common Name	Genus	Species	Surrogate Species	LC50 or EC50 (µg/L)	95% CI	CI Diff	\mathbb{R}^2	MSE	Slope
Oligochaete	Lumbriculus	variegatus	Fathead minnow (Pimephales promelas)	119,654.23	28,703.38–498,803.53	1	0.81	0.43	0.94
Swamp lymnaea	Lymnaea	stagnalis	Daphnid (<i>Daphnia magna</i>)	140,785.29	44,279.27–447,629.61	1	0.95	0.22	0.94
Swamp lymnaea	Lymnaea	stagnalis	Fathead minnow (Pimephales promelas)	43,503.66	4,552.02–415,772.35	2	0.84	0.59	1.2
Oriental river shrimp	Macrobrachiu m	nipponense	Daphnid (Daphnia magna)	150,464.42	50,574.73–447,651.17	1	0.98	0.05	1.14
Western pearlshell	Margaritifera	falcata	Daphnid (Daphnia magna)	76,786.02	35,816.24–164,622.31	1	0.95	0.15	0.87
Washboard	Megalonaias	nervosa	Daphnid (Daphnia magna)	66,456.23	36,331.52–121,560.51	1	0.97	0.12	0.96
Washboard	Megalonaias	nervosa	Fathead minnow (Pimephales promelas)	14,751.2	1,574.98–138,160.88	2	0.73	0.88	1.14
Largemouth bass	Micropterus	salmoides	Rainbow trout (Oncorhynchus mykiss)	122,645.94	48,554.03–309,799.73	1	0.88	0.2	0.94
Water flea	Moina	тасгосора	Daphnid (Daphnia magna)	74,941.32	12,959.43–433,371.44	1	0.96	0.1	0.72
Striped bass	Morone	saxatilis	Rainbow trout (Oncorhynchus mykiss)	420,540.94	209,099.78–845,790.84	0	0.99	0.01	1.06
Cape Fear shiner	Notropis	mekistocholas	Rainbow trout (Oncorhynchus mykiss)	1,124,400.54	227,237.79– 55,63,672.09	1	0.99	0.01	1.17
Cutthroat trout	Oncorhynchus	clarkii	Rainbow trout (Oncorhynchus mykiss)	172,849.67	106,687.91–280,041.19	0	0.95	0.07	0.94
Cutthroat trout	Oncorhynchus	clarkii	Fathead minnow (Pimephales promelas)	40,119.28	12,512.99–128,632.83	1	0.82	0.34	0.99
Apache trout	Oncorhynchus	gilae	Rainbow trout (Oncorhynchus mykiss)	336,019.51	49,794.94– 2,267,481.36	2	0.98	0.01	1.09
Coho salmon	Oncorhynchus	kisutch	Rainbow trout (Oncorhynchus mykiss)	366,642.51	265,876.89–505,597.63	0	0.98	0.03	1.02
Coho salmon	Oncorhynchus	kisutch	Fathead minnow (Pimephales promelas)	26,526.27	4,057.97–173,400.22	2	0.64	0.69	0.91
Chinook salmon	Oncorhynchus	tshawytscha	Rainbow trout (Oncorhynchus mykiss)	290,680.89	147,262.14–573,775.3	0	0.95	0.1	1.01
Chinook salmon	Oncorhynchus	tshawytscha	Fathead minnow (Pimephales promelas)	50,391.13	3,594.71–706,401.87	2	0.7	0.82	1.16

