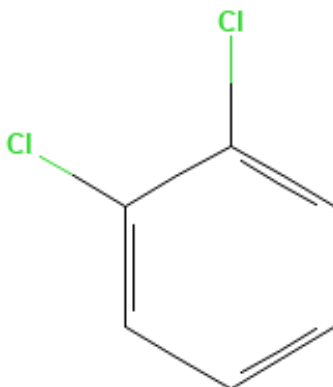




Draft Systematic Review Protocol for *o*-Dichlorobenzene

Systematic Review Support Document for the Draft Risk Evaluation

CASRN 95-50-1



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TABLE OF CONTENTS

1	INTRODUCTION.....	4
2	CLARIFICATIONS AND UPDATES TO THE 2021 DRAFT SYSTEMATIC REVIEW PROTOCOL.....	5
2.1	Clarifications.....	5
3	DATA SEARCH.....	8
3.1	Multi-Disciplinary Updates and Clarifications to the Data Search	9
3.2	Physical and Chemical Properties.....	11
3.3	Environmental Fate and Transport Properties	12
3.4	Environmental Release and Occupational Exposure	12
3.4.1	Environmental Release and Occupational Exposure Updated Literature Search	12
3.5	General Population, Consumer, and Environmental Exposure	12
3.5.1	General Population, Consumer, and Environmental Exposure Updated Literature Search Strings	13
3.6	Environmental and Human Health Hazard.....	15
3.6.1	Environmental and Human Health Hazard Updated Literature Search.....	15
3.7	Dermal Absorption	20
3.7.1	Dermal Absorption Search String.....	20
4	DATA SCREENING.....	20
4.1	Multi-disciplinary Updates and Clarifications to the Data Screening	21
4.2	Physical and Chemical Properties.....	22
4.3	Environmental Fate and Transport Properties	24
4.4	Environmental Release and Occupational Exposure	25
4.5	General Population, Consumer, and Environmental Exposure	27
4.6	Environmental and Human Health Hazard.....	29
4.6.1	Hazard Targeted PECO Screening Criteria Updates	30
4.6.2	Further Filtering: Human Health Hazard	36
4.7	Dermal Absorption	41
5	DATA EVALUATION AND DATA EXTRACTION	43
5.1	Physical and Chemical Properties.....	44
5.2	Environmental Fate and Transport Properties	44
5.3	Environmental Release and Occupation Exposure	44
5.4	General Population, Consumer, and Environmental Exposure	44
5.4.1	Data Quality Evaluation Metric Updates	46
5.5	Environmental and Human Health Hazard.....	67
5.5.1	Environmental Hazard	68
5.5.2	Human Health Hazard.....	69
5.6	Dermal Absorption	71
5.6.1	Data Quality Metrics - <i>In Vitro/Ex Vivo</i>	72
5.6.1	Data quality metrics- animal <i>in vivo</i>	88
5.6.2	Data quality metrics- human <i>in vivo</i>	88
6	EVIDENCE INTEGRATION.....	89
6.1	Physical and Chemical Properties.....	89

6.2	Environmental Fate and Transport	89
6.3	Environmental Release and Occupational Exposure	89
6.4	General Population, Consumer, and Environmental Exposure	90
6.4.1	General Population and Environmental Exposure: Surface, Groundwater, and Drinking Water 90	
6.4.2	General Population and Environmental Exposure: Ambient Air.....	90
6.4.3	Consumer Exposure Assessment	90
6.5	Environmental and Human Health Hazard	91
6.5.1	Environmental Hazard	91
6.5.2	Human Health Hazard.....	93
6.1	Dermal Absorption	93
7	REFERENCES	95

LIST OF TABLES

Table 2-1. Terminology Clarifications between the 2021 Draft Systematic Review Protocol and the Draft Risk Evaluation for <i>o</i> -Dichlorobenzene	6
Table 3-1. Peer Literature Search Strategies for <i>o</i> -Dichlorobenzene.....	9
Table 3-2 Targeted Peer Literature Search Strategies for <i>o</i> -Dichlorobenzene	13
Table 4-1. PECO Statement for Dermal Exposure References for <i>o</i> -Dichlorobenzene	42
Table 4-2. Major categories of “potentially relevant supplemental material”	42
Table 5-1. Updated Data Quality Evaluation Criteria for Monitoring Data Sources.....	46
Table 5-2. Updated Evaluation Criteria for Experimental Data Sources.....	54
Table 5-3. Updated Data Evaluation Criteria for Database Data.....	62
Table 5-4. Updated Data Quality Evaluation Criteria for Animal Toxicity Studies.....	70
Table 5-5. Updated Data Evaluation Criteria for <i>In Vitro/Ex Vivo</i> Dermal Absorption Studies	72
Table 6-1. Querying the Evidence to Organize Integration for Environmental Data and Information	91

LIST OF FIGURES

Figure 1-1. Overview of the TSCA Risk Evaluation Process with Identified Systematic Review Steps... 4	
Figure 4-1. Literature Inventory Tree – Physical and Chemical Properties for <i>o</i> -Dichlorobenzene	23
Figure 4-2. Literature Inventory Tree – Environmental Fate and Transport Properties for <i>o</i> - Dichlorobenzene.....	25
Figure 4-3. Literature Inventory Tree – Environmental Release and Occupational Exposure for <i>o</i> - Dichlorobenzene.....	26
Figure 4-4. Literature Inventory Tree – General Population, Consumer, and Environmental Exposure Search Results for <i>o</i> -Dichlorobenzene.....	28
Figure 4-5. Literature Inventory Tree – Environmental and Human Health Hazard for <i>o</i> - Dichlorobenzene.....	30
Figure 4-6. Literature Inventory Tree – Dermal Absorption for <i>o</i> -Dichlorobenzene	43
Figure 5-1. Data Evaluation and Data Extraction Cross Walk Workflow for Environmental Hazard	69

1 INTRODUCTION

The U.S. EPA's Office of Pollution Prevention and Toxics (OPPT) applies systematic review principles in the development of risk evaluations under the amended Toxic Substances Control Act (TSCA). TSCA section 26(h) requires EPA to use scientific information, technical procedures, measures, methods, protocols, methodologies, and models consistent with the best available science and base decisions under Section 6 on the weight of the scientific evidence. Within the TSCA risk evaluation context, the weight of the scientific evidence is defined as "a systematic review method, applied in a manner suited to the nature of the evidence or decision, that uses a pre-established protocol to comprehensively, objectively, transparently, and consistently identify and evaluate each stream of evidence, including strengths, limitations, and relevance of each study and to integrate evidence as necessary and appropriate based upon strengths, limitations, and relevance" (40 CFR 702.33).

To meet the TSCA section 26(h) science standards, EPA used the TSCA systematic review process described in the *Draft Systematic Review Protocol Supporting TSCA Risk Evaluations for Chemical Substances* (U.S. EPA, 2021) (hereinafter referred to as "2021 Draft Systematic Review Protocol"). Section 3 of the 2021 Draft Systematic Review Protocol depicts the steps in which information is identified and whether it undergoes the formal systematic review process (U.S. EPA, 2021). Information attained via the systematic review process is integrated with information attained from sources of information that do not undergo systematic review (e.g., EPA-generated model outputs) to support a weight of the scientific evidence analysis (Figure 1-1).

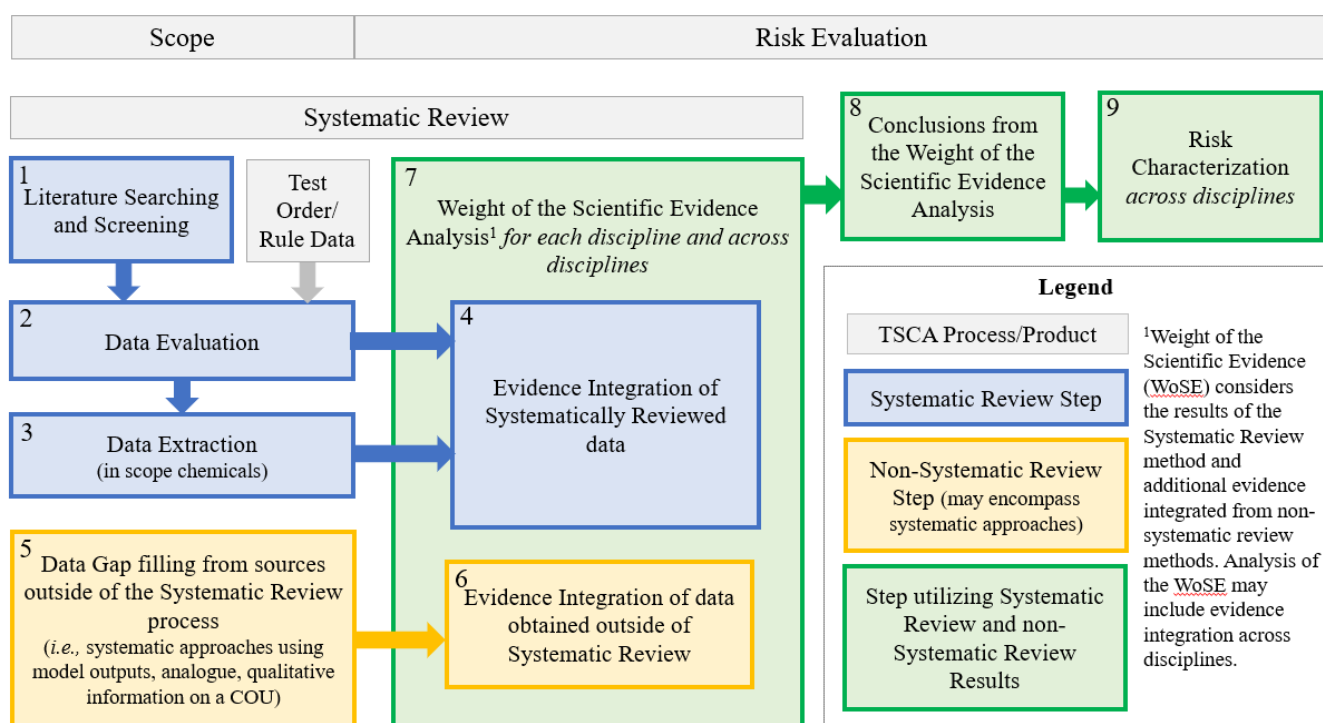


Figure 1-1. Overview of the TSCA Risk Evaluation Process with Identified Systematic Review Steps

The process complements the risk evaluation process in that it is used to develop the exposure and hazard assessments based on reasonably available information. EPA defines "reasonably available information" to mean information that EPA possesses or can reasonably obtain and synthesize for use in risk evaluations, considering the deadlines for completing the evaluation (40 CFR 702.33).

2 CLARIFICATIONS AND UPDATES TO THE 2021 DRAFT SYSTEMATIC REVIEW PROTOCOL

In 2021, EPA released the *Draft Systematic Review Protocol Supporting TSCA Risk Evaluations for Chemical Substances* ([U.S. EPA, 2021](#)), a framework of systematic review approaches under TSCA, to address comments received on a precursor systematic review approaches framework, the *Application of Systematic Review in TSCA Risk Evaluations* ([U.S. EPA, 2018](#)). In April 2022, the SACC provided comments on the 2021 Draft Systematic Review Protocol and additional comments on OPPT's systematic review approaches were garnered during the public comment period. In lieu of an update to the 2021 Draft Systematic Review Protocol, this systematic review protocol for the *Draft Risk Evaluation for o-Dichlorobenzene* ([U.S. EPA, 2026n](#)) describes some clarifications and different approaches that were implemented than those described in the 2021 Draft Systematic Review Protocol in response to (1) SACC comments, (2) public comments, or (3) to reflect chemical-specific risk evaluation needs.

2.1 Clarifications

The chemical-specific systematic review protocol is used to transparently document any updates or clarifications made to the systematic review process used for considering information identified for a given TSCA risk evaluation, as compared to those published in the *Draft Systematic Review Protocol Supporting TSCA Risk Evaluations for Chemical Substances* ([U.S. EPA, 2021](#)) (aka, 2021 Draft Systematic Review Protocol). Throughout the 2021 Draft Systematic Review Protocol, there were some terms used that were not explicitly defined, resulting in their different uses within the document ([U.S. EPA, 2021](#)). Table 2-1 lists the terms that were updated to resolve some of the confusion expressed by the public and SACC comments regarding the implementation of the respective systematic review-related step. One main clarification is that *all references that undergo systematic review are considered for use in the risk evaluation*, even those that do not meet the various discipline and sub-discipline screening criteria or those that are categorized as supplemental information at title and abstract (TIAB) or full-text screening.

Section 4.2.5 of the 2021 Draft Systematic Review Protocol describes how data sources (e.g., individual references, databases) may be tagged and linked in when the same information is present in multiple publications ([U.S. EPA, 2021](#)). References will generally undergo data quality evaluation and extraction if there are data that pass screening criteria; however, to prevent the same data from being represented multiple times and conflating the amount of available information there is on a subject area, if two or more references contain the same results tables, EPA selects the reference(s) that most thoroughly describes the extractable results (indicated as the parent reference in DistillerSR). If two references portray the same information from the same dataset, only one is counted in the overall dataset (i.e., deduplication). If two references contain information about the same dataset, but one of those references only provides additional contextual information or summary statistics (e.g., mean), both data sources are linked but the extractable information from both may be combined in DistillerSR. This enables the capture of key information while avoiding double-counting the data of interest. The linked reference containing most of the data, which are evaluated and extracted, is identified in DistillerSR as the parent reference; the “complementary child reference” in DistillerSR does not undergo independent data evaluation and extraction but is evaluated and extracted in combination with the parent reference. Linking the references in DistillerSR allows the reference with more limited information or only contextual information to be tracked and utilized to evaluate the extracted data in the other related studies. The child reference may undergo data quality evaluation and extraction if there are additional unique and original data that pass screening criteria.

Section 4.5 of the 2021 Draft Systematic Review Protocol describes how data may be obtained using TSCA authorities and test orders. One update to that section is that in addition to requiring data reporting

under TSCA sections 4 (test order), 8(a) (Chemical Data Reporting) and 8(d) (Health and Safety Data Reporting), *EPA may also require data reporting under TSCA section 8(c)* (Call-in of Adverse Reactions Records). Appendix 5.3 also describes how information may be submitted to EPA under other TSCA authorities (e.g., TSCA sections 4, 5, 6, 8(d) and 8 (e), as well as FYI submissions).

Section 5 of the 2021 Draft Systematic Review Protocol describes how EPA conducts data quality evaluation of data/information sources considered for a respective chemical risk evaluation, with Section 5.2 specifically explaining the terminology used to describe both metric and overall data/information source quality determinations ([U.S. EPA, 2021](#)). To respond to both SACC and public comments regarding the inappropriate use of quantitative methodologies to calculate both “metric rankings” and “overall study rankings,” *EPA decided to not implement quantitative methodologies to attain either metric and overall data/information source quality determinations* and therefore updated the terminology used for both metric (“metric ranking”) and overall data/information source (“overall study ranking”) quality determinations (Table 2-1). Subsequently terminology for both individual metric and overall information source quality determinations has been updated to “metric rating” and “overall quality determination,” respectively. The word “level” was also often used synonymously and inconsistently with the word “ranking” in the 2021 Draft Systematic Review Protocol; that inconsistency has been rectified, resulting in the word “level” no longer being used to indicate either metric or overall data/information source quality determinations ([U.S. EPA, 2021](#)).

Sections 4.3.2.1.3 and 6 of the 2021 Draft Systematic Review Protocol describe when EPA may reach out to authors of data/information sources to obtain raw data or missing elements that are important to support the data evaluation and data integration steps ([U.S. EPA, 2021](#)). In such cases, the request(s) for additional data/information, number of contact attempts, and responses from the authors are documented. EPA’s outreach is considered unsuccessful if those contacted do not respond to email or phone requests within one month of initial attempt(s) of contact. One important clarification to this guidance is that *EPA may reach out to authors anytime during the systematic review process for a given data/information source or reference, and that contacting authors does not explicitly happen during the data quality evaluation or extraction step*.

Table 2-1. Terminology Clarifications between the 2021 Draft Systematic Review Protocol and the Draft Risk Evaluation for *o*-Dichlorobenzene

2021 Draft Systematic Review Protocol Term	<i>o</i> -Dichlorobenzene Systematic Review Protocol Term Update	Clarification
“Title and abstract” or “title/abstract”	“Title and abstract”	To increase consistency, the term “title and abstract” will be used to refer to information specific to “title and abstract” screening.
Variations of how “include,” “on topic” or “PECO ^a /PESO ^b /RESO ^c relevant” implied a reference was considered for use in the risk evaluation, whereas “exclude,” “off topic” or “not PECO ^a /PESO ^b /RESO ^c ”	Meets/does not meet PECO ^a /PESO ^b /RESO ^c screening criteria	The term “include” or “exclude” falsely suggests that a reference was or was not, respectively, considered in the risk evaluation. There was also confusion regarding whether “on topic” and “PECO ^a /PESO ^b /RESO ^c relevant” were synonymous and suggested those references were explicitly considered for use in the risk evaluation (and by default, “off topic” and “not PECO ^a /PESO ^b /RESO ^c relevant” references were not). References that meet the screening criteria proceed to

2021 Draft Systematic Review Protocol Term	<i>o</i> -Dichlorobenzene Systematic Review Protocol Term Update	Clarification
relevant” implied a reference was <i>not</i> considered for use in the risk evaluation.		the next systematic review step; however, all references that undergo systematic review at any time are considered in the risk evaluation. Information that is categorized as supplemental or does not meet screening criteria are generally less relevant for quantitative use in the risk evaluation but may be considered if there is a data need identified. For instance, mechanistic studies are generally categorized as supplemental information at either title and abstract or full-text screening steps but may undergo the remaining systematic review steps if there is a relevant data need for the risk evaluation (<i>e.g.</i> , dose response, mode of action).
Database source not unique to a chemical	Database	Updated term and definition of “Database”: Data obtained from databases that collate information for the chemical of interest using methods that are reasonable and consistent with sound scientific theory and/or accepted approaches and are from sources generally using sound methods and/or approaches (<i>e.g.</i>, state or federal governments, academia). Example databases include STORET (STORage and RETrieval) and the Massachusetts Energy and Environmental Affairs Data Portal. The term in the 2021 Draft Systematic Review Protocol (Table_Apx N-1) incorrectly suggested that databases that contain information on a singular chemical are not considered (U.S. EPA, 2021). Furthermore, the wording “large” was removed to prevent confusion and the incorrect suggestion that there is a data size requirement for databases that contain information that may be considered for systematic review.
Metric Ranking or Level	Metric Rating	As explained above, EPA is not implementing quantitative methodologies to indicate metric quality determinations, therefore the term “ranking” is inappropriate. The term “level” was inconsistently used to indicate metric quality determinations previously; therefore, EPA is removing the use of this term to reduce confusion when referring to metric quality determinations. The term “Rating” is more appropriate to indicate the use of professional judgement to determine a quality level for individual metrics.

2021 Draft Systematic Review Protocol Term	<i>o</i> -Dichlorobenzene Systematic Review Protocol Term Update	Clarification
Overall Study Ranking or Level	Overall Quality Determination (OQD)	As explained above, EPA is not implementing quantitative methodologies to indicate overall data/information source quality determinations, therefore the term “ranking” is inappropriate. The term “level” was inconsistently used to indicate overall data/information source quality determinations previously; therefore, EPA is removing the use of this term to reduce confusion when referring to overall data/information source quality determinations. The term “Rating” is more appropriate to indicate the use of professional judgement to determine a quality level for the overall data/information source quality determination.
Sub-discipline	No change in term	Sub-discipline explicitly indicates the two categories of receptor-based studies relevant to evaluate human health hazard (discipline): epidemiological (human receptor) or human health animal model toxicological studies (non-human animal receptor). Although environmental hazard is a discipline, Appendix T incorrectly suggested that environmental hazard is a sub-discipline in the 2021 Draft Systematic Review Protocol.
Evidence Stream	No change in term	Evidence streams were updated for both environmental and human health hazard disciplines to more appropriately categorize the hazardous endpoints that were considered. Please see additional descriptions of the evidence stream updates in Section 0 below.
^a “PECO” stands for Population, Exposure, Comparator or Scenario, and Outcomes. ^b “PESO” stands for Pathways or Processes, Exposure, Setting or Scenario, and Outcomes. ^c “RESO” stands for Receptors, Exposure, Setting or Scenario, and Outcomes.		

3 DATA SEARCH

As described in Section 4 of the 2021 Draft Systematic Review Protocol ([U.S. EPA, 2021](#)), EPA conducts a comprehensive search for reasonably available information to support the TSCA risk evaluations. Chemical-specific literature searches are conducted as described in Section 4.2.1 of the 2021 Draft Systematic Review Protocol for all disciplines (*i.e.*, physical and chemical properties, environmental fate and transport properties, engineering, exposure, environmental hazard, and human health hazard) ([U.S. EPA, 2021](#)). Additional details on the chemical verification process, and the methodology used to search for chemical specific peer-reviewed and gray literature is available in Sections 4.2 and 4.3 of the 2021 Draft Systematic Review Protocol, respectively ([U.S. EPA, 2021](#)). The search for peer-reviewed and gray literature relevant references was completed in September and May 2019, respectively. Appendix Section C.1.24 contains the specific search strings used to identify peer-reviewed literature on *o*-dichlorobenzene

([U.S. EPA, 2021](#)). All reasonably available information submitted to EPA under TSCA authorities was considered.

An updated literature search for potential additional sources of information and data that might support the risk evaluation for *o*-dichlorobenzene was conducted in May 2025. Details for the updated literature search and consideration of the new information are described in Section 3.1 of this chemical-specific systematic review protocol.

3.1 Multi-Disciplinary Updates and Clarifications to the Data Search

For the *Draft Risk Evaluation for o-Dichlorobenzene* ([U.S. EPA, 2026n](#)), the literature search was conducted as described in Section 4 of the 2021 Draft Systematic Review Protocol ([U.S. EPA, 2021](#)), where the peer-reviewed and gray literature updated search followed the approach outlined in Sections 4.2 and 4.3 of the 2021 Draft Systematic Review Protocol, respectively ([U.S. EPA, 2021](#)). Occasionally additional data sources relevant for the risk evaluation may be identified after the initial search for peer-reviewed and gray literature; these data sources will then undergo systematic review for the relevant discipline(s). Additionally, each discipline utilizes different strategies (*e.g.*, search strings) to attain their discipline-specific pools of data sources that undergo systematic review.

Updated Literature Search

An update to the peer-reviewed literature search to capture information published since September 2019 was performed in May 2025 to identify any potential additional data sources available since September 2019 for *o*-dichlorobenzene and relevant to environmental release and occupational exposure; general population, consumer, and environmental exposure; and human health hazard. EPA considered to have sufficient information on physical and chemical properties, environmental fate and transport properties, as well as environmental hazard to support the *Draft Risk Evaluation for o-Dichlorobenzene* ([U.S. EPA, 2026n](#)) and did not proceed with an update to the peer-reviewed literature. Table 3-1 lists the details for the literature search strategies for *o*-dichlorobenzene. To clarify, the literature search strategy as described in Section 4 of the 2021 Draft Systematic Review Protocol ([U.S. EPA, 2021](#)) was the same for the initial search in 2019 as it was for the search in May 2025. For full transparency, the literature results in Table 3-1 indicate the number of references obtained during the initial search, the updated search, as well as the total number of references identified for *o*-dichlorobenzene. The literature search strategies described in Table 3-1 are chemical-specific but discipline-agnostic. To identify discipline-specific pools of data sources that underwent systematic review, EPA applied discipline-specific strategies (*e.g.*, search strings) to prioritize the type of studies from the updated peer literature search that were of interest for the *o*-dichlorobenzene risk evaluation. Details on the number of references identified for environmental release and occupational exposure; general population, consumer, and environmental exposure; and human health hazard as a result of the updated peer literature search are described in Sections 3.4, 3.5, and 3.6, respectively.

Table 3-1. Peer Literature Search Strategies for *o*-Dichlorobenzene

Source	Search Strategy
ProQuest	TIAB("95-50-1" OR "2-Dichlorobenzene" OR "1,2-Dichlorobenzene" OR "Paracrystals" OR "1,4-Dichlorobenzene" OR "o-dichlorobenzene" OR "1,3-Dichlorobenzene" OR "o-DCB" OR "m-Dichlorobenzene" OR "Orthodichlorobenzene" OR "ortho-dichlorobenzene" OR "Cloroben" OR "meta-Dichlorobenzene" OR "metadichlorobenzene" OR "Chloroben" OR "Dichlorobenzene, 1,2-" OR "1,2-Dichlorbenzene" OR "Para crystals" OR "Dizene" OR "dichlorobenzene, o-" OR "2,6-Dichlorobenzene" OR "2,4-Dichlorobenzene" OR "1,4-Chlorobenzene" OR "Benzene, 1,2-dichloro")
PubMed	("95-50-1"[rn] OR "2-Dichlorobenzene"[tw] OR "1,2-Dichlorobenzene"[tw] OR "Paracrystals"[tw] OR "1,4-Dichlorobenzene"[tw] OR "o-dichlorobenzene"[tw] OR "1,3-Dichlorobenzene"[tw] OR "o-DCB"[tw] OR "m-Dichlorobenzene"[tw] OR "Orthodichlorobenzene"[tw] OR "ortho-dichlorobenzene"[tw] OR

Source	Search Strategy
	"Cloroben"[tw] OR "meta-Dichlorobenzene"[tw] OR "metadichlorobenzene"[tw] OR "Chloroben"[tw] OR "Dichlorobenzene, 1,2-"[tw] OR "1,2-Dichlorobenzene"[tw] OR "Para crystals"[tw] OR "Dizene"[tw] OR "dichlorobenzene, o-"[tw] OR "2,6-Dichlorobenzene"[tw] OR "2,4-Dichlorobenzene"[tw] OR "1,4-Chlorobenzene"[tw] OR "Benzene, 1,2-dichloro"[tw])
Scopus	TITLE-ABS({95-50-1} OR {2-Dichlorobenzene} OR {1,2-Dichlorobenzene} OR {Paracrystals} OR {1,4-Dichlorobenzene} OR {o-dichlorobenzene} OR {1,3-Dichlorobenzene} OR {o-DCB} OR {m-Dichlorobenzene} OR {Orthodichlorobenzene} OR {ortho-dichlorobenzene} OR {Cloroben} OR {meta-Dichlorobenzene} OR {metadichlorobenzene} OR {Chloroben} OR {Dichlorobenzene, 1,2-} OR {1,2-Dichlorbenzene} OR {Para crystals} OR {Dizene} OR {dichlorobenzene, o-} OR {2,6-Dichlorobenzene} OR {2,4-Dichlorobenzene} OR {1,4-Chlorobenzene} OR {Benzene, 1,2-dichloro})
WoS	TS=("95-50-1" OR "2-Dichlorobenzene" OR "1,2-Dichlorobenzene" OR "Paracrystals" OR "1,4-Dichlorobenzene" OR "o-dichlorobenzene" OR "1,3-Dichlorobenzene" OR "o-DCB" OR "m-Dichlorobenzene" OR "Orthodichlorobenzene" OR "ortho-dichlorobenzene" OR "Cloroben" OR "meta-Dichlorobenzene" OR "metadichlorobenzene" OR "Chloroben" OR "Dichlorobenzene, 1,2-" OR "1,2-Dichlorbenzene" OR "Para crystals" OR "Dizene" OR "dichlorobenzene, o-" OR "2,6-Dichlorobenzene" OR "2,4-Dichlorobenzene" OR "1,4-Chlorobenzene" OR "Benzene, 1,2-dichloro")
Literature Results	<i>Initial Search: 4,620, Update Search: 1,196, Total Literature: 5,816</i>

SWIFT-Review Validation

EPA received comments regarding the lack of detail on the use and validation of SWIFT-Review to determine discipline-specific peer-reviewed reference set considered for use in TSCA risk evaluations. In response to those comments, EPA conducted validation exercises to clarify the search process and build consistency among all the disciplines. The 2021 Draft Systematic Review Protocol contains validation results for the use of SWIFT-Review to determine which peer-reviewed references may be relevant for the characterization of occupational exposure and environmental releases and general population, consumer, and environmental exposure for the respective chemical risk evaluations. However, to expand upon the information provided in the 2021 Draft Systematic Review Protocol, EPA validated references relevant for determining chemical-specific peer-reviewed reference set for the characterization of physical and chemical properties, environmental fate and transport properties, and environmental and human health hazard. EPA manually screened the references that were found in the overall peer-reviewed search results that did not undergo TIAB screening (*i.e.*, references that were not identified using a discipline-specific search string). If a reference that did not undergo further review after TIAB screening was found to meet the screening criteria for a respective discipline (*e.g.*, data needs on physical chemical properties, environmental fate and transport properties, and environmental and human health hazard) and identified for the chemical of interest, it was flagged as a false negative. This analysis validated and verified the use of the search terms in SWIFT-Review, as it showed that less than 5 percent of references were false negatives across all three disciplines. This method was repeated for several of the TSCA High Priority Substances to build confidence in our discipline-specific search strings.

Supplemental Filtering of 2019 Literature Search for Dermal Absorption

EPA uses dermal absorption studies to accurately assess dermal exposure resulting from certain conditions of use. These studies are identified as supplemental studies within the human health hazard discipline. However, dermal absorption data may not meet screening criteria for other disciplines and even for the human health discipline (see criteria in Appendix H of the 2021 Draft Systematic Review Protocol ([U.S. EPA, 2021](#))). Therefore, EPA developed search strings specific for dermal absorption (see Section 3.7) that were used to filter data sources excluded from the original literature search conducted in 2019. This filtering method was conducted using SWIFT-Review and the general process is explained in Section 4.2.4 of the 2021 Draft Systematic Review Protocol ([U.S. EPA, 2021](#)).

Additional Gray Literature Sources

Physical and Chemical Properties: In addition to the gray literature sources listed in Appendix E of the 2021 Draft Systematic Review Protocol, an additional database was added to the list of gray literature sources for physical and chemical properties. The National Institutes for Standards and Technology (NIST) Chemistry Webbook was searched in September 2021 to capture spectroscopic data, specifically ultra-violet and visible absorption (UV-Vis) data, if recorded. This source may also provide thermodynamic data that informs chemical stability and behavior under various conditions.

General Population, Consumer, and Environmental Exposure: In addition to the gray literature sources listed in Appendix E of the 2021 Draft Systematic Review Protocol ([U.S. EPA, 2021](#)), three sources were added in 2023 to capture database outputs from several governmental sources. All three datasets were accessed directly and uploaded into HERO. EPA used data it collected in support of compliance with the Safe Drinking Water Act. This includes data for *o*-dichlorobenzene collected pursuant to the EPA's Six-Year Review 3 of Drinking Water, which includes national compliance monitoring data. EPA also downloaded data from the Centers for Disease Control (CDC) and Prevention's National Health and Nutrition Examination Survey (NHANES) and the Water Quality Portal (WQP), which results from a collaboration between EPA, the U.S. Geological Survey, and the National Water Quality Monitoring Council.

