PUBLIC RELEASE DRAFT
~~August~~September 2024

***DRAFT CHARGE to the TOXIC SUBSTANCES CONTROL ACT (TSCA) SCIENCE ADVISORY COMMITTEE ON CHEMICALS (SACC)***

***Peer Review of 2024 Draft Risk Evaluation for 1,1-Dichloroethane and 2024 Draft Human Health Hazard Assessment for 1,2-Dichloroethane Technical Support Document***

## Background

The U.S. Environmental Protection Agency (EPA or the Agency) has evaluated risks posed by 1,1-dichloroethane under the Toxic Substances Control Act to human health and environment, as presented in the *Draft Risk Evaluation for 1,1-Dichloroethane* (U.S. EPA, 2024b) ("draft risk evaluation"). The Agency is requesting peer review by the TSCA SACC of the *Draft Risk Evaluation for 1,1-Dichloroethane*. Additionally, EPA is requesting SACC peer review of the *Draft Human Health Hazard Assessment for 1,2-Dichloroethane Technical Support Document* (U.S. EPA, 2024a) (TSD).

1,1-Dichloroethane is a chlorinated solvent that is manufactured and used primarily in industrial applications, such as a reactant for the manufacture of other chemicals or as a laboratory chemical. The reported total production volume (PV) of 1,1-dichloroethane in 2016 and 2020 was between 100 million and one billion pounds. Based on submitted data under EPA's Chemical Data Reporting rule, a high percentage of the production volume is used for processing as a reactive intermediate, and a small percentage is used for commercial use as a laboratory chemical. EPA has not identified any consumer uses of 1,1-dichloroethane.

The draft risk evaluation includes analyses of physical and chemical properties; the fate and transport in the environment; exposure to workers, and general population including potentially exposed or susceptible subpopulations; releases to the environment; environmental hazard and risk characterization for terrestrial and aquatic species; and human health hazard and risk characterization for workers and the general population.

Given that the largest reported environmental releases of 1,1-dichloroethane are to air, a major exposure pathway to 1,1-dichloroethane is through releases to air. Based on its physical and chemical properties—including water solubility, vapor pressure, and Henry's Law constant—1,1-dichloroethane released to air is expected to remain primarily in air. Some 1,1-dichloroethane released to water will remain in water as it is water soluble. Continuous releases of 1,1-dichloroethane to water are expected to volatilize to air at rates dependent on environmental conditions; however, a portion of 1,1-dichloroethane will remain in the water column (maximum solubility is 5,000 mg/L). EPA, therefore, assessed relevant air, surface water, and land exposure pathways. The Agency relied on databases reporting multi-year 1,1-dichloroethane releases to ambient air, surface water, and disposal to land, such as the Toxic Release Inventory (TRI), the National Emissions Inventory (NEI), and Discharge Monitoring Reports (DMR), among others, to conduct major portions of its exposure analysis.

Due to limited empirical data for human health and portions of the environmental hazard assessments, EPA is proposing to rely on read-across. Specifically, for human health assessment, EPA is proposing to use 1,2-dichloroethane as an analog for a read-across method to supplement the non-cancer and cancer hazard information for 1,1-dichloroethane. The Agency is therefore submitting the draft human health hazard TSD for 1,2-dichloroethane for peer review. EPA is in the process of preparing a draft risk

evaluation for 1,2-dichloroethane that will be subsequently released for public comment and peer review.

EPA is releasing the draft risk evaluation for 1,1-dichloroethane for public comment and independent, expert peer review. EPA is focusing its peer review charge questions on specific scientific areas and analyses. Many of the methods and analyses used in these evaluations are not novel and have been reviewed in the development of previous TSCA assessments. EPA is requesting feedback on approaches, results, and calculations associated with the exposure, human health hazard, and environmental hazard analyses not previously peer reviewed. Once EPA receives input from public comment and peer review, revisions will be made, and the Agency will finalize the 1,1-dichloroethane risk evaluation. EPA will also incorporate information from the draft 1,2-dichloroethane human health hazard assessment TSD into the draft risk evaluation for 1,2-dichloroethane.

