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Supplemental Information for the Exposure and Use Assessment of Five Persistent, Bioaccumulative and Toxic Chemicals

Peer Review Draft

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Appendix A. Supplemental Document for Decabromodiphenyl ethers (DecaBDE)

A.1 Literature Search Strategy

This document describes the literature search strategy to support the exposure assessments for five persistent, bioaccumulative, and toxic (PBT) chemicals. The intent of the search is to assess the likely exposure of the general population, consumers, occupational populations, potentially exposed or susceptible subpopulations, and the environment to the conditions of use of PBT chemicals based on the criteria outlined in the Toxic Substances Control Act (TSCA) section 6(h) (OLRC, 2016). The conditions of use are defined as the circumstances under which a chemical substance is intended, known or reasonably foreseen to be manufactured, processed, distributed in commerce, used or disposed of.

Data sources in the peer-reviewed (open) and gray literature were considered as shown in Figure A-1. In addition to the primary searches of the peer-reviewed literature in Web of Science, PubMed, and Toxline, there were additional supplemental searches that were used to complement and/or evaluate the primary peer-reviewed search strategy. These were: backward searches of frequently used sources[1], a Google Scholar search of the top 100 results by chemical, and public comments and associated references cited in those comments submitted to the dockets by mid-January 2018.

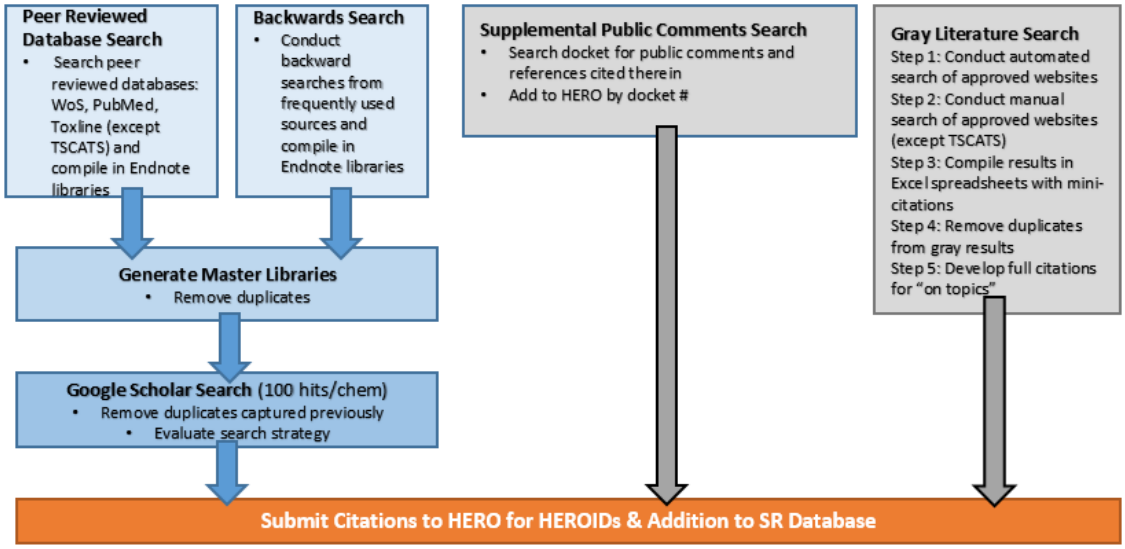

Figure A-1. Literature Search Strategy Workflow

[1]Frequently used sources are sources expected to be of high quality, such as assessments conducted by other government agencies.

An additional search of the gray literature was conducted as described in the Gray Literature Search Strategy section and was based off the protocol developed for the Systematic Review of the "First 10" chemicals under TSCA.

The results of the literature searches were compiled into Endnote libraries (database searches) and Excel spreadsheets (gray literature.)

A.1.1. Database (Peer-reviewed) Search Strategies

The literature searches for the five PBT chemicals were designed to be as broad as possible, searching only for the chemical name and synonyms, but not including any limiters such as terms describing expected uses or dates. For DecaBDE, the chemical class name, polybrominated diphenyl ethers (PBDE), was also included as a supplementary search. The class name was included because DecaBDE is expected to behave similarly in the environment as other PBDEs, as well as degrade to lower-brominated PBDEs. This also follows precedent set by other DecaBDE assessments previously conducted by EPA and others (see frequently used sources in Table A-7.) The search strategies are presented in Table A-1 and Table A-2.

Table A-1. DecaBDE Open Literature Search Strategy

Date of Search: December 15, 2017

Database	Search Strategy
PubMed	(1163-19-5[rn] OR BDE-209[tiab] OR DecaBDE[tiab] OR Deca-BDE[tiab] OR Decabromobiphenyl-ether[tiab] OR Decabromobiphenyl-ether[nm] OR Decabromodiphenylether[tiab] OR Decabromodiphenyl-ether[tiab] OR Decabromodiphenyl-oxide[tiab] OR PBDE-209[tiab] OR Pentabromophenyl-ether[tiab]) AND (English[lang])
Web of Science	("1,1'-Oxybis(2,3,4,5,6-pentabromobenzene)" OR "2,2',3,3',4,4',5,5',6,6'-Decabrominated diphenyl ether" OR "2,2',3,3',4,4',5,5',6,6'-Decabromobiphenyl ether" OR "2,2',3,3',4,4',5,5',6,6'-Decabromodiphenyl ether" OR "Benzene, 1,1'-oxybis(2,3,4,5,6-pentabromo-" OR "Bis(pentabromophenyl) ether" OR "Bis(pentabromophenyl)ether" OR "Ether, bis(pentabromophenyl)" OR "Ether, decabromodiphenyl" OR "FR-PE(H)" OR Adine-505 OR AFR-1021 OR AI3-27894 OR Berkflam-B-10E OR BR-55N OR BRN-2188438 OR Bromkal-82-0DE OR Bromkal-83-10DE OR DB-10 OR DB-101 OR DB-102 OR DE-83 OR De-83R OR Decabrom OR Decabromdiphenyl-oxide OR Decabromobiphenyl-oxide OR Decabromophenyl-ether OR DP-10F OR EB-10 OR EB-10FP OR EB-10W OR EB-10WS OR EBR-700 OR Fire-Cut-83D OR Flame-Cut-110R OR Flame-Cut-Br-100 OR FR-10 OR FR-300 OR FR-300BA OR FR-300-BA OR FRP-53 OR FR-PE OR Nonnen-DP-10 OR Nonnen-DP-10(F) OR PBED-209 OR Planelon-DB OR Planelon-DB-100 OR Planelon-DB-101 OR Plasafety-EB-10 OR Plasafety-EBR-700 OR Saytex-102 OR Saytex-102E OR Tardex-100 OR 1163-19-5 OR BDE-209 OR DecaBDE OR Deca-BDE OR Decabromobiphenyl-ether OR Decabromodiphenylether OR Decabromodiphenyl-ether OR Decabromodiphenyl-oxide OR PBDE-209 OR Pentabromophenyl-ether) AND English
Toxline	1163-19-5
	Include Synonyms Exclude PubMed Records from TSCATS and NIH Reporter Database removed in EndNote

Table A-2. PBDE Open Literature Search Strategy

Additional PBDE terms only
Date of Search: December 15, 2017

Database	Search Strategy
PubMed	(PBDE[tiab] OR PBDEs[tiab] OR Halogenated-Diphenyl-Ethers[mh] OR Brominated-Diphenyl-Ethers[tiab] OR Polybrominated-Diphenyl-Ethers[tiab] OR BDEs[tiab]) AND (English[lang]) NOT (1163-19-5[rn] OR BDE-209[tiab] OR DecaBDE[tiab] OR Deca-BDE[tiab] OR Decabromobiphenyl-ether[tiab] OR Decabromobiphenyl-ether[nm] OR Decabromodiphenylether[tiab] OR Decabromodiphenyl-ether[tiab] OR Decabromodiphenyl-oxide[tiab] OR PBDE-209[tiab] OR Pentabromophenyl-ether[tiab])
Web of Science	(PBDE OR PBDEs OR Brominated-Diphenyl-Ethers OR Polybrominated-Diphenyl-Ethers OR BDEs) AND English NOT ("1,1'-Oxybis(2,3,4,5,6-pentabromobenzene)" OR "2,2',3,3',4,4',5,5',6,6'-Decabrominated diphenyl ether" OR "2,2',3,3',4,4',5,5',6,6'-Decabromobiphenyl ether" OR "2,2',3,3',4,4',5,5',6,6'-Decabromodiphenyl ether" OR "Benzene, 1,1'-oxybis(2,3,4,5,6-pentabromo-" OR "Bis(pentabromophenyl) ether" OR "Bis(pentabromophenyl)ether" OR "Ether, bis(pentabromophenyl)" OR "Ether, decabromodiphenyl" OR "FR-PE(H)" OR Adine-505 OR AFR-1021 OR AI3-27894 OR Berkflam-B-10E OR BR-55N OR BRN-2188438 OR Bromkal-82-0DE OR Bromkal-83-10DE OR DB-10 OR DB-101 OR DB-102 OR DE-83 OR De-83R OR Decabrom OR Decabromdiphenyl-oxide OR Decabromobiphenyl-oxide OR Decabromophenyl-ether OR DP-10F OR EB-10 OR EB-10FP OR EB-10W OR EB-10WS OR EBR-700 OR Fire-Cut-83D OR Flame-Cut-110R OR Flame-Cut-Br-100 OR FR-10 OR FR-300 OR FR-300BA OR FR-300-BA OR FRP-53 OR FR-PE OR Nonnen-DP-10 OR Nonnen-DP-10(F) OR PBED-209 OR Planelon-DB OR Planelon-DB-100 OR Planelon-DB-101 OR Plasafety-EB-10 OR Plasafety-EBR-700 OR Saytex-102 OR Saytex-102E OR Tardex-100 OR 1163-19-5 OR BDE-209 OR DecaBDE OR Deca-BDE OR Decabromobiphenyl-ether OR Decabromodiphenylether OR Decabromodiphenyl-ether OR Decabromodiphenyl-oxide OR PBDE-209 OR Pentabromophenyl-ether)
Toxline	(PBDE OR PBDEs OR Brominated-Diphenyl-Ethers OR Polybrominated-Diphenyl-Ethers OR BDEs) NOT 1163-19-5
	Include Synonyms Exclude PubMed Records from TSCATS and NIH Reporter Database removed in EndNote

A.1.2. Gray Literature Search Strategies

The five PBT chemicals searched were targeted to relevant sources and the approach was adapted from the first 10 chemicals to optimize efficiency by eliminating redundancy. Gray literature screening criteria excluded peer-reviewed journal articles that were expected to be caught in the database searches. Mini citations, containing author, title, year, were generated as a preliminary step to aid in identification and removal of duplicate records prior to tagging. Automated searches via the Google search Application Programming Interface (API) were employed where possible in favor of manual search sources. A summary of sources and search result counts after the removal of duplicates is presented in Table A-3. All results were

reviewed from each source. The search strings used for manual and automated searches are found in Table A-4.

EPA is aware of information submitted by companies as part of TSCA requirements under sections 4, 8(d), 8(e) or as part of an FYI ("TSCATS Submissions data"). This information was not considered as part of the literature search and screening strategy. EPA plans to consider this information in the future.

Public comments submitted to the Docket (by Docket Number) were captured and HERO records were created including the title, author and docket number. The results were then compared to those of other searches to determine whether references cited in those public comments were already identified by other searches or need to be included. PDFs of the individual comments were not captured; instead a special "Public Comment" tag in HERO which specifies the corresponding round of public comments was used. Detailed results of the Public Comments submitted with the number of cited references for DecaBDE is shown in Table A-5.

Table A-3. Summary of Gray Literature Sources and Search Results for Automated and Manual Searches for DecaBDE

Source ID[1]	Source Category	Website	Description	Search type	Search Result Counts[2]
6000	US States Government Resources	States website custom search engine, see Summary of State Sources tab	Custom search engine using States sites	Automated	69
1000	US EPA Resources	epa.gov	US Environmental Protection Agency	Automated	124
1150	US EPA Resources	http://aqsdr1.epa.gov/aqsweb/aqstmp/airdata/download_files.html#Annual	Office of Air: AQS	Manual	0
1101	US EPA Resources	https://chemview.epa.gov/chemview	ChemView (CDR/IUR)	Manual	29
1083	US EPA Resources	https://actor.epa.gov/cpcat/faces/search.xhtml	CPDat	Manual	1
1154	US EPA Resources	https://comptox.epa.gov/dashboard/	Chemistry Dashboard	Manual	1
1148	US EPA Resources	https://iaspub.epa.gov/oppthpv/existchem_hpv_prioritizations.report	EPA HPVIS	Manual	0
1001	US EPA Resources	https://www.epa.gov/ground-water-and-drinking-water/table-regulated-drinking-water-contaminants	Office of Water: EPA Clean Water Act	Manual	0
1008	US EPA Resources	https://www.waterqualitydata.us/portal/	Office of Water: STORET and WQX	Manual	1
1155	US EPA Resources	https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/persistent-bioaccumulative-and-toxic-pbt-chemicals-under	TSCA PBT Use Documents	Manual	1
2150	Other US Agency Resources	cdc.gov	Centers for Disease Control (includes NIOSH and ATSDR)	Automated	40
2511	Other US Agency Resources	energy.gov	Department of Energy	Automated	6
2300	Other US Agency Resources	fda.gov	US Food and Drug Administration	Automated	4
2050	Other US Agency Resources	niehs.nih.gov	NIH National Institute of Environmental Health and Safety	Automated	19
2400	Other US Agency Resources	osha.gov	OSHA Occupational Safety and Health Administration	Automated	1

Source ID[1]	Source Category	Website	Description	Search type	Search Result Counts[2]
2521	Other US Agency Resources	pnnl.gov	Pacific Northwest National Laboratory	Automated	1
2509	Other US Agency Resources	usgs.gov	US Geological Survey	Automated	27
2027	Other US Agency Resources	https://ntp.niehs.nih.gov/pubhealth/roc/index-1.html#C	NIH Report on Carcinogens	Manual	1
2414	Other US Agency Resources	https://www.osha.gov/opengov/healthsamples.html	OSHA Chemical Exposure Health Data	Manual (inclusive of all results; not limited to first 100)	0
2123	Other US Agency Resources	https://www2a.cdc.gov/hhe/search.asp	CDC NIOSH Health Hazard Evaluations	Manual and Automated (inclusive of all results; not limited to first 100)	0
2104	Other US Agency Resources	www.atsdr.cdc.gov/hac/pha/	CDC ATSDR Health Hazard Consultations	Manual and Automated (inclusive of all results; not limited to first 100)	1
3160	Other Resources	oecd.org	The Organisation for Economic Co-operation and Development (OECD)	Automated	20
5000	Other Resources	sustainableproduction.org	Lowell Center for Sustainable Production	Automated	8
5020	Other Resources	Infohouse.p2ric.org	Pollution Prevention Infohouse	Automated	17
3600	Other Resources	http://www.spin2000.net/spinmyphp/	Substances in Preparations in Nordic Countries (SPIN) Database	Manual	1
5027	Other Resources	Kirk Othmer Encyclopedia	Book	Manual	2
5028	Other Resources	Ashford's Dictionary of Industrial Chemicals, 2001	Book	Manual	1

Source ID[1]	Source Category	Website	Description	Search type	Search Result Counts[2]
5029	Other Resources	Hawley's Chemical Dictionary, 2016	Book	Manual	0
3425	International Resources	carexcanada.ca	Carex Canada	Automated	0
3520	International Resources	env.go.jp	Government of Japan: Ministry of the Environment	Automated	12
3050	International Resources	europa.eu	European Union	Automated	164
3057	International Resources	https://echa.europa.eu/information-on-chemicals/registered-substances	ECHA	Manual	1
3100	International Resources	iarc.fr	International Agency for Research on Cancer	Automated	8
3350	International Resources	nicnas.gov.au	Australian Government: Department of Health, National Industrial Chemicals; NICNAS	Automated	11
3250	International Resources	who.int	World Health Organization	Automated	18
3421	International Resources	https://www.canada.ca/en/health-canada/services/chemical-substances/fact-sheets/chemicals-glance.html#interest	Canada Chemicals Portal	Manual	12
3450	International Resources	http://limitvalue.ifa.dguv.de/	GESTIS Database	Manual	0
			Total Unique (Duplicates Removed)		**601**

[1]"Source ID" refers to an internal ID assigned to each source for tracking purposes.

[2] Search result counts represent totals after removal of duplicate records.

Table A-4. Gray Literature Search Strings

Chemical	Manual Search Terms	Google Search Terms (up to 128 characters)
Decabromodiphenyl ethers (DecaBDE)	Search database by CAS or chemical name, or select from a list on the website	"1163-19-5" OR "DecaBDE" OR "PBDE-209" OR "Decabromodiphenyl-ether" OR "Decabromobiphenyl-oxide"

Table A-5. Detailed Results from Public Comments Backwards Search for DecaBDE

Public Comment Title	Publisher	Comment ID	References Cited Count
Comment submitted by Christina Franz, Senior Director, Regulatory & Technical Affairs, American Chemistry Council (ACC)	American Chemistry Council (ACC)	EPA-HQ-OPPT-2016-0724-0006	10
Comment submitted by Patrick Morrison, Assistant to the General President, Health, Safety and Medicine, International Association of Fire Fighters (IAFF)	International Association of Fire Fighters (IAFF)	EPA-HQ-OPPT-2016-0724-0005	6
Comment submitted by Veena Singla, PhD, Associate Director, Science and Policy, Program on Reproductive Health and the Environment, University of California, San Francisco (UCSF) et al.	UCSF Program on Reproductive Health and the Environment, academics, scientists and clinicians	EPA-HQ-OPPT-2016-0724-0007	45
Comment submitted by Dianne Barton, Chair, National Tribal Toxics Council (NTTC)	National Tribal Toxics Council (NTTC)	EPA-HQ-OPPT-2016-0724-0010	18
Comment submitted by Laurie Valeriano, Executive Director et al., Toxic-Free Future	Toxic-Free Future	EPA-HQ-OPPT-2016-0724-0009	14
Comment submitted by Elizabeth Hitchcock, Acting Director, Safer Chemicals Healthy Families (SCHF) et al.	Safer Chemicals Healthy Families (SCHF), Alaska Community Action on Toxics, Center for Environmental Health, Earthjustice, Environmental Health Strategy Center, Natural Resources Defense Council, Toxic-Free Future	EPA-HQ-OPPT-2016-0724-0008	7
Comment submitted by Jyotsna Jagai, Research Assistant Professor University of Illinois, Chicago Chair, Environment Section, American Public Health Association et al.		EPA-HQ-OPPT-2016-0724-0014	6

Public Comment Title	Publisher	Comment ID	References Cited Count
Comment submitted by Pamela Miller, Executive Director, Alaska Community Action on Toxics (ACAT)	Alaska Community Action on Toxics (ACAT)	EPA-HQ-OPPT-2016-0724-0011	4
Comment submitted by Jessica Helm et al., Silent Spring Institute	Silent Spring Institute	EPA-HQ-OPPT-2016-0724-0015	13
Comment submitted by Robert Stockman, Senior Attorney, Environmental Defense Fund (EDF)	Environmental Defense Fund (EDF)	EPA-HQ-OPPT-2016-0724-0020	8
Comment submitted by Catherine Karr, Sheela Sathyanarayana and Olivia Halas, Northwest Pediatric Environmental Health Specialty Unit	Northwest Pediatric Environmental Health Specialty Unit	EPA-HQ-OPPT-2016-0724-0018	9
Comment submitted by Leslie Riegle, Director of Environmental Policy, Aerospace Industries Association (AIA)	Aerospace Industries Association (AIA)	EPA-HQ-OPPT-2016-0724-0016	0
Comment submitted by Ken Zarker, Section Manager, Hazardous Waste and Toxics Reduction Program, State of Washington Department of Ecology	State of Washington Department of Ecology	EPA-HQ-OPPT-2016-0724-0017	21
TOTAL		13	161
Total Unique (Duplicates Removed)			**138**

A.1.3. Supplemental Search Strategy

Backward Search

To both supplement and test the database and gray literature searches, backward searches of frequently used sources were conducted. These sources consist of previous risk assessments, systematic reviews, and other assessments, generally conducted by EPA or other government agencies of the chemicals of interest and presented in Table A-7. The references that are cited within sections deemed relevant to this assessment were gathered into Endnote libraries for title abstract review.

Google Scholar Search

To further supplement and test the database searches, a Google Scholar search was conducted for each of the five PBT chemicals. The top 100 results returned by Google Scholar for each chemical were exported into Endnote libraries. These results were compared to the references identified in the database, backward, and gray literature searches to identify references not found by the previous searches. While Google Scholar results are expected to be primarily peer-reviewed rather than gray literature, the results were still compared to all searches.

A.1.4. Literature Search Results

The literature searches were conducted, and for PubMed, Web of Science, ToxLine, Backwards searches, and Google Scholar searches, the results were imported into one Endnote library per

chemical. After the results were combined, duplicates were removed and TSCATS/NIH Reporter data, a subset of ToxLine, were moved into a separate folder. The resulting counts are presented in **Error! Reference source not found.**. Detailed results for the DecaBDE backwards search are presented in **Error! Reference source not found.**.

Table A-6. Count of Peer-reviewed Literature Search Results by Search Type for DecaBDE and PBDE

Chemical	PubMed	WoS	ToxLine	TSCATS/ NIH Reporter	Backwards	Google Scholar
DecaBDE	1259	995	89	325	694	5
PBDE	3863	3419	8	236	NA	NA

Table A-7. Detailed Results of Backwards Search of Frequently Used Sources for DecaBDE

HERO ID	Document Title	Reference Count
4197019	AN ALTERNATIVES ASSESSMENT FOR THE FLAME RETARDANT DECABROMODIPHENYL ETHER (DecaBDE)	130
1003344	Ecological State of the Science Report on decabromodiphenyl Ether (decaBDE) Bioaccumulation and Transformation	181
4180691	ECHA ANNEX XV RESTRICTION REPORT PROPOSAL FOR A RESTRICTION	48
4161055	A Human Mixture Risk Assessment for Neurodevelopmental Toxicity Associated with Polybrominated Diphenyl Ethers Used as Flame Retardants	43
4180692	Risk profile on decabromodiphenyl ether (commercial mixture, c-decaBDE)	287
4182591	Environmental risk evaluation report: Decabromodiphenyl ether	309
956687	An Exposure Assessment of Polybrominated Diphenyl Ethers	364
4182466	VCCEP DecaBDE Assessment	3
	TOTAL	1365
	Total Unique (Duplicates Removed)	**1021**
	EndNote Library: Total Unique (Duplicates Removed)	**694**

A.2 Literature Screening Strategy

A.2.1. Development of the Literature Screening Approach

The steps involved in developing the title abstract screening approach are:

1. Define inclusion/exclusion criteria.
2. Conduct the pilot using 10 randomly selected studies for each chemical from both the peer-reviewed and gray literature that are screened by EPA experts.

3. Use the results of the pilot to refine the inclusion/exclusion criteria.
4. Use the refined pilot to train screeners in applying the tags.

The overall workflow of the systematic review process including the literature screening is presented in Appendix F.

In these assessments, the results of the title/abstract literature screening will be used to develop the PECO statement. The PECO statement is included in Appendix A.3. Four tags were used at the title-abstract phase: Peer On Topic, Peer Off Topic, Gray On Topic, and Gray Off Topic and recorded on the HERO project pages. Title abstract screening was conducted in DRAGON[2]. A screenshot of the DRAGON form and all DRAGON tags is presented in Appendix H.

The inclusion/exclusion criteria for title/abstract and full text screening are included in Appendix F. During full text screening, studies were also screened for "Red Flag Criteria," which represent the "Unacceptable" criteria from the Data Evaluation criteria (U.S. EPA, 2018).

A.2.2. Literature Screening Pilot

A pilot with 100 results representative of the five chemicals and the peer, backwards, and gray literature search results was developed by EPA. Two exposure experts scored the pilot, and met with EPA to refine the criteria and application of the criteria.

Before screening, all screeners were required to meet a 90% accuracy in tagging the pilot screening studies. Screeners who met this level of proficiency could begin title abstract screening. Screeners who do not meet this level of proficiency, continued to train, using the studies screened by screeners who had passed the pilot as additional training studies. Documentation of all pilot tagging results was maintained in Excel spreadsheets for both the peer-reviewed and gray literature.

A.2.3. Literature Screening

Title abstract screening of the peer-reviewed and gray literature occurred in DRAGON, an online tool for systematic review. Results of the DecaBDE search were manually screened with one screener who has been trained via the pilot process. Additionally, a subject matter expert reviewed 10% of the references deemed to be On Topic and Off Topic as a quality assurance check to ensure that they have been categorized appropriately.

For gray literature, title/abstract and full text screening was done simultaneously, and tags for screening are included in Appendix H. For peer-reviewed literature, title/abstract and full text screening were done separately, and tags for each stage are included in Appendix H.2.

[2]DRAGON is an online tool for systematic review developed by ICF that stores qualitative and quantitative data from literature to help scientists implement the elements of systematic review, including problem formulation, literature screening, risk of bias evaluation, and data integration.

A.2.4. Prioritization

The database search strategy for DecaBDE is returned approximately 2,500 results. Adding search terms for the chemical class PBDEs to the DecaBDE search increased the number of results to approximately 13,000. Few of the results added by including terms for chemical class are likely to be relevant to an exposure assessment of DecaBDE; therefore, the results of the title abstract screening of the DecaBDE search results were used to prioritize the results added by including chemical class search terms using text analytics in the DoCTER tool and SWIFTActive.