Because the literature pool for many chemicals, including *o*-dichlorobenzene, includes a record from EPA's STORET database, which has been retired, EPA downloaded all the data for this chemical from the WQP, the successor database that now contains data from STORET. This data was uploaded into HERO and added to the literature pool that is considered for systematic review. In addition, to obtain information on *o*-dichlorobenzene exposures to the U.S. population, EPA added data from the Centers for Disease Control and Prevention's National Health and Nutrition Examination Survey (NHANES) to its literature set. At the time of download, the tables with data for *o*-dichlorobenzene available from CDC included "Analysis of Whole Blood, Serum, and Urine Samples, NHANES 1999-2018," and "Analysis of Chemicals Found in Cigarette Smoke in a Special Sample of U.S. Adults, NHANES 2011-2016."

3.2 Physical and Chemical Properties

The search for peer-reviewed and gray literature are as described in Sections 4.2 and 4.3, respectively, in the 2021 Draft Systematic Review Protocol ([U.S. EPA, 2021](#)). SWIFT-Review was used to identify peer-reviewed references that are predicted to be the most relevant for evaluating physical and chemical properties for the *Draft Risk Evaluation for o-Dichlorobenzene* ([U.S. EPA, 2026n](#)). Specifically, the search string used to identify data sources that potentially contain physical and chemical property information on *o*-dichlorobenzene in SWIFT-Review was developed by EPA's ORD in collaboration with Sciome and is presented in Appendix G, Section G-1, Table_Apx G-1 of the 2021 Draft Systematic Review Protocol ([U.S. EPA, 2021](#)). As mentioned above in Section 3.1, the search string used to identify potentially relevant peer-reviewed data references for evaluation of the physical and chemical properties of *o*-dichlorobenzene was validated. When the search string terms are identified in the title, abstract or as a keyword of a given reference in SWIFT-Review, those references proceed with title and abstract screening.

EPA considered to have sufficient information on physical and chemical properties to support the *Draft Risk Evaluation for o-Dichlorobenzene* ([U.S. EPA, 2026n](#)) and did not proceed with an update to the peer-reviewed literature.

3.3 Environmental Fate and Transport Properties

The search for peer-reviewed and gray literature are as described in Sections 4.2 and 4.3, respectively, in the 2021 Draft Systematic Review Protocol ([U.S. EPA, 2021](#)). Specifically, SWIFT-Review was used to identify peer-reviewed references that are predicted to be the most relevant for evaluating environmental fate and transport properties for the *Draft Risk Evaluation for o-Dichlorobenzene* ([U.S. EPA, 2026n](#)). The search string used for environmental fate and transport literature in SWIFT-Review was developed by EPA's ORD in collaboration with Sciome and is presented in Appendix G, Section G.2, Table_Apx G2 of the 2021 Draft Systematic Review Protocol ([U.S. EPA, 2021](#)). As mentioned above in Section 3.1, the search string used to identify potentially relevant peer-reviewed data references for evaluation of the environmental fate and transport properties of *o*-dichlorobenzene were validated. When the search string terms are identified in the title, abstract or as a keyword of a given reference in SWIFT-Review, those references proceed with TIAB screening.

EPA considered to have sufficient information on environmental fate and transport properties to support the *Draft Risk Evaluation for o-Dichlorobenzene* ([U.S. EPA, 2026n](#)) and did not proceed with an update to the peer-reviewed literature.

3.4 Environmental Release and Occupational Exposure

The searches for peer-reviewed and gray literature are described in Sections 4.2 and 4.3, respectively, in the 2021 Draft Systematic Review Protocol ([U.S. EPA, 2021](#)). Specifically, SWIFT-Review was used to identify peer-reviewed references that are predicted to be the most relevant for evaluating environmental release and occupational exposure for the *Draft Risk Evaluation for o-Dichlorobenzene* ([U.S. EPA, 2026n](#)). As described in Sections 4.2.4.2 of the 2021 Draft Systematic Review Protocol ([U.S. EPA, 2021](#)), EPA identified on-topic and off-topic references from the broad search results of the *o*-dichlorobenzene peer-reviewed literature as positive and negative "seeds" to classify which references contained environmental release and occupational exposure to prioritize for further review. When the relevant references were identified in SWIFT Review, those references proceeded with title and abstract screening.

3.4.1 Environmental Release and Occupational Exposure Updated Literature Search

As described in Section 3.1, an update to the peer-reviewed literature search to capture information published since September 2019 was performed in May 2025 to identify any potential additional data sources for environmental release and occupational exposure that might have been identified since the initial literature search was conducted in 2019 for *o*-dichlorobenzene. The literature search strategy was the same for the initial search in 2019 as it was for the search in May 2025. EPA then identified discipline-specific relevant references in SWIFT Review (independent of data type and based on positive/negative seeds) consistent with the Agency's standard process to identify information for environmental release and occupational exposure. From the update to the peer-reviewed literature search and SWIFT Review step, EPA identified 69 new additional sources of data that were screened as described in Section 4.4.

3.5 General Population, Consumer, and Environmental Exposure

The peer-reviewed and gray literature searches for general population, consumer, and environmental exposure are as described in Sections 4.2 and 4.3, respectively, in the 2021 Draft Systematic Review Protocol ([U.S. EPA, 2021](#)). Specifically, SWIFT-Review was used to identify peer-reviewed references that are predicted to be the most relevant for evaluating general population, consumer, and environmental exposures to *o*-dichlorobenzene. As described in Sections 4.2.4.2 of the 2021 Draft Systematic Review Protocol ([U.S. EPA, 2021](#)), EPA identified on-topic and off-topic references from the broad search results

of the peer-reviewed literature as positive and negative “seeds” to classify which references on general population, consumer, and environmental exposures to prioritize for further review. As noted previously in Section 3.1, three additional references were added to the literature search protocol to capture database data from the Six-Year Review 3, WQP and NHANES. The database data were compared to other database and monitoring data found during the literature search to ensure no duplication of data. A record from a predecessor database to Water Quality Portal, EPA’s STORET database, that was found during the literature search was not counted as a separate reference, to avoid double-counting data. There were no other changes to the process identified in the 2021 Draft Systematic Review Protocol for information considered for the evaluation of general population, consumer, and environmental exposure to *o*-dichlorobenzene ([U.S. EPA, 2021](#)).

3.5.1 General Population, Consumer, and Environmental Exposure Updated Literature Search Strings

As noted in Section 3.1, the updated literature search performed in May 2025 to identify information considered for the evaluation of general population, consumer, and environmental exposure, included additional search strategies to prioritize specific needs and to fill data gaps for the information supporting the risk evaluation of *o*-dichlorobenzene. The priority was to identify data sources for indoor and ambient air studies that are newer than 1990 and reporting data from the U.S. and Canada. As such, references identified by any one of the targeted areas below and that were also identified by the “U.S. & Canada” search strategy were sent forward to screening. Details on the targeted search strategies are listed in Table 3-2. A total of 252 references were identified using these search strings.

Table 3-2 Targeted Peer Literature Search Strategies for *o*-Dichlorobenzene

Targeted Area	Search Strategy
Ambient Outdoor Air	tiab:(("airborne" OR "airflow" OR "air flow" OR "atmosphere" OR "atmospheric" OR "pm10" OR "pm(10)" OR "pm2.5" OR "pm(2.5)" OR ("air" AND ("particulate*" OR "outdoor" OR "particle" OR "gaseous" OR "saml*")) OR "ambient air" OR "fume*") NOT "marine air")
Consumer Product or Article	tiab:("consumer exposure*" OR "consumer product" OR "chamber study" OR "chamber studies" OR "product emission*" OR "migration rate*" OR "product use*" OR "weight fraction*" OR "use pattern*" OR "source characterization*" OR "emission*" OR "emission rate*") OR tiab:(("consumer exposure*" OR "consumer product" OR "chamber study" OR "chamber studies" OR "product emission*" OR "migration rate*" OR "product use*" OR "weight fraction*" OR "use pattern*" OR "source characterization*" OR "emission*" OR "emission rate*" OR "consumer" OR "source*") AND ("textile*" OR "fabric*" OR "clothes" OR "clothing" OR "leather*" OR "shoe*" OR "plastic*" OR "paper*" OR "rubber*" OR "soap*" OR "bar soap*" OR "dish soap*" OR "detergent*" OR "lubricant*" OR "grease*" OR "degreaser*" OR "ink*" OR "toner*" OR "pigment*" OR "dye*" OR "appliance*" OR "electronic*" OR "battery" OR "batteries" OR "automo*" OR "automobile*" OR "automotive*" OR "car*" OR "motor*" OR "adhesive*" OR "sealant*" OR "glue*" OR "toy*"))
Human Biomonitoring (Exposure & Dose)	tiab:(("dose" OR "doses" OR "dosing" OR "dosage*" OR "expose" OR "exposed" OR "exposing" OR "exposure" OR "daily dos*" OR "daily intake" OR "kg/d" OR "kg/day" OR "g/d" OR "g/day" OR "mg/d" OR "mg/day" OR "ug/d" OR "ug/day" OR "µg/d" OR "µg/day" OR "l/d" OR "l/day" OR "ml/d" OR "ml/day" OR "ul/d" OR "ul/day" OR "µl/d" OR "µl/day" OR "exposure time" OR "inhalation rate" OR "food intake" OR "water intake" OR "soil intake rate" OR "dust" OR "intake rate" OR "skin absorption" OR "dermal absorption fraction" OR "skin permeation coefficient" OR "liquid-phase transfer coefficient*" OR "gas-phase transfer coefficient*" OR "overall mass transfer coefficients"

Targeted Area	Search Strategy
	OR "KOL" OR "solid-phase diffusion coefficient" OR "material-air partition coefficient" OR "gas-phase mass transfer coefficient" OR "equilibrium partition coefficient" OR "permeability coefficient" OR ("Kp" AND ("skin" OR "neat" OR "aqueous")) OR "average daily dose" OR "lifetime average daily dose" OR "dosimetry" OR "average daily dose" OR "LADD" OR "metabolite*" OR "BW" OR "body weight" OR "acute exposure" OR "chronic exposure" OR "activity pattern" OR "cumulative exposure" OR "aggregate exposure" OR "exposure duration" OR "personal exposure" OR "exposure factor" OR "exposure event" OR "exposure frequency" OR "assessment" OR "benchmark dose" OR "time averaged exposure" OR "TWA" OR "bioavailability" OR "exposure pathway" OR "reference concentration*" OR "reference dose" OR "sampl*") AND ("human" OR "biological marker*" OR "biomonitor*" OR "bio-monitor*" OR "biological monitor*" OR "biomark*" OR "bio-mark*" OR "bio mark*" OR "NHANES" OR "blood" OR "serum" OR "plasma" OR "urine" OR "tissue" OR "breast milk" OR "human milk" OR "breastmilk" OR "colostrum" OR "foremilk" OR "hindmilk" OR "cord blood" OR "umbilical blood" OR "bioaccum*" OR "bio-accum*")) OR ("human" AND "transfer*")
Human Biomonitoring (General)	tiab:("biological marker*" OR "biomonitor*" OR "bio-monitor*" OR "biological monitor*" OR "biomark*" OR "bio-mark*" OR "bio mark*" OR "NHANES" OR "bioaccum*" OR "bio-accum*") OR tiab:("biological marker*" OR "biomonitor*" OR "bio-monitor*" OR "biological monitor*" OR "biomark*" OR "bio-mark*" OR "bio mark*" OR "NHANES" OR "bioaccum*" OR "bio-accum*") AND ("blood" OR "serum" OR "plasma" OR "urine" OR "breast milk" OR "human milk" OR "breastmilk" OR "colostrum" OR "foremilk" OR "hindmilk" OR "cord blood" OR "umbilical blood" OR "lung tissue" OR "saliva" OR "bone*" OR "exhaled breath" OR "feces" OR "hair" OR "nails" OR "fingernail*" OR "placenta" OR "semen" OR "skin" OR "dermal wipe" OR "tissue*" OR "tooth" OR "teeth" OR "wipe" OR "skin wipe" OR "wristband" OR "dosimetry" OR "exhaled breath" OR "exhalation study" OR "metabolite*" OR "metabolise*" OR "metabolism" OR "amniotic" OR "body" OR "excret*" OR "human matrix" OR "human matrices" OR "human"))
Human Biomonitoring (Routes of Exposure)	tiab:("ate" OR "drank" OR "drink" OR "drinking" OR "drinks" OR "eat" OR "eaten" OR "eating" OR "eats" OR "swallow" OR "swallowed" OR "swallowing" OR "breastfed" OR "breast fed" OR "breastfeed*" OR "exposure route" OR "feed" OR "fed" OR "adherence factor" OR "absorption barrier" OR "pica" OR ("consume*" OR "consuming" OR "consumpt*" OR "ingest*" OR "intake*") AND ("mouth" OR "mouthing" OR "oral" OR "orally")) OR ("absorb*" OR "adsorb*" OR "adher*" OR "contact" OR "expose*" OR "exposu*") AND ("human" OR "dermal" OR "dermis" OR "epidermal" OR "epidermis" OR "skin" OR "contact" OR "touch" OR "surface area")) OR ("expose*" OR "exposu*" OR "intake*") AND ("breath*" OR "inhal*" OR "respiration" OR "sniff*"))
Indoor Air	tiab:(("air" OR "airborne" OR "airflow" OR "particulate*" OR "pm10" OR "pm(10)" OR "pm2.5" OR "pm(2.5)") AND ("indoor" OR "office" OR "house" OR "home" OR "living room" OR "kitchen" OR "residential" OR "apartment" OR "daycare" OR "gym" OR "classroom" OR "university"))
United States & Canada	tiab:("U.S." OR "United States" OR "North America*" OR "American" OR "Canada" OR "Canadian" OR "Continental U.S." OR "Continental United States" OR "Alabama" OR "Alaska" OR "Arizona" OR "Arkansas" OR "California" OR "Colorado" OR "Connecticut" OR "Delaware" OR "Florida" OR "Georgia" OR "Hawaii" OR "Idaho" OR "Illinois" OR "Indiana" OR "Iowa" OR "Kansas" OR "Kentucky" OR "Louisiana" OR "Maine" OR "Maryland" OR "Massachusetts" OR "Michigan" OR "Minnesota" OR "Mississippi" OR "Missouri" OR "Montana" OR "Nebraska" OR "Nevada" OR "New Hampshire" OR "New Jersey" OR "New Mexico" OR "New York" OR "North Carolina" OR "North Dakota" OR "Ohio" OR "Oklahoma" OR "Oregon" OR "Pennsylvania" OR "Rhode Island" OR "South

Targeted Area	Search Strategy
	Carolina" OR "South Dakota" OR "Tennessee" OR "Texas" OR "Utah" OR "Vermont" OR "Virginia" OR "Washington" OR "West Virginia" OR "Wisconsin" OR "Wyoming")
Total Results for Discipline	252 references

3.6 Environmental and Human Health Hazard

The search for peer-reviewed and gray literature are as described in Sections 4.2 and 4.3, respectively, in the 2021 Draft Systematic Review Protocol ([U.S. EPA, 2021](#)). Specifically, SWIFT-Review was used to identify peer-reviewed references that are predicted to be the most relevant for evaluating environmental and human health hazard for *o*-dichlorobenzene. Specifically, search strings were developed for the two hazard disciplines by EPA's Office of Research and Development (ORD) in collaboration with SWIFT-Review developer, Sciome. As mentioned above in Section 3.1, the search string used to identify potentially relevant peer-reviewed data references for evaluation of the environmental and human health hazard of *o*-dichlorobenzene were validated. When the search string terms are identified in the title, abstract or as a keyword of a given reference in SWIFT-Review, those references proceed with TIAB screening. The environmental and human health hazard search strings are provided [online](#).

3.6.1 Environmental and Human Health Hazard Updated Literature Search

As described in Section 3.1, an update to the peer-reviewed literature search was performed in May 2025 to identify any potential additional data sources for human health hazard that might have become available since the initial literature search was conducted in September 2019 for *o*-dichlorobenzene. To identify discipline-specific pools of data sources that underwent systematic review, EPA applied human health hazard strategies (e.g., search strings) in the updated literature search performed in May 2025. Specifically, EPA applied additional targeted keyword queries to identify and prioritize cancer-related literature within the update. Search queries were adapted from NIEHS's most recent Report on Carcinogens standard search strings ([NIEHS, 2023](#)). Literature detailing *in vitro* studies were deprioritized. A revision was also made to improve an epidemiological information filter that is part of the standard filter set for human health hazard. The improved filter aimed to increase the sensitivity of the search for epidemiologic quantitative analysis information. Also, eight additional references that were identified by the literature search for the Exposure discipline also were screened to determine whether they met PECO criteria for epidemiology. For environmental hazard, EPA considered to have sufficient information to support the *Draft Risk Evaluation for o-Dichlorobenzene* ([U.S. EPA, 2026n](#)) and did not proceed with an update to the peer-reviewed literature. Details on the targeted search strategies for *o*-dichlorobenzene to identify human health hazard information are listed Table 3-3. From the update to the peer-reviewed literature search, EPA identified 106 new additional sources of data that were screened as described in Section 4.6.

Also, as described in Sections 6.5.1 and 6.5.2, data needs were identified during evidence integration, where information from sources that either did or did not undergo systematic review on *o*-dichlorobenzene was considered.

Table 3-3. Targeted Peer Literature Search Strategies for *o*-Dichlorobenzene

Targeted Area	Search Strategy
Cancer (General)	tiab:(("angiogenesis inducing agents" OR "myelodysplastic-myeloproliferative diseases" OR "neoplasms" OR "carcinogenicity tests" OR "carcinogens" OR ("sentinel-lymph-node" NOT "biopsy") OR ("ASCO" NOT "fungi") OR ("WAGR" AND "syndrome") OR "5q-syndrome" OR "leukostasis")) OR (("acanthoma" OR "acanthomas" OR "acrochordon" OR "acrochordons" OR "acrospiroma" OR

Targeted Area	Search Strategy
	"acrospiomas" OR "adamantinoma" OR "adamantinomas" OR "adenoacanthoma" OR "adenoacanthomas" OR "adenoameloblastoma" OR "adenoameloblastomas" OR "adenocanthoma" OR "adenocanthomas" OR "adenocarcinoma" OR "adenocarcinomas" OR "adenofibroma" OR "adenofibromas" OR "adenolipoma" OR "adenolipomas" OR "adenolymphoma" OR "adenolymphomas" OR "adenoma" OR "adenomas" OR "adenomatosis" OR "adenomatous" OR "adenomyoepithelioma" OR "adenomyoepitheliomas" OR "adenomyoma" OR "adenomyomas" OR "adenosarcoma" OR "adenosarcomas" OR "adenosis" OR "aesthesioneuroblastoma" OR "aesthesioneuroblastomas" OR "ameloblastoma" OR "ameloblastomas" OR "amyloidoses" OR "amyloidosis" OR "anaplasia" OR "androblastoma" OR "androblastomas" OR "angioblastoma" OR "angioblastomas" OR "angioendothelioma" OR "angioendotheliomas" OR "angioendotheliomatosis" OR "angiofibroma" OR "angiofibromas" OR "angiofibrosarcoma" OR "angiokeratoma" OR "angiokeratomas" OR "angioleiomyoma" OR "angioleiomyomas" OR "angioliipoma" OR "angioliipomas" OR "angioma" OR "angiomas" OR "angiomatosis" OR "angiomylipoma" OR "angiomylipomas" OR "angiomyoma" OR "angiomyomas" OR "angiomyxoma" OR "angiomyxomas" OR "angioreticuloma" OR "angioreticulomas" OR "angiosarcoma" OR "angiosarcomas" OR "apudoma" OR "apudomas" OR "argentaftinoma" OR "argentaftinomas" OR "arrhenoblastoma" OR "arrhenoblastomas" OR "astroblastoma" OR "astroblastomas" OR "astrocytoma" OR "astrocytomas" OR "astroglioma" OR "astrogliomas" OR "baltoma" OR "basiloma" OR "basilomas" OR "blastoma" OR "blastomas" OR "Buschke-Lowenstein" OR "cancer" OR "cancerous" OR "cancers" OR "carcinogen" OR "carcinogenesis" OR "carcinogenic" OR "carcinogenicity-test*" OR "carcinogens" OR "carcinoid" OR "carcinoma" OR "carcinomas" OR "carcinomatosis" OR "carcinosarcoma" OR "carcinosarcomas" OR "cavernoma" OR "cavernomas" OR "cementoma" OR "cementomas" OR "ceruminoma" OR "ceruminomas" OR "chemodectoma" OR "chemodectomas" OR "cherubism" OR "chloroma" OR "chloromas" OR "cholangiocarcinoma" OR "cholangiocarcinomas" OR "cholangiohepatoma" OR "cholangioma" OR "cholangiomas" OR "cholangiosarcoma" OR "cholesteatoma" OR "cholesteatomas" OR "chondroblastoma" OR "chondroblastomas" OR "chondroma" OR "chondromas" OR "chondrosarcoma" OR "chondrosarcomas" OR "chordoma" OR "chordomas" OR "chorioadenoma" OR "chorioadenomas" OR "chorioangioma" OR "chorioangiomas" OR "choriocarcinoma" OR "choriocarcinomas" OR "chorioepithelioma" OR "chorioepitheliomas" OR "chorionepithelioma" OR "chorionepitheliomas" OR "choristoma" OR "choristomas" OR "chromaffinoma" OR "chromaffinomas" OR "CIN" OR "CLL" OR "cocarcinogenesis" OR "collagenoma" OR "collagenomas" OR "comedocarcinoma" OR "comedocarcinomas" OR "condyloma" OR "condylomas" OR "corticotropinoma" OR "corticotropinomas" OR "craniopharyngioma" OR "craniopharyngiomas" OR "cylindroma" OR "cylindromas" OR "cystadenocarcinoma" OR "cystadenocarcinomas" OR "cystadenofibroma" OR "cystadenofibromas" OR "cystadenoma" OR "cystadenomas" OR "cystoma" OR "cystomas" OR "cystosarcoma" OR "cystosarcomas" OR "dentinoma" OR "dentinomas" OR "dermatofibroma" OR "dermatofibromas" OR "dermatofibrosarcoma" OR "dermatofibrosarcomas" OR "dermoid" OR "dictyoma" OR "dysgerminoma" OR "dysgerminomas" OR "dyskeratoma" OR "dyskeratomas" OR "dysmyelopoiesis" OR "ectomesenchymoma" OR "ectomesenchymomas" OR "elastofibroma" OR "elastofibromas" OR "enchondroma" OR "enchondromas" OR "enchondromatosis" OR "endothelioma" OR "endotheliomas" OR "ependymblastoma" OR "ependymblastomas" OR "ependymoma" OR "ependymomas" OR "epidermoid" OR "epithelioma" OR "epitheliomas" OR "erythroleukaemia" OR "erythroleukaemias" OR "erythro leukemia" OR "erythro leukemias" OR "erythroplakia" OR "erythroplakias" OR "erythroplasia" OR "essentialthrombocythemia" OR "esthesioneuroblastoma" OR "esthesioneuroblastomas" OR "esthesioneuroepithelioma" OR "esthesioneuroepitheliomas" OR "exostosis" OR "fibroadenoma" OR "fibroadenomas" OR "fibroadenosarcoma" OR "fibroadenosis" OR "fibrochondrosarcoma" OR "fibroelastoma" OR "fibroelastomas" OR "fibroepithelioma" OR "fibroepitheliomas" OR "fibrofolliculoma" OR "fibrofolliculomas" OR "fibroid" OR "fibroids" OR "fibrolipoma" OR "fibrolipomas" OR "fibroliposarcoma" OR "fibroma" OR "fibromas" OR "fibromatosis" OR "fibromyoma" OR "fibromyomas" OR "fibromyxolipoma" OR "fibromyxoma" OR "fibromyxomas" OR "fibroodontoma" OR "fibroodontomas" OR "fibrosarcoma" OR "fibrosarcomas" OR "fibrothecoma" OR "fibrothecomas" OR "fibroxanthoma" OR "fibroxanthomas" OR "fibroxanthosarcoma" OR "fibroxanthosarcomas" OR "ganglioblastoma" OR "ganglioblastomas" OR "gangliocytoma" OR "gangliocytomas" OR "ganglioglioma" OR "gangliogliomas" OR

Targeted Area	Search Strategy
	"ganglioneuroblastoma" OR "ganglioneuroblastomas" OR "ganglioneurofibroma" OR "ganglioneurofibromas" OR "ganglioneuroma" OR "ganglioneuromas" OR "gastrinoma" OR "gastrinomas" OR "germinoma" OR "germinomas" OR "glioblastoma" OR "glioblastomas" OR "gliofibroma" OR "gliofibromas" OR "glioma" OR "gliomas" OR "gliomatosis" OR "glioneuroma" OR "glioneuromas" OR "gliosarcoma" OR "gliosarcomas" OR "glomangioma" OR "glomangiomas" OR "glomangiomatosis" OR "glomangiomyoma" OR "glomangiomyomas" OR "glomangiosarcoma" OR "glomangiosarcomas" OR "glucagonoma" OR "glucagonomas" OR "gonadoblastoma" OR "gonadoblastomas" OR "gonocytoma" OR "gonocytomas" OR "granuloma" OR "granulomas" OR "granulomatosis" OR "gynaecomastia" OR "gynandroblastoma" OR "gynecomastia" OR "haemangioblastoma" OR "haemangioblastomas" OR "haemangioma" OR "haemangiomas" OR "haemangiopericytoma" OR "haemangiopericytomas" OR "haemangiosarcoma" OR "haemangiosarcomas" OR "hamartoma" OR "hamartomas" OR "hemangioblastoma" OR "hemangioblastomas" OR "hemangioendothelioma" OR "hemangioendotheliomas" OR "hemangioendoteliosarcoma" OR "hemangioendoteliosarcomas" OR "hemangioma" OR "hemangiomas" OR "hemangiomatosis" OR "hemangiopericytoma" OR "hemangiopericytomas" OR "hemangioperithelioma" OR "hemangiosarcoma" OR "hemangiosarcomas" OR "hepatoblastoma" OR "hepatoblastomas" OR "hepatocarcinoma" OR "hepatocarcinomas" OR "hepatocholangiocarcinoma" OR "hepatocholangiocarcinomas" OR "hepatoma" OR "hepatomas" OR "hibernoma" OR "hibernomas" OR "hidradenoma" OR "hidradenomas" OR "hidrocystoma" OR "hidrocystomas" OR "histiocytoma" OR "histiocytomas" OR "hodgkin" OR "hodgkins" OR "hydradenoma" OR "hydradenomas" OR "hypernephroma" OR "hypernephromas" OR "immunocyoma" OR "immunocyomas" OR "insulinomas" OR "keratoacanthoma" OR "keratoacanthomas" OR "leiomyoblastoma" OR "leiomyoblastomas" OR "leiomyofibroma" OR "leiomyofibromas" OR "leiomyoma" OR "leiomyomas" OR "leiomyomatosis" OR "leiomyosarcoma" OR "leiomyosarcomas" OR "leukaemia" OR "leukaemias" OR "leukemia" OR "leukemias" OR "leukoplakia" OR "leukoplakias" OR "lipoadenoma" OR "lipoadenomas" OR "lipoblastoma" OR "lipoblastomas" OR "lipoblastomatosis" OR "lipoma" OR "lipomas" OR "lipomatosis" OR "liposarcoma" OR "liposarcomas" OR "luteinoma" OR "luteoma" OR "luteomas" OR "lymphangioendothelioma" OR "lymphangioendotheliomas" OR "lymphangioleiomyomatosis" OR "lymphangioma" OR "lymphangiomas" OR "lymphangiomatosis" OR "lymphangiomyoma" OR "lymphangiomyomas" OR "lymphangiomyomatosis" OR "lymphangiosarcoma" OR "lymphangiosarcomas" OR "lymphoepithelioma" OR "lymphoepitheliomas" OR "lymphoma" OR "lymphomas" OR "lymphoproliferation" OR "lymphoproliferations" OR "lymphoproliferative" OR "lymphoscintigraphic" OR "lymphoscintigraphy" OR "macroglobulinemia" OR "macroglobulinemias" OR "macroprolactinoma" OR "malignancies" OR "malignancy" OR "malignant" OR "maltoma" OR "maltomas" OR "masculinovoblastoma" OR "mastocytoma" OR "mastocytomas" OR "mastocytosis" OR "medulloblastoma" OR "medulloblastomas" OR "medulloctoma" OR "medulloctomas" OR "medulloepithelioma" OR "medulloepitheliomas" OR "medullomyoblastoma" OR "medullomyoblastomas" OR "meigs-syndrome" OR "melanoacanthoma" OR "melanoacanthomas" OR "melanoameloblastoma" OR "melanocytoma" OR "melanocytomas" OR "melanoma" OR "melanomas" OR "melanomatosis" OR "meningioblastoma" OR "meningioma" OR "meningiomas" OR "meningiomatosis" OR "mesenchymoma" OR "mesenchymomas" OR "mesonephroma" OR "mesonephromas" OR "mesothelioma" OR "mesotheliomas" OR "metaplasia" OR "microglioma" OR "microgliomas" OR "micrometastases" OR "micrometastasis" OR "mycosisfungoides" OR "myelodysplasia" OR "myelodysplasias" OR "myelodysplastic" OR "myelofibrosis" OR "myelolipoma" OR "myelolipomas" OR "myeloma" OR "myelomas" OR "myelomatosis" OR "myeloproliferation" OR "myeloproliferations" OR "myeloproliferative" OR "myelosuppression" OR "myoblastoma" OR "myoblastomas" OR "myoepithelioma" OR "myoepitheliomas" OR "myofibroblastoma" OR "myofibroblastomas" OR "myofibroma" OR "myofibromas" OR "myofibromatosis" OR "myofibrosarcoma" OR "myofibrosarcomas" OR "myolipoma" OR "myolipomas" OR "myoma" OR "myomas" OR "myosarcoma" OR "myosarcomas" OR "myxofibroma" OR "myxofibromas" OR "myxolipoma" OR "myxolipomas" OR "myxoliposarcoma" OR "myxoma" OR "myxomas" OR "neoplasia" OR "neoplasia" OR "neoplasm" OR "neoplasms" OR "neoplastic" OR "nephroblastoma" OR "nephroblastomas" OR "neurilemmoma" OR "neurilemmomas" OR "neurilemmomatosis" OR "neurilemoma" OR "neurilemmas" OR "neurinoma" OR "neurinomas" OR "neuroblastoma" OR "neuroblastomas" OR "neurocytoma" OR

