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Pollution Prevention

Systematic Review Protocol for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos

Systematic Review Support Document for the Risk Evaluation

CASRN: 1332-21-4

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1 INTRODUCTION

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

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

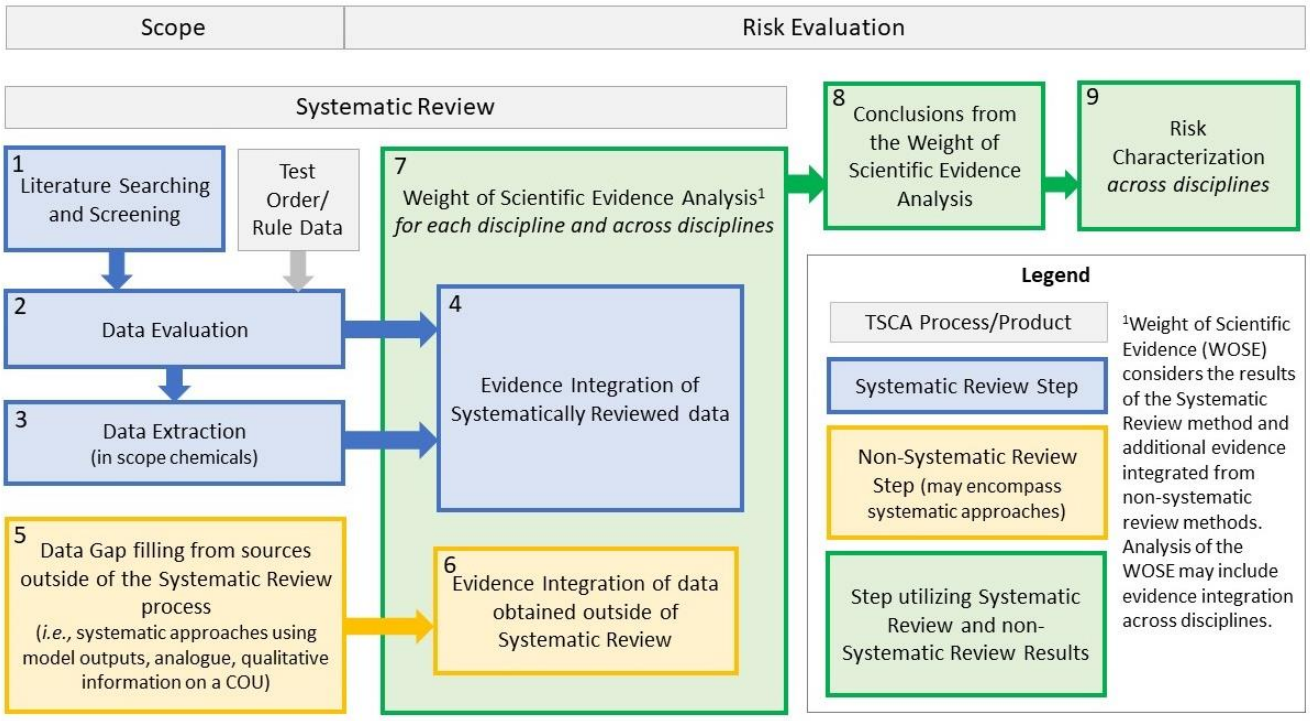

Figure 1-1. Overview of the TSCA Risk Evaluation Process with Identified Systematic Review Steps

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

2 CLARIFICATION AND UPDATES TO THE 2021 DRAFT SYSTEMATIC REVIEW PROTOCOL

In 2021, EPA released the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021), a framework of systematic review approaches under TSCA, to address comments received on a precursor systematic review approaches framework, the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a). In April 2022, the Science Advisory Committee on Chemicals (SACC) provided comments on the 2021 Draft Systematic Review Protocol and additional comments on OPPT's systematic review approaches were garnered during the public comment period. In lieu of an update to the 2021 Draft Systematic Review Protocol, this systematic review protocol for the *Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos* (U.S. EPA, 2024i) (hereinafter referred to as "Risk Evaluation for Asbestos Part 2") describes some clarifications and different approaches that were implemented than those described in the 2021 Draft Systematic Review Protocol in response to (1) SACC comments, (2) public comments, or (3) to reflect chemical-specific risk evaluation needs.

2.1 Clarifications

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

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

evaluation under TSCA (not just epidemiological cohort studies). Also, this procedure may apply when there is duplicative information in two references even if it is more than just "contextual." A modification specifically for asbestos epidemiology studies is that references that assessed the same cohort of participants (such as a group or cohort of people followed over time) were grouped together and linked for non-independent review even if those references included different results. Cohort or sub-cohort groups of references underwent data quality evaluation and extraction together rather than as independent references.

Section 4.5 of the 2021 Draft Systematic Review Protocol describes how data may be obtained using TSCA authorities and test orders. One update to that section is that in addition to requiring data reporting under TSCA sections 4 (test order), 8(a) (Chemical Data Reporting) and 8(d) (Health and Safety Data Reporting), *EPA may also require data reporting under TSCA section 8(c)* (Call-in of Adverse Reactions Records). Appendix 5.3 also describes how information may be submitted to EPA under other TSCA authorities (*e.g.*, TSCA sections 4, 5, 6, 8(d) and 8 (e), as well as FYI submissions).

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

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

Table 2-1. Terminology Clarifications between the 2021 Draft Systematic Review Protocol and the Risk Evaluation for Asbestos Part 2

2021 Draft Systematic Review Protocol Term	Asbestos Systematic Review Protocol Term Update	Clarification
"Title and abstract" or "title/abstract"	"Title and abstract"	To increase consistency, the term "title and abstract" will be used to refer to information specific to "title and abstract" screening.

2021 Draft Systematic Review Protocol Term	Asbestos Systematic Review Protocol Term Update	Clarification
Variations of how "include," "on topic" or "PECO[a]/PESO[b]/RESO[c] relevant" implied a reference was considered for use in the risk evaluation, whereas "exclude," "off topic" or "not PECO[a]/PESO[b]/RESO[c] relevant" implied a reference was *not* considered for use in the risk evaluation.	Meets/does not meet PECO[a]/PESO[b]/RESO[c] screening criteria	The term "include" or "exclude" falsely suggests that a reference was or was not, respectively, considered in the risk evaluation. There was also confusion regarding whether "on topic" and "PECO[a]/PESO[b]/RESO[c] relevant" were synonymous and suggested those references were explicitly considered for use in the risk evaluation (and by default, "off topic" and "not PECO[a]/PESO[b]/RESO[c] relevant" references were not). References that meet the screening criteria proceed to the next systematic review step; however, all references that undergo systematic review at any time are considered in the risk evaluation. Information that is categorized as supplemental or does not meet screening criteria are generally less relevant for quantitative use in the risk evaluation but may be considered if there is a data need identified. For instance, mechanistic studies are generally categorized as supplemental information at either title and abstract or full-text screening steps but may undergo the remaining systematic review steps if there is a relevant data need for the risk evaluation (*e.g.*, dose response, mode of action).
Database source not unique to a chemical	Database	Updated term and definition of "Database": Data obtained from databases that collate information for the chemical of interest using methods that are reasonable and consistent with sound scientific theory and/or accepted approaches and are from sources generally using sound methods and/or approaches (*e.g.*, state or federal governments, academia). Example databases include STORET (STOrage and RETrieval) and the Massachusetts Energy and Environmental Affairs Data Portal. The term in the 2021 Draft Systematic Review Protocol (Table_Apx N-1) incorrectly suggested that databases that contain information on a singular chemical are not considered (U.S. EPA, 2021). Furthermore, the wording "large" was removed to prevent confusion and the incorrect suggestion that there is a data size requirement for databases that contain information that may be considered for systematic review.
Metric ranking or level	Metric rating	As explained above, EPA is not implementing quantitative methodologies to indicate metric quality determinations, therefore the term "ranking" is inappropriate. The term "level" was inconsistently used to indicate metric quality determinations previously; therefore, EPA is removing the use of this term to reduce confusion when referring to metric quality

2021 Draft Systematic Review Protocol Term	Asbestos Systematic Review Protocol Term Update	Clarification
		determinations. The term "Rating" is more appropriate to indicate the use of professional judgement to determine a quality level for individual metrics.
Overall study ranking or level	Overall quality determination (OQD)	As explained above, EPA is not implementing quantitative methodologies to indicate overall data/information source quality determinations, therefore the term "ranking" is inappropriate. The term "level" was inconsistently used to indicate overall data/information source quality determinations previously; therefore, EPA is removing the use of this term to reduce confusion when referring to overall data/information source quality determinations. The term "Rating" is more appropriate to indicate the use of professional judgement to determine a quality level for the overall data/information source quality determination.
Sub-discipline	No change in term	Sub-discipline explicitly indicates the two categories of receptor-based studies relevant to evaluate human health hazard (discipline): epidemiological (human receptor) or human health animal model toxicological studies (non-human animal receptor). Although environmental hazard is a discipline, Appendix T incorrectly suggested that environmental hazard is a sub-discipline in the 2021 Draft Systematic Review Protocol.
Evidence stream	No change in term	Evidence streams were updated for both environmental and human health hazard disciplines to more appropriately categorize the hazardous endpoints that were considered. Please see additional descriptions of the evidence stream updates in Section 6.5 below.

[a] "PECO" stands for Population, Exposure, Comparator or Scenario, and Outcomes.
[b] "PESO" stands for Pathways or Processes, Exposure, Setting or Scenario, and Outcomes.
[c] "RESO" stands for Receptors, Exposure, Setting or Scenario, and Outcomes.

3 DATA SEARCH

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

reviewed literature on asbestos (U.S. EPA, 2021). All reasonably available information submitted to EPA under TSCA authorities was considered.

3.1 Multi-disciplinary Updates and Clarifications to the Data Search

For the Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2024i) the literature search was conducted as described in Section 4 of the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021), where the peer-reviewed and gray literature updated search followed the approach outlined in Sections 4.2 and 4.3 of the 2021 Draft Systematic Review Protocol, respectively (U.S. EPA, 2021). After the initial search for peer-reviewed and gray literature, additional sources relevant to the risk evaluation were identified; these sources went through the systematic review process for the appropriate discipline(s). Additionally, each discipline utilized different strategies (*e.g.*, search strings) to attain their discipline-specific pool of data sources that underwent systematic review.

SWIFT-Review Validation

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

Additional Gray Literature Sources

Physical and Chemical Properties: In addition to the gray literature sources listed in Appendix E of the 2021 Draft Systematic Review Protocol, an additional database was added to the list of gray literature sources for physical and chemical properties. The National Institutes for Standards and Technology (NIST) Chemistry Webbook was searched in September 2021 to capture spectroscopic data, specifically ultra-violet and visible absorption (UV-Vis) data, if recorded. This source may also provide thermodynamic data that informs chemical stability and behavior under various conditions. However, no data was found for asbestos in the NIST Chemistry Webbook.

Environmental Release and Occupational Exposure: In addition to the gray literature sources listed in Appendix E of the 2021 Draft Systematic Review Protocol, two additional databases were included in the list of gray literature sources for environmental release and occupational exposure. In December 2022, Google Scholar and CDC's NIOSHTic were searched to gather data about the average estimate for the release duration and release frequency for handling asbestos during construction, renovation,

demolition activities, firefighting, or other disaster response-related activities. Appendix G of the Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2024i) describes the sources used in the release assessment for these cases in detail.

