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Approach Document for Screening Hazard Information for Low-Priority Substances Under TSCA

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1. General Process

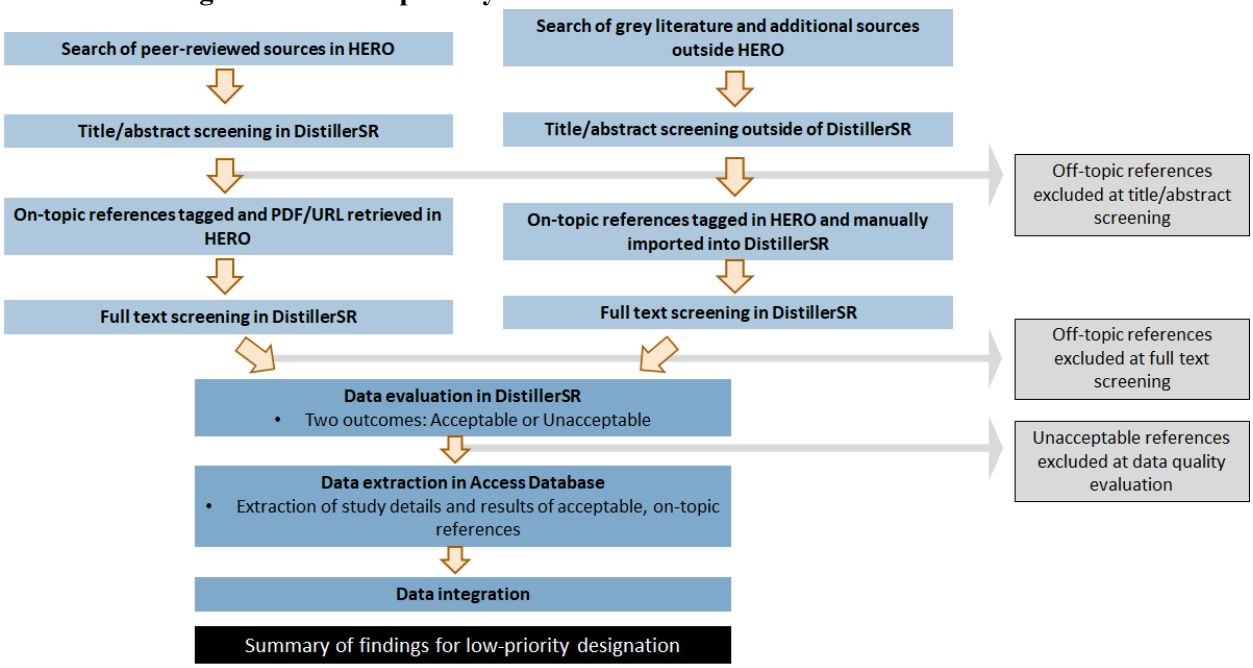
EPA's Office of Pollution Prevention and Toxics is implementing processes and regulations (40 CFR Part 702) to support the prioritization of chemical substances under the Lautenberg amendments to the Toxic Substances Control Act (TSCA) (section 6(b)(1)). The purpose of prioritization under TSCA is to designate chemical substances as either high-priority substances for risk evaluation, or low-priority substances for which risk evaluations are not warranted at the time of designation.

EPA created a fit-for-purpose literature search and review approach to document health and environmental hazard and fate information for risk-based screening reviews that support low-priority substance proposed designations. This approach involves a comprehensive review of the literature, tailored to capture the reasonably available information typically associated with low-hazard chemicals. EPA also used this approach to assess reliability, completeness, and consistency.

EPA used tools such as the Health & Environmental Research Online (HERO) database and DistillerSR to implement this literature search and review process. HERO, which is managed by EPA's Office of Research and Development (ORD), includes more than three million scientific references and associated data from the peer-reviewed, grey literature, and other sources. HERO maintains this repository of scientific references by chemical or project area to improve public access to data supporting EPA's scientific products. HERO provides an interface with other reference managers and systematic review programs such as Endnote and DistillerSR. DistillerSR is a software that helps screen, review, and manage references efficiently.

In this literature review document, the term "low-priority substance candidate" is used to refer to chemical substances in the low-priority substance proposal and final designation process. This document outlines EPA's approach for identifying, screening, evaluating, and integrating the relevant reasonably available health and environmental hazard and fate information to support low-priority substance designations (Figure 1). This document also describes the general literature search strategies, the inclusion and exclusion criteria to identify information sufficient to establish low-priority designation, and the criteria for assessing the quality of the information. Chemical-specific details, such as the literature search terms, are noted for each chemical substance in their respective proposal screening reviews and supporting documents.

Figure 1: General approach to gather, screen, evaluate, extract and integrate information sufficient to establish designation for low-priority substances



2. Data Search

Per 40 CFR section 702.9, EPA will use reasonably available information to screen candidate substances against the seven regulatory criteria and considerations for prioritization. Reasonably available information is defined as "information that EPA possesses or can reasonably generate, obtain and synthesize for use, considering the deadlines in 15 U.S.C. 2605(b) for prioritization" (40 CFR section 702.3). Reasonably available information includes information received during public comment and confidential business information (CBI) which may appear, for example, in submissions under TSCA section 8.

Data search is an important component of collecting reasonably available information. EPA defined strategies to identify relevant information in public databases and other sources across three broad subject-area disciplines: a) health hazard; b) environmental hazard; and c) fate.

2.1 Chemical Identification

Establishing the identity of the chemical substance under review is the first step in the literature search, and includes verifying the chemical name, Chemical Abstracts Service (CAS) Registry number, chemical structure, and molecular weight and formula. EPA conducted chemical identification for the low-priority substance candidates as described below.

Chemical Name. A chemical name was assigned to the substance and used consistently throughout the profile to describe the chemical substance. Typically, the name was a recognizable common name, although an abbreviation could be used to shorten lengthy names (example, C10-13 Linear alcohol ethoxylates shortened to *C10-13 LAE*). The chemical name listed on the TSCA inventory[1] was included in the assessment, along with other common synonyms. For use in the literature search, a list of chemical name synonyms was also compiled using the ChemIDplus[2], Substance Registry Services (SRS),[3] and Common Chemistry[4] databases.

Chemical Abstracts Service (CAS) Registry Number. EPA used the CAS registry number corresponding to the appropriate TSCA inventory listing for the literature search. Alternate CAS number(s) were also included if they represented old or inactive designations. To avoid potential mischaracterization, related but unconfirmed CAS numbers were excluded. Discrepancies were resolved after consultation with EPA chemistry experts who helped verify CAS numbers.

Chemical structure. Expert judgment was used to determine the chemical structure. Structures were provided in each chemical substance's screening review during prioritization in the form of 2-D image and by the simplified molecular-input line-entry system (SMILES) notation.

2.2 Literature Search Strategy

EPA searched for publicly available information in the peer-reviewed databases, grey literature and additional sources. The peer-reviewed databases contain primary data that have been reviewed by scientific experts and is commonly referred to as peer-reviewed literature. The peer-reviewed database searches were conducted across the three subject-area disciplines mentioned previously. A professional

[1] https://www.epa.gov/tsca-inventory/how-access-tsca-inventory
[2] https://chem.nlm.nih.gov/chemidplus/
[3] https://ofmpub.epa.gov/sor_internet/registry/substreg/LandingPage.do
[4] http://www.commonchemistry.org/

librarian developed the discipline-specific database search strategies by incorporating known chemical synonyms for the chemical substance of interest (section 2.1), and tailoring terms for each database, including applicable indexing keywords or categories available in that database (e.g., Medical Subject Headings (MeSH) terms for the PubMed search strategy). Each chemical's search terms were provided in the chemical substance's screening review published during the proposed priority designation. Table 1 provides the list of peer-reviewed databases that were searched for all the low-priority substance candidates.