Targeted Area	Search Strategy
	"neurocytomas" OR "neuroepithelioma" OR "neuroepitheliomas" OR "neurofibroma" OR "neurofibromas" OR "neurofibromatosis" OR "neurofibrosarcoma" OR "neurofibrosarcomas" OR "neurolipocytoma" OR "neuroma" OR "neuromas" OR "neuronevus" OR "neurothekeoma" OR "neurothekeomas" OR "nonhodgkin" OR "nonhodgkins" OR "nonseminoma" OR "nonseminomas" OR "nonseminomatous" OR "NSCLC" OR "odontoameloblastoma" OR "odontoma" OR "oligoastrocytoma" OR "oligoastrocytomas" OR "oligodendroglioma" OR "oligodendrogliomas" OR "oncocyoma" OR "oncocyomas" OR "opsoclonus-myoclonus" OR "orchioblastoma" OR "orchioblastomas" OR "osteoblastoma" OR "osteoblastomas" OR "osteochondroma" OR "osteochondromas" OR "osteochondrosarcoma" OR "osteochondrosarcomas" OR "osteoclastoma" OR "osteoclastomas" OR "osteofibrosarcoma" OR "osteoma" OR "osteomas" OR "osteosarcoma" OR "osteosarcomas" OR "pancreatoblastoma" OR "pancreatoblastomas" OR "papillomas" OR "papillomata" OR "papillomatosis" OR "parachordoma" OR "parachordomas" OR "paraganglioma" OR "paragangliomas" OR "paraneoplastic" OR "perineurioma" OR "perineuriomas" OR "peutz-jeghers" OR "phaeochromocytoma" OR "phaeochromocytomas" OR "pheochromoblastoma" OR "pheochromoblastomas" OR "pheochromocytoma" OR "pheochromocytomas" OR "pilomatricoma" OR "pilomatricomas" OR "pilomatrixoma" OR "pilomatrixomas" OR "pinealblastoma" OR "pinealoblastoma" OR "pinealoblastomas" OR "pinealoma" OR "pinealomas" OR "pineoblastoma" OR "pineoblastomas" OR "pineocytoma" OR "pineocytomas" OR "plasmacytoma" OR "plasmacytomas" OR "pneumoblastoma" OR "pneumoblastomas" OR "pneumocytoma" OR "polyembryoma" OR "polyembryomas" OR "polyhistioma" OR "polyhistiomas" OR "polyposis" OR "porocarcinoma" OR "porocarcinomas" OR "poroma" OR "poromas" OR "precancer" OR "precancerous" OR "reninoma" OR "reninomas" OR "reticuloendothelioma" OR "reticuloendotheliomas" OR "reticulohistiocytoma" OR "reticulohistiocytomas" OR "retinoblastoma" OR "retinoblastomas" OR "rhabdomyoma" OR "rhabdomyomas" OR "rhabdomyosarcoma" OR "rhabdomyosarcomas" OR "rhabdosarcoma" OR "rhabdosarcomas" OR "sarcoma" OR "sarcomas" OR "sarcomatosis" OR "schwannoma" OR "schwannomas" OR "schwannomatosis" OR "seminoma" OR "seminomas" OR "seminomatous" OR "sezary-syndrome" OR "somatostatinoma" OR "somatostatinomas" OR "somatotropinoma" OR "somatotropinomas" OR "spermatocytoma" OR "spiradenoma" OR "spiradenomas" OR "spongioblastoma" OR "spongioblastomas" OR "steatocystoma" OR "steatocystomas" OR "struma-ovarii" OR "subependymoma" OR "subependymomas" OR "syringadenoma" OR "syringadenomas" OR "syringocystadenoma" OR "syringocystadenomas" OR "syringoma" OR "syringomas" OR "teratocarcinoma" OR "teratocarcinomas" OR "teratoma" OR "teratomas" OR "thecoma" OR "thecomas" OR "thymolipoma" OR "thymolipomas" OR "thymoma" OR "thymomas" OR "trichilemmoma" OR "trichilemmomas" OR "trichoadenoma" OR "trichoblastoma" OR "trichoblastomas" OR "trichodiscoma" OR "trichodiscomas" OR "trichoepithelioma" OR "trichoepitheliomas" OR "trichofolliculoma" OR "trichofolliculomas" OR "tricholemmoma" OR "tricholemmomas" OR "tumor" OR "tumorigenesis" OR "tumorigenic" OR "tumorigenesis" OR "tumorigenic" OR "tumor-marker*" OR "tumorigenesis" OR "tumorigenic" OR "tumors" OR "tumour" OR "tumours" OR "vipoma" OR "vipomas" OR "waldenstrom" OR "waldenstroms" OR "xanthoastrocytoma" OR "xanthoastrocytomas" OR "xanthofibroma" OR "xanthofibromas" OR "xanthogranuloma" OR "xanthogranulomas" OR "xanthoma" OR "xanthomas" OR "xanthosarcoma" OR "xanthosarcomas" OR "oncogene-fusion"))
Cancer in Experimental Animals	tiab:("mice" OR "mouse" OR "rats" OR "rat" OR "hamster" OR "hamsters" OR "guinea pig*" OR "gerbil*" OR "rabbits" OR "rabbit" OR "dogs" OR "dog" OR "monkey" OR "monkeys" OR "pongo pygmaeus" OR "sow" OR "sows" OR "boar" OR "boars" OR "animal stud*" OR "murine" OR "wood-mouse" OR "murinae" OR "muridae" OR "cricetinae" OR "rodentia" OR "rodent" OR "rodents" OR "ferrets" OR "ferret" OR "polecat*" OR "mustela putorius" OR "cavia" OR "callithrix" OR "marmoset*" OR "chinchilla*" OR "jird" OR "jirds" OR "merione" OR "meriones" OR "cats" OR "cat" OR "felis" OR "canis" OR "sheep" OR "sheeps" OR "goats" OR "goat" OR "capra" OR "saguinus" OR "tamarin*" OR "leontopithecus" OR "ape" OR "apes" OR "pan paniscus" OR "bonobo*" OR "pan troglodytes" OR "gibbon*" OR "siamang*" OR "nomascus" OR "symphalangus" OR "chimpanzee*" OR "orangutan*" OR "horse" OR "horses" OR "equus" OR "cow" OR "cows" OR "chicken" OR "chickens" OR "wistar" OR "balb" OR "C57" OR "C57bl" OR "quail" OR "long-evans" OR "guppy" OR "medaka" OR "zebrafish" OR "flying fox" OR "Fruit bat" OR "non-human-primate*" OR

Targeted Area	Search Strategy
	"capuchin*" OR "rhesus" OR "macaque*" OR "cattle" OR "bovine" OR "pigs" OR "pig" OR "swine" OR "swines" OR "piglet*" OR "Sprague-Dawley" OR "vervet*" OR "chimera")
Human Cancer Studies	tiab:(("Epidemiologic Studies" OR "epidemiology" OR "Meta-Analysis" OR "Case Reports" OR "workmen*" OR "Worker*" OR "Seroepidemiologic Stud*" OR "retrospective stud*" OR "prospective stud*" OR "Mortality" OR "longitudinal stud*" OR "follow up stud*" OR "ecological study" OR "ecological studies" OR "Cross Sectional Stud*" OR "Correlation stud*" OR "cohort*" OR "case-control*" OR "cancer registr*" OR "case series" OR "case referent" OR "record link*")) OR ((("metaanalysis" OR "case-report*" OR "metaanalyses" OR "meta-analysis") OR ("randomized controlled trial") OR ("case-crossover") OR ("systematic review")))
Epidemiologic Quantitative Analysis	tiab:(("human health" OR "dose response" OR "human studies" OR "human study" OR "human data" OR "human development" OR ("human" AND ("person" OR "people" OR "pediatric*" OR "paediatric*" OR "baby" OR "babies" OR "toddler*" OR "child*" OR "youngster*" OR "teen" OR "teens" OR "teenager*" OR ((("in utero" OR "prenat*" OR "perinat*" OR "neonat*" OR "postnat*") AND NOT ("mice" OR "mouse" OR "rat" OR "rats"))) OR "preschool*" OR "pre-school*" OR "kindergarten*" OR "schoolchild*" OR "student*" OR "elder*" OR "senior citizen*" OR "seniors" OR "retiree*" OR "septuagenarian*" OR "octagenarian*" OR "sexagenarian*" OR "nonagenarian*" OR "centenarian*" OR "father*" OR "mother*" OR "sibling*" OR "brother*" OR "sister*" OR "twin" OR "twins" OR "grandparent*" OR "grandfather*" OR "grandmother*" OR "grandchild*" OR "granddaughter*" OR "grandson*" OR "caregiver*" OR "care giver*" OR "men" OR "women" OR "man" OR "boy" OR "boys" OR "boyhood" OR "woman" OR "girl" OR "girls" OR "girlhood" OR "population groups" OR "vulnerable populations" OR "african american*" OR "asian american*" OR "hispanic*" OR "latina*" OR "latino*" OR "mexican american*" OR "underserved" OR "disadvantaged" OR "epidemiologic studies" OR "double-blind method" OR "single-blind method" OR "epidemiology" OR "case control*" OR "case-control*" OR "cohort" OR "cross sectional" OR "cross-sectional" OR "follow-up study" OR "longitudinal study" OR "prospective study" OR "retrospective study" OR "case reports" OR "clinical trial" OR "observational study" OR "randomized control trial" OR "twin study" OR "clinical trial*" OR "randomized control trial*" OR "research subjects" OR "human experimentation" OR "Patient Participation" OR "human subject*" OR "research subject*" OR "patient*" OR "inpatient*" OR "outpatient*" OR "participant*" OR "volunteer*" OR "occupational groups" OR "professional" OR "staff" OR "technician*" OR "worker*" OR "educator*" OR "instructor*" OR "teacher*" OR "clinician*" OR "doctor*" OR "physician*" OR "pharmacist*" OR "nurs*" OR "residents" OR "veterinarian*" OR "human experimentation")) AND ("meta-analysis" OR "Systematic review" OR "prevalence ratio*" OR "hazard ratio*" OR "odds ratio*" OR "risk ratio*" OR "relative risk*" OR "covariate*" OR "adjust*" OR "control* for" OR "associat*" OR "confound*" OR "CI" OR "confidence interval*" OR "credible interval" OR "regression*" OR "explanatory variable*" OR "dose-response" OR "nonsignificant" OR "RR" OR "RRs" OR "SMR" OR "SMRs" OR "rate ratio*" OR "significan*" OR tiab_punct:"P <" OR tiab_punct:"p <" OR tiab_punct:"P <=" OR tiab_punct:"p <=" OR tiab_punct:"P >*" OR tiab_punct:"p >*" OR tiab_punct:"p=*" OR tiab_punct:"P =" OR tiab_punct:"p =" OR tiab_punct:"p>*" OR tiab_punct:"p<*""))
<i>in vitro</i> (for the purposes of exclusion)	tiab:(("Cell line" OR "tumor cells, cultured" OR "cultured tumor cells" OR "in vitro techniques" OR "saccharomyces cerevisiae" OR "cells, cultured" OR "cultured cells" OR "micronucleus tests" OR "comet assay" OR "primary cells" OR "cell culture" OR "cultured" OR "in vitro" OR "3T3" OR "A549" OR "BEAS-2B" OR "CACO-2" OR "CHO cells" OR "HELA" OR "HepG2" OR "HepaRG" OR "Jurkat" OR "MCF-7" OR "stem cells" OR "tissues" OR "tissue" OR "assay" OR "assays" OR "culture media")tiab:(("Cell line" OR "tumor cells, cultured" OR "cultured tumor cells" OR "in vitro techniques" OR "saccharomyces cerevisiae" OR "cells, cultured" OR "cultured cells" OR "micronucleus tests" OR "comet assay" OR "primary cells" OR "cell culture" OR "cultured" OR "in vitro" OR "3T3" OR "A549" OR "BEAS-2B" OR "CACO-2" OR "CHO cells" OR "HELA" OR "HepG2" OR "HepaRG" OR "Jurkat" OR "MCF-7" OR "stem cells" OR "tissues" OR "tissue" OR "assay" OR "assays" OR "culture media"))
Total Results for Discipline	106 references

3.7 Dermal Absorption

As described in Section 3.1, an updated literature search was performed from our existing literature pool to identify potentially relevant information for the characterization of dermal absorption of *o*-dichlorobenzene. The search string used is listed below in Section 3.7.1.

3.7.1 Dermal Absorption Search String

"Dermal flux" OR "Skin flux" OR "Dermal penetration" OR "Skin penetration" OR "Dermal absorption fraction" OR "Absorption fraction" OR "Neat Kp" OR "Aqueous Kp" OR "Kp" OR "Skin permeability coefficient" OR "Permeability coefficient" OR "Skin permeation coefficient" OR "Permeation coefficient" OR "Skin permeation" OR "Skin absorption" OR "Dermal absorption" OR "Dermal permeation" OR "OECD 427" OR "OECD 428"

4 DATA SCREENING

Sections 4.2.5 and 4.3.2 of the 2021 Draft Systematic Review Protocol describe how TIAB and full-text screening respectively, are conducted to identify references that may contain relevant information for use in risk evaluations under TSCA using discipline-specific screening criteria ([U.S. EPA, 2021](#)). Specifically, TIAB screening efforts may be conducted using the specialized web-based software programs DistillerSR¹ and SWIFT-Active-Screener,^{2,3} and the below sub-sections will describe whether TIAB screening was done manually in DistillerSR or utilized machine learning to help prioritize reference screening in SWIFT-Active-Screener. Additional details on how SWIFT Active-Screener utilizes a machine-learning algorithm to automatically compute which unscreened documents are most likely to be relevant⁴ are available in Section 4.2.5 of the 2021 Draft Systematic Review Protocol ([U.S. EPA, 2021](#)). During TIAB screening, if it was unclear whether a reference met the screening criteria (*e.g.*, PECO/RESO/PESO statements) without having the full reference to review, or if a reference was determined to meet the screening criteria, that reference advanced to full-text screening if the full reference could be retrieved and generated into a Portable Document Format (PDF).

Literature inventory trees were introduced in the scoping process for the risk evaluations that began systematic review in 2019 in response to comments received from the SACC and public to better illustrate how references underwent various systematic review steps (*e.g.*, TIAB and full-text screening). As explained in Section 2.1.2 of the *Final Scope of the Risk Evaluation for o-Dichlorobenzene* ([U.S. EPA, 2020b](#)), literature inventory trees demonstrate how references that meet screening criteria progress to the next systematic review step. EPA used the Health Assessment Workplace Collaborative⁵ (HAWC) tool to

¹ As noted on the [DistillerSR web page](#), this systematic review software “automates the management of literature collection, triage, and assessment using AI and intelligent workflows...to produce transparent, audit ready, and compliant literature reviews.” EPA uses DistillerSR to manage the workflow related to screening and evaluating references; the literature search is conducted external to DistillerSR.

² SWIFT-Active Screener is another systematic review software that EPA is adopting in the TSCA systematic review process. From Sciome’s [SWIFT-Active Screener](#) web page: “As screening proceeds, reviewers include or exclude articles while an underlying statistical model in SWIFT-Active Screener automatically computes which of the remaining unscreened documents are most likely to be relevant. This ‘Active Learning’ model is continuously updated during screening, improving its performance with each reference reviewed. Meanwhile, a separate statistical model estimates the number of relevant articles remaining in the unscreened document list.”

³ SWIFT is an acronym for “*Sciome Workbench for Interactive Computer-Facilitated Text-mining*.” SWIFT-Active Screener uses machine learning approaches to save screeners’ time and effort.

⁴ Description comes from the [SWIFT-Active Screener](#) web page.

⁵ [EPA HAWC](#) is an application that allows to record and share the results of the systematic literature search, data extraction, and analyses that can then be publicly accessed online.

develop web-based literature inventory trees that enhance the transparency of the decisions resulting from the screening processes; details on the application of the tool were described by Shapiro et al ([2018](#)).

Additional references identified outside of the literature searches in September 2019 or May 2025 on *o*-dichlorobenzene, but that that EPA has obtained via public and other sources (*e.g.*, chemical assessor identified, backward searches) were also considered in the systematic review process and are reflected in the interactive HAWC hyperlinks available in the figure captions below each respective literature inventory tree. The web-based interactive literature inventory trees in HAWC also allow users to directly access the references in the Health & Environmental Research Online (HERO) database (more details available in Section 1 of the 2021 Draft Systematic Review Protocol). Instructions for accessing information about references and data sources in each node via HERO are available in HAWC for each respective literature inventory tree. Each node indicates whether a reference has met screening criteria at different screening steps and/or contains types of content that may be discerned at that respective systematic review step ([U.S. EPA, 2021](#)). Furthermore, the sum of the numbers for the various nodes in the literature inventory trees may be smaller or larger than the preceding node because some studies may have unclear relevance or be relevant for many categories of information. The screening process for each discipline varies and the nodes in the literature inventory tree indicate the screening decisions determined for each reference and whether specific content could be determined; if no references had a specific screening decision and/or contained specific content relevant for a respective discipline, a node will not be present on the literature tree to depict this.

Occasionally some references or data sources are identified in the literature search because of the availability of the title and abstract, however EPA may not be able to always locate the entire or original version. Therefore, references or data sources that meet TIAB screening criteria may be unattainable for full-text screening. The “PDF not available” node within the literature inventory tree refers to references that were identified in the literature search, but which EPA was unable to obtain the entire reference or source of information.

While all information contained in references that enter systematic review is considered for use in the risk evaluation, the references that satisfy the screening criteria are generally deemed to contain the most relevant and useful information for characterizing the uses of, exposure to, and hazard associated with a chemical of interest and are generally utilized in the risk evaluation or to identify further data needs. On the other hand, data or information sources that do not satisfy the screening criteria outlined below may undergo data quality evaluation and extraction should a data need arise for the risk evaluation.

4.1 Multi-disciplinary Updates and Clarifications to the Data Screening

As stated above in Section 0, all references that are found in the initial chemical-specific searches are considered for use in the respective chemical risk evaluation. Previously Section 4.2.5 of the 2021 Draft Systematic Review Protocol explained that references tagged as potentially having supplemental information may be considered for data quality evaluation and extraction. However, one clarification to that description is that even references that are tagged as not meeting TIAB or full-text screening criteria (*e.g.*, PECO/PESO/RESO) for a respective discipline or sub-discipline may also undergo additional screening to meet information needs that were not stated in the original screening criteria and be considered for data quality evaluation and extraction, should there be additional relevant information that may not have met the original screening criteria.

Section **Error! Reference source not found.** described that an updated peer literature search was conducted in May 2025 to identify any potential additional data sources

for *o*-dichlorobenzene relevant to environmental release and occupational exposure; general population, consumer, and environmental exposure; and human health hazard that might not have been identified since the initial literature search that was conducted in 2019. Any additional references identified from the updated literature search were screened as previously described in Section 4.2 and Appendix H of the 2021 Draft Systematic Review Protocol ([U.S. EPA, 2021](#)) unless otherwise stated that updates were made. Any updates to the screening process since the publication of the 2021 Draft Systematic Review Protocol for environmental release and occupational exposure; general population, consumer, and environmental exposure; and human health hazard are described below in Sections 4.4, 4.5. and 4.6, respectively.

4.2 Physical and Chemical Properties

During data screening, EPA followed the process described in Appendix H, Section H-1 of the 2021 Draft Systematic Review Protocol ([U.S. EPA, 2021](#)), to conduct title and abstract and full-text screening for *o*-dichlorobenzene guided by the data or information needs on various physical and chemical properties or endpoints as listed in Table_Apx H-1 of the protocol. The same screening criteria was used during TIAB and FT screening for references considered for the evaluation of physical and chemical properties of *o*-dichlorobenzene. Title and abstract screening was performed using SWIFT Active-Screener. Upon meeting screening criteria during full-text screening, data or information sources then undergo data quality evaluation and extraction. Figure 4-1 presents the number of references that report general physical and chemical property information that fulfilled the data needs for *o*-dichlorobenzene and passed these criteria for TIAB and FT screening.

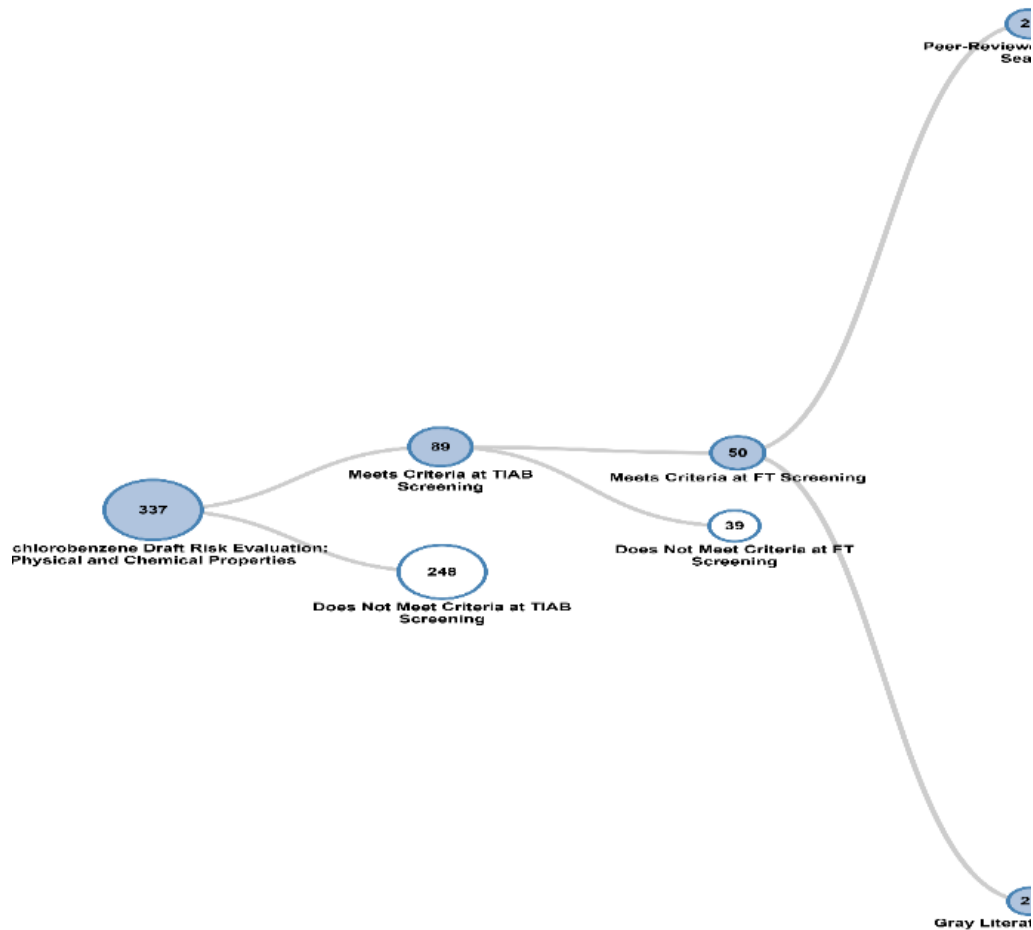


Figure 4-1. Literature Inventory Tree – Physical and Chemical Properties for *o*-Dichlorobenzene
View the interactive literature inventory tree in [HAWC](#). Data in this figure represent all references obtained from the publicly available databases and gray literature reference searches that were included in systematic review as of April

24, 2026. Additional data may be added to the interactive version as they become available. Some studies may be found through multiple searches and may have more than one source tag in HERO.

4.3 Environmental Fate and Transport Properties

During data screening, EPA followed the process described in Appendix H, Section H.2 of the 2021 Draft Systematic Review Protocol ([U.S. EPA, 2021](#)), to conduct TIAB and FT screening for *o*-dichlorobenzene literature search results, as guided by the PESO statement. PESO stands for **P**athways or **P**rocesses, **E**xposure, **S**etting or **S**cenario, and **O**utcomes (see Table_Apx H2 in 2021 Draft Systematic Review Protocol). The same PESO screening criteria was used during TIAB and FT screening for references considered for the evaluation of environmental fate and transport properties of *o*-dichlorobenzene. TIAB screening was performed using SWIFT Active-Screener. Data or information sources that comply with the screening criteria specified in the PESO statement then undergo data quality evaluation and extraction. Figure 4-2 presents the number of references that report *o*-dichlorobenzene fate processes and endpoints, or environmental and exposure pathways that passed PESO screening criteria at TIAB and FT screening.

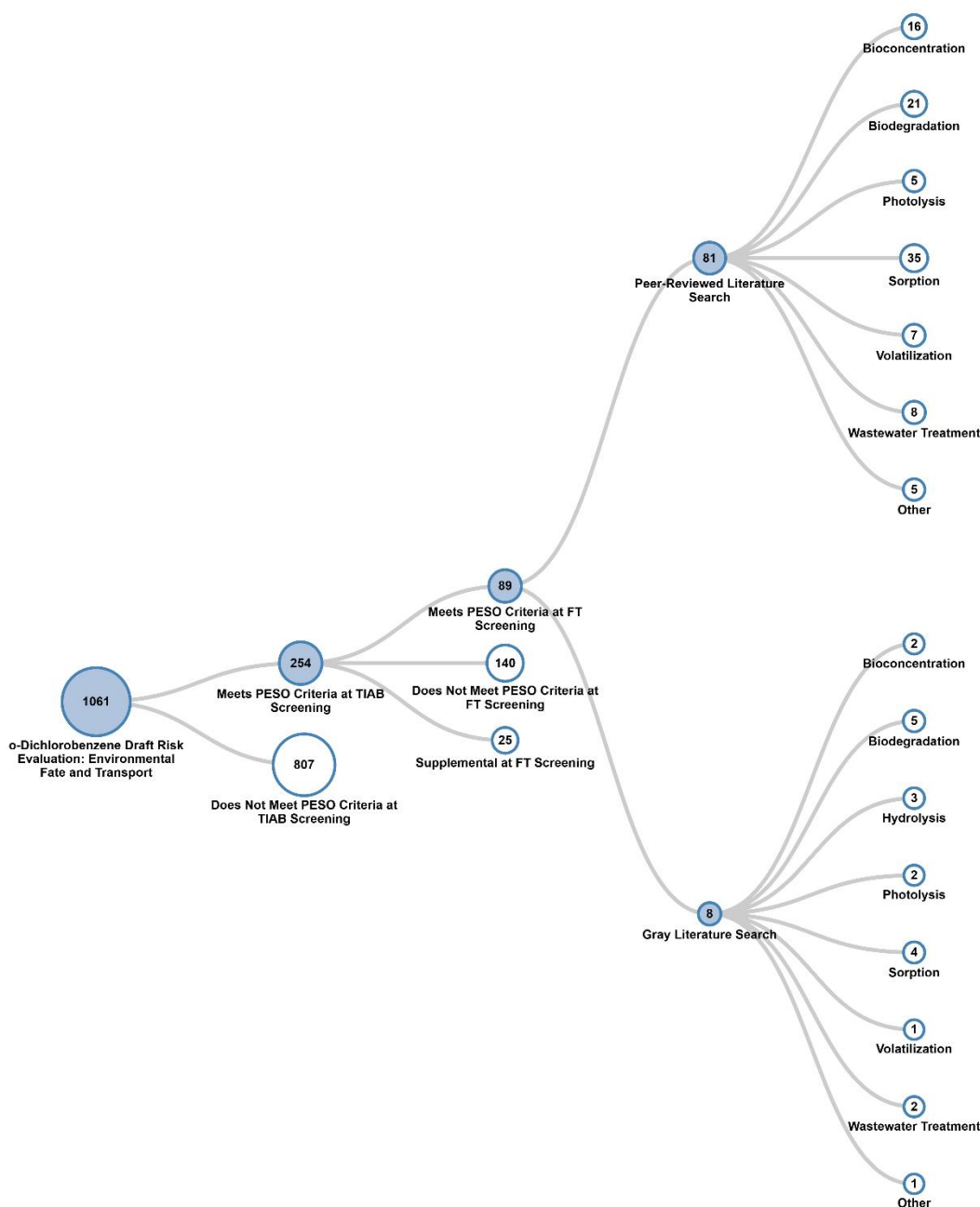


Figure 4-2. Literature Inventory Tree – Environmental Fate and Transport Properties for *o*-Dichlorobenzene

View the interactive literature inventory tree in [HAWC](#). Data in this figure represent all references obtained from the publicly available databases and gray literature references searches that were included in systematic review as of April 24, 2026. Additional data may be added to the interactive version as they become available.

4.4 Environmental Release and Occupational Exposure

During data screening, EPA followed the process described in Appendix H, Section H.3 of the 2021 Draft Systematic Review Protocol ([U.S. EPA, 2021](#)), to conduct title and abstract, and full-text screening for *o*-dichlorobenzene literature search results, as guided by the RESO statement. RESO stands for **R**eceptors,

Exposure, **S**etting or Scenario, and **O**utcomes. The same RESO statement was used during title and abstract, and full-text screening for references considered for the evaluation of environmental release and occupational exposure information for *o*-dichlorobenzene. TIAB were performed using SWIFT Active-Screener. Data or information sources that comply with the screening criteria specified in the RESO statement then undergo data quality evaluation and extraction. Figure 4-3 presents the number of references that report general engineering data, environmental release, and occupational exposure data that passed RESO screening criteria at TIAB, and full-text screening.

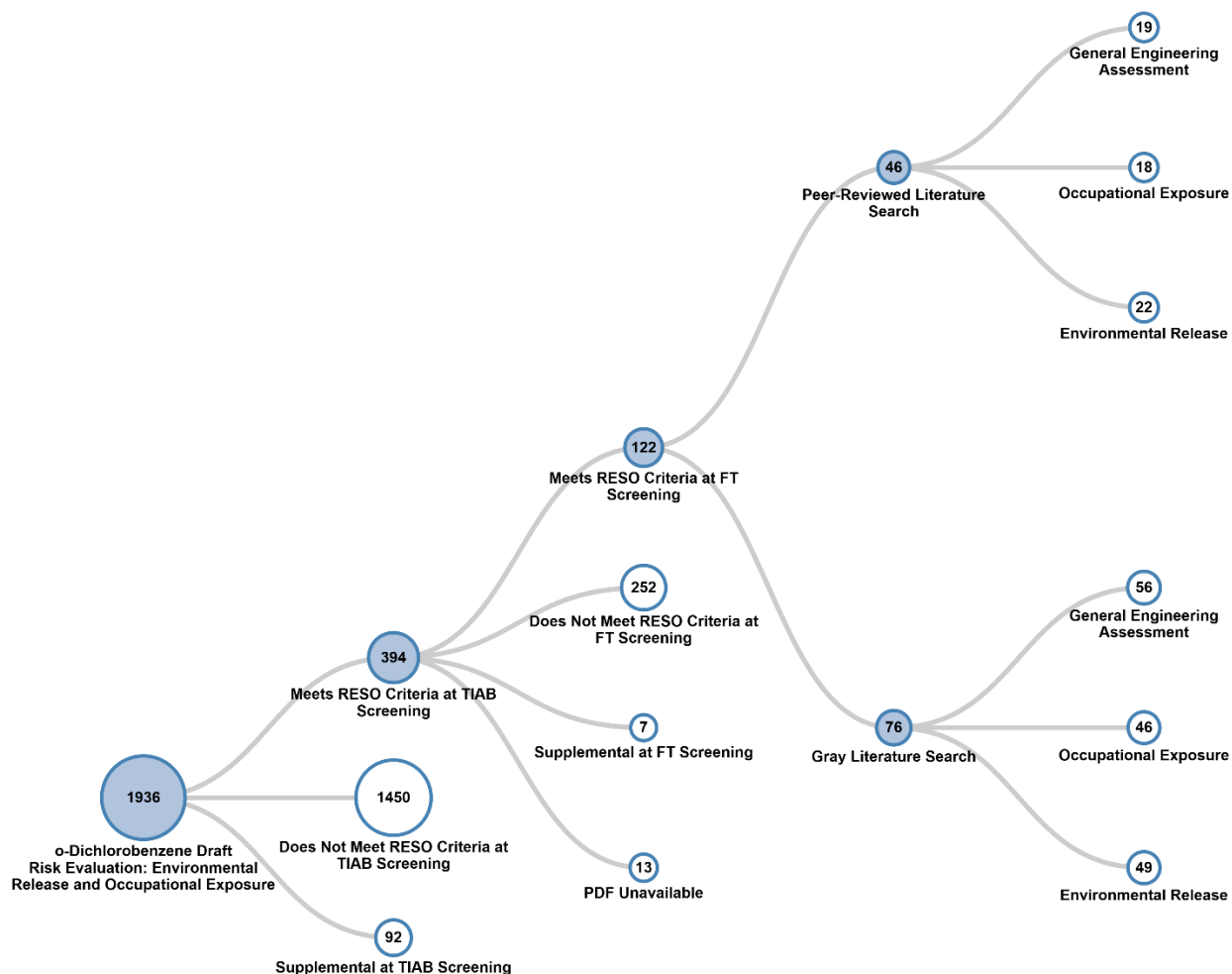


Figure 4-3. Literature Inventory Tree – Environmental Release and Occupational Exposure for *o*-Dichlorobenzene

View the interactive literature inventory tree in [HAWC](#). Data in this figure represents all references obtained from the publicly available databases and gray literature references searches that were included in systematic review as of April 14, 2026. Additional data may be added to the interactive version as they become available.