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

Because the literature pool for many chemicals, including asbestos, includes a record from EPA's STORET (STOrage and RETrieval) database, which has been retired, EPA downloaded all the data for this chemical from the WQP, the successor database that now contains data from STORET. This data was uploaded into HERO and added to the literature pool that is considered for systematic review.

Additional Data Sources Identified Through the TSCA Data Gathering Authorities and Public Comments

Under the one-time asbestos reporting rule under TSCA section 8(a), exposure-related information—including information on the presence, types, and quantities of asbestos (including asbestos that is a component of a mixture) and asbestos-containing articles that have been manufactured (including imported) or processed—was provided to the Agency. In total, 71 submissions were received and considered in the Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2024i), consistent with TSCA sections 26(h), (i), and (k), 15 U.S.C. 2625. EPA reviewed each submission to determine the relevant condition(s) of use (COU), how asbestos was identified in the products, and the level of asbestos measured in the product or occupational setting. Submissions with potential asbestos exposures not previously considered in the Risk Evaluation for Asbestos, Part 1: Chrysotile asbestos (U.S. EPA, 2020), and Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2024i) were used to inform the selection of new COUs in the Risk Evaluation for Asbestos Part 2. Two criteria were used to determine if the exposure data (*e.g.*, weight fraction of asbestos in a product and air monitoring data in a workplace) should be considered quantitatively in the Risk Evaluation for Asbestos Part 2 exposure levels above those considered in the draft risk evaluation for a given COU or exposure levels for a COU that previously had no underlying exposure data. No new data were identified for quantitative evaluation in Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2024i) using these criteria.

To inform the Risk Evaluation for Asbestos Part 2, there were two public comment periods in which EPA received additional potentially relevant information. A letter peer review of the quantitative human health approach to be applied in the Risk Evaluation for Asbestos Part 2 was conducted in October and November of 2023 with a 60-day public comment period of the associated white paper opened on August 3, 2024. Additionally, the Draft Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2023a) was released on April 16, 2024, and was accompanied by a 60-day public comment period. References submitted during these public comment periods not previously considered using the systematic review approaches implemented to inform the Risk Evaluation for Asbestos, Part 1: Chrysotile asbestos (U.S. EPA, 2020) or Draft Risk Evaluation for Asbestos Part 2 were reviewed for relevancy to the Risk Evaluation for Asbestos Part 2. For consumer, occupational, and general population exposure, the criteria for consideration for quantitative analysis were references relevant to exposure outside the range

of what was previously considered in the Draft Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2023a). Similarly, the criteria for use in quantitative analyses for human health assessment were epidemiology references that identified a health effect at a lower asbestos exposure level than was previously evaluated in either the cancer or non-cancer assessments in the Draft Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2023a). No new references were identified for quantitative evaluation in the Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2024i) using these criteria.

3.2 Physical and Chemical Properties

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

3.3 Environmental Fate and Transport Properties

The search for peer-reviewed and gray literature are as described in Sections 4.2 and 4.3, respectively, in the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021). Specifically, SWIFT-Review was used to identify peer-reviewed references that are predicted to be the most relevant for evaluating environmental fate and transport properties for the Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2024i). The search string used for environmental fate and transport literature in SWIFT-Review was developed by EPA's ORD in collaboration with Sciome and is presented in Appendix G, Section G.2, Table_Apx G2 of the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021). As mentioned above in Section 3.1, the search string used to identify potentially relevant peer-reviewed data references for evaluation of the environmental fate and transport properties of Asbestos were validated. When the search string terms are identified in the title, abstract or as a keyword of a given reference in SWIFT-Review, those references proceed with TIAB screening.

3.4 Environmental Release and Occupational Exposure

The search for peer-reviewed and gray literature are as described in Sections 4.2 and 4.3, respectively, in the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021). Specifically, SWIFT-Review was used to identify peer-reviewed references that are predicted to be the most relevant for evaluating environmental release and occupational exposure for the Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2024i). As described in Sections 4.2.4.2 of the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021), EPA identified on-topic and off-topic references from the broad search results of the asbestos peer-reviewed literature as positive and negative "seeds" to classify which references contained environmental release and occupational exposure to prioritize for further review. When the relevant references were identified in SWIFT Review, those references proceeded with title and abstract screening.

3.5 General Population, Consumer, and Environmental Exposure

The peer-reviewed and gray literature searches for general population, consumer, and environmental exposure are as described in Sections 4.2 and 4.3, respectively, in the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021). Specifically, SWIFT-Review was used to identify peer-reviewed references that are predicted to be the most relevant for evaluating general population, consumer, and

environmental exposures to asbestos. As described in Section 4.2.4.2 of the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021), EPA identified on-topic and off-topic references from the broad search results of the peer-reviewed literature as positive and negative "seeds" to classify which references on general population, consumer, and environmental exposures to prioritize for further review. As noted previously in Section 3.1, eight additional references were added to the literature search protocol to capture database data from the WQP and Six-Year Review 3. The database data were compared to other database and monitoring data found during the literature search to ensure no duplication of data. A record from a predecessor database to Water Quality Portal, EPA's STORET database, that was found during the literature search was not counted as a separate reference, to avoid double-counting data. There were no other changes to the process identified in the 2021 Draft Systematic Review Protocol for information considered for the evaluation of general population, consumer, and environmental exposure for the Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2021).

3.6 Environmental and Human Health Hazard

The search for peer-reviewed and gray literature are as described in Sections 4.2 and 4.3, respectively, in the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021). Specifically, SWIFT-Review was used to identify peer-reviewed references that are predicted to be the most relevant for evaluating environmental and human health hazard for the Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2024i). Specifically, search strings were developed for the two hazard disciplines by EPA's Office of Research and Development (ORD) in collaboration with SWIFT-Review developer, Sciome. As mentioned above in Section 3.1, the search string used to identify potentially relevant peer-reviewed data references for evaluation of the environmental and human health hazard of asbestos were validated by EPA. When the search string terms are identified in the title, abstract or as a keyword of a given reference in SWIFT-Review, those references proceed with TIAB screening. The environmental and human health hazard search strings are provided online.

4 DATA SCREENING

Sections 4.2.5 and 4.3.2 of the 2021 Draft Systematic Review Protocol describe how TIAB and full-text screening respectively, are conducted to identify references that may contain relevant information for use in risk evaluations under TSCA using discipline-specific screening criteria (U.S. EPA, 2021). Specifically, TIAB screening efforts may be conducted using the specialized web-based software programs DistillerSR[1] and SWIFT-Active-Screener,[2, 3] and the below sub-sections will describe whether TIAB screening was done manually in DistillerSR or utilized machine learning to help prioritize reference screening in SWIFT-Active-Screener. Additional details on how SWIFT Active-Screener utilizes a machine-learning algorithm to automatically compute which unscreened documents are most likely to be relevant[4] are available in Section 4.2.5 of the 2021 Draft Systematic Review Protocol (U.S.

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

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

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

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

EPA, 2021). During TIAB screening, if it was unclear whether a reference met the screening criteria (*e.g.,* PECO/RESO/PESO statements) without having the full reference to review, or if a reference was determined to meet the screening criteria, that reference advanced to full-text screening if the full reference could be retrieved and generated into a Portable Document Format (PDF).

Literature inventory trees were introduced in the scoping process for the risk evaluations that began systematic review in 2019 in response to comments received from the SACC and public to better illustrate how references underwent various systematic review steps (*e.g.,* TIAB and full-text screening). As explained in Section 2.1.2 of the *Final Scope of the Risk Evaluation for Asbestos. Part 2: Supplemental evaluation including legacy uses and associated disposal of asbestos* (U.S. EPA, 2022), literature inventory trees demonstrate how references that meet screening criteria progress to the next systematic review step. EPA used the Health Assessment Workplace Collaborative (HAWC) tool to develop web-based literature inventory trees that enhance the transparency of the decisions resulting from the screening processes. Additional references that EPA has obtained via public comments and other sources were also considered in the systematic review process and are reflected in the interactive HAWC hyperlinks available in the figure captions below each respective literature inventory tree. The web-based interactive literature inventory trees in HAWC also allow users to directly access the references in the Health & Environmental Research Online (HERO) database (more details available in Section 1 of the 2021 Draft Systematic Review Protocol). Instructions for accessing information about references and data sources in each node via HERO are available in HAWC for each respective literature inventory tree. Each node indicates whether a reference has met screening criteria at different screening steps and/or contains types of content that may be discerned at that respective systematic review step (U.S. EPA, 2021). Furthermore, the sum of the numbers for the various nodes in the literature inventory trees may be smaller or larger than the preceding node because some studies may have unclear relevance or be relevant for many categories of information. The screening process for each discipline varies and the nodes in the literature inventory tree indicate the screening decisions determined for each reference and whether specific content could be determined; if no references had a specific screening decision and/or contained specific content relevant for a respective discipline, a node will not be present on the literature tree to depict this.

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

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

4.1 Multi-disciplinary Updates and Clarifications to the Data Screening

As stated above in Section 1, all references that are found in the initial chemical-specific searches are considered for use in the respective chemical risk evaluation. Previously Section 4.2.5 of the 2021 Draft Systematic Review Protocol explained that references tagged as potentially having supplemental

information may be considered for data quality evaluation and extraction. However, one clarification to that description is that even references that are tagged as not meeting TIAB or full-text screening criteria (*e.g.*, PECO/PESO/RESO) for a respective discipline or sub-discipline may also undergo additional screening to meet information needs that were not stated in the original screening criteria and be considered for data quality evaluation and extraction, should there be additional relevant information that may not have met the original screening criteria.

4.2 Physical and Chemical Properties

During data screening, EPA followed the process described in Appendix H, Section H-1 of the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021), to conduct TIAB and full-text screening for asbestos guided by the data or information needs on various physical and chemical properties or endpoints as listed in Table_Apx H-1 of the protocol. The same screening criteria was used during TIAB and full-text screening for references considered for the evaluation of physical and chemical properties of asbestos. TIAB screening was performed using SWIFT Active-Screener. Upon meeting screening criteria during full-text screening, data or information sources then undergo data quality evaluation and extraction. Figure 4-1 presents the number of references that report general physical and chemical property information that fulfilled the data needs for the Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2024i) and passed these criteria for TIAB and full-text screening.