Table 1: Peer-reviewed Databases Searched for Low-Priority Substance Candidates	
Health Hazard	
Pubmed	https://www.ncbi.nlm.nih.gov/pubmed/
Web of Science	https://login.webofknowledge.com/
Toxline	https://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?TOXLINE
TSCATS	https://cfpub.epa.gov/si/si_public_record_Report.cfm?Lab=&dirEntryId=2855
Environmental Hazard	
Web of Science	https://login.webofknowledge.com/
Toxline	https://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?TOXLINE
TSCATS	https://cfpub.epa.gov/si/si_public_record_Report.cfm?Lab=&dirEntryId=2855
Proquest	https://www.proquest.com/
Fate	
Web of Science	https://login.webofknowledge.com/

Grey literature and additional sources are the broad category of studies not found in standard, peer-reviewed literature database searches. This includes U.S. and international government agency websites, non-government organization (NGO) websites, and data sources that are difficult to find, or are not included, in the peer-reviewed databases, such as white papers, conference proceedings, technical reports, reference books, dissertations, and information on various stakeholder websites. EPA used the chemical identification information as described in Section 2.1 to search the grey literature and other sources (Table 2). The search results were either PDFs or URLs containing potentially relevant information.

Table 2: Grey Literature and Additional Sources Searched for Low-Priority Substance Candidates	
Source	**Link**
Ulmann's	https://onlinelibrary.wiley.com/doi/book/10.1002/14356007
Kirk-Othmer	https://onlinelibrary.wiley.com/doi/book/10.1002/0471238961
Patty's	https://onlinelibrary.wiley.com/doi/book/10.1002/0471125474
ChemIDplus	https://chem.nlm.nih.gov/chemidplus/
Agency for Toxic Substances and Disease Registry (ATSDR)	https://www.atsdr.cdc.gov/toxprofiledocs/index.html
ChemAgora portal	http://chemagora.jrc.ec.europa.eu/chemagora/
Cosmetic Ingredient Review (CIR)	https://www.cir-safety.org/ingredients
Chemtrack	http://www.chemtrack.org/White/CMR.pdf
European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC) publications	http://www.ecetoc.org/publications
European Chemical Agency (ECHA)	https://echa.europa.eu/web/guest/information-on-chemicals/registered-substances
ECOTOXicology knowledgebase (ECOTOX)	https://cfpub.epa.gov/ecotox/
EPA ChemView	https://chemview.epa.gov/chemview

Table 2: Grey Literature and Additional Sources Searched for Low-Priority Substance Candidates	
Source	**Link**
EPA-High Production Volume Information System (HPVIS)	via ChemView
European Food Safety Authority (EFSA)	http://www.efsa.europa.eu/
US Food and Drug Administration (FDA)	https://www.fda.gov/
Human and Environmental Risk Assessment (HERA)	https://www.heraproject.com/RiskAssessment.cfm
High Production Volume (HPV) Hazard Characterization	https://iaspub.epa.gov/oppthpv/hpv_hc_characterization.get_report?doctype=2
HPV Risk-Based Prioritization	https://iaspub.epa.gov/oppthpv/hpv_hc_characterization.get_report?doctype=1
Hazardous Substances Data Bank (HSDB)	https://toxnet.nlm.nih.gov/newtoxnet/hsdb.htm
INCHEM	http://www.inchem.org/
Japan existing chemical database	http://dra4.nihs.go.jp/mhlw_data/jsp/SearchPageENG.jsp
National Industrial Chemicals Notification and Assessment Scheme (NICNAS)	https://www.nicnas.gov.au/
National Institute of Environmental Health Sciences (NIEHS)	https://www.niehs.nih.gov/index.cfm
Japan National Institute of Technology and Evaluation (NITE)	https://www.nite.go.jp/chem/jcheck/search.action?request_locale=en
National Toxicology Program (NTP)	https://ntpsearch.niehs.nih.gov/home
Organisation for Economic Co-operation and Development (OECD)/Screening Information Dataset (SIDS)	https://hpvchemicals.oecd.org/ui/SponsoredChemicals.aspx

2.3 Search Execution, Retrieval or Results, and Storage in HERO

EPA used the HERO database to search, retrieve, and/or store data sources supporting scientific assessments. EPA used HERO to search peer-reviewed databases for potentially relevant data sources (Table 1). Search results were given a unique reference identifier (or HERO identification number) and organized into a separate HERO chemical page. The references on the HERO chemical page were further organized by discipline (i.e., health hazard; environmental hazard; and fate). Citations were then exported to EndNote to identify duplicates, and any duplicate citations were removed from the HERO chemical page.

EPA searched the grey literature and additional sources outside of HERO. Potentially relevant citations from the sources listed in Table 2 were then manually imported into HERO. Like the references from the peer-reviewed databases, references were assigned a unique reference identifier and organized on the relevant chemical page by discipline.

The HERO low-priority substance candidate project pages are accessible to the public at https://hero.epa.gov/hero/.

3. Data Screening and Evaluation

Following the literature search, EPA screened references through a two-step process using discipline-specific information need criteria (Tables A1-A3). Off topic studies were excluded from further review at both screening steps. Following the initial screening steps, EPA conducted data evaluation and excluded references with unacceptable data quality.

In the first of the screening steps (title/abstract screening, discussed in Section 3.2), EPA reviewed reference titles and abstracts for relevance (see Appendix B). In the second screening step (full-text screening, discussed in Section 3.3), references identified as relevant were subjected to a more detailed relevance check. At this step, EPA reviewed the entirety of a given reference using a more detailed set of questions (see Appendix C).

EPA used DistillerSR to conduct both the title/abstract and full-text screening and data evaluation. DistillerSR helps manage the screening work flow by asking a series of questions based on pre-determined criteria or information needs, and then documenting eligibility decisions for each reference. The program also tracks any conflicts on literature interpretation (i.e. whether a study is on- or off-topic, acceptable or unacceptable) arising between reviewers. For each low-priority substance candidate, two screeners reviewed each reference. Review teams resolved conflicts on literature interpretation through discussion and arriving at mutual agreement or through consultation with peers or subject matter experts.

3.1 Information Needs and Criteria

For each step of the initial screening process, reviewers categorized the references into on-topic for included sources or off-topic for excluded sources. On-topic references are those that may contain information to address the hazard potential of low-priority substance candidates. Off-topic references are those that do not contain relevant information, and thus are excluded from further consideration. The criteria for on-topic and off-topic sources at data screening were developed based on pre-determined information needs. The information needs for each discipline include characteristics pertaining to the study population/test organism, types of exposures and routes, use of controls, type and level of effects, associated media/exposure pathways, and other processes. A complete list of the information needs is provided in Appendix A Tables A1-A3. These information needs helped guide the development of questions for title/abstract and full-text screening.

3.2 Initial Screening by Title and Abstract

Title/abstract screening is the first screening step performed in DistillerSR for peer-reviewed sources only (discussed further below). The results from the peer-reviewed database search were imported from HERO into DistillerSR. For the initial screening, EPA developed questions based on the information needs for each discipline. These high-level title/abstract screening questions were applied to refine references and address:

- Type of data source such as peer-reviewed or grey literature or other data sources;
- Experimental study information based on:
    - Type of test species (i.e. human, animal, *in vitro*, aquatic, terrestrial);
    - Type of hazard outcomes and endpoints;
- Availability of quantitative data (for environmental hazard and fate); and
- Presence of information from other disciplines.