The Existing Chemicals Risk Assessment Division (ECRAD) has received input from senior scientists and technical experts from EPA's Office of Chemical Safety and Pollution Prevention and across EPA. Specifically, ECRAD has received input from the OCSPP Senior Science Advisors, OCSPP's Science Policy Council, and through the intra-agency review process. The areas of analysis contained in this risk evaluation reflect some of the revisions received throughout review and during scientific deliberations, however, there are some significant aspects of the draft 1,1-dichloroethane risk evaluation and the draft 1,2-dichloroethane human health hazard assessment TSD for which there is not agreement between ECRAD scientists and senior scientists and technical experts. In accordance with EPA's Scientific Integrity Policy (https://www.epa.gov/scientific-integrity/epas-scientific-integrity-policy), the areas of scientific disagreement are described in relevant charge questions below and are intended to guide the scientific peer review by the SACC. EPA is requesting the SACC provide input on these science issues—including the differences of scientific opinion —which relate specifically to 1,1-dichloroethane and 1,2-dichloroethane but also more broadly in the application of risk assessment practices and use of existing EPA and internally accepted guidance documents.

**Charge Questions**

1. **Environmental Exposure:** As described in Section 2 of the draft risk evaluation, 1,1-dichloroethane is a volatile liquid with appreciable water solubility. Depending on which environmental compartment(s) receive the release, 1,1-dichloroethane is expected to partition primarily to air; however, environmental partitioning analysis shows continuous releases of 1,1-dichloroethane to water have the potential to remain in water. Additional discussion of the evidence of 1,1-dichloroethane in various media, including water is presented in Sections 1.1.2.1 and 2.2.2 of the draft risk evaluation. As described in Section 3.3.3.2.1 of the draft risk evaluation, to estimate exposures from releases to surface water for the one facility representing the manufacturing condition of use, EPA used this facility's second highest recorded release, which took place in 2016, as more representative of release conditions for this facility. The highest release from this facility located in Lake Charles, Louisiana, was associated with a storm event that is not representative of usual operating conditions and was considered an outlier in the analysis. The analysis includes consideration of the facility's operating days. However, since extreme storm events do occur with regularity in the region of the country where the manufacturing facility is located (and may be expected to occur with higher frequency and intensity in the future due to climate change), EPA is seeking comments on this approach. The analysis also includes consideration of the facility's operating days.

Please comment on the use, representativeness, and relevancy of the 2016 annual release data for estimating environmental exposure in the draft risk evaluation via surface water for this facility over its operating days.

2. **Read-Across Analysis for Environmental Hazard Assessment:** Limited empirical toxicity data are available for 1,1-dichloroethane in aquatic organisms for developing the environmental hazard values (see Appendix J.1 of the draft risk evaluation*)*. EPA selected 1,2-dichloropropane and 1,1,2-trichloroethane as analogs to read-across environmental hazard to 1,1-dichloroethane.

    a. Please comment on the strengths and uncertainties related to the read-across approaches used for the selection of the analogs for aquatic organisms and environmental assessment as outlined in Appendix J.1 of the draft risk evaluation. If appropriate, please provide additional methodologies that EPA could use to identify analogs for 1,1-dichloroethane for use in the ecological risk assessment.

    b. Please comment on the selection of 1,2-dichloropropane and 1,1,2-trichloroethane as analogs to support the 1,1-dichloroethane aquatic hazard database. Please also comment on the steps in the analysis, robustness, transparency of assumptions, and uncertainties of the conclusions, as well as the overall clarity with which the results are communicated.