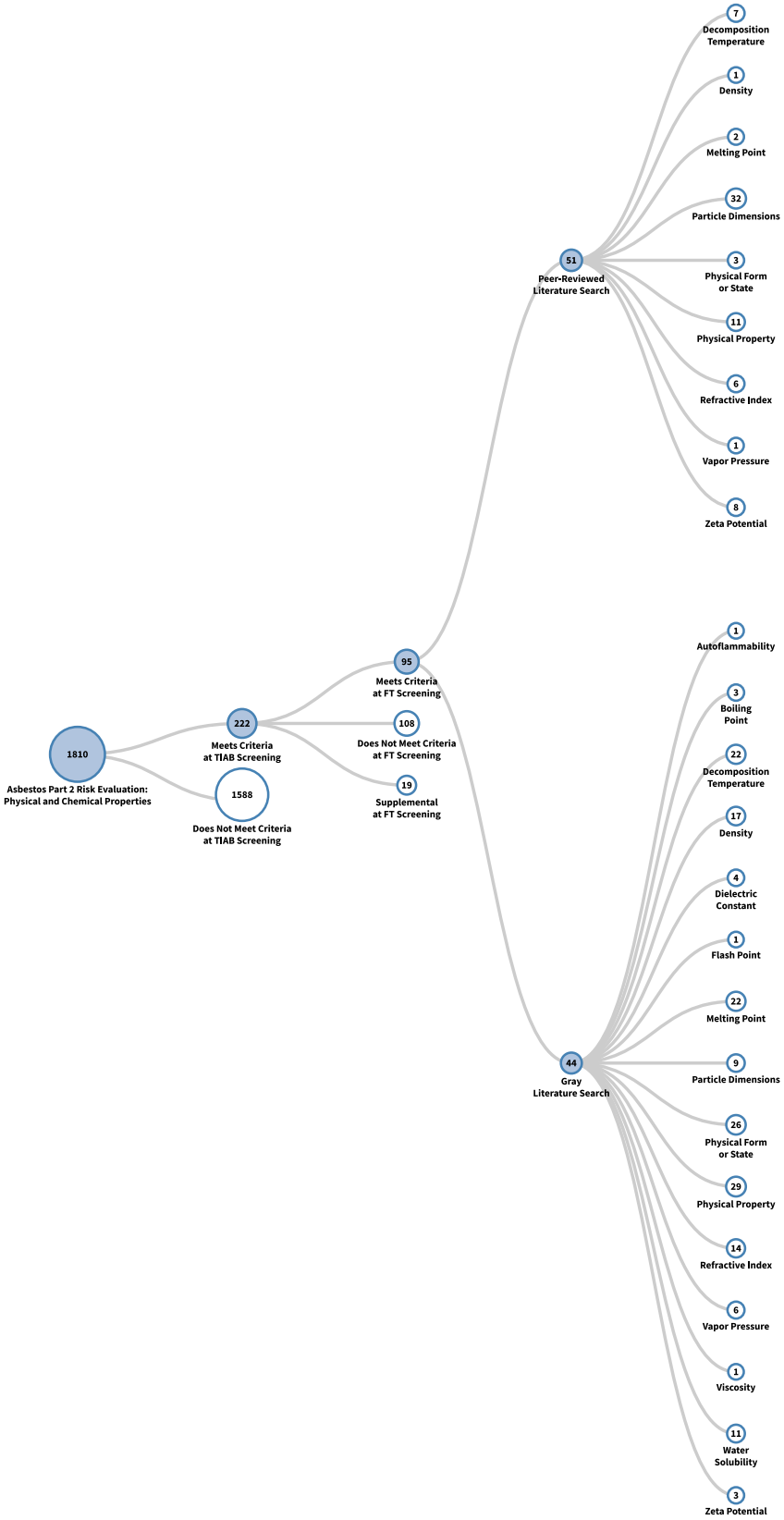

Figure 4-1. Literature Inventory Tree – Physical and Chemical Properties for Asbestos Part 2
View the interactive literature inventory tree in HAWC. Data in this figure represent all references obtained from the publicly available databases and gray literature references searches that were included in systematic review as of February 14, 2023.

4.3 Environmental Fate and Transport Properties

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

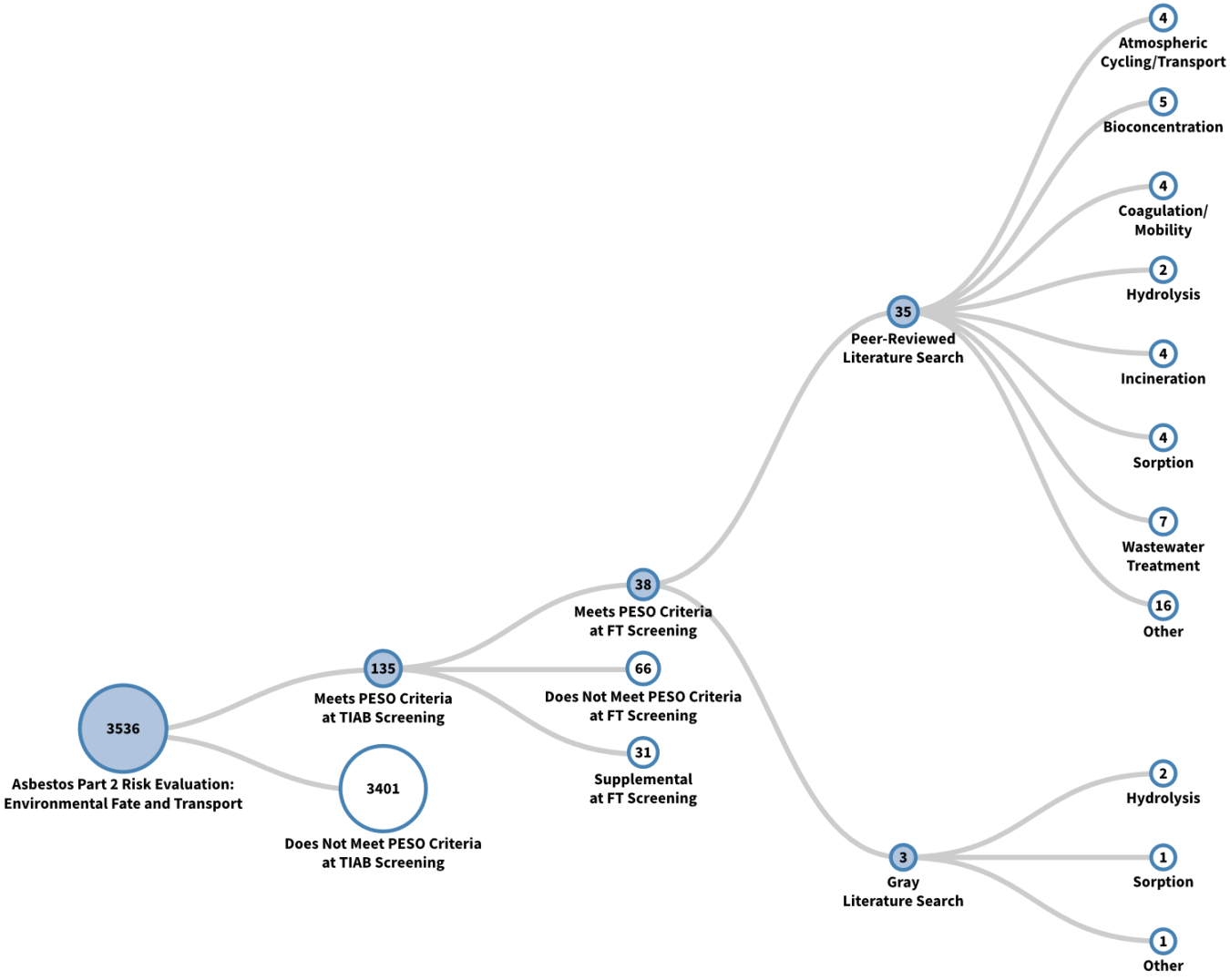

Figure 4-2. Literature Inventory Tree – Environmental Fate and Transport Properties for Asbestos Part 2

View the interactive literature inventory tree in HAWC. Data in this figure represent all references obtained from the publicly available databases and gray literature references searches that were included in systematic review as of March 13, 2023.

4.4 Environmental Release and Occupational Exposure

During data screening, EPA followed the process described in Appendix H, Section H.3 of the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021), to conduct title and abstract, and full-text screening for asbestos literature search results, as guided by the RESO statement. RESO stands for **R**eceptors, **E**xposure, **S**etting or Scenario, and **O**utcomes. The same RESO statement was used during title and abstract, and full-text screening for references considered for the evaluation of environmental release and occupational exposure information for asbestos. TIAB were performed using SWIFT Active-Screener. Data or information sources that comply with the screening criteria specified in the RESO statement then undergo data quality evaluation and extraction. Figure 4-3 presents the number of references that report general engineering data, environmental release, and occupational exposure data that passed RESO screening criteria at TIAB, and full-text screening.

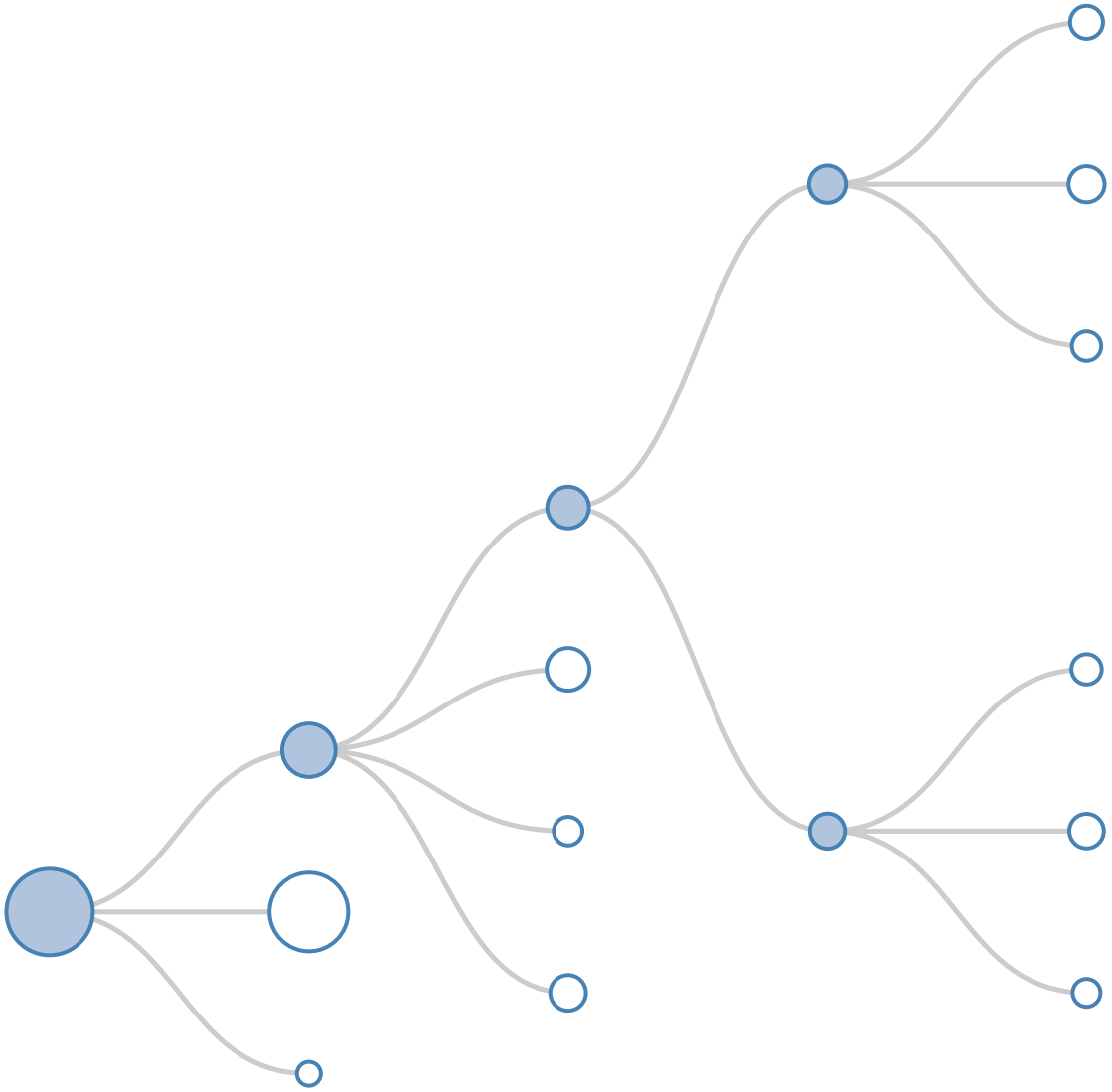

Figure 4-3. Literature Inventory Tree – Environmental Release and Occupational Exposure Search Results for Asbestos Part 2

View the interactive literature inventory tree in HAWC. Data in this figure represent all references obtained from the publicly available databases and gray literature references searches that were included in systematic review as of September 6, 2024.