For prioritization, multiple text analytic algorithms can be used to find studies with titles and abstracts similar to seed studies previously identified as On Topic by EPA experts. DoCTER employs two main metrics, ensemble clustering and machine learning, including active machine learning. Ensemble clustering uses multiple algorithms in Varghese et al. (2017) to prioritize references for review. The prioritization strategy is shown in Figure A-2**Error! Reference source not found.** and presented in Varghese et al. (2017). These algorithms create a user-defined number of clusters based on similarities in the text of the title and abstract, and each algorithm is broadly-accepted in the text analytics scientific field, as described in Varghese et al. (2017). The clusters are populated by the algorithms that first convert the text in each title and abstract into a numerical matrix (using binary or 0s and 1s to represent the text) and then identifies similarities or similar numerical strings between each matrix representation of a title and abstract. Based on the similarities, the reference is assigned to a cluster. In the example, each of the algorithms was used to bin the studies into 10, 20, or 30 clusters, for a total of six different cluster analyses (six large circles in the figure). A random sample of studies identified as relevant serve as “tracer” or “seed” studies (pink circles in the figure). The tracer method involves following these relevant studies and determining the clusters the majority occur in; these clusters are then deemed more likely to contain other (as-yet unidentified) relevant studies. Off topic references, or negative seeds, can be used to estimate performance of the tool using the metric of precision, but are not required for clustering.

To identify these high-priority clusters, the clusters containing a given fraction (75% in the example) of the relevant tracer studies are identified for each of the six analyses and termed “high concentration of tracer” clusters. All non-tracer studies in those high-concentration clusters can then be marked as “high priority” for further screening. This ensemble method is used to increase confidence in the selection of prioritized studies by mitigating uncertainty from each individual analysis. Additionally, studies in the “low priority” clusters can be further analyzed using machine learning algorithms that also use the “tracer” studies in conjunction with Off Topic references, or negative seeds, and assign a probability score to each of the remaining studies as likely to be On Topic.

DoCTER also employs machine learning, which uses a training data set of studies identified as both On and Off Topic, to identify studies that are most likely to be On Topic. This data set can be identified prior to conducting prioritization in traditional machine learning or can be conducted as part of the prioritization process, as in active machine learning.

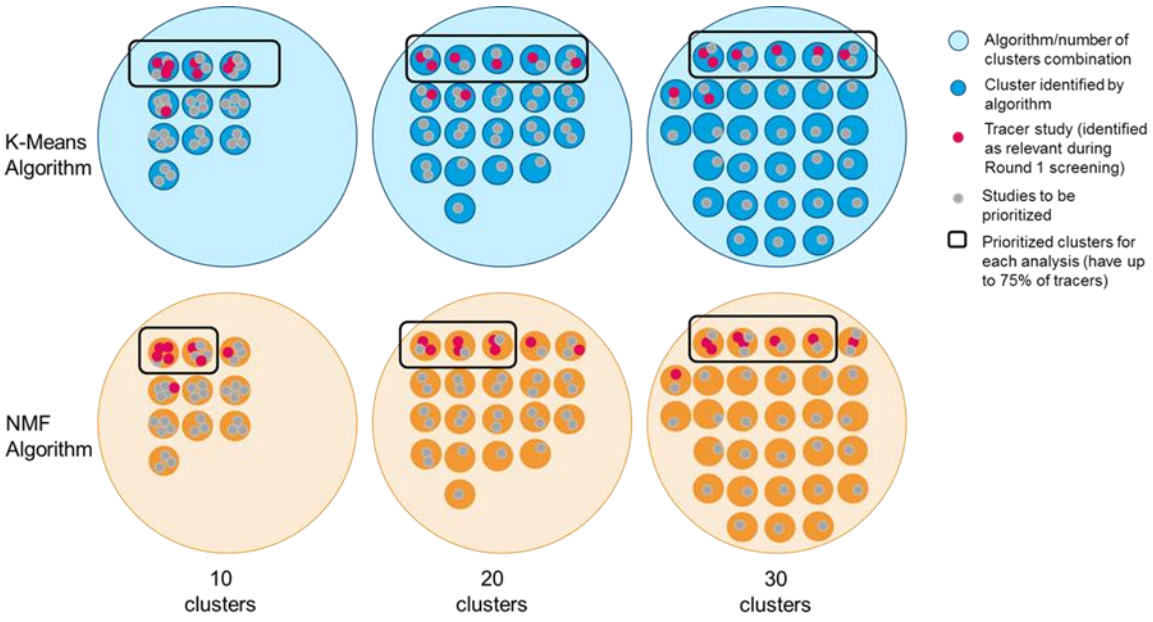

Figure A-2. Ensemble text analytics method for prioritizing studies for screening.

Studies were also prioritized independently using SWIFT-Review. The same training data of On Topic and Off Topic studies used in DoCTER were also used for prioritization in SWIFT-Review. Using the training set, SWIFT-Review builds a statistical log-linear model that is used to estimate the probability that an unlabeled document is relevant (Howard et al., 2016).

The overall correlation between DoCTER and SWIFT-Review scoring and percentile rank was very high and any reference that was flagged as high priority by either DoCTER or SWIFT-Review was loaded into DRAGON for title abstract screening.

After full-text screening was complete, EPA prioritized the following studies with the following criteria:

- Sample size of >10
- Study published after 2000
- Quantitative data was available in a table, rather than graph or chart.

Using these criteria, approximately 150 studies were not prioritized for data extraction and data evaluation. Due to the large number of studies, it is likely the overall magnitude and trends of reported exposure are well represented by the studies that were evaluated and extracted.

Any reference that was flagged as high priority by either DoCTER or SWIFT was loaded into DRAGON for title abstract screening.

A.3 PECO Statement

PECO statements were written after full-text screening and informed how articles were identified for inclusion in the exposure characterization.

Chemical	**DecaBDE**
PECO Element	**Evidence**
Population	**Human:** Children; infants; pregnant women; lactating women; women of childbearing age; general population; consumers and bystanders in residential settings; workers and occupational non-users; near-facility populations (including industrial and commercial facilities manufacturing, processing, or using DecaBDE); populations exposed from transfer from workplaces through take home exposures; populations in co-located residences or businesses. No chemical-specific exclusions are suggested at present.
	Ecological: Aquatic organisms (edible and nonedible fish, aquatic invertebrates (daphnia), amphibians); terrestrial organisms (plants, soil invertebrates (worms), birds, mammals). No chemical specific exclusions are suggested at present.
Exposure	**Expected Exposure Sources, Pathways, Routes**
	Source: Indoor sources/materials that are abraded during use or have high potential for direct contact; industrial activities (manufacturing, processing, recycling, treatment, disposal of products); commercial and consumer uses of consumer products containing decaBDE and associated releases to air, dust, water, or wastes (wastewater/liquid wastes, solid wastes).
	Pathway: dust; contact with products; indoor air; food (breastmilk, fish, meat, eggs, dairy); waste streams (landfills, biosolids); outdoor air (fugitive/stack emissions); soil/sediment contact.
	Routes: inhalation (indoor air and dust); oral (dietary ingestion of breastmilk, food, incidental ingestion of contaminated soil and dust); mouthing of consumer articles; dermal (contact with dust, soil, consumer products containing DecaBDE); hand-to-mouth contact, ingestion of suspended particles.
Comparator (Scenario)	**Human:** Populations in alternative geographic regions and differing age groups. Populations at different distances from industrial and recycling sites. Populations occupationally exposed. Populations with alternative diets.
	Ecological: Receptors in alternative geographical locations. Receptors with differing levels of proximity to sources and releases.
Outcomes for Exposure Concentration or Dose	**Human:** Acute, subchronic, and/or chronic external dose estimates (mg/kg/day); acute, subchronic, and/or chronic internal dose based on biomonitoring and reverse dosimetry (mg/kg/day); acute, subchronic, and/or chronic air, soil, dust, water and biomonitoring concentration estimates (mg/m^3 or mg/L).
	Ecological: A wide range of ecological receptors will be considered using surface water, sediment, soil, and air concentrations. Targeted use of wildlife biomonitoring data will also be explored.

A.4 PRISMA Diagram

The PRISMA Diagram for DecaBDE, including literature counts from search, screening and included phases from all sources, is presented in Figure A-3. A subset of studies that passed the screening phase were not extracted or evaluated due to the ready availability of the full text and supplemental information. Due to time constraints, studies that did not include data in text or tables, and studies that had fewer than 10 observations were not extracted or evaluated.

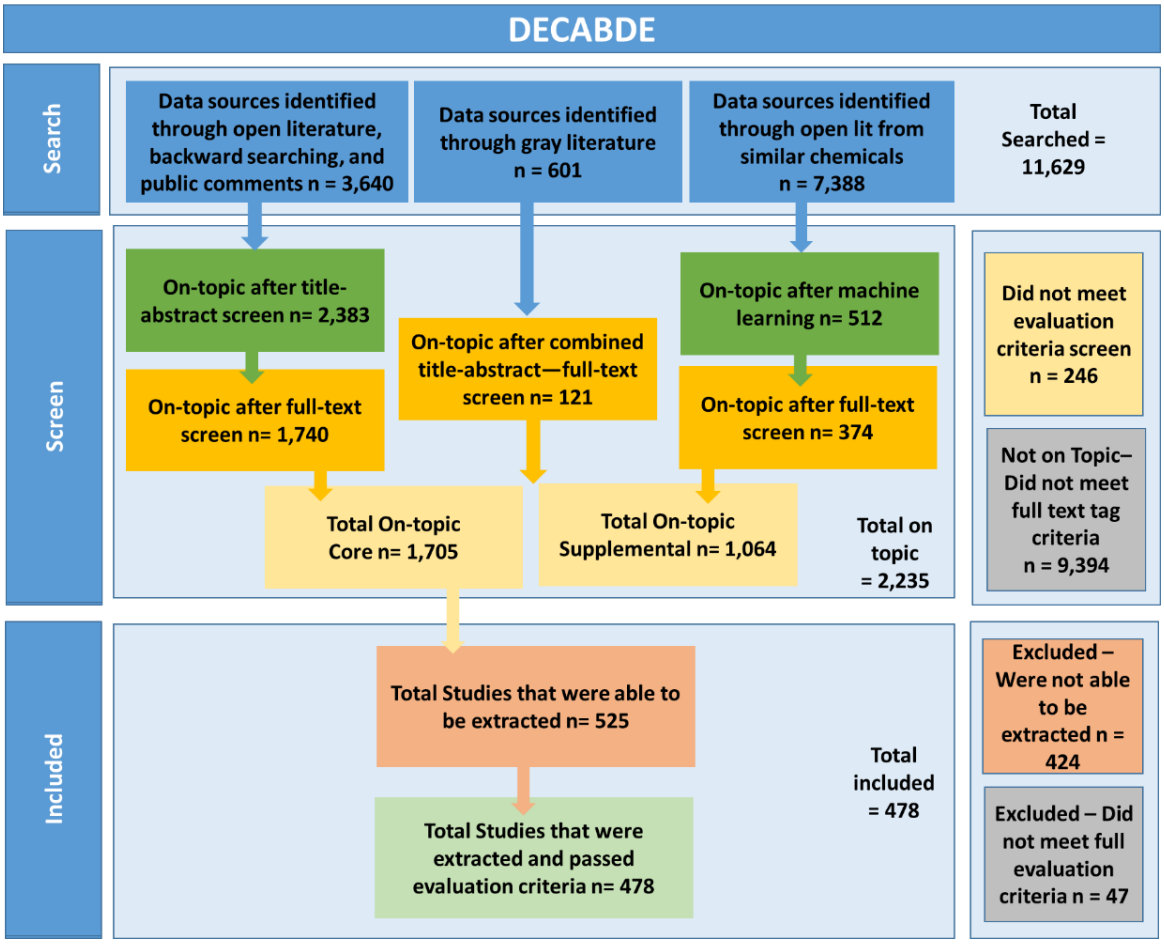

Figure A-3. PRISMA Diagram for DecaBDE

A.5 Data Evaluation Criteria

Core exposure data includes the following exposure data types:

- Environmental monitoring
- Biomonitoring
- Database Sources
- Completed Assessments
- Modeling

Assessors evaluated the extracted core exposure data for evaluation criteria specific to the data type. The data evaluation criteria are included in (U.S. EPA, 2018).

A.6 Data Extraction Fields

Core exposure data, including monitoring data and modeled estimates of concentration or dose, was extracted in DRAGON. The data extraction fields are included in Appendix I.

Appendix B. Supplemental Document for Hexachlorobutadiene (HCBD) Literature Search Strategy

This document describes the literature search strategy to support the exposure assessments for five persistent, bioaccumulative, and toxic (PBT) chemicals. The intent of the search is to assess the likely exposure of the general population, consumers, occupational populations, potentially exposed or susceptible subpopulations, and the environment to the conditions of use of PBT chemicals based on the criteria outlined in the Toxic Substances Control Act (TSCA) section 6(h) (OLRC, 2016). The conditions of use are defined as the circumstances under which a chemical substance is intended, known or reasonably foreseen to be manufactured, processed, distributed in commerce, used or disposed of.

Data sources in the peer-reviewed (open) and gray literature were considered as shown in Figure B-1. In addition to the primary searches of the peer-reviewed literature in Web of Science, PubMed, and Toxline, there were additional supplemental searches that were used to complement and/or evaluate the primary peer-reviewed search strategy. These were: backward searches of frequently used sources[3], a Google Scholar search of the top 100 results by chemical, and public comments and associated references cited in those comments submitted to the dockets by mid-January 2018.

An additional search of the gray literature was conducted as described in the Gray Literature Search Strategy section and was based off the protocol developed for the Systematic Review of the "First 10" chemicals under TSCA.

The results of the literature searches were compiled into Endnote libraries (database searches) and Excel spreadsheets (gray literature).

B.1.1. Database (Peer-reviewed) Search Strategies

The literature searches for the five PBT chemicals were designed to be as broad as possible, searching only for the chemical name and synonyms, but not including any limiters such as terms describing expected uses or dates. For HCBD, no chemical category name was included in the search. The search strategy for HCBD is presented in Table B-1.

[3] Frequently used sources are sources expected to be of high quality, such as assessments conducted by other government agencies.

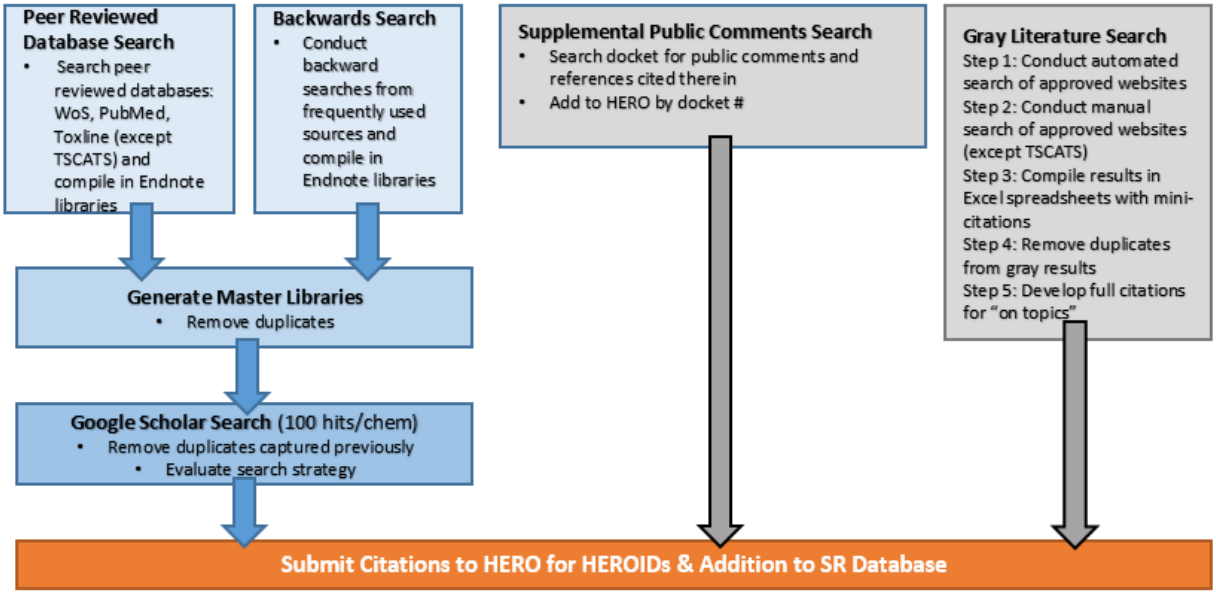

Figure B-1. Literature Search Strategy Workflow

Table B-1. HCBD Open Literature Search Strategy

Date of Search: December 15, 2017

Database	Search Strategy
PubMed	("1,1,2,3,4,4-Hexachloro-1,3-butadiene"[tiab] OR "1,3-Hexachlorobutadiene"[tiab] OR "Hexachloro-1,3-butadiene"[tiab] OR "Hexachlorobuta-1,3-diene"[tiab] OR 87-68-3[rn] OR Dolen-pur[tiab] OR HCBD[tiab] OR Hexachlorobutadiene[tiab] OR Hexachlorobutadiene[nm] OR Perchlorobutadiene[tiab]) AND (English[lang])
Web of Science	("1,1,2,3,4,4-Hexachloro-1,3-butadien" OR "1,1,2,3,4,4-Hexachlorobuta-1,3-diene" OR "1,3-Butadiene, 1,1,2,3,4,4-hexachloro-" OR "1,3-Butadiene, hexachloro-" OR "BUTADIENE, HEXACHLORO-" OR "Hexachlor-1,3-butadien" OR "Hexachlorbuta-1,3-dien" OR "Hexacloro-1,3-butadieno" OR "hexaclorobuta-1,3-dieno" OR "Perchloro-1,3-butadiene" OR "1,1,2,3,4,4-Hexachloro-1,3-butadiene" OR "1,3-Hexachlorobutadiene" OR "Hexachloro-1,3-butadiene" OR "Hexachlorobuta-1,3-diene" OR 87-68-3 OR Dolen-pur OR HCBD OR Hexachlorobutadiene OR Perchlorobutadiene) AND English
Toxline	87-68-3
	Include Synonyms Exclude PubMed Records from TSCATS and NIH Reporter Database removed in EndNote

B.1.2. Gray Literature Search Strategies

The five PBT chemicals searched were targeted to relevant sources and the approach was adapted from the first 10 chemicals to optimize efficiency by eliminating redundancy. Gray literature screening criteria excluded peer-reviewed journal articles that were expected to be caught in the database searches. Mini citations, containing author, title, year, were generated

as a preliminary step to aid in identification and removal of duplicate records prior to tagging. Automated searches via the Google search API were employed where possible in favor of manual search sources. A summary of sources and search result counts after the removal of duplicates is presented in Table B-2.All results were reviewed from each source. The search strings used for manual and automated searches are found in Table B-3.

EPA is aware of information submitted by companies as part of TSCA requirements under sections 4, 8(d), 8(e) or as part of an FYI ("TSCATS Submissions data"). This information was not considered as part of the literature search and screening strategy. EPA plans to consider this information in the future.

Public comments submitted to the Docket (by Docket Number) were captured and HERO records were created including the title, author and docket number. The results were then compared to those of other searches to determine whether references cited in those public comments were already identified by other searches or need to be included. PDFs of the individual comments were not captured; instead a special "Public Comment" tag in HERO which specifies the corresponding round of public comments was used. Detailed results of the Public Comments submitted with the number of cited references for HCBD is shown in Table B-4.

Table B-2. Summary of Gray Literature Sources and Search Results for Automated and Manual Searches for HCBD

Source ID[1]	Source Category	Website	Description	Search type	Search Result Counts[2]
6000	US States Government Resources	States website custom search engine, see Summary of State Sources tab	Custom search engine using States sites	Automated	97
1000	US EPA Resources	epa.gov	US Environmental Protection Agency	Automated	283
1150	US EPA Resources	http://aqsdr1.epa.gov/aqsweb/aqstmp/airdata/download_files.html#Annual	Office of Air: AQS	Manual	1
1101	US EPA Resources	https://chemview.epa.gov/chemview	ChemView (CDR/IUR)	Manual	1
1083	US EPA Resources	https://actor.epa.gov/cpcat/faces/search.xhtml	CPDat	Manual	1
1154	US EPA Resources	https://comptox.epa.gov/dashboard/	Chemistry Dashboard	Manual	1
1148	US EPA Resources	https://iaspub.epa.gov/oppthpv/existchem_hpv_prioritizations.report	EPA HPVIS	Manual	0
1001	US EPA Resources	https://www.epa.gov/ground-water-and-drinking-water/table-regulated-drinking-water-contaminants	Office of Water: EPA Clean Water Act	Manual	0
1008	US EPA Resources	https://www.waterqualitydata.us/portal/	Office of Water: STORET and WQX	Manual	1
1155	US EPA Resources	https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/persistent-bioaccumulative-and-toxic-pbt-chemicals-under	TSCA PBT Use Documents	Manual	0
2150	Other US Agency Resources	cdc.gov	Centers for Disease Control (includes NIOSH and ATSDR)	Automated	63
2511	Other US Agency Resources	energy.gov	Department of Energy	Automated	108
2300	Other US Agency Resources	fda.gov	US Food and Drug Administration	Automated	14
2050	Other US Agency Resources	niehs.nih.gov	NIH National Institute of Environmental Health and Safety	Automated	17
2400	Other US Agency Resources	osha.gov	OSHA Occupational Safety and Health Administration	Automated	6

Source ID[1]	Source Category	Website	Description	Search type	Search Result Counts[2]
2521	Other US Agency Resources	pnnl.gov	Pacific Northwest National Laboratory	Automated	11
2509	Other US Agency Resources	usgs.gov	US Geological Survey	Automated	63
2027	Other US Agency Resources	https://ntp.niehs.nih.gov/pubhealth/roc/index-1.html#C	NIH Report on Carcinogens	Manual	0
2414	Other US Agency Resources	https://www.osha.gov/opengov/healthsamples.html	OSHA Chemical Exposure Health Data	Manual (inclusive of all results; not limited to first 100)	1
2123	Other US Agency Resources	https://www2a.cdc.gov/hhe/search.asp	CDC NIOSH Health Hazard Evaluations	Manual and Automated (inclusive of all results; not limited to first 100)	0
2104	Other US Agency Resources	www.atsdr.cdc.gov/hac/pha/	CDC ATSDR Health Hazard Consultations	Manual and Automated (inclusive of all results; not limited to first 100)	51
3160	Other Resources	oecd.org	The Organisation for Economic Co-operation and Development (OECD)	Automated	21
5000	Other Resources	sustainableproduction.org	Lowell Center for Sustainable Production	Automated	2
5020	Other Resources	Infohouse.p2ric.org	Pollution Prevention Infohouse	Automated	50
3600	Other Resources	http://www.spin2000.net/spinmyphp/	Substances in Preparations in Nordic Countries (SPIN) Database	Manual	0
5027	Other Resources	Kirk Othmer Encyclopedia	Book	Manual	0
5028	Other Resources	Ashford's Dictionary of Industrial Chemicals, 2001	Book	Manual	0
5029	Other Resources	Hawley's Chemical Dictionary, 2016	Book	Manual	1
3425	International Resources	carexcanada.ca	Carex Canada	Automated	0

Source ID[1]	Source Category	Website	Description	Search type	Search Result Counts[2]
3520	International Resources	env.go.jp	Government of Japan: Ministry of the Environment	Automated	8
3050	International Resources	europa.eu	European Union	Automated	162
3057	International Resources	https://echa.europa.eu/information-on-chemicals/registered-substances	ECHA	Manual	0
3100	International Resources	iarc.fr	International Agency for Research on Cancer	Automated	52
3350	International Resources	nicnas.gov.au	Australian Government: Department of Health, National Industrial Chemicals; NICNAS	Automated	2
3250	International Resources	who.int	World Health Organization	Automated	36
3421	International Resources	https://www.canada.ca/en/health-canada/services/chemical-substances/fact-sheets/chemicals-glance.html#interest	Canada Chemicals Portal	Manual	1
3450	International Resources	http://limitvalue.ifa.dguv.de/	GESTIS Database	Manual	10
			Total Unique (Duplicates Removed)		**1064**

[1]"Source ID" refers to an internal ID assigned to each source for tracking purposes.

[2] Search result counts represent totals after removal of duplicate records.