Appendix B lists the title/abstract screening questions in detail for each of the three disciplines. Specifically, the health hazard questions are provided in Table B1, the environmental hazard questions are provided in Table B2, and the fate questions are provided in Table B3.

For references retrieved from the grey literature and additional sources, EPA manually conducted the initial screening on the title and abstract (if available) using the same set of screening questions without using DistillerSR. This approach reduced the number of uploads into DistillerSR initially and focused on uploading only on-topic data sources for full-text screening. In some cases, EPA bypassed the title/abstract screening and initiated full-text screening if the grey literature data source had no abstract and/or the title lacked specificity.

3.3 Full-Text Screening

The relevant references from title/abstract screening were further screened for relevance at the full text level. On-topic references from peer-reviewed databases identified during the title/abstract screening process were uploaded as pdfs into HERO. Two reviewers performed full-text screening on the HERO-tagged pdf in DistillerSR. For grey literature and additional sources, results from manual searches were uploaded in HERO and directly imported to DistillerSR for full-text screening.

Full-text screening questions were developed in DistillerSR and applied to on-topic references for both peer-reviewed and grey literature sources. The full-text screening questions were created to address the remaining information needs for a given discipline. For example, the questions helped identify the presence of detailed information on substance composition, exposure routes, relevant hazard/fate endpoints, and controls in a reference. See Appendix C for full-text screening questions on each of the three disciplines, with health hazard in Table C1, environmental hazard in Table C2, and fate in Table C3. During the full-text screening step, EPA also conducted a quality check where screeners noted supplementary information, inaccessible references (i.e. foreign language, incorrect links, or mismatched pdfs and title/abstract citations), and discussion of unrelated chemicals in the reference.

3.4 Data Evaluation

The quality of individual studies was assessed at the data evaluation stage in the screening review of low-priority substance candidates. For each on-topic study, EPA applied a data quality check using metrics most appropriate for low-hazard chemicals. EPA observed that low-priority substance candidates had fewer peer-reviewed data but had a greater number of grey literature and other sources as compared to chemicals with known hazards, so information from both sources were weighed equally in accordance with TSCA 26(i). Given these differences in information availability, data quality metrics were chosen to capture information from peer-reviewed and grey literature sources for evaluation of low-priority substance candidates.

The unique set of metrics for low-priority substance candidates were organized into a broader category of metrics (domains) that describe study attributes such as the test substance, test design, test condition, test organism, outcome, data presentation, and other attributes. Across each domain, metrics slightly varied from one discipline to another to accommodate the types of information typically present in publicly available sources, as seen on Table 3. Detailed questions and answers associated with data quality metrics are documented in Appendix D, with those for health hazard animal data in Table D1, health hazard *in vitro* data in Table D2, environmental hazard data in Table D3, and environmental fate data in Table D4.

Table 3: Data Quality Evaluation Domains and Metrics by Discipline				
Domain or metric category	**Unique Metrics**			
	Health Hazard- animal	**Health Hazard-*in vitro***	**Environmental Hazard**	**Fate**
Test substance	1. Test substance identity	1. Test substance identity	1. Test substance identity	1. Test substance identity
Test design	2. Negative and vehicle controls 3. Positive controls	2. Negative controls 3. Positive controls 4. Assay type	2. Negative controls	2. Study controls 3. Test substance stability
Test conditions	4. Reporting of doses/concentrations 5. Exposure duration	5. Reporting of concentrations 6. Exposure duration 7. Metabolic activation (if application)	3. Experimental system 4. Reporting of concentrations 5. Exposure duration	4. Test method suitability 5. Testing conditions 6. System type and design- partitioning
Test organisms	6. Test animal characteristics 7. Number of animals per group	8. Test model	6. Test organism characteristics	7. Test organism – degradation 8. Test organism – partitioning
Outcome assessment	8. Outcome assessment methodology	8. Outcome assessment methodology	7. Outcome assessment methodology	9. Outcome assessment methodology
Data presentation	9. Reporting of data	9. Reporting of data	9. Reporting of data	10. Reporting of data
Other				11. Confounding variables 12. Verification or plausibility of results

For data evaluation for low-priority substance candidate references, EPA assessed references against the quality metrics listed in Table 3 to determine whether a source was acceptable for subsequent data extraction. On-topic references for low-priority substance candidates were evaluated and categorized as unacceptable or acceptable for data extraction based on the data quality metrics in Appendix D.

4. Data Extraction and Integration

4.1 Data Extraction

Data extraction is the process in which quantitative and qualitative information are identified from each on-topic, acceptable source and extracted. EPA implemented data extraction during the screening review for each low-priority substance candidate. Only sources containing information that met data quality metrics went through the data extraction process.

For on-topic, acceptable sources, data evaluators extracted relevant details concerning the study method and approach, such as:

- Test substance ID as reported in the study
- Test substance purity, if reported
- GLP compliance, if reported
- Concentration, unit conversions, and calculations
- Critical health effects
- Routes of exposure
- Media/exposure pathways (in the context of hazard studies)
- Author noted method deviations
- Evaluator noted deviations
- Any assumptions made about the study details. For example, duration or use of controls was not explicitly stated but was assumed to be acceptable based on the reported test method.

4.2 Data Integration into Summary Findings

After evaluating all references, EPA implemented a data integration strategy in the screening review for each low-priority substance candidate. Data integration activities included development of endpoint summaries and weight of the scientific evidence (WoSE) analysis taking into account the data's quality, consistency, relevancy, coherence and biological plausibility. Specifically,

- When multiple references provided the same study (e.g., multiple grey literature and additional sources), EPA integrated and collapsed the information into one study summary and provided all relevant HERO IDs;
- EPA described the data for each endpoint in each chemical substance's screening review published at proposal (described further below); and
- EPA applied WoSE analysis[5] when needed to ensure that the reasonably available information was considered and appropriately weighed in the evaluation.

EPA's proposed priority designations under 40 CFR section 702.9 and final priority designations under 40 CFR section 702.11 will be consistent with the scientific standards provision in 15 U.S.C. 2625(h) and the weight of the scientific evidence provision in 15 U.S.C. 2625(i). EPA reviewed reasonably available information, consistent with 15 U.S.C. 2625(k), to identify relevant, quality studies to evaluate the hazard potential for each chemical substance against the endpoints listed in each chemical's screening review. EPA's New Chemicals Program has used these endpoints for decades to evaluate chemical substances

[5] WoSE analysis is an integrative and interpretive process that considers information in favor (e.g., positive study) or against (e.g., negative study) a given hypothesis within the context of the assessment question(s) being evaluated.

under TSCA[6] and EPA toxicologists rely on these endpoints as key indicators of potential human health and environmental effects. These endpoints also align with internationally accepted hazard characterization criteria, such as the Globally Harmonized System of Classification and Labelling of Chemicals,[7] and form the basis of the comparative hazard assessment of chemicals.

As a last step, EPA prepared a summary of findings to present the evidence for each of the statutory considerations and criteria described in 40 CFR section 702.9. The summary of findings also described the basis for the conclusion(s) and recommendation(s) supporting the designation of the low-priority substance.

[6] https://www.epa.gov/sustainable-futures/sustainable-futures-p2-framework-manual
[7] https://www.unece.org/fileadmin/DAM/trans/danger/publi/ghs/ghs_rev07/English/ST_SG_AC10_30_Rev7e.pdf

Appendix A: Information Needs

For the screening review of low-priority substance candidates, EPA identified health hazards, environmental hazards, and fate characteristics associated with exposures from relevant routes (e.g., oral, inhalation, dermal). The type of information needed to conduct a screening review of low-priority substance candidates varied across the three hazard and fate disciplines. Discipline-specific information needs are listed below in Tables A.1-A.3. To properly screen a study, the information needs include: a description of the test species (e.g. human, animal, aquatic, terrestrial); hazard endpoints (e.g. acute and chronic toxicity, cancer vs. non-cancer health outcomes, mortality); controls; and associated media and exposure pathways in the context of hazard studies.