4.5 General Population, Consumer, and Environmental Exposure

During data screening, EPA followed the process described in Appendix H.4 of the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021), to conduct TIAB and full-text screening for asbestos literature search results, as guided by the PECO statement. PECO stands for **P**opulation, **E**xposure, **C**omparator or Scenario, and **O**utcomes for Exposure Concentration or Dose. The same PECO statement was used during TIAB and full-text screening for references considered for the evaluation of general population, consumer, and environmental exposure information for asbestos. TIAB screening was performed using SWIFT Active-Screener. Figure 4-4 presents the number of references that report general population, consumer, and environmental exposure data that passed PECO screening criteria at TIAB and full-text screening.

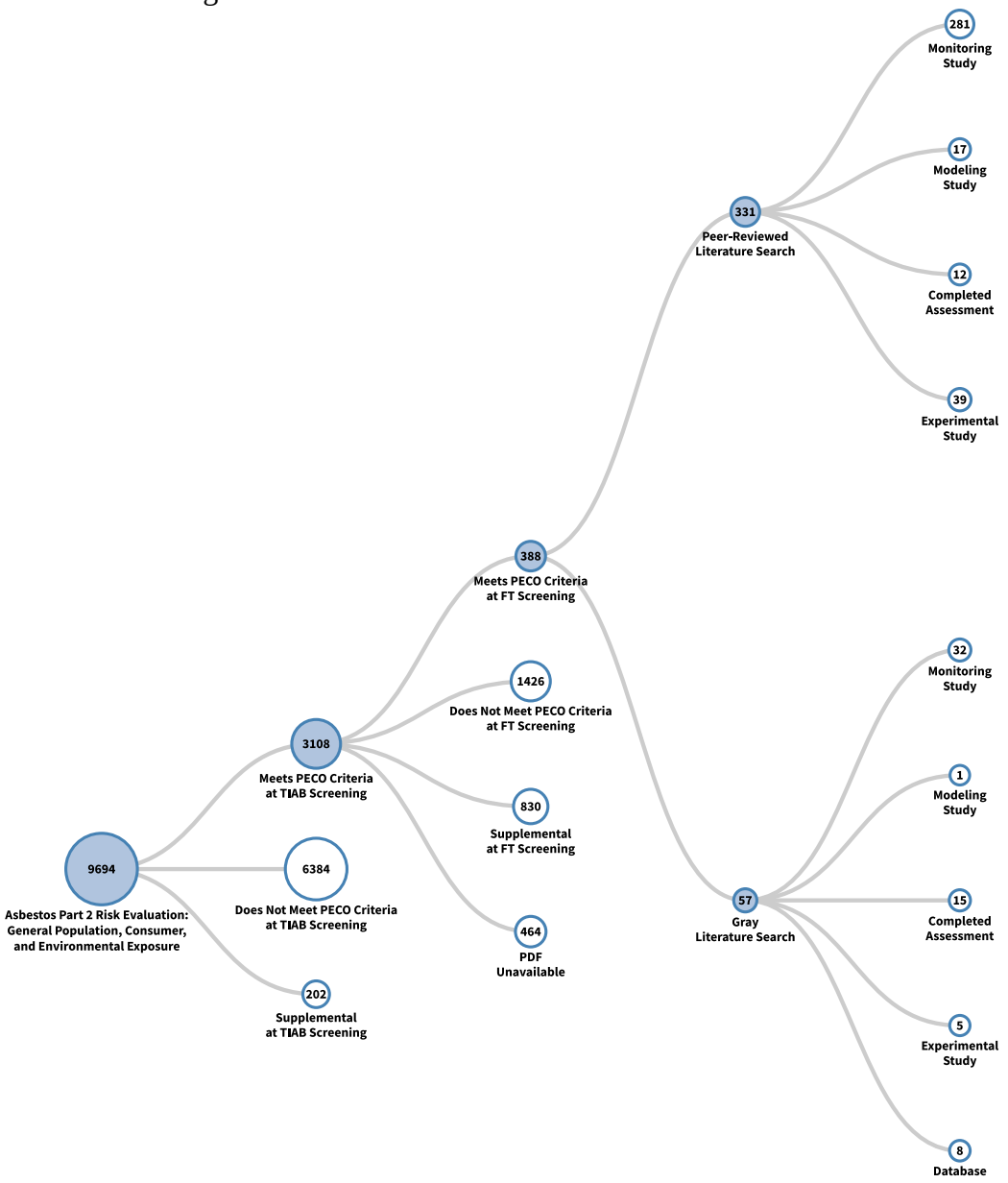

Figure 4-4. Literature Inventory Tree – General Population, Consumer, and Environmental Exposure Search Results for Asbestos Part 2

View the interactive literature inventory tree in HAWC. Data in this figure represent all references obtained from the publicly available databases and gray literature reference searches that were included in systematic review as of August 23, 2024.

4.6 Environmental and Human Health Hazard

During data screening, EPA followed the process described in Section 4 of the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021), to conduct TIAB and full-text screening for the Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2024i) literature search results, as guided by the PECO statement. PECO stands for **P**opulation, **E**xposure, **C**omparator or Scenario, and **O**utcomes for Exposure Concentration or Dose. Regarding animal toxicological studies, there are many receptors that may be used to characterize both human and environmental hazard, exposure and risk. Non-mammalian model systems are increasingly used to identify potential human health hazards (*e.g.*, Xenopus, zebrafish), and traditional human health models (*e.g.*, rodents) can be used to identify potential environmental hazard for terrestrial organisms. For the Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2024i) there were sufficient data to characterize human hazard and risk due to asbestos exposure using epidemiological information, therefore all data that met PECO screening criteria for non-human receptors were considered for the characterization of environmental hazard.

The same PECO statement was used during TIAB and full-text screening for references considered for the evaluation of environmental and human health hazard resulting from exposure to asbestos. TIAB was performed using SWIFT-ActiveScreener. Full-text screening occurred in DistillerSR for references that either met the PECO screening criteria during TIAB screening or if it was unclear to EPA whether the reference would meet the PECO screening criteria based on the information available in the title and abstract. Since the publication of the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021), the PECO screening criteria used to conduct TIAB and full-text screening was updated from what was published in Appendix H, Section 5.13 of the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021). Additional clarifications and updates regarding the PECO screening criteria are described below in Section 4.6.1. Figure 4-5 presents the number of references that report environmental and human health hazard data that passed PECO screening criteria at TIAB and full-text screening.

4.6.1 Hazard PECO Screening Criteria Updates

As stated above, following the publication of the 2021 Draft Systematic Review Protocol, EPA updated the PECO screening criteria statement (Table 4-1) for the Risk Evaluation for Asbestos Part 2, including the major categories of "potentially relevant supplemental material" (Table 4-2) to prioritize the information that is the most relevant for characterizing both environmental and human health hazard resulting from asbestos exposure scenarios presented in the Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2021). To make it easier for the reader to see changes made to the data evaluation metrics, the following conventions are used: text inserted is underlined, and text deleted is in ~~strikethrough~~.

Regarding the "exposure" PECO element, an update made was that exposure to any singular or combination of asbestos fibers listed in Table 4-1 was considered to be potentially relevant for the characterization of human and environmental health hazard outcomes. Another update made to the exposure considerations is that for terrestrial organisms, it is unlikely that exposure to the fiber types listed in Table 4-2 will occur via non-oral exposure routes in the environment. EPA expects that there is no potential for dermal or inhalation exposures to animals under the COUs for asbestos, as defined by the 9 fiber types in the PECO screening criteria (see Section 6.5.1 for further rationale regarding exposure routes most relevant for characterizing terrestrial organism exposure to asbestos), therefore only data sources that identified health outcomes resulting from oral exposures would meet PECO screening criteria for both TIAB and full-text screening of references identified to be potentially relevant for the characterization of environmental hazard.

Additional minor modifications were made to the wording of the case reports/case series supplemental category to clarify that all references, regardless of sample size, containing epidemiological data without a comparison group should be supplemental information. The additional study designs of case-case and case-only studies were also added to this category because they only include cases and don't include an unexposed or lower exposed comparison group.

Table 4-1. Populations, Exposures, Comparators, and Outcomes (PECO) Criteria for the Risk Evaluation for Asbestos Part 2

PECO Element	Evidence
Population	**Human:** Any population and life stage (*e.g.,* occupational or general population, including children and other sensitive populations). **Animal:** Aquatic and terrestrial species (live, whole organism) from any lifestage (*e.g.,* preconception, in utero, lactation, peripubertal, and adult stages). Animal models will be inventoried according to the categorization below: • **Ecotoxicological models**: invertebrates (*e.g.*, insects, spiders, crustaceans, mollusks, and worms) and vertebrates (*e.g.,* mammals and all amphibians, birds, fish, and reptiles). ~~All hen studies (including neurotoxicity studies) will be included for ecotoxicological models~~. **Plants:** All aquatic and terrestrial species (live), including algal, moss, lichen and fungi species. **Screener note:** • <u>All non-human animal (*e.g.*, rodents, rabbits, hens, amphibians, fish, insects) and plant models listed above are relevant as an ecotoxicological model</u>. • ~~To identify human health and ecological hazards, other organisms not listed above in their respective categories can also be used. Non-mammalian model systems are increasingly used to identify potential human health hazards (*e.g., Xenopus,* zebrafish), and traditional human health models (*e.g.*, rodents) can be used to identify potential ecological hazard. Neurotoxicity studies performed in hens (e.g, OECD 418 and 419) are considered relevant to both human and eco hazard~~. • PECO considerations should be directed toward effects on target species only and not on the indirect effects expressed in taxa as a result of chemical treatment (*e.g.,* substance is lethal to a targeted pest species leading to positive effects on plant growth due to diminished presence of the targeted pest species). • Tests of single toxicants in *in vitro* and *ex vivo* systems or on gametes, embryos, or plant or fungal sections capable of forming whole, new organisms will be tagged as potentially supplemental (mechanistic studies). Bacteria and yeast studies specific for assessing genotoxicity or mutagenicity (*e.g.,* Ames assay) will also be tagged as potentially supplemental (mechanistic studies) but are otherwise excluded. Studies on viruses are excluded.
Exposure	**Relevant forms:** Asbestos, as defined by the following fiber types (or mixtures of fiber types): • asbestos: 1332-21-4 • chrysotile (serpentine): 12001-29-5 • crocidolite (riebeckite): 12001-28-4 • amosite (grunerite): 12172-73-5