3. **Read-Across Analysis for Human Health Assessment:** Limited non-cancer empirical toxicity data are available for 1,1-dichloroethane for oral exposures and ECRAD did not identify available data for dermal and inhalation exposures. The Agency for Toxics Substances and Disease Registry (ATSDR) completed a *Toxicological Profile for 1,1-Dichloroethane* in August 2015 (ATSDR, 2015). EPA identified 1,2-dichloroethane as an analog for reading-across to 1,1-dichloroethane non-cancer human health using the methodology found in Section 5.2.1.3 of the draft risk evaluation.

    a. Please comment on strengths and uncertainties related to the read-across approach and methodologies (Appendix J.2) used for structural similarities (Section 5.2.1.3.1), physical and chemical properties (Section 5.2.1.3.2), metabolic similarities (Section 5.2.1.3.3), and non-cancer toxicological similarities (Sections 5.2.1.3.5) in the draft risk evaluation. If appropriate, please provide additional methodologies that EPA could use to identify analogs for 1,1-dichloroethane for use in the human health risk assessment.

    b. Please comment on the selection of 1,2-dichoroethane as the analog to support the 1,1-dichloroethane non-cancer hazard database. Please also comment on the steps in the analysis, robustness, transparency of assumptions and uncertainties of the conclusions, as well as the overall clarity with which the results are communicated.

    c. Please include in your comments the extent to which the ATSDR (2015) Toxicological Profile for 1,1-Dichloroethane provides information relevant to support the risk evaluation under TSCA.

4. **Human Health Assessment: Oral, Non-cancer (Acute):** As described in Section 5.2.3 and Section 5.2.6 of the draft risk evaluation, ECRAD is proposing to rely on dose-related changes in kidney weights from Storer et al. (1984) for the acute oral point of departure (Table 5-42).

    a. Please comment on the study quality, study protocol, study conduct, and data interpretation of the Storer et al. (1984) for 1,2-dichloroethane. Please include in your comments information about the appropriateness of using the findings from Storer et al. (1984) for deriving an acute oral point of departure(s) (PODs) for extrapolating non-cancer risk to 1,1-dichloroethane and 1,2-dichloroethane.

    b. Please also include comments on the selection of the BMR (benchmark response) selected, benchmark dose (BMD) analyses models used, and those selected. Please comment, on clarity and completeness of the description of the BMD analysis.

    c. If appropriate, please suggest alternative study or studies for use in deriving an acute oral point of departure (POD) for 1,1-dichloroethane and 1,2-dichloroethane.

5. **Human Health Assessment: Oral, Non-cancer (Short-Term and Chronic):** As described in Section 5.2.3 and Section 5.2.6 of the draft risk evaluation, ECRAD is proposing to rely on the immunological effects identified in the 1,2-dichloroethane 14-day gavage study within Munson et al. (1982) for the oral non-cancer short-term and chronic points of departure (LOAEL = 4.89 mg/kg/day).

    ECRAD's conclusion about the Munson et al. (1982) drinking water study differs from EPA's Office of Research and Development (ORD) 2010 Provisional Peer-Reviewed Toxicity Value (PPRTV) (U.S. EPA, 2010) and the 2022 Draft Toxicological Profile from ATSDR (ATSDR, 2022). For example, the ORD PPRTV (p. 33) provides a summary of Munson et al (1982) and concluded: "The NOAEL for this study would be the highest dose tested, 189 mg/kg-day." ATSDR (2022; pp. 166–168) did not select the Munson et al. (1982) study for POD derivation and provided an explanation of why the immunological findings were not selected for sub-chronic or chronic POD derivation (ATSDR defines a 14-day study as acute) that included scientific issues surrounding human relevance, dose selection, metabolism and unknown mechanistic understanding.