Common Name	Genus	Species	Surrogate Species	LC50 or EC50 (µg/L)	95% CI	CI Diff	\mathbb{R}^2	MSE	Slope
Mozambique tilapia	Oreochromis	mossambicus	Fathead minnow (Pimephales promelas)	57,935.82	8,402.23–399,489.41	2	0.72	0.33	0.86
Pheasantshell	Ortmanniana	pectorosa	Daphnid (<i>Daphnia magna</i>)	109,652.75	23,210.04–518,045.51	1	0.97	0.11	0.96
Pheasantshell	Ortmanniana	pectorosa	Fathead minnow (Pimephales promelas)	51,226.5	4,095.81–640,708.1	2	0.97	0.07	1.58
Medaka	Oryzias	latipes	Rainbow trout (Oncorhynchus mykiss)	30,8671.3	37,743.82– 2,524,332.59	2	0.94	0.15	0.91
Medaka	Oryzias	latipes	Fathead minnow (Pimephales promelas)	96,417.29	57,829.08–160,756.85	1	0.98	0.04	0.85
Mississippi grass shrimp	Palaemonetes	kadiakensis	Daphnid (<i>Daphnia magna</i>)	27,618.42	2261.9–337230.4	2	0.63	0.71	0.75
Midge	Paratanytarsu s	dissimilis	Rainbow trout (Oncorhynchus mykiss)	596,295.55	152,447.33– 2,332,401.52	1	0.9	0.33	0.88
Midge	Paratanytarsu s	dissimilis	Fathead minnow (Pimephales promelas)	228,979.52	49,796.25– 1,052,937.48	2	0.84	0.52	0.86
Midge	Paratanytarsu s	parthenogenet icus	Daphnid (<i>Daphnia magna</i>)	466,644.19	198,320.3– 1,098,017.81	1	0.98	0.05	0.97
Midge	Paratanytarsu s	parthenogenet icus	Fathead minnow (Pimephales promelas)	401,683	82,343.92– 1,959,486.14	2	0.98	0.09	0.98
Bryozoan	Pectinatella	magnifica	Daphnid (Daphnia magna)	491,272.68	26,280.94– 9,183,506.25	2	0.98	0	0.86
Yellow perch	Perca	flavescens	Rainbow trout (Oncorhynchus mykiss)	128,283.21	20,532.59-801,485.85	1	0.76	0.58	0.89
Yellow perch	Perca	flavescens	Fathead minnow (Pimephales promelas)	25,231.57	2,836.64–224,435.04	2	0.73	0.54	0.93
Tadpole physa	Physella	gyrina	Daphnid (<i>Daphnia magna</i>)	142,420.26	59,814.7–339,109.78	1	0.95	0.19	0.96
Tadpole physa	Physella	gyrina	Fathead minnow (Pimephales promelas)	43,315.93	6,524.71–287,568.98	2	0.84	0.58	1.22
Guppy	Poecilia	reticulata	Rainbow trout (Oncorhynchus mykiss)	113,530.47	20,815.97–619,195.99	1	0.63	0.68	0.71
Guppy	Poecilia	reticulata	Fathead minnow (Pimephales promelas)	48,786.48	19,551.77–121,735.94	1	0.78	0.38	0.84
Water flea	Pseudosida	ramosa	Daphnid (Daphnia magna)	57,686.1	4,928.67–675,175.36	2	0.86	0.56	0.88