PECO Element	Evidence
	• anthophyllite: 17068-78-9 • tremolite: 14567-73-8 • actinolite: 12172-67-7 • winchite: 12425-92-2 • richterite: 17068-76-7 • Libby amphibole: 1318-09-8 • Exposure reported as PCM or TEM (including conversion factors for dust) • Talc (or Magnesium silicate) contaminated with asbestos For **synonyms** see a list of validated synonyms on the EPA Chemistry Dashboard. **Human:** Any exposure to one or more of the ~~8~~ 9 asbestos fiber types, singularly or mixed, that meets the following conditions: • Exposure based on measured or estimated concentrations of asbestos • May be combined with estimates of duration of exposure, such as exposure biomonitoring data (*e.g.*, lung tissue specimens), environmental or occupational-setting monitoring data (*e.g.*, ambient air levels), job title or residence. • Quantitative measures or estimates of exposure *only* • For categorical exposures, a minimum of 2 exposure groups (referent group + 1) **Ecotoxicological Animal Model:** ~~Any exposure to asbestos fiber types including via water (including environmental aquatic exposures), soil or sediment, diet, gavage, injection, dermal, and inhalation.~~ Any oral exposure to one or more of the 9 asbestos fiber types, regardless of the exposure media (*e.g.*, water, diet, soil, sediment), singularly or mixed. All other exposure pathways (*e.g.*, dermal, inhalation, injection) should be tagged as excluded ~~(please select the correct supplemental tag: apical/mechanistic and the non-oral exposure pathway).~~ For organism exposures to asbestos or PECO-relevant asbestos fibers where oral exposures cannot be discerned from other exposure pathways that are more characteristic of mammalian and avian studies, please select include (*e.g.*, fish or invertebrates exposed to asbestos in surface water, sediment, and/or soil. **Plants:** ~~Any exposure to asbestos fiber types including via water, soil, sediment.~~ Any exposure to one or more of the 9 asbestos fiber types, regardless of the exposure media (*e.g.*, water, soil, sediment), singularly or mixed. **Screener note:** • Field studies with media concentrations (*e.g.*, surface water, interstitial water, soil, sediment) and/or body/tissue concentrations of animals or plants are to be identified as **Supplemental** if any biological effects are reported. • ~~Studies involving exposures to mixtures (with other chemicals or fiber types other than the ones listed above) will be included only if they also include exposure to any of the 8 asbestos fiber types (alone or in combination). Otherwise, mixture studies will be as **Supplemental**.~~ • Controlled outdoor experimental studies (*e.g.*, controlled

PECO Element	Evidence
	crop/greenhouse studies, mesocosm studies, artificial stream studies) are considered to be laboratory studies (**not field studies**) because there is a known and prescribed exposure dose(s) and an evaluation of hazardous effect(s). Whereas field studies (*e.g.*, biomonitoring) where there is no prescribed exposure dose(s) will be **excluded** if there is no evaluated hazardous effect, and tagged as **Supplemental** field, if there is an evaluated hazardous effect. • Papers reporting exposure to "asbestos" generally and not specific fiber type of asbestos will be included for further consideration.
Comparator	**Human:** the source meets either of the following conditions: • Contains a comparison or referent population exposed to lower levels (or no exposure/exposure below detection limits) of asbestos, and other relevant forms listed above. **Ecotoxicological Animal Model and Plants:** A concurrent control group exposed to vehicle-only treatment and/or untreated control (control could be a baseline measurement). **Screener note:** • If no control group is explicitly stated or implied (*e.g.*, by mention of statistical results that could only be obtained if a control group was present), the study will be marked as **Unclear** during Title/Abstract Screening. • ~~All case reports and case studies/series describing findings in a sample size of less than 20 people in any setting (*e.g.*, occupation, general population) will be tracked as "potentially relevant supplemental information".~~
Outcome	**Human**: Health outcomes including cancer (*e.g.*, lung cancer, mesothelioma, laryngeal cancer, and ovarian cancer) and all non-cancer at the ~~system~~ organ level (*e.g.*, immune, cardiovascular, respiratory) or higher. **Eco Animal and Plants**: All apical biological effects (effects measured at the organ level or higher) and bioaccumulation from laboratory studies with concurrently measured media and/or tissue concentrations. Apical endpoints include but are not limited to reproduction, survival, and growth. **Screener note:** • **Measurable biological effects relevant for humans, animals and plants may include but are not limited to:** mortality, behavioral, population, physiological, growth, reproduction, systemic, point of contact (irritation and sensitization) effects. • Effects measured at the cellular level of biological organization and below are to be tagged as supplemental, mechanistic. **However, if there are apical and mechanistic endpoints, the study will be marked as Yes- PECO relevant/include**.

Table 4-2. Major categories of "potentially relevant supplemental material" for the Risk Evaluation for Asbestos Part 2

Category	Evidence
Mechanistic studies	All studies that report results at the cellular level and lower in both mammalian and non-mammalian model systems, including *in vitro*, *in vivo*, *ex vivo*, and *in silico* studies. These studies include assays for genotoxicity or mutagenicity using bacteria or yeast.
ADME, PBPK, and toxicokinetic	Studies designed to capture information regarding absorption, distribution, metabolism, and excretion (ADME), toxicokinetic studies, or physiologically based pharmacokinetic (PBPK) models.
Case reports, ~~or~~ case series, case-case, or case-only study designs	Case reports, ~~(n ≤ 3 cases) and~~ case series, ~~(non-occupational)~~ case-case, and case-only study designs will be tracked as potentially relevant supplemental information. (Does NOT include case-control, case-referent or case-crossover study designs, which would be PECO includes if they meet criteria).
Susceptible populations (no health outcome)	Studies that identify potentially susceptible subgroups; for example, studies that focus on a specific demographic, lifestage, or genotype. This tag applies primarily during full text screening. **Screener note:** if biological susceptibility issues are clearly present or *strongly* implied in the title/abstract, this supplemental tag may be applied at the title abstract level. If uncertain at title/abstract, do not apply this tag to the reference during title/abstract screening.
Non-English records	Non-English records will be tracked as potentially relevant supplemental information.
Records with no original data	Records that do not contain original data, such as other agency assessments, informative scientific literature reviews, editorials or commentaries.
Conference abstracts	Records that do not contain sufficient documentation to support study evaluation and data extraction.
Field Studies	Field studies with media concentrations (*e.g.*, surface water, interstitial water, soil, sediment) and/or body/tissue concentrations of animals or plants if biological effects reported
Studies that investigate talc or magnesium silicate	Studies with measured hazard endpoints (apical or mechanistic) where the exposure is to talc or magnesium silicate as defined below should be tagged as supplemental: • *Talc:* 14807-96-6, 35592-05-3, talcum, agalite, antimyst, asbestine, trimagnesium, soapstone, steatite, French chalk • *Magnesium silicate:* 1343-88-0, Magnesium silicate, Magnesium oxosilanediolate, Silicic acid, magnesium salt, Florisil, magnesium silandiolate However, please exclude synthetic magnesium silicate (lab-synthesized and thus, not asbestos-relevant) or synthetic magnesium silicate-products.

Category	Evidence
Other relevant structures	If another asbestos fiber type or talc/magnesium silicate are mentioned with resulting biological effects reported. However, please exclude synthetic magnesium silicate (lab-synthesized and thus, not asbestos-relevant) or synthetic magnesium silicate-products. Studies with measured hazard endpoints (apical or mechanistic) where the exposure is to asbestos fibers not listed above as being PECO-relevant, talc (CASRN: 14807-96-6) or magnesium silicate (CASRN: 1343-88-0) should be tagged as supplemental. If talc is the source of any of the 8 asbestos types, the reference should be included.

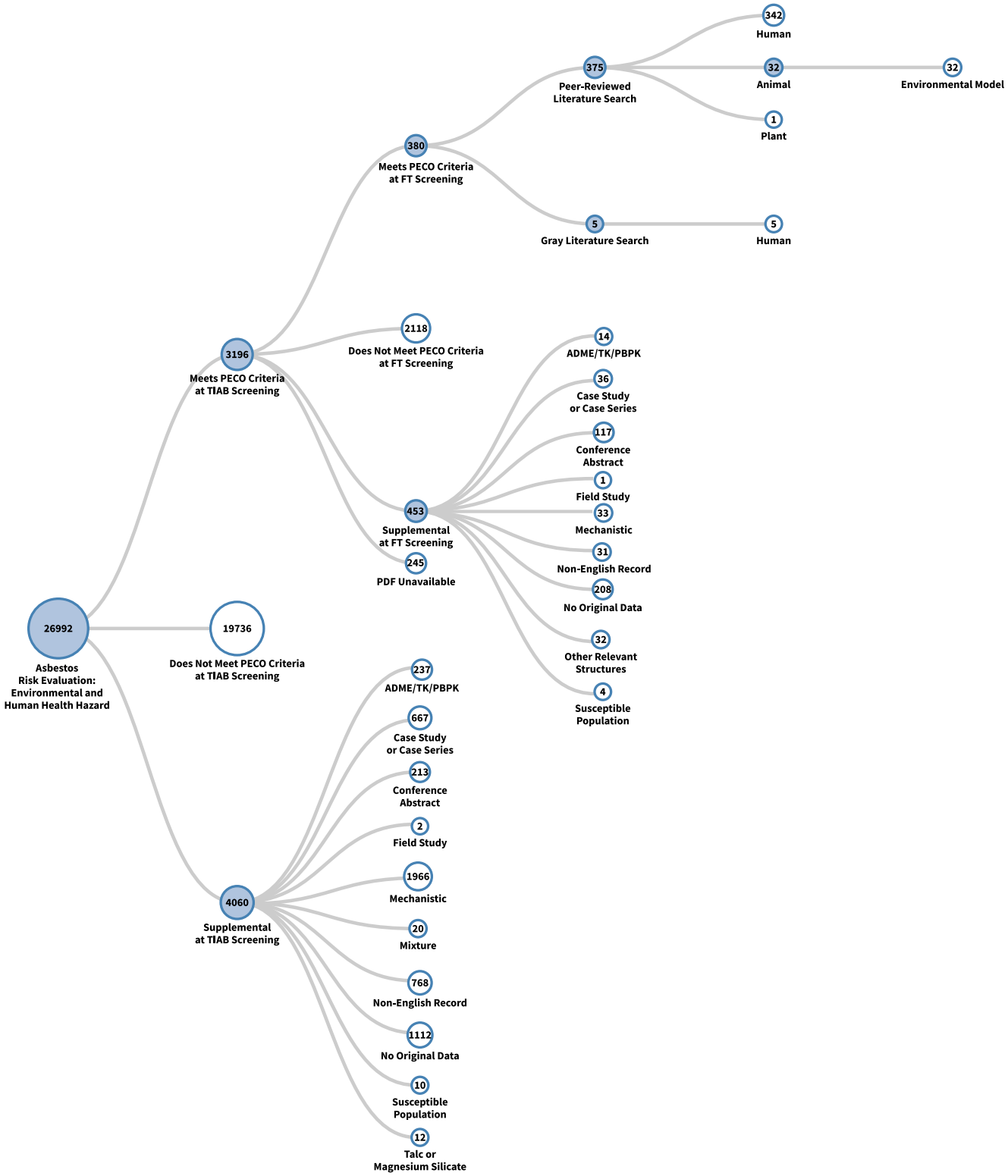

Figure 4-5. Literature Inventory Tree – Environmental and Human Health Hazard for Asbestos Part 2

View the interactive literature inventory tree in HAWC. Data in this figure represent all references obtained from the publicly available databases and gray literature references searches that were included in systematic review as of March 20, 2023.

