Questions by Committee to EPA; September 17, 2024

MEETING TITLE: SACC REVIEW OF THE 2024 DRAFT RISK EVALUATION FOR 1,1-DICHLOROETHANE AND DRAFT HUMAN HEALTH HAZARD ASSESSMENT FOR 1,2-DICHLOROETHANE

The SACC requested confidence intervals for aquatic hazard data.

RESPONSE: Confidence intervals (if available) are added in red text to table below. Confidence intervals on the modeled data sourced from WebICE are available in Appendix K.2.1.1 of the Draft Risk Evaluation.

Table_Apx J-1. Empirical Acute (EC50, LC50) and Chronic (ChV) Hazard Comparison for Various Aquatic Species Exposed to 1,1-Dichloroethane or Analogs 1,2-Dichloropropane and 1,1,2-Trichloroethane

Species	Endpoint	1,1-Dichloroethane (Target)	1,2-Dichloropropane (Analog)		1,1,2-Trichloropropane (Analog)	
		Empirical Toxicity (mg/L)	Empirical Toxicity (mg/L)	Ratio to 1,1-Dichloroethane	Empirical Toxicity (mg/L)	Ratio to 1,1-Dichloroethane
Poecila reticulata (guppy) [a i]	LC50	202	116	0.57	94.4	0.47
Daphnia magna	EC50	34 (30.0-39.1) [c]	29.5 (26.5-32.8)[e]	0.87	81.6[k] (81 [58-97]; 18 [11-32]; 190 [160-210]; 170 [150-200]; 81 [58-110]; 78 [57-110]) [g h]	2.40
Pseudokirchneriella subcapitata [b i]	EC50	49.92	34.42	0.69	105.42	2.11
Daphnia magna	ChV	0.93[d]	1.52[f]	1.63	3.2 (2.4-4.2)[h]	3.44

[a] Data are from (1981).
[b] Data are from (2007).
[c] Data are from (2009a).
[d] Data are from (2009d).
[e] Data are from (1995a).
[f] Data are from (1995b).
[g] Data are from (1983; 1980).
[h] Data are from (3M Environmental Lab, 1984).
[i] These studies were rated uninformative for not stating the doses and/or number of doses utilized in the dose-response (Tsai and Chen, 2007; Könemann, 1981) and not stating inclusion of a control group (Könemann, 1981); however, EPA finds other aspects of both studies otherwise useful for comparing the relative toxicity of 1,1-dichloroethane and 1,2-dichloropropane or 1,1,2-trichloroethane.
[k] This value represents the geometric mean of hazard values from the referenced studies.

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The SACC requested information on the databases and data sources that get searched.

RESPONSE: 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* (HEROID 10415760) was reviewed by the TSCA Scientific Advisory Committee on Chemicals (SACC) in 2021 and received public comment. This draft document describes the process used to identify potentially relevant information when conducting a systematic review in Section 4. Furthermore, Appendix E of the *Draft Systematic Review Protocol Supporting TSCA Risk Evaluations for Chemical Substances* document contains a list and description of databases identified for each discipline. Additional data sources and/or databases evaluated to inform the risk evaluation of 1,1-dichloroethane are described in the *Draft Systematic Review Protocol for 1,1-Dichloroethane: Systematic Review Support Document for the Draft Risk Evaluation* (HEROID 11151731).

The SACC requested information on what is involved in Full Text Screening. At what point is EPA OPPT using artificial intelligence tools and when are humans reading and evaluating the studies?

RESPONSE: Sections 4.2.5 and 4.3.2 of 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* (HEROID 10415760) and Section 4 of the *Draft Systematic Review Protocol for 1,1-Dichloroethane: Systematic Review Support Document for the Draft Risk Evaluation* (HEROID 11151731) describe how title-and-abstract screening and full-text screening are conducted to identify references that may contain relevant information for use in risk evaluations under TSCA using discipline-specific screening criteria. EPA uses machine learning in the identification and title-and-abstract screening of potentially relevant information for risk evaluations. EPA does not use generative AI for this or other purposes in the systematic review process. Full-text screening is conducted manually by two independent technical experts in a respective discipline. If the independent screeners' responses differ, they may collaborate to resolve the conflict. If the independent screeners cannot reach consensus or encounter situations that may be common to multiple screeners, they may consult discipline-specific experts or the full screening team. Some disciplines (*e.g.*, physical and chemical properties) may use a third independent reviewer to resolve conflicts.

The SACC requested information on metabolic and toxicologic similarities for the other analogs. Why did EPA OPPT not evaluate toxicological similarities for all assessed possible analogs?

RESPONSE: The process EPA used to identify an analog for both environmental hazard and human health hazard start with the same step - structural similarity analyses. The analyses were completed using four programs. AIM analysis was performed on CBI-side and analogs were described as 1st or 2nd pass. 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. Analogs that appeared in three out of four programs were identified as potential analog candidates. Using these parameters, 17 analogs were identified as potentially suitable analog candidates for 1,1-dichloroethane based on structural similarity. Only the results for structural comparison are shown for chemicals that have completed data evaluation and extraction as part of the OPPT Systematic Review process or were previously evaluated by OPPT with final published risk evaluations. This was necessary as it was not

possible to complete data evaluation and extraction for all possible analogs and complete the risk evaluation within the required timeline.

The SACC requested clarification on the qualitative evaluation vs quantitative evaluation of toxicological similarities as part of the analog selection process mentioned in one of the presentations. The SACC requested to see the quantitative evaluation of the target/analog chemicals if it is available.

RESPONSE: Due to limited human health hazard information for 1,1-dichloroethane, quantitative comparisons between 1,1-dichloroethane and 1,2-dichloroethane are only available for one oral study (Muralidhara et al. (2001)). Evaluation of the entire database for both 1,1-dichloroethane and 1,2-dichloroethane can be found starting in Section 5.2.3 and continuing through Section 5.2.5. Quantitative comparisons of the oral toxicity of 1,1-dichloroethane from this one study to data for 1,2-dichloroethane is shown in Section 5.2.6.1.2 to 5.2.6.1.4 for acute, short-term, and chronic oral exposures, respectively. The primary comparisons of toxicological similarities as part of the analog selection process are qualitative. Qualitative comparisons of the oral toxicity of 1,1-dichloroethane compared to 1,2-dichloroethane is detailed in Section 5.2.2 for toxicokinetics, Section 5.2.3.1 for non-cancer critical health outcomes, Section 5.2.4 for genotoxicity and Section 5.2.5.1.1 for cancer. This information is summarized as part of the analog selection process in Section 5.2.1.3.4 for cancer and Section 5.2.1.3.5 for non-cancer.

The SACC requested specific information on where the application of body weight scaling is described in the risk evaluation.

RESPONSE: The application of body weight scaling in the calculation of human equivalent doses (HEDs) and human equivalent concentrations (HECs) are provided in Appendix M.3.1.3 of the risk evaluation document. The conversion can also be found in Tables 5-49 thru 5-51 in the footnotes to the 1,1-dichloroethane draft risk evaluation.