Table B-3. Gray Literature Search Strings

Chemical	Manual Search Terms	Google Search Terms (up to 128 characters)
Hexachlorobutadiene (HCBD)	Search database by CAS or chemical name, or select from a list on the website	"87-68-3" OR "Hexachlorobutadiene" OR "HCBD" OR "Perchlorobutadiene" OR "Hexachloro-1,3-butadiene"

Table B-4. Detailed Results from Public Comments Backwards Search for HCBD

Public Comment Title	Publisher	Comment ID	References Cited Count
Comment submitted by Christina Franz, Senior Director, Regulatory & Technical Affairs, American Chemistry Council (ACC)	American Chemistry Council (ACC)	EPA-HQ-OPPT-2016-0738-0007	10
Comment submitted by Sarah E. Amick, Vice President EHS&S and Senior Counsel, Rubber Manufacturers Association (RMA)	Rubber Manufacturers Association (RMA)	EPA-HQ-OPPT-2016-0738-0003	0
Comment submitted by Veena Singla, PhD, Associate Director, Science and Policy, Program on Reproductive Health and the Environment, University of California, San Francisco (UCSF) et al.	UCSF Program on Reproductive Health and the Environment, academics, scientists and clinicians	EPA-HQ-OPPT-2016-0738-0008	45
Comment submitted by Robert Stockman, Senior Attorney on behalf of Environmental Defense Fund (EDF)	Environmental Defense Fund (EDF)	EPA-HQ-OPPT-2016-0738-0011	8
Comment submitted by Jyotsna S. Jagai, PhD, Research Assistant Professor, University of Illinois, Chicago Chair, Environment Section, American Public Health Association		EPA-HQ-OPPT-2016-0738-0016	6
Comment submitted by Elizabeth Hitchcock, Acting Director, Safer Chemicals Healthy Families (SCHF) et al.	Safer Chemicals Healthy Families (SCHF), Alaska Community Action on Toxics, Center for Environmental Health, Earthjustice, Environmental Health Strategy Center, Natural Resources Defense Council, Toxic-Free Future	EPA-HQ-OPPT-2016-0738-0012	27
Comment submitted by Ken Zarker, Section Manager, Hazardous Waste and Toxics Reduction Program, Washington State Department of Ecology	Washington State Department of Ecology	EPA-HQ-OPPT-2016-0738-0009	114
Comment submitted by Dianne C. Barton, Chair, National Tribal Toxics Council (NTTC)	National Tribal Toxics Council (NTTC)	EPA-HQ-OPPT-2016-0738-0013	18
TOTAL		8	228
Total Unique (Duplicates Removed)			**218**

B.1.3. Supplemental Search Strategy

Backward Search

To both supplement and test the database and gray literature searches, backward searches of frequently used sources were conducted. These sources consist of previous risk assessments, systematic reviews, and other assessments, generally conducted by EPA or other government agencies of the chemicals of interest and presented in Table B-6. The references that are cited within sections deemed relevant to this assessment were gathered into Endnote libraries for title abstract review.

Google Scholar Search

To further supplement and test the database searches, a Google Scholar search was conducted for each of the five PBT chemicals. The top 100 results returned by Google Scholar for each chemical were exported into Endnote libraries. These results were compared to the references identified in the database, backward, and gray literature searches to identify references not found by the previous searches. While Google Scholar results are expected to be primarily peer-reviewed rather than gray literature, the results were still compared to all searches.

B.1.4. Literature Search Results

The literature searches were conducted, and for PubMed, Web of Science, ToxLine, Backwards searches, and Google Scholar searches, the results were imported into one Endnote library per chemical. After the results were combined, duplicates were removed and TSCATS/NIH Reporter data, a subset of ToxLine, were moved into a separate folder. The resulting counts are presented in Table B-5. Detailed results for the HCBD backwards search are presented in Table B-6.

Table B-5. Count of Peer-reviewed Literature Search Results by Search Type for HCBD

Chemical	PubMed	WoS	ToxLine	TSCATS/ NIH Reporter	Backwards	Google Scholar
HCBD	246	189	511	94	53	17

Table B-6. Detailed Results of Backwards Search of Frequently Used Sources for HCBD

HERO ID	Document title	Reference count
1464554	PRIORITY SUBSTANCES LIST ASSESSMENT REPORT Canadian Environmental Protection Act, 1999 Hexachlorobutadiene	54
4182482	Euro Chlor Risk Assessment for the Marine Environment OSPARCOM Region - North Sea	19
	TOTAL	73
	Total Unique (Duplicates Removed)	**65**
	EndNote Library: Total Unique (Duplicates Removed)	**53**

B.2 Literature Screening Strategy

B.2.1. Development of the Literature Screening Approach

The steps involved in developing the title abstract screening approach are:

1. Define inclusion/exclusion criteria.
2. Conduct the pilot using 10 randomly selected studies for each chemical from both the peer-reviewed and gray literature that are screened by EPA experts.
3. Use the results of the pilot to refine inclusion/exclusion criteria.
4. Use the refined pilot to train screeners in applying the tags.

The overall workflow of the systematic review process including the literature screening is presented in Appendix F.

In these assessments, the results of the title/abstract literature screening will be used to develop the PECO statement. The PECO statement is included in Appendix 0. Four tags were used at the title-abstract phase: Peer On Topic, Peer Off Topic, Gray On Topic, and Gray Off Topic and recorded on the HERO project pages. Title abstract screening was conducted in DRAGON[4]. A screenshot of the DRAGON form and all DRAGON tags is presented in Appendix H.

The inclusion/exclusion criteria for title/abstract and full text screening are included in Appendix G. During full text screening, studies were also screened for "Red Flag Criteria," which represent the "Unacceptable" criteria from the Data Evaluation criteria (U.S. EPA, 2018).

B.2.2. Literature Screening Pilot

A pilot with 100 results representative of the five chemicals and the peer, backwards, and gray literature search results was developed by EPA. Two exposure experts scored the pilot, and met with EPA to refine the criteria and application of the criteria.

Before screening, all screeners were required to meet a 90% accuracy in tagging the pilot screening studies. Screeners who met this level of proficiency were able to begin title abstract screening. Screeners who do not meet this level of proficiency, continued to train, using the studies screened by screeners who had passed the pilot as additional training studies. Documentation of all pilot tagging results was maintained in Excel spreadsheets for both the peer-reviewed and gray literature.

B.2.3. Literature Screening

Title abstract screening of the peer-reviewed and gray literature occurred in DRAGON, an online tool for systematic review. Results of the HCBD search were manually screened with one screener who has been trained via the pilot process. Additionally, a subject matter expert

[4] DRAGON is an online tool for systematic review developed by ICF that stores qualitative and quantitative data from literature to help scientists implement the elements of systematic review, including problem formulation, literature screening, risk of bias evaluation, and data integration.

reviewed 10% of the references deemed to be On Topic and Off Topic as a quality assurance check to ensure that they have been categorized appropriately.

For gray literature, title/abstract and full text screening was done simultaneously, and tags for screening are included in Appendix H. For peer-reviewed literature, title/abstract and full text screening were done separately, and tags for each stage are included in Appendix H.2.

B.3 PECO Statement

PECO statements were written after full-text screening and informed how articles were identified for inclusion in the exposure characterization.

Chemical	**HCBD**
PECO Element	**Evidence**
Population	**Human:** Women of child-bearing age (WOCBA) with occupational exposure; WOCBA, children, infants living at or near hazardous waste, industrial or chemical waste disposal sites, or who consume contaminated fish. WOCBA and children who use consumer products containing HCBD. No chemical-specific exclusions are suggested at present.
	Ecological: Aquatic organisms (edible and nonedible fish, aquatic invertebrates (daphnia), amphibians); terrestrial organisms (plants, soil invertebrates (worms), birds, mammals). No chemical specific exclusions are suggested at present.
Exposure	**Expected Exposure Sources, Pathways, Routes**
	Source Hazardous waste sites, contaminated industrial sites, waste management sites, and associated releases from such sites to air, water, or wastes (wastewater/liquid wastes, solid wastes). Contact with consumer products containing HCBD. Consumption of contaminated fish and shellfish products.
	Pathway: Inhalation of vapors in indoor and outdoor air; contact with consumer products; ingestion of contaminated soil, water, fish, shellfish; waste streams (landfills, biosolids); outdoor air (fugitive/stack emissions); soil/sediment contact.
	Routes: Inhalation (outdoor and indoor air and dust); oral (dietary ingestion of breastmilk, food, incidental ingestion of contaminated soil and dust); mouthing of consumer articles; hand-to-mouth contact.
Comparator (Scenario)	**Human:** Populations in alternative geographic regions and differing age groups. Populations at different distances from industrial and recycling sites. Populations occupationally exposed. Populations with alternative diets.
	Ecological: Receptors in alternative geographical locations. Receptors with differing levels of proximity to sources and releases.
Outcomes for Exposure Concentration or Dose	**Human:** Acute, subchronic, and/or chronic external dose estimates (mg/kg/day); acute, subchronic, and/or chronic internal dose based on biomonitoring and reverse dosimetry (mg/kg/day); acute, subchronic, and/or chronic air, soil, dust, water and biomonitoring concentration estimates (mg/m^3 or mg/L).
	Ecological: A wide range of ecological receptors will be considered using surface water, sediment, soil, and air concentrations. Targeted use of wildlife biomonitoring data will also be explored.

B.4 PRISMA Diagram

The PRISMA Diagram for HCBD, including literature counts from search, screening and included phases from all sources, is presented in Figure B-2. A subset of studies that passed the screening phase were not extracted or evaluated due to the ready availability of the full text and supplemental information. Due to time constraints, studies that did not include data in text or tables, and studies that had fewer than 10 observations were not extracted or evaluated.

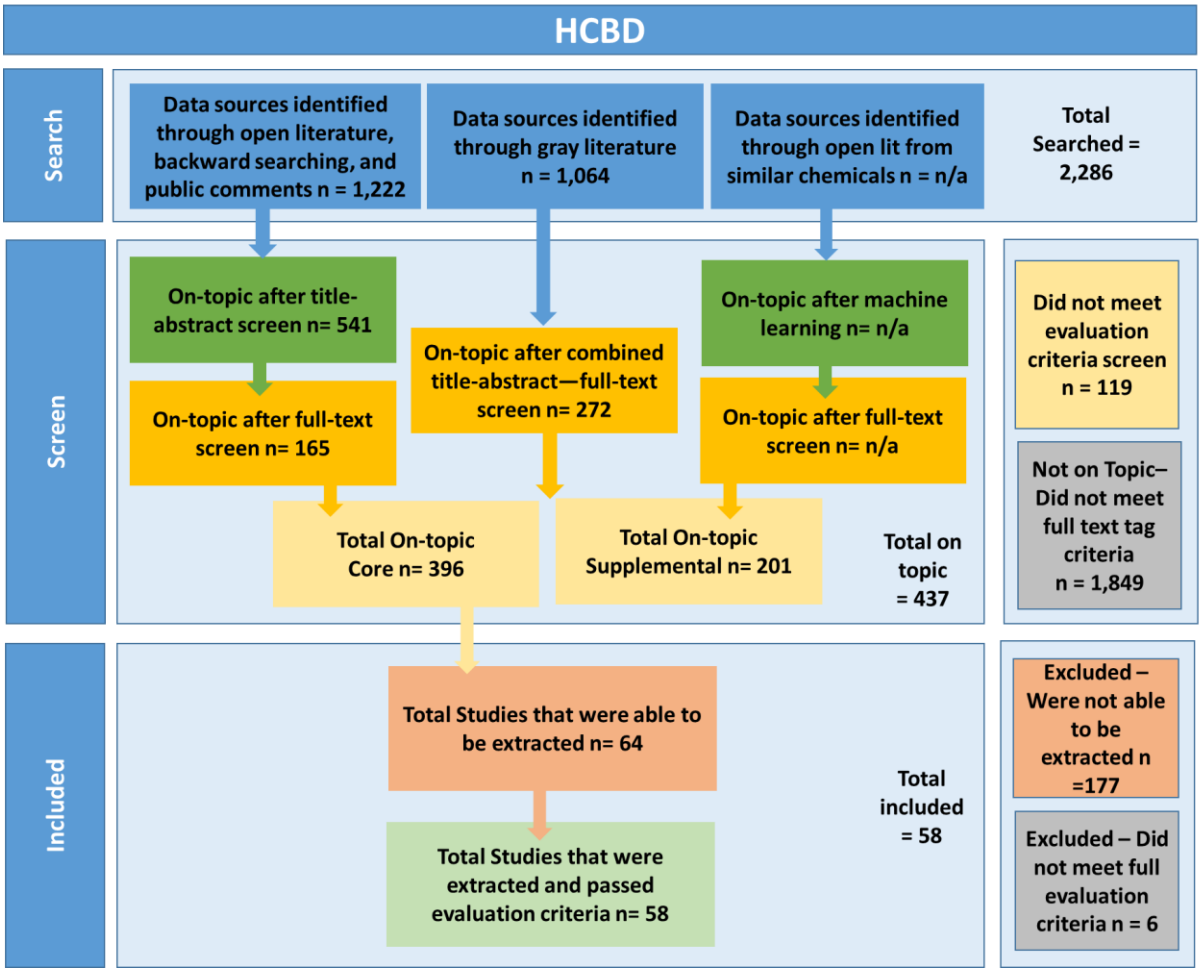

Figure B-2. PRISMA Diagram for HCBD

B.5 Data Evaluation Criteria

Core exposure data includes the following exposure data types:

- Environmental monitoring
- Biomonitoring
- Database Sources
- Completed Assessments
- Modeling

Assessors evaluated the extracted core exposure data for evaluation criteria specific to the data type. The data evaluation criteria are included in (U.S. EPA, 2018).

B.6 Data Extraction Fields

Core exposure data, including monitoring data and modeled estimates of concentration or dose, was extracted in DRAGON. The data extraction fields are included in Appendix I.

Appendix C. Supplemental Document for Phenol, isopropylated, phosphate (3:1) (ITPP)

C.1 Literature Search Strategy

This document describes the literature search strategy to support the exposure assessments for five persistent, bioaccumulative, and toxic (PBT) chemicals. The intent of the search is to assess the likely exposure of the general population, consumers, occupational populations, potentially exposed or susceptible subpopulations, and the environment to the conditions of use of PBT chemicals based on the criteria outlined in the Toxic Substances Control Act (TSCA) section 6(h) (OLRC, 2016). The conditions of use are defined as the circumstances under which a chemical substance is intended, known or reasonably foreseen to be manufactured, processed, distributed in commerce, used or disposed of.

Data sources in the peer-reviewed (open) and gray literature were considered as shown in Figure C-1. In addition to the primary searches of the peer-reviewed literature in Web of Science, PubMed, and Toxline, there were additional supplemental searches that were used to complement and/or evaluate the primary peer-reviewed search strategy. These were: backward searches of frequently used sources[5], a Google Scholar search of the top 100 results by chemical, and public comments and associated references cited in those comments submitted to the dockets by mid-January 2018.

An additional search of the gray literature was conducted as described in the Gray Literature Search Strategy section and was based off the protocol developed for the Systematic Review of the "First 10" chemicals under TSCA.

The results of the literature searches were compiled into Endnote libraries (database searches) and Excel spreadsheets (gray literature).

C.1.1. Database (Peer-reviewed) Search Strategies

The literature searches for the five PBT chemicals were designed to be as broad as possible, searching only for the chemical name and synonyms, but not including any limiters such as terms describing expected uses or dates. For ITPP, no chemical category name was included in the search, but a series of similar chemicals were searched for potential information.

The search strategies for ITPP are presented in Table C-1 and Table C-2.

[5] Frequently used sources are sources expected to be of high quality, such as assessments conducted by other government agencies.

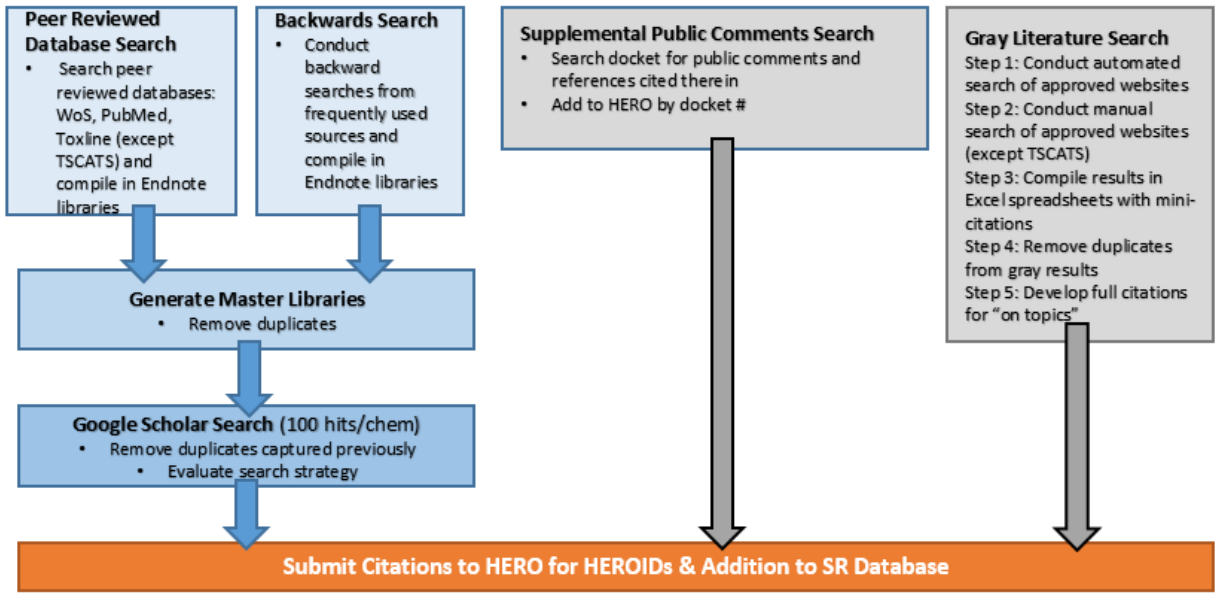

Figure C-1. Literature Search Strategy Workflow

Table C-1. ITPP Open Literature Search Strategy

Date of Search: December 15, 2017

Database	Search Strategy
PubMed	("isopropylated phenyl phosphates"[tiab] OR OS-70[tiab]) AND (English[lang])
Web of Science	("Duran MP280(sup R)" OR "fenol, isopropilado, fosfato (3:1)" OR "Isopropylated phenol phosphate (3:1)" OR "Isopropylated phenol, phosphate" OR "Phenol Isopropylated phosphate" OR "Phenol isopropyle, phosphate (3:1)" OR "Phenol, isopropylated, phosphate (3:1)" OR "PHENOL, ISOPROPYLATED, PHOSPHATE" OR "Phenol, isopropyliert, Phosphate (3:1)" OR "Triphenyl phosphates isopropylated" OR 68937-41-7 OR Durad-100 OR "isopropylated phenyl phosphates" OR OS-70) AND English
Toxline	68937-41-7
	Include Synonyms Exclude PubMed Records from TSCATS and NIH Reporter Database removed in EndNote

Table C-2. PIP3 Supplemental Literature Search Strategy

Date of Search: April 5, 2018

Database	Search Strategy
PubMed	("115-86-6"[rn] OR "Phenyl phosphate"[tiab] OR "Triphenyl phosphate"[tiab] OR "Triphenyl phosphate"[nm] OR "Triphenylphosphate"[tiab]) AND (English[lang])
Web of Science	("(1-Methylethyl)phenol phosphate (3:1)" OR "101299-37-0" OR "115-86-6" OR "2-(1-Methylethyl)phenyl diphenyl phosphate" OR "2502-15-0" OR "26967-76-0" OR "28108-99-8" OR "28109-00-4" OR "2-Isopropylphenyl diphenyl phosphate" OR "3,4-Di(propan-2-yl)phenyl diphenyl phosphate" OR "3,4-Diisopropylphenyl diphenyl phosphate" OR "4-isopropylphenyl diphenyl phosphate" OR "55864-04-5" OR "64532-94-1" OR "66797-44-2" OR "68155-51-1" OR "69500-29-4" OR "72668-27-0" OR "96300-97-9" OR "Bis(2-isopropylphenyl) phenyl phosphate" OR "Bis(isopropylphenyl) phenyl phosphate" OR "Bis(isopropylphenyl)phenylphosphat" OR "Bis(o-isopropylphenyl) phenyl phosphate" OR "Celluflex TPP" OR "DI(2-ISOPROPYLPHENYL)PHENYLPHOSPHATE" OR "Di(isopropylphenyl) phenyl phosphate" OR "Di-isopropyltriphenyl phosphate" OR "Diphenyl (2-propan-2-ylphenyl) phosphate" OR "Diphenyl 2-(propan-2-yl)phenyl phosphate" OR "Diphenyl 4-(propan-2-yl)phenyl phosphate" OR "Diphenyl o-isopropylphenylphenyl phosphate" OR "Diphenyl p-isopropylphenyl phosphate" OR "Disflamoll TP" OR "fosfato de fenilo y bis(isopropilfenilo)" OR "fosfato de trifenilo" OR "Isopropyl phenyl diphenyl phosphate" OR "Isopropylphenyl diphenyl phosphate" OR "Kronitex 100" OR "Kronitex 200" OR "o-Isopropylphenyl diphenyl phosphate mixt. with triphenyl phosphate" OR "o-Isopropylphenyl diphenyl phosphate" OR "p-Cumenyl phenyl phosphate (7CI)" OR "p-Cumenyl phosphate ((C9H11O)3PO)" OR "Phenol, (1-methylethyl)-, phosphate (3:1" OR "Phenol, (1-methylethyl)-, phosphate (3:1)" OR "Phenol, 3-(1-methylethyl)-, phosphate (3:1)" OR "Phenol, 4-(1-methylethyl)-, phosphate (3:1)" OR "Phenyl bis[2-(propan-2-yl)phenyl] phosphate" OR "Phenyl di(isopropylphenyl) phosphate" OR "Phenyl phosphate ((PhO)3PO)" OR "Phenyl phosphate" OR "Phoscon FR 903N" OR "Phosflex 31P" OR "Phosflex 41P" OR "Phosflex TPP" OR "phosphate de bis(isopropylphenyle) et de phenyle" OR "Phosphate de triphenyle" OR "Phosphate, tris(isopropylphenyl)" OR "Phosphoric acid, (1-methylethyl)phenyl diphenyl ester (9CI)" OR "Phosphoric acid, (1-methylethyl)phenyl diphenyl ester" OR "Phosphoric acid, 2-(1-methylethyl)phenyl diphenyl ester" OR "Phosphoric acid, 2-(1-methylethyl)phenyl diphenyl ester, mixt. with triphenyl phosphate" OR "Phosphoric acid, 3,4-bis(1-methylethyl)phenyl diphenyl ester" OR "Phosphoric acid, 4-(1-methylethyl)phenyl diphenyl ester" OR "Phosphoric acid, bis((1-methylethyl)phenyl) phenyl ester (9CI)" OR "Phosphoric acid, bis((1-methylethyl)phenyl) phenyl ester" OR "Phosphoric acid, bis(2-(1-methylethyl)phenyl) phenyl ester" OR "Phosphoric acid, bis[2-(1-methylethyl)phenyl] phenyl ester" OR "Phosphoric acid, bis[2-(1-methylethyl)phenyl] phenyl ester" OR "Phosphoric acid, triphenyl ester" OR "p-Isopropylphenyl diphenyl phosphate" OR "Reofos 95" OR "Reofos TPP" OR "Sumilizer TPP" OR "TP (VAN)" OR "Tri(isopropylphenyl) phosphate" OR "Trifenylfosfat" OR "Triphenoxyphosphine oxide" OR "Triphenyl phosphate" OR "Triphenylphosphat" OR "Triphenylphosphate" OR "Tris(3-isopropylphenyl) phosphate" OR "Tris(4-isopropylphenyl) phosphate" OR "Tris(isopropylphenyl) phosphate" OR "Tris(isopropylphenyl)phosphate" OR "Tris(isopropylphenyl)phosphates" OR "Tris(p-isopropylphenyl) phosphate" OR "Tris(p-isopropylphenyl)phosphate" OR "Tris[4-(propan-2-yl)phenyl] phosphate" OR "Wako TPP") AND English
Toxline	("101299-37-0" OR "115-86-6" OR "2502-15-0" OR "26967-76-0" OR "28108-99-8" OR "28109-00-4" OR "55864-04-5" OR "64532-94-1" OR "66797-44-2" OR "68155-51-1" OR "69500-29-4" OR "72668-27-0" OR "96300-97-9")
	Include Synonyms Exclude PubMed Records

C.1.2. Gray Literature Search Strategies

The five PBT chemicals searched were targeted to relevant sources and the approach was adapted from the first 10 chemicals to optimize efficiency by eliminating redundancy. Gray literature screening criteria excluded peer-reviewed journal articles that were expected to be caught in the database searches. Mini citations, containing author, title, year, were generated as a preliminary step to aid in identification and removal of duplicate records prior to tagging. Automated searches via the Google search API were employed where possible in favor of manual search sources. A summary of sources and search result counts after the removal of duplicates is presented in Table C-3. All results were reviewed from each source. The search strings used for manual and automated searches are found in Table C-4.

EPA is aware of information submitted by companies as part of TSCA requirements under sections 4, 8(d), 8(e) or as part of an FYI ("TSCATS Submissions data"). This information was not considered as part of the literature search and screening strategy. EPA plans to consider this information in the future.

Public comments submitted to the Docket (by Docket Number) were captured and HERO records were created including the title, author and docket number. The results were then compared to those of other searches to determine whether references cited in those public comments were already identified by other searches or need to be included. PDFs of the individual comments were not captured; instead a special "Public Comment" tag in HERO which specifies the corresponding round of public comments was used. Detailed results of the Public Comments submitted with the number of cited references for ITPP is shown in Table C-5.