As described in Section 3.4, an update to the peer-reviewed literature search to capture information published since September 2019 was performed in May 2025. Of the new additional sources of data that EPA identified for *o*-dichlorobenzene from the update peer-reviewed literature search for environmental release and occupational exposure information, 69 references went through TIAB screening. Of these 69 references, 4 references met the RESO screening criteria during TIAB screening or were unclear to EPA whether the reference met the RESO screening criteria and proceeded to full-text screening. Upon

completion of full-text screening, EPA identified 1 reference (HERO ID: 11457810) that met the full-text screening criteria and moved to the data evaluation and extraction step of the systematic review process.

4.5 General Population, Consumer, and Environmental Exposure

During data screening, EPA followed the process described in Appendix H.4 of the 2021 Draft Systematic Review Protocol ([U.S. EPA, 2021](#)), to conduct TIAB and full-text screening for *o*-dichlorobenzene literature search results from the initial search in 2019 as well as the updated literature search in May 2025, as guided by the PECO statement. PECO stands for **P**opulation, **E**xposure, **C**omparator or Scenario, and **O**utcomes for Exposure Concentration or Dose. The same PECO statement was used during TIAB and full-text screening for references considered for the evaluation of general population, consumer, and environmental exposure information for *o*-dichlorobenzene. TIAB screening was performed using SWIFT Active-Screener.

Figure 4-4 presents the number of references that report general population, consumer, and environmental exposure data that passed PECO screening criteria at TIAB and full-text screening.

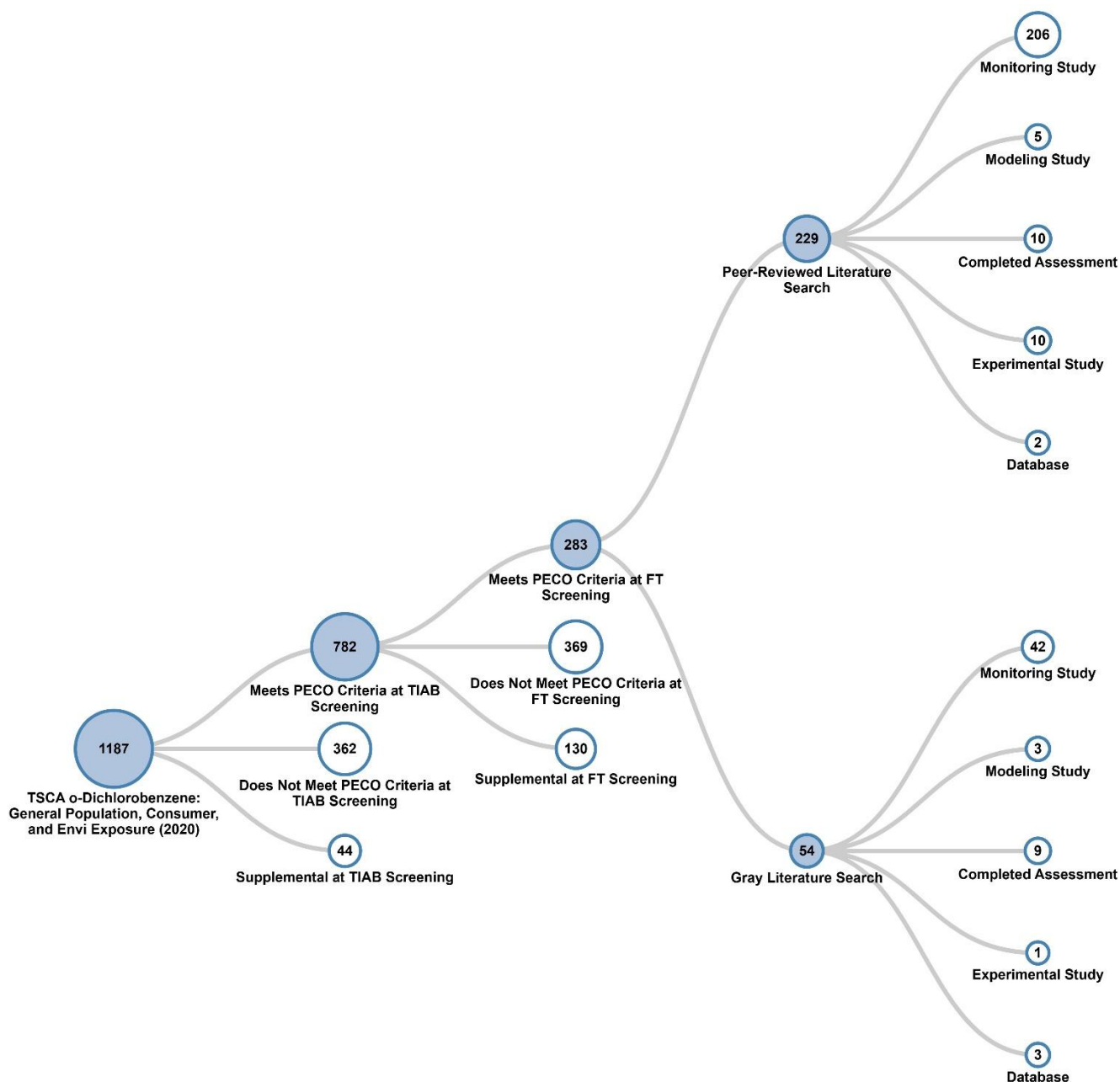


Figure 4-4. Literature Inventory Tree – General Population, Consumer, and Environmental Exposure Search Results for *o*-Dichlorobenzene

View the interactive literature inventory tree in [HAWC](#). Data in this figure represent all references obtained from the publicly available databases and gray literature references searches that were included in systematic review as of May 1, 2026. Additional data may be added to the interactive version as they become available.

As described in Section 3.5, an update to the peer-reviewed literature search to capture information published since September 2019 was performed in May 2025, and EPA identified 252 new additional sources of data. Of the new additional sources of data that EPA identified for *o*-dichlorobenzene from the updated peer-reviewed literature search for general population, consumer, and environmental exposure information, 252 references went through TIAB screening. Of these 252 references, 13 references met the PECO screening criteria during TIAB screening or were unclear to EPA whether the reference met the

PECO screening criteria and proceeded to full-text screening. Upon completion of full-text screening, EPA identified 4 references (HERO ID: 6938836, 6952657, 12830425 and 12952530) that met the full-text screening criteria and moved to the data evaluation and extraction step of the systematic review process.

4.6 Environmental and Human Health Hazard

During data screening of the references identified in the initial literature search in 2019, EPA followed the process described in Appendix H, Section H.5.1 of the 2021 Draft Systematic Review Protocol ([U.S. EPA, 2021](#)), to conduct TIAB and full-text screening for *o*-dichlorobenzene literature search results, as guided by the PECO statement. PECO stands for **P**opulation, **E**xposure, **C**omparator or Scenario, and **O**utcomes. The same PECO statement was used during TIAB and full-text screening for references considered for the evaluation of environmental and human health hazard resulting from exposure to *o*-dichlorobenzene. For TIAB screening, EPA utilized machine learning to help prioritize reference screening in SWIFT-Active-Screener. Full-text screening occurred in DistillerSR for references that either met the PECO screening criteria during TIAB screening or if it was unclear to EPA whether the reference would meet the PECO screening criteria based on the information available in the title and abstract.

As described in Section 3.1 and 3.6, in addition to the sources identified in the initial literature search in 2019, EPA conducted an updated literature search for peer-reviewed literature in May 2025. The PECO statement used to conduct TIAB and full-text screening for the updated literature search was updated from what was published in Appendix H.5.1 of the 2021 Draft Systematic Review Protocol ([U.S. EPA, 2021](#)). Specific updates to the PECO screening criteria that were used to screen references from the updated literature search in May 2025 are described below in Section 4.6.1.

Figure 4-5 represents the number of references at TIAB and full-text screening for *o*-dichlorobenzene that report environmental and human health hazard data that met the original PECO screening criteria for references identified in the original literature search in 2019 as well as human health hazard data that met the updated PECO screening criteria for the references identified in the updated literature search in May 2025 for *o*-dichlorobenzene.

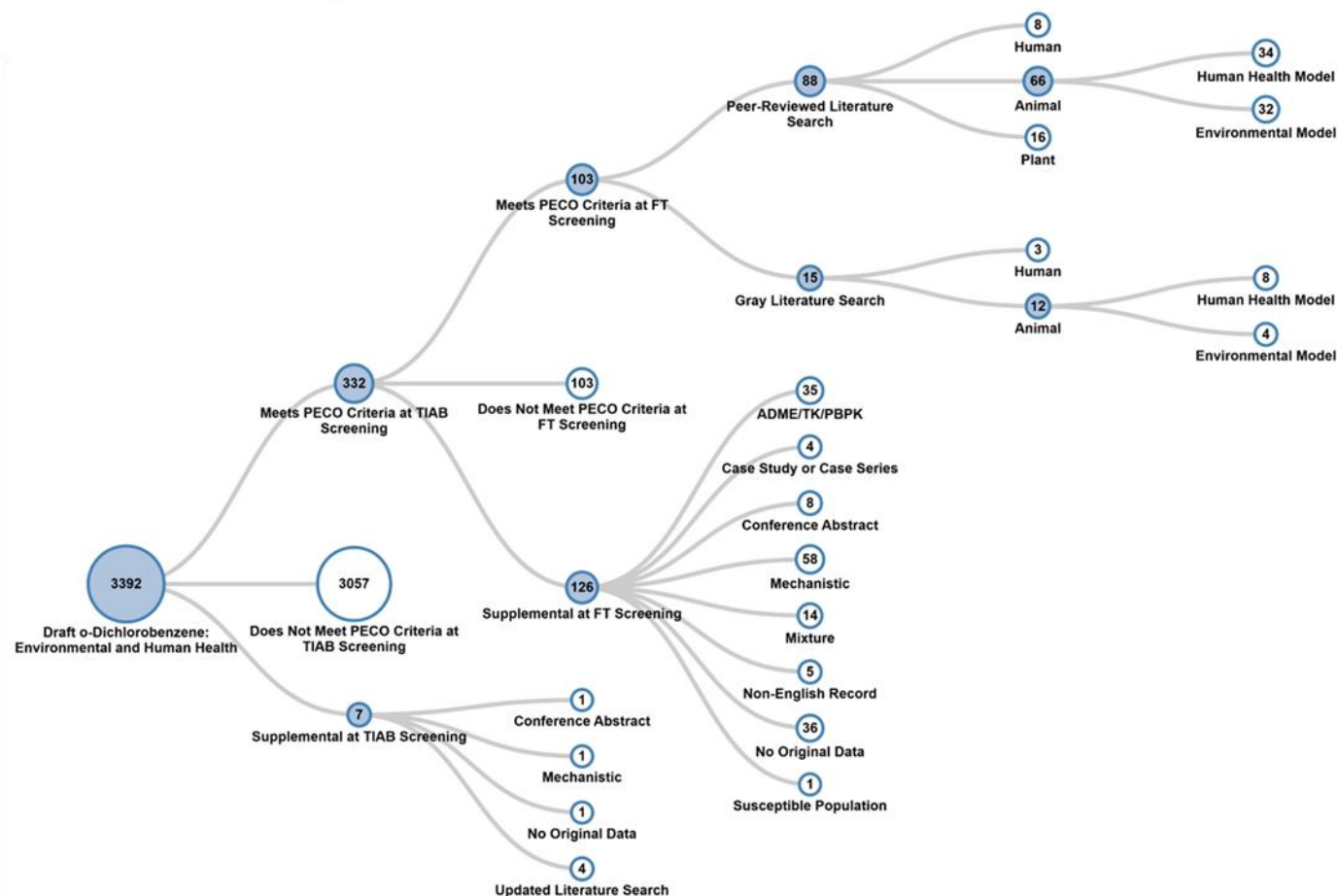


Figure 4-5. Literature Inventory Tree – Environmental and Human Health Hazard for *o*-Dichlorobenzene

View the interactive literature inventory tree in [HAWC](#). Data in this figure represents all references obtained from the publicly available databases and gray literature references searches that were included in systematic review as of February 11, 2026. Additional data may be added to the interactive version as they become available.

As described in Section 3.6, an update to the peer-reviewed literature search to capture human health information published since September 2019 was performed in May 2025. EPA applied targeted keyword queries to identify and prioritize cancer-related literature and identified 106 new additional sources of data. The new additional sources of data that EPA identified for *o*-dichlorobenzene from the updated peer-reviewed literature search for human health hazard information went through TIAB screening. Of these 106 references, 10 references met the PECO screening criteria during TIAB screening or were unclear to EPA whether the reference met the PECO screening criteria and proceeded to full-text screening. Upon completion of full-text screening, EPA identified 1 reference (HERO ID: 10096148) that met the full-text screening criteria and moved to the data evaluation and extraction step of the systematic review process.

4.6.1 Hazard Targeted PECO Screening Criteria Updates

As stated in the previous paragraph, for references identified during the updated peer literature search in May 2025, EPA updated the PECO statement for *o*-dichlorobenzene (Error! Reference source not found. and Error! Reference source not found.). The screening criteria were developed as a targeted approach to prioritize the information that was most relevant and presented new information for characterizing cancer-

related human health hazards for the risk evaluation for *o*-dichlorobenzene. As stated previously, EPA considered to have sufficient information from the initial literature search results and studies submitted under TSCA authorities (e.g., TSCA Section 4 test order, TSCA Section 8(d) Health and Safety Data Reporting) for environmental hazard to support the *Draft Risk Evaluation for o-Dichlorobenzene* ([U.S. EPA, 2026n](#)) and did not proceed with an update to the peer-reviewed literature.

The PECO statement published in Appendix H.5.1 of the 2021 Draft Systematic Review Protocol ([U.S. EPA, 2021](#)) applies to information for both *p*-dichlorobenzene and *o*-dichlorobenzene, and the updated PECO statement also applies to both *p*-dichlorobenzene and *o*-dichlorobenzene. To make it easier for the reader to see changes made or clarifications added to the screening criteria published in Appendix H.5.1 of the 2021 Draft Systematic Review Protocol ([U.S. EPA, 2021](#)), the following conventions are used in Error! Reference source not found. and Error! Reference source not found.: text inserted is underlined, and text deleted is in ~~striketrough~~.

The updated literature search conducted in May 2025 to identify new information that would fill data gaps for characterizing cancer-related human health hazards did not include a search targeted on environmental hazard, and therefore the updated PECO statement in Table 4-1 does not include any screening criteria for environmental hazard studies (this is indicated with N/A in Table 4-1).

Table 4-1. Updated PECO Criteria for the 2025 Updated Literature Searches for *o*-Dichlorobenzene (CASRN 95-50-1) and *p*-Dichlorobenzene (CASRN 106-46-7) – Title and Abstract and Full-Text Screening

PECO Element	Evidence
Population	Human: Any population and lifestage (e.g., occupational or general population, including children and other sensitive populations). Animal: Aquatic and terrestrial species (live, whole organism) from any lifestage (e.g., preconception, in utero, lactation, peripubertal, and adult stages). ~~Include insects, spiders, amphibians, birds, crustaceans, fish, mollusks, reptiles, worms and invertebrates. Bacteria and viruses are not included. In most cases, transgenic animal models will get screened as “yes” or “unclear” at TIAB level.~~ <u>Animal models will be inventoried according to the categorization below:</u> <u><i>Human health models:</i> rat, mouse, rabbit, dog, hamster, guinea pig, cat, non-human primate, pig, and zebrafish ~~hen (neurotox only)~~.</u> <u><i>Ecotoxicological models:</i> N/A. (Studies on ecotoxicological models were not considered for systematic review of the 2025 updated literature search. At this time for the 2025 updated literature search, ecotoxicological studies that would have otherwise met the original PECO criteria will be tagged as <i>Supplemental, Updated literature search: Meets original PECO criteria but does not fill a critical data gap.</i></u> ~~Plant: Aquatic and terrestrial species (live), all plants including algal, moss, lichen and fungi species.~~ <u>N/A. (Studies on plants were not considered for systematic review of the 2025 updated literature search. At this time for the 2025 updated literature search, plant studies that would have otherwise met the original PECO criteria will be tagged as <i>Supplemental, Updated literature search: Meets original PECO criteria but does not fill a critical data gap.</i></u> Screener note:

PECO Element	Evidence
	• <u>Human Health Animal Hazard: To identify human health hazards, other organisms not listed above might also be considered. Non-mammalian model systems such as the zebrafish animal model are increasingly used to identify potential human health hazards. Any zebrafish studies reporting cancer, tumor, or any other <i>in vivo</i> apical health outcome indicative of cancer or pre-cancerous lesions meet the PECO screening criteria.</u> • <u>Human Health Animal Hazard: Studies on gametes, embryos, or plant (e.g., ungerminated seeds, harvested fruit, cut flowers, and potato tubers) or fungal sections capable of forming whole, new organisms will be tagged as potentially Supplemental, Mechanistic.</u> • <u>Human Health Animal Hazard: Bacteria and yeast studies specific for assessing genotoxicity, mutagenicity (e.g., Ames assay), or hormone assay will be tagged as potentially Supplemental, Mechanistic. Otherwise, bacteria and yeast studies that are not used for assessing genotoxicity, mutagenicity, or hormone assays do not meet the PECO criteria.</u> • <u>Human Health Animal Hazard: Studies on viruses and any pathogenic microbes (unless bacteria or yeast used for assessing genotoxicity, mutagenicity, or hormone assay; see bullet above) do not meet the PECO screening criteria.</u>
Exposure	Relevant forms: • <u><i>o</i>-Dichlorobenzene or 1, 2-dichlorobenzene (CASRN 95-50-1)</u> • <u><i>p</i>-Dichlorobenzene or 1, 4-dichlorobenzene (CASRN 106-46-7)</u> • <u><i>o</i>-Dichlorobenzene (CASRN 95-50-1) has a number of synonyms that can be found on the EPA Chemistry Dashboard. <i>p</i>-Dichlorobenzene (CASRN 106-46-7) has a number of synonyms that can be found on the EPA Chemistry Dashboard.</u> • <u>Forms that should be excluded: <i>m</i>-Dichlorobenzene or 1,3-dichlorobenzene (CASRN 541-73-1) and chlorobenzene (CASRN 108-90-7)</u> • <u>No isomers were included for <i>o</i>-dichlorobenzene (CASRN 95-50-1) and <i>p</i>-dichlorobenzene (CASRN 106-46-7)</u> Human: <u>Any exposure to dichlorobenzene, <i>o</i>-dichlorobenzene (95-50-1), or <i>p</i>-dichlorobenzene (106-46-7), singularly or in mixture (including co-occurrence and mixtures as defined under TSCA), including exposure as measured by internal concentrations of these chemicals or metabolites of these chemicals in a biological matrix (i.e., urine, blood, semen, etc.) where the dichlorobenzenes or synonyms listed above are mentioned).</u> Animal Human Health Models: <u>Any exposure to dichlorobenzene, <i>o</i>-dichlorobenzene (95-50-1), or <i>p</i>-dichlorobenzene (106-46-7) including via water, soil or sediment, diet, gavage, injection, dermal, and inhalation.</u> Animal Ecotoxicological Models and Plants: <u>N/A. (Studies on ecotoxicological animal models or plants were not considered for systematic review of the 2025 updated literature search. At this time for the 2025 updated literature search, ecotoxicological animal model and plant studies that would have otherwise met the original PECO criteria will be tagged as Supplemental, Updated literature search: Meets original PECO criteria but does not fill a critical data gap.</u> Plants: <u>Exposure to dichlorobenzene, <i>o</i>-dichlorobenzene (95-50-1), or <i>p</i>-dichlorobenzene (106-46-7) including via water or soil, with reported concentration and duration. Studies involving exposures to mixtures will be included only if they include exposure to dichlorobenzene, <i>o</i>-</u>

PECO Element	Evidence
	dichlorobenzene (95-50-1), or <i>p</i>-dichlorobenzene (106-46-7) alone. Chemical exposures for aquatic plants where only sediment concentrations are reported from field studies are excluded; laboratory based sediment studies are retained. Screener note: • <u>Environmental Hazard:</u> N/A. Field studies with media concentrations (e.g., surface water, interstitial water, soil, sediment) and/or body/tissue concentrations of animals or plants are to be identified as <u>Supplemental, Field Study</u> only if any biological effects are reported. • <u>Environmental Hazard:</u> N/A. Controlled outdoor experimental studies (e.g., controlled crop/greenhouse studies, mesocosm studies, artificial stream studies) are considered to be laboratory studies (<u>not field studies</u>) because there is a known and prescribed exposure dose(s) and an evaluation of hazardous effect(s). Whereas field studies (e.g., biomonitoring) where there is no prescribed exposure dose(s) do not meet the PECO screening criteria if there is no evaluated hazardous effect, and tagged as <u>Supplemental, Field study</u> if there is an evaluated hazardous effect. • <u>Human Health Animal Hazard:</u> Studies involving exposures to mixtures will be included only if they also include exposure to dichlorobenzene, <i>o</i>-dichlorobenzene (95-50-1), or <i>p</i>-dichlorobenzene (106-46-7) alone. Otherwise, mixture studies in <u>human health animal models</u> will be tagged as <u>Supplemental, Mixture study (human health animal models)</u> and mixture studies in ecotoxicological animal models and in plants will be tagged as <u>Supplemental, Mixture study (plants and eco health animal models)</u>.
Comparator	Human: A comparison or referent population exposed to lower levels (or no exposure/exposure below detection limits) of dichlorobenzene, <i>o</i>-dichlorobenzene (95-50-1), or <i>p</i>-dichlorobenzene (106-46-7) or exposure to dichlorobenzene, <i>o</i>-dichlorobenzene (95-50-1), or <i>p</i>-dichlorobenzene (106-46-7) for shorter periods of time. Any study with a comparison group, control group, or referent group, including: • A comparison group that does not have the disease or outcome of interest (such as a case-control study); or Any study comparing exposed individuals to unexposed or lower-exposed individuals including: • A comparison group with no exposure to the chemical of interest or exposure below detection limits, or • A comparison group exposed to lower levels of the chemical of interest; or • A comparison group exposed to the chemical of interest for shorter periods of time; or Any study assessing the association between a continuous measure of exposure and a health outcome; or For studies in which humans are intentionally exposed to the chemical of interest, an individual can serve as their own control Animal <u>Human Health Models</u> and Plants: A concurrent control group exposed to vehicle-only

PECO Element	Evidence
	treatment and/or untreated control (control could be a baseline measurement). Animal Ecotoxicological Models and Plants: ~~A concurrent control group exposed to vehicle-only treatment and/or untreated control (control could be a baseline measurement).~~ N/A. (Studies on ecotoxicological animal models or plants were not considered for systematic review of the 2025 updated literature search. At this time for the 2025 updated literature search, ecotoxicological animal model and plant studies that would have otherwise met the original PECO criteria will be tagged as <i>Supplemental, Updated literature search: Meets original PECO criteria but does not fill a critical data gap.</i> Screener note: - Human Health Animal Hazard: If no control group is explicitly stated (implied (<i>e.g.</i>, by mention of statistical results that could only be obtained if a control group was present), the study will be marked as <i>Unclear</i> during Title/Abstract Screening. During Full-text Screening, if no control group is explicitly stated, then the study does not meet PECO screening criteria. - Human Health Animal Hazard: For studies in which human health animal models are intentionally exposed to a chemical, the control could be a baseline measurement of the same individual (<i>i.e.</i>, the individual is assessed pre- and post-exposure), and these studies do meet the PECO screening criteria. Also, for studies in which human health animal models are intentionally exposed to a chemical, references that contain experimental designs that do not require a negative or vehicle control group (<i>i.e.</i>, skin sensitization (such as LLNA), LC50 and LD50 completed within an acute timeframe, or dermal irritation studies in which the experimental individual serves as their own control) do meet the PECO screening criteria.
Outcome	Human: All health outcomes (cancer and noncancer) at the organ level or higher. Cancer, tumors, or any other apical health outcome indicative of cancer or pre-cancerous lesions in human study participants. Animal Human Health Models: Only cancer, tumor, or any other <i>in vivo</i> apical health outcome indicative of cancer or pre-cancerous lesions. Studies reporting only mechanistic or <i>in vitro</i> cancer data (<i>e.g.</i>, key characteristics of cancer, mode of action analyses) are to be tagged as <i>Supplemental, Mechanistic</i>. At this time for the 2025 updated literature search, studies reporting data on apical health outcomes NOT related to cancer but that would have otherwise met all other original PECO criteria will be tagged as <i>Supplemental, Updated literature search: Meets original PECO criteria but does not fill a critical data gap.</i> Animal Ecotoxicological Models and Plants: N/A. (Studies on ecotoxicological animal models or plants were not considered for systematic review of the 2025 updated literature search. At this time for the 2025 updated literature search, ecotoxicological animal model and plant studies that would have otherwise met the original PECO criteria will be tagged as <i>Supplemental, Updated literature search: Meets original PECO criteria but does not fill a critical data gap.</i> Screener note: Human Health Animal Hazard: Effects measured at the cellular level of biological

PECO Element	Evidence
	<u>organization and below are to be tagged as <i>Supplemental, Mechanistic</i>.</u>

Table 4-2. Major categories of Potentially Relevant Supplemental Material for *o*-Dichlorobenzene (CASRN 95-50-1) and *p*-Dichlorobenzene (CASRN 106-46-7) – Title and Abstract and Full-Text Screening

Category	Evidence
Mechanistic studies	~~Studies reporting measurements related to a health outcome that inform the biological or chemical events associated with phenotypic effects, in both mammalian and non-mammalian model systems, including <i>in vitro</i>, <i>in vivo</i> (by various non-inhalation routes of exposure), <i>ex vivo</i>, and <i>in silico</i> studies. All studies that report results at the cellular level and lower in both mammalian and non-mammalian model systems, including <i>in vitro</i>, <i>in vivo</i>, <i>ex vivo</i>, and <i>in silico</i> studies. These studies include assays for genotoxicity or mutagenicity using bacteria or yeast.~~
ADME, PBPK, and toxicokinetic	Studies designed to capture information regarding absorption, distribution, metabolism, and excretion (ADME), toxicokinetic studies, or physiologically based pharmacokinetic (PBPK) models.
Field studies	Field studies with media concentrations (<i>e.g.</i> , surface water, interstitial water, soil, sediment) and/or body/tissue concentrations of animals or plants if biological effects reported.
Mixture studies	<u>Experimental</u> mixture studies that are not considered PECO-relevant because they do not contain an exposure or treatment group assessing only the chemical of interest. <u>Human health animal models and ecotoxicological animal models/plants will be tagged separately for mixture studies.</u>
Non-English records	Non-English records will be tracked as potentially relevant supplemental information.
Records with no original data	Records that do not contain original data, such as other agency assessments, informative scientific literature reviews, editorials or commentaries, <u>and also those that may cite secondary data on dermal absorption. This also includes studies of dermal exposure, risk, or modeling that may cite dermal absorption studies.</u>
Conference abstracts	Records that <u>would otherwise meet PECO criteria, but</u> do not contain sufficient documentation to support study evaluation and data extraction.
Case reports or case series	~~Case reports ($n \leq 3$ cases) and case series (non-occupational) will be tracked as potentially relevant supplemental information.~~ <u>Epidemiology:</u> Study designs such as case reports, case series, and case studies without a comparison group will be tagged as Supplemental.

Category	Evidence
	(This Supplemental category does NOT include cohort (prospective cohort, retrospective cohort, etc.), case-control, case-crossover, case-reference, case-cohort, cross-sectional, nested case control, regression, relative risk, risk ratio, odds ratio, hazard ratio, or standardized mortality ratio (SMR) study designs, which if they report cancer related health outcomes will meet the PECO screening criteria but if they report health outcomes NOT related to cancer will be tagged as <i>Supplemental, Updated literature search: Meets original PECO criteria but does not fill a critical data gap</i> .
Susceptible population (no health outcome)	~~Studies that identify potentially susceptible subgroups; for example, studies that focus on a specific demographic, lifestage, or genotype.~~ <u>Epidemiology and Human Health Animal Hazard:</u> Studies that identify potentially susceptible subgroups but do not report a health outcome. Screening note: If biological susceptibility issues are clearly present or <i>strongly</i> implied in the title/abstract, this supplemental tag may be applied at the Title/Abstract Screening. If uncertain at title/abstract, do not apply this tag to the reference during the Title/Abstract Screening.
<u>Updated literature search: Meets original PECO criteria but does not fill a critical data gap</u>	<u>Studies that met the original PECO as published in the <i>Draft Systematic Review Protocol Supporting TSCA Risk Evaluations for Chemical Substances (U.S. EPA, 2021)</i>, however, they did not fill critical data gaps as per the additional criteria described in the revised PECO statement after the updated literature search was completed in 2025.</u>

4.6.2 Further Filtering: Human Health Hazard

References that met the PECO screening criteria and were categorized as having epidemiology information for the evaluation of human health hazard went through a fit-for-purpose further filtering step to determine which studies would move forward to data quality evaluation and data extraction.

4.6.2.1 Epidemiology Studies

To streamline the identification of studies containing dose-response data that had not previously been evaluated by EPA, modifications were implemented to the process described in the 2021 Draft Systematic Review Protocol ([U.S. EPA, 2021](#)). Following PECO-based screening, references that met PECO screening criteria for epidemiology underwent a further filtering process to identify the subset of potentially relevant references that proceeded to data quality evaluation:

4.6.2.1.1 Epidemiology Further Filtering Process

All references that met PECO screening criteria for epidemiology proceeded to a further filtering form in DistillerSR.

The questions on the further filtering form are presented in Table below. This form includes questions to confirm that the initial PECO-based screening determination was correct; identify the exposure routes in the study and the duration for inhalation exposures; tag cancer and non-cancer studies; determine whether the reference contains dose-response data; and identify any intentional dosing studies.

JUNE 2026

References that met PECO screening criteria and also met further filtering criteria proceeded to data quality evaluation and extraction. To proceed to data quality evaluation and extraction, references had to meet the further filtering criteria of containing potentially relevant dose-response data, which was defined based on the study using quantitative information to determine three or more levels of exposure that were used in the analysis or an exposure-response model using a continuous measure of exposure.