Table A.1: Information Needs for Health Hazard Data

Type	Information Needs

Hazard Effects	• Identify and document health hazards associated with exposure[8] to the chemical substance using:
	  • Test organisms or species, including:
	  • *Humans*: Epidemiological and intentional human dosing studies,[9] if available
	  ▪ Potentially exposed or susceptible subpopulations such as infants, children, pregnant women, occupational workers, the elderly, etc.
	  • *Animals*: Standard mammalian animal models, including rat, mouse, rabbit, guinea pig, hamster, monkey, dog
	  • *in vitro*: Human or animal cells, tissues or organs (not whole animals); bacteria, nonmammalian eukaryotes; other nonmammalian laboratory studies
	  • Endpoint-specific effects, including:
	  • Acute effects, sub-chronic effects, chronic effects
	  • Carcinogenicity, mutagenicity/genotoxicity, reproductive and developmental toxicity, neurotoxicity
	  • Skin sensitization, eye and skin irritation
	  • Dose (or concentration) response data
	  • Proper negative or positive controls, as appropriate

Toxicokinetics, if available	• Identify toxicokinetic data, i.e. on absorption, distribution, metabolism, excretion (ADME):
	  • Animal and human studies
	  • *in vitro* studies
	  • Modelled ADME data
	  • Physiologically-based pharmacokinetic (PBPK) models

Mechanistic evidence, if available	• Identify studies that support the mode of action (MOA) for health effects (e.g., for threshold or non-threshold cancer and non-cancer effects) from:
	  • Genotoxicity studies
	  • *in vitro* mechanistic studies *in vivo* mechanistic studies

[8] Exposure to the chemical substance via all relevant routes such as oral, inhalation, or dermal routes. This also includes exposure in air, dust, drinking water, diet, or gavage.
[9] Ethical considerations were part of EPA's evaluation of human data.

Table A.2: Information Needs for Environmental Hazard Data	
Type	**Information Needs**

Hazard Effects	• Identify and document environmental hazards associated with exposure to the chemical substance using:
	  • Test organisms or species, including:
	  • Standard and non-standard species for fish, invertebrates, microorganisms in freshwater and marine environments or media
	  • Benthic organisms or relevant sediment species in freshwater and marine environments or media, if available
	  • Relevant non-aquatic or non-mammalian terrestrial species (e.g., earthworms), if available
	  • Endpoint-specific effects, including:
	  • Acute and chronic effects
	  • Mortality, immobilization, development/growth rate/yield, biomass, reproduction/fertility
	  • Dose (or concentration) response data
	  • Proper negative or positive controls, as appropriate

Table A.3: Information Needs for Fate Data	
Type	**Information Needs**

Characteristics or Parameters	• Identify and document environmental fate characteristics or parameters associated with exposure to the chemical substance using:
	  • Associated Media/Exposure Pathways:
	  • Surface water, sediment
	  • Soil, biosolids
	  • Groundwater
	  • Air
	  • Other (e.g., biota)
	  • Associated Processes, such as:
	  • Hydrolysis, photolysis, biodegradation (aerobic and anaerobic), atmospheric deposition, sorption, mobility, partitioning, bioaccumulation and bioconcentration
	  • Engineering processes, if available (e.g., wastewater treatment, incineration)
	  • Proper negative or positive controls, as appropriate

Appendix B: Title/Abstract Screening Questions

The information needs in Appendix A guided the development of the initial screening questions across disciplines. Tables B.1-B.3 describe the title/abstract screening questions that were either applied to all grey literature (and other) sources manually or applied to peer-reviewed sources in DistillerSR. The initial screening questions, detailed below, address information such as type of data source (peer-reviewed vs. grey literature), type of evidence (e.g. quantitative vs. qualitative; or by outcome), and presence of data for other disciplines in each reference.

Table B.1: Low-Priority Substance Title/Abstract Screening Questions for Health Hazard Data

Question	Answer
Is information presented related to the health hazard information needs?	Yes
	No*
What is the source of the health hazard information?	Peer-reviewed literature source or robust summary
	Grey literature and additional sources
	Unclear (e.g., no abstract)
What kind of evidence does this reference primarily contain?	Human
	Animal
	in vitro
	*in silico**
Based on title and abstract screening, which health outcome(s) apply? (check all that apply)	Acute toxicity
	Repeat dose (chronic/sub-chronic)
	Neurotoxicity
	Carcinogenicity
	Reproductive toxicity
	Developmental toxicity (including developmental neurotoxicity)
	Irritation (skin, eye, respiratory)
	Sensitization (skin, respiratory)
	Immunotoxicity
	Absorption, Distribution, Metabolism, and Excretion (ADME)
	Genotoxicity
	Mechanisms of toxicity (e.g. mechanisms of action, adverse outcome pathways)
	Unclear (e.g. no abstract)
Is information for another discipline presented?	Environmental Hazard
	Fate
	Other (e.g. Exposure, Chemistry)

* If this answer was selected, the reference was excluded from EPA's screening review.

Table B.2: Low-Priority Substance Title/ Abstract Screening for Environmental Hazard Data	
Question	**Answer**
Is information presented related to the environmental hazard information needs?	Yes
	No*
What is the source of the environmental hazard information?	Peer reviewed literature source or robust summary
	Grey literature and additional sources
	Unclear
Is quantitative environmental hazard data presented?	Yes
	No*
	Maybe
Is information for another discipline presented?	Fate
	Health Hazard
	Other (e.g. Exposure, Chemistry)

* If this answer was selected, the reference was excluded from EPA's screening review.

Table B.3: Low-Priority Substance Title/Abstract Screening for Fate Data	
Question	**Answer**
Is information presented related to the fate information needs?	Yes
	No*
What is the source of the fate information?	Peer-reviewed literature source or Robust Summary
	Grey literature and additional sources
	Unclear
Is quantitative fate data presented?	Yes
	No*
	Maybe
Is information for another discipline presented?	Environmental Hazard
	Health Hazard
	Other (e.g. Exposure, Chemistry)

* If this answer was selected, the reference was excluded from EPA's screening review.

Appendix C: Full-Text Screening Questions in DistillerSR

The information needs (in Appendix A) were also used to develop full-text screening questions. These questions were applied to references from both peer-reviewed and grey literature sources in DistillerSR for health hazard (human, animal, and *in vitro*) as described in Table C.1, environmental hazard as described in Table C.2, and environmental fate as described in Table C.3. The typical questions addressed during full-text screening helped identify information such as substance composition, type of exposure route, relevant hazard/fate endpoints, and use of appropriate controls and models.