Table C-3. Summary of Gray Literature Sources and Search Results for Automated and Manual Searches for ITPP

Source ID[1]	Source Category	Website	Description	Search type	Search Result Counts[2]
6000	US States Government Resources	States website custom search engine, see Summary of State Sources tab	Custom search engine using States sites	Automated	6
1000	US EPA Resources	epa.gov	US Environmental Protection Agency	Automated	39
1150	US EPA Resources	http://aqsdr1.epa.gov/aqsweb/aqstmp/airdata/download_files.html#Annual	Office of Air: AQS	Manual	0
1101	US EPA Resources	https://chemview.epa.gov/chemview	ChemView (CDR/IUR)	Manual	6
1083	US EPA Resources	https://actor.epa.gov/cpcat/faces/search.xhtml	CPDat	Manual	1
1154	US EPA Resources	https://comptox.epa.gov/dashboard/	Chemistry Dashboard	Manual	1
1148	US EPA Resources	https://iaspub.epa.gov/oppthpv/existchem_hpv_prioritizations.report	EPA HPVIS	Manual	0
1001	US EPA Resources	https://www.epa.gov/ground-water-and-drinking-water/table-regulated-drinking-water-contaminants	Office of Water: EPA Clean Water Act	Manual	0
1008	US EPA Resources	https://www.waterqualitydata.us/portal/	Office of Water: STORET and WQX	Manual	0
1155	US EPA Resources	https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/persistent-bioaccumulative-and-toxic-pbt-chemicals-under	TSCA PBT Use Documents	Manual	1
2150	Other US Agency Resources	cdc.gov	Centers for Disease Control (includes NIOSH and ATSDR)	Automated	2
2511	Other US Agency Resources	energy.gov	Department of Energy	Automated	0
2300	Other US Agency Resources	fda.gov	US Food and Drug Administration	Automated	0

Source ID[1]	Source Category	Website	Description	Search type	Search Result Counts[2]
2050	Other US Agency Resources	niehs.nih.gov	NIH National Institute of Environmental Health and Safety	Automated	20
2400	Other US Agency Resources	osha.gov	OSHA Occupational Safety and Health Administration	Automated	1
2521	Other US Agency Resources	pnnl.gov	Pacific Northwest National Laboratory	Automated	0
2509	Other US Agency Resources	usgs.gov	US Geological Survey	Automated	3
2027	Other US Agency Resources	https://ntp.niehs.nih.gov/pubhealth/roc/index-1.html#C	NIH Report on Carcinogens	Manual	0
2414	Other US Agency Resources	https://www.osha.gov/opengov/healthsamples.html	OSHA Chemical Exposure Health Data	Manual (inclusive of all results; not limited to first 100)	0
2123	Other US Agency Resources	https://www2a.cdc.gov/hhe/search.asp	CDC NIOSH Health Hazard Evaluations	Manual and Automated (inclusive of all results; not limited to first 100)	0
2104	Other US Agency Resources	www.atsdr.cdc.gov/hac/pha/	CDC ATSDR Health Hazard Consultations	Manual and Automated (inclusive of all results; not limited to first 100)	0
3160	Other Resources	oecd.org	The Organisation for Economic Co-operation and Development (OECD)	Automated	3
5000	Other Resources	sustainableproduction.org	Lowell Center for Sustainable Production	Automated	0
5020	Other Resources	Infohouse.p2ric.org	Pollution Prevention Infohouse	Automated	0

Source ID[1]	Source Category	Website	Description	Search type	Search Result Counts[2]
3600	Other Resources	http://www.spin2000.net/spinmyphp/	Substances in Preparations in Nordic Countries (SPIN) Database	Manual	1
5027	Other Resources	Kirk Othmer Encyclopedia	Book	Manual	1
5028	Other Resources	Ashford's Dictionary of Industrial Chemicals, 2001	Book	Manual	0
5029	Other Resources	Hawley's Chemical Dictionary, 2016	Book	Manual	0
3425	International Resources	carexcanada.ca	Carex Canada	Automated	0
3520	International Resources	env.go.jp	Government of Japan: Ministry of the Environment	Automated	0
3050	International Resources	europa.eu	European Union	Automated	32
3057	International Resources	https://echa.europa.eu/information-on-chemicals/registered-substances	ECHA	Manual	1
3100	International Resources	iarc.fr	International Agency for Research on Cancer	Automated	0
3350	International Resources	nicnas.gov.au	Australian Government: Department of Health, National Industrial Chemicals; NICNAS	Automated	3
3250	International Resources	who.int	World Health Organization	Automated	0
3421	International Resources	https://www.canada.ca/en/health-canada/services/chemical-substances/fact-sheets/chemicals-glance.html#interest	Canada Chemicals Portal	Manual	0
3450	International Resources	http://limitvalue.ifa.dguv.de/	GESTIS Database	Manual	0
			Total Unique (Duplicates Removed)		121

[1]"Source ID" refers to an internal ID assigned to each source for tracking purposes.

[2] Search result counts represent totals after removal of duplicate records.

Table C-4. Gray Literature Search Strings

Chemical	Manual Search Terms	Google Search Terms (up to 128 characters)
Phenol, isopropylated, phosphate (3:1)	Search database by CAS or chemical name, or select from a list on the website	"68937-41-7" OR "Phenol, isopropylated, phosphate (3:1)" OR "isopropylated triphenyl phosphate"

Table C-5. Detailed Results of Public Comments Backwards Search for ITPP

Public Comment Title	Publisher	Comment ID	References Cited Count
Comment submitted by Derek D. Swick, PhD, Manager, Regulatory and Scientific Affairs, American Petroleum Institute (API)	American Petroleum Institute (API)	EPA-HQ-OPPT-2016-0730-0008	1
Comment submitted by Christina Franz, Senior Director, Regulatory & Technical Affairs, American Chemistry Council (ACC)	American Chemistry Council (ACC)	EPA-HQ-OPPT-2016-0730-0010	11
Comment submitted by David H. Quigley, Akin Gump, Strauss Hauer & Feld LLP	Akin Gump, Strauss Hauer & Feld LLP	EPA-HQ-OPPT-2016-0730-0007	0
Comment submitted by Rick Brown, PhD, Global Product Stewardship Manager, ExxonMobil Fuels & Lubricants Company	ExxonMobil Fuels & Lubricants Company	EPA-HQ-OPPT-2016-0730-0009	1
Comment submitted by David H. Quigley, Akin Gump, Strauss Hauer & Feld LLP	Akin Gump, Strauss Hauer & Feld LLP	EPA-HQ-OPPT-2016-0730-0006	0
Comment submitted by Ryan J. Carra, Beveridge & Diamond PC	Beveridge & Diamond PC	EPA-HQ-OPPT-2016-0730-0002	3
Anonymous public comment	Anonymous	EPA-HQ-OPPT-2016-0730-0004	0
Comment submitted by Veena Singla, PhD, Associate Director, Science and Policy, Program on Reproductive Health and the Environment, University of California, San Francisco (UCSF) et al.	UCSF Program on Reproductive Health and the Environment, academics, scientists and clinicians	EPA-HQ-OPPT-2016-0730-0011	45
Comment submitted by Leslie Riegle, Director of Environmental Policy Aerospace Industries Association (AIA)	Aerospace Industries Association (AIA)	EPA-HQ-OPPT-2016-0730-0012	0
Comment submitted by Dianne C. Barton, Chair, National Tribal Toxics Council (NTTC)	National Tribal Toxics Council (NTTC)	EPA-HQ-OPPT-2016-0730-0015	18
Comment submitted by Robert Stockman, Senior Attorney, Environmental Defense Fund (EDF)	Environmental Defense Fund (EDF)	EPA-HQ-OPPT-2016-0730-0014	8

Public Comment Title	Publisher	Comment ID	References Cited Count
Comment submitted by Levi Howell, Regulatory Affairs Specialist, ICL-IP America Inc.	ICL-IP America Inc.	EPA-HQ-OPPT-2016-0730-0013	0
Comment submitted by Jyotsna S. Jagai, Research Assistant Professor, University of Illinois, Chicago Chair, Environment Section, American Public Health Association et al.		EPA-HQ-OPPT-2016-0730-0019	6
Comment submitted by Ken Zarker, Section Manager, Hazardous Waste and Toxics Reduction Program, Washington State Department of Ecology	Washington State Department of Ecology	EPA-HQ-OPPT-2016-0730-0018	3
Comment submitted by Elizabeth Hitchcock, Acting Director, Safer Chemicals Healthy Families (SCHF) et al.	Safer Chemicals Healthy Families (SCHF), Alaska Community Action on Toxics, Center for Environmental Health, Earthjustice, Environmental Health Strategy Center, Natural Resources Defense Council, Toxic-Free Future	EPA-HQ-OPPT-2016-0730-0022	51
TOTAL		15	147
Total Unique (Duplicates Removed)			**135**

C.1.3. Supplemental Search Strategy

Backward Search

To both supplement and test the database and gray literature searches, backward searches of frequently used sources were conducted. These sources consist of previous risk assessments, systematic reviews, and other assessments, generally conducted by EPA or other government agencies of the chemicals of interest and presented in Table C-7. The references that are cited within sections deemed relevant to this assessment were gathered into Endnote libraries for title abstract review.

Google Scholar Search

To further supplement and test the database searches, a Google Scholar search was conducted for each of the five PBT chemicals. The top 100 results returned by Google Scholar for each chemical were exported into Endnote libraries. These results were compared to the references identified in the database, backward, and gray literature searches to identify references not found by the previous searches. While Google Scholar results are expected to be primarily peer-reviewed rather than gray literature, the results were still compared to all searches.

C.1.4. Literature Search Results

The literature searches were conducted, and for PubMed, Web of Science, ToxLine, Backwards searches, and Google Scholar searches, the results were imported into one Endnote library per chemical. After the results were combined, duplicates were removed and TSCATS/NIH Reporter data, a subset of ToxLine, were moved into a separate folder. The resulting counts are presented in Table C-6. Detailed results for the ITPP backwards search are presented in Table C-7.

Table C-6. Count of Peer-reviewed Literature Search Results by Search Type for ITPP

Chemical	PubMed	WoS	ToxLine	TSCATS/ NIH Reporter	Backwards	Google Scholar
ITPP	4	43	1	27	129	100

Table C-7. Detailed Results of Backwards Search of Frequently Used Sources for ITPP

HEROID	Document title	Reference Count
4182594	Environmental risk evaluation report: Isopropylated triphenyl phosphate	23
4182605	Indoor emissions and fate of flame retardants: A modelling approach	106
	TOTAL	129
	Total Unique (Duplicates Removed)	**129**
	EndNote Library: Total Unique (Duplicates Removed)	**129**

C.2 Literature Screening Strategy

C.2.1. Development of the Literature Screening Approach

The steps involved in developing the title abstract screening approach are:

1. Define inclusion/exclusion criteria.
2. Conduct the pilot using 10 randomly selected studies for each chemical from both the peer-reviewed and gray literature that are screened by EPA experts.
3. Use the results of the pilot to refine inclusion/exclusion criteria.
4. Use the refined pilot to train screeners in applying the tags.

The overall workflow of the systematic review process including the literature screening is presented in Appendix F.

In these assessments, the results of the title/abstract literature screening will be used to develop the PECO statement. The PECO statement is included in Appendix 0. Four tags were used at the title-abstract phase: Peer On Topic, Peer Off Topic, Gray On Topic, and Gray Off Topic and recorded on the HERO project pages. Title abstract screening was conducted in DRAGON[6]. A screenshot of the DRAGON form and all DRAGON tags is presented in Appendix H.

The inclusion/exclusion criteria for title/abstract and full text screening are included in Appendix G. During full text screening, studies were also screened for "Red Flag Criteria," which represent the "Unacceptable" criteria from the Data Evaluation criteria (U.S. EPA, 2018).

C.2.2. Literature Screening Pilot

A pilot with 100 results representative of the five chemicals and the peer, backwards, and gray literature search results was developed by EPA. Two exposure experts scored the pilot, and met with EPA to refine the criteria and application of the criteria.

Before screening, all screeners were required to meet a 90% accuracy in tagging the pilot screening studies. Screeners who met this level of proficiency were able to begin title abstract screening. Screeners who do not meet this level of proficiency, continued to train, using the studies screened by screeners who had passed the pilot as additional training studies. Documentation of all pilot tagging results was maintained in Excel spreadsheets for both the peer-reviewed and gray literature.

C.2.3. Literature Screening

Title abstract screening of the peer-reviewed and gray literature occurred in DRAGON, an online tool for systematic review. Results of the ITPP search were manually screened with one screener who has been trained via the pilot process. Additionally, a subject matter expert

[6] DRAGON is an online tool for systematic review developed by ICF that stores qualitative and quantitative data from literature to help scientists implement the elements of systematic review, including problem formulation, literature screening, risk of bias evaluation, and data integration.

reviewed 10% of the references deemed to be On Topic and Off Topic as a quality assurance check to ensure that they have been categorized appropriately.

For gray literature, title/abstract and full text screening was done simultaneously, and tags for screening are included in Appendix H. For peer-reviewed literature, title/abstract and full text screening were done separately, and tags for each stage are included in Appendix H.2.

C.2.4. Prioritization

The database search strategy for ITPP returned approximately 50 results. The supplemental search for related chemicals returned approximately 1,600 results. Few of the results added by the related chemicals search are likely to be relevant to an exposure assessment of ITPP; therefore, the results from title abstract screening of the ITPP search results were used to prioritize the related chemicals search results using text analytics in DoCTER.

For prioritization, multiple text analytic algorithms can be used to find studies with titles and abstracts similar to seed studies previously identified as On Topic by EPA experts. DoCTER employs two main metrics, ensemble clustering and machine learning, including active machine learning. Supervised clustering using an ensemble approach uses multiple algorithms in Varghese et al. (2017) to prioritize references for review. The prioritization strategy is shown in Figure C-2 and presented in Varghese et al. (2017). These algorithms create a user-defined number of clusters based on similarities in the text of the title and abstract, and each algorithm is broadly-accepted in the text analytics scientific field, as described in Varghese et al. (2017). The clusters are populated by the algorithms that first convert the text in each title and abstract into a numerical matrix (using binary or 0s and 1s to represent the text) and then identifies similarities or similar numerical strings between each matrix representation of a title and abstract. Based on the similarities, the reference is assigned to a cluster. In the example, each of the algorithms was used to bin the studies into 10, 20, or 30 clusters, for a total of six different cluster analyses (six large circles in the figure). A random sample of studies identified as relevant serve as “tracer” or “seed” studies (pink circles in the figure). The tracer method involves following these relevant studies and determining the clusters the majority occur in; these clusters are then deemed more likely to contain other (as-yet unidentified) relevant studies. Off topic references, or negative seeds, can be used to estimate performance of the tool using the metric of precision, but are not required for clustering.

To identify these high-priority clusters, the clusters containing a given fraction (75% in the example) of the relevant tracer studies are identified for each of the six analyses and termed “high concentration of tracer” clusters. All non-tracer studies in those high-concentration clusters can then be marked as “high priority” for further screening. This ensemble method is used to increase confidence in the selection of prioritized studies by mitigating uncertainty from each individual analysis. Additionally, studies in the “low priority” clusters can be further analyzed using machine learning algorithms that also use the “tracer” studies in conjunction with Off Topic references, or negative seeds, and assign a probability score to each of the remaining studies as likely to be On Topic.

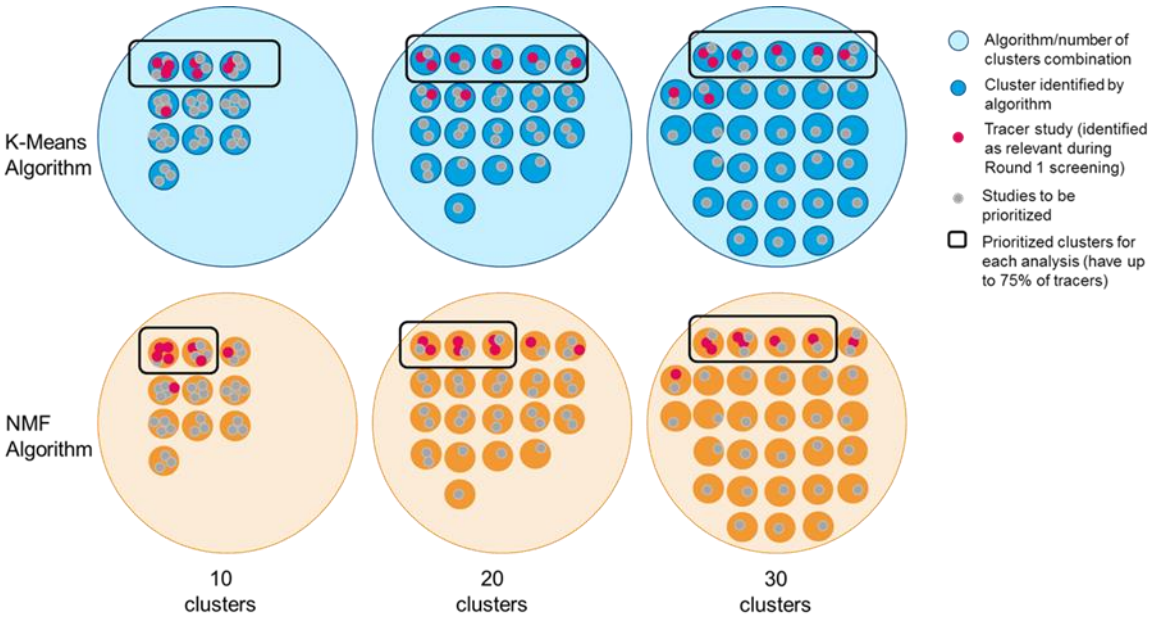

Figure C-2. Ensemble text analytics method for prioritizing studies for screening

Any reference that was flagged as high priority by DoCTER was loaded into DRAGON for title abstract screening.

C.3 PECO Statement

Chemical	PIP3
PECO Element	**Evidence**
Population	**Human:** Workers and occupational non-users (e.g., fire fighters); general population; consumers and bystanders in residential settings; near-facility populations (includes industrial and commercial facilities manufacturing, processing, or using PIP3); populations exposed from transfer from workplaces through take home exposures; populations in co-located residences or businesses; populations with subsistence diets; children; infants; pregnant women; lactating women; women of childbearing age; susceptible populations (life stages, preexisting conditions, genetic factors). No chemical-specific exclusions are suggested at present.
	Ecological: Aquatic organisms (edible and nonedible fish, aquatic invertebrates (daphnia), amphibians); terrestrial organisms (plants, soil invertebrates (worms), birds, mammals). No chemical specific exclusions are suggested at present.
Exposure	**Expected Exposure Sources, Pathways, Routes**
	Source: Industrial activities (manufacturing, processing, recycling, treatment, disposal of products); commercial and consumer uses of consumer products containing PIP3 and associated releases to air, water, or wastes (wastewater/liquid wastes, solid wastes); indoor sources/materials that cover a large surface area, are abraded during use, or have high potential for direct contact.
	Pathway: Waste streams (e.g., landfills, biosolids); outdoor air (fugitive/stack emissions); drinking water; surface water/groundwater (transfer from outdoor air/soil); indoor air (transfer from outdoor air); soil/sediment; dust; contact with products; liquid contact; vapor intrusion; food (breastmilk, fish, meat, eggs, dairy); media-specific background and source attribution to be considered.
	Routes: Inhalation (indoor air, smoke from burning buildings or PVC products); oral (dietary ingestion of food or breastmilk, incidental ingestion of contaminated soil and dust, hand-to-mouth contact, ingestion of drinking water, ingestion of suspended particles, mouthing of consumer articles); dermal (contact with dust, soil, consumer products containing PIP3 or other secondary vectors)
Comparator (Scenario)	**Human:** Consider media-specific background exposure scenarios and use/source specific exposure scenarios as well as which receptors are and are not reasonably exposed across the projected exposure scenarios.
	Ecological: Consider media-specific background exposure scenarios and use/source specific exposure scenarios as well as which receptors are and are not reasonably exposed across the projected exposure scenarios.
Outcomes for Exposure Concentration or Dose	**Human:** Acute, subchronic, and/or chronic external dose estimates (mg/kg/day); acute, subchronic, and/or chronic internal dose based on biomonitoring and reverse dosimetry (mg/kg/day); acute, subchronic, and/or chronic air, soil, dust, and water concentration estimates (mg/m^3 or mg/L).
	Ecological: A wide range of ecological receptors will be considered using surface water, sediment, soil, and air concentrations. Targeted use of wildlife biomonitoring data will also be explored.

C.4 PRISMA Diagram

The PRISMA Diagram for ITPP, including literature counts from search, screening and included phases from all sources, is presented in Figure C-3. A subset of studies that passed the screening phase were not extracted or evaluated due to the ready availability of the full text and supplemental information. Due to time constraints, studies that did not include data in text or tables, and studies that had fewer than 10 observations were not extracted or evaluated.

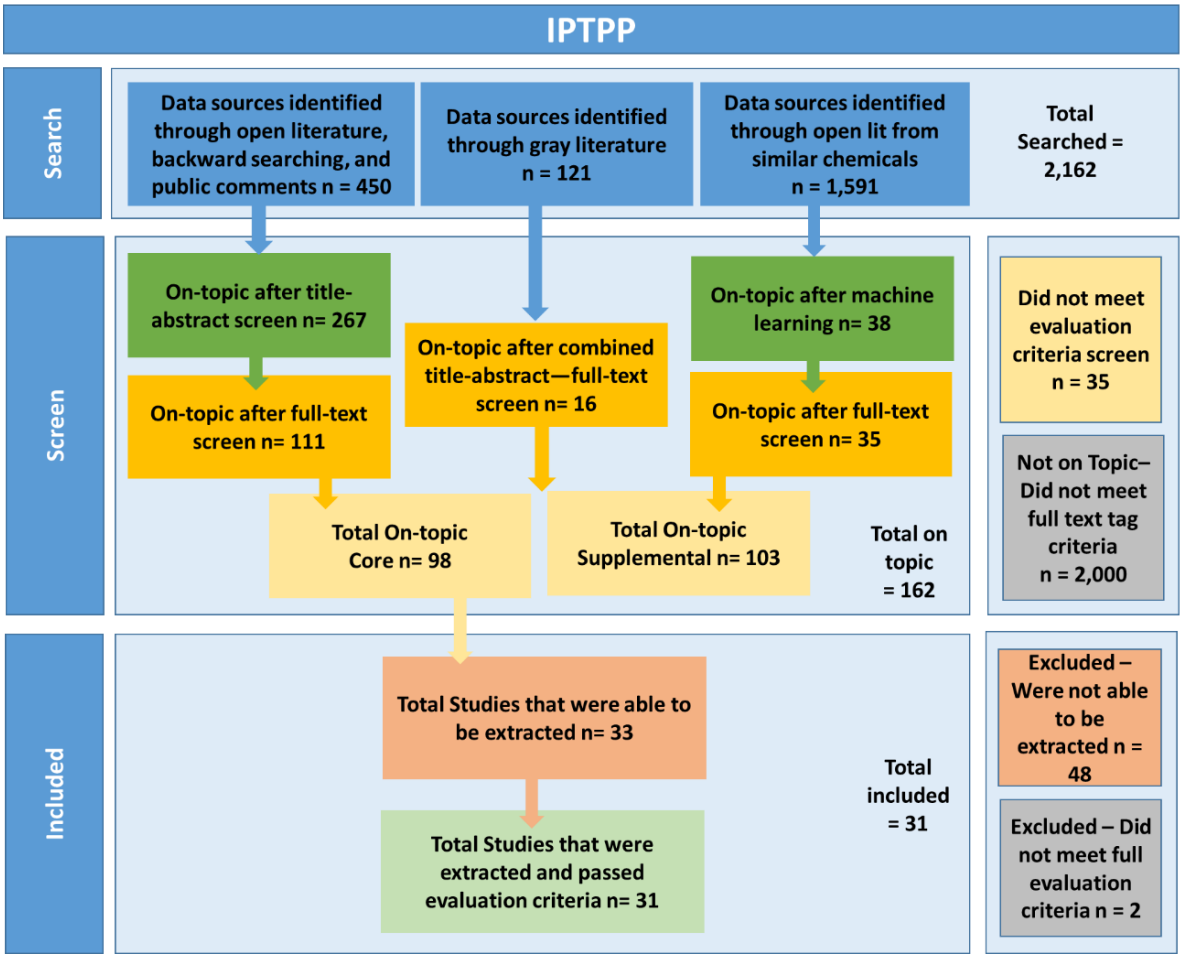

Figure C-3. PRISMA Diagram for ITPP

C.5 Data Evaluation Criteria

Core exposure data includes the following exposure data types:

- Environmental monitoring
- Biomonitoring
- Database Sources
- Completed Assessments
- Modeling

Assessors evaluated the extracted core exposure data for evaluation criteria specific to the data type. The data evaluation criteria are included in (U.S. EPA, 2018).

C.6 Data Extraction Fields

Core exposure data, including monitoring data and modeled estimates of concentration or dose, was extracted in DRAGON. The data extraction fields are included in Appendix I.

Appendix D. Supplemental Document for 2,4,6-Tris(tert-butyl) phenol (TTBP)

D.1 Literature Search Strategy

This document describes the literature search strategy to support the exposure assessments for five persistent, bioaccumulative, and toxic (PBT) chemicals. The intent of the search is to assess the likely exposure of the general population, consumers, occupational populations, potentially exposed or susceptible subpopulations, and the environment to the conditions of use of PBT chemicals based on the criteria outlined in the Toxic Substances Control Act (TSCA) section 6(h) (OLRC, 2016).The conditions of use are defined as the circumstances under which a chemical substance is intended, known or reasonably foreseen to be manufactured, processed, distributed in commerce, used or disposed of.

Data sources in the peer-reviewed (open) and gray literature were considered as shown in **Error! Reference source not found.**. In addition to the primary searches of the peer-reviewed literature in Web of Science, PubMed, and Toxline, there were additional supplemental searches that were used to complement and/or evaluate the primary peer-reviewed search strategy. These were: backward searches of frequently used sources[7], a Google Scholar search of the top 100 results by chemical, and public comments and associated references cited in those comments submitted to the dockets by mid-January 2018.