Table Epidemiology Further Filtering Form

Epidemiology Further Filtering Form
1. Please select all chemicals that are in the reference.
☐ o-DCB
☐ p-DCB
1a. Does this reference meet PECO and require further filtering? (Select all that Apply)
☐ Yes, meets PECO screening criteria ☐ Supplemental - Mechanistic studies ☐ Supplemental - ADME, PBPK, and toxicokinetic ☐ Supplemental - Susceptible populations (no health outcome) ☐ Supplemental - Mixture studies ☐ Supplemental - Case reports or case series/studies ☐ Supplemental - Non-English records ☐ Supplemental - Records with no original data ☐ Supplemental - Conference abstracts ☐ Supplemental - Exposure studies ☐ NO, DOES NOT meet PECO screening criteria AND doesn't satisfy a data need ☐ Does not meet original PECO but satisfies a data need
[The form ends here unless the “Yes, meets PECO screening criteria” or the “Does not meet original PECO but satisfies a data need” answer is selected.]
1b. Is there missing supporting/supplemental info (SI)? <i>Answer yes if the article has a SI file that is NOT included in the PDF.</i>
☐ Yes
☐ No
2a. Potential Exposure Routes for the Condition of Use (COU) in the study (select <u>all</u> potential routes via which exposure could have occurred in the study population)
<i>Use your best judgment to decide the appropriate exposure route(s).</i>
☐ Inhalation
☐ Dermal/Skin
☐ Ocular/Eye
☐ Food
☐ Drinking water
☐ Teeth or dental patient
☐ Comment if there is substantial uncertainty on your selection [free text]

Epidemiology Further Filtering Form
2b. Exposure Routes specifically assessed via exposure measurement (select all routes that were specifically assessed via exposure measurement in the study)
☐ Inhalation (air sampling, personal air monitoring, area air monitoring, inhalation chamber studies, shower studies, questionnaire assessing inhalation exposure, lung tissue exposure biomarkers, etc.) Check all inhalation exposure durations that apply: ☐ acute inhalation (exposure duration of 24 hours or less) (For a study to be classified as an acute exposure study, the exposure duration must be 24 hours or less at the time of outcome measurement. The outcome doesn't need to be measured immediately after exposure ends, but further exposure cannot occur before outcome measurement. Examples of exposures that might be 24 hours or less include accidental spills and studies in which participants are intentionally dosed with the chemical of interest for 24 hours or less.) ☐ short-term inhalation (exposure duration of more than 24 hours and up to and including 28 days) ☐ chronic inhalation (exposure duration of more than 28 days) ☐ If the duration of exposure is unclear, please select the most relevant choice from the list above. ☐ Acute inhalation (24 hours or less) ☐ Short-term inhalation (>24 hours and <=28 days) ☐ Chronic inhalation (more than 28 days)
Dermal/Skin (wipe sampling, questionnaire assessing dermal exposure, patch testing (intentional dosing), dermal chamber studies, shower studies, skin permeability coefficient, skin exposure biomarkers, etc.)
Ocular/Eye (ocular chamber studies, etc.)
Food (duplicate diet, food sampling, etc.)
Drinking water (water sampling, etc.)
Teeth or dental patient
Other (duration, non-route-specific biomarker (matrices such as blood, urine, etc.), etc.)
3. Does the study assess occupational exposure?
<i>Office workers in their workplace <u>are</u> occupational exposures.</i>
☐ Yes
☐ No
4. Endpoints Analyzed (check all that apply)
☐ Cancer/carcinogenesis Select all cancer health outcome categories included in the study (CANCER ONLY) ☐ Neurological/behavioral ☐ Cardiovascular ☐ Thyroid ☐ Cancer of the Reproductive System ☐ Childhood cancer (before birth through age 18) ☐ Gastrointestinal ☐ Immune/hematological ☐ Hepatic/liver ☐ Mortality ☐ Musculoskeletal ☐ Nutritional/metabolic

Epidemiology Further Filtering Form
☐ Ocular/sensory ☐ Renal/kidney ☐ Lung/respiratory ☐ Skin & connective tissue ☐ Other [free text to specify]
☐ Non-cancer Select all non-cancer health outcome categories included in the study (NON-CANCER ONLY) ☐ Neurological/behavioral ☐ Cardiovascular ☐ Thyroid ☐ Reproductive/developmental ☐ Gastrointestinal ☐ Immune/hematological ☐ Hepatic/liver ☐ Mortality ☐ Musculoskeletal ☐ Nutritional/metabolic ☐ Ocular/sensory ☐ Renal/kidney ☐ Lung/respiratory ☐ Skin & connective tissue ☐ Irritation ☐ Sensitization ☐ Other [free text to specify]
5. Does the study report a quantitative measurement of exposure?
☐ No What non-quantitative exposure data does the study have? ☐ Measure of exposure with only binary data (detected/undetected or exposed/unexposed) ☐ Other - no quantitative measurement
☐ Yes What type(s) of quantitative measurement does the study report (check all that apply)? ☐ Duration of exposure ☐ Quantitative measurement or estimate of concentration or dose of the chemical of interest ▪ Please select any of the following quantitative methods that apply. ☐ Measured concentration or dose ☐ Modeled concentration or dose ☐ Job-Exposure Matrix (JEM) or similar ☐ Concentration or dose per time period (ex: mg/day, mg/kg/day, ml/hour, ml/year, TWA, etc.) ☐ Biomarker of exposure with quantitative data ☐ Other (please specify) [free text]
6. Did the study <u>report</u> any of the following exposure levels (check all that apply)?
☐ Three or more levels of exposure (<i>i.e.</i>, referent group + 2 or more groups) but didn't use these levels in any analyses of the association between the chemical of interest and a health outcome
☐ Three or more levels of exposure (<i>i.e.</i>, referent group + 2 or more groups), which were used in the analyses of the association between the chemical of interest and a health outcome

Epidemiology Further Filtering Form
☐ A continuous measure of exposure but didn't use this measurement in any model or analyses of the association between the chemical of interest and a health outcome
☐ An exposure-response model using a continuous measure (or estimate) of exposure
☐ Other
7. Questions addressing whether the study assesses the association between the exposure to the chemical of interest and a health outcome:
7a. Is the exposure only assessed as part of a mixture and the specific contribution of the chemical of interest is not separated out?
☐ Yes ☐ No
7b. Does the study only focus on exposure to a different chemical with the chemical of interest as an effect modifier?
☐ Yes ☐ No
7c. Does the study only focus on a third variable's effect on the relationship between exposure to the chemical of interest and an outcome?
☐ Yes ☐ No
8. Did the study report a quantitative measurement or estimate of concentration or dose of the chemical of interest (based on Question 5) AND Use this quantitative information to define three or more levels of exposure (<i>i.e.</i> , referent group + 2 or more groups) or an exposure-response model using a continuous measure of exposure, which were used in the analyses of the association between exposure to the chemical of interest and a health outcome (based on Question 6)? THIS ANSWER IS AUTO-CALCULATED > DO NOT EDIT ANSWER
☐ Yes
☐ No
9. Please comment on whether the study contains potentially useful dose-response data and note any questions you have. [free text]
10. Select the applicable study design:
☐ This reference contains only observational epidemiology data
☐ This reference contains only human intentional dosing or controlled exposure epidemiology data (studies in which people were intentionally exposed to the chemical of interest)
☐ This reference contains BOTH observational and intentional dosing epidemiology data
11. Please select all {Potentially Exposed and Susceptible Subpopulations} PESS categories relevant to the reference.
Lifestage (select all that apply) (Specific ages for the categories below may vary. Select the category if the study included analyses for that particular category) Select all lifestages
☐ Pregnant people (parent) or embryo/fetus (developmental) (conception through birth)
☐ Infants (birth through <12 months)

Epidemiology Further Filtering Form
○ Children (age 1 year through <11 years) ○ Adolescents (age 11 years through <21 years) ○ Older adults (>=65 years) ○ Other PESS lifestage specified in the reference (such as studies specifying a certain age range as being more likely to be either exposed or susceptible)
○ Studies focusing on reproductive parameters
○ Pre-existing Disease (ex. altered metabolism, behaviors, treatments related to condition)
○ Lifestyle Activities (ex. exercise, smoking)
○ Occupational
○ Consumers of targeted/niche products
○ Geography/site-specific (ex. downstream of release sites)
○ Sociodemographic status (ex. home near exposure source)
○ Nutrition (ex. contaminated food source)
○ Genetics/Epigenetics (ex. genetic variants that increase susceptibility)
○ Unique Activities (ex. sweat lodges)
○ Aggregate Exposures (ex. multiple air exposure sources)
○ Other Chemical and Non-chemical stressors (ex. exposure to other substances that affect same organ as test chemical)
○ Tribal Affiliation
○ Other PESS category specified in the reference
12. Should this reference move on to data quality evaluation and extraction?
○ Yes, this reference meets the PECO screening criteria AND MEETS further filtering criteria
○ Yes, this reference doesn't meet PECO screening criteria BUT satisfies a data need
○ No, not at this time. This reference meets the PECO screening criteria but DOES NOT meet further filtering criteria
○ No, this reference does NOT meet the PECO screening criteria or is Supplemental
13. Comments (optional)
[free text]

4.6.2.1.2 Epidemiology Further Filtering Results

Of the eleven references that met epidemiology PECO screening criteria for *o*-dichlorobenzene, three references ([Rodrigues et al., 2020](#); [Von Ehrenstein et al., 2016](#); [Heck et al., 2015](#)) met the further filtering criteria. These three references proceeded to data quality evaluation and extraction. The other eight references that met PECO screening criteria did not meet further filtering criteria and thus are not in the data quality evaluation and extraction tables.

4.7 Dermal Absorption

EPA developed a PECO statement (Table 4-1 and Table 4-2) to screen references for dermal absorption resulting from *o*-dichlorobenzene exposure. Screening was conducted on the combined set of references that included (1) data sources from the additional filtering exercise described in Section 3.1; (2) references tagged as absorption, distribution, metabolism, and elimination (ADME) data; and (3) sources submitted in the 2021 8(d) rule. Two reviewers manually screen each study at both the TIAB and full-text screening

steps. Figure 4-6 presents the number of references screened and those that passed PECO screening criteria at TIAB and full-text screening steps.

Table 4-1. PECO Statement for Dermal Exposure References for *o*-Dichlorobenzene

PECO Element	Evidence
P	Tests of the single toxicants on <i>ex vivo</i> tissues (including permeation and retention studies) or on live, whole, taxonomically verifiable organisms are included. Human: Any population and life stage (occupational or general population, including children and other sensitive populations). Animal: All human health models, including (but not limited to) rat, mouse, rabbit, dog, hamster, guinea pig, cat, non-human primate, and pig. Supplemental: Tests using 3D human skin equivalent/reconstructed tissue models (<i>e.g.</i>, EpiDerm, EPISKIN) or any other <i>in vitro</i> systems are considered supplemental.
E	Human and Animal: Any quantified dermal exposure to <i>o</i>-dichlorobenzene or 1, 2-dichlorobenzene (CASRN 95-50-1) or in a vehicle, including exposure that occurs <i>in vivo</i> or <i>ex vivo</i> for any duration. Studies are included only if exposure is intentional and quantified. If exposure is not intentional and is not experimentally controlled, the study is excluded. For example, studies of absorption in workers will be excluded, even if exposure has been quantified. Studies assessing exposures to mixtures (<i>i.e.</i>, containing substances other than a vehicle) will be included only if they also contain an exposure or treatment group assessing the chemical of interest alone or in aqueous solution. Supplemental: <i>In vitro</i> exposures and/or studies in which exposure occurs only to a mixture containing one or more of the chemicals of interest.
C	Human and Animal: Any or no comparison group.
O	Human and Animal: Any quantitative assessment of the rate or extent of dermal absorption of the substance. Measurements may include the amount of substance that has passed through the skin, or was retained in the skin, distributed within the organism (<i>e.g.</i>, blood and tissue concentrations), and/or excreted by the organism (<i>e.g.</i>, through urine, feces, or expired air). Absorption may be measured directly (by chemical analysis for the substance and/or its metabolites) or indirectly (<i>e.g.</i>, measurement of radioactivity if using a radio-labelled test substance). Absorption may be quantified via determination of percent absorption, dermal/penetrative flux rate, or dermal penetration coefficient (Kp).

Table 4-2. Major categories of “potentially relevant supplemental material”

Category	Evidence
<i>In vitro</i> studies	Tests using 3D human skin equivalent/reconstructed tissue models (<i>e.g.</i> , EpiDerm, EPISKIN) or any other <i>in vitro</i> systems.
Mixture studies	Experimental mixture studies that are not considered PECO-relevant because they do not contain an exposure or treatment group assessing only the chemical of interest, but that otherwise meet PECO criteria.
Non-English records	Non-English records that appear to meet PECO criteria.
Records with no original data	Records that do not contain original data, such as other agency assessments, informative scientific literature reviews, editorials, or commentaries, but may cite secondary data on dermal absorption. This also includes studies of dermal exposure,

	risk, or modeling that may cite dermal absorption studies.
Conference abstracts	Records that would otherwise meet PECO criteria, but do not contain sufficient documentation to support study evaluation and data extraction.

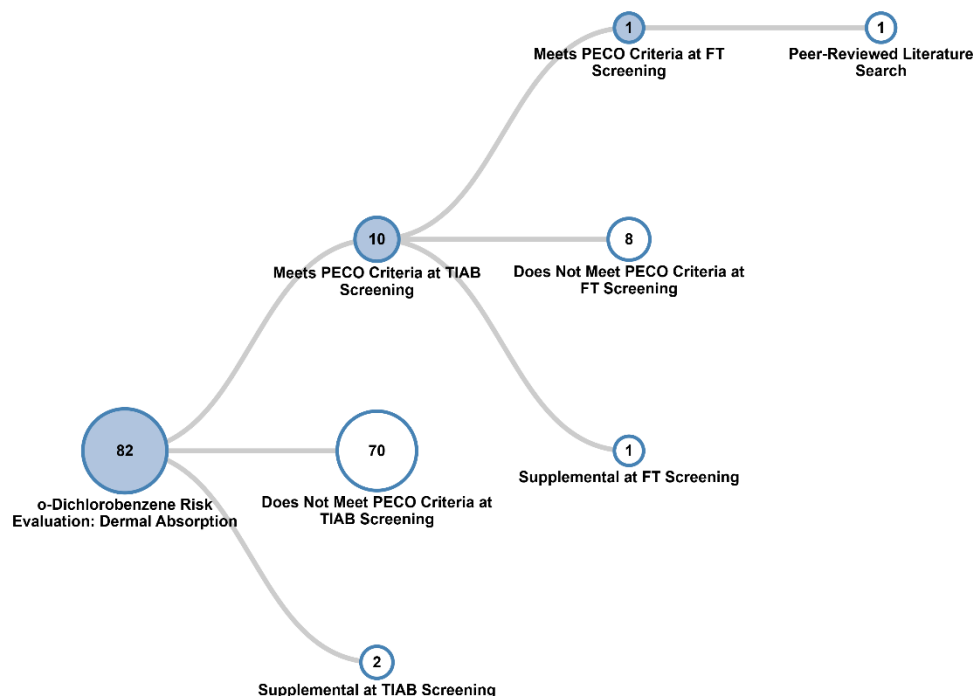


Figure 4-6. Literature Inventory Tree – Dermal Absorption for *o*-Dichlorobenzene

View the interactive literature inventory tree in [HAWC](#). Data in this figure represents all references obtained from the publicly available databases and gray literature references searches that were included in systematic review as of December 22, 2025. Additional data may be added to the interactive version as they become available.

5 DATA EVALUATION AND DATA EXTRACTION

Data evaluation and extraction were conducted as described in Sections 5 and 6 of the *2021 Draft Systematic Review Protocol* (U.S. EPA, 2021). Data evaluation is the systematic review step in which EPA assesses quality of the individual data sources using the evaluation strategies and criteria for each discipline (e.g., physical and chemical property data; fate and transport data; occupational exposure and environmental release data; general population, consumer, and environmental exposure data; environmental hazard; human health hazard) or sub-discipline (e.g., animal toxicity or epidemiology). The data quality evaluation method uses a structured framework with predefined criteria for each type of data/information source. Data extraction is the systematic review step in which EPA uses structured forms or templates to extract quantitative and qualitative data and information from references that meet screening criteria. The overall goal is to provide transparency, consistency, and as much objectivity as possible to the data quality evaluation and extraction processes along with meeting the TSCA scientific standards in section 26(h).

References that meet screening criteria following full-text screening will generally proceed to data quality evaluation and extraction steps, however one clarification to the procedures outlined in Section 6 of the *2021 Draft Systematic Review Protocol* is that in situations where EPA is unable to extract data/information from sources that meet screening criteria (e.g., formatting prohibits accurate extraction), that source may not have extracted data to present in the risk evaluation or respective supplemental

documents. The systematic review supplemental files that contain results from the data quality evaluation and extraction systematic review steps may use updated templates from those that were provided in the *2021 Draft Systematic Review Protocol* ([U.S. EPA, 2021](#)) because the purpose of these supplemental documents is to accommodate the data needs for each respective risk evaluation. The following sections describe the data quality and extraction process followed by each discipline or sub-discipline to address various information needs for the Draft Risk Evaluation for *o*-dichlorobenzene ([U.S. EPA, 2026n](#)) and any clarifications or updates regarding these systematic review steps as described in the *2021 Draft Systematic Review Protocol* ([U.S. EPA, 2021](#)).

5.1 Physical and Chemical Properties

As described in the *2021 Draft Systematic Review Protocol*, evaluation and extraction followed the steps outlined in Sections 5, 6, and 6.1 ([U.S. EPA, 2021](#)). The data quality criteria for physical and chemical property data are summarized in Appendix K of the *2021 Draft Systematic Review Protocol*. The *Data Quality Evaluation and Data Extraction Information for Physical and Chemical Properties for o-Dichlorobenzene* ([U.S. EPA, 2026g](#)) provides details of the data extracted and evaluated, including metric ratings and the overall study quality determination for each data source.

5.2 Environmental Fate and Transport Properties

As described in the *2021 Draft Systematic Review Protocol*, evaluation and extraction followed the steps outlined in Sections 5, 6, and 6.2 ([U.S. EPA, 2021](#)). The data quality criteria for environmental fate data are summarized in Appendix L of the systematic review protocol. Appendix L.4 describes how the overall quality of fate data or information were weighted according to an ordinal system corresponding to *High* (1), *Medium* (2), or *Low* (3) to quantitatively or qualitatively support the risk evaluations. EPA does not plan to use data rated as *Uninformative* (4). Table_Apx L4 illustrates the possible quality rankings across the selected metrics for environmental fate data with examples in Table_Apx L5, Table_Apx L6 and Table_Apx L7 ([U.S. EPA, 2021](#)). Specific fate data quality ranking quality criteria are in Table_Apx L8. The *Data Quality Evaluation and Data Extraction Information for Environmental Fate and Transport for o-Dichlorobenzene* ([U.S. EPA, 2026e](#)) provides details of the data extracted and evaluated, including metric rating and the overall study quality determination for each data source.

5.3 Environmental Release and Occupation Exposure

As described in the *2021 Draft Systematic Review Protocol*, evaluation and extraction followed the steps outlined in Sections 5, 6, and 6.2 ([U.S. EPA, 2021](#)). The data quality criteria for environmental release and occupational exposure data are summarized in Appendix M of the *2021 Draft Systematic Review Protocol* ([U.S. EPA, 2021](#)). The *Data Quality Evaluation and Data Extraction Information for Environmental Release and Occupational Exposure for o-Dichlorobenzene* ([U.S. EPA, 2026f](#)) details the data extracted and evaluated, including metric rating and the overall study quality determination for each data source.

5.4 General Population, Consumer, and Environmental Exposure

As described in the *2021 Draft Systematic Review Protocol*, data quality evaluation and extraction generally followed the steps outlined in Section 5 and 6 ([U.S. EPA, 2021](#)). However, a few updates were made to the data quality evaluation metrics for some evidence streams (*i.e.*, study types) since the metrics were published in the *2021 Draft Systematic Review Protocol* ([U.S. EPA, 2021](#)). Most of the changes were editorial or minor clarifications, including the standardization of some metrics that apply to multiple evidence streams, where appropriate. For example, in the quality assurance/quality control (QA/QC) metric for evaluating monitoring and experimental evidence streams, the acronym QA/QC was defined and

replaced all references to quality assurance and quality control when occurring separately or together, and the term “QA/QC techniques” was changed to “QA/QC measures,” which already appeared in the metrics.

A few metrics applicable to multiple evidence streams were slightly modified to better fit some of the unique situations that frequently arise for a certain type of evidence stream (*e.g.*, databases). For example, some metrics were updated to clarify the intent of the metric and better account for variation in types of evidence included in one grouping (*e.g.*, experiments involving chamber studies vs. product concentration assessments). The domains did not change, however see below for the changes and updates made to the data evaluation metrics for the respective evidence types (*i.e.*, monitoring, experimental studies and databases) as presented in Section 5.4.1. No changes were made to the data evaluation metrics for modeling data, as described in Appendix N.6.2, or to the data evaluation metrics for completed exposure assessments and risk characterizations, as described in Appendix N.6.7 in the *2021 Draft Systematic Review Protocol*, respectively ([U.S. EPA, 2021](#)). Data quality evaluations for references that met PECO screening criteria are included in the *Data Quality Evaluation Information for General Population, Consumer, and Environmental Exposure for o-Dichlorobenzene* ([U.S. EPA, 2026i](#)), referred to hereafter as the “*o*-Dichlorobenzene Data Quality Evaluation Information for General Population, Consumer, and Environmental Exposure.”

Data extraction of general population, consumer, and environmental exposure data and information was conducted as described in Section 6 of the *2021 Draft Systematic Review Protocol* ([U.S. EPA, 2021](#)). However, with respect to information stored within databases, if EPA has access to the data tables, EPA does not conduct a separate data extraction because the data are more accessible and have additional context in the original database format. Data present in the database when the database underwent full-text screening are available in the HERO database ([CDC, 2022](#); [U.S. EPA, 2022](#); [U.S. EPA et al., 2022](#); [QuanTech, 2021](#)), along with the date the data were downloaded. If a reference (*e.g.*, peer-reviewed reference) presents data from a database that did not undergo systematic review directly (*e.g.*, a foreign database that is not publicly accessible), the data would be extracted from the reference to the extent possible; this did not apply to references that underwent systematic review for this chemical.

As mentioned above in Section 5, references may not undergo data extraction, regardless of the overall quality determination, if they contain no extractable data points (*e.g.*, values are contained in a non-digitizable figure or are representative of unspecified media or treatment processes). On the other hand, there are references that have many reported endpoints that meet PECO screening criteria for a respective chemical risk evaluation, making it difficult to include all the data in the chemical-specific data extraction supplemental file. When a reference meets PECO screening criteria, the reference receives a data quality evaluation, and the data in the reference are still considered in the Risk Evaluation, whether or not the included data are extracted in DistillerSR and appear among the chemical-specific extractions in the Systematic Review Supplemental File: Data Extraction Information for General Population, Consumer, and Environmental Exposure. In addition, there may be other reasons that EPA decides not to extract all the data from a reference that undergoes data evaluation; EPA extracts the data that are most relevant, given the needs of the assessment. As seen in Figure 4-5, the extracted *o*-dichlorobenzene data are from targeted evaluated references that have an OQD of High assuming that such studies would be distinctly supportive to the *o*-dichlorobenzene exposure assessment. The extracted data provide a high level of confidence for characterizing general population, consumer, and environmental exposure and for meeting assessment needs. This constitutes an update to Section 6 of the *2021 Draft Systematic Review Protocol* ([U.S. EPA, 2021](#)). Extraction forms, templates, and decisions are tailored to fit the data extraction needs for each risk evaluation.

The types of fields extracted vary by evidence stream and generally followed Section 6.3 of the *2021 Draft Systematic Review Protocol* with regard to the data characteristics captured ([U.S. EPA, 2021](#)). Examples of types of data extracted and the extraction formats for the evidence streams identified through systematic review to evaluate environmental, general population, and consumer exposure data are listed in the extraction tables provided in the *Data Extraction Information for General Population, Consumer, and Environmental Exposure for o-Dichlorobenzene* ([U.S. EPA, 2026d](#)), referred to hereafter as the “o-Dichlorobenzene Data Extraction Information for General Population, Consumer, and Environmental Exposure.”

5.4.1 Data Quality Evaluation Metric Updates

The data evaluation metrics for the monitoring, experimental, and database evidence streams, are presented below in Table 5-1, Table 5-2, and Table 5-3, respectively. Each table shows which data evaluation metrics changed since the publication of the *2021 Draft Systematic Review Protocol* ([U.S. EPA, 2021](#)). Other data quality criteria for studies on consumer, general population, and environmental exposure appear in Appendix N of the *2021 Draft Systematic Review Protocol* ([U.S. EPA, 2021](#)). For the modeling, completed exposure assessments, and risk characterization evidence streams, there were no changes made to the data evaluation metrics since the *2021 Draft Systematic Review Protocol* was published. The criteria for modeling studies appear in Table_Apx N-9 of the *2021 Draft Systematic Review Protocol*, and criteria for completed exposure assessments and risk characterizations appear in Table_Apx N-19. In some cases, references can meet the criteria for two exposure evidence streams, and they can also be reviewed and meet criteria for other disciplines. Upon review, each study is evaluated and extracted using the criteria for the most appropriate and applicable evidence streams given the information therein. In order to make it easier for the reader to see changes made to the data evaluation metrics, the following conventions are used: text inserted is underlined, and text deleted is in ~~striketrough~~.

Table 5-1. Updated Data Quality Evaluation Criteria for Monitoring Data Sources

Data Quality Rating	Description
<u>Domain 1. Reliability</u>	
<u>Metric 1. Sampling methodology</u>	
High	Samples were collected according to publicly available SOPs that are scientifically sound and widely accepted (<i>i.e.</i>, from a source generally ~~using~~ <u>known to use</u> sound methods and/or approaches) for the chemical and media of interest. Example SOPs include U.S. Geological Survey (USGS) “National Field Manual for the Collection of Water-Quality Data,” EPA’s “Ambient Air Sampling” (SESDPROC-303-R5), etc. OR The sampling protocol used was not a publicly available SOP from a source generally ~~known to use~~ <u>using</u> sound methods and/or approaches, but the sampling methodology is clear, appropriate (<i>i.e.</i>, scientifically sound), and similar to widely accepted protocols for the chemical and media of interest. All pertinent sampling information is provided in the data source or companion source. Examples include: • sampling equipment • sampling procedures/regimen • sample storage conditions/duration • performance/calibration of sampler • study site characteristics • matrix characteristics

Data Quality Rating	Description
Medium	Sampling methodology is discussed in the data source or companion source and is generally appropriate (<i>i.e.</i>, scientifically sound) for the chemical and media of interest; however, one or more pieces of sampling information is not described. The missing information is unlikely to have a substantial impact on results. OR Standards, methods, protocols, or test guidelines may not be widely accepted, but a successful validation study for the new/unconventional procedure was conducted prior to the sampling event and is consistent with sound scientific theory and/or accepted approaches. Or a review of information indicates the methodology is acceptable and differences in methods are not expected to lead to lower quality data.
Low	Sampling methodology is only briefly discussed; therefore, most sampling information is missing and likely to have a substantial impact on results. AND/OR The sampling methodology does not represent best sampling methods, protocols, or guidelines for the chemical and media of interest (<i>e.g.</i>, outdated [but still valid] sampling equipment or procedures, long storage durations). AND/OR There are some inconsistencies in the reporting of sampling information (<i>e.g.</i>, differences between text and tables in data source, differences between standard method and actual procedures reported to have been used, etc.) that led to a low confidence in the sampling methodology used.
Critically Deficient	The sampling methodology is not discussed in the data source or companion source. AND/OR Sampling methodology is not scientifically sound or is not consistent with widely accepted methods/approaches for the chemical and media being analyzed (<i>e.g.</i>, inappropriate sampling equipment, improper storage conditions). AND/OR There are numerous inconsistencies in the reporting of sampling information, resulting in high uncertainty in the sampling methods used.
Not rated/not applicable	
Reviewer's comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
Metric 2. Analytical methodology	

Data Quality Rating	Description
High	Samples were analyzed according to publicly available analytical methods that are scientifically sound and widely accepted (<i>i.e.</i>, from a source generally <u>using known to use</u> sound methods and/or approaches) and are appropriate for the chemical and media of interest. Examples include EPA SW-846 Methods, NIOSH Manual of Analytical Methods 5th Edition, etc. OR The analytical method used was not a publicly available method from a source generally <u>using known to use</u> sound methods and/or approaches, but the methodology is clear and appropriate (<i>i.e.</i>, scientifically sound) and similar to widely accepted protocols for the chemical and media of interest. All pertinent sampling information is provided in the data source or companion source. Examples include: • extraction method • analytical instrumentation (required) • instrument calibration • limit of quantitation (LOQ), LOD, detection limits, and/or reporting limits • recovery samples • biomarker used (if applicable) • matrix-adjustment method (<i>i.e.</i>, creatinine, lipid, moisture)
Medium	Analytical methodology is discussed in detail and is clear and appropriate (<i>i.e.</i>, scientifically sound) for the chemical and media of interest; however, one or more pieces of analytical information is not described. The missing information is unlikely to have a substantial impact on results. AND/OR The analytical method may not be standard/widely accepted, but a method validation study was conducted prior to sample analysis and is expected to be consistent with sound scientific theory and/or accepted approaches. AND/OR Samples were collected at a site and immediately analyzed using an on-site mobile laboratory, rather than shipped to a stationary laboratory.
Low	Analytical methodology is only briefly discussed. Analytical instrumentation is provided and consistent with accepted analytical instrumentation/methods. However, most analytical information is missing and likely to have a substantial impact on results. AND/OR Analytical method is not standard/widely accepted, and method validation is limited or not available. AND/OR Samples were analyzed using field screening techniques. AND/OR LOQ, LOD, detection limits, and/or reporting limits not reported. AND/OR There are some inconsistencies or possible errors in the reporting of analytical information (<i>e.g.</i>, differences between text and tables in data source, differences between standard method and actual procedures reported to have been used, etc.) which leads to a lower confidence in the method used.

Data Quality Rating	Description
Critically Deficient	Analytical methodology is not described, including analytical instrumentation (<i>i.e.</i>, HPLC, GC). AND/OR Analytical methodology is not scientifically appropriate for the chemical and media being analyzed (<i>e.g.</i>, method not sensitive enough, not specific to the chemical, out of date). AND/OR There are numerous inconsistencies in the reporting of analytical information, resulting in high uncertainty in the analytical methods used.
Not rated/ Not applicable	
Reviewer's comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
Metric 3. Selection of biomarker of exposure	
High	Biomarker in a specified matrix is known to have an accurate and precise quantitative relationship with external exposure, internal dose, or target dose (<i>e.g.</i>, previous studies (or the current study) have indicated the biomarker of interest reflects external exposures). AND Biomarker (parent chemical or metabolite) is derived from exposure to the chemical of interest.
Medium	Biomarker in a specified matrix has accurate and precise quantitative relationship with external exposure, internal dose, or target dose. AND Biomarker is derived from multiple parent chemicals, not only the chemical of interest, but there is a stated method to apportion the estimate to only the chemical of interest
Low	Biomarker in a specified matrix has accurate and precise quantitative relationship with external exposure, internal dose, or target dose. AND Biomarker is derived from multiple parent chemicals, not only the chemical of interest, and there is NOT an accurate method to apportion the estimate to only the chemical of interest. OR Biomarker in a specified matrix is a poor surrogate (low accuracy and precision) for exposure/dose.
Critically Deficient	Not applicable. A study will not be deemed critically deficient based on the use of biomarker of exposure.
Not rated/ applicable	Metric is not applicable to the data source.