Common Name	Genus	Species	Surrogate Species	LC50 or EC50 (µg/L)	95% CI	CI Diff	\mathbb{R}^2	MSE	Slope
Atlantic salmon	Salmo	salar	Rainbow trout (Oncorhynchus mykiss)	223,068.14	92,794.8–536,230.41	1	0.96	0.11	1.01
Brown trout	Salmo	trutta	Rainbow trout (Oncorhynchus mykiss)	232,475.73	121,031.18–446,537.51	0	0.97	0.07	0.99
Brook trout	Salvelinus	fontinalis	Rainbow trout (Oncorhynchus mykiss)	219,732.21	111,781.11–431,935.63	0	0.94	0.1	0.99
Brook trout	Salvelinus	fontinalis	Fathead minnow (Pimephales promelas)	26,928.82	4,822.39–150,375.94	2	0.7	0.74	0.95
Lake trout	Salvelinus	namaycush	Rainbow trout (Oncorhynchus mykiss)	102,905.22	56,217.5–188,366.32	1	0.94	0.07	0.89
Lake trout	Salvelinus	namaycush	Fathead minnow (Pimephales promelas)	9,297.5	1,861.5–46,437.95	1	0.65	0.33	0.76
Daphnid	Simocephalus	serrulatus	Daphnid (Daphnia magna)	78,750.89	14,816.91–418,560.09	1	0.85	0.28	0.93
Daphnid	Simocephalus	vetulus	Daphnid (Daphnia magna)	35,264.06	1,764.67–704,700.43	2	0.88	0.34	0.75
Beaver-tail fairy shrimp	Thamnocepha lus	platyurus	Daphnid (Daphnia magna)	101,312.19	60,549.74–169,517.91	1	0.97	0.12	0.91
Copepod	Tigriopus	japonicus	Fathead minnow (Pimephales promelas)	169,058.01	166,51.39– 1,716,430.43	2	0.72	0.13	0.77
Oligochaete	Tubifex	tubifex	Daphnid (Daphnia magna)	1,131,962.05	114,352.37– 11,205,286.61	2	0.79	0.77	0.89
Oligochaete	Tubifex	tubifex	Fathead minnow (Pimephales promelas)	154,230.29	28,108.44-846,271.49	1	0.86	0.52	1.03
Paper pondshell	Utterbackia	imbecillis	Daphnid (Daphnia magna)	85,634.43	52,801.19–138,885.7	1	0.97	0.08	0.88
Paper pondshell	Utterbackia	imbecillis	Fathead minnow (Pimephales promelas)	17,533.51	2,347.7–130,948.4	2	0.65	0.85	0.86
African clawed frog	Xenopus	laevis	Fathead minnow (Pimephales promelas)	44,609.74	9,882.41–201,373.23	2	0.91	0.14	0.76
Razorback sucker	Xyrauchen	texanus	Rainbow trout (Oncorhynchus mykiss)	121,656.13	14,368.55– 1,030,042.16	2	0.87	0.18	0.78

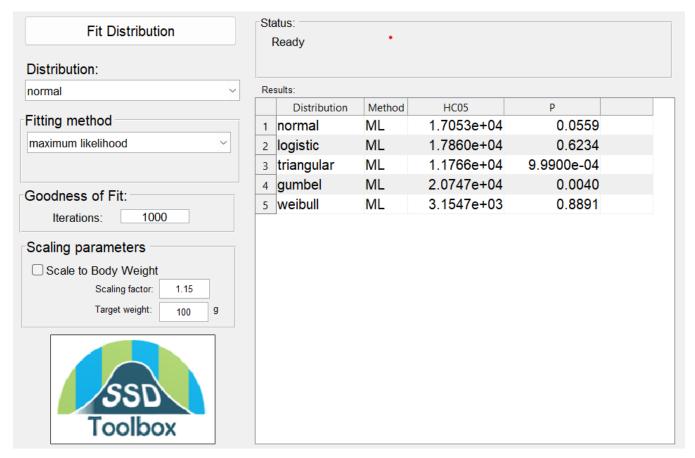
B.1.1.2 Species Sensitivity Distribution (SSD)

The SSD Toolbox is a resource created by EPA's ORD that can fit SSDs to environmental hazard data (Etterson, 2020a). The SSD Toolbox runs on Matlab 2018b (9.5) for Windows 64 bit. For the draft 1,2-dichloroethane risk evaluation, EPA calculated an SSD representing aquatic and benthic species with the SSD Toolbox using acute EC50 and LC50 hazard data for 1,2-dichloroethane and the analogs 1,1-dichloroethane and 1,2-dichloropropane from systematic review. The Agency estimated data from the Web-ICE application (Appendix B.1.1.1) that included 37 fish, 5 amphibians, and 45 invertebrate species. The SSD was used to calculate an HC05. In other words, HC05 estimates the concentration that is expected to be protective for 95 percent of species.