An additional search of the gray literature was conducted as described in the Gray Literature Search Strategy section and was based off the protocol developed for the Systematic Review of the "First 10" chemicals under TSCA.

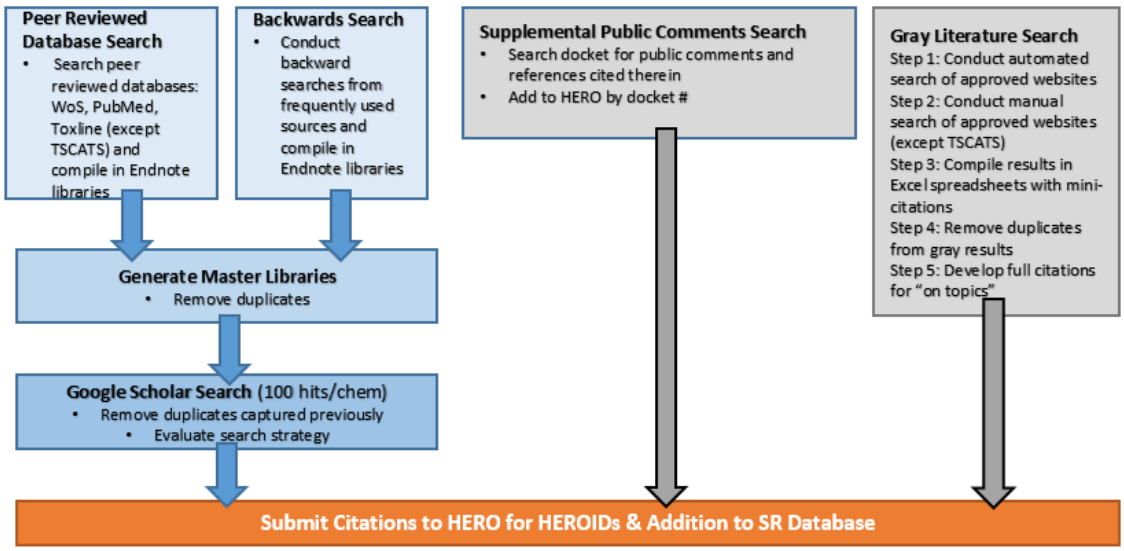

Figure D-1. Literature Search Strategy Workflow

[7] Frequently used sources are sources expected to be of high quality, such as assessments conducted by other government agencies.

The results of the literature searches were compiled into Endnote libraries (database searches) and Excel spreadsheets (gray literature.)

D.1.1. Database (Peer-reviewed) Search Strategies

The literature searches for the five PBT chemicals were designed to be as broad as possible, searching only for the chemical name and synonyms, but not including any limiters such as terms describing expected uses or dates. For TTBP, no chemical category name was included in the search, but a series of similar chemicals were searched for potential information. The search strategies for TTBP are presented in Table D-1 and Table D-2.

Table D-1. TTBP Open Literature Search Strategy

Date of Search: December 15, 2017

Database	Search Strategy
PubMed	(2,4,6-tri-tert-butylphenol[nm] OR "2,4,6-Tri-t-butylphenol"[tiab] OR "2,4,6-TRI-TERT.-BUTYLPHENOL"[tiab] OR "2,4,6-TRI-TERT-BUTYL PHENOL"[tiab] OR "2,4,6-Tri-tert-butylphenol"[tiab] OR 732-26-3[rn] OR Tri-tert-butylphenol[tiab]) AND (English[lang])
Web of Science	("2,4,6-Tris(1,1-dimethylethyl)phenol" OR "2,4,6-Tris(tert-butyl)phenol" OR "2,4,6-tri-terc-butilfenol" OR "2,4,6-Tri-tert-butyl-1-hydroxybenzene" OR "Phenol, 2,4,6-tri(1,1-dimethylethyl)-" OR "Phenol, 2,4,6-tris(1,1-dimethylethyl)-" OR "Phenol, 2,4,6-tri-tert-butyl-" OR "Phenol, tris(1,1-dimethylethyl)-" OR "Tris(1,1-dimethylethyl)phenol" OR Alkofen-B OR Voidox OR "2,4,6-Tri-t-butylphenol" OR "2,4,6-TRI-TERT.-BUTYLPHENOL" OR "2,4,6-TRI-TERT-BUTYL PHENOL" OR "2,4,6-Tri-tert-butylphenol" OR 732-26-3 OR Tri-tert-butylphenol) AND English
Toxline	732-26-3
	Include Synonyms Exclude PubMed Records from TSCATS and NIH Reporter Database removed in EndNote

Table D-2. TTBP Supplemental Literature Search Strategy

Date of Search: April 5, 2018

Database	Search Strategy
PubMed	("Topanol"[tiab] OR "Tonarol"[tiab] OR "Sustane"[tiab] OR "Phenol, 2,6-bis(1,1-dimethylethyl)-4-methyl-"[tiab] OR "Phenol, 2,4-bis(1,1-dimethylethyl)-"[tiab] OR "p-Cresol, 2,6-di-tert-butyl-"[tiab] OR "o-t-Butylphenol"[tiab] OR "Ionole"[tiab] OR "Ionol"[tiab] OR "Di-tert-butylphenol"[tiab] OR "Di-tert-butyl-p-cresol"[tiab] OR "Dibunol"[tiab] OR "CAO 3"[tiab] OR "CAO 1"[tiab] OR "Butylhydroxytoluene"[tiab] OR "Butylated hydroxytoluene"[mh] OR "Butylated hydroxytoluene"[tiab] OR "AO 4"[tiab] OR "Agidol"[tiab] OR "96-76-4"[rn] OR "96-70-8"[rn] OR "88-18-6"[rn] OR "6-tert-Butyl-2,4-xylenol"[tiab] OR "6-tert-Butyl-2,4-dimethylphenol"[tiab] OR "4-Methyl-2,6-di-tert-butylphenol"[tiab] OR "4-Methyl-2,6-ditertbutylphenol"[tiab] OR "4 Methyl 2,6 ditertbutylphenol"[tiab] OR "3,5-Di-tert-butyl-4-hydroxytoluene"[tiab] OR "2-tert-Butylphenol"[tiab] OR "2-tert-Butylphenol"[nm] OR "2-tert-Butyl-p-cresol"[tiab] OR "2-tert-Butyl-4-methylphenol"[tiab] OR "2-tert-Butyl-4-methylphenol"[nm] OR "2-tert-Butyl-4-ethylphenol"[tiab] OR "2-tert-Butyl-4-ethylphenol"[nm] OR "2-tert-Butyl-4,6-dimethylphenol"[tiab] OR "2-t-Butylphenol"[tiab] OR "2-t-Butyl-4-methylphenol"[tiab] OR "2409-55-4"[rn] OR "2,6-Di-tert-butylphenol"[tiab] OR "2,6-Di-tert-

Database	Search Strategy
	butylphenol"[nm] OR "2,6-Di-tert-butyl-p-cresol"[tiab] OR "2,6-Di-tert-butyl-4-methylphenol"[tiab] OR "2,6-Di-tert-butyl-4-hydroxytoluene"[tiab] OR "2,6-Di-tert-butyl-4-ethylphenol"[tiab] OR "2,6-Di-t-butylphenol"[tiab] OR "2,6-Di-t-butyl-p-cresol"[tiab] OR "2,6-Di-t-butyl-4-methylphenol"[tiab] OR "2,6-Bis(1,1-dimethylethyl)phenol"[tiab] OR "2,6-Bis(1,1-dimethylethyl)-4-methylphenol"[tiab] OR "2,6 Di-tert-butylphenol"[tiab] OR "2,6 Di tert butyl p cresol"[tiab] OR "2,6 Di t butyl 4 methylphenol"[tiab] OR "2,4-Di-tert-butylphenol"[tiab] OR "2,4-Di-tert-butylphenol"[nm] OR "1879-09-0"[rn] OR "128-39-2"[rn] OR "128-37-0"[rn] OR "2,4-Bis(1,1-dimethylethyl)phenol"[tiab] OR "2,4-DI-TERT-BUTYL PHENOL"[tiab] OR "2,6-bis(1,1-Dimethylethyl)-4-methyl-phenol"[tiab] OR "2,6-Bis(tert-butyl)-4-methylphenol"[tiab] OR "2,6-Di(tert-butyl)hydroxytoluene"[tiab] OR "2,6-DI-TERT BUTYL-4-METHYLPHENOL"[tiab] OR "2,6-DI-TERT.-BUTYLPHENOL"[tiab] OR "2,6-DI-TERT-BUTYL-4-METHYL PHENOL"[tiab] OR "2,6-Di-tert-butylcresol"[tiab] OR "2,6-tert-Butyl-4-methylphenol"[tiab] OR "Butyl hydroxy toluene"[tiab] OR "DIBUTYL HYDROXYTOLUENE"[tiab] OR "Dibutylhydroxytoluene"[tiab] OR "Di-tert-Butyl-4-methylphenol"[tiab] OR "Di-tert-butylcresol"[tiab] OR "DITERTIARY BUTYL P-CRESOL"[tiab] OR "E321"[tiab] OR "Popol"[tiab]) AND (English[lang])
Web of Science	("Vulkanox KB" OR "Vianol" OR "Vanlube PCX" OR "Vanlube PC" OR "Toxolan P" OR "Topanol" OR "Topanol OC" OR "Topanol O" OR "Tonarol" OR "Tenox BHT" OR "Tenamene 3" OR "Tenamen 3" OR "Swanox BHT" OR "Sustane" OR "Sustane BHT" OR "Sumilizer BHT" OR "Stavox" OR "Prodox 340" OR "Prodox 146A-85X" OR "Prodox 146" OR "Phenol, o-tert-butyl-" OR "Phenol, o-(tert-butyl)-" OR "Phenol, 2-tert-butyl-4-ethyl-" OR "Phenol, 2,6-di-tert-butyl-4-ethyl-" OR "Phenol, 2,6-di-tert-butyl-4-ethyl- (8CI)" OR "Phenol, 2,6-di-tert-butyl-" OR "Phenol, 2,6-bis(1,1-dimethylethyl)-4-methyl-" OR "Phenol, 2,6-bis(1,1-dimethylethyl)-4-ethyl-" OR "Phenol, 2,6-bis(1,1-dimethylethyl)-" OR "Phenol, 2,4-di-tert-butyl-" OR "Phenol, 2,4-di(1,1-dimethylethyl)-" OR "Phenol, 2,4-bis(1,1-dimethylethyl)-" OR "Phenol, 2-(1,1-dimethylethyl)-4-methyl-" OR "Phenol, 2-(1,1-dimethylethyl)-4-ethyl-" OR "Phenol, 2-(1,1-dimethylethyl)-4,6-dimethyl-" OR "Phenol, 2-(1,1-dimethylethyl)-" OR "p-Cresol, 2-tert-butyl-" OR "p-Cresol, 2,6-di-tert-butyl-" OR "Paranox 441" OR "Parabar 441" OR "o-tert-Butylphenol" OR "o-tert-Butyl-p-cresol" OR "o-t-Butylphenol" OR "o-Di-tert-butyl-p-methylphenol" OR "Nonox TBC" OR "Nocrac 200" OR "Kerabit" OR "Isonox 103" OR "Ionole" OR "Ionol" OR "Ionol 2" OR "Impruvol" OR "Hitec 4701" OR "Ethyl AN 701" OR "Ethyl 701" OR "Ethanox 701" OR "Di-tert-butyl-p-methylphenol" OR "Di-tert-butylphenol" OR "Di-tert-butyl-p-cresol" OR "Dibutylated hydroxytoluene" OR "Dibunol" OR "Deenax" OR "Dalpac" OR "Chemanox 11" OR "Catalin cao-3" OR "Catalin antioxydant 1" OR "CAO 3" OR "CAO 1" OR "Butylohydroksytoluenu" OR "Butylhydroxytoluene" OR "Butylated hydroxytoluol" OR "Butylated hydroxytoluene" OR "BUKS" OR "BHT 264" OR "BHT (food grade)" OR "Benzene, 2-tert-butyl-4-ethyl-1-hydroxy-" OR "Benzene, 1-tert-butyl-2-hydroxy-" OR "AOX 4K" OR "AOX 4" OR "AO 4K" OR "AO 4" OR "AO 29" OR "Antrancine 8" OR "Antox QT" OR "Antioxidant T 501" OR "Antioxidant No. 33" OR "Antioxidant MPJ" OR "Antioxidant KB" OR "Antioxidant DBPC" OR "Antioxidant 4K" OR "Antioxidant 4" OR "Antioxidant 30" OR "Antioxidant 29" OR "Antioxidant 264" OR "Alkofen BP" OR "Agidol" OR "Advastab 401" OR "96-76-4" OR "96-70-8" OR "88-18-6" OR "6-tert-Butyl-2,4-xylenol" OR "6-tert-Butyl-2,4-dimethylphenol" OR "6-t-Butyl-2,4-xylenol" OR "6-t-Butyl-2,4-dimethylphenol" OR "4-Methyl-6-t-butylphenol" OR "4-Methyl-2-tert-butylphenol" OR "4-Methyl-2-t-butylphenol" OR "4-Methyl-2,6-tert-butylphenol" OR "4-Methyl-2,6-di-tert-butylphenol" OR "4-Methyl-2,6-ditertbutylphenol" OR "4-Methyl-2,6-di-terc. butylfenol" OR "4-Methyl-2-(1,1-dimethylethyl)phenol" OR "4-Hydroxy-3,5-di-tert-butyltoluene" OR "4-Ethyl-2-tert-butylphenol" OR "4-Ethyl-2,6-di-tert-butylphenol" OR "4130-42-1" OR "4 Methyl 2,6 ditertbutylphenol" OR "3,5-Di-tert-butyl-4-hydroxytoluene" OR "2-tert-Butylphenol" OR "2-tert-Butyl-p-cresol" OR "2-tert-Butyl-4-methylphenol" OR "2-tert-Butyl-4-methyl-1-phenol" OR "2-tert-Butyl-4-ethylphenol" OR "2-tert-Butyl-4,6-dimethylphenol" OR "2-tert-Butyl-1-

Database	Search Strategy
	hydroxybenzene" OR "2-terc.Butyl-p-kresol" OR "2-t-Butylphenol" OR "2-t-Butyl-p-cresol" OR "2-t-Butyl-4-methylphenol" OR "2-t-Butyl-4-ethylphenol" OR "2409-55-4" OR "2,6-Di-tert-butyl-p-methylphenol" OR "2,6-Di-tert-butylphenol" OR "2,6-Di-tert-butyl-p-cresol" OR "2,6-Di-tert-butyl-4-methylphenol" OR "2,6-Di-tert-butyl-4-methylhydroxybenzene" OR "2,6-Di-tert-butyl-4-hydroxytoluene" OR "2,6-Di-tert-butyl-4-ethylphenol" OR "2,6-Di-tert-butyl-4-cresol" OR "2,6-Di-tert-butyl-1-hydroxy-4-methylbenzene" OR "2,6-Di-terc.butyl-p-kresol" OR "2,6-Di-t-butylphenol" OR "2,6-Di-t-butyl-p-cresol" OR "2,6-Di-t-butyl-4-methylphenol" OR "2,6-Bis(tert-butyl)phenol" OR "2,6-Bis(1,1-dimethylethyl)phenol" OR "2,6-Bis(1,1-dimethylethyl)-4-methylphenol" OR "2,6-Bis(1,1-dimethylethyl)-4-ethylphenol" OR "2,6 Di-tert-butylphenol" OR "2,6 Di tert butyl p cresol" OR "2,6 Di t butyl 4 methylphenol" OR "2,4-Xylenol, 6-tert-butyl-" OR "2,4-Di-tert-butylphenol" OR "2,4-Dimethyl-6-tert-butylphenol" OR "2-(1,1-Dimethylethyl)phenol" OR "2-(1,1-Dimethylethyl)-4-methylphenol" OR "1-Hydroxy-4-methyl-2,6-di-tert-butylbenzene" OR "1-Hydroxy-4-ethyl-2,6-di-tert-butylbenzene" OR "1-Hydroxy-2-tert-butyl-4-methylbenzene" OR "1-Hydroxy-2,4-di-tert-butylbenzene" OR "1879-09-0" OR "128-39-2" OR "128-37-0" OR "2-(1,1-Dimethylethyl)-4-methyl-phenol" OR "2,4-BIS(TERT-BUTYL)PHENOL" OR "2,4-di-terc-butilfenol" OR "2,4-Di-tert-butylhydroxybenzene" OR "2,6-Bis(1,1-dimethylethyl)-4-methylphenol, 9CI" OR "2,6-di-terc-butilfenol" OR "2,6-di-terc-butil-p-cresol" OR "2,6-DI-TERT.-BUTYL-P-KRESOL" OR "2,6-Di-tert-butyl-4-methyl-1-hydroxybenzene" OR "2,6-DI-TERT-BUTYL-4-METHYLPHENOL(3,5-DI-TERT-BUTYL-4-HYDROXYTOLUENE)(2,6-DI-TERT-BUTYL-P-CRESOL)" OR "2,6-Di-tert-butyl-4-methyphenol" OR "2,6-Di-tert-butylmethylphenol" OR "2,6-Di-tert-butyl-p-cresol, 8CI" OR "2,6-Di-tert-butyl-p-cresole" OR "2,6-Di-tert-butyl-p-kresol" OR "2-terc-butilfenol" OR "3,5-Di-tert-butyl-p-hydroxytoluene" OR "4-Methyl-2,6-bis(1,1-dimethylethyl)phenol" OR "Antage BHT" OR "Antioxidant 246" OR "BHT Swanox" OR "B-NOX BHT-P" OR "BRN 1910383" OR "Catalin CAO 3" OR "DIBUTYL PARACRESOL" OR "Dibutylcresol" OR "FEMA 2184" OR "Ionol K" OR "K-NOX-BHT" OR "Lowinox BHT" OR "Lubrizol 817" OR "Naugard BHT" OR "Nipanox" OR "Nocrac 2000" OR "Permanax BHT" OR "PHENOL, 2,6-DI-TERT-BUTYL-4-METHYL" OR "PHENOL, 2,6-DI-TERT-BUTYL-4-METHYL-" OR "Phenol, bis(1,1-dimethylethyl)methyl-" OR "Ralox BHT" OR "Reaction product from p-cresol and isobutylene" OR "Selosol H 633" OR "Sumilizer BHT-R" OR "TOLUENE, 3,5-DI-TERTIARY-BUTYL-4-HYDROXY-" OR "Topanol BHT" OR "Topanol O-FG" OR "Topanol OL" OR "Ultranox 226" OR "Vanox PC" OR "Yoshinox BHT" OR "2,4-Bis(1,1-dimethylethyl)phenol" OR "2,4-DI-TERT-BUTYL PHENOL" OR "2,6-bis(1,1-Dimethylethyl)-4-methyl-phenol" OR "2,6-Bis(tert-butyl)-4-methylphenol" OR "2,6-Di(tert-butyl)hydroxytoluene" OR "2,6-DI-TERT BUTYL-4-METHYLPHENOL" OR "2,6-DI-TERT.-BUTYLPHENOL" OR "2,6-DI-TERT-BUTYL-4-METHYL PHENOL" OR "2,6-Di-tert-butylcresol" OR "2,6-tert-Butyl-4-methylphenol" OR "Butyl hydroxy toluene" OR "DIBUTYL HYDROXYTOLUENE" OR "Dibutylhydroxytoluene" OR "Di-tert-Butyl-4-methylphenol" OR "Di-tert-butylcresol" OR "DITERTIARY BUTYL P-CRESOL" OR "E321" OR "PHENOL,2,6-BIS(1,1-DIMETHYL-ETHYL)-4-METHYL" OR "Popol") AND English
Toxline	("96-76-4" OR "96-70-8" OR "88-18-6" OR "4130-42-1" OR "2409-55-4" OR "1879-09-0" OR "128-39-2" OR "128-37-0")
	Include Synonyms Exclude PubMed Records

D.1.2. Gray Literature Search Strategies

The five PBT chemicals searched were targeted to relevant sources and the approach was adapted from the first 10 chemicals to optimize efficiency by eliminating redundancy. Gray literature screening criteria excluded peer-reviewed journal articles that were expected to be

caught in the database searches. Mini citations, containing author, title, year, were generated as a preliminary step to aid in identification and removal of duplicate records prior to tagging. Automated searches via the Google search API were employed where possible in favor of manual search sources. A summary of sources and search result counts after the removal of duplicates is presented in Table D-3. All results were reviewed from each source. The search strings used for manual and automated searches are found in Table D-4.

EPA is aware of information submitted by companies as part of TSCA requirements under sections 4, 8(d), 8(e) or as part of an FYI ("TSCATS Submissions data"). This information was not considered as part of the literature search and screening strategy. EPA plans to consider this information in the future.

Public comments submitted to the Docket (by Docket Number) were captured and HERO records were created including the title, author and docket number. The results were then compared to those of other searches to determine whether references cited in those public comments were already identified by other searches or need to be included. PDFs of the individual comments were not captured; instead a special "Public Comment" tag in HERO which specifies the corresponding round of public comments was used. Detailed results of the Public Comments submitted with the number of cited references for Tris is shown in Table D-5.

Table D-3. Summary of Gray Literature Sources and Search Results for Automated and Manual Searches for TTBP

Source ID[1]	Source Category	Website	Description	Search type	Search Result Counts[2]
6000	US States Government Resources	States website custom search engine, see Summary of State Sources tab	Custom search engine using States sites	Automated	7
1000	US EPA Resources	epa.gov	US Environmental Protection Agency	Automated	8
1150	US EPA Resources	http://aqsdr1.epa.gov/aqsweb/aqstmp/airdata/download_files.html#Annual	Office of Air: AQS	Manual	0
1101	US EPA Resources	https://chemview.epa.gov/chemview	ChemView (CDR/IUR)	Manual	5
1083	US EPA Resources	https://actor.epa.gov/cpcat/faces/search.xhtml	CPDat	Manual	1
1154	US EPA Resources	https://comptox.epa.gov/dashboard/	Chemistry Dashboard	Manual	1
1148	US EPA Resources	https://iaspub.epa.gov/oppthpv/existchem_hpv_prioritizations.report	EPA HPVIS	Manual	0
1001	US EPA Resources	https://www.epa.gov/ground-water-and-drinking-water/table-regulated-drinking-water-contaminants	Office of Water: EPA Clean Water Act	Manual	0
1008	US EPA Resources	https://www.waterqualitydata.us/portal/	Office of Water: STORET and WQX	Manual	1
1155	US EPA Resources	https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/persistent-bioaccumulative-and-toxic-pbt-chemicals-under	TSCA PBT Use Documents	Manual	1
2150	Other US Agency Resources	cdc.gov	Centers for Disease Control (includes NIOSH and ATSDR)	Automated	0
2511	Other US Agency Resources	energy.gov	Department of Energy	Automated	0
2300	Other US Agency Resources	fda.gov	US Food and Drug Administration	Automated	0
2050	Other US Agency Resources	niehs.nih.gov	NIH National Institute of Environmental Health and Safety	Automated	0
2400	Other US Agency Resources	osha.gov	OSHA Occupational Safety and Health Administration	Automated	0

Source ID[1]	Source Category	Website	Description	Search type	Search Result Counts[2]
2521	Other US Agency Resources	pnnl.gov	Pacific Northwest National Laboratory	Automated	0
2509	Other US Agency Resources	usgs.gov	US Geological Survey	Automated	5
2027	Other US Agency Resources	https://ntp.niehs.nih.gov/pubhealth/roc/index-1.html#C	NIH Report on Carcinogens	Manual	0
2414	Other US Agency Resources	https://www.osha.gov/opengov/healthsamples.html	OSHA Chemical Exposure Health Data	Manual (inclusive of all results; not limited to first 100)	0
2123	Other US Agency Resources	https://www2a.cdc.gov/hhe/search.asp	CDC NIOSH Health Hazard Evaluations	Manual and Automated (inclusive of all results; not limited to first 100)	0
2104	Other US Agency Resources	www.atsdr.cdc.gov/hac/pha/	CDC ATSDR Health Hazard Consultations	Manual and Automated (inclusive of all results; not limited to first 100)	0
3160	Other Resources	oecd.org	The Organisation for Economic Co-operation and Development (OECD)	Automated	4
5000	Other Resources	sustainableproduction.org	Lowell Center for Sustainable Production	Automated	0
5020	Other Resources	Infohouse.p2ric.org	Pollution Prevention Infohouse	Automated	3
3600	Other Resources	http://www.spin2000.net/spinmyphp/	Substances in Preparations in Nordic Countries (SPIN) Database	Manual	1
5027	Other Resources	Kirk Othmer Encyclopedia	Book	Manual	0
5028	Other Resources	Ashford's Dictionary of Industrial Chemicals, 2001	Book	Manual	0

Source ID[1]	Source Category	Website	Description	Search type	Search Result Counts[2]
5029	Other Resources	Hawley's Chemical Dictionary, 2016	Book	Manual	0
3425	International Resources	carexcanada.ca	Carex Canada	Automated	0
3520	International Resources	env.go.jp	Government of Japan: Ministry of the Environment	Automated	17
3050	International Resources	europa.eu	European Union	Automated	32
3057	International Resources	https://echa.europa.eu/information-on-chemicals/registered-substances	ECHA	Manual	1
3100	International Resources	iarc.fr	International Agency for Research on Cancer	Automated	0
3350	International Resources	nicnas.gov.au	Australian Government: Department of Health, National Industrial Chemicals; NICNAS	Automated	4
3250	International Resources	who.int	World Health Organization	Automated	0
3421	International Resources	https://www.canada.ca/en/health-canada/services/chemical-substances/fact-sheets/chemicals-glance.html#interest	Canada Chemicals Portal	Manual	0
3450	International Resources	http://limitvalue.ifa.dguv.de/	GESTIS Database	Manual	0
			Total Unique (Duplicates Removed)		91

[1]"Source ID" refers to an internal ID assigned to each source for tracking purposes.