Data Quality Rating	Description
Reviewer's comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
<u>Domain 2.</u> Representative	
<u>Metric 4.</u> Geographic area	
High	Geographic location(s) is reported, discussed, or referenced.
Medium	Not applicable. This metric is dichotomous (<i>i.e.</i> , high vs. critically deficient).
Low	Not applicable. This metric is dichotomous (<i>i.e.</i> , high vs. critically deficient).
Critically Deficient	Geographic location is not reported, discussed, or referenced.
Not rated/ not applicable	
Reviewer's comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
<u>Metric 5.</u> Temporality	
High	Timing of sample collection for monitoring data is consistent with current or recent exposures (within 5 years) may be expected.
Medium	Timing of sample collection for monitoring data is less consistent with current or recent exposures (>5 to 15 years) may be expected.
Low	Timing of sample collection for monitoring data is not consistent with when current exposures (>15 years old) may be expected and likely to have a substantial impact on results.
Critically Deficient	Timing of sample collection for monitoring data is not reported, discussed, or referenced.
Not rated/ Not applicable	
Reviewer's comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
<u>Metric 6.</u> Spatial and temporal variability	
High	Sampling approach accurately captures variability of environmental contamination in population/scenario/media of interest based on the heterogeneity/homogeneity and dynamic/static state of the environmental system. For example: • Large sample size (<i>i.e.</i>, ≥ 10 or <u>more</u> samples for a single scenario). • Use of replicate samples. • Use of systematic or continuous monitoring methods. • Sampling over a sufficient period of time to characterize trends. • For urine, 24-hour samples are collected (vs. first morning voids or spot).

Data Quality Rating	Description
	For biomonitoring studies, the timing of sample collected is appropriate based on chemical properties (e.g., half-life), the pharmacokinetics of the chemical (e.g., rate of uptake and elimination), and when the exposure event occurred.
Medium	Sampling approach likely captures variability of environmental contamination in population/scenario/media of interest based on the heterogeneity/homogeneity and dynamic/static state of the environmental system. Some uncertainty may exist, but it is unlikely to have a substantial impact on results. For example: Moderate sample size (i.e., 5–10 samples for a single scenario), or - Use of judgmental (non-statistical) sampling approach, or - No replicate samples. - For urine, first morning voids or pooled spot samples.
Low	Sampling approach poorly captures variability of environmental contamination in population/scenario/media of interest. For example: Small sample size (i.e., <5 samples), or - Use of haphazard sampling approach, or - No replicate samples, or - Grab or spot samples in single space or time, or - Random sampling that does not include all periods of time or locations, or - For urine, un-pooled spot samples.
Critically Deficient	Sample size is not reported. Single sample collected per data set. For biomonitoring studies, the timing of sample collected is not appropriate based on chemical properties (e.g., half-life), the pharmacokinetics of the chemical (e.g., rate of uptake and elimination), and when the exposure event occurred.
Not rated/not applicable	
Reviewer's comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
Metric 7. Exposure scenario	
High	The data closely represent relevant exposure scenario (i.e., the population/scenario/media of interest). Examples include: - amount and type of chemical/product used - source of exposure - method of application or by-stander exposure - use of exposure controls - microenvironment (location, time, climate)
Medium	The data likely represent the relevant exposure scenario (i.e., population/scenario/media of interest). One or more key pieces of information may not be described but the deficiencies are unlikely to have a substantial impact on the characterization of the exposure scenario. AND/OR

Data Quality Rating	Description
	If surrogate data, activities seem similar to the activities within scope.
Low	The data lack multiple key pieces of information, and the deficiencies are likely to have a substantial impact on the characterization of the exposure scenario. AND/OR There are some inconsistencies or possible errors in the reporting of scenario information (<i>e.g.</i>, differences between text and tables in data source, differences between standard method and actual procedures reported to have been used, etc.) which leads to a lower confidence in the scenario assessed. AND/OR If surrogate data, activities have lesser similarity but are still potentially applicable to the activities within scope.
Critically Deficient	If reported, the exposure scenario discussed in the monitored study does not represent the exposure scenario of interest for the chemical.
Not rated/ Not applicable	
Reviewer's comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
Domain 3. Accessibility/clarity	
Metric 8. Reporting of results	
High	Supplementary or raw data (<i>i.e.</i>, individual data points) are reported, allowing summary statistics to be calculated or reproduced. AND Summary statistics are detailed and complete. Example parameters include: • Description of data set summarized (<i>i.e.</i>, location, population, dates, etc.) • Range of concentrations or percentiles • Number of samples in data set • Frequency of detection • Measure of variation (coefficient of variation [CV], standard deviation) • Measure of central tendency (mean, geometric mean, median) • Test for outliers (if applicable) AND Both adjusted and unadjusted results are provided (<i>i.e.</i>, correction for void completeness in urine biomonitoring, whole-volume or lipid adjusted for blood biomonitoring, wet or dry weight for environmental tissue samples or soil samples) [only if applicable].
Medium	Supplementary or raw data (<i>i.e.</i>, individual data points) are not reported, and therefore summary statistics cannot be reproduced. AND/OR Summary statistics are reported but are missing one or more parameters (see description for high). AND/OR Only adjusted or unadjusted results are provided, but not both [only if applicable].

Data Quality Rating	Description
Low	Supplementary data are not provided, and summary statistics are missing most parameters (see description for high). AND/OR There are some inconsistencies or errors in the results reported, resulting in low confidence in the results reported (e.g., differences between text and tables in data source, less appropriate statistical methods).
Critically Deficient	There are numerous inconsistencies or errors in the calculation and/or reporting of results, resulting in highly uncertain reported results.
Not Rated/ Not Applicable	
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
Metric 9. Quality assurance	
High	The study quality assurance/quality control (QA/QC) measures and all pertinent ~~quality assurance~~ QA/QC information is provided in the data source or companion source. Examples include: • Field, laboratory, and/or storage recoveries. • Field and laboratory control samples. • Baseline (pre-exposure) samples. • Biomarker stability • Completeness of sample (i.e., creatinine, specific gravity, osmolality for urine samples) AND No QA/QC ~~quality control~~ issues were identified, or any identified issues were minor and adequately addressed (i.e., correction for low recoveries, correction for completeness).
Medium	The study applied and documented ~~quality assurance/quality control~~ QA/QC measures; however, one or more pieces of QA/QC information is not described . Missing information is unlikely to have a substantial impact on results. AND No QA/QC ~~quality control~~ issues were identified, or any identified issues were minor and addressed (i.e., correction for low recoveries, correction for completeness).
Low	~~QA/QC measures~~ ~~Quality assurance/quality control techniques~~ and results were not directly discussed but <u>are</u> implied through the study's use of standard field and laboratory protocols. AND/OR Deficiencies were noted in ~~quality assurance/quality control~~ QA/QC measures that are likely to have a substantial impact on results. AND/OR There are some inconsistencies in the ~~quality assurance~~ QA/QC measures reported, resulting in low confidence in the QA/QC ~~quality assurance/control~~ measures taken and results (e.g., differences between text and tables in data source).

Data Quality Rating	Description
Critically Deficient	QA/QC issues have been identified which significantly interfere with the overall reliability of the study.
Not Rated/ Not Applicable	
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
Domain 4. Variability and uncertainty	
Metric 10. Variability and uncertainty	
High	The study characterizes variability in the population/media studied. AND Key uncertainties, limitations, and data gaps have been identified. AND The uncertainties are minimal and have been characterized.
Medium	The study has limited characterization of variability in the population/media studied. AND/OR The study has limited discussion of key uncertainties, limitations, and data gaps. AND/OR Multiple uncertainties have been identified but are unlikely to have a substantial impact on results.
Low	The characterization of variability is absent. AND/OR Key uncertainties, limitations, and data gaps are not discussed. AND/OR Uncertainties identified may have a substantial impact on the exposure the exposure assessment
Critically Deficient	Estimates are highly uncertain based on characterization of variability and uncertainty.
Not Rated/ Not Applicable	
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>

Table 5-2. Updated Evaluation Criteria for Experimental Data Sources

Data Quality Rating	Metric Description
Domain 1. Reliability	
Metric 1. Sampling Methodology and Conditions	

Data Quality Rating	Metric Description
High	Samples were collected according to publicly available SOPs, methods, protocols, or test guidelines that are scientifically sound and widely accepted from a source generally known to use sound methods and/or approaches such as EPA, NIST, American Society for Testing and Materials, ISO, and ACGIH. OR The sampling protocol used was not a publicly available SOP from a source generally known to use sound methods and/or approaches, but the sampling methodology is clear, appropriate (<i>i.e.</i>, scientifically sound), and similar to widely accepted protocols for the chemical and media of interest. All pertinent sampling information is provided in the data source or companion source. Examples include: • sampling conditions (<i>e.g.</i>, temperature, humidity) • sampling equipment and procedures • sample storage conditions/duration • performance/calibration of sampler
Medium	Sampling methodology is discussed in the data source or companion source and is generally appropriate (<i>i.e.</i>, scientifically sound) for the chemical and media of interest, however, one or more pieces of sampling information is not described. The missing information is unlikely to have a substantial impact on results. OR Standards, methods, protocols, or test guidelines may not be widely accepted, but a successful validation study for the new/unconventional procedure was conducted prior to the sampling event and is consistent with sound scientific theory and/or accepted approaches.
Low	Sampling methodology is only briefly discussed. Therefore, most sampling information is missing and likely to have a substantial impact on results. AND/OR The sampling methodology does not represent best sampling methods, protocols, or guidelines for the chemical and media of interest (<i>e.g.</i>, outdated (but still valid) sampling equipment or procedures, long storage durations). AND/OR There are some inconsistencies in the reporting of sampling information (<i>e.g.</i>, differences between text and tables in data source, differences between standard method and actual procedures reported to have been used, etc.) which lead to a low confidence in the sampling methodology used.
Critically Deficient	The sampling methodology is not discussed in the data source or companion source. AND/OR Sampling methodology is not scientifically sound or is not consistent with widely accepted methods/approaches for the chemical and media being analyzed (<i>e.g.</i>, inappropriate sampling equipment, improper storage conditions). AND/OR There are numerous inconsistencies in the reporting of sampling information, resulting in high uncertainty in the sampling methods used.
Not Rated/Not Applicable	

Data Quality Rating	Metric Description
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
Metric 2. Analytical methodology	
High	Samples were analyzed according to publicly available analytical methods that are scientifically sound and widely accepted (<i>i.e.</i>, from a source generally using sound methods and/or approaches) and are appropriate for the chemical and media of interest. Examples include EPA SW-846 Methods, NIOSH Manual of Analytical Methods 5th Edition, etc. OR The analytical method used was not a publicly available method from a source generally known to use sound methods and/or approaches, but the methodology is clear and appropriate (<i>i.e.</i>, scientifically sound) and similar to widely accepted protocols for the chemical and media of interest. All pertinent <u>analytical sampling</u> information is provided in the data source or companion source. Examples include: • extraction method • analytical instrumentation (required) • instrument calibration • LOQ, LOD, detection limits, and/or reporting limits • recovery samples • biomarker used (if applicable) • matrix-adjustment method (<i>i.e.</i>, creatinine, lipid, moisture)
Medium	Analytical methodology is discussed in detail and is clear and appropriate (<i>i.e.</i>, scientifically sound) for the chemical and media of interest; however, one or more pieces of analytical information is not described. The missing information is unlikely to have a substantial impact on results. AND/OR The analytical method may not be standard/widely accepted, but a method validation study was conducted prior to sample analysis and is expected to be consistent with sound scientific theory and/or accepted approaches. AND/OR Samples were collected at a site and immediately analyzed using an on-site mobile laboratory, rather than shipped to a stationary laboratory.
Low	Analytical methodology is only briefly discussed. Analytical instrumentation is provided and consistent with accepted analytical instrumentation/methods. However, most analytical information is missing and likely to have a substantial impact on results. AND/OR Analytical method is not standard/widely accepted, and method validation is limited or not available. AND/OR Samples were analyzed using field screening techniques. AND/OR LOQ, LOD, detection limits, and/or reporting limits not reported.

Data Quality Rating	Metric Description
	AND/OR There are some inconsistencies or possible errors in the reporting of analytical information (e.g., differences between text and tables in data source, differences between standard method and actual procedures reported to have been used, etc.) which leads to a lower confidence in the method used.
Critically Deficient	Analytical methodology is not described, including analytical instrumentation (i.e., HPLC, GC). AND/OR Analytical methodology is not scientifically appropriate for the chemical and media being analyzed (e.g., method not sensitive enough, not specific to the chemical, out of date). AND/OR There are numerous inconsistencies in the reporting of analytical information, resulting in high uncertainty in the analytical methods used.
Not Rated/Not Applicable	
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
Metric 3. Selection of biomarker of exposure	
High	Biomarker in a specified matrix is known to have an accurate and precise quantitative relationship with external exposure, internal dose, or target dose (e.g., previous studies (or the current study) have indicated the biomarker of interest reflects external exposures). AND Biomarker (parent chemical or metabolite) is derived from exposure to the chemical of interest.
Medium	Biomarker in a specified matrix has accurate and precise quantitative relationship with external exposure, internal dose, or target dose. AND Biomarker is derived from multiple parent chemicals, not only the chemical of interest, but there is a stated method to apportion the estimate to only the chemical of interest
Low	Biomarker in a specified matrix has accurate and precise quantitative relationship with external exposure, internal dose, or target dose. AND Biomarker is derived from multiple parent chemicals, not only the chemical of interest, and there is NOT a stated method to apportion the estimate to only the chemical of interest. <u>OR</u> <u>Biomarker in a specified matrix is a poor surrogate (low accuracy and precision) for exposure/dose.</u>

Data Quality Rating	Metric Description
Critically Deficient	<u>Not applicable. A study will not be deemed critically deficient based on the use of biomarker of exposure. Biomarker in a specified matrix is a poor surrogate (low accuracy and precision) for exposure/dose.</u>
Not Rated/Not Applicable	Metric is not applicable to the data source.
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
<u>Domain 2. Representative</u>	
<u>Metric 4. Testing scenario</u>	
High	Testing conditions closely represent relevant exposure scenarios (<i>i.e.</i>, population/scenario/media of interest). Examples include: • amount and type of chemical/product used • source of exposure/test substance • method of application or by-stander exposure • use of exposure controls • microenvironment (location, time, climate, temperature, humidity, pressure, airflow) AND Testing conducted under a broad range of conditions for factors such as temperature, humidity, pressure, airflow, and chemical mass/weight fraction (if appropriate).
Medium	The data likely represent the relevant exposure scenario (<i>i.e.</i>, population/scenario/media of interest). One or more key pieces of information may not be described but the deficiencies are unlikely to have a substantial impact on the characterization of the exposure scenario. AND/OR If surrogate data, activities seem similar to the activities within scope.
Low	The data lack multiple key pieces of information, and the deficiencies are likely to have a substantial impact on the characterization of the exposure scenario. AND/OR There are some inconsistencies or possible errors in the reporting of scenario information (<i>e.g.</i>, differences between text and tables in data source, differences between standard method and actual procedures reported to have been used, etc.) which leads to a lower confidence in the scenario assessed. AND/OR If surrogate data, activities have lesser similarity but are still potentially applicable to the activities within scope. AND/OR Testing conducted under a single set of conditions, <u>except for experiments to determine a weight fraction or concentration in a product.</u>
Critically Deficient	Testing conditions are not relevant to the exposure scenario of interest for the chemical.

Data Quality Rating	Metric Description
Not Rated/Not Applicable	
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
Metric 5. Sample size and variability	
High	Sample size is reported and large enough (<i>i.e.</i> , ≥ 10 samples) to be reasonably assured that the samples represent the scenario of interest. AND Replicate tests performed and variability across tests is characterized (if appropriate).
Medium	Sample size is moderate (<i>i.e.</i> , 5 to ~~40~~ <u><10</u> samples), thus the data are likely to represent the scenario of interest. AND Replicate tests performed and variability across tests is characterized (if appropriate).
Low	Sample size is small (<i>i.e.</i> , <5 samples), thus the data are likely to poorly represent the scenario of interest. AND/OR Replicate tests were not performed.
Critically Deficient	Sample size is not reported. AND/OR Single sample collected per data set, <u>except for experiments to determine a weight fraction or concentration in a product.</u> AND/OR For biomonitoring studies, the timing of sample collected is not appropriate based on chemical properties (<i>e.g.</i> , half-life), the pharmacokinetics of the chemical (<i>e.g.</i> , rate of uptake and elimination), and when the exposure event occurred.
Not Rated/Not Applicable	
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
Metric 6. Temporality	
High	Source(s) of tested items appears to be current (within 5 years).
Medium	Source(s) of tested items is less consistent with when current or recent exposures (>5 to 15 years) are expected.

Data Quality Rating	Metric Description
Low	Source(s) of tested items is not consistent with when current or recent exposures (>15 years) are expected or is not identified.
Critically Deficient	Temporality of tested items is not reported, discussed, or referenced.
Not Rated/Not Applicable	
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
Domain 3. Accessibility/clarity	
Metric 7. Reporting of results	
High	Supplementary or raw data (<i>i.e.</i>, individual data points) are reported, allowing summary statistics to be calculated or reproduced. AND Summary statistics are detailed and complete. Example parameters include: • Description of data set summarized (<i>i.e.</i>, location, population, dates, etc.) • Range of concentrations or percentiles • Number of samples in data set • Frequency of detection • Measure of variation (CV, standard deviation) • Measure of central tendency (mean, geometric mean, median) • Test for outliers (if applicable) AND Both adjusted and unadjusted results are provided (<i>i.e.</i>, correction for void completeness in urine biomonitoring, whole-volume or lipid adjusted for blood biomonitoring) [only if applicable].
Medium	Supplementary or raw data (<i>i.e.</i>, individual data points) are not reported, and therefore summary statistics cannot be reproduced. AND/OR Summary statistics are reported but are missing one or more parameters (see description for high). AND/OR Only adjusted or unadjusted results are provided, but not both [only if applicable].
Low	Supplementary data are not provided, and summary statistics are missing most parameters (see description for high). AND/OR There are some inconsistencies or errors in the results reported, resulting in low confidence in the results reported (<i>e.g.</i>, differences between text and tables in data source, less appropriate statistical methods).
Critically Deficient	There are numerous inconsistencies or errors in the calculation and/or reporting of results, resulting in highly uncertain reported results.

Data Quality Rating	Metric Description
Not Rated/Not Applicable	
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
Metric 8. Quality assurance	
High	The study applied quality assurance/quality control (<u>QA/QC</u>) measures and all pertinent <u>QA/QC</u> ~~quality assurance~~ information is provided in the data source or companion source. Examples include: • Laboratory, and/or storage recoveries. • Laboratory control samples. • Baseline (pre-exposure) samples. • Biomarker stability • Completeness of sample (<i>i.e.</i>, creatinine, specific gravity, osmolality for urine samples) AND No <u>QA/QC</u> ~~quality control~~ issues were identified, or any identified issues were minor and adequately addressed (<i>i.e.</i>, correction for low recoveries, correction for completeness).
Medium	The study applied and documented ~~quality assurance/quality control~~ <u>QA/QC</u> measures; however, one or more pieces of QA/QC information is not described. Missing information is unlikely to have a substantial impact on results. AND No <u>QA/QC</u> ~~quality control~~ issues were identified, or any identified issues were minor and addressed (<i>i.e.</i>, correction for low recoveries, correction for completeness).
Low	<u>QA/QC</u> ~~Quality assurance/quality control techniques~~ <u>measures</u> and results were not directly discussed but <u>are</u> ~~can be~~ implied through the study's use of standard field and laboratory protocols. AND/OR Deficiencies were noted in <u>QA/QC</u> ~~quality assurance/quality control~~ measures that are likely to have a substantial impact on results. AND/OR There are some inconsistencies in the <u>QA/QC</u> ~~quality assurance~~ measures reported, resulting in low confidence in the ~~quality assurance/control~~ <u>QA/QC</u> measures taken and results (<i>e.g.</i>, differences between text and tables in data source).
Critically Deficient	QA/QC issues have been identified which significantly interfere with the overall reliability of the study.
Not Rated/Not Applicable	

Data Quality Rating	Metric Description
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
<u>Domain 4.</u> Variability and uncertainty	
<u>Metric 9.</u> Variability and uncertainty	
High	The study characterizes variability in the population/media studied. AND Key uncertainties, limitations, and data gaps have been identified. AND The uncertainties are minimal and have been characterized.
Medium	The study has limited characterization of variability in the population/media studied. AND/OR The study has limited discussion of key uncertainties, limitations, and data gaps. AND/OR Multiple uncertainties have been identified but are unlikely to have a substantial impact on results.
Low	The characterization of variability is absent. AND/OR Key uncertainties, limitations, and data gaps are not discussed. AND/OR Uncertainties identified may have a substantial impact on ~~the exposure~~ the exposure assessment
Critically Deficient	Estimates are highly uncertain based on characterization of variability and uncertainty.
Not Rated/Not Applicable	
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>

Table 5-3. Updated Data Evaluation Criteria for Database Data

Data Quality Rating	Description
<u>Domain 1.</u> Reliability	
<u>Metric 1.</u> Sampling methodology	
High	Widely accepted sampling methodologies (<i>i.e.</i> , from a source generally <u>known to use</u> ~~using~~ sound methods and/or approaches) were used to generate the data presented in the

Data Quality Rating	Description
	database. Example SOPs include USGS's "National Field Manual for the Collection of Water-Quality Data," EPA's "Ambient Air Sampling" (SESDPROC-303-R5), etc.
Medium	One or more pieces of sampling methodology information is not described, but missing information is unlikely to have a substantial impact on results. OR The sampling methodologies were consistent with sound scientific theory and/or accepted approaches based on the reported sampling information but may not have followed published procedures from a source generally known to use sound methods and/or approaches.
Low	The sampling methodology was not reported in data source or <u>readily available</u> companion data source.
Critically Deficient	The sampling methodologies used were not appropriate for the chemical/media of interest in the database (e.g., inappropriate sampling equipment, improper storage conditions).
Not Rated/Not Applicable	
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
Metric 2. Analytical methodology	
High	Widely accepted analytical methodologies (i.e., from a source generally using sound methods and/or approaches) were used to generate the data presented in the database. Example SOPs include EPA SW-846 Methods, NIOSH Manual of Analytical Methods 5th Edition, etc.
Medium	The analytical methodologies were consistent with sound scientific theory and/or accepted approaches based on the reported analytical information but may not have followed published procedures from a source generally known to use sound methods and/or approaches.
Low	The analytical methodology was not reported in data source or companion data source.
Critically Deficient	The analytical methodologies used were not appropriate for the chemical/media of interest in the database (e.g., method not sensitive enough, not specific to the chemical, out of date).
Not Rated/Not Applicable	
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>

Data Quality Rating	Description
<u>Domain 2. Representative</u>	
<u>Metric 3. Geographic area</u>	
High	Geographic location(s) is reported, discussed, or referenced.
Medium	Not applicable. This metric is dichotomous (<i>i.e.</i> , high vs. critically deficient).
Low	Not applicable. This metric is dichotomous (<i>i.e.</i> , high vs. critically deficient).
Critically Deficient	Geographic location is not reported, discussed, or referenced.
Not Rated/Not Applicable	
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
<u>Metric 4. Temporal</u>	
High	The data reflect current conditions (within 5 years) AND/OR Database contains robust historical data for spatial and temporal analyses (if applicable).
Medium	The data are less consistent with current or recent exposures (>5 to 15 years) AND/OR Database contains sufficient historical data for spatial and temporal analyses (if applicable).
Low	Data are not consistent with when current exposures (>15 years old) may be expected AND/OR Database does not contain enough historical data for spatial and temporal analyses (if applicable).
Critically Deficient	Timing of sample data is not reported, discussed, or referenced.
Not Rated/Not Applicable	
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
<u>Metric 5. Exposure scenario</u>	
High	The data closely represent relevant exposure scenario (<i>i.e.</i> , the population/scenario/media of interest). Examples include: • Amount and type of chemical/product used • Source of exposure • Method of application or by-stander exposure • Use of exposure controls

Data Quality Rating	Description
	Microenvironment (location, time, climate)
Medium	The data likely represent the relevant exposure scenario (<i>i.e.</i>, population/scenario/media of interest). One or more key pieces of information may not be described but the deficiencies are unlikely to have a substantial impact on the characterization of the exposure scenario. AND/OR If surrogate data, activities seem similar to the activities within scope.
Low	The data lack multiple key pieces of information and the deficiencies are likely to have a substantial impact on the characterization of the exposure scenario. AND/OR There are some inconsistencies or possible errors in the reporting of scenario information (<i>e.g.</i>, differences between text and tables in data source, differences between standard method and actual procedures reported to have been used, etc.) which leads to a lower confidence in the scenario assessed. AND/OR If surrogate data, activities have lesser similarity but are still potentially applicable to the activities within scope.
Critically Deficient	If reported, the exposure scenario discussed in the monitored study does not represent the exposure scenario of interest for the chemical.
Not Rated/Not Applicable	
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
Domain 3. Accessibility/clarity	
Metric 6. Availability of database and supporting documents	
High	Database is widely accepted and/or from a source generally known to use sound methods and/or approaches (<i>e.g.</i> , <u>raw data from</u> NHANES, STORET).
Medium	The database may not be widely known or accepted (<i>e.g.</i>, state-maintained databases), but the database is adequately documented with <u>most or all of</u> the following information: - Within the database, metadata is present (sample identifiers, annotations, flags, units, matrix descriptions, etc.) and data fields are generally clear and defined. - A user manual <u>and</u> other supporting documentation is available, or there is sufficient documentation in the data source or companion source. Database quality assurance and data quality control measures are defined and/or a QA/QC protocol was followed.
Low	The database may not be widely known or accepted, and only limited database documentation is available (see the medium rating).
Critically Deficient	No information is provided on the database source or availability to the public.

Data Quality Rating	Description
Not Rated/ Applicable	
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
Metric 7. Reporting of results	
High	The <u>database or</u> information source reporting the analysis of the database data is well organized and understandable by the target audience. AND Summary statistics in the data source are detailed and complete. Example parameters include: • Description of data set summarized (<i>i.e.</i>, location, population, dates, etc.) • Range of concentrations or percentiles • Number of samples in data set • Frequency of detection • Measure of variation (CV, standard deviation) • Measure of central tendency (mean, geometric mean, median) • Test for outliers (if applicable)
Medium	The <u>database or</u> information source reporting the analysis of the database data is well organized and understandable by the target audience. AND/OR Summary statistics are missing one or more parameters (see description for high).
Low	The <u>database or</u> information source reporting the analysis of the database data is unclear or not well organized. AND/OR Summary statistics are missing most parameters (see description for high) AND/OR There are some inconsistencies or errors in the results reported, resulting in low confidence in the results reported (<i>e.g.</i>, differences between text and tables in data source, less appropriate statistical methods).
Critically Deficient	There are numerous inconsistencies or errors in the calculation and/or reporting of results, resulting in highly uncertain reported results. AND/OR The information source reporting the analysis of the database data is missing key sections or lacks enough organization and clarity to locate and extract necessary information.
Not Rated/Not Applicable	
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>

Data Quality Rating	Description
<u>Domain 4</u> . Variability and uncertainty	
<u>Metric 8</u> . Variability and uncertainty	
High	<u>Variability</u> , key uncertainties, limitations, and/or data gaps have been identified. AND/OR The uncertainties are minimal and have been characterized.
Medium	The study has limited discussion of <u>variability</u> , key uncertainties, limitations, and/or data gaps. AND/OR Multiple uncertainties have been identified but are unlikely to have a substantial impact on results.
Low	<u>Variability</u> , key uncertainties, limitations, and data gaps are not discussed. AND/OR Uncertainties identified may have a substantial impact on the exposure the exposure assessment
Critically Deficient	Estimates are highly uncertain based on characterization of variability and uncertainty.
Not Rated/Not Applicable	
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>

5.5 Environmental and Human Health Hazard

Details regarding the evaluation and extraction of environmental and human health hazard information from references that met PECO screening criteria are available in Sections 5 and 6.4 of the *2021 Draft Systematic Review Protocol*. Data quality criteria for environmental studies, animal and *in vitro* toxicity studies and epidemiological studies are available in Appendix P, Q, and R in the *2021 Draft Systematic Review Protocol*, respectively ([U.S. EPA, 2021](#)). Any updates made to the data quality evaluation and extraction forms for human health hazard information since the *2021 Draft Systematic Review Protocol* was published ([U.S. EPA, 2021](#)) are described below in Section 5.5.2. The below-listed supplemental documents provide details of the data evaluated and extracted. Data evaluation information for each discipline (*i.e.*, environmental and human health hazard) is contained in separate supplemental documents and includes metric ratings and the overall study quality determination for each data source. On the other hand, data extraction information for both disciplines are contained in a single supplemental document to increase the ease of accessing hazard data that may be relevant for both environmental- and human health-related receptors. One clarification that applies to the data extraction of human health hazard data is that all the data extraction was conducted in DistillerSR. In regard to the environmental hazard data, for references that meet PECO screening criteria at full text screening, the available environmental hazard data were extracted from those references in the ECOTOXicology Knowledgebase (ECOTOX) database and then imported into DistillerSR.

- *Data Quality Evaluation Information for Environmental Hazard for o-Dichlorobenzene* ([U.S. EPA, 2026h](#))

- *Data Quality Evaluation Information for Human Health Hazard Epidemiology for o-Dichlorobenzene* ([U.S. EPA, 2026k](#))
- *Data Quality Evaluation Information for Human Health Hazard Animal Toxicology for o-Dichlorobenzene* ([U.S. EPA, 2026j](#))
- *Data Extraction Information for Environmental Hazard and Human Health Hazard Animal Toxicology and Epidemiology for o-Dichlorobenzene* ([U.S. EPA, 2026c](#))
- *Data Quality Evaluation and Data Extraction Information for Dermal Absorption for o-Dichlorobenzene* ([U.S. EPA, 2026a](#))

5.5.1 Environmental Hazard

As described in Appendix R of the *2021 Draft Systematic Review Protocol*, references that met PECO criteria at full-text screening underwent data quality evaluation ([U.S. EPA, 2021](#)). Likewise, for references that met PECO criteria at full-text screening underwent data extraction as described in Section 6.4.1 of the *2021 Draft Systematic Review Protocol* ([U.S. EPA, 2021](#)). This section describes any updates made to the data quality evaluation and data extraction process since the *2021 Draft Systematic Review Protocol* was published.

Data Evaluation and Data Extraction Cross Walk

As per the established systematic review process described in the *2021 Draft Systematic Review Protocol*, data extraction is completed for all health outcomes regardless of the overall quality determination a study has received during data quality evaluation (*i.e.*, rating of high, medium, low, or uninformative). Moreover, initial data extractions for environmental hazard are completed outside of DistillerSR by contractors that support ECOTOX, database managed by EPA's ORD. Data extraction QC for *o*-dichlorobenzene was completed within DistillerSR by EPA staff in OPPT.

Since the *2021 Draft Systematic Review Protocol* was published, an additional process improvement step has been incorporated into the environmental hazard TSCA systematic review process. EPA staff that perform the data extraction QC need to cross walk data evaluation forms to data extraction forms to ensure that health outcomes for each experimental condition reported in the study match in both the data evaluation and extraction forms; this step is necessary because the initial data extractions are completed outside of DistillerSR independently of the data evaluation process within DistillerSR. In addition, EPA staff completing the cross walk during the data extraction QC need to ensure that the rating for the health outcome in the data evaluation forms is also reported in the data extraction forms.