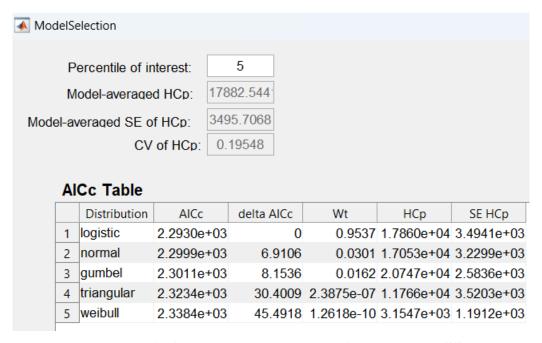
The SSD Toolbox contains functions for fitting up to six distributions (normal, logistic, triangular, Gumbel, Weibull, and Burr) across four model estimation methods (maximum likelihood, moment estimators, graphical methods, and Bayesian methods, in this case the Metropolis-Hastings algorithm). Maximum likelihood was used to model the data for 1,2-dichloroethane due to its general acceptance for fitting SSDs (Etterson, 2020b), its low sampling variance, and the fact that models can also be compared a posteriori using information theoretic methods, in this case Akaike's Information Criterion corrected for sample size (AICc). AICc was used along with a comparison of p-values and a visual assessment of Q-Q plots, which are methods available to all model estimation methods, to select the distribution used to calculate the HC05 for this analysis. Based on the guidance documents for use of the SSD Toolbox (Etterson, 2020b), the Burr distribution is provided only for comparison and is not used for modeling; thus, it was not included.

The SSD Toolbox uses a parametric bootstrap method to calculate a p-value to compare goodness-of-fit across distributions. In this type of test, p-values exceeding 0.05 are required (Etterson, 2020b). The normal, (p = 0.06), logistic (p = 0.62), and Weibull (p = 0.89) distributions all passed this initial screening (Figure_Apx B-1). The sample-size corrected AICc was lowest for the logistic distribution (Figure_Apx B-2). Because numerical methods may lack statistical power for small sample sizes, a visual inspection of the data was also used to assess goodness-of-fit, in this case a comparison of Q-Q plots between the three distributions. In a Q-Q plot, the horizontal axis gives the empirical quantiles, and the vertical axis gives the predicted quantiles (from the fitted distribution). A good model fit shows the data points in close proximity to the diagonal line across the data distribution. Comparison of Q-Q plots between the three distributions identified the logistic distribution as the best distribution, with the data closely fitting the line across the center of the plot (Figure_Apx B-3).

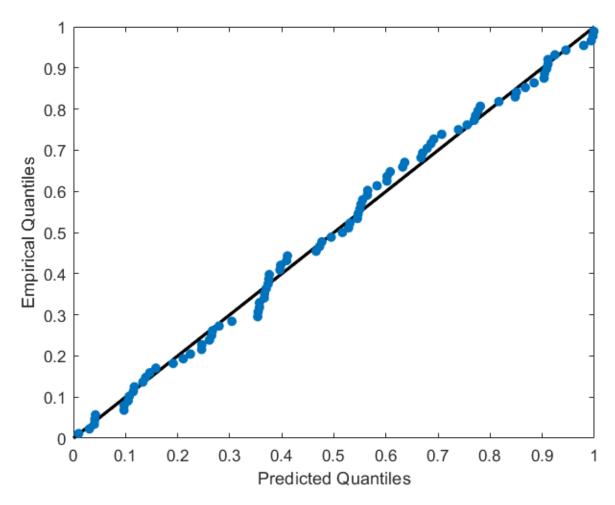
This distribution was then plotted along with data points for both measured and modeled species. Life history information was attached to each species, indicating an even distribution of various life history strategies along the curve (Figure_Apx B-4). The calculated HC05 was 17,860 μ g/L (95% CI = 11,909– 26,445 μ g/L). The lower 95 percent CI of the HC05 (11,909 μ g/L) was then selected as the acute aquatic COC.