[2] Search result counts represent totals after removal of duplicate records.

Table D-4. Gray Literature Search Strings

Chemical	Manual Search Terms	Google Search Terms (up to 128 characters)
2,4,6-Tris(tert-butyl) phenol	Search database by CAS or chemical name, or select from a list on the website	"732-26-3" OR "2,4,6-Tris(tert-butyl) phenol" OR "2,4,6-tri-tert-butylphenol" OR "Tri-tert-butylphenol"

Table D-5. Detailed Results of Public Comments Backwards Search for TTBP

Public Comment Title	Publisher	Comment ID	References Cited Count
Comment submitted by Christina Franz, Senior Director, Regulatory & Technical Affairs, American Chemistry Council (ACC)	American Chemistry Council (ACC)	EPA-HQ-OPPT-2016-0734-0007	10
Comment submitted by Derek D. Swick, Manager, American Petroleum Institute (API)	American Petroleum Institute (API)	EPA-HQ-OPPT-2016-0734-0006	0
Anonymous public comment	Anonymous	EPA-HQ-OPPT-2016-0734-0004	0
Comment submitted by Veena Singla, PhD, Associate Director, Science and Policy, Program on Reproductive Health and the Environment, University of California, San Francisco (UCSF) et al.	UCSF Program on Reproductive Health and the Environment, academics, scientists and clinicians	EPA-HQ-OPPT-2016-0734-0008	45
Comment submitted by Dianne C. Barton, Chair, National Tribal Toxics Council (NTTC)	National Tribal Toxics Council (NTTC)	EPA-HQ-OPPT-2016-0734-0014	18
Comment submitted by Elizabeth Hitchcock, Acting Director, Safer Chemicals Healthy Families (SCHF) et al.	Safer Chemicals Healthy Families (SCHF), Alaska Community Action on Toxics, Center for Environmental Health, Earthjustice, Environmental Health Strategy Center, Natural Resources Defense Council, Toxic-Free Future	EPA-HQ-OPPT-2016-0734-0013	21
Comment submitted by Jyotsna S. Jagai, Research Assistant Professor, University of Illinois, Chicago Chair, Environment Section, American Public Health Association et al.		EPA-HQ-OPPT-2016-0734-0011	6

Public Comment Title	Publisher	Comment ID	References Cited Count
Comment submitted by Leslie Riegle, Director of Environmental Policy, Aerospace Industries Association (AIA)	Aerospace Industries Association (AIA)	EPA-HQ-OPPT-2016-0734-0010	0
Comment submitted by Robert Stockman, Senior Attorney, Environmental Defense Fund (EDF)	Environmental Defense Fund (EDF)	EPA-HQ-OPPT-2016-0734-0012	8
Comment submitted by Craig Bernard, PhD, Vice President, Global Regulatory Affairs, Dorf Ketal Chemicals	Dorf Ketal Chemicals	EPA-HQ-OPPT-2016-0734-0015	0
Comment submitted by Ken Zarker, Section Manager, Hazardous Waste and Toxics Reduction Program, Washington State Department of Ecology	Washington State Department of Ecology	EPA-HQ-OPPT-2016-0734-0009	3
Comment submitted by Kevin M. Kransler, PhD, Regulatory Affairs Manager, SI Group	SI Group	EPA-HQ-OPPT-2016-0734-0020	0
TOTAL		12	111
Total Unique (Duplicates Removed)			**101**

D.1.3. Supplemental Search Strategy

Backward Search

To both supplement and test the database and gray literature searches, backward searches of frequently used sources were conducted. These sources consist of previous risk assessments, systematic reviews, and other assessments, generally conducted by EPA or other government agencies of the chemicals of interest and presented in Table D-7. The references that are cited within sections deemed relevant to this assessment were gathered into Endnote libraries for title abstract review.

Google Scholar Search

To further supplement and test the database searches, a Google Scholar search was conducted for each of the five PBT chemicals. The top 100 results returned by Google Scholar for each chemical were exported into Endnote libraries. These results were compared to the references identified in the database, backward, and gray literature searches to identify references not found by the previous searches. While Google Scholar results are expected to be primarily peer-reviewed rather than gray literature, the results were still compared to all searches.

D.1.4. Literature Search Results

The literature searches were conducted, and for PubMed, Web of Science, ToxLine, Backwards searches, and Google Scholar searches, the results were imported into one Endnote library per chemical. After the results were combined, duplicates were removed and TSCATS/NIH Reporter data, a subset of ToxLine, were moved into a separate folder. The resulting counts are presented Table D-6. Detailed results for the TTBP backwards search are presented in Table D-7.

Table D-6. Count of Peer-reviewed Literature Search Results by Search Type for TTBP

Chemical	PubMed	WoS	ToxLine	TSCATS/ NIH Reporter	Backwards	Google Scholar
246-Tris	24	82	20	5	71	80

Table D-7. Detailed Results of Backwards Search of Frequently Used Sources for TTBP

HEROID	Document title	Reference count
4182671	Canada Screening Assessment	43
4182739	EU Risk Assessment	28
4198468	NICNAS (2013)	1
	TOTAL	72
	Total Unique (Duplicates Removed)	**71**
	EndNote Library: Total Unique (Duplicates Removed)	**71**

D.2 Literature Screening Strategy

D.2.1. Development of the Literature Screening Approach

The steps involved in developing the title abstract screening approach are:

1. Define inclusion/exclusion criteria.
2. Conduct the pilot using 10 randomly selected studies for each chemical from both the peer-reviewed and gray literature that are screened by EPA experts.
3. Use the results of the pilot to refine inclusion/exclusion criteria.
4. Use the refined pilot to train screeners in applying the tags.

In these assessments, the results of the title/abstract literature screening will be used to develop the PECO statement. The overall workflow of the systematic review process including the literature screening is presented in Appendix F.

The PECO statement is included in Appendix D.3. Four tags were used at the title-abstract phase: Peer On Topic, Peer Off Topic, Gray On Topic, and Gray Off Topic and recorded on the HERO project pages. Title abstract screening was conducted in DRAGON[8]. A screenshot of the DRAGON form and all DRAGON tags is presented in Appendix H.

The inclusion/exclusion criteria for title/abstract and full text screening are included in Appendix G. During full text screening, studies were also screened for "Red Flag Criteria," which represent the "Unacceptable" criteria from the Data Evaluation criteria (U.S. EPA, 2018).

D.2.2. Literature Screening Pilot

[8] DRAGON is an online tool for systematic review developed by ICF that stores qualitative and quantitative data from literature to help scientists implement the elements of systematic review, including problem formulation, literature screening, risk of bias evaluation, and data integration.

A pilot with 100 results representative of the five chemicals and the peer, backwards, and gray literature search results was developed by EPA. Two exposure experts scored the pilot, and met with EPA to refine the criteria and application of the criteria.

Before screening, all screeners were required to meet a 90% accuracy in tagging the pilot screening studies. Screeners who met this level of proficiency were able to begin title abstract screening. Screeners who do not meet this level of proficiency, continued to train, using the studies screened by screeners who had passed the pilot as additional training studies. Documentation of all pilot tagging results was maintained in Excel spreadsheets for both the peer-reviewed and gray literature.

D.2.3. Literature Screening

Title abstract screening of the peer-reviewed and gray literature occurred in DRAGON, an online tool for systematic review. Results of the TTBP search were manually screened with one screener who has been trained via the pilot process. Additionally, a subject matter expert reviewed 10% of the references deemed to be On Topic and Off Topic as a quality assurance check to ensure that they have been categorized appropriately.

For gray literature, title/abstract and full text screening was done simultaneously, and tags for screening are included in Appendix H. For peer-reviewed literature, title/abstract and full text screening were done separately, and tags for each stage are included in Appendix H.2.

D.2.4. Prioritization

The database search strategy for TTBP returned approximately 125 results. The supplemental search for related chemicals returned approximately 7,800 results. Few of the results added by the related chemicals search are likely to be relevant to an exposure assessment of TTBP; therefore, the results from title abstract screening of the TTBP search results were used to prioritize the related chemicals search results using text analytics in DoCTER.

For prioritization, multiple text analytic algorithms can be used to find studies with titles and abstracts similar to seed studies previously identified as On Topic by EPA experts. DoCTER employs two main metrics, ensemble clustering and machine learning, including active machine learning. Supervised clustering using an ensemble approach uses multiple algorithms in Varghese et al. (2017) to prioritize references for review. The prioritization strategy is shown in Figure D-2 and presented in Varghese et al. (2017). These algorithms create a user-defined number of clusters based on similarities in the text of the title and abstract, and each algorithm is broadly-accepted in the text analytics scientific field, as described in Varghese et al. (2017). The clusters are populated by the algorithms that first convert the text in each title and abstract into a numerical matrix (using binary or 0s and 1s to represent the text) and then identifies similarities or similar numerical strings between each matrix representation of a title and abstract. Based on the similarities, the reference is assigned to a cluster. In the example, each of the algorithms was used to bin the studies into 10, 20, or 30 clusters, for a total of six different cluster analyses (six large circles in the figure). A random sample of studies identified as relevant serve as “tracer” or “seed” studies (pink circles in the figure). The tracer method

involves following these relevant studies and determining the clusters the majority occur in; these clusters are then deemed more likely to contain other (as-yet unidentified) relevant studies. Off topic references, or negative seeds, can be used to estimate performance of the tool using the metric of precision, but are not required for clustering.

To identify these high-priority clusters, the clusters containing a given fraction (75% in the example) of the relevant tracer studies are identified for each of the six analyses and termed "high concentration of tracer" clusters. All non-tracer studies in those high-concentration clusters can then be marked as "high priority" for further screening. This ensemble method is used to increase confidence in the selection of prioritized studies by mitigating uncertainty from each individual analysis. Additionally, studies in the "low priority" clusters can be further analyzed using machine learning algorithms that also use the "tracer" studies in conjunction with Off Topic references, or negative seeds, and assign a probability score to each of the remaining studies as likely to be On Topic.

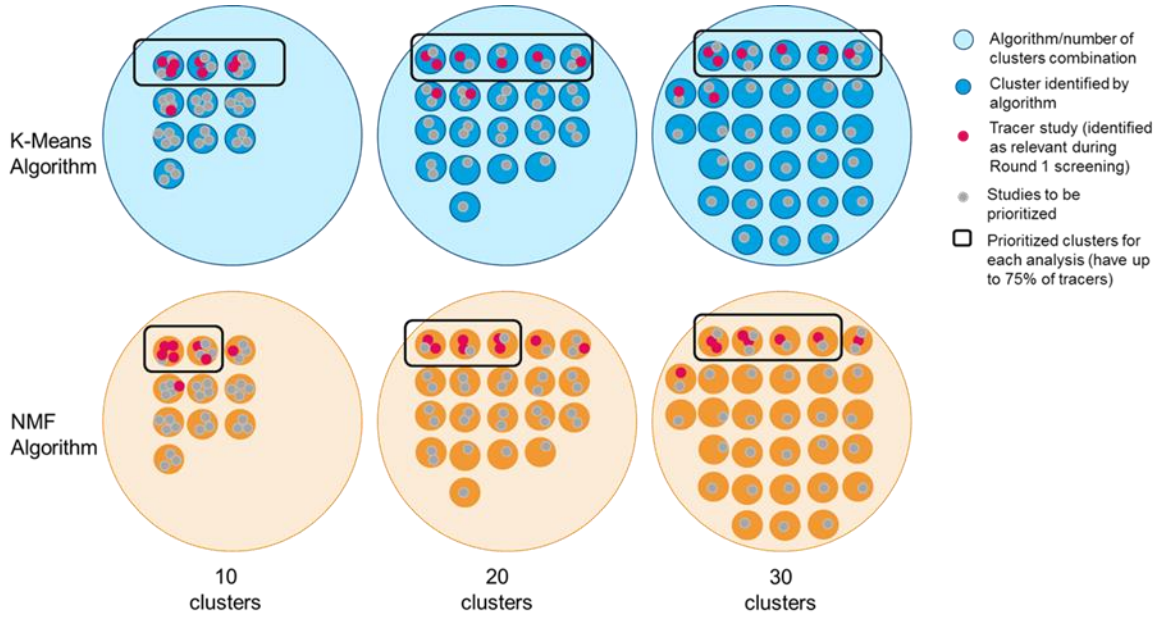

Figure D-2. Ensemble text analytics methods for prioritizing studies for screening

Any reference that was flagged as high priority by DoCTER was loaded into DRAGON for title abstract screening.

D.3 PECO Statement

Chemical	**2,4,6 TRIS**
PECO Element	**Evidence**
Population	**Human:** Workers and occupational non-users; general population; consumers and bystanders in residential settings; near-facility populations (includes industrial and commercial facilities manufacturing, processing, or using 2,4,6 TRIS); populations exposed from transfer from workplaces through take home exposures; populations in co-located residences or businesses; populations with subsistence diets; children; infants; pregnant women; lactating women; women of childbearing age; susceptible populations (life stages, preexisting conditions, genetic factors). No chemical-specific exclusions are suggested at present. **Ecological:** Aquatic organisms (edible and nonedible fish, aquatic invertebrates (daphnia), amphibians); terrestrial organisms (plants, soil invertebrates (worms), birds, mammals). No chemical specific exclusions are suggested at present.
Exposure	**Expected Exposure Sources, Pathways, Routes** Source: Industrial activities (manufacturing, processing, recycling, treatment, disposal of products); commercial and consumer uses of consumer products containing 2,4,6 TRIS and associated releases to air, soil, water, or wastes (wastewater/liquid wastes, solid wastes); historical use in pesticides and agricultural products Pathway: Waste streams (e.g., landfills, biosolids); outdoor air (fugitive/stack emissions); surface water/groundwater (transfer from outdoor air/soil); indoor air (transfer from outdoor air); soil/sediment; dust; contact with products; vapor intrusion from moist soil or aqueous solution; food (breastmilk, fish, meat, eggs, dairy, crops) Routes: Inhalation (indoor air); oral (dietary ingestion of food or breastmilk, incidental ingestion of contaminated soil and dust, hand-to-mouth contact, ingestion of suspended particles); dermal (contact with dust, soil, consumer products containing 2,4,6 TRIS or other secondary vectors) **Expected Lesser Exposure Sources, Pathways, Routes** • Source: impurity in 2,6 di-tert-butylphenol • Pathway: outdoor air; drinking water • Routes: inhalation of outdoor air; ingestion of drinking water
Comparator (Scenario)	**Human:** Consider media-specific background exposure scenarios and use/source specific exposure scenarios as well as which receptors are and are not reasonably exposed across the projected exposure scenarios. **Ecological:** Consider media-specific background exposure scenarios and use/source specific exposure scenarios as well as which receptors are and are not reasonably exposed across the projected exposure scenarios.
Outcomes for Exposure Concentration or Dose	**Human:** Acute, subchronic, and/or chronic external dose estimates (mg/kg/day); acute, subchronic, and/or chronic internal dose based on biomonitoring and reverse dosimetry (mg/kg/day); acute, subchronic, and/or chronic air, soil, dust, and water concentration estimates (mg/m^3 or mg/L). **Ecological:** A wide range of ecological receptors will be considered using surface water, sediment, soil, and air concentrations. Targeted use of wildlife biomonitoring data will also be explored.

D.4 PRISMA Diagram

The PRISMA Diagram for TTBP, including literature counts from search, screening and included phases from all sources, is presented in Figure D-3. A subset of studies that passed the screening phase were not extracted or evaluated due to the ready availability of the full text and supplemental information. Due to time constraints, studies that did not include data in text or tables, and studies that had fewer than 10 observations were not extracted or evaluated.

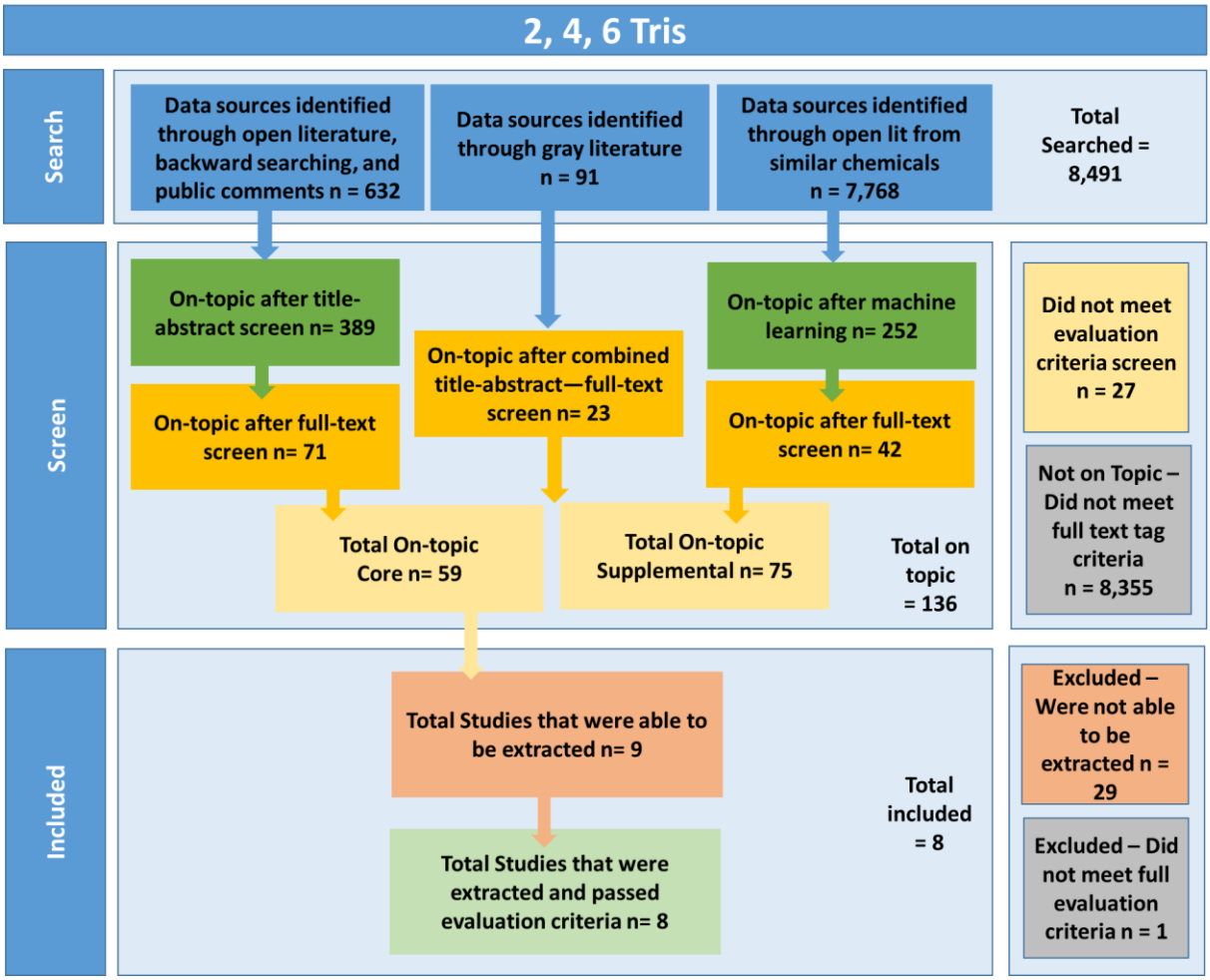

Figure D-3. PRISMA Diagram for TTBP

D.5 Data Evaluation Criteria

Core exposure data includes the following exposure data types:

- Environmental monitoring
- Biomonitoring
- Database Sources
- Completed Assessments
- Modeling

Assessors evaluated the extracted core exposure data for evaluation criteria specific to the data type. The data evaluation criteria are included in (U.S. EPA, 2018).

D.6 Data Extraction Fields

Core exposure data, including monitoring data and modeled estimates of concentration or dose, was extracted in DRAGON. The data extraction fields are included in Appendix I.

Appendix E. Supplemental Document for Pentachlorothiophenol (PCTP)

E.1 Literature Search Strategy

This document describes the literature search strategy to support the exposure assessments for five persistent, bioaccumulative, and toxic (PBT) chemicals. The intent of the search is to assess the likely exposure of the general population, consumers, occupational populations, potentially exposed or susceptible subpopulations, and the environment to the conditions of use of PBT chemicals based on the criteria outlined in the Toxic Substances Control Act (TSCA) section 6(h) (OLRC, 2016).The conditions of use are defined as the circumstances under which a chemical substance is intended, known or reasonably foreseen to be manufactured, processed, distributed in commerce, used or disposed of.

Data sources in the peer-reviewed (open) and gray literature were considered as shown in Figure E-1. In addition to the primary searches of the peer-reviewed literature in Web of Science, PubMed, and Toxline, there were additional supplemental searches that were used to complement and/or evaluate the primary peer-reviewed search strategy. These were: backward searches of frequently used sources[9], a Google Scholar search of the top 100 results by chemical, and public comments and associated references cited in those comments submitted to the dockets by mid-January 2018.

An additional search of the gray literature was conducted as described in the Gray Literature Search Strategy section and was based off the protocol developed for the Systematic Review of the "First 10" chemicals under TSCA.

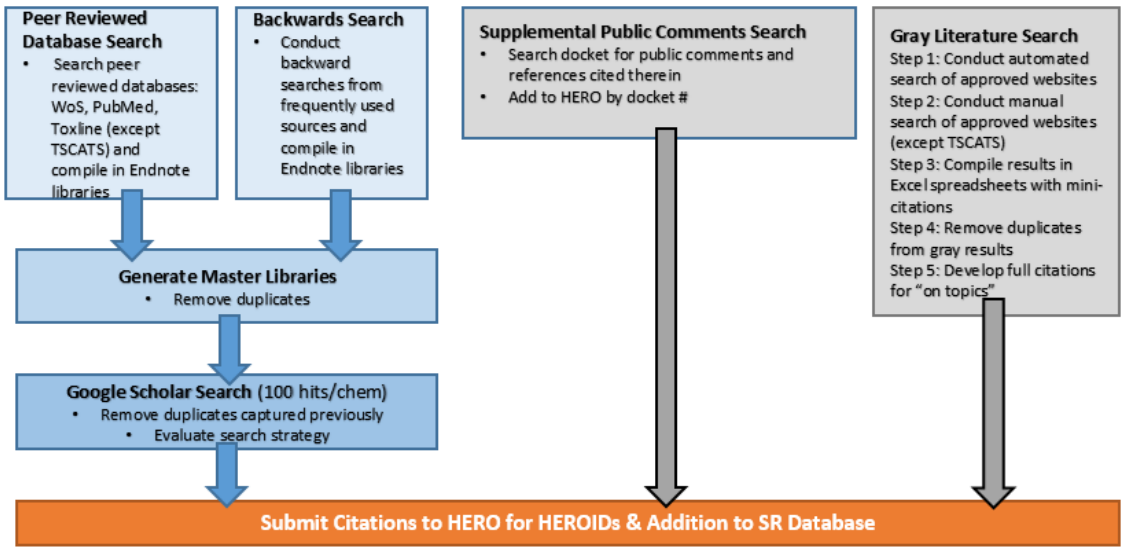

Figure E-1. Literature Search Strategy Workflow

[9] Frequently used sources are sources expected to be of high quality, such as assessments conducted by other government agencies.

The results of the literature searches were compiled into Endnote libraries (database searches) and Excel spreadsheets (gray literature.)

E.1.1. Database (Peer-reviewed) Search Strategies

The literature searches for the five PBT chemicals were designed to be as broad as possible, searching only for the chemical name and synonyms, but not including any limiters such as terms describing expected uses or dates. For PCTP, no chemical category name was included in the search. The search strategy for PCTP is presented in**Error! Reference source not found.** Table E-1.

Table E-1. PCTP Open Literature Search Strategy

Date of Search: December 15, 2017

Database	Search Strategy
PubMed	(133-49-3[rn] OR PCTP[tiab] OR Pentachlorobenzenethiol[tiab] OR Pentachlorothiophenol[nm] OR Pentachlorothiophenol[tiab]) AND (English[lang])
Web of Science	("2,3,4,5,6-Pentachlorobenzene-1-thiol" OR "Benzenethiol, 2,3,4,5,6-pentachloro-" OR "Benzenethiol, pentachloro-" OR AI3-23118 OR BRN-1108638 OR Pentachloro-benzenethiol OR Pentachlorthiofenol OR RPA-6 OR 133-49-3 OR PCTP OR Pentachlorobenzenethiol OR Pentachlorothiophenol) AND English
Toxline	133-49-3
	Include Synonyms Exclude PubMed Records from TSCATS and NIH Reporter Database removed in EndNote

E.1.2. Gray Literature Search Strategies

The five PBT chemicals searched were targeted to relevant sources and the approach was adapted from the first 10 chemicals to optimize efficiency by eliminating redundancy. Gray literature screening criteria excluded peer-reviewed journal articles that were expected to be caught in the database searches. Mini citations, containing author, title, year, were generated as a preliminary step to aid in identification and removal of duplicate records prior to tagging. Automated searches via the Google search API were employed where possible in favor of manual search sources. A summary of sources and search result counts after the removal of duplicates is presented in Table E-2. All results were reviewed from each source. The search strings used for manual and automated searches are found in **Error! Reference source not found.**.