To maximize efficiency for the completion of the data evaluation and data extraction cross walk, an external (outside of DistillerSR) automated function has been added. Figure 5-1 summarizes the steps that a study that meets the PECO screening criteria for environmental hazard (green circle in Figure 5-1) follows until completion of the data evaluation and data extraction cross walk (gray oval with check mark in Figure 5-1). The initial data extractions by ECOTOX contractors occur outside of DistillerSR (orange ECOTOX box in Figure 5-1), and data converted into a JSON file are later imported into DistillerSR in preparation for the data extraction QC by EPA staff (second blue square in the red DistillerSR box in Figure 5-1).

The light purple box with the label "External processing" in Figure 5-1 illustrates the steps that occur outside of DistillerSR including the automated crosswalk function (blue square with an asterisk). Specifically, this automated function starts with a data extraction form and compares to the corresponding data evaluation form by first filtering by HERO ID, then filtering by species name, followed by lifestage of the organism, exposure duration, health outcome and chemical type. For each of these filtering levels as the matching function is run, if there is a data evaluation form that corresponds to the data extraction criteria,

there is a successful match and the health outcomes in the data extraction form and data evaluation forms are aligned and, the rating is also added in the data extraction forms. On the contrary, if there is no data evaluation that corresponds to the data extraction criteria, the automated cross walk stops, and the outcome of the function is “No Match”. If there is no match by the automated function, the cross walk is completed manually at the final step. Once the automated cross walk function is complete, the data are converted to a JSON file that is uploaded into DistillerSR. For the final step, the QCer reviews the data extraction forms for the successful automated matches and completes the cross walk manually for the forms that did not match (blue square with double asterisks in Figure 5-1), at which point the data evaluation and data extraction cross walk is complete.

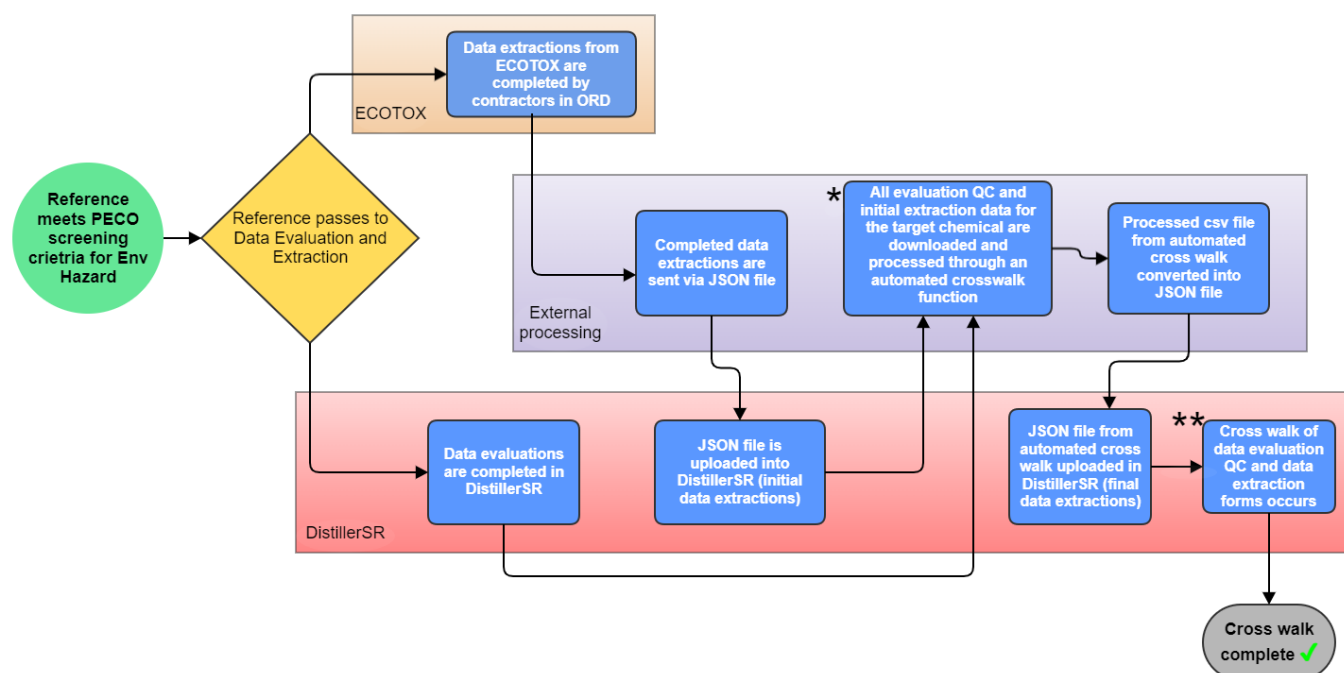


Figure 5-1. Data Evaluation and Data Extraction Cross Walk Workflow for Environmental Hazard

At the completion of the data evaluation and data extraction cross walk for *o*-dichlorobenzene, the data extraction information was included in the *Data Extraction Information for Environmental Hazard and Human Health Hazard Animal Toxicology and Epidemiology for o-Dichlorobenzene* ([U.S. EPA, 2026c](#)).

5.5.2 Human Health Hazard

As described in Appendices Q and R of the *2021 Draft Systematic Review Protocol*, references that met PECO screening criteria at full text screening underwent data quality evaluation ([U.S. EPA, 2021](#)). Likewise, for references that met PECO screening criteria at full text screening underwent data extraction as described in Section 6.4.1 of the *Draft Systematic Review Protocol* ([U.S. EPA, 2021](#)). Any clarifications or updates regarding the data quality evaluation or extraction of data from references that met PECO screening criteria at full text screening will be discussed further below for epidemiological and animal toxicity studies.

The data evaluation and extraction information for all *o*-dichlorobenzene references can be found in the supplemental files:

- *Data Quality Evaluation Information for Human Health Hazard Epidemiology for o-Dichlorobenzene* ([U.S. EPA, 2026k](#))

- *Data Quality Evaluation Information for Human Health Hazard Animal Toxicology for o-Dichlorobenzene* ([U.S. EPA, 2026j](#))
- *Data Extraction Information for Environmental Hazard and Human Health Hazard Animal Toxicology and Epidemiology for o-Dichlorobenzene* ([U.S. EPA, 2026c](#))
- *Data Quality Evaluation and Data Extraction Information for Dermal Absorption for o-Dichlorobenzene* ([U.S. EPA, 2026a](#))

5.5.2.1 Epidemiology Studies

For *o*-Dichlorobenzene, all references that met PECO screening criteria and further filtering criteria for epidemiology underwent data quality evaluation and data extraction as described in Appendix Section R and Section 6.4.1 of the *2021 Draft Systematic Review Protocol*, respectively ([U.S. EPA, 2021](#)). Although the studies that did not meet further filtering criteria do not have overall quality determinations from data quality evaluation, these references were considered in hazard identification for the risk evaluation and contribute to the overall weight of scientific evidence for the health effects that they assessed.

Additionally, case reports and case series were not evaluated for data quality because they were screened as Supplemental based on the PECO screening criteria described in the *2021 Draft Systematic Review Protocol* ([U.S. EPA, 2021](#)). There were no changes to the data evaluation domains and metrics or data extraction methodologies since the *2021 Draft Systematic Review Protocol* was published.

5.5.2.2 Animal Toxicity Studies

Although there were no updates made to the data extraction methodologies described in the *2021 Draft Systematic Review Protocol* for references with potentially relevant animal toxicity studies for the evaluation of human health hazard, EPA did update language in some of the metrics used to conduct data quality evaluation for those references. Updates to the data evaluation metrics from the versions published in Appendix Q.4.2 of the *2021 Draft Systematic Review Protocol* ([U.S. EPA, 2021](#)) are shown below in Table 5-4. Language that was inserted since the draft protocol was published is **bolded**, and language removed is shown in ~~strike through~~. Language was removed from metric 12 to ensure the metric rating was not discounted due to assessment of liver metabolism via an injection pathway. The description for the rating of high for metric 12 was updated to clarify that the caveat of 10 or more air changes/hour applies only to dynamic whole-body chambers. For metrics not listed below, no changes were made since the *2021 Draft Systematic Review Protocol* was published ([U.S. EPA, 2021](#)).

Table 5-4. Updated Data Quality Evaluation Criteria for Animal Toxicity Studies

Data Quality Rating	Description
Metric 12. Exposure route and method Were the route and method of exposure reported and suited to the test substance (<i>e.g.</i> , accounting for volatility, ~~injection was not used for assays of liver metabolism~~ , an appropriate vehicle was used when necessary)? For nose-only or head-only inhalation studies, were the animals appropriately acclimated or was the lack of acclimation controlled for?	
High	The route and method of exposure were reported and were suited to the test substance (see above) For inhalation studies, a dynamic, nose-only or head-only chamber was used, ~~with greater than 10 or more air changes/hour~~ . While dynamic nose-only (or head-only) studies are generally preferred, dynamic whole-body chambers are acceptable for gases as long as there were 10 or more air changes/hour .

Data Quality Rating	Description
Medium	There were minor limitations regarding the route and method of exposure, but the researchers took appropriate steps to mitigate the problem (<i>e.g.</i>, attempted to minimize headspace for volatile compounds in drinking water). These limitations are unlikely to have a substantial impact on results. For inhalation studies, a dynamic whole-body chamber was used for vapors that may condense (assume most will condense at high concentrations unless otherwise stated) or for aerosols, having 10 or more air changes/hour. A medium rating can also be assigned if the study indicates a dynamic chamber but not the number of air changes.
Low	There were deficiencies regarding the route and method of exposure that are likely to have a substantial effect on results. Researchers may have attempted to correct the problem, but the success of the mitigating action was unclear. For inhalation studies, there are significant flaws in the design or operation of the inhalation chamber, such as uneven distribution of test substance in a whole-body chamber, having less than 10 air changes/hour in a whole-body chamber, or using a whole-body chamber that is too small for the number and volume of animals exposed. OR Only very minimal if any details about the methods for inhalation exposure administration (as described above) were reported, resulting in significant uncertainty about the true exposure parameters.
Critically Deficient	The route or method of exposure was not reported OR An inappropriate route or method (<i>e.g.</i>, administration of a volatile organic compound via the diet) was used for the test substance <u>without</u> taking steps to correct the problem (<i>e.g.</i>, mixing fresh diet). These are serious flaws that makes the study unusable. For inhalation studies, either a static chamber was used, there is no description of the inhalation chamber, or an atypical exposure method was used, such as allowing a container of test substance to evaporate in a room.
Not Rated/Not Applicable	Do not select for this metric.
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>

5.6 Dermal Absorption

As described in the *2021 Draft Systematic Review Protocol*, evaluation and extraction of dermal absorption studies follow the steps outlined in Sections 5 and 6 ([U.S. EPA, 2021](#)) for all studies that meet the dermal absorption PECO screening criteria. Data evaluation metrics for *in vitro/ex vivo* dermal absorption studies have been updated from those described in Appendix S and the *in vivo* criteria are based on the *in vivo* animal toxicity study criteria in Appendix Q of the *2021 Draft Systematic Review Protocol* ([U.S. EPA, 2021](#)). OECD guidelines were used to develop the criteria for the evaluation of dermal absorption references ([OECD, 2022](#), [2011](#), [2004a](#), [b](#), [c](#)).

As indicated in Section 5.3 of the *2021 Draft Systematic Review Protocol*, initial and QC reviews are conducted for each reference ([U.S. EPA, 2021](#)). The sections below identify updates to the criteria made since publication of the *2021 Draft Systematic Review Protocol*.

The 3D human skin equivalent models are not recommended by OECD Guidance (OECD Series on Testing and Assessment No. 156 (September 2022) ([OECD, 2022](#)) for use in evaluating risks. Therefore, if adequate data are available from *in vivo* or *in vitro/ex vivo* (excised skin) studies, EPA will not evaluate studies using 3D human skin for data quality or extract information from the studies. However, EPA may discuss the 3D models when integrating evidence and may consider evaluating them if no other experimental dermal absorption information is available. The *Data Quality Evaluation and Data Extraction Information for Dermal Absorption for o-Dichlorobenzene* ([U.S. EPA, 2026a](#)) provides details of the data extracted and evaluated, including metric ratings and overall study quality determination(s) for each data source.

5.6.1 Data Quality Metrics - *In Vitro/Ex Vivo*

Table 5-5 shows the dermal absorption *in vitro/ex vivo* data evaluation criteria and revisions from Appendix S in the *2021 Draft Systematic Review Protocol* ([U.S. EPA, 2021](#)). Language that was inserted is **bolded** and language removed is shown as ~~struckthrough~~. For metrics 1,3,5, 6, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, and 21 changes to the wording were made to provide context and/or clarity to the evaluation question and/or rankings for the metric. For metrics 4, 5,7, and 10 language was added in the places that were marked as TBD in Appendix S. For metric 4, the wording used for the ranking for medium was changed to the ranking for high and wording was added for the ranking of medium. Clarifications were also made to the wording for the ranking of low and critically deficient. For metric 8, the ranking of high was removed, and the language was incorporated into the ranking for medium.

EPA did not perform data extraction on dermal absorption data because interpretation of dermal absorption results is complex and often requires additional interpretation or statistical adjustment. For these reasons, results are presented distinct from the systematic review process.

Table 5-5. Updated Data Evaluation Criteria for *In Vitro/Ex Vivo* Dermal Absorption Studies

Data Quality Rating	Description
<u>Domain 1</u> . Test substance	
<u>Metric 1</u> . Test substance identity Was the test substance identified definitively (<i>i.e.</i> , established nomenclature, CASRN, physical nature, physical and chemical properties, and/or structure reported, including information on the specific form tested [<i>e.g.</i> , salt or base, valence state, isomer, if applicable] for materials that may vary in form)? If test substance was a mixture, were mixture components and ratios characterized?	
High	The test substance (<i>i.e.</i> , chemical of interest) was identified definitively (<i>i.e.</i> , nomenclature, CASRN, structure) and where applicable the specific form (<i>e.g.</i> , particle characteristics for solid state materials, salt or base, valence state, hydration state, isomer, radiolabel, etc.) was definitively and completely characterized. For mixtures, the components and ratios were characterized (<i>i.e.</i> , provided as concentration, ratio of percentage of the mixture or product).

Data Quality Rating	Description
	Additionally, for radiolabeled substances, the location of the radiolabel within the substance should be indicated, ideally with the radiolabel ¹⁴ C in a metabolically stable position.
Medium	The test substance (<i>i.e.</i> , chemical of interest) was identified and the specific form was characterized (where applicable). For mixtures, some components and components and ratios were identified and characterized but at least the chemical of interest has a percentage/concentration reported. There were minor uncertainties (<i>e.g.</i> , minor characterization details were omitted such as about the radiolabel details) that were unlikely to have a substantial impact on results.
Low	The test substance and form (if applicable) were identified, and the components and ratios of mixtures were characterized, but there were uncertainties regarding test substance identification or characterization that are likely to have a substantial impact on the results (<i>e.g.</i> , no information on isomer (or enantiomer) composition of differences could affect toxicokinetic properties, limited particle size information, omitted details regarding branched or straight chain structure).
Critically Deficient	The test substance identity and form (the latter if applicable) could not be determined from the information provided (<i>e.g.</i> , nomenclature was unclear and CASRN or structure were not reported) OR For mixtures, the components and ratios were not characterized.
Not Rated/Not Applicable	Do not select for this metric
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
Metric 2. Test substance source Was the source of the test substance reported, including manufacturer and batch/lot number for materials that may vary in composition? If synthesized or extracted, was test substance identity verified by analytical methods?	
High	The source of the test substance was reported as a manufacturer or the production process was specifically identified. The batch/lot number was identified (for materials that may vary in composition), and the chemical identity was either certified by the source in the publication or could be verified on a manufacturer's website. OR The test substance identity was analytically verified by the laboratory that performed the toxicity study.

Data Quality Rating	Description
Low	The test substance was synthesized or extracted by a source other than the manufacturer [and no production process was identified]. OR The source was not reported. AND The test substance identity was NOT analytically verified by the performing laboratory.
Not Rated/Not Applicable	Do not select for this metric
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
Metric 3. Test substance purity Was the purity or grade (<i>i.e.</i> , analytical, technical) of the test substance (including the radiolabeled substance) reported and adequate? Were impurities identified? Were impurities present in quantities that could influence the results?	
High	For discrete substances, the test substance (including radiolabel) purity and composition were such that any observed effects were highly likely to be due to the nominal test substance itself (<i>e.g.</i> , highly pure at >98% or analytical grade test substance or a formulation of lower purity that contains ingredients considered to be inert, such as water). All components, including impurities and residual chemicals, were identified and the chemical of interest was the main component.
Medium	The nature and quantity of reported impurities are such that study results were not likely to be substantially impacted by the impurities (impurities not known to induce outcome of interest at low levels, impurities are inert or GRAS, etc.). Regardless of the nature and purity, for discrete chemicals, the purity of the chemical of interest should be >70%, unless water is the only impurity.
Low	Purity and/or grade of test substance were not reported
Critically Deficient	The nature and quantity of reported impurities were such that study results were likely to be due to one or more of the impurities. ~~This is a serious flaw that makes the study unusable.~~ AND/OR For discrete chemicals, purity was <70% with an impurity other than water.
Not Rated/Not Applicable	Do not select for this metric
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
Domain 2. Test design	
Metric 4. Reference compounds Were the results of a reference compound (<i>e.g.</i> , caffeine, testosterone, benzoic acid) run concurrently or separately and recently by the same laboratory and reported in the study? Was the absorption response appropriate?	

Data Quality Rating	Description
Alternately, has the performing lab demonstrated previous technical sufficiency in dermal absorption studies? [TBD: need to decide how important it is to have reference compounds]	
High	An appropriate concurrent reference compound was tested or data from a historical reference compound was provided, and an appropriate response was observed. Any uncertainties (e.g., omission of minor details regarding exposure or response) are minor.
Medium	~~When applicable, an appropriate concurrent or historical reference compound was used, and an appropriate response was observed. Any uncertainties (e.g., omission of minor details regarding exposure or response) are minor.~~ An appropriate concurrent or historical reference compound was used, but there were some deficiencies regarding the reference compound exposure or response (e.g., the response was not well described, it is unclear whether the response was acceptable).
Low	~~When applicable, an appropriate concurrent or historical reference compound was used, but there were deficiencies regarding the reference compound exposure or response (e.g., the response was not described).~~ ~~OR~~ ~~No reference compound was used or reported.~~ No appropriate reference compound was used or reported AND there is no established history of test performance in the performing laboratory.
Critically Deficient	~~Reference compounds were run but an inadequate response for the reference compounds (outside historical controls results) indicates that the assay would not accurately measure absorption. the response was unacceptable (e.g., outside historical control results), raising concerns about the validity of the assay.~~
Not Rated/Not Applicable	Do not select for this metric.
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
<u>Metric 5. Assay procedures</u> Were assay methods and procedures (e.g., diffusion cell set up, temperature, humidity, physiological conductivity compatibility of receptor fluid, volumes applied and surface area of skin, amount of test substance per surface area of skin , use/measurement of occlusion or carbon trap, materials and procedures used for tape stripping, capture of volatile compounds if required) described in detail and applicable/justified? ~~See other metrics for additional assay procedures (e.g., metrics 1–3 for test substance information; metric 11 for exposure duration; metric 15 for replicates per group).~~ Do the study methods describe how they ensure that quantification of the receptor fluid is adequately sensitive (e.g., sufficient signal-to-noise ratio, high enough specific activity of radiolabel, sufficient amount of time or number of scintillations detected). Diffusion cell setup should indicate static vs flow-through, and for flow-through the flow rate should be indicated. ~~OECD 428, OECD GD28 and OECD GD156 should be consulted and used to consider quality ratings.~~	
High	Study authors described the methods and procedures (e.g., diffusion cell set up, temperature, humidity, physiological conductivity compatibility of receptor fluid, volumes applied and surface area of skin, use/measurement of occlusion or carbon trap,

Data Quality Rating	Description
	specific activity of radiolabel , materials and procedures used for tape stripping, capture of volatile compounds if required) used for the test in detail and justified any relevant choices . Either a static cell or flow-through system was used, with either constant stirring (static cell) or an appropriate flow- rate (flow-through). These methods were appropriate based on the TGs and GDs above.
Medium	Methods and procedures were partially described (<i>e.g., all but temperature and humidity are described</i>) but appeared to be appropriate (<i>e.g., TBD</i>), so the omission of details is unlikely to have a substantial impact on results.
Low	The methods and procedures were not well described or deviated from customary practices (<i>e.g., TBD absence of occlusion or carbon trap for volatile test substance</i>) and this is likely to have a substantial impact on results, however conservative statistical adjustments could possibly account for these deviations.
Critically Deficient	Assay methods and procedures were not appropriate and would result in unusable data that cannot be statistically accounted for (<i>e.g., TBD failure to use a diffusion cell with sufficient seal, too low volume/mass of test substance applied per surface area, tape stripping and wash fractions combined and not measured independently</i>).
Not Rated/Not Applicable	Do not select for this metric
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
Metric 6. Standards for tests For assays with established criteria, were the test validity, acceptability, reliability, and/or QC criteria reported and consistent with current standards and guidelines? Were sufficient data provided to determine that the standards/guidelines have been met? <u>Example criteria:</u> <i>Percent recovery:</i> 100±10% of the radioactivity as stated in OECD TG 428; 100±20% for volatile and unlabeled compounds as stated in OECD GD 28. <i>Coefficient of Variation:</i> Variance across replicates should be measured and indicated when standard deviation exceeds 25%. <i>Skin integrity:</i> (1) Tritiated water – a.) a ‘limit value’ for a maximum Kp of 4.5 x10⁻³ cm/h (Guth et al. 2015 [Tox In Vitro 29:113-23]; Meidan and Roper, 2008 [Tox In Vitro 22:1062-9]) and mean Kp of 2.5 x 10⁻³ cm/h (Bronaugh et al. 1986 [Br J Dermatol 115:1-11]) for human <i>ex vivo</i> skin and b.) percent absorption (≤ 0.6% of applied dose in 1 hr) (Learn et al.– Poster from Charles River Labs). (2) Electrical conductance - minimal threshold of 17 kilo-ohms (Fasano et al., 2002) [Tox In Vitro 16:731-740]). (3) Trans-epidermal water loss - Less than 10 grams/m²/hr (Zhang, 2018) [Tox In Vitro 51: 129-135] (4) Other internal reference standard methods (<i>e.g., 3H-labeled compounds, methylene blue</i>) as cited in Guth et al. 2015. ~~<i>Skin integrity:</i> (1) Tritiated water – minimal flux threshold TBD (2) Electrical conductance – minimal threshold of 17 kilo-ohms (Fasano et al., 2002).~~ ~~OECD 428, OECD GD28, and OECD GD156 should be consulted; deviations should be explained.~~	
Medium	Criteria used to determine the test validity acceptability, reliability, and/or quality of the experiment QC criteria (<i>e.g., threshold for skin integrity, percent recovery considered acceptable</i>) were reported and consistent with current standards and

Data Quality Rating	Description
	guidelines, as/if applicable and authors stated that results met those criteria or the results provided enough detail to compare with the criteria
Low	Few or no QC criteria were reported, however, the reported results provided enough information to evaluate how the study compared against the criteria stated in the study and/or external criteria and standards. ~~Some QC criteria were not reported.~~
Critically Deficient	Inadequate information was provided on the standards used to evaluate the study results AND 1) the authors did not report whether the test met pre-established criteria, OR 2) inadequate data on results were presented ~~provided~~ to demonstrate the validity, acceptability, and reliability of the test when compared with current standards and guidelines or the pre-established standards/criteria identified by the authors. In this case, adequate QC cannot be performed.
Not Rated/Not Applicable	Do not select for this metric
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
<u>Domain 3. Exposure characterization</u>	
<u>Metric 7. Preparation and storage of test substance (chemical)</u> Did the study characterize preparation of the test substance and storage conditions? Were the frequency of preparation and/or storage conditions appropriate to the test substance stability and solubility (if applicable)?	
High	The test substance preparation and/or storage conditions (<i>e.g.</i> , test substance stability, homogeneity, mixing temperature, stock concentration, stirring methods, storage conditions) were reported and appropriate for the test substance (<i>e.g.</i> , stability and solubility in diluents or solvents confirmed especially if they differ from what is used commercially; volatile test substances prepared and stored in sealed containers; same stock solution for all exposure concentrations).
Medium	The test substance preparation and storage conditions were reported, but minor limitations in the test substance preparation and/or storage conditions were identified (<i>e.g.</i> , test substance formulations were stirred instead of centrifuged for a specific number of rotations per minute ~~TBD~~). OR There is an omission of details that are unlikely to have a substantial impact on results (<i>e.g.</i> , preparation/administration of test substance is described, but storage is not reported; however, storage is unlikely to affect results based on likely stability over the time frame of the test or the physical and chemical properties of the chemical make concerns about volatility or solubility unlikely).
Low	Deficiencies in reporting of test substance preparation, and/or storage conditions are likely to have a substantial impact on results (<i>e.g.</i> , available information on physical and

Data Quality Rating	Description
	chemical properties suggests that stability and/or solubility of test substance in diluent/solvent may be poor). OR Information on preparation and storage was <i>not</i> reported and lack of details could substantially impact results (e.g., preparation for volatile or low-solubility chemicals).
Critically Deficient	Serious flaws reported regarding test substance preparation and/or storage conditions will have critical impacts on dose/concentration estimates and make the study unusable (e.g., instability of test substance, test substance volatilized rapidly from storage containers).
Not Rated/Not Applicable	Do not select for this metric
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
Metric 8. Consistency of exposure administration Were exposures administered consistently across study groups (e.g., consistent volumes and area of skin surface for application)?	
High	~~Details of exposure administration were reported and exposures were administered consistently across study groups in a scientifically sound manner (e.g., consistent volumes, thickness and area of skin surface for application).~~
Medium	Details of exposure administration were reported or inferred from the text, ~~and but the minor limitations in administration of exposures~~ were administered consistently across study groups in a scientifically sound manner (e.g., consistent volumes slight variation in volume, thickness and area of or skin surface used for application). Any minor deviations/limitations are considered) that were identified are unlikely to have a substantial impact on results. OR Details of exposure administration are incompletely reported, but the missing information is unlikely to have a substantial impact on results.
Low	Details of exposure administration were reported, but deficiencies in administration of exposures (e.g., moderate differences in volume, thickness, and area of skin surface used for application) that were reported or inferred from the text are likely to have a substantial impact on results. OR Details of exposure administration are insufficiently reported and the missing information is likely to have a substantial impact on results
Critically Deficient	Exposures were not administered consistently across and/or within study groups (e.g., large differences in volume, thickness, and area of skin surface used for application) resulting in serious flaws that make the study unusable.
Not Rated/Not Applicable	Do not select for this metric.

Data Quality Rating	Description
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
Metric 9. Reporting of concentrations Were exposure doses/concentrations or amounts of test substance reported without ambiguity (e.g., point estimate instead of range, analytical instead of nominal)? Note: Ambiguity also applies to doses/concentrations if values were only reported as points on a figure without numerical values.	
High	The exposure doses/concentrations or amounts of test substance were reported without ambiguity (e.g., point estimate instead of range, analytical/measured instead of nominal).
Medium	The exposure doses/concentrations or amounts of test substance were reported with some ambiguity (e.g., range instead of point estimate OR nominal instead of analytical/measured).
Low	The exposure doses/concentrations or amounts of test substance were reported but with substantial ambiguity about precision (e.g., only an estimated range AND only nominal instead of analytical measurements).
Critically Deficient	The exposure doses/concentrations or amounts of test substance were not reported, resulting in serious flaws that make the study unusable.
Not Rated/Not Applicable	Do not select for this metric.
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
Metric 10. Exposure duration Was the exposure duration (e.g., hours) reported and was it appropriate for this study type and/or outcome(s) of interest? Was the duration of exposure relevant to conditions of use and physical-chemical properties of the test substance? Did measurements continue post-exposure to account for retained dose in skin? ~~[TBD: add text about human exposure relevancy].~~	
High	The exposure duration (e.g., hours) was reported and was appropriate for the study type and/or outcome(s) of interest (e.g., at least 6 to 10 hours prior to washing and up to at least 24 hours total including post-washing). A shorter exposure duration may also be included but is less useful unless the substance is demonstrated to be volatile, the results demonstrate that absorption approached completion (e.g., nothing left in the skin wash or tape strip samples) , or the timepoint is used only for Kp/flux measurements.
Low	The duration(s) of exposure differed slightly from current standards and guidelines for studies of this type (e.g., <6 to 10 hours prior to washing and less than 24 hours total including post-washing), and but the differences may are unlikely to have a substantial impact on results.
Critically Deficient	No information on exposure duration(s) was reported OR the exposure duration was not appropriate OR Duration(s) differed significantly from studies of the same or similar types and these differences (most likely shorter duration) .

Data Quality Rating	Description
	~~These deficiencies~~ are likely to have a substantial impact on interpretation of results.
Not Rated/Not Applicable	Do not select for this metric.
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
Metric 11. Number of exposure groups and concentrations spacing Were the number of exposure groups/ tested concentrations and dose/concentration spacing appropriate and justified by study authors (<i>e.g.</i> , to mimic a specific type of human exposure) and adequate for addressing the purpose of the study across a wide range of conditions of use (COUs) (e.g., dilute, concentrated, and neat)? (<i>e.g.</i> , to evaluate dermal absorption)?	
High	There were three or more dose ~~The number of exposure groups tested~~ and dose/concentration spacing were justified by study authors (<i>e.g.</i> , to mimic a specific type of human exposure) and ~~were~~ was adequate for addressing the purpose of the study.
Low	There were ~~minor~~ limitations regarding the number of exposure groups and/or applied dose/concentration spacing (<i>e.g.</i> , unclear if lowest dose was low enough or the highest dose was high enough, or less than three doses/concentrations tested), restricting the applicability of the results to only a subset of COUs and weight fractions.), ~~but the number of exposure groups and spacing of exposure levels were adequate and are unlikely to have a substantial impact on results.~~
Critically Deficient	The number of exposure groups and dose/concentration spacing were not reported OR ~~the number of exposure groups and dose/concentration spacing were not adequate and did not mimic expected human exposures.~~
Not Rated/Not Applicable	Do not select for this metric.
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
Domain 4. Test model	
Metric 12. Test model (skin) Were the test models (<i>e.g.</i> , viable skin, cadaver/cosmetic surgery skin, animal skin) and descriptive information (<i>e.g.</i> , tissue origin, anatomical site, tissue storage, initial integrity or viability) reported? What was the source of the test model? Was the model routinely used for the outcome of interest? For example, for human skin, split thickness (200–400µm), dermatomed skin is preferred.	
High	The test model (<i>e.g.</i> , viable skin, cadaver skin, cosmetic surgery skin, animal skin) and descriptive information (<i>e.g.</i> , tissue origin, anatomical site, tissue storage, integrity or viability, lot/batch used) were reported and the test model was routinely used for the outcome of interest.