    The U.S. EPA (2010) PPRTV relied on the drinking water study within the NTP (1991) study for their provisional reference dose (RfD). Similarly, ATSDR (2022) in their 2022 Toxicological Profile for 1,2-dichloroethane relied on the increase in kidney weight from the same drinking water study within NTP (1991) for their oral intermediate minimal risk level (MRL) for 1,2-dichloroethane (LOAEL = 58 mg/kg/day). ECRAD evaluated the drinking water study within Munson et al. (1982) and NTP (1991) according to OPPT's systematic review process to be "uninformative."

    a. Please comment on the study quality of drinking water and gavage experiments in the same study, study protocol, study conduct, and data interpretation of the Munson et al. (1982) for 1,2-dichloroethane. Please include in your comments information about the appropriateness of using the findings from Munson et al. (1982) for deriving short-term and chronic POD(s) for extrapolating non-cancer risk to 1,1-dichloroethane and 1,2-dichloroethane.

b. Please comment on the study quality, study protocol and conduct, and data interpretation of the drinking water study within NTP (1991). Please include in your comments information about the appropriateness of using the findings from the drinking water study within NTP (1991) for deriving short-term and chronic POD(s) for extrapolating non-cancer risk to 1,1-dichloroethane and 1,2-dichloroethane.

c. Pending your comments on 4.a and 4.b and if appropriate, please suggest any alternative study or studies [*e.g.*, ATSDR (2015) Toxicological Profile for 1,1-Dichloroethane] for use in deriving oral short-term and chronic PODs for 1,1-dichloroethane and 1,2-dichloroethane.

d. Please comment on the extent to which there is potential for uncertainty associated using short-term and sub-chronic studies for assessing chronic, long-term exposure to 1,1-dichloroethane.

6. **Human Health Assessment: Inhalation, Non-cancer (Acute):** As described in Section 5.2.6 of the draft risk evaluation, Appendix F in the draft human health hazard technical support document (TSD) for 1,2-dichloroethane, and in *Draft Risk Evaluation for 1,1-Dichloroethane – Supplemental Information File: Benchmark Dose Modeling* (U.S. EPA, 2024c), BMD modeling was completed and used for several non-cancer points of departure inhalation (Dow Chemical, 2006). In these cases, the statistical benchmark concentration lower confidence limit (BMCL) on the concentration at the benchmark concentration (BMC) used as the POD is lower than the No Observed Adverse Effect Levels (NOAELs) of each of the studies (See Table 5-43; Appendix F of the draft TSD). The U.S. EPA (2012) Benchmark Dose Technical Guidance states (p. 20): "extrapolation sufficiently below the observable range may be too uncertain to reliably estimate the BMCs/BMCLs for the selected BMR (e.g., when all the dosed groups have near-maximal responses). In such cases, BMD modeling is not recommended and obtaining more data or using the NOAEL/Lowest Observed Adverse Effect Level (LOAEL) approach, while recognizing the inabilities of that approach to resolve the data limitations, may be warranted."

   a. Please comment on the study quality, study protocol, study conduct, and data interpretation of the Dow Chemical (2006) for 1,2-dichloroethane. Please include in your comments information about the appropriateness of using the findings from Dow Chemical (2006) for deriving an acute inhalation point of departure(s) for extrapolating non-cancer risk to 1,1-dichloroethane and 1,2-dichloroethane.

   b. Please also include comments on the selection of the BMR selected, BMC analyses used, and the clarity and completeness of the description of the BMC analysis.

   c. If appropriate, please suggest alternative study or studies for use in deriving an acute inhalation POD for 1,1-dichloroethane and 1,2-dichloroethane.

7. **Human Health Assessment: Inhalation, Non-cancer (Short-Term and Chronic):** As described in Section 5.2.6 of the draft risk evaluation, Appendix F in the draft human health hazard TSD for 1,2-dichloroethane, and in *Draft Risk Evaluation for 1,1-Dichloroethane – Supplemental Information File: Benchmark Dose Modeling* (U.S. EPA, 2024c), BMD modeling was completed and used for

short-term and chronic inhalation (Zhang et al., 2017) exposure durations (See Table 5-45; Appendix F of the draft TSD).

a. Please comment on the study quality, study protocol, study conduct, and data interpretation of the Zhang et al. (2017) for 1,2-dichloroethane. Please include in your comments information about the appropriateness of using the findings from Zhang et al. (2017) for deriving short-term and chronic inhalation PODs for extrapolating non-cancer risk to 1,1-dichloroethane and 1,2-dichloroethane.

b. Please also include comments on the selection of the BMR selected, BMC analyses used, and the clarity and completeness of the description of the BMC analysis.

c. If appropriate, please suggest alternative study or studies [e.g., ATSDR (2015) ATSDR Toxicological Profile for 1,1-Dichloroethane] for use in deriving short-term and chronic inhalation points of departure for 1,1-dichloroethane and 1,2-dichloroethane.