EPA is aware of information submitted by companies as part of TSCA requirements under sections 4, 8(d), 8(e) or as part of an FYI (“TSCATS Submissions data”). This information was not considered as part of the literature search and screening strategy. EPA plans to consider this information in the future.

Public comments submitted to the Docket (by Docket Number) were captured and HERO records were created including the title, author and docket number. The results were then compared to those of other searches to determine whether references cited in those public comments were already identified by other searches or need to be included. PDFs of the individual comments were not captured; instead a special “Public Comment” tag in HERO which specifies the corresponding round of public comments was used. Detailed results of the Public Comments submitted with the number of cited references for PCTP is shown in Table E-4

Table E-2. Summary of Gray Literature Sources and Search Results for Automated and Manual Searches for PCTP

Source ID[1]	Source Category	Website	Description	Search type	Search Result Counts[2]
6000	US States Government Resources	States website custom search engine, see Summary of State Sources tab	Custom search engine using States sites	Automated	4
1000	US EPA Resources	epa.gov	US Environmental Protection Agency	Automated	46
1150	US EPA Resources	http://aqsdr1.epa.gov/aqsweb/aqstmp/airdata/download_files.html#Annual	Office of Air: AQS	Manual	0
1101	US EPA Resources	https://chemview.epa.gov/chemview	ChemView (CDR/IUR)	Manual	0
1083	US EPA Resources	https://actor.epa.gov/cpcat/faces/search.xhtml	CPDat	Manual	1
1154	US EPA Resources	https://comptox.epa.gov/dashboard/	Chemistry Dashboard	Manual	1
1148	US EPA Resources	https://iaspub.epa.gov/oppthpv/existchem_hpv_prioritizations.report	EPA HPVIS	Manual	0
1001	US EPA Resources	https://www.epa.gov/ground-water-and-drinking-water/table-regulated-drinking-water-contaminants	Office of Water: EPA Clean Water Act	Manual	0
1008	US EPA Resources	https://www.waterqualitydata.us/portal/	Office of Water: STORET and WQX	Manual	0
1155	US EPA Resources	https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/persistent-bioaccumulative-and-toxic-pbt-chemicals-under	TSCA PBT Use Documents	Manual	1
2150	Other US Agency Resources	cdc.gov	Centers for Disease Control (includes NIOSH and ATSDR)	Automated	6
2511	Other US Agency Resources	energy.gov	Department of Energy	Automated	7
2300	Other US Agency Resources	fda.gov	US Food and Drug Administration	Automated	1
2050	Other US Agency Resources	niehs.nih.gov	NIH National Institute of Environmental Health and Safety	Automated	1

Source ID[1]	Source Category	Website	Description	Search type	Search Result Counts[2]
2400	Other US Agency Resources	osha.gov	OSHA Occupational Safety and Health Administration	Automated	0
2521	Other US Agency Resources	pnnl.gov	Pacific Northwest National Laboratory	Automated	0
2509	Other US Agency Resources	usgs.gov	US Geological Survey	Automated	6
2027	Other US Agency Resources	https://ntp.niehs.nih.gov/pubhealth/roc/index-1.html#C	NIH Report on Carcinogens	Manual	0
2414	Other US Agency Resources	https://www.osha.gov/opengov/healthsamples.html	OSHA Chemical Exposure Health Data	Manual (inclusive of all results; not limited to first 100)	0
2123	Other US Agency Resources	https://www2a.cdc.gov/hhe/search.asp	CDC NIOSH Health Hazard Evaluations	Manual and Automated (inclusive of all results; not limited to first 100)	0
2104	Other US Agency Resources	www.atsdr.cdc.gov/hac/pha/	CDC ATSDR Health Hazard Consultations	Manual and Automated (inclusive of all results; not limited to first 100)	0
3160	Other Resources	oecd.org	The Organisation for Economic Co-operation and Development (OECD)	Automated	2
5000	Other Resources	sustainableproduction.org	Lowell Center for Sustainable Production	Automated	0
5020	Other Resources	Infohouse.p2ric.org	Pollution Prevention Infohouse	Automated	0
3600	Other Resources	http://www.spin2000.net/spinmyphp/	Substances in Preparations in Nordic Countries (SPIN) Database	Manual	1
5027	Other Resources	Kirk Othmer Encyclopedia	Book	Manual	0
5028	Other Resources	Ashford's Dictionary of Industrial Chemicals, 2001	Book	Manual	1
5029	Other Resources	Hawley's Chemical Dictionary, 2016	Book	Manual	0
3425	International Resources	carexcanada.ca	Carex Canada	Automated	0

Source ID[1]	Source Category	Website	Description	Search type	Search Result Counts[2]
3520	International Resources	env.go.jp	Government of Japan: Ministry of the Environment	Automated	4
3050	International Resources	europa.eu	European Union	Automated	23
3057	International Resources	https://echa.europa.eu/information-on-chemicals/registered-substances	ECHA	Manual	0
3100	International Resources	iarc.fr	International Agency for Research on Cancer	Automated	0
3350	International Resources	nicnas.gov.au	Australian Government: Department of Health, National Industrial Chemicals; NICNAS	Automated	0
3250	International Resources	who.int	World Health Organization	Automated	1
3421	International Resources	https://www.canada.ca/en/health-canada/services/chemical-substances/fact-sheets/chemicals-glance.html#interest	Canada Chemicals Portal	Manual	0
3450	International Resources	http://limitvalue.ifa.dguv.de/	GESTIS Database	Manual	0
			Total Unique (Duplicates Removed)		106

[1]"Source ID" refers to an internal ID assigned to each source for tracking purposes.
[2] Search result counts represent totals after removal of duplicate records.

Table E-3. Gray Literature Search Strings

Chemical	Manual Search Terms	Google Search Terms (up to 128 characters)
Pentachlorothiophenol (PCTP)	Search database by CAS or chemical name, or select from a list on the website	"133-49-3" OR "Pentachlorothiophenol" OR "PCTP"

Table E-4. Detailed Results from Public Comments Backwards Search for PCTP

Public Comment Title	Publisher	Comment ID	References Cited Count
Comment submitted by Christina Franz, Senior Director, Regulatory & Technical Affairs, American Chemistry Council (ACC)	American Chemistry Council (ACC)	EPA-HQ-OPPT-2016-0739-0006	10
Comment submitted by Sarah E. Amick, Vice President EHS&S and Senior Counsel, Rubber Manufacturers Association (RMA)	Rubber Manufacturers Association (RMA)	EPA-HQ-OPPT-2016-0739-0002	0
Comment submitted by Veena Singla, PhD, Associate Director, Science and Policy, Program on Reproductive Health and the Environment, University of California, San Francisco (UCSF) et al.	UCSF Program on Reproductive Health and the Environment, academics, scientists and clinicians	EPA-HQ-OPPT-2016-0739-0007	45
Comment submitted by Jyotsna S. Jagai, PhD, Research Assistant Professor, University of Illinois, Chicago Chair, Environment Section, American Public Health Association		EPA-HQ-OPPT-2016-0739-0013	6
Comment submitted by Robert Stockman, Senior Attorney on behalf of Environmental Defense Fund (EDF)	Environmental Defense Fund (EDF)	EPA-HQ-OPPT-2016-0739-0009	8
Comment submitted by Elizabeth Hitchcock, Acting Director, Safer Chemicals Healthy Families (SCHF) et al.	Safer Chemicals Healthy Families (SCHF), Alaska Community Action on Toxics, Center for Environmental Health, Earthjustice, Environmental Health Strategy Center, Natural Resources Defense Council, Toxic-Free Future	EPA-HQ-OPPT-2016-0739-0010	19
Comment submitted by Dianne C. Barton, Chair, National Tribal Toxics Council (NTTC)	National Tribal Toxics Council (NTTC)	EPA-HQ-OPPT-2016-0739-0011	18
Comment submitted by Dr. Alan Hocknell, Senior Vice President, Research & Development, Callaway Golf Company	Callaway Golf Company	EPA-HQ-OPPT-2016-0739-0015	0
TOTAL		8	106
Total Unique (Duplicates Removed)			**97**

E.1.3. Supplemental Search Strategy

Backward Search

To both supplement and test the database and gray literature searches, backward searches of frequently used sources were conducted. Candidate sources consist of previous risk assessments, systematic reviews, and other assessments, generally conducted by EPA or other government agencies of the chemicals of interest, although no frequently used sources were identified for PCTP.

Google Scholar Search

To further supplement and test the database searches, a Google Scholar search was conducted for each of the five PBT chemicals. The top 100 results returned by Google Scholar for each chemical were exported into Endnote libraries. These results were compared to the references identified in the database, backward, and gray literature searches to identify references not found by the previous searches. While Google Scholar results are expected to be primarily peer-reviewed rather than gray literature, the results were still compared to all searches.

E.1.4. Literature Search Results

The literature searches were conducted, and for PubMed, Web of Science, ToxLine, Backwards searches, and Google Scholar searches, the results were imported into one Endnote library per chemical. After the results were combined, duplicates were removed and TSCATS/NIH Reporter data, a subset of ToxLine, were moved into a separate folder. The resulting counts are presented in**Error! Reference source not found.** Table E-5. Backwards searching was not conducted for PCTP.

Table E-5. Count of Peer-reviewed Literature Search Results by Search Type for PCTP

Chemical	PubMed	WoS	ToxLine	TSCATS/ NIH Reporter	Backwards	Google Scholar
PCTP	92	47	24	0	0	81

E.2 Literature Screening Strategy

E.2.1. Development of the Literature Screening Approach

The steps involved in developing the title abstract screening approach are:

1. Define inclusion/exclusion criteria.
2. Conduct the pilot using 10 randomly selected studies for each chemical from both the peer-reviewed and gray literature that are screened by EPA experts.
3. Use the results of the pilot to refine inclusion/exclusion criteria.
4. Use the refined pilot to train screeners in applying the tags.

The overall workflow of the systematic review process including the literature screening is presented in Appendix F.

In these assessments, the results of the title/abstract literature screening will be used to develop the PECO statement. The PECO statement is included in Appendix E.3. Four tags were used at the title-abstract phase: Peer On Topic, Peer Off Topic, Gray On Topic, and Gray Off Topic and recorded on the HERO project pages. Title abstract screening was conducted in DRAGON[10]. A screenshot of the DRAGON form and all DRAGON tags is presented in Appendix H.

The inclusion/exclusion criteria for title/abstract and full text screening are included in g. During full text screening, studies were also screened for "Red Flag Criteria," which represent the "Unacceptable" criteria from the Data Evaluation criteria (U.S. EPA, 2018).

E.2.2. Literature Screening Pilot

A pilot with 100 results representative of the five chemicals and the peer, backwards, and gray literature search results was developed by EPA. Two exposure experts scored the pilot, and met with EPA to refine the criteria and application of the criteria.

Before screening, all screeners were required to meet a 90% accuracy in tagging the pilot screening studies. Screeners who met this level of proficiency were able to begin title abstract screening. Screeners who do not meet this level of proficiency, continued to train, using the studies screened by screeners who had passed the pilot as additional training studies. Documentation of all pilot tagging results was maintained in Excel spreadsheets for both the peer-reviewed and gray literature.

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Title abstract screening of the peer-reviewed and gray literature occurred in DRAGON, an online tool for systematic review. Results of the PCTP search were manually screened with one screener who has been trained via the pilot process. Additionally, a subject matter expert reviewed 10% of the references deemed to be On Topic and Off Topic as a quality assurance check to ensure that they have been categorized appropriately.

For gray literature, title/abstract and full text screening was done simultaneously, and tags for screening are included in Appendix G For peer-reviewed literature, title/abstract and full text screening were done separately, and tags for each stage are included in Appendix H.2.

[10] DRAGON is an online tool for systematic review developed by ICF that stores qualitative and quantitative data from literature to help scientists implement the elements of systematic review, including problem formulation, literature screening, risk of bias evaluation, and data integration.

E.3 PECO Statement

Chemical	PCTP
PECO Element	**Evidence**
Population	**Human:** Workers and occupational non-users; general population; consumers and bystanders in residential settings; near-facility populations (includes industrial and commercial facilities manufacturing, processing, or using PCTP); populations living at or near hazardous waste, industrial or chemical waste disposal sites; populations with subsistence diets; children; infants; pregnant women; lactating women; women of childbearing age; susceptible populations (life stages, preexisting conditions, genetic factors). No chemical-specific exclusions are suggested at present. **Ecological:** Aquatic organisms (edible and nonedible fish, aquatic invertebrates (daphnia), amphibians); terrestrial organisms (plants, soil invertebrates (worms), birds, mammals). No chemical specific exclusions are suggested at present.
Exposure	**Expected Exposure Sources, Pathways, Routes** Source: Industrial activities (manufacturing, processing, recycling, treatment, disposal of products); commercial and consumer uses of consumer products containing PCTP and associated releases to air, water, or wastes (wastewater/liquid wastes, solid wastes); use as a soil fungicide, herbicide, and slime prevention in industrial waters; metabolite of hexachlorobenzene; metabolite and degradation product of pentachloronitrobenzene Pathway: Waste streams (e.g., landfills, biosolids); outdoor air (fugitive/stack emissions); drinking water; surface water/groundwater (transfer from outdoor air/soil); indoor air (transfer from outdoor air); soil/sediment; dust; contact with products; liquid contact; vapor intrusion; food (breastmilk, fish, meat, eggs, dairy); media-specific background and source attribution to be considered. Routes: Inhalation (indoor and ambient air); oral (dietary ingestion of food or breastmilk, incidental ingestion of contaminated soil and dust, hand-to-mouth contact, ingestion of drinking water, ingestion of suspended particles, mouthing of consumer articles); dermal (contact with dust, soil, consumer products containing PCTP or other secondary vectors)
Comparator (Scenario)	**Human:** Consider media-specific background exposure scenarios and use/source specific exposure scenarios as well as which receptors are and are not reasonably exposed across the projected exposure scenarios. **Ecological:** Consider media-specific background exposure scenarios and use/source specific exposure scenarios as well as which receptors are and are not reasonably exposed across the projected exposure scenarios.
Outcomes for Exposure Concentration or Dose	**Human:** Acute, subchronic, and/or chronic external dose estimates (mg/kg/day); acute, subchronic, and/or chronic internal dose based on biomonitoring and reverse dosimetry (mg/kg/day); acute, subchronic, and/or chronic air, soil, dust, and water concentration estimates (mg/m^3 or mg/L). **Ecological:** A wide range of ecological receptors will be considered using surface water, sediment, soil, and air concentrations. Targeted use of wildlife biomonitoring data will also be explored.

E.4 PRISMA Diagram

The PRISMA Diagram for PCTP, including literature counts from search, screening and included phases from all sources, is presented in**Error! Reference source not found.** Figure E-2. A subset of studies that passed the screening phase were not extracted or evaluated due to the ready availability of the full text and supplemental information. Due to time constraints, studies that did not include data in text or tables, and studies that had fewer than 10 observations were not extracted or evaluated.

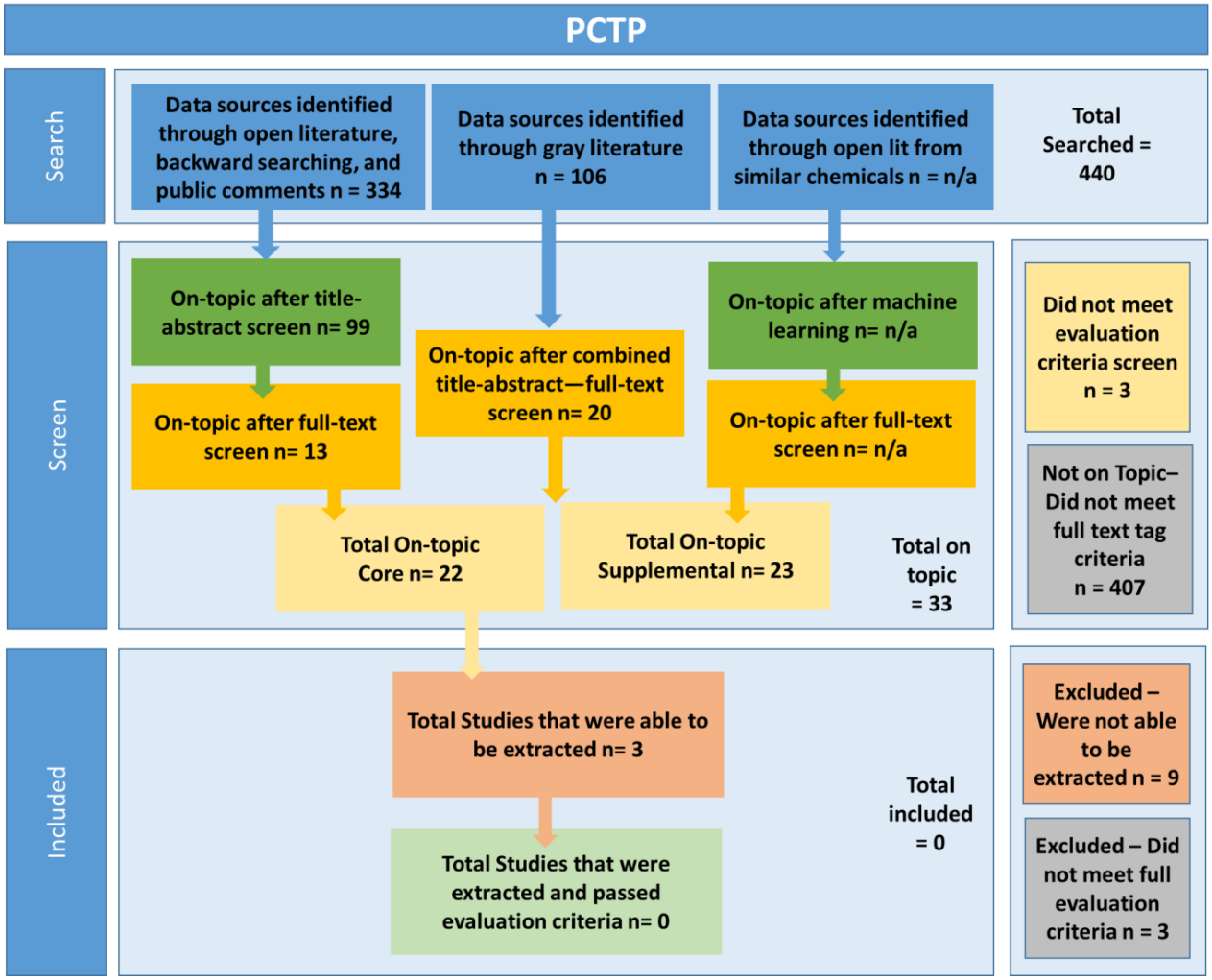


Figure E-2. PRISMA Diagram for PCTP

E.5 Data Evaluation Criteria

Core exposure data includes the following exposure data types:

- Environmental monitoring
- Biomonitoring
- Database Sources

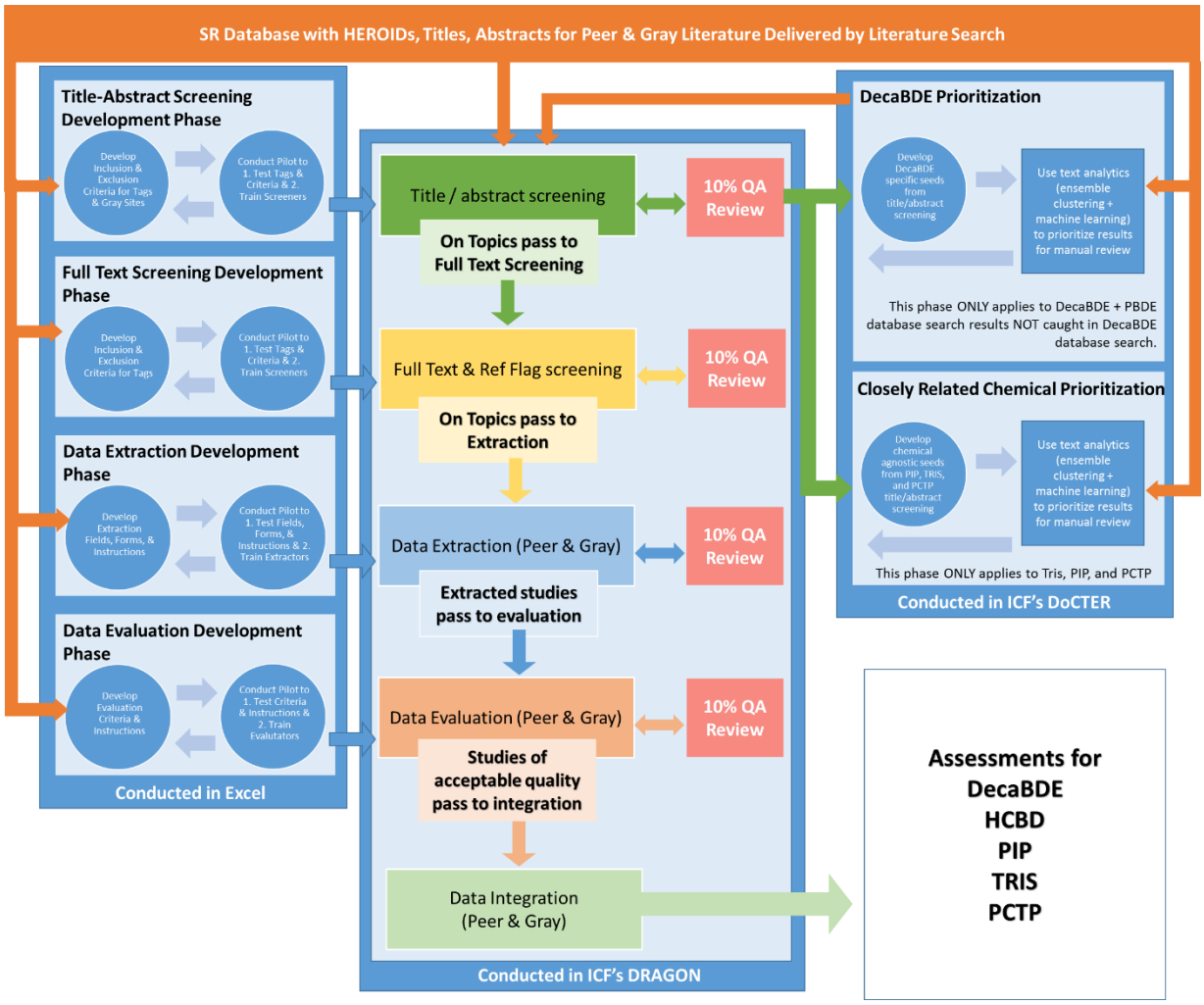
- Completed Assessments
- Modeling

Assessors evaluated the extracted core exposure data for evaluation criteria specific to the data type. The data evaluation criteria are included in (U.S. EPA, 2018).

E.6 Data Extraction Fields

Core exposure data, including monitoring data and modeled estimates of concentration or dose, was extracted in DRAGON. The data extraction fields are included in Appendix I.

Appendix F. Overall Workflow for Systematic Review



Appendix G. Inclusion and Exclusion Criteria for Title/Abstract and Full Text Screening

For title/abstract screening, references were classified as either On Topic or Off Topic with regards to the criteria presented in Table G-1. Although multiple tags were not introduced at this stage, the inclusion and exclusion criteria were organized around subject matter areas for purposed of presentation. Full text PDFs will be sought for references that are determined to be On Topic at the title/abstract stage via HERO's "Fetch" feature, Endnote "Find Full Text", and Reprintz. Only references determined to be On Topic with a full text PDF available will be considered for full text screening.