Data Quality Rating	Description
Low	The test model was insufficiently reported ~~and reporting along with limited descriptive information.~~ OR The test model was routinely used for the outcome of interest. reporting limitations may ~~are unlikely to~~ have a substantial impact on results.
Critically Deficient	The test model and necessary descriptive information were not at all reported. OR the test model was not appropriate for evaluation of dermal absorption ~~the specific outcome of interest.~~
Not Rated/Not Applicable	Do not select for this metric.
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
Metric 13. Number/Replicates per group Was the number of replicates per dose/concentration group appropriate for the study type and outcome analysis?	
Medium	The number of replicates per dose/concentration were reported and was appropriate (e.g., acceptable data from a minimum of four replicates per test preparation).
Low	The number of replicates per dose/concentration and timepoint was reported but was less than recommended by current standards and guidelines (i.e., less than four replicates for each test preparation according to OECD TG 428). This is likely to have an impact on results. OR The number of replicates per dose/concentration was not reported.
Critically Deficient	The number of organisms or tissues per study group and/or replicates per study group was insufficient to characterize dermal absorption (e.g., less than four replicates per test preparation produced acceptable data).
Not Rated/Not Applicable	Do not select for this metric. Not applicable for qualitative studies not requiring any statistics.
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
Domain 5. Outcome assessment	
Metric 14. Outcome assessment methodology Did the outcome assessment methodology address or report the intended outcome(s) of interest? Was the outcome assessment methodology (including ~~nature of endpoints evaluated,~~ measurement technique and timing of measurement[s]) appropriate sensitive for the associated conditions of use (COUs) ~~outcome(s) of interest (e.g., measured endpoints that are able to detect a true effect)?~~ OECD 428, OECD GD28 and the dosing scenario? ~~OECD-GD156 should be consulted, and deviations should be documented and explained.~~	

Data Quality Rating	Description
High	The outcome assessment methodology addressed the intended outcome(s) of interest AND was sensitive for the outcome(s) of interest and followed OECD guidance documents. The selected formulations are reasonable for the chemical of interest and would result in dosing reflected a sufficiently conservative estimate representative range of conditions of use for the chemical of interest (e.g., use of IPM diluent). ~~(COUs) to which humans are exposed. The infinite dose scenario should be used is optimum for Kp determinations while finite dosing is required optimal for percent% absorption calculations. For finiteThe dose conditions, normally 1-5 mg/cm² of in the skin for a solid, and up to 10 µL/cm² for liquids of test material should be loaded, unless otherwise justified. For dilutions (i.e., not neat test material), finite should be considered to be the potentially absorbable dose testing for each concentration of should ideally be conducted with application of 10 µL/cm² test material. For infinite dose testing of solids, it is required that at least 10 mg/cm² of pure substance be used to establish an undepletable dose, regardless of concentration. For infinite dose testing of liquids, at least 100 µL/cm² of pure substance should be used to establish an undepletable dose, regardless of concentration. calculate the final % absorption. Recovery is 90±10% or 80±20% for volatile substances.~~
Medium	The outcome assessment methodology used partially addressed the intended outcomes(s) of interest and deviations were explained, ~~(e.g., mutation frequency evaluated in the absence of cytotoxicity in a gene mutation test)~~, but minor uncertainties (e.g., dosing was slightly below or above the recommendations for finite or infinite scenarios) are unlikely to have a substantial impact on results.
Low	Significant deficiencies in the implementation of the reported outcome assessment methodology were identified ~~(e.g., a volatile diluent was used with a volatile test substance matrix/assay interference, assay yielded anomalous results, etc.)~~ OR The outcome assessment methodology was not clearly reported and it was unclear whether methods were sensitive for the outcome of interest. This is likely to have a substantial impact on results.
Critically Deficient	The reported assessment methodology was not sensitive to the outcome(s) of interest. For example, percentage absorption was determined only from an infinite dose, and/the reported measurement endpoint(s) or Kp/flux was derived from a finite dose, and statistics could timing were not easily be calculated independently. sensitive for the outcome(s) of interest (e.g., cells were evaluated for chromosomal aberrations immediately after exposure to the test substance instead of after post exposure incubation period). These are serious flaws that make the study unusable.
Not Rated/Not Applicable	Do not select for this metric.
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
<u>Metric 15. Consistency of outcome assessment</u> Was the outcome assessment carried out consistently (i.e., using the same protocol) across study groups (e.g., assessment at the same time after initial exposure in all study groups)?	

Data Quality Rating	Description
High	Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups (e.g., at the same time after initial exposure) using the same protocol in all study groups. All study groups utilized the same vehicle for the blank formulation as for the study concentration groups a vehicle , the duration of exposure was the same across groups, the same receptor fluid composition was used ~~utilized~~ for each group, the sampling period was consistent across groups, etc.
Medium	There were minor differences in the timing of outcome assessment across study groups, or incomplete reporting of minor details of outcome assessment protocol execution were explained, but these uncertainties or limitations are unlikely to have substantial impact on results.
Low	Details regarding the execution of the study protocol for outcome assessment (e.g., timing of assessment across groups) were confusing, limited, or not reported nor deviations explained (or cited to another publication with no description in the paper itself), and these deficiencies are likely to have a substantial impact on results.
Critically Deficient	There were large inconsistencies in the execution of study protocols for outcome assessment across study groups. These are serious flaws that make the study unusable.
Not Rated/Not Applicable	Do not select for this metric.
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
Metric 16. Sampling adequacy and sensitivity Was the reported sampling size adequate for the outcome(s) of interest, including number of evaluations per exposure group, and endpoint (e.g., scintillation counts/sample)? ~~number of slides/cells/metaphases evaluated per test concentration)? OECD 428, OECD GD28, and OECD GD156 should be consulted, deviations should be explained.~~	
High	The study reported adequate sampling for the outcome(s) of interest including number of evaluations per exposure group, and measurement sensitivity endpoint (e.g., scintillation counts/sample and/or duration of radioactivity detection, adequate signal to noise [i.e., background] ratio for detection [e.g., signal 3x noise]). The sampling intervals should be adequate to allow accurately graphically representing the results of the receptor fluid content of the test article versus time.
Medium	Details regarding sampling for the outcome(s) of interest were reported, but minor limitations were identified in the reported sampling of the outcome(s) of interest and were explained. However, those limitations are unlikely to have a substantial impact on results.
Low	Details regarding sampling of outcomes were not fully reported nor explained and the omissions are likely to have a substantial impact on results.

Data Quality Rating	Description
Critically Deficient	Reported sampling was not adequate for the outcome(s) of interest and/or serious uncertainties or limitations were identified in how the study carried out the sampling of the outcome(s) of interest (e.g., replicates from control and test concentrations were evaluated at different times).
Not Rated/Not Applicable	N/A NA should be used for assays/studies that do not require a certain number of slides/cells/metaphases etc. be sampled for scoring (i.e., mutagenicity assays, mechanistic studies).
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
<u>Domain 6. Confounding/variable control</u>	
Metric 17. Confounding variables in test design and procedures Were there confounding differences among the study groups in the size, and/or quality of tissues exposed that could influence the outcome assessment, (e.g., skin integrity)?	
High	There were no differences reported among study group parameters (e.g., test substance lot or batch, strain/batch/ lot number of ~~organisms or models used per group or size~~ skin samples used per group or size , and/or quality of tissues exposed) that could influence the outcome assessment. Skin integrity was ~~acceptable~~ measured by preferable methods (e.g., electrical resistance and TEWL). Results of skin integrity testing were acceptable for all replicates and exposure groups (e.g., > 17 kilo-ohms based on electrical resistance, less than 10 grams/m2/hr)
Medium	Minor differences were reported and explained in initial conditions that are unlikely to have a substantial impact on results (e.g., tissues from two different lots were used and QC data were similar for both lots). Skin integrity ~~had variability but were acceptable~~ was measured by a less desirable method (e.g., tritiated water) , but results were acceptable (e.g., a 'limit value' for Kp of 4.5×10^{-3} cm/h or percent absorption of $\leq 0.6\%$ of applied dose in 1 hr) . Outliers were statistically evaluated. Most results of skin integrity testing were acceptable, and the number of replicates/donors was adequate after excluding any unacceptable results.
Low	Initial strain/batch/lot number skin samples used per group, size, and/or quality of tissues exposed was not reported. These deficiencies are likely to have a substantial impact on results.
Critically Deficient	There were significant differences among the study groups with respect to the strain/batch/lot number of ~~organisms or models used per group or size and/or quality of tissues exposed (e.g., initial number of viable bacterial cells were different for each replicate [105 cells in replicate 1, 108 cell in replicate 2, and 103 cells in replicate 3]; tissues from two different lots were used for in vitro skin corrosion test, but the control batch quality for one lot was outside of the acceptability range)~~ . Skin integrity results were below thresholds. Recovery was below guidance limits or not quantified. ~~Exposures did not reflect worker COUs.~~ skin samples used per group or size and/or quality of tissues exposed (e.g., several replicates demonstrated integrity issues). Recovery varied greatly among replicates (i.e., >10%). In this situation, results are not reliable for estimating actual absorption.

Data Quality Rating	Description
Not Rated/Not Applicable	Do not select for this metric.
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
Metric 18. Confounding variables in outcomes unrelated to exposure Were there differences among the study groups unrelated to exposure to test substance (e.g., solubility in receptor fluid contamination) that could influence the outcome assessment? Did the test material interfere in the assay (e.g., altering fluorescence or absorbance, signal quenching by heavy metals, altering pH, solubility, or stability issues)?	
High	There were no reported differences among the study replicates or groups in test model unrelated to exposure (e.g., solubility in receptor fluid contamination) and the test substance did not interfere with the assay (e.g., signal quenching by heavy metals). The test substance was demonstrated to be soluble in the receptor fluid.
Medium	Authors reported that one or more replicates or groups experienced disproportionate outcomes unrelated to exposure (e.g., solubility issues contamination), but data from the remaining exposure replicates or groups were valid and is unlikely to have a substantial impact on results. OR The test material interfered in the assay, but the interference did not cause substantial differences among the groups. OR Solubility in the receptor fluid was not demonstrated, but solubility is not likely to be an issue based on the expected concentration relative to the receptor fluid formulation.
Low	Data on outcome differences unrelated to exposure (including receptor fluid formulation) were not reported for each study replicate or group and the missing information is likely to have a substantial impact on results. OR Assay interference was present or inferred resulting in large variabilities among the groups.
Critically Deficient	There were indications of assay interference several replicates or groups or there is evidence of insolubility in the receptor fluid such that no outcomes could be assessed.
Not Rated/Not Applicable	Do not select for this metric.
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
Domain 7. Data presentation and analysis	
Metric 19. Data analysis Were statistical methods, calculations methods, and/or data manipulation clearly described and appropriate for dataset(s)? Were absorption estimates presented across a time series for each compartment of the test system?	

Data Quality Rating	Description
High	Statistical methods (including any calculations or data transformations) were clearly described or had only minor omissions and were appropriate for the dataset(s). Percentage absorption estimates were presented across a time series for each compartment of the test system, and Kp/flux measurements were based on the linear/steady-state part of the absorption curve. Calculated absorption estimates properly accounted for outliers consistently across replicates/timepoints ~~Any selection of outliers was justified.~~
Low	Statistical analysis was performed but not described adequately to understand what was performed or whether it was properly applied (e.g., determination of outliers). OR Statistical analysis was inconsistently/inappropriately applied across replicates and datasets (e.g., absorption not measured across time series, inconsistent exclusion of outliers {perhaps due to integrity failure} across measurements, but coefficient of variation for several replicates (SD relative to mean) was $\leq 25\%$). OR Absorption estimates were not presented across a time series for each component.
Critically Deficient	Statistical analysis was performed using an inappropriate method (e.g., parametric test for non-normally distributed data), and/or coefficient of variation for several replicates (SD relative to mean) was $>25\%$. OR Statistical analysis was not performed. AND Data enabling an independent statistical analysis were not provided. These are serious flaws that make the study unusable.
Not Rated/Not Applicable	Statistical analysis was not possible (n = 1–2) or not necessary (clearly negative findings across all groups; Ames assay using 2-fold increase as benchmark).
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
Metric 20. Data interpretation Is ~~Were the evaluation criteria reported and~~ is the interpretation of results consistent with standards and guidelines? For example, did reported absorption estimates account for sufficient recovery? Was the combined amount of test substance in the skin and receptor fluid counted in the overall estimate? Was derivation of Kp vs fractional absorption applied to the appropriate exposure conditions (infinite dose vs finite dose, respectively)?	
High	~~Study authors followed evaluation criteria for the test, and these were consistent with established practices*.~~ Recovery of applied test substance was adequate (90% for occluded or non-volatile substance, 80% for non-occluded, volatile ~~substance or~~ unlabeled substance) or the absorption estimate was normalized to account for any reduction below these levels. Both the skin compartment and any tape-stripping washes after the first two were included in the absorption estimate. AND Assay results were correctly interpreted relative to the properties of the test substance and the assay setup (sufficient duration to capture all absorption if not evaporated, proper interpretation of finite vs infinite dose).

Data Quality Rating	Description
Medium	Absorption estimates were reported improperly or incompletely (e.g., skin compartment not included, values not normalized if recovery less than adequate), however simple independent data analysis is possible to overcome these issues.
Low	Measurements of permeability flux/Kp were evaluated from a finite dose or fractional absorption estimates were included from a single and/or infinite dose. ~~Complex reanalysis of the data is required in order to obtain usable interpretations (e.g., external outlier analysis may be required, Kp determination must be recalculated from the time series).~~
Critically Deficient	The reported ~~scoring~~ rating and/or evaluation criteria were very inconsistent with established practices, resulting in the interpretation of data results that are seriously flawed and highly misleading relative to the properly interpreted results (e.g., study author claims 5% absorption but correct analysis results in 40% absorption, only percentage absorption is reported from a finite dose) and therefore not usable for any scenarios.
Not Rated/Not Applicable	Do not select for this metric.
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>
Metric 21. Reporting of data Were the data for all outcomes presented? Were data reported by exposure group?	
High	Data for exposure-related findings were presented for all outcomes by exposure group (e.g., all timepoints, formulations, concentrations, finite vs infinite dose) . Negative findings were reported qualitatively or quantitatively.
Medium	Data for exposure-related findings were reported for most, but not all, outcomes by exposure group (e.g., both short and long-term exposures). The minor uncertainties in outcome reporting are unlikely to have substantial impact on results (e.g., intermediate timepoints not included in the data tables but the full curve is included).
Low	Data for exposure-related findings were not shown for each study group, but results were described in the text. OR Data were only reported for some outcomes. OR Continuous data were presented without measures of variability or n/group.
Critically Deficient	Data presentation was inadequate (e.g., the report does not differentiate among findings in multiple exposure groups) OR Major inconsistencies were present in reporting of results that render the findings uncertain regarding hazard identification or dose- response.
Not Rated/Not Applicable	Do not use for this metric.

Data Quality Rating	Description
Reviewer's Comments	<i>[Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance]</i>

5.6.1 Data quality metrics- animal *in vivo*

Animal *in vivo* dermal absorption data was not identified through systematic review, test order data, or public comment submissions.

5.6.2 Data quality metrics- human *in vivo*

Human *in vivo* dermal absorption data was not identified through systematic review, test order data, or public comment submissions.

6 EVIDENCE INTEGRATION

As described in Section 7 of the *2021 Draft Systematic Review Protocol* ([U.S. EPA, 2021](#)), evidence integration refers to the consideration of evidence obtained from systematic review and scientific information obtained from sources that did not undergo systematic review to implement a weight of the scientific evidence approach. The weight of the scientific evidence is defined as “a systematic review method, applied in a manner suited to the nature of the evidence or decision, that uses a pre-established protocol to comprehensively, objectively, transparently, and consistently identify and evaluate each stream of evidence, including strengths, limitations, and relevance of each study and to integrate evidence as necessary and appropriate based upon strengths, limitations, and relevance” (40 CFR 702.33). The consideration of the quality and relevance of the data, while taking into account the strengths and limitations of the data, to appropriately evaluate the evidence for this supplement, is described in Section 7 of the *2021 Draft Systematic Review Protocol* ([U.S. EPA, 2021](#)).

6.1 Physical and Chemical Properties

The systematic review process identified multiple data for each of the physical-chemical properties analyzed in the risk evaluation. Relevant data types used for the physical-chemical assessment are discussed in Appendix K of the *2021 Draft Systematic Review Protocol* ([U.S. EPA, 2021](#)). When a specific datum is cited for a given physical-chemical parameter, priority is given to data from expert-curated, peer-reviewed databases that have been identified as “trusted sources”. Sources of uncertainty are discussed, when appropriate, in the risk evaluation.

6.2 Environmental Fate and Transport

Relevant data types used for environmental fate and transport assessment are listed in Table 7-1 of the *2021 Draft Systematic Review Protocol* ([U.S. EPA, 2021](#)). Systematic review data as well as data gaps filled using evidence streams outside systematic review are incorporated as described in Figure 7-1. Quality of these data are determined based on whether they are measured or estimated data, and further broken down based on consistency, study design, study conditions and uncertainty (Figure 7-2).

6.3 Environmental Release and Occupational Exposure

To evaluate environmental releases and occupational exposures for the various COUs, EPA first mapped the COUs to broader occupational exposure scenario (OES) categories. Specifically, EPA developed OES categories to group processes or applications with similar sources of environmental releases and occupational exposures. For each OES, EPA integrated the occupational exposure results for various job classifications to be representative of all U.S. workers and sites within that OES.

The EPA utilized release data from programmatic databases (DMR, TRI, and NEI databases) and used identified air, water, and land release data to estimate releases for OESs where they were applicable ([U.S. EPA, 2023a](#), [b](#), [2020c](#)). To estimate the number of sites within an OES, EPA used TRI, DMR, and CDR data.

EPA assessed OES-specific exposures to workers and occupational non-users (ONUs) based on monitoring data, analogous monitoring data, and modeling approaches. EPA developed worker activity information using test order data, GSs, ESD, and other systematic review literature. When sufficient monitoring data for an OES were available, EPA gave preference to monitoring data more recent than 1989, as the Occupational Safety and Health Administration (OSHA) set a permissible exposure limit (PEL) for DBP of 5 mg/m³ in 1989. For the assessment of dermal exposures, EPA used the fractional absorption dermal model and performed a Monte Carlo simulation with 100,000 iterations for each OES.

6.4 General Population, Consumer, and Environmental Exposure

o-Dichlorobenzene concentrations in ambient air, surface water, sediment, soil, landfills, and biosolids were gathered and summarized within each environmental media pathway ([U.S. EPA, 2026b](#)). The sources and approaches to gather monitoring data from peer-reviewed publications, government reports, and/or databases were classified as monitoring and mainly used to compare with modeling results or to support qualitative assessments. Consumer products containing *o*-dichlorobenzene were identified through review and searches of a variety of sources, such as completed assessments, 2016 and 2020 Chemical Data Reporting ([U.S. EPA, 2020a, 2016](#)). General population and environmental exposures were evaluated for the inhalation, dermal and ingestion exposure pathways based on environmental release data. In summary, modeled environmental release estimates were used as inputs for the general population exposure modeling.

6.4.1 General Population and Environmental Exposure: Surface, Groundwater, and Drinking Water

For the drinking and surface water exposure assessment, EPA conducted a screening-level approach. The drinking water assessment used reported environmental data and an equation to calculate intake dose. Concentrations were taken from the highest reported study and additional inputs were used from the Exposure Factors Handbook (EFH) ([U.S. EPA, 2011](#)). The surface water assessment used the maximum annual release of *o*-dichlorobenzene to surface water from DMR and a mass balance model. EPA then compared the reported environmental monitoring data and reported environmental modeling data with EPA modeled media concentrations. Section 5 of the *Draft Chemistry, Fate, Release, and Exposure Assessment for o-Dichlorobenzene* ([U.S. EPA, 2026b](#)) summarizes measured concentrations of *o*-Dichlorobenzene within published literature for surface water, drinking water, wastewater, groundwater and soil.

6.4.2 General Population and Environmental Exposure: Ambient Air

EPA evaluated general population and environmental exposures based on measured and predicted concentrations of *o*-dichlorobenzene in ambient air. Measured concentrations for ambient air were found in the peer-reviewed literature obtained through systematic review, from the EPA Ambient Monitoring Technology Information Center (AMTIC) archive, and from the EPA estimated ambient air concentrations ([U.S. EPA, 2026b](#)). Air release estimates were used as inputs for estimating ambient air concentrations and deposition fluxes via American Meteorological Society/Environmental Protection Agency Regulatory Model (AERMOD) and Human Exposure Model (HEM). Modeled ambient air concentrations were used to estimate inhalation exposure. Modeled deposition fluxes were used to estimate soil concentrations and in-stream concentrations of *o*-dichlorobenzene. Where available, EPA compared reported environmental monitoring and modeling data with EPA modeled ambient air concentrations.

6.4.3 Consumer Exposure Assessment

EPA assessed consumer exposure to *o*-dichlorobenzene for both users and bystanders, resulting from use of consumer products and articles. The major routes of exposure considered were via inhalation and dermal exposure. Consumer products containing *o*-dichlorobenzene were identified through review and searches of a variety of sources, such as completed assessments, 2016 and 2020 Chemical Data Reporting ([U.S. EPA, 2020a, 2016](#)), in addition to chemical safety data sheets (SDSs) identified through product-specific internet searches. Chemical weight fractions were gathered from SDSs and completed assessments and used to tailor COU-specific consumer exposure scenarios for products and articles identified in the consumer market. The dermal assessment was based on ([Elsisi et al., 1989](#)), which was an *in vivo* absorption study using male F344 rats.

6.4.3.1 Other data sources

The exposure models relied heavily on the physical chemical and fate properties as input parameters. Sections 5.1 and 5.2 describe how the physical chemical and fate properties were selected. Where applicable, EPA relied on model defaults, exposure factors and activity patterns available from EPA's Exposure Factors Handbook ([U.S. EPA, 2017](#)). As mentioned previously, these physical chemical and fate parameters are used as inputs for modeling.

6.5 Environmental and Human Health Hazard

Sections 7.4 and 7.5, the *2021 Draft Systematic Review Protocol* explain how information from data sources that undergo systematic review and those that do not are considered for use in risk evaluations under TSCA, specifically, for evaluating environmental and human health hazard, respectively ([U.S. EPA, 2021](#)).

The environmental hazard evidence streams, as described in Table 7-8 of the *2021 Draft Systematic Review Protocol*, have been updated to increase the level of clarity and consistency of granularity ([U.S. EPA, 2021](#)). Table 6-1 the updated environmental hazard evidence streams that parses out the types of mechanistic data evidence streams.

6.5.1 Environmental Hazard

Section 7.4.1 of the *2021 Draft Systematic Review Protocol* describes how environmental hazard integration is organized into different evidence streams. The environmental hazard evidence streams for risk evaluations conducted under TSCA, as described in Table 7-8 of the *2021 Draft Systematic Review Protocol*, have been updated (Table 6-1; updates are represented in bold text) to increase the level of clarity and consistency of granularity ([U.S. EPA, 2021](#)). These updated environmental hazard evidence streams more clearly reflect how apical and mechanistic hazardous endpoints (as defined by the screening PECO statement) that result from either controlled field/laboratory or uncontrolled exposure field studies are binned to better consider the relevancy of the data for the respective risk evaluation.

Table 6-1. Querying the Evidence to Organize Integration for Environmental Data and Information

Evidence Stream	Questions
Apical endpoints (controlled field/laboratory conditions)	Of the available data, are there endpoints that could have population level effects such as reproduction, growth, and/or mortality?
Mechanistic data (controlled field/laboratory conditions)	Is the mechanistic endpoint linked to an apical endpoint? Is it part of an AOP? If not, can you instead use it qualitatively? If a transcriptomic point of departure (tPOD) is available, is it appropriate to use quantitatively?
Apical endpoints (uncontrolled exposure field conditions)	Are there any field studies available showing adverse effects? How does exposure to the chemical of interest affect the community of organisms? Are there any co-occurring adverse environmental conditions other than exposure to the chemical of interest that should be taken into consideration?

Evidence Stream	Questions
Mechanistic endpoints (uncontrolled exposure field conditions)	Is the mechanistic endpoint linked to an apical endpoint? Is it part of an AOP? If not, can you instead use it qualitatively? If a transcriptomic point of departure (tPOD) is available, is it appropriate to use quantitatively? Are there any co-occurring adverse environmental conditions other than exposure to the chemical of interest that should be taken into consideration?

As described in the *Draft Human Health and Environmental Hazard Assessment for o-Dichlorobenzene* ([U.S. EPA, 2026I](#)), streams for environmental hazard included empirical data with apical endpoints for aquatic and terrestrial organisms that were reviewed following the TSCA systematic review process.

EPA reviewed potential environmental health hazards associated with *o*-dichlorobenzene ([U.S. EPA, 2026I](#)). Studies identified as meeting PECO screening criteria and evaluated for data quality received an overall quality determination of high, medium, low, or uninformative. Data on the toxicity of *o*-dichlorobenzene were limited and only high and medium-quality studies were used for purposes of hazard and risk characterization ([U.S. EPA, 2026I](#)). An OQD of high and medium were assigned to 19 aquatic studies and 12 terrestrial studies. Due to a lack of wildlife terrestrial mammalian studies, controlled laboratory studies that used rats as human health model organisms were used to assess terrestrial hazards. When high and/or medium-quality empirical data were not readily available for *o*-dichlorobenzene, modeled data were incorporated into the evidence stream. Predictive models represented within the body of evidence included American Meteorological Society/Environmental Protection Agency Regulatory Model (AERMOD). Modeled data served as evidence streams that fall outside of systematic review but include systematically reviewed methods and were integrated with evidence streams that fall within the TSCA systematic review process.

A SSD analysis was used to derive an acute aquatic hazard threshold. An SSD is a type of probability distribution of toxicity values from multiple species that models the variation in sensitivity of species to a particular chemical stressor and is generated by fitting a statistical distribution function to the proportion of species affected as a function of concentration or dose. It can be used to visualize which species are most sensitive to toxic chemical exposure and to predict a concentration of a toxic chemical that is hazardous to a percentage of test species. Empirical data included in the SSD analysis were limited to LC50 (concentration which is lethal to 50% of test organisms) values at or below the limit of water solubility. Predicted acute hazard data for aquatic invertebrates and vertebrates were also generated using EPA's Web-Based Interspecies Correlation Estimation Web-ICE (v 4.0) toxicity predictions tool ([U.S. EPA, 2024](#)). Web-ICE is a tool developed by the U.S. EPA that estimates the acute toxicity of a chemical to a species, genus, or family from known toxicity of the chemical to a surrogate species. A deterministic approach was used to derive all other environmental hazard thresholds.

Using empirical and modeled evidence streams, EPA characterized the environmental hazards of *o*-dichlorobenzene to surrogate species representing various receptor groups ([U.S. EPA, 2026I](#)), including, freshwater vertebrates (fish, acute and chronic; amphibian, acute); freshwater invertebrates (acute and chronic); freshwater algae (acute and chronic); a terrestrial invertebrate (earthworm); and terrestrial vertebrates ((mammalian (rat): oral routes of exposure)).

Evaluations of the strength of evidence and weight of scientific evidence for environmental hazard was conducted as described within Section 7.4.2 of the *2021 Draft Systematic Review Protocol* ([U.S. EPA, 2021](#)). For additional details on the application of this methodology, please see *Draft Human Health and Environmental Hazard Assessment for o-Dichlorobenzene* ([U.S. EPA, 2026l](#)).

6.5.2 Human Health Hazard

In addition to individual studies identified through the literature search process, EPA also integrated evidence from previous governmental assessments, primarily the ATSDR *Toxicological Profile for Dichlorobenzenes* ([ATSDR, 2006](#)). EPA's 2006 Integrated Risk Information System (IRIS) *Draft Health Assessment of Dichlorobenzenes* ([U.S. EPA, 2006](#)) was also consulted for purposes of considering the database of available studies; however, as a draft document, it does not constitute an official Agency assessment. In some cases, EPA utilized study summaries and conclusions from these prior assessments for hazard information on non-critical hazard outcomes and supporting mechanistic/toxicokinetic information. To support the cancer analysis, a read-across analysis was also performed as part of the Rethinking Chronic Toxicity and Carcinogenicity Assessment for Agrochemicals Project (ReCAAP) framework for evaluating *o*-dichlorobenzene carcinogenicity. The read-across analysis searched for cancer and inhalation toxicity information on structural analogs of *o*-dichlorobenzene to address the data gap from the absence of a chronic inhalation study.

Section 7.5 of the *2021 Draft Systematic Review Protocol* describes how EPA considers individual evidence streams (human, animal toxicity, and mechanistic/supplemental studies) when integrating evidence ([U.S. EPA, 2021](#)), including the use of standardized tables with causality statements indicating weight of scientific evidence conclusions across evidence streams.

For the human health hazard assessment of *p*-dichlorobenzene, EPA decided that given the breadth, diversity, and variety of study types used to support multiple hazard domains/organ systems, a narrative format was better suited for hazard characterization and evidence integration. Therefore, evidence integration tables were not created for the *Draft Human Health and Environmental Hazard Assessment for o-Dichlorobenzene* ([U.S. EPA, 2026l](#)). Additionally, EPA did not make causality statements indicating weight of scientific evidence conclusions across evidence streams because the process described in Section 7.5 of the *2021 Draft Systematic Review Protocol* was determined to be too rigid (*i.e.*, the overall weight of the scientific evidence judgement was dictated based on the specific within-stream strength of the evidence judgement ratings) and did not allow for full consideration of nuanced differences between evidence databases that might all fall under the same judgement/conclusion.

EPA did retain the within-stream strength of the evidence judgements (indeterminate, slight, moderate, robust), applied based on the considerations described in Table 7-13 of the *2021 Draft Systematic Review Protocol*. EPA then decided whether the evidence supported dose-response analysis of the hazard outcome based both on the strength of the evidence judgements and other considerations as discussed in the human health hazard assessment.

6.1 Dermal Absorption

There were no dermal absorption studies identified specific to *o*-dichlorobenzene. However, one study that used a unique *in vitro* system with pig skin (considered more relevant than rodents when compared to humans) inside a "cradle chamber" tested absorption of "dichlorobenzene" without identifying the isomer ([Riviere et al., 2000](#)). The specific isomer used was either *o*-dichlorobenzene, *m*-dichlorobenzene (*i.e.*, 1,3-dichlorobenzene), or a mixture, based on being in a liquid state. The study quality was rated

“uninformative for dose-response” in *Data Quality Evaluation Information for Dermal Absorption for o-Dichlorobenzene* ([U.S. EPA, 2026a](#)), so EPA instead utilized read-across from *p*-dichlorobenzene.

Two dermal absorption studies were available for *p*-dichlorobenzene. As described in Section 2.2.1 of the *Draft Human Health and Environmental Hazard Assessment for p-Dichlorobenzene* ([U.S. EPA, 2026m](#)), test order data ([Charles River Laboratories, 2025](#)) was developed in consultation with EPA in order to cover a range of potential formulations and exposure durations relevant to TSCA exposure scenarios for unoccluded, finite dose loading relevant to fractional absorption. An older study ([CPA, 2005](#)) utilized occluded, infinite dosing relevant to deriving permeability coefficient (K_p)/flux values. Both of these studies were considered in an exposure-scenario specific manner, and the results were compared to modeling estimates from Part E of the Risk Assessment Guidance for Superfund Volume I ([U.S. EPA, 2004](#)) and IHSkinPerm.

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