Table C.1: Low-Priority Substance Full-Text Screening Questions for Health Hazard Data

Question	Answer
Does the reference contain information pertaining to a low-priority substance candidate?	Yes
	No*
What type of source is this reference?	Peer-reviewed literature source
	Robust summary (e.g. HPVIS, ECHA DB)
	Government or other reliable assessment [Note: this should include any assessment containing unpublished data]
	Review article or book chapter that contains only citations to peer-reviewed literature sources* [excluded to help remove duplicates]
	Unclear
Does the reference contain supplemental human health hazard information?	Yes
	No
What kind of evidence does this reference primarily contain?	Human
	Animal
	in vitro
	in silico studies that DO NOT contain experimental verification*
The following questions apply to HUMAN evidence only	
Does the reference report an exposure route that is or is presumed to be by an inhalation, oral, or dermal route?	Yes
	No*
Does the reference report both test substance exposure(s) AND related health outcome(s)?	Yes
	No*
If the reference reports an exposure to a chemical mixture, are measures of the test substance or related metabolite(s) reported independently of other chemicals? Note: If the paper does not pertain to mixtures, choose "Not Applicable".	Yes
	No*
	Not Applicable
Does the reference have an appropriate study population based on the information needs (e.g., mammalian whole-animal)?	Yes
	No*
The following questions apply to ANIMAL evidence only	
Does the reference report an exposure route that is by inhalation, oral, or dermal route?	Yes
	No*

Table C.1: Low-Priority Substance Full-Text Screening Questions for Health Hazard Data	
Question	**Answer**
Does the reference report both test substance-related exposure(s) AND related health outcome(s)?	Yes
	No*
Does the reference report the duration of exposure?	Yes
	No*
Does the reference report an exposure to the test substance only (i.e. no mixtures with the exception of aqueous solutions and reasonable impurities and byproducts)?	Yes
	No*
Does the paper report a negative control that is a vehicle control or no treatment control?	Yes
	No*[10]
The following questions apply to MECHANISTIC/ALTERNATIVE TEST METHODS evidence only	
Does the reference report a negative control that is a vehicle control or no treatment control?	Yes
	No*
Does the reference report an exposure to the test substance only (i.e. no mixtures with the exception of aqueous solutions and reasonable impurities and byproducts)?	Yes
	No*
For genotoxicity studies only: Does the study use a positive control?	Yes
	No*
	Not applicable
Based on full-text screening, which health outcome(s) apply? (check all that apply)	Acute toxicity
	Repeat dose (chronic/sub-chronic)
	Neurotoxicity
	Carcinogenicity
	Genotoxicity
	Reproductive toxicity
	Developmental toxicity (including developmental neurotoxicity)
	Irritation (skin, eye, respiratory)
	Sensitization (respiratory, skin)
	Immunotoxicity
	Absorption, Distribution, Metabolism, and Excretion (ADME)
	Mechanistic toxicity (e.g. mechanisms of action)

* If this answer was selected, the reference was excluded from EPA's screening review.

[10] Except for acute mammalian toxicity and skin and eye irritation studies, where the use of a negative control may not be required (e.g., OECD 403 Acute Inhalation Toxicity Guidelines).

Table C2: Low-Priority Substance Full-Text Screening Questions for Environmental Hazard Data	
Question	**Answer**
Does the reference contain information pertaining to a low-priority substance candidate?	Yes
	No*
What type of source is this reference?	Peer-reviewed literature source
	Robust summary (e.g. HPVIS, ECHA DB)
	Government or other reliable assessment [Note: this includes any assessment that contains unpublished data]
	Review article or book chapter that contains only citations to peer-reviewed literature sources* [excluded to help remove duplicates]
	Unclear
Does the reference contain supplemental environmental hazard information?	Yes
	No
Is quantitative environmental hazard data presented?	Yes
	No*
Is this primarily a modeling/simulation study? [Note: select "No" if experimental verification was included in the study]	Yes*
	No
Is environmental hazard data presented for standard or non-standard aquatic or terrestrial species (fish, invertebrates, microorganisms, non-mammalian terrestrial species)?	Yes
	No*
Is exposure measured for the target substance or is the test substance a mixture (except for reasonable impurities, byproducts, and aqueous solutions) or formulated product?	Target substance
	Mixture*
	Formulated Product*
	Unclear
Does the reference report a duration of exposure?	Yes
	No*
Does the reference report a negative control that is a vehicle control or no treatment control?	Yes
	No*
Does the reference include endpoints in the information needs?	Yes
	No*
Which types of evidence are reported?	Acute fish toxicity
	Acute invertebrate toxicity
	Acute algae/microorganism toxicity
	Chronic fish toxicity
	Chronic invertebrate toxicity
	Chronic algae/microorganism toxicity
	Benthic or relevant sediment species (marine or freshwater)
	Non-mammalian species

* If this answer was selected, the reference was excluded from EPA's screening review.

Table C.3: Low-Priority Substance Full-Text Screening Questions for Fate Data	
Question	**Answer**
Does the reference contain information pertaining to a low-priority substance candidate?	Yes
	No*
What type of source is this reference?	Peer-reviewed literature source
	Robust summary (e.g. HPVIS, ECHA DB)
	Government or other reliable assessment [Note: this includes any assessment that contains unpublished data]
	Review article or book chapter that contains only citations to peer-reviewed literature sources* [excluded to help remove duplicates]
	Unclear
Does the reference contain supplemental fate information?	Yes
	No
Is quantitative fate data presented?	Yes
	No*
Is this primarily a modeling/simulation study? [Note: Select "Yes" only if there is no experimental verification]	Yes*
	No
For which medium/media is information presented?	Air
	Biosolids/Sludge
	Biota/Tissues
	Drinking water
	Groundwater
	Sediment
	Soil
	Surface water
	Wastewater
	Other media (explain other media)
Which fate data endpoints are reported?	Ready biodegradation (OECD 301 series; OECD 310)
	Inherent biodegradation (OECD 302 series)
	Aerobic biodegradation (excluding ready and inherent standard tests)
	Aerobic biotransformation products
	Anaerobic biodegradation
	Anaerobic biotransformation products
	Aqueous photolysis
	Atmospheric photolysis (direct, indirect)
	Hydrolysis
	Abiotic transformation products (includes photolysis, hydrolysis)
	Photolysis - Soil
	Bioconcentration Factor (BCF)/Bioaccumulation Factor (BAF)

Table C.3: Low-Priority Substance Full-Text Screening Questions for Fate Data	
Question	**Answer**
	Biomagnification Factor (BMF)
	Henry's Law Constant
	Volatilization
	Koc/Soil absorption
	Soil mobility (suspension/resuspension)
	Wastewater treatment removal
	Incineration removal information
	Other fate information

* If this answer was selected, the reference was excluded from EPA's screening review.

Appendix D: Data Quality Metrics

During data evaluation, references were evaluated against a unique set of metrics (Table 3) for each of the hazard and fate disciplines. The metrics are designed to further describe study characteristics and define the quality of the data. The data quality of a study was assessed across a general category of metrics (or domains) that include information about the test substance, test design, test conditions, test organism, test outcome, and data presentation. References were excluded when unacceptable for at least one metric. The tables below include metrics in question form for the data quality evaluation of health hazard-animal data (Table D.1), health hazard-*in vitro* data (Table D.2), environmental hazard data (Table D.3), and fate (Table D.4).