Table G-1. Inclusion/Exclusion Criteria for PBT 5

Tier 2 Screening Category	Exposure Category	Inclusion Criteria	Exclusion Criteria	Example Keywords
Core	Ecological Exposure	Covers ecological exposure, including exposure to aquatic and terrestrial flora and fauna and media where these organisms live (water, soil, sediment)	Toxicity studies that describe hazards to ecological organisms.	Concentration with associated units, e.g., mg/m3, mg/g, etc., mammal, avian, fish, aquatic
		Covers is measurements were taken, even if data not reported		
		Covers any supplemental data on exposure sources, pathways, routes, or populations that could be used to construct an ecological exposure scenario (uses, releases, outdoor fate).		
Core	General Population Exposure	Covers exposure to the general population due to concentrations in outdoor and indoor environmental media.	Method validation studies involving exposures to laboratory-produced chemical or chemical mixture in a lab setting, rather than environmentally-derived samples	general population exposure/dose with associated units, e.g., mg/kg, m/kg/day, etc., blood, urine, tissue, releases, background levels, ambient/outdoor air, deposition, surface water, drinking water, ground water, soil, dust, sediment, sludge, disposal, life cycle
		Covers exposure to the general population due to concentrations in other edible species and food through dietary uptake.	Toxicity studies that describe hazards to animals (usually terrestrial mammals) used to assess toxicity to humans	

Tier 2 Screening Category	Exposure Category	Inclusion Criteria	Exclusion Criteria	Example Keywords
		Covers estimated doses to humans through biomonitoring and/or PBPK or quasi-PBPK modeling, Toxicokinetics studies using environmentally relevant exposures.	Toxicokinetic studies that describe ADME using spiked doses	
		Covers any supplemental data on exposure sources, pathways, routes, or populations that could be used to construct a general population exposure scenario (uses, releases, outdoor fate).		
Core	Consumer Exposure	Covers exposure to consumers who use a product or article containing the chemical	Method validation studies involving exposures to laboratory-produced chemical, rather than environmentally-derived samples	consumer product exposure/dose with associated units, e.g., mg/kg, m/kg/day, etc., indoor/residential, product, article, aerosol, dust, indoor air, hand-to-mouth, surface, shower, dermal loading, blood, urine, tissue
		Covers exposure to consumers who are close proximity of a product or article present in their living space	Unverifiable or anecdotal reports of consumer use. For example, secondary sources that do not cite a source.	
		Covers any supplemental data on exposure sources, pathways, routes, or populations that could be used to construct a consumer exposure scenario (uses, consumer surveys on use patterns, releases/emissions from experimental data, indoor fate).	Toxicity studies that describe hazards to animals (usually terrestrial mammals) used to assess toxicity to humans	
			Toxicokinetic studies that describe ADME using spiked doses	
Core	Potentially exposed and susceptible subpopulations	Covers exposure for a potentially exposed and susceptible subpopulation exposed at a higher level than the general population [Include above]		susceptible/sensitive subpopulation, infants, children, pregnancy, senior, aged, elderly, older women, men, gender, immunocompromised, diseased population, preexisting

Tier 2 Screening Category	Exposure Category	Inclusion Criteria	Exclusion Criteria	Example Keywords
				disease, genetics, socioeconomic status, race
				highly-exposed sub population, near-facility population, higher-than-average exposure, above background, populations near manufacturing facilities
Supplemental - Engineering	Process Information	Studies pertaining to chemical processes containing information on life cycle, production volume (including HPV status), descriptions of processes, and manufacturing sites		Life cycle, production volume, use volume, import, process description, process flow diagram, product concentration, sites, manufacture, process, release, emission, industry, facility
Supplemental - Engineering	Occupational exposure	Occupational exposure studies that contain or may contain information on breathing zone (personal sample) measurements of occupational exposures to the chemical(s) of interest, measured as time-weighted averages (TWAs), dermal exposure estimates (skin loading), and/or biological monitoring as part of occupational surveillance.	Mentions toxicity-based exposure regulatory limits only but does not contain exposure values/estimates;	Worker, worker activities, worker exposure, occupational exposure, inhalation, dermal, personal sample, time-weighted average, breathing zone, PPE, personal protective equipment, engineering controls, exposure reduction, ventilation
		Covers any supplemental data on exposure sources, pathways, routes, or populations that could be used to construct an occupational exposure scenario (uses, occupational surveys, process description, process-flow diagram, emissions, indoor fate). See below	Toxicity studies that describe hazards to animals (usually terrestrial mammals) used to assess toxicity to humans	
		Description of worker activities with exposure potential during the manufacture, processing, or use of the chemical(s) of interest in each industrial/commercial life cycle stage.	Toxicokinetic studies that describe ADME using spiked doses	

Tier 2 Screening Category	Exposure Category	Inclusion Criteria	Exclusion Criteria	Example Keywords
		Physical form of the chemical(s) of interest for each exposure activity (e.g., liquid, vapor, mist) and activity.		
		For solids, bulk and dust particle size characterization data.		
		Information on short-term exposures, or peak exposures in each occupational life cycle stage (or in a workplace scenario like an occupational life cycle stage).		
Supplemental - Engineering	Occupational Exposure Modeling	Worker exposure duration for specific tasks (hr/day)		
		Exposure frequency for specific tasks (days/yr).		
		Number of workers who potentially handle or have exposure to the chemical(s) of interest in each occupational life cycle stage.		
		Personal protective equipment (PPE) types employed by the industries within scope.		
		Engineering controls employed to reduce occupational exposures in each occupational life cycle stage (or in a workplace scenario similar to the life cycle stage of interest), and associated data or estimates of exposure reductions.		
Supplemental - Engineering	Environmental Releases	Studies pertaining to releases from industrial facilities that manufacture, process, use, or dispose the chemical substance across the life-cycle of the chemical.		Release, emission, release rate, release frequency, point source, area source, , landfill, incineration, POTW, WWTP, on-site treatment, sewage or

Tier 2 Screening Category	Exposure Category	Inclusion Criteria	Exclusion Criteria	Example Keywords
		The total annual U.S. volume (lb/yr) or kg/yr) of the chemical(s) of interest manufactured, imported, processed, and used		wastewater treatment, disposal, pretreatment program, recycling, sludge, effluent, process diagram, process flow, loss fraction, emission rate, flux
		The share of total annual manufacturing and import volume that is processed or used in each life cycle step.		
		Description of processes, equipment, unit operations, and material flows and frequencies of the chemical(s) of interest during each industrial/ commercial life cycle step.		
		Number of sites that manufacture, process, or use the chemical(s) of interest for each industrial/ commercial life cycle step and site locations.		
		Description of sources of potential environmental releases, including cleaning of residues from process equipment and transport containers, involved during the manufacture, processing, or use of the chemical(s) of interest in each life cycle stage.		
		Estimated mass of the chemical(s) of interest released from industrial and commercial sites to each environmental medium (air, water, land) and treatment and disposal methods (POTW, incineration, landfill), including releases per site and aggregated over all sites (annual release rates, daily release rates)		
		Release or emission factors, loss fractions.		

Tier 2 Screening Category	Exposure Category	Inclusion Criteria	Exclusion Criteria	Example Keywords
		Number of release days per year for industrial process of interest.		
		Waste treatment methods and pollution control devices employed by the industries within scope and associated data on release/emission reductions.		
Supplemental - Fate	Fate & Transport	Any fate information that could be used to inform an exposure scenario. Studies that characterize transport and transformation in the environment or through organisms, including if the chemical of interest is a metabolite	Secondary physical-chemical property information for chemical substances	KOA, KOW, KAW, KOC, Kd, partitioning coefficient, fugacity, flux, groundwater, migration, sediment, leach, soil, sorb, sorption, adsorption, dust, particles, aerosol, volatility, solubility;
		Primary physical-chemical property information for chemical substances	Studies that are solely for the purpose of quantifying a fate parameter above, but are laboratory experiments using laboratory-derived chemicals or laboratory simulations, and do not put the results in context of environmentally relevant conditions	Persistence, half-life, hydrolysis, photolysis, photostability, biodegradation, aerobic, anaerobic, metabolism, reduction, degradation, transformation;
		Any fate information that could be used to inform an exposure scenario.	Laboratory experiments using environmental sample under non-natural conditions or added substrates, not naturally occurring in environment Test systems, laboratory experiments, or demonstrations where conditions are clearly not	BCF, BAF, BSAF, trophic magnification, biomagnification, bioaccumulation, bioconcentration, biota sediment accumulation factor, biotransfer
		Studies that characterize transport and transformation in the environment or through organisms.		

Tier 2 Screening Category	Exposure Category	Inclusion Criteria	Exclusion Criteria	Example Keywords
		The types of data for how chemicals are transported or transformed in and through environmental media are listed below: abiotic reduction rates or half-lives, abiotic dehalogentation, aerobic biodegradation or half-lives, anaerobic biodegradation rates or half-lives, direct and indirect aqueous photolysis, direct and indirect atmospheric photolysis or half-lives, bioconcentration factors and bioaccumulation factors, hydrolysis rates, or half-lives, volatilization rates, sorption rates to organic matter in outdoor environments, diffusion and sorption rates and sink information in indoor environments (material-air partition coefficient, diffusion-coefficient, mass-transfer), source degradation through abrasion, direct-transfer of dust to surfaces, abiotic transformation, aerobic biotransformation, atmospheric deposition, atmospheric flux, biomagnification and trophic magnification, coagulation, desorption, suspension and resuspensions, incineration removal information, and wastewater treatment removal information.	relevant to naturally-occurring conditions	
		Physical Chemical Properties		
Supplemental - Other	Use	Contains information related to uses described in EPA's "Preliminary information on Use" Documents. Screeners should read these documents prior to screening. Contains information about potential use scenarios, even if not chemical specific.	Anecdotal information (without a reference) about a chemical's use across its lifecycle.	
Supplemental - Other	Pathways and Settings	Contains exposure scenarios information or pathways of Emission to receptor.		

Appendix H. DRAGON Form and Screening Tags

H.1 DRAGON Screening Form

The user interface for the screening forms in DRAGON is presented in Figure H-1.

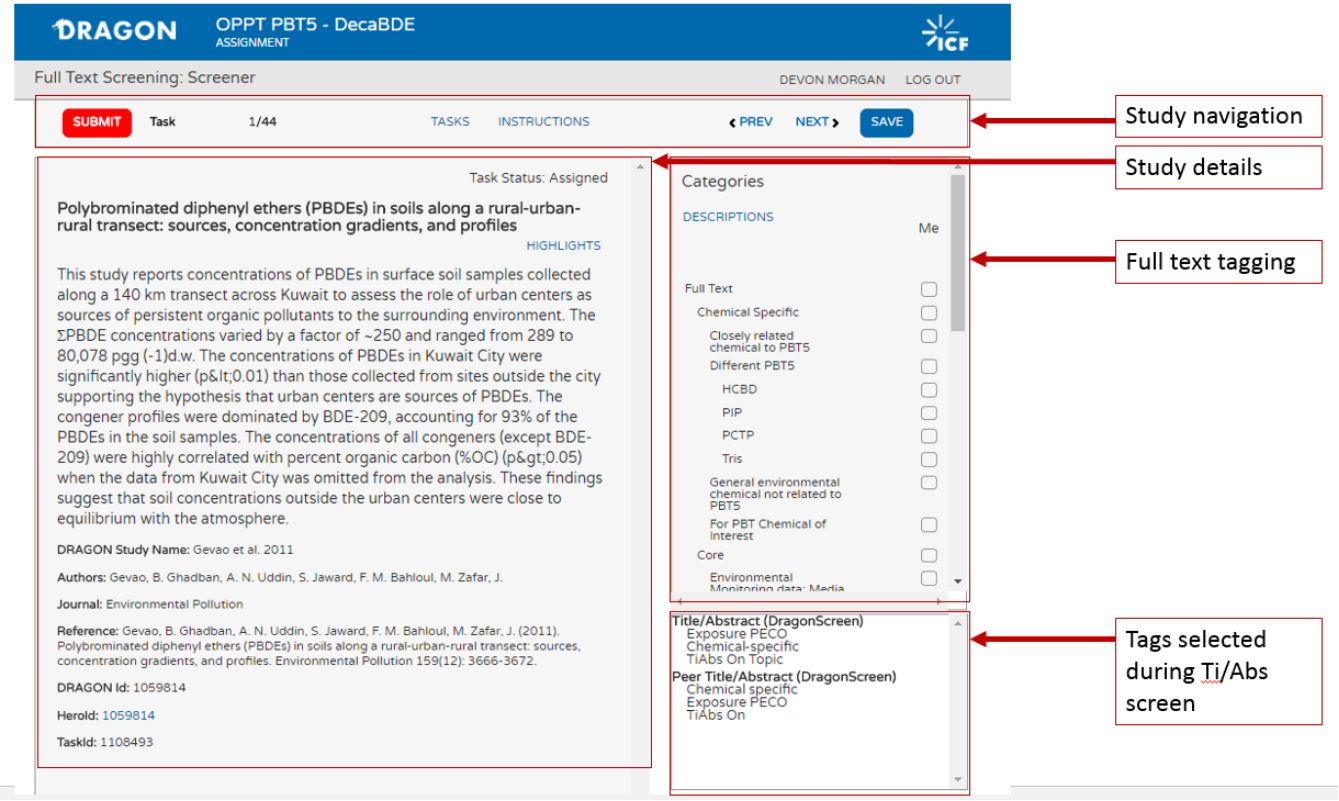


Figure H-1. DRAGON Full Text Screening User Interface

H.2 Peer-Reviewed and Gray Literature Tagging Structures in DRAGON

The title/abstract screening and full text screening occurred separately for peer-reviewed literature. The title/abstract screening and full text screening occurred simultaneously for gray literature. The full text screening tagging structure for screeners in DRAGON is displayed in Figure H-2 .

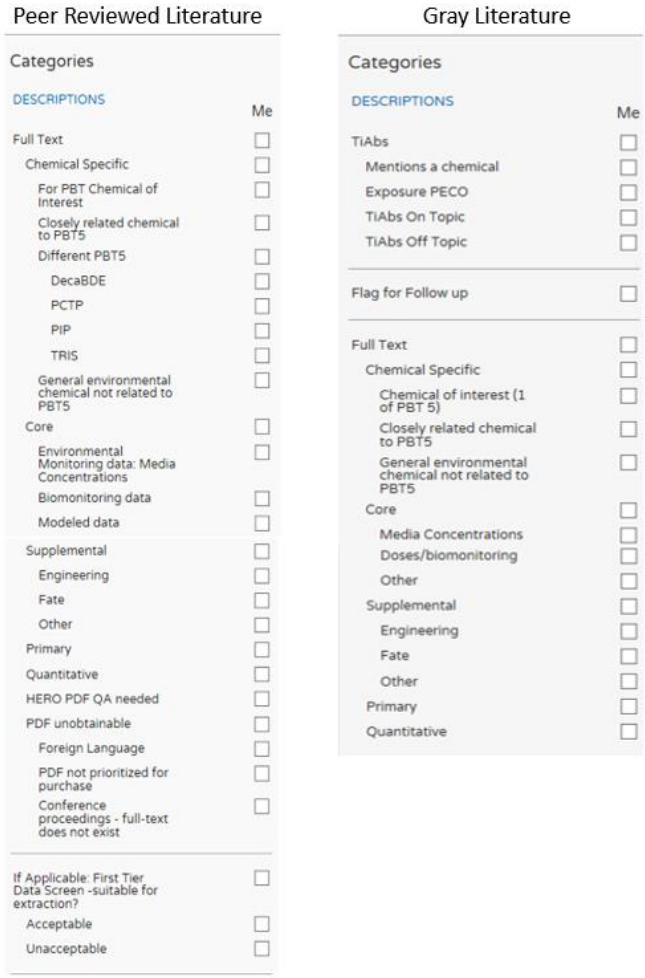


Figure H-2. Full Text Tagging Structure in DRAGON

H.3 DRAGON Extraction Form

The user interface for the data extraction forms in DRAGON is presented in Figure H-3.

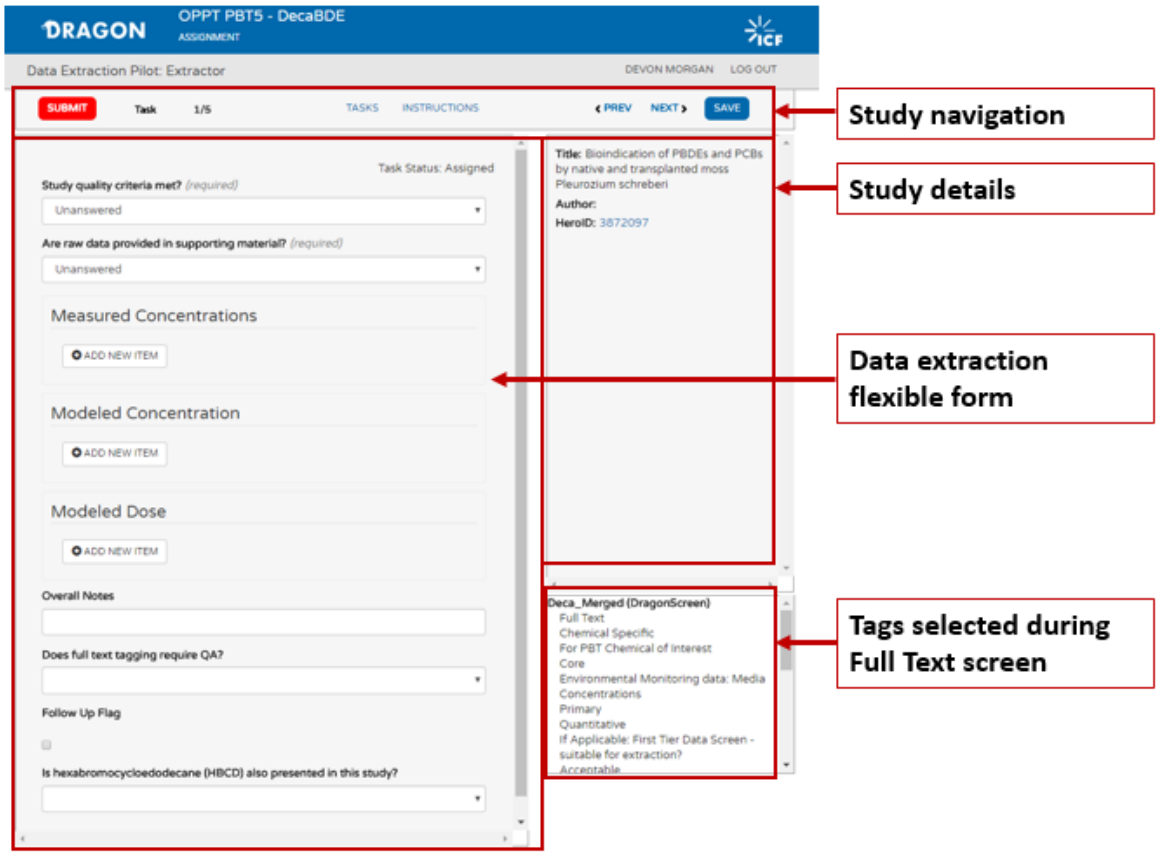


Figure H-3. Data Extraction Form Structure in DRAGON

H.4 DRAGON Evaluation Form

The user interface for the data extraction forms in DRAGON is presented in Figure H-4.

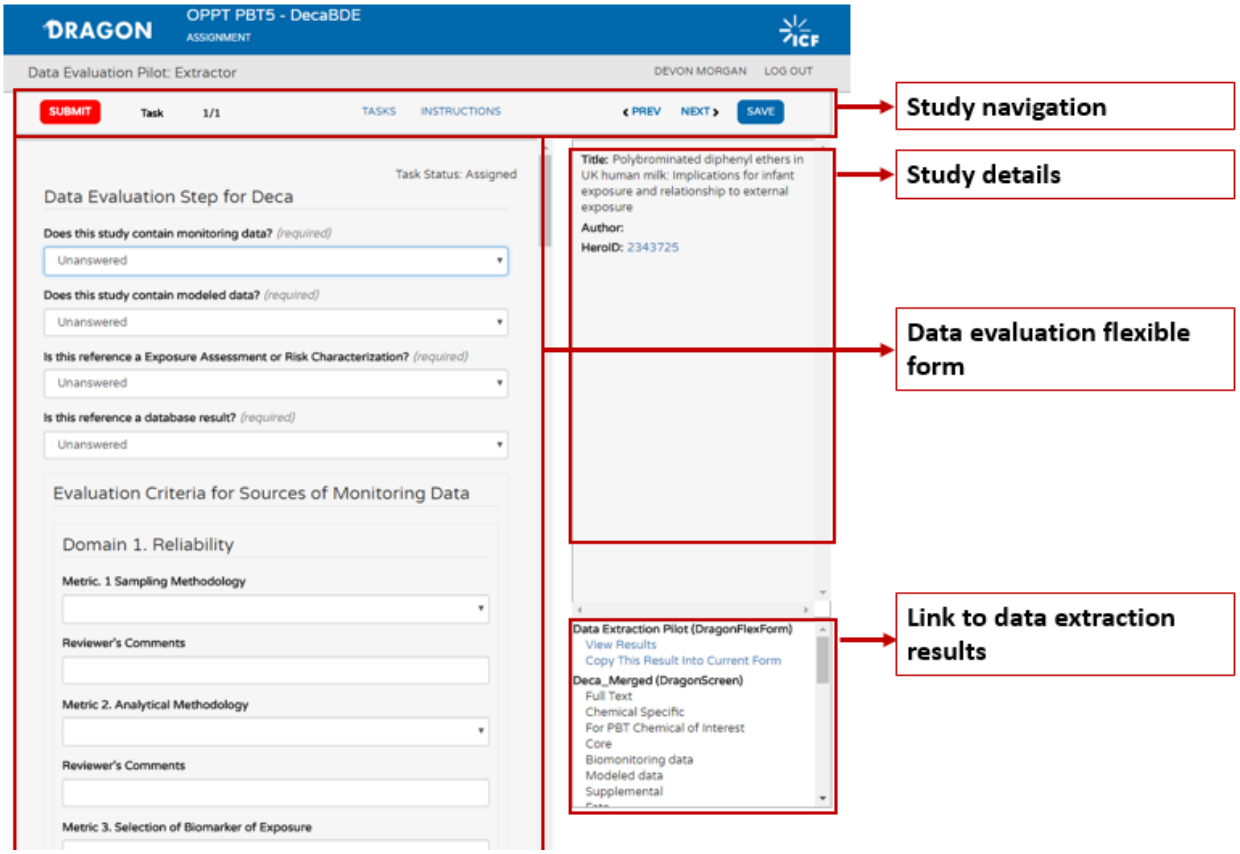


Figure H-4. Data Evaluation Form Structure in DRAGON

Appendix I. Data Extraction Fields

Field Name	Descriptor
Study quality Criteria Met?	Yes/No
Are raw data provided in supporting material?	Yes/No
Study Populations	
Population	Homes in Wisconsin, Hispanic Mothers, West Virginia Miners, Coho Salmon from Great Lakes, Degreasing products,…etc.
Country	USA
Locations Details	Madison, WI
Location Type	For monitoring studies: Rural, Urban, Near Facility, Remote, Mixed For Biomonitoring: Occupational Exposure, Studies: Occupational For … etc.
Description	Description
Medium	
Matrix	Air, water, sediment, soil, blood, urine, fish tissue,…etc.
Matrix Type	Environmental sample (monitoring)|Biological sample (biomonitoring)|Consumer Product
Number of Samples	#
Sampling year (Dates of collection)	01/1996-06/1998
Sampling Notes **(expand)**	Description
Chemistry	
Chemical Name	HCBD, Deca, PIP, TRIS, PCTP
CAS number (if study provided)	#
Mean	#
Reported Mean?	Study Reported|ICF Calculated
Median	#
Reported Median?	Study Reported|ICF Calculated

Central Tendency Unit	e.g. µg/g or µg/m^3…etc.
Central Tendency Notes	Description
Min	#
Max	#
Total observations reported	#
Number of non-detects reported	#
Is the analytical method described or referenced?	Yes|No
Analytical Method name	OCs by GC-ECD or VOCs by GC-MS…etc.
Analytical method description (Combine extraction, Instrument, Type)	EPA Method 6000, FDA Fish Tissue method, Accelerated solvent extraction and analysis via LC-MSMS…etc.
Detection Limit	#
Detection Limit Unit	ug/g
Detection Limit Type	Method detection limit|Method reporting limit|Instrument detection limit|Instrument reporting limit
Method Reporting notes	Authors also reported method detection limit of 0.005 µg/g
Modeled Media Concentrations	
Matrix	Air, water, sediment, soil, blood, urine, fish,…etc.
MatrixType	Environmental sample (monitoring)|Biological sample (biomonitoring)|Consumer Product
Modeling Notes	Description
Chemistry	
Chemical Name	HCBD, Deca, PIP, TRIS, PCTP
CAS number (if provided)	#
Model Estimate	
Estimate Name	50th Percentile, 95th Percentile, High estimate
Estimate	#
Estimate Unit	µg/g
Estimate Notes	Description

Modeled Dose	
Receptor Name	3-year old children, adults…etc.
Receptor Type	Species (e.g., Human)
Receptor notes	Description
Chemistry	
Chemical Name	HCBD, Deca, PIP, TRIS, PCTP
CAS number (if provided)	#
Chemical Notes	Description (e.g., Bioavailable concentration)
Dose Estimate	
Dose Name	Inhalation (air), inhalation (particulate), food ingestion, total exposure,…etc
Dose Estimate	#
Dose Unit	(µg/kg)/day
Dose Notes	Description
Overall Study	
Overall Notes	Description (e.g., Raw data provided in Table 3, could calculate mean and median.)
Does full text tagging require QA?	Yes|No
Follow up flag	Description

Appendix J. References

Howard, BE; Phillips, J; Miller, K; Tandon, A; Mav, D; Shah, MR; Holmgren, S; Pelch, KE; Walker, V; Rooney, AA; Macleod, M; Shah, RR; Thayer, K. (2016). SWIFT-Review: a text-mining workbench for systematic review. Systematic Reviews. 5: 87. http://dx.doi.org/10.1186/s13643-016-0263-z.

OLRC (Office of the Law Revision Counsel). (2016). Toxic substances control. Prioritization, risk evaluation, and regulation of chemical substances and mixtures. (15 USC Ch. 53 2605). http://uscode.house.gov/view.xhtml?path=/prelim%40title15/chapter53&edition=prelim.

U.S. EPA (U.S. Environmental Protection Agency). (2018). Application of systematic review in TSCA risk evaluations. (740-P1-8001). Washington, D.C.: U.S. Environmental Protection Agency, Office of Chemical Safety and Pollution Prevention. https://www.epa.gov/sites/production/files/2018-06/documents/final_application_of_sr_in_tsca_05-31-18.pdf.

Varghese, A; Cawley, M; Hong, T. (2017). Supervised clustering for automated document classification and prioritization: A case study using toxicological abstracts. Environ Syst Decis. http://dx.doi.org/10.1007/s10669-017-9670-5.