4.6.2 Further Filtering

To streamline the identification of studies relevant to dose-response assessment, EPA implemented modifications to the process described in the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021). Following PECO-based screening, epidemiologic studies were further characterized according to exposure route, outcome assessed, analysis type, and cohort. References that assessed the same cohort of participants were grouped together and evaluated as cohort groups or sub-groups of references instead of as individual independent references as mentioned above in Section 2.1. For the 347 references that met PECO screening criteria, a total of 159 epidemiologic cohorts were identified and references from the same cohort were grouped together for data quality evaluation as described in the *White Paper: Quantitative Human Health Approach to be Applied in the Risk Evaluation for Asbestos Part 2 – Supplemental Evaluation including Legacy Uses and Associated Disposals of Asbestos* (U.S. EPA, 2023b).

Further screening of studies that met PECO criteria was conducted to identify cohorts that contained dose-response data. The further screening was based on the data analysis method used in the study (regression and standardized mortality ratio (SMR) studies were included), the method of exposure measurement (based on Data Quality Evaluation Metric 4), and the range, distribution, and levels of exposure in the analysis (based on Data Quality Evaluation Metric 5). These modifications and the rationale for their development and use are described in detail in Section 3 and Appendix B of the *White Paper: Quantitative Human Health Approach to be Applied in the Risk Evaluation for Asbestos Part 2 – Supplemental Evaluation including Legacy Uses and Associated Disposals of Asbestos* (U.S. EPA, 2023b). A brief description of these further screening steps is presented here:

Step 1 of Further Screening for Fit for Purpose Context: Identification of Studies that Used Standardized Mortality Ratios and Regression Analysis

Prior asbestos assessments, including the Risk Evaluation for Asbestos Part 1: Chrysotile Asbestos, hereinafter referred to as Risk Evaluation Asbestos Part 1 (U.S. EPA, 2020), focused their dose-response analyses on studies that assessed exposure-response relationships using either SMRs or regression analyses. Because of the utility of SMR and regression studies in dose-response assessment, EPA further screened PECO-relevant studies to identify the subset of these studies that used SMR or regression analyses.

Step 2 of Further Screening for Fit for Purpose Context: Identification of Studies with Sufficient Exposure Measurement and Range

For all studies identified as regression or SMR studies, for each outcome assessed in the paper or cohort group, Metrics 4 and 5 were evaluated before other data quality evaluation metrics. Each paper or cohort group of papers was evaluated by two epidemiologists: an initial evaluator and a quality control (QC) reviewer. If the paper or cohort group was rated as medium or high for Metrics 4 and 5, then the initial evaluator moved on to data quality evaluation for all metrics, and then all data quality evaluation metrics and comments went on to QC review. If either Metric 4 or 5 was rated low or critically deficient, then the initial reviewer submitted for QC without evaluation of the remaining metrics. If the QC reviewer determined that Metrics 4 and 5 should have been rated medium or high, then the paper or cohort group was sent back to the initial reviewer for evaluation of the remaining metrics prior to completion of QC.

Because of the importance of the exposure measurement in dose-response assessment, OPPT evaluated the exposure measurement metric (Metric 4) before evaluating other data quality evaluation metrics to focus on the subset of studies with the most reliable asbestos fiber detection and quantification methods (*i.e.*, use of phase-contrast microscopy (PCM) or transmission electron microscopy (TEM)). Studies that were rated low or critically deficient for Metric 4 did not move on to data quality evaluation.

Metric 5 explicitly assesses whether the study includes a sufficient range, distribution, and levels of exposure for dose-response assessment, and thus assesses study relevance, rather than risk of bias. Thus, Metric 5 was evaluated before the other data quality evaluation metrics, and only those studies that were rated as medium (high is not an option) for Metric 5 moved on to data quality evaluation.

Six references from two cohorts were evaluated in the Risk Evaluation Asbestos Part 1 (U.S. EPA, 2020) and didn't include any additional Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2021) outcomes. Data quality evaluation wasn't conducted for these 6 references because the data quality evaluation results from the Risk Evaluation Asbestos Part 1 (U.S. EPA, 2020) were used for the Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2021).

The further screening to identify cohorts that proceeded to data quality evaluation is illustrated in Figure 4-6 below.

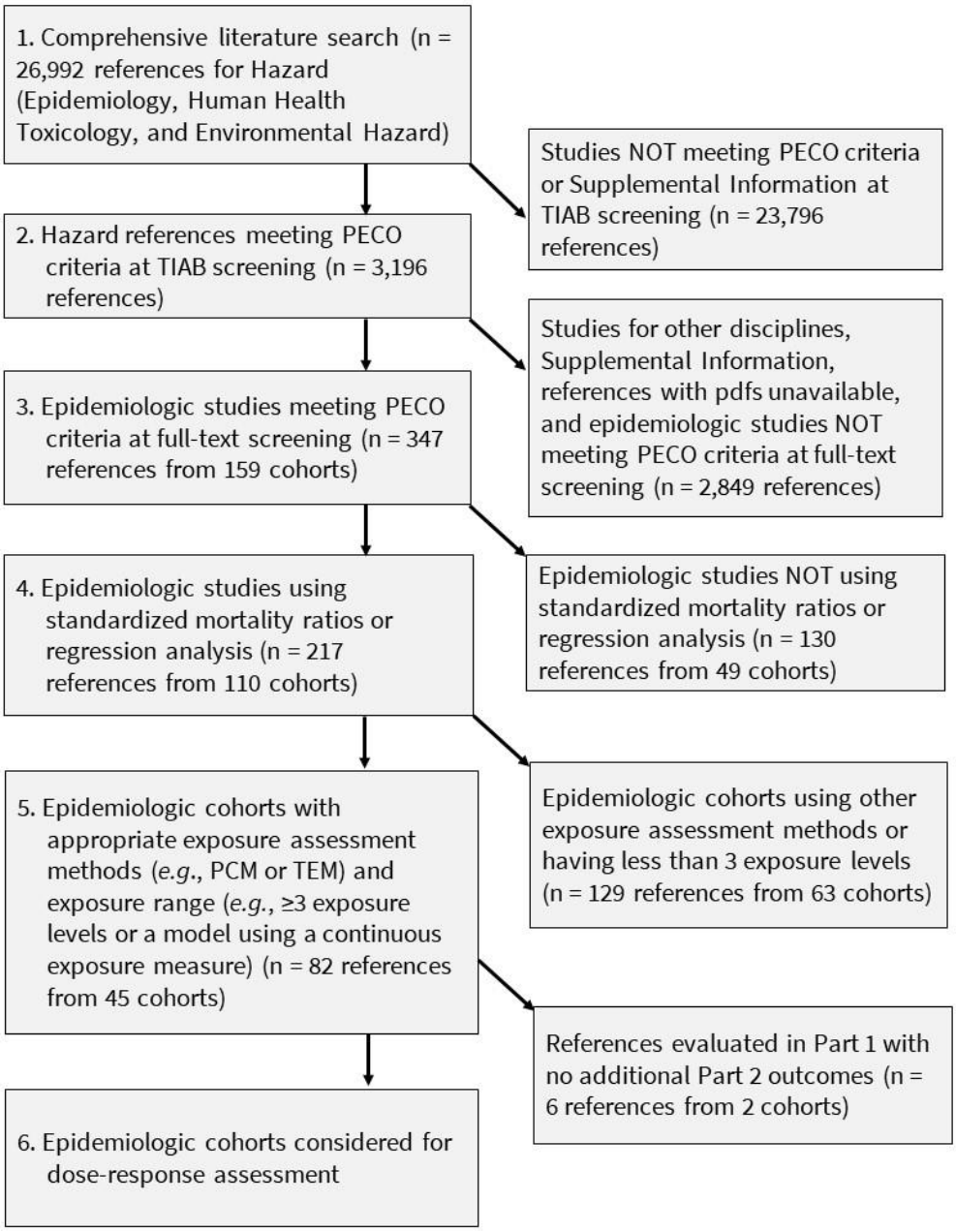

Figure 4-6. Schematic of the Approach Used to Identify Epidemiologic Studies for Dose-Response Consideration

TIAB = title/abstract (screening); PCM = phase-contrast microscopy; TEM = transmission electron microscopy

5 DATA EVALUATION AND DATA EXTRACTION

Data evaluation and extraction were conducted as described in Sections 5 and 6 of the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021). Data evaluation is the systematic review step in which EPA assesses quality of the individual data sources using the evaluation strategies and criteria for each discipline (*e.g.*, physical and chemical property data; fate and transport data; occupational exposure and environmental release data; general population, consumer, and environmental exposure data;

environmental hazard; human health hazard) or sub-discipline (*e.g.*, animal toxicity or epidemiology). The data quality evaluation method uses a structured framework with predefined criteria for each type of data/information source. Data extraction is the systematic review step in which EPA uses structured forms or templates to extract quantitative and qualitative data and information from references that meet screening criteria. The overall goal is to provide transparency, consistency, and as much objectivity as possible to the data quality evaluation and extraction processes along with meeting the TSCA scientific standards in section 26(h).

References that meet screening criteria following full-text screening will generally proceed to data quality evaluation and extraction steps, however one clarification to the procedures outlined in Section 6 of the 2021 Draft Systematic Review Protocol is that in situations where EPA is unable to extract data/information from sources that meet screening criteria (*e.g.*, formatting prohibits accurate extraction), that source may not have extracted data to present in the risk evaluation or respective supplemental documents. The systematic review support documents that contain results from the data quality evaluation and extraction systematic review steps may use updated templates from those that were provided in the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021) because the purpose of these supplemental documents is to accommodate the data needs for each respective risk evaluation. The following sections describe the data quality and extraction process followed by each discipline or sub-discipline to address various information needs for the Risk Evaluation of Asbestos Part 2 (U.S. EPA, 2024i)and any clarifications or updates regarding these systematic review steps as described in the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021).

5.1 Physical and Chemical Properties

As described in the 2021 Draft Systematic Review Protocol, evaluation and extraction followed the steps outlined in Sections 5, 6, and 6.1 (U.S. EPA, 2021). The data quality criteria for physical and chemical property data are summarized in Appendix K of the 2021 Draft Systematic Review Protocol. The *Data Quality Evaluation and Data Extraction Information for Physical and Chemical Properties for Asbestos Part 2 – Supplemental Including Legacy Uses and Associated Disposal of Asbestos - Systematic Review Support Document for the Risk Evaluation* (U.S. EPA, 2024e) provides details of the data extracted and evaluated, including metric ratings and the overall study quality determination for each data source.

5.2 Environmental Fate and Transport Properties

As described in the 2021 Draft Systematic Review Protocol, evaluation and extraction followed the steps outlined in Sections 5, 6, and 6.2 (U.S. EPA, 2021). The data quality criteria for environmental fate data are summarized in Appendix L of the systematic review protocol. Appendix Section L.4 describes how the overall quality of fate data or information were weighted according to an ordinal system corresponding to *high (1)*, *medium (2)*, or *low (3)* to support the risk evaluations quantitatively or qualitatively. EPA does not plan to use data rated as *critically deficient* (4). Table_Apx L4 illustrates the possible quality rankings across the selected metrics for environmental fate data with examples in Table_Apx L5, Table_Apx L6 and Table_Apx L7 (U.S. EPA, 2021). Specific fate data quality ranking quality criteria are in Table_Apx L8 (U.S. EPA, 2021). The *Data Quality Evaluation and Data Extraction Information for Environmental Fate and Transport for Asbestos Part 2 - Supplemental Including Legacy Uses and Associated Disposal of Asbestos - Systematic Review Support Document for the Risk Evaluation* (U.S. EPA, 2024c) provides details of the data extracted and evaluated, including metric rating and the overall study quality determination for each data source.