Table D.1: Low-Priority Substance Data Quality Evaluation of Health Hazard – Animal Data

Question	Answer
Metric 1: Test Substance Identity • Was the test substance identified (i.e., established nomenclature, CASRN or other registry number, and/or structure) definitively reported? • If test substance is a mixture, were mixture components characterized?	Acceptable if: • The test substance identity could be determined from the information provided. **OR** • For mixtures, the components were characterized, or the test substance identity or description included molecular boundaries of the mixture or source material in such a manner that a reasonable approximation of components can be determined.
	Unacceptable if: • The test substance identity cannot be determined from the information provided (e.g., nomenclature was unclear and CASRN or structure were not reported). **OR** • For mixtures, the components and ratios were not characterized or did not include information that could result in a reasonable approximation of components.
	Not applicable
Metric 2: Negative and Vehicle Controls • Was an appropriate concurrent negative control group included? • If a vehicle was used, was the control group exposed to the vehicle? • For inhalation and gavage studies, were controls sham-exposed?	Acceptable if: • Study authors reported using an appropriate concurrent negative control group (e.g.., all conditions are equal except for chemical exposure). For gavage or inhalation study, a vehicle and/or sham-treated control group was included.
	Unacceptable if: • A concurrent negative control group was not included or reported. **OR** • The reported negative control group was not appropriate (e.g., age/weight of animals differed between control and treated groups).
	Not applicable
Metric 3: Positive Controls • Was an appropriate concurrent positive control group included, if necessary, based on study type (e.g., certain neurotoxicity studies)?	Acceptable if: • When applicable, a concurrent positive control was used (if necessary for the study type) and a positive response was observed.
	Unacceptable if:

Table D.1: Low-Priority Substance Data Quality Evaluation of Health Hazard – Animal Data	
Question	**Answer**
	• When applicable, an appropriate concurrent positive control (i.e., inducing a positive response) was not used.
	Not applicable: • This metric is not rated/applicable if positive control was not indicated by study type.
Metric 4: Reporting of Doses/Concentrations • Were doses/concentrations reported without ambiguity (e.g., point estimate in addition to a range)? • In oral studies, if doses were not reported, was information reported that enabled dose estimation (e.g., test animal dietary intake and body weight monitoring data in dietary studies)?	Acceptable if: • Doses/concentrations were reported or could be calculated using default or reported estimates of body weight and diet/water intake. Note: Dose calculations based on default estimates of body weight and food/water intake are acceptable for grey literature.
	Unacceptable if: • Doses/concentrations were not reported and could not be calculated using default or reported estimates of body weight and diet/water intake (e.g., default intake values are not available for pregnant animals).
	Not applicable
Metric 5: Exposure Duration • Was the duration of exposure reported and appropriate for this study type and/or outcome(s) of interest?	Acceptable if: • The exposure duration was reported and appropriate for this study type and/or outcome(s) of interest (e.g., > 28 days duration for repeat dose).
	Unacceptable if: • The duration of exposure was not reported. **OR** • The reported exposure duration was not suited to the study type and/or outcome(s) of interest (e.g., <28 days for repeat dose).
	Not applicable
Metric 6: Test Animal Characteristics • Were the test animal species, strain, sex, health status, age, and starting body weight reported? • Was the test species and strain an appropriate animal model for the evaluation of the specific outcome(s) of interest (e.g., routinely used for similar study types)?	Acceptable if: • The test animal species was reported and was appropriate for the evaluation of the specific outcome(s) of interest (e.g., routinely used for the study type).
	Unacceptable if: • The test animal species was not reported. **OR** • The test animal (species, strain, sex, life-stage, source) was not appropriate for the evaluation of the specific outcome(s) of interest (e.g., genetically modified animals, strain was uniquely susceptible or resistant to one or more outcome of interest).
	Not applicable
Metric 7: Number of Animals Per Group • Was the number of animals per study group appropriate for the study type and outcome analysis?	Acceptable if: • The number of animals per study group was reported and was sufficient to characterize toxicological effects.
	Unacceptable if:

Table D.1: Low-Priority Substance Data Quality Evaluation of Health Hazard – Animal Data	
Question	**Answer**
	• The number of animals per study group was not reported. **OR** • The number of animals per study group was insufficient to characterize toxicological effects (e.g., 1-2 animals in each group).
	Not applicable
Metric 8: Outcome Assessment Methodology • Did the outcome assessment methodology address or report the intended outcome(s) of interest? • Was the outcome assessment methodology (including endpoints and timing of assessment) sensitive for the outcome(s) of interest (e.g., measured endpoints that are able to detect a true health effect or hazard)? Note: Outcome refers to health effects measured in an animal study (e.g., acute toxicity/lethality, organ-specific toxicity, reproductive and developmental toxicity).	Acceptable if: • The outcome assessment methodology addressed or reported (at least partially) the intended outcome(s) of interest and was sensitive for the outcomes(s) of interest (e.g., serum chemistry and organ weight evaluated in the absence of histology).
	Unacceptable if: • The outcome assessment methodology was not sensitive for the outcome(s) of interest (e.g., evaluation of endpoints outside the critical window of development, a systemic toxicity study that evaluated only grossly observable endpoints, such as clinical signs and mortality, etc.).
	Not applicable
Metric 9: Reporting of Data • Were the data for all outcomes presented? • Were data reported by exposure group and sex (if applicable)?	Acceptable if: • A description of exposure-related findings was presented for most outcomes by exposure group and sex (if applicable).
	Unacceptable if: • 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.
	Not applicable
Comment: Please list any strengths and/or deficiencies identified for each metric, or if the metric is "not applicable", explain why.	

Table D.2: Low-Priority Substance Data Quality Evaluation of Health Hazard – *in vitro* Data	
Questions	**Answer**
Metric 1: Test Substance Identity • Was the test substance identified (i.e., established nomenclature, CASRN, and/or structure) definitively reported? • If test substance is a mixture, were mixture components characterized?	Acceptable if: • The test substance identity could be determined from the information provided. **OR** • For mixtures, the components were characterized, or the test substance identity or description included molecular boundaries of the mixture or source material in such a manner that a

Table D.2: Low-Priority Substance Data Quality Evaluation of Health Hazard – *in vitro* Data	
Questions	**Answer**
	reasonable approximation of components can be determined.
	Unacceptable if: • The test substance identity or description cannot be determined from the information provided (e.g., nomenclature was unclear and CASRN or structure were not reported). **OR** • For mixtures, the components and ratios were not characterized or did not include information that could result in a reasonable approximation of components.
	Not applicable
Metric 2: Negative Controls • Was a concurrent negative (untreated, sham-treated, and/or vehicle, as necessary) control group included?	Acceptable if: • Study authors reported using an appropriate concurrent negative control group (i.e., all conditions are equal except for chemical exposure).
	Unacceptable if: • A concurrent negative control group was not included or reported. **OR** • The reported negative control group was not appropriate (e.g., different cell lines used for controls and test substance exposure).
	Not applicable
Metric 3: Positive Controls • Was a concurrent positive or proficiency control group included, *if applicable*, based on study type, and was the response appropriate in this group (e.g., induction of positive effect)?	Acceptable if: • A concurrent positive or proficiency control group, if applicable, was used and the intended positive response was induced.
	Unacceptable if: • A concurrent positive control or proficiency group was not used.
	Not applicable
Metric 4: Assay Type • Were assay types (e.g., bacterial mutagenicity assay, chromosomal aberration assay, comet assay, unscheduled DNA repair assay, etc.) reported?	Acceptable if: • The assay type was reported and was appropriate for the study type and/or outcome(s) of interest.
	Unacceptable if: • The assay type was not reported. **OR** • The assay type was not appropriate for the study type or outcome of interest (e.g., *in vitro* skin corrosion protocol used for *in vitro* skin irritation assay).
	Not applicable
Metric 5: Reporting of Concentration • Were exposure doses/concentrations or amounts of test substance reported without ambiguity (e.g., point estimate instead of range, analytical instead of nominal)?	Acceptable if: • The exposure doses/concentrations or amounts of test substance were reported without ambiguity (e.g., point estimate instead of range).
	Unacceptable if:

Table D.2: Low-Priority Substance Data Quality Evaluation of Health Hazard – *in vitro* Data	
Questions	**Answer**
	• The exposure doses/concentrations or amounts of test substance were not reported.
	Not applicable
Metric 6: Exposure Duration • Was the exposure frequency (hours/day and days/week) and duration of exposure reported and appropriate for this study type and/or outcome(s) of interest?	Acceptable if: • The exposure duration (e.g., min, hours, days) was reported and appropriate for the study type and/or outcome(s) of interest (e.g., 48-72-hour exposure for bacterial reverse mutation assay).
	Unacceptable if: • No information on exposure duration(s) was reported. **OR** • The exposure duration was not appropriate for the study type and/or outcome of interest (e.g., 24 hours exposure for bacterial reverse mutation test).
	Not applicable
Metric 7: Metabolic Activation • Were exposures conducted in the presence and absence of a metabolic activation system, if applicable, for the study type? • Was the source, method of preparation, concentration or volume in final culture, and quality control information on the metabolic activation system reported?	Acceptable if: • Study authors reported exposures were conducted in the presence of metabolic activation and the type and source.
	Unacceptable if: • No information on the characterization and use of a metabolic activation system was reported. **OR** • The exposure duration was not appropriate for the study type and/or outcome of interest (e.g., 24 hours exposure for bacterial reverse mutation test).
	Not applicable
Metric 8: Test Model • Were the test models (e.g., cell types or lines, tissue models) reported? • Was the model routinely used for the outcome of interest (e.g., Chinese hamster ovary cells for micronucleus formation)?	Acceptable if: • The test model was reported and is routinely used for the outcome of interest.
	Unacceptable if: • The test model was not reported OR • The test model was not routinely used for evaluation of the specific outcome of interest.
	Not applicable
Metric 9: Outcome Assessment Methodology • Did the outcome assessment methodology address or report the intended outcome(s) of interest? • Was the outcome assessment methodology (including endpoints and timing of assessment) sensitive for the outcome(s) of interest (e.g., measured endpoints that are able to detect a true health effect or hazard)? Note: Outcome refers to health effects measured in an animal study (e.g., acute toxicity/lethality, organ-specific toxicity, reproductive and developmental toxicity).	Acceptable if: • The outcome assessment methodology addressed or reported (at least partially) the intended outcome(s) of interest and was sensitive for the outcomes(s) of interest (e.g., mutation frequency evaluated in the absence of cytotoxicity in a gene mutation test).
	Unacceptable if: • The outcome assessment methodology was not reported. **OR** • The assessment methodology was not appropriate for the outcome(s) of interest (e.g., cells were

Table D.2: Low-Priority Substance Data Quality Evaluation of Health Hazard – *in vitro* Data	
Questions	**Answer**
	evaluated for chromosomal aberrations immediately after exposure to the test substance instead of after post-exposure incubation period).
	Not applicable
Comment: Please list any strengths and/or deficiencies identified for each metric, or if the metric is "not applicable", explain why.	

Table D.3: Low-Priority Substance Data Quality Evaluation of Environmental Hazard Data	
Question	**Answer**
Metric 1: Test Substance Identity • Was the test substance identified (i.e., established nomenclature, CASRN or other registry number, and/or structure) definitively reported? • If test substance is a mixture, were mixture components characterized?	Acceptable if: • The test substance identity could be determined from the information provided. **OR** • For mixtures, the components were characterized, or the test substance identity or description included molecular boundaries of the mixture or source material in such a manner that a reasonable approximation of components can be determined.
	Unacceptable if: • The test substance identity or description cannot be determined from the information provided (e.g., nomenclature was unclear, CASRN or structure were not reported, substance name/ description does not match CASRN). **OR** • For mixtures, the components and ratios were not characterized or did not include information that could result in a reasonable approximation of components.
	Not applicable
Metric 2: Negative Controls • Was a concurrent negative control group tested?	Acceptable if: • Study authors reported using a concurrent negative control group.
	Unacceptable if: • A concurrent negative control group was not included or reported
	Not applicable
Metric 3: Experimental System • Was the experimental system (e.g., static, semi-static, or flow-through regime) described?	Acceptable if: • The experimental system (e.g., static, semi-static, or flow-through regime) was described.
	Unacceptable if: • The experimental system (e.g., static, semi-static, or flow-through regime) was not described.
	Not applicable

Table D.3: Low-Priority Substance Data Quality Evaluation of Environmental Hazard Data	
Question	**Answer**
Metric 4: Reporting of Concentrations • Were test substance concentrations reported (nominal and/or measured)?	Acceptable if: • Test concentrations were reported (nominal and/or measured).
	Unacceptable if: • Test concentrations were not reported.
	Not applicable
Metric 5: Exposure Duration • Was the duration of exposure reported and appropriate for this study type and/or outcome(s) of interest?	Acceptable if: • The duration of exposure was reported and appropriate for the study type and/or outcome(s) of interest (e.g., acute daphnid study of 48-hour duration).
	Unacceptable if: • The duration of exposure was not reported. **OR** • The reported exposure duration was not suited to the study type and/or outcome(s) of interest (e.g., study intended to assess effects on reproduction did not expose organisms for an acceptable period of time prior to mating).
	Not applicable
Metric 6: Test Organism Characteristics • Was the test species reported and appropriate for this study type and/or outcome(s) of interest? • If available, is the life stage or age of the test organisms appropriate for the study?	Acceptable if: • The test species was reported and appropriate for this study type and/or outcome(s) of interest. If reported, the organism life stage or age was appropriate for the outcome(s) of interest.
	Unacceptable if: • The test species was not reported. **OR** • The test species, life stage, or age was not appropriate for the outcome(s) of interest.
	Not applicable
Metric 7: Outcome Assessment Methodology • Did the outcome assessment methodology address or report the intended outcome(s) of interest? Note: Outcome refers to biological effects measured in an ecotoxicity study (e.g., reproductive toxicity).	Acceptable if: • The outcome assessment methodology addressed or reported (at least partially) the intended outcome(s) of interest.
	Unacceptable if: • The outcome assessment methodology was not reported.
	Not applicable
Metric 8: Reporting of Data • Were exposure-related findings reported as effect levels for the endpoint(s) of interest (e.g., LOEC, NOEC, LC_{50}, EC_{50})?	Acceptable if: • Exposure-related findings were reported as effect levels for the endpoint(s) of interest (e.g., LOEC, NOEC, LC_{50}, EC_{50}).
	Unacceptable if: • Data presentation was inadequate. **OR** • Major inconsistencies were present in reporting of results.
	Not applicable

Table D.3: Low-Priority Substance Data Quality Evaluation of Environmental Hazard Data	
Question	**Answer**
Comment: Please list any strengths and/or deficiencies identified for each metric, or if the metric is "not applicable", explain why.	

Table D.4: Low-Priority Substance Data Quality Evaluation of Fate Data	
Question	**Answer**
Metric 1: Test Substance Identity • Was the test substance identified (i.e., established nomenclature, CASRN or other registry number, and/or structure) definitively reported? • If test substance is a mixture, were mixture components characterized?	Acceptable if: • The test substance identity could be determined from the information provided. **OR** • For mixtures, the components were characterized, or the test substance identity or description included molecular boundaries of the mixture or source material in such a manner that a reasonable approximation of components can be determined.
	Unacceptable if: • The test substance identity or description cannot be determined from the information provided (e.g., nomenclature was unclear and CASRN or structure were not reported). **OR** • For mixtures, the components and ratios were not characterized or did not include information that could result in a reasonable approximation of components.
	Not applicable
Metric 2: Study Controls • Was a concurrent negative control or blank group included? • Were positive controls included (if applicable)? • If a vehicle was used was it unlikely to influence the study results, stability, bioavailability or/toxicity of the test substance?	Acceptable if: • The study included a negative control or blank group. If applicable, a positive control group was included. **AND** • The selected vehicle was unlikely to influence the study results.
	Unacceptable if: • The study did not include or report crucial control groups that consequently made the study unusable (e.g., no positive control for a biodegradation study reporting 0% removal). **OR** • The vehicle used in the study was likely to unduly influence the study results.
	Not applicable
Metric 3: Test Substance Stability • Did the study characterize and accommodate the test substance stability, homogeneity, preparation, and storage conditions?	Acceptable if: • The test substance stability, homogeneity, preparation, and storage conditions were reported, and were appropriate for the study (e.g., a test substance known to degrade in light was stored in dark or amber bottles).