Figure_Apx B-1. SSD Toolbox Interface Showing HC05s and P Values for Each Distribution Using Maximum Likelihood Fitting Method Using Acute Aquatic Hazard Data (<u>Etterson</u>, 2020a)



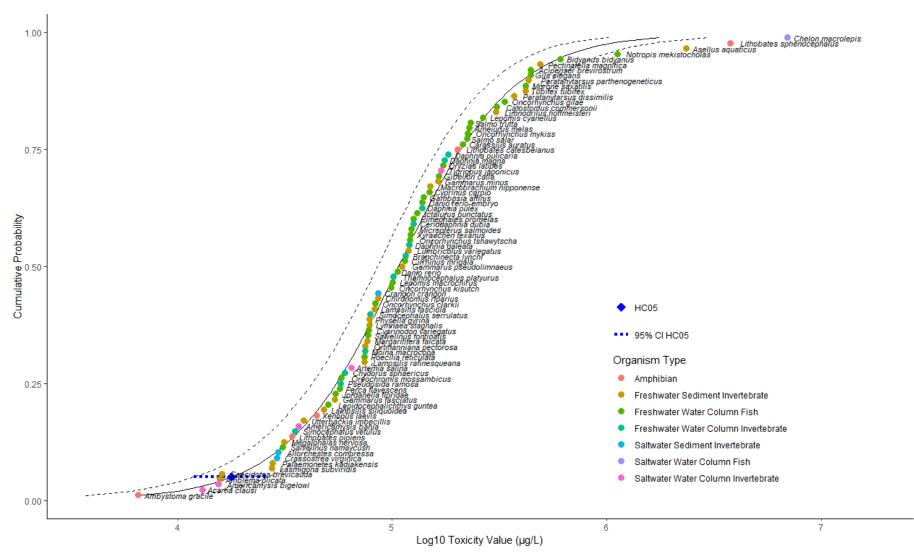
Figure_Apx B-2. AICc for the Five Distribution Options in the SSD Toolbox for Acute Aquatic Hazard Data (<u>Etterson, 2020a</u>)



Figure_Apx B-3. Q-Q Plot of 1,2-Dichloroethane Acute Aquatic Hazard Data With the Logistic Distribution (<u>Etterson, 2020a</u>)

1555

1556



Figure_Apx B-4. SSD Distribution for 1,2-Dichloroethane Acute Hazard Data in μg/L (Etterson, 2020a; Wickham, 2016)