5.3 Environmental Release and Occupation Exposure

As described in the 2021 Draft Systematic Review Protocol, evaluation and extraction followed the steps outlined in Sections 5, 6, and 6.2 (U.S. EPA, 2021). The data quality criteria for environmental release and occupational exposure data are summarized in Appendix M of the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021). The *Data Quality Evaluation and Data Extraction Information for Environmental Release and Occupational Exposure for Asbestos Part 2 - Supplemental Including Legacy Uses and Associated Disposal of Asbestos - Systematic Review Support Document for the Risk Evaluation* (U.S. EPA, 2024d) details the data extracted and evaluated, including metric rating and the overall study quality determination for each data source.

5.4 General Population, Consumer, and Environmental Exposure

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

A few metrics applicable to multiple evidence streams were slightly modified to better fit some of the unique situations that frequently arise for a certain type of evidence stream (*e.g.*, databases). For example, some metrics were updated to clarify the intent of the metric and better account for variation in types of evidence included in one grouping (*e.g.*, experiments involving chamber studies vs. product concentration assessments). The domains did not change; however, see below for the changes and updates made to the data evaluation metrics for the respective evidence types (*i.e.*, monitoring, experimental studies and databases) as presented in Section 5.4.1. No changes were made to the data evaluation metrics for modeling data, as described in Appendix N.6.2, or to the data evaluation metrics for completed exposure assessments and risk characterizations, as described in Appendix N.6.7 in the 2021 Draft Systematic Review Protocol, respectively (U.S. EPA, 2021). Data quality evaluations for all the references that met PECO screening criteria are included in the *Data Quality Evaluation Information for General Population, Consumer, and Environmental Exposure for Asbestos Part 2 - Supplemental Including Legacy Uses and Associated Disposal of Asbestos - Systematic Review Support Document for the Risk Evaluation* (U.S. EPA, 2024g), hereinafter referred to as "Asbestos Part 2 Data Quality Evaluation Information for General Population, Consumer, and Environmental Exposure."

Data extraction of general population, consumer, and environmental exposure data and information was conducted as described in Section 6 of the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021). However, with respect to information stored within databases, if EPA has access to the data tables, EPA does not conduct a separate data extraction because the data are more accessible and have additional context in the original database format. Data present in the database when the database underwent full-text screening are available in the HERO database (*e.g.*, HERO IDs: 10692772, 10692770, 10692769, 10692779, 10692774, 10692785, 10692790, and 11143231), along with the date the data were downloaded. If a reference (*e.g.*, peer-reviewed reference) presents data from a database that did not undergo systematic review directly (*e.g.*, a foreign database that is not publicly accessible), the data

would be extracted from the reference to the extent possible; this did not apply to references that underwent systematic review for this chemical.

As mentioned above in Section 5, references may not undergo data extraction, regardless of the overall quality determination, if they contain no extractable data points (*e.g.*, values are contained in a non-digitizable figure or are representative of unspecified media or treatment processes). On the other hand, there are references that have many reported endpoints that meet PECO screening criteria for a respective chemical risk evaluation, making it difficult to include all the data in the chemical-specific data extraction systematic review support document. When a reference meets PECO screening criteria, the reference receives a data quality evaluation, and the data in the reference are still considered in the Risk Evaluation, whether or not the included data are extracted in DistillerSR and appear among the chemical-specific extractions in the Systematic Review Support Document: Data Extraction Information for General Population, Consumer, and Environmental Exposure. For example, some raw data was not extracted from HERO IDs 3580701, 3581418, 3585730, 6896139, and 7481806 because no summary statistics were provided, and unique exposure scenarios presented reported more than twenty data point values. In addition, there may be other reasons that EPA decides not to extract all the data from a reference that undergoes data evaluation; EPA extracts the data that are most relevant, given the needs of the assessment. Decisions about whether to limit extractions to certain timeframes or certain countries were made on an evidence stream by evidence stream basis based on available data and the conditions of use being evaluated to better characterize general population, consumer, and environmental exposure and meet assessment needs. This constitutes an update to Section 6 of the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021). While EPA may not extract all the data from all sources, EPA extracted data from studies from the U.S. and other high-income countries that are most relevant for characterizing exposure, use conditions, patterns of use, and product characteristics in the U.S. for legacy uses of asbestos and associated disposals. EPA did not extract data from studies about human or animal biomonitoring because asbestos is a mineral and there are no associated metabolites, transformation products, or byproducts. Additionally, since the Risk Evaluation for Asbestos, Part I: Chrysotile Asbestos assessed car clutches, brakes, and gaskets, data regarding these products were not extracted in this supplement (U.S. EPA, 2020). Current asbestos mining/manufacturing/processing is not a condition of use for consumers or the general population for the Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2024i), and thus, data associated with those uses were not extracted after evaluation. Extraction forms, templates, and decisions are tailored to fit the data extraction needs for each risk evaluation.

The types of fields extracted vary by evidence stream and generally followed Section 6.3 of the 2021 Draft Systematic Review Protocol with regard to the data characteristics captured (U.S. EPA, 2021). Examples of types of data extracted and the extraction formats for the evidence streams identified through systematic review to evaluate environmental, general population, and consumer exposure data are listed in the extraction tables provided in the *Data Extraction Information for General Population, Consumer, and Environmental Exposure Risk Evaluation for Asbestos Part 2 - Supplemental Including Legacy Uses and Associated Disposal of Asbestos - Systematic Review Support Document for the Risk Evaluation* (U.S. EPA, 2024b), hereinafter referred to as "Asbestos Part 2 Data Extraction Information for General Population, Consumer, and Environmental Exposure."

5.4.1 Data Quality Evaluation Metric Updates

The data evaluation metrics for the monitoring, experimental, and database evidence streams, are presented below in Table 5-1, Table 5-2, Table 5-3, respectively. Each table shows which data evaluation metrics changed since the publication of the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021). Other data quality criteria for studies on consumer, general population, and environmental exposure appear in Appendix N of the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021). For

the modeling and completed exposure assessments and risk characterization evidence streams, there were no changes made to the data evaluation metrics since the 2021 Draft Systematic Review Protocol was published (U.S. EPA, 2021). The criteria for modeling studies appear in Table_Apx N-9 of the 2021 Draft Systematic Review Protocol, and criteria for completed exposure assessments and risk characterizations appear in Table_Apx N-19 (U.S. EPA, 2021). In some cases, references can meet the criteria for two exposure evidence streams, and they can also be reviewed and meet criteria for other disciplines. Upon review, each study is evaluated and extracted using the criteria for the most appropriate and applicable evidence streams given the information therein. In order to make it easier for the reader to see changes made to the data evaluation metrics, the following conventions are used: text inserted is underlined, and text deleted is in ~~strikethrough~~.

5.4.1.1 Data Evaluation Criteria for Monitoring Data, as Revised

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

Data Quality Rating	Description
Domain 1. Reliability	
Metric 1. Sampling methodology	
High	Samples were collected according to publicly available SOPs that are scientifically sound and widely accepted (*i.e.*, from a source generally ~~using~~ known to use sound methods and/or approaches) for the chemical and media of interest. Example SOPs include U.S. Geological Survey (USGS') "National Field Manual for the Collection of Water-Quality Data," EPA's "Ambient Air Sampling" (SESDPROC-303-R5), etc. **OR** The sampling protocol used was not a publicly available SOP from a source generally known to use ~~using~~ sound methods and/or approaches, but the sampling methodology is clear, appropriate (*i.e.*, scientifically sound), and similar to widely accepted protocols for the chemical and media of interest. All pertinent sampling information is provided in the data source or companion source. Examples include: • sampling equipment • sampling procedures/regime • sample storage conditions/duration • performance/calibration of sampler • study site characteristics • matrix characteristics
Medium	Sampling methodology is discussed in the data source or companion source and is generally appropriate (*i.e.*, scientifically sound) for the chemical and media of interest; however, **one or more pieces of sampling information is not described.** The missing information is unlikely to have a substantial impact on results. **OR** Standards, methods, protocols, or test guidelines may not be widely accepted, but a successful validation study for the new/unconventional procedure was conducted prior to the sampling event and is consistent with sound scientific theory and/or accepted approaches. Or a review of information indicates the methodology is acceptable and differences in methods are not expected to lead to lower quality data.

Data Quality Rating	Description
Low	Sampling methodology is only briefly discussed; therefore, **most sampling information is missing** and likely to have a substantial impact on results. **AND/OR** The sampling methodology **does not represent best sampling methods, protocols, or guidelines** for the chemical and media of interest (*e.g.*, outdated [but still valid] sampling equipment or procedures, long storage durations). **AND/OR** There are **some inconsistencies** in the reporting of sampling information (*e.g.*, differences between text and tables in data source, differences between standard method and actual procedures reported to have been used, etc.) that led to a low confidence in the sampling methodology used.
Critically deficient	The sampling methodology is not discussed in the data source or companion source. **AND/OR** Sampling methodology is not scientifically sound or is not consistent with widely accepted methods/approaches for the chemical and media being analyzed (*e.g.*, inappropriate sampling equipment, improper storage conditions). **AND/OR** There are **numerous inconsistencies** in the reporting of sampling information, resulting in high uncertainty in the sampling methods used.
Not rated/not applicable	
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 2. Analytical methodology	
High	Samples were analyzed according to publicly available analytical methods that are scientifically sound and widely accepted (*i.e.*, from a source generally ~~using~~ known to use sound methods and/or approaches) and are appropriate for the chemical and media of interest. Examples include EPA SW-846 Methods, NIOSH Manual of Analytical Methods 5th Edition, etc. **OR** The analytical method used was not a publicly available method from a source generally ~~using~~ known to use sound methods and/or approaches, but the methodology is clear and appropriate (*i.e.*, scientifically sound) and similar to widely accepted protocols for the chemical and media of interest. All pertinent sampling information is provided in the data source or companion source. Examples include: • extraction method • analytical instrumentation (required) • instrument calibration • limit of quantitation (LOQ), LOD, detection limits, and/or reporting limits • recovery samples • biomarker used (if applicable) matrix-adjustment method (*i.e.*, creatinine, lipid, moisture)

Data Quality Rating	Description
Medium	Analytical methodology is discussed in detail and is clear and appropriate (*i.e.*, scientifically sound) for the chemical and media of interest; however, **one or more pieces of analytical information is not described**. The missing information is unlikely to have a substantial impact on results. **AND/OR** The analytical **method may not be standard/widely accepted, but a method validation study was conducted** prior to sample analysis and is expected to be consistent with sound scientific theory and/or accepted approaches. **AND/OR** Samples were collected at a site and immediately analyzed using an on-site mobile laboratory, rather than shipped to a stationary laboratory.
Low	Analytical methodology is only briefly discussed. Analytical instrumentation is provided and consistent with accepted analytical instrumentation/methods. However, **most analytical information is missing** and likely to have a substantial impact on results. **AND/OR** Analytical method **is not s**tandard/widely accepted, and method validation is limited or not available. **AND/OR** Samples were analyzed using field screening techniques. **AND/OR** LOQ, LOD, detection limits, and/or reporting limits not reported. **AND/OR** There are **some inconsistencies or possible errors** in the reporting of analytical information (*e.g.*, differences between text and tables in data source, differences between standard method and actual procedures reported to have been used, etc.) which leads to a lower confidence in the method used.
Critically deficient	Analytical methodology is not described, **including analytical instrumentation** (*i.e.*, HPLC, GC). **AND/OR** Analytical methodology is not scientifically appropriate for the chemical and media being analyzed (*e.g.*, method not sensitive enough, not specific to the chemical, out of date). **AND/OR** There are numerous inconsistencies in the reporting of analytical information, resulting in high uncertainty in the analytical methods used.
Not rated/ Not applicable	
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*