Table D.4: Low-Priority Substance Data Quality Evaluation of Fate Data	
Question	**Answer**
	OR • The test substance stability, homogeneity, preparation or storage conditions were not reported; however, these factors were not likely to have a substantial impact on study results.
	Unacceptable if: • There were problems with test substance stability, homogeneity, or preparation that had an impact on concentration or dose estimates and interfered with interpretation of study results.
	Not applicable
Metric 4: Test Method Suitability • Was the test method reported and suitable for the test material? • Was the target chemical tested at concentrations below its aqueous solubility?	Acceptable if: • The test method was suitable for the test substance**.** The measured or nominal concentrations of the test substance were provided, but these concentrations did not greatly exceed the water solubility of the test substance.
	Unacceptable if: • The test method was not reported or not suitable for the test substance. **OR** • The test concentrations were not reported. **OR** • The reported test concentrations were not measured, and the nominal concentrations reported greatly exceeded the substances water solubility, which would greatly inhibit meaningful interpretation of the outcomes.
	Not applicable
Metric 5: Testing Conditions • Were the test conditions reported and appropriate for the study method (e.g., temperature, dissolved organic matter, aeration, total organic matter, pH or water hardness reported and maintained throughout the test)?	Acceptable if: • Reported testing conditions were appropriate for the study method. Deviations or omissions were minor and were not likely to have substantial impact on study results.
	Unacceptable if: • Testing conditions were not reported, and the omission would likely have a substantial impact on study results. **OR** • Testing conditions were not appropriate for the method (e.g., a biodegradation study at temperatures that inhibit the microorganisms).
	Not applicable
Metric 6: System Type and Design- for partitioning studies • Was equilibrium established? • Were the system type and design capable of appropriately maintaining substance concentrations for experimental studies?	Acceptable if: • Equilibrium was established. The system type and design (e.g.., static, semi-static, and flow-through; sealed, open) were capable of appropriately maintaining substance concentrations. **OR**

Table D.4: Low-Priority Substance Data Quality Evaluation of Fate Data	
Question	**Answer**
	• Equilibrium or system type/design was not established or reported, but this was not likely to have a substantial impact on study results.
	Unacceptable if: • Equilibrium was not established or reported, preventing meaningful interpretation of study results. **OR** • The system type and design (e.g. static, semi-static, and flow-through; sealed, open) were not capable of appropriately maintaining substance concentrations, preventing meaningful interpretation of study results.
	Not applicable
Metric 7: Test Organism- for degradation studies • Was information about the test organism, species or inoculum reported? • Was inoculum source and any pre-conditioning or pre-adaptation procedures reported? • Are the test organism, species or inoculum source routinely used for similar study types or outcome(s) of interest? • Were the chosen organisms or inoculum appropriate for the study method or route?	Acceptable if: • The test organism, species, or inoculum source were reported, including information concerning any pre-conditioning or pre-adaptation procedures. In general, the species or inoculum source are routinely used for similar study types or were otherwise appropriate for the study method. **OR** • The information above was only partially disclosed but would not prevent meaningful interpretation of the study results (e.g., an adapted inoculum in a ready test would not be excluded, but reviewer comments should note that the study could only be used to evaluate inherent biodegradation).
	Unacceptable if: • The test organism, species, or inoculum source were not reported, preventing meaningful interpretation of the study results.
	Not applicable
Metric 8: Test Organism-for partitioning studies • Was information about the test organism reported? • Is the test organism or species routinely used for similar study types or outcome(s) of interest?	Acceptable if: • The test organism was reported and is routinely used for similar study types or outcome(s) of interest. **OR** • The test organism is not routinely used, but this deviation is not likely to prevent meaningful interpretation of the study results.
	Unacceptable if: • The test organism information was not reported. **OR** • The test organism is not routinely used and would likely prevent meaningful interpretation of the study results.
	Not applicable
Metric 9: Outcome Assessment Methodology • Did the outcome assessment methodology address and report the outcome(s) of interest?	Acceptable if: • The outcome assessment methodology addressed or reported the intended outcome(s) of interest.

Table D.4: Low-Priority Substance Data Quality Evaluation of Fate Data	
Question	**Answer**
	OR • There was incomplete reporting of outcome assessment methods; however, such differences or absence of details were not likely to be severe or have a substantial impact on the study results.
	Unacceptable if: • The assessment methodology did not address or report the outcome(s) of interest.
	Not applicable
Metric 10: Data Reporting • Were the reported data sufficient to evaluate the outcome of interest or is there sufficient data to reasonably infer an outcome of interest (e.g. is lipid content sufficient to calculate a BCF if not explicitly reported)? • Were the target chemical concentrations or relevant transformation products (if required) reported for the outcome of interest? • Was the analytical method used suitable for detection and capable of identifying or quantifying the parent or transformation products? • Was sufficient evidence presented to confirm that the disappearance or transformation of the parent compound was not due to some other process (e.g., sorption; hydrolytic degradation in a biodegradation process)?	Acceptable if: • The target chemical or relevant transformation product(s) concentrations (if required), extraction efficiency, percent recovery, or mass balance were reported. **OR** • The target chemical concentrations and transformation product(s) (if required) were not reported; however, these omissions were not likely to have a substantial impact on study results. **OR** • The lipid content or lipid normalized BCF was not reported for BCF studies, but these deficiencies or omissions were not likely to have a substantial impact on study results.
	Unacceptable if: • Insufficient data were reported to evaluate the outcome of interest or to reasonably infer an outcome of interest. **OR** • The analytical method used was not suitable for detection or quantification of the test substance. **OR** • Data indicate that disappearance or transformation of the parent compound was likely due to some other process.
	Not applicable
Metric 11: Confounding Variables • Were sources of variability or uncertainty noted in the study? • Did confounding differences among the study groups influence the outcome assessment?	Acceptable if: • Sources of variability and uncertainty in the measurements and statistical techniques and between study groups (if applicable) were reported in the study. **OR** • The differences in the measurements and statistical techniques and between study groups were considered or accounted for in data evaluation with minor deviations or omissions. **OR** • The minor deviations or omissions were not likely to have a substantial impact on study results.
	Unacceptable if:

Table D.4: Low-Priority Substance Data Quality Evaluation of Fate Data	
Question	**Answer**
	• There were sources of variability and uncertainty in the measurements and statistical techniques or between study groups.
	Not applicable
Metric 12: Verification or Plausibility of Results • Were the study results plausible? For example, a study concluded that disappearance was due to hydrolytic degradation, but the test substance lacks functional groups susceptible to hydrolysis. • Were the results consistent with the study design and details?	Acceptable if: • Reported values were within the expected range as defined by reference substance(s), related physical-chemical properties, and the reported design and details. **OR** • The reported value was outside the expected range; however, no serious study deficiencies were identified, and the value was plausible given the outcome of interest. **OR** • Due to limited information, evaluation of the reasonableness of the study results was not possible (e.g. reference substance(s) not used or physical-chemical properties unknown and unable to be estimated).
	Unacceptable if: • Reported value was completely inconsistent with reference substance data, related physical-chemical properties, or otherwise implausible, suggesting that a serious study deficiency exists (identified or not).
	Not applicable
Comment: Please list any strengths and/or deficiencies identified for each metric, or if the metric is "not applicable", explain why.	