8. **Dermal Absorption: Interpretation and Use of the New *In Vitro* Study:** As described in Section 5.1.1.1.5, of the draft risk evaluation, new data are available for an *in vitro* dermal absorption study using frozen human skin for conducted in accordance with OECD TG 428 and conditions of use (COU) information. The *1,1-Dichloroethane Test Order – Rates of Penetration through Human Skin Using a Flow Through in vitro System Study Report* (Labcorp Early Development, 2024), the *Draft Risk Evaluation for 1,1-Dichloroethane – Supplemental Information: in vitro Dermal Absorption Study Analysis* (U.S. EPA, 2024~~e~~), and *Draft Risk Evaluation for 1,1-Dichloroethane – Supplemental Information: in vitro Dermal Absorption Calculation Sheet* (U.S. EPA, 2024f) are available for review. As described in the study analysis, ECRAD has proposed to use a dermal absorption factor 0.3% in the oral to dermal route to route extrapolation. In the neat COU exposure portion of the *in vitro* study, a total of 0.13% was recovered in the receptor fluid over 24 hours with an overall recovery of 58.42%. For the draft risk evaluation, ECRAD adjusted the dermal absorption factor to 0.3% to develop an upper bound value to account for mass recovery. In the other non-COU components of the study (*e.g.,* diluted in isopropyl myristate [IPM] and 1,2-dichloroethane at various concentrations) where the recovery was >80% the dermal absorption ranged from <0.01 to 0.06%.

The OECD 2022 *Guidance Notes On Dermal Absorption Studies* (OECD, 2022) states the following: "If recovery is <95% but a robust explanation demonstrating the missing material would not have been or is very unlikely to have been absorbed, then the inclusion of the missing material might not be required." Similarly, the European Food Safety Authority *Guidance on Dermal Absorption* (EFSA, 2017) states that (p. 13) "Losses that are considered to be from non-absorbed material will have no impact on the results." In the case of 1,1-dichloroethane, loss is expected to be due to volatility. The study authors did not conduct the recovery calculations (which were performed by ECRAD) because "The missing radioactivity was most likely due to loss of volatile test item at sampling. It is therefore considered that the losses would be associated with the non-absorbed fraction and no correction for the losses has been made to the absorption value (p. 31)."

With regard to overall recovery, EFSA (2017) (p. 13) states that "If no clear conclusion can be drawn, only values from high recovery samples should be used to derive the absorption and

replicates with low recoveries should be excluded entirely." OECD (2022) (p. 39) provides similar guidance. In the case of the 1,1-dichloroethane study where the recovery was >80%, the dermal absorption ranged from <0.01 to 0.06%.

a. Please comment on the selection and derivation of ECRAD's 0.3% dermal absorption factor and its appropriateness for developing the dermal exposure and risk assessments for 1,1-dichloroethane, considering the range of replicate values for conditions of use testing, % mass recovery and data variability. If appropriate, please provide comments on an alternative dermal absorption factor.