1559

B.1.1.3 Dose-Response Curve Fit Methods

1562

1563

1564

1565

1566

1567 1568

1569

15701571

15721573

1574

15751576

1577

1578 1579

1580

15811582

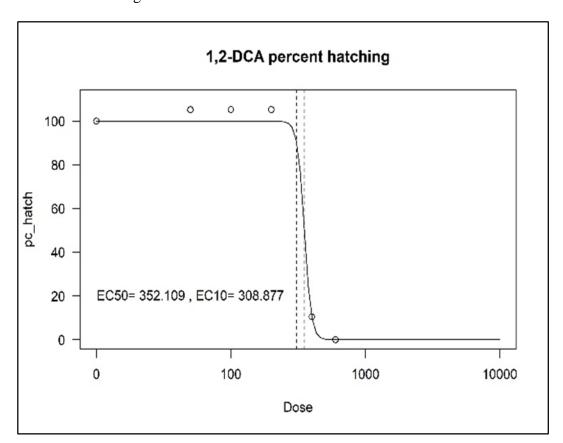
1583

1584

1585

1586

The hatching rate endpoint for *Ophryotrocha labronica* exposed to 1,2-dichloroethane was further analyzed to derive EC50 and EC10 values by fitting a dose-response curve. The authors of the original dose-response study (Rosenberg et al., 1975) reported for each concentration of 1,2-dichloroethane the hatching percent of O. labronica eggs. The hatching rate endpoint is expressed as percent relative to control response. Hormetic observations (i.e., treatments having a response exceeding that of the control) were not censored. Characterizing EC50 and EC10 values required defining both the 0 percent effect and 100 percent effect. Estimated between these two thresholds are the EC50, or the 50 percent inhibition of egg hatching, and EC10, 10 percent inhibition of egg hatching. Responses plateaued as concentration increased. Because zero was the minimum possible realistic value, the 100 percent effect (i.e., lower asymptote) was set at zero. The 0 percent effect was defined as the control response; therefore, the upper asymptote was fixed at 100 percent of the control response. Hatching percent followed a decreasing logistic shape. Several functions were tested using R v4.2.1, with and without upper and lower asymptotes (R. Core Team, 2022; Ritz et al., 2015). A log-logistic curve was ultimately fit to the data with slope and inflection point as the estimated parameters. The EC50 was calculated as the concentration along the curve halfway between 0 and 100 percent control response and the EC10 as the concentration a tenth of the way along the curve. Figure Apx B-5 shows the log-logistic curve, with vertical dotted lines indicating the EC50 and EC10.



Figure_Apx B-5. Log-Logistic Curve Fit to Hatching Percent Data From *Ophryotrocha labronica* Exposed to 1,2-Dichloroethane (Rosenberg et al., 1975)

B.1.2 Evidence Integration

Data integration includes analysis, synthesis, and integration of information for the risk evaluation. During data integration, EPA considers quality, consistency, relevancy, coherence, and biological

- plausibility to make final conclusions regarding the weight of scientific evidence. As stated in the Draft Systematic Review Protocol (<u>U.S. EPA, 2021</u>), data integration involves transparently discussing the significant issues, strengths, and limitations, as well as the uncertainties of the reasonably available information and the major points of interpretation.
- The general analytical approaches for integrating evidence for environmental hazard is discussed in Section 7.4 of the Draft Systematic Review Protocol (U.S. EPA, 2021).

- The organization and approach to integrating hazard evidence is determined by the reasonably available evidence regarding routes of exposure, exposure media, duration of exposure, taxa, metabolism and distribution, effects evaluated, the number of studies pertaining to each effect, as well as the results of the data quality evaluation.
- The environmental hazard integration is organized around effects to aquatic and terrestrial organisms as well as the respective environmental compartments (*e.g.*, water column, benthic, soil). Environmental hazard assessment may be complex based on the considerations of the quantity, relevance, and quality of the available evidence.
- For 1,2-dichloroethane, environmental hazard data from toxicology studies identified during systematic review have used evidence that characterizes apical endpoints; that is, hazard endpoints that could have population level effects such as reproduction, growth, or mortality. EPA also considered predictions from Web-ICE to supplement the empirical data found during systematic review.

B.1.2.1 Rubric for Weight of Scientific Evidence

The weight of scientific evidence fundamentally means that the evidence is weighed (*i.e.*, ranked), and weighted (*i.e.*, a piece or set of evidence or uncertainty may have more importance or influence in the result than another). Based on the weight of scientific evidence and uncertainties, a confidence statement was developed that qualitatively ranks (*i.e.*, robust, moderate, slight, or indeterminate) the confidence in the hazard threshold. The qualitative confidence levels are described below and illustrated in Table_Apx B-2.

- The evidence considerations and criteria detailed within (<u>U.S. EPA, 2021</u>) will guide the application of strength-of-evidence judgments for environmental hazard effect within a given evidence stream and were adapted from Table 7-10 of the Draft Systematic Review Protocol (<u>U.S. EPA, 2021</u>).
- EPA used the strength-of-evidence and uncertainties from (U.S. EPA, 2021) for the hazard assessment to qualitatively rank the overall confidence using evidence for environmental hazard. Confidence levels of robust (+ + +), moderate (+ +), slight (+), or indeterminant are assigned for each evidence property that corresponds to the evidence considerations (U.S. EPA, 2021). The rank of the Quality of the Database consideration is based on the systematic review data quality rank (high, medium, or low) for studies used to calculate the hazard threshold, and whether there are data gaps in the toxicity dataset. Another consideration in the Quality of the Database is the risk of bias (*i.e.*, how representative is the study to ecologically relevant endpoints). Additionally, because of the importance of the studies used for deriving hazard thresholds, the Quality of the Database consideration may have greater weight than the other individual considerations. The high, medium, and low systematic review ranks correspond to the evidence table ranks of robust (+ + +), moderate (+ +), or slight (+), respectively. The evidence considerations are weighted based on professional judgement to obtain the Overall Confidence for each hazard threshold. In other words, the weights of each evidence property relative to the other properties are dependent on the specifics of the weight of scientific evidence and uncertainties that are described in