9. **Cancer Assessment:** The available rodent cancer studies for 1,1-dichloroethane have been determined to be inappropriate for deriving quantitative cancer risk estimates. EPA identified 1,2-dichloroethane as a proposed analog for reading-across to 1,1-dichloroethane based on the methodology found in Section 5.2.1.3 of the draft risk evaluation. The 1,1-dichloroethane draft risk evaluation includes a review of the cancer hazard data gaps identified for 1,1-dichloroethane (Section 5.2.1.2.2) and outlines cancer hazard identification and evidence integration for 1,1-dichloroethane and 1,2-dichloroethane (Section 5.2.5). Additional relevant information on 1,2-dichloroethane can be found in the draft TSD. In the fall of 2023, ECRAD conducted an internal peer review of the available rodent cancer studies available for 1,1-dichloroethane and 1,2-dichloroethane by agency experts outside OPPT. While the internal peer reviewers and the ECRAD assessment team came to the same conclusion about the quality and utility of most of the rodent cancer studies, there was a differing scientific opinion (DSO) about the NTP (1978) mouse study with 1,2-dichloroethane. Three documents are available for review by the SACC related to this internal peer review within *EPA Peer Review of Carcinogenicity Studies for 1,1-Dichloroethane and 1,2-Dichloroethane* (2024) available on EPA-HQ-OPPT-2024-0114: the original charge to the independent EPA reviewers, a review memo developed by those internal peer reviewers, and a response developed by the ECRAD assessment team.

a. Please comment on strengths and uncertainties related to the read-across methodology used for selection of the analog for the cancer assessment as outlined in Section 5.2.1.3 and Appendix J.2. of the draft risk evaluation. If appropriate, please provide additional methodologies which EPA could use to identify analogs for 1,1-dichloroethane.

b. Please comment on the selection of 1,2-dichoroethane as the analog to support the 1,1-dichloroethane cancer hazard database. Please also comment on the steps in the analysis, robustness and uncertainties of the conclusions, and the clarity with which they are communicated.

c. Please comment on EPA's preliminary conclusion that the NTP (1978) mouse and rat cancer studies for 1,1-dichloroethane are not appropriate for use to quantitative risk assessment. Please also comment on the extent to which the 1,1-dichloroethane rat and mouse studies are or are not useful qualitatively in hazard identification and characterization.

d. Please comment on the strengths and uncertainties and use of the Nagano et al. (2006) study with 1,2-dichloroethane to develop an Inhalation Unit Risk for inhalation cancer assessment of 1,1-dichloroethane and 1,2-dichloroethane.

e. Please comment on EPA's preliminary conclusion that the NTP rat cancer study for 1,2-dichloroethane is not appropriate for use to quantitative risk assessment. Please also

comment on the extent to which the 1,2-dichloroethane rat study is or is not useful qualitatively in hazard identification and characterization.

f. Although internal peer reviewers recommended against using the NTP (1978) mouse cancer study to develop quantitative risk estimates. ECRAD has proposed to use it in the draft risk evaluation. Please comment on the quality, study protocol, study conduct, and data interpretation of the NTP (1978) mouse cancer study for 1,2-dichloroethane. Please include in your comments on the extent to which the 1,2-dichloroethane NTP (1978) mouse study is or is not useful qualitatively and/or quantitatively in hazard identification, dose-response, and characterization.

g. Pending your comments on 9.c, 9.e, and 9.f and if the panel determines that NTP (1978) rat and mouse cancer studies are not appropriate for use in human health risk assessment, please provide additional comment on the extent to which the oral cancer risk can be and/or needs to be assessed for in the risk evaluations for 1,1-dichloroethane and 1,2-dichloroethane.

**10. Occupational Exposure**

a. As described in Section 5.1.1.1.2 of the draft risk evaluation and in the Draft Risk Evaluation for 1,1-Dichloroethane – Supplemental Information File: Environmental Releases and Occupational Exposure Assessment (U.S. EPA, 2024d), EPA obtained primary inhalation exposure monitoring data for 1,1-dichloroethane for the occupational exposure scenario (OES) of Manufacture through a test order. EPA prioritized the use of these occupational inhalation monitoring data for the intended condition of use and other appropriate exposure scenarios (*e.g.*, Processing as a Reactant and Laboratory Use OESs). Please comment on the study protocol and conduct of the study. Please also comment on ECRAD's interpretation, use, and representativeness of the manufacturing inhalation exposure monitoring data received through the test order as applied to other exposure scenarios.