the narrative and may or may not be equal. Therefore, the overall score is not necessarily a mean or 1635 1636 defaulted to the lowest score. The confidence levels and uncertainty type examples are described below.

1637 1638

1643

1644 1645

1646

1647

1648 1649

1650

1651

1656

1657

1658

1659

1660

1661

1662

1663

1664

Confidence Levels

- 1639 Robust (+++) confidence suggests thorough understanding of the scientific evidence and 1640 uncertainties. The supporting weight of scientific evidence outweighs the uncertainties to the point where it is unlikely that the uncertainties could have a significant effect on the exposure or 1641 hazard estimate. 1642
 - Moderate (++) confidence suggests some understanding of the scientific evidence and uncertainties. The supporting scientific evidence weighed against the uncertainties is reasonably adequate to characterize exposure or hazard estimates.
 - Slight (+) confidence is assigned when the weight of scientific evidence may not be adequate to characterize the scenario, and when the assessor is making the best scientific assessment possible in the absence of complete information. There are additional uncertainties that may need to be considered.
 - Indeterminant (NA) corresponds to entries in evidence tables where information is not available within a specific evidence consideration.

Types of Uncertainties 1652

- The following uncertainties may be relevant to one or more of the weight of scientific evidence 1653 1654 considerations listed above and will be integrated into that property's rank in the evidence (Table Apx 1655 B-2).
 - Scenario uncertainty: Uncertainty regarding missing or incomplete information needed to fully define the exposure and dose.
 - o The sources of scenario uncertainty include descriptive errors, aggregation errors, errors in professional judgment, and incomplete analysis.
 - Parameter uncertainty: Uncertainty regarding some parameter.
 - Sources of parameter uncertainty include measurement errors, sampling errors, variability, and use of generic or surrogate data.
 - Model uncertainty: Uncertainty regarding gaps in scientific theory required to make predictions on the basis of causal inferences.
 - o Modeling assumptions may be simplified representations of reality.

1665 1666

1669

1671

1667 Table Apx B-2 summarizes the weight of scientific evidence and uncertainties, while increasing 1668 transparency on how EPA arrived at the overall confidence level for each exposure hazard threshold. Symbols are used to provide a visual overview of the confidence in the body of evidence, while de-1670 emphasizing an individual ranking that may give the impression that ranks are cumulative (e.g., ranks of different categories may have different weights).

Page **69** of **71**

Table_Apx B-2. Considerations That Inform Evaluations of the Strength of the Evidence Within an Evidence Stream

Consideration	Increased Evidence Strength (of the Apical Endpoints, Mechanistic, or Field Studies Evidence)	Decreased Evidence Strength (of the Apical Endpoints, Mechanistic, or Field Studies Evidence)				
The evidence considerations and criteria provided below guide the application of strength-of-evidence judgments for an outcome or environmental hazard effect within a given evidence stream. Evidence integration or synthesis results that do not warrant an increase or decrease in evidence strength for a given consideration are considered "neutral" and are not described (and, in general, are captured in the assessment-specific evidence profile table						
Quality of the database ^a (risk of bias)	 A large evidence base of high- or medium-quality studies increases strength. Strength increases if relevant species are represented in a database. 	 An evidence base of mostly <i>low</i>-quality studies decreases strength. Strength also decreases if the database has data gaps for relevant species (<i>i.e.</i>, a trophic level that is not represented). Decisions to increase strength for other considerations in this table should generally not be made if there are serious concerns for risk of bias; in other words, all the other considerations in this table are dependent upon the quality of the database. ^a 				
Consistency	Similarity of findings for a given outcome (<i>e.g.</i> , of a similar magnitude, direction) across independent studies or experiments increases strength, particularly when consistency is observed across species, life stage, sex, wildlife populations, and across or within aquatic and terrestrial exposure pathways.	 Unexplained inconsistency (<i>i.e.</i>, conflicting evidence; see (<u>U.S. EPA</u>, 2005) decreases strength. Strength should not be decreased if discrepant findings can be reasonably explained by study confidence conclusions; variation in population or species, sex, or life stage; frequency of exposure (<i>e.g.</i>, intermittent or continuous); exposure levels (low or high); or exposure duration. 				
Strength (effect magnitude) and precision	 Evidence of a large magnitude effect (considered either within or across studies) can increase strength. Effects of a concerning rarity or severity can also increase strength, even if they are of a small magnitude. Precise results from individual studies or across the set of studies increases strength, noting that biological significance is prioritized over statistical significance. Use of probabilistic model (e.g., Web-ICE, SSD) may increase strength. 	Strength may be decreased if effect sizes that are small in magnitude are concluded not to be biologically significant, or if there are only a few studies with imprecise results.				
Biological gradient/dose- response	• Evidence of dose-response increases strength.	A lack of dose-response when expected based on biological understanding and having a wide range of doses/exposures evaluated in the evidence base can decrease strength.				

Consideration	Increased Evidence Strength (of the Apical Endpoints, Mechanistic, or Field Studies Evidence)	Decreased Evidence Strength (of the Apical Endpoints, Mechanistic, or Field Studies Evidence)				
	 Dose-response may be demonstrated across studies or within studies and it can be dose- or duration-dependent. Dose-response may not be a monotonic dose-response (monotonicity should not necessarily be expected; for example, different outcomes may be expected at low vs. high doses due to activation of different mechanistic pathways or induction of systemic toxicity at very high doses). Decreases in a response after cessation of exposure (e.g., return to baseline fecundity) also may increase strength by increasing certainty in a relationship between exposure and outcome (this particularly applicable to field studies). 	 In experimental studies, strength may be decreased when effects resolve under certain experimental conditions (<i>e.g.</i>, rapid reversibility after removal of exposure). However, many reversible effects are of high concern. Deciding between these situations is informed by factors such as the toxicokinetics of the chemical and the conditions of exposure, see (U.S. EPA, 1998), endpoint severity, judgments regarding the potential for delayed or secondary effects, as well as the exposure context focus of the assessment (<i>e.g.</i>, addressing intermittent or short-term exposures). In rare cases, and typically only in toxicology studies, the magnitude of effects at a given exposure level might decrease with longer exposures (<i>e.g.</i>, due to tolerance or acclimation). Like the discussion of reversibility above, a decision about whether this decreases evidence strength depends on the exposure context focus of the assessment and other factors. If the data are not adequate to evaluate a dose-response pattern, then strength is neither increased nor decreased. 				
Biological relevance	Effects observed in different populations or representative species suggesting that the effect is likely relevant to the population or representative species of interest (<i>e.g.</i> , correspondence among the taxa, life stages, and processes measured or observed and the assessment endpoint).	An effect observed only in a specific population or species without a clear analogy to the population or representative species of interest decreases strength.				
Physical/chemical relevance	Correspondence between the substance tested and the substance constituting the stressor of concern.	The substance tested is an analog of the chemical of interest or a mixture of chemicals which include other chemicals besides the chemical of interest.				
Environmental relevance	Correspondence between test conditions and conditions in the region of concern.	The test is conducted using conditions that would not occur in the environment.				
^a Database refers to the entire da	Database refers to the entire dataset of studies integrated in the environmental hazard assessment and used to inform the strength of the evidence. In this					

^a Database refers to the entire dataset of studies integrated in the environmental hazard assessment and used to inform the strength of the evidence. In this context, database does *not* refer to a computer database that stores aggregations of data records such as the ECOTOX Knowledgebase.