b. As described in Section 5.1.1.1.3 of the draft risk evaluation and in the Draft Risk Evaluation for 1,1-Dichloroethane – Supplemental Information File: Environmental Releases and Occupational Exposure Assessment (U.S. EPA, 2024d), EPA used surrogate chlorinated solvent inhalation monitoring data to estimate occupational exposures for the General waste handling, treatment, and disposal OES where there were a lack of inhalation monitoring data. EPA also applied a vapor pressure correction factor to account for vapor pressure differences between 1,1-dichloroethane and the surrogate chemicals methylene chloride and 1,2-dichloroethane. Please comment on the appropriateness and representativeness of the surrogate data to estimate occupational exposures.

c. As described in Section 5.1.1.1.5 of the draft risk evaluation and in the Draft Risk Evaluation for 1,1-Dichloroethane – Supplemental Information File: Environmental Releases and Occupational Exposure Assessment (U.S. EPA, 2024d), EPA used the Dermal Exposure to Volatile Liquids Model (DEVL) and applied the model to all OESs; however, values for fraction absorbed and weight fraction of the chemical can differ among OESs. In particular, a key parameter in the model is the dermal loading on the skin per exposure event. The values that EPA currently uses are based on experimental studies done with oils of different viscosities (U.S. EPA, 1992).

i. Please comment on the appropriateness of using a dermal loading value based on generic scenario of oils for risk assessment of 1,1-dichloroethane. If appropriate, please provide any information on dermal loading values that may be more applicable for 1,1-dichloroethane in the conditions of use assessed in this draft risk evaluation.

ii. Please also provide comment on additional available data, models and/or references on dermal exposure assessment, dermal loading, and/or dermal fraction absorbed, which could be used in the future to improve and refine the dermal exposure potential in risk evaluation of other chemicals and across various conditions of use.

The following two charge questions were added after comments received during the August 27, 2024 Public Preparatory Meeting.

**11.** In 2015 OPPT received an OECD guideline 443 study entitled "An extended one-generation drinking water reproductive toxicity study of ethylene dichloride in rats" (WIL Research, 2015). This study was conducted to fulfill one of the requirements of an Enforceable Consent Agreement (ECA) under Section 4 of TSCA. During the Agency's review of the draft protocol for this study, the Agency identified palatability and volatility as possible issues to be addressed. The 2024 data evaluation for the extended one-generation study is contained pp. 919-938 in the *1,1-Dichloroethane - Draft Data Quality Evaluation Information for Human Health Hazard Animal Toxicology* supplemental file. Specifically, the draft data quality evaluation notes the following: "The study authors did note that concentration-dependent reductions in water intake throughout the study period were likely due to issues with palatability. This resulted in exposure levels that were generally below the target. Water intake was reduced by >20% in the mid-and high-dose groups, and there were corresponding reductions in body weights. The authors noted that many of the effects observed (decreased body weights, organ weight changes etc.,) stemmed from the reduced water intake and likely dehydration. Several other minor protocol deviations or errors were detailed; none of these was considered to have a significant impact on the study results."

a. Please comment on how the data quality evaluation criteria were applied to evaluate the extended one-generation study. Please include in your comments the extent to which OPPT has transparently and comprehensively documented the justification for categorizing the extended one-generation study as "uninformative." Please also include in your comments the extent to which this study is (or is not) useful for hazard characterization and identification.

**12.** EPA's OPPT is committed to continuous improvement of risk assessment methods and processes. The 2016 revisions to TSCA require the Agency to use the best available science and to base decisions on the scientific weight of evidence.

~~ii.~~a. In light of your comments in Questions 4 through 9 and 11, please describe whether the information rated "uninformative" in the above-mentioned studies is appropriate for use in quantitative analysis and include suggestions for how OPPT might improve its approach to use of studies ranked as "uninformative".

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