Data Quality Rating	Description
Metric 3. Selection of biomarker of exposure	
High	Biomarker in a specified matrix is known to have an accurate and precise quantitative relationship with external exposure, internal dose, or target dose (*e.g.*, previous studies (or the current study) have indicated the biomarker of interest reflects external exposures). **AND** Biomarker (parent chemical or metabolite) is derived from exposure to the chemical of interest.
Medium	Biomarker in a specified matrix has accurate and precise quantitative relationship with external exposure, internal dose, or target dose. **AND** Biomarker is derived from multiple parent chemicals, not only the chemical of interest, **but** there is a stated method to apportion the estimate to only the chemical of interest
Low	Biomarker in a specified matrix has accurate and precise quantitative relationship with external exposure, internal dose, or target dose. **AND** Biomarker is derived from multiple parent chemicals, not only the chemical of interest, **and** there is NOT an accurate method to apportion the estimate to only the chemical of interest. **OR** Biomarker in a specified matrix is a poor surrogate (low accuracy and precision) for exposure/dose.
Critically deficient	Not applicable. A study will not be deemed critically deficient based on the use of biomarker of exposure.
Not rated/ applicable	Metric is not applicable to the data source.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Domain 2. Representative	
Metric 4. Geographic area	
High	Geographic location(s) is reported, discussed, or referenced.
Medium	Not applicable. This metric is dichotomous (*i.e.*, high vs. critically deficient).
Low	Not applicable. This metric is dichotomous (*i.e.*, high vs. critically deficient).
Critically deficient	Geographic location is not reported, discussed, or referenced.
Not rated/ not applicable	
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*

Data Quality Rating	Description
Metric 5. Temporality	
High	Timing of sample collection for monitoring data is consistent with current or recent exposures **(within 5 years)** may be expected.
Medium	Timing of sample collection for monitoring data **is less consistent** with current or recent exposures **(>5 to 15 years)** may be expected.
Low	Timing of sample collection for monitoring data is not consistent with when current exposures **(>15 years old)** may be expected and likely to have a substantial impact on results.
Critically deficient	Timing of sample collection for monitoring data is **not reported, discussed, or referenced.**
Not rated/ not applicable	
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 6. Spatial and temporal variability	
High	Sampling approach accurately captures variability of environmental contamination in population/scenario/media of interest based on the heterogeneity/homogeneity and dynamic/static state of the environmental system. For example: • **Large sample size** (*i.e.,* ≥10 or more samples for a single scenario). • Use of replicate samples. • Use of systematic or continuous monitoring methods. • Sampling over a sufficient period of time to characterize trends. • For urine, 24-hour samples are collected (vs. first morning voids or spot). • For biomonitoring studies, the timing of sample collected is appropriate based on chemical properties (*e.g.*, half-life), the pharmacokinetics of the chemical (*e.g.*, rate of uptake and elimination), and when the exposure event occurred.
Medium	Sampling approach likely captures variability of environmental contamination in population/scenario/media of interest based on the heterogeneity/homogeneity and dynamic/static state of the environmental system. Some uncertainty may exist, but it is unlikely to have a substantial impact on results. For example: • **Moderate sample size** (*i.e.,* 5–10 samples for a single scenario), or • Use of judgmental (non-statistical) sampling approach, or • No replicate samples. • For urine, first morning voids or pooled spot samples.
Low	Sampling approach poorly captures variability of environmental contamination in population/scenario/media of interest. For example: • **Small sample size** (*i.e.,* <5 samples), or • Use of haphazard sampling approach, or • No replicate samples, or • Grab or spot samples in single space or time, or • Random sampling that does not include all periods of time or locations, or

Data Quality Rating	Description
	• For urine, un-pooled spot samples.
Critically deficient	Sample size is not reported. **Single sample** collected per data set. For biomonitoring studies, the timing of sample collected is not appropriate based on chemical properties (*e.g.*, half-life), the pharmacokinetics of the chemical (*e.g.*, rate of uptake and elimination), and when the exposure event occurred.
Not rated/not applicable	
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 7. Exposure scenario	
High	The data closely represent relevant exposure scenario (*i.e.*, the population/scenario/media of interest). Examples include: • amount and type of chemical/product used • source of exposure • method of application or by-stander exposure • use of exposure controls • microenvironment (location, time, climate)
Medium	The data likely represent the relevant exposure scenario (*i.e.*, population/scenario/media of interest). **One or more key pieces of information may not be described** but the deficiencies are unlikely to have a substantial impact on the characterization of the exposure scenario. **AND/OR** If surrogate data, activities seem similar to the activities within scope.
Low	The data lack multiple key pieces of information, and the deficiencies are likely to have a substantial impact on the characterization of the exposure scenario. **AND/OR** There are **some inconsistencies or possible errors** in the reporting of scenario information (*e.g.*, differences between text and tables in data source, differences between standard method and actual procedures reported to have been used, etc.) which leads to a lower confidence in the scenario assessed. **AND/OR** If surrogate data, activities have lesser similarity but are still potentially applicable to the activities within scope.
Critically deficient	If reported, the exposure scenario discussed in the monitored study does not represent the exposure scenario of interest for the chemical.
Not rated/ not applicable	
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*

Data Quality Rating	Description
Domain 3. Accessibility/clarity	
Metric 8. Reporting of results	
High	Supplementary or raw data (*i.e.*, individual data points) are reported, allowing summary statistics to be calculated or reproduced. **AND** Summary statistics are detailed and complete. Example parameters include: • Description of data set summarized (*i.e.*, location, population, dates, etc.) • Range of concentrations or percentiles • Number of samples in data set • Frequency of detection • Measure of variation (coefficient of variation [CV], standard deviation) • Measure of central tendency (mean, geometric mean, median) • Test for outliers (if applicable) **AND** Both adjusted and unadjusted results are provided (*i.e.*, correction for void completeness in urine biomonitoring, whole-volume or lipid adjusted for blood biomonitoring, wet or dry weight for environmental tissue samples or soil samples) (only if applicable).
Medium	Supplementary or raw data (*i.e.*, individual data points) are not reported, and therefore summary statistics cannot be reproduced. **AND/OR** Summary statistics are reported but are missing one or more parameters (see description for high). **AND/OR** Only adjusted or unadjusted results are provided, but not both (only if applicable).
Low	Supplementary data are not provided, and summary statistics are missing most parameters (see description for high). **AND/OR** There are some inconsistencies or errors in the results reported, resulting in low confidence in the results reported (*e.g.*, differences between text and tables in data source, less appropriate statistical methods).
Critically deficient	There are numerous inconsistencies or errors in the calculation and/or reporting of results, resulting in highly uncertain reported results.
Not rated/ not applicable	
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 9. Quality assurance	
High	The study quality assurance/quality control (QA/QC) measures and all pertinent ~~quality assurance~~ QA/QC information is provided in the data source or companion source. Examples include: • Field, laboratory, and/or storage recoveries. • Field and laboratory control samples.

Data Quality Rating	Description
	• Baseline (pre-exposure) samples. • Biomarker stability • Completeness of sample (*i.e.*, creatinine, specific gravity, osmolality for urine samples) **AND** No QA/QC ~~quality control~~ issues were identified, or any identified issues were minor and adequately addressed (*i.e.*, correction for low recoveries, correction for completeness).
Medium	The study applied and documented ~~quality assurance/quality control~~ QA/QC measures; however, **one or more pieces of QA/QC information is not described.** Missing information is unlikely to have a substantial impact on results. **AND** No QA/QC ~~quality control~~ issues were identified, or any identified issues were minor and addressed (*i.e.*, correction for low recoveries, correction for completeness).
Low	QA/QC measures ~~Quality assurance/quality control techniques~~ and results were not directly discussed but are implied through the study's use of standard field and laboratory protocols. **AND/OR** Deficiencies were noted in ~~quality assurance/quality control~~ QA/QC measures that are likely to have a substantial impact on results. **AND/OR** There are some inconsistencies in the ~~quality assurance~~ QA/QC measures reported, resulting in low confidence in the QA/QC ~~quality assurance/control~~ measures taken and results (*e.g.*, differences between text and tables in data source).
Critically deficient	QA/QC issues have been identified which significantly interfere with the overall reliability of the study.
Not rated/ not applicable	
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Domain 4. Variability and uncertainty	
Metric 10. Variability and uncertainty	
High	The study characterizes variability in the population/media studied. **AND** Key uncertainties, limitations, and data gaps have been identified. **AND** The uncertainties are minimal and have been characterized.
Medium	The study has limited characterization of variability in the population/media studied. **AND/OR** The study has limited discussion of key uncertainties, limitations, and data gaps. **AND/OR** Multiple uncertainties have been identified but are unlikely to have a substantial impact on results.

Data Quality Rating	Description
Low	The characterization of variability is absent. **AND/OR** Key uncertainties, limitations, and data gaps are not discussed. **AND/OR** Uncertainties identified may have a substantial impact on the exposure the exposure assessment
Critically deficient	Estimates are highly uncertain based on characterization of variability and uncertainty.
Not rated/ not applicable	
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*

5.4.1.2 Data Evaluation Criteria for Experimental Data, as Revised

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

Data Quality Rating	Metric Description
Domain 1. Reliability	
Metric 1. Sampling Methodology and Conditions	
High	Samples were collected according to publicly available SOPs, methods, protocols, or test guidelines that are scientifically sound and widely accepted from a source generally known to use sound methods and/or approaches such as EPA, NIST, American Society for Testing and Materials, ISO, and ACGIH. **OR** The sampling protocol used was not a publicly available SOP from a source generally known to use sound methods and/or approaches, but the sampling methodology is clear, appropriate (*i.e.*, scientifically sound), and similar to widely accepted protocols for the chemical and media of interest. All pertinent sampling information is provided in the data source or companion source. Examples include: • sampling conditions (*e.g.*, temperature, humidity) • sampling equipment and procedures • sample storage conditions/duration • performance/calibration of sampler
Medium	Sampling methodology is discussed in the data source or companion source and is generally appropriate (*i.e.*, scientifically sound) for the chemical and media of interest, however, one or more pieces of sampling information is not described. The missing information is unlikely to have a substantial impact on results. **OR** Standards, methods, protocols, or test guidelines may not be widely accepted, but a successful validation study for the new/unconventional procedure was conducted prior to the sampling event and is consistent with sound scientific theory and/or accepted approaches.

Data Quality Rating	Metric Description
Low	Sampling methodology is only briefly discussed. Therefore, most sampling information is missing and likely to have a substantial impact on results. **AND/OR** The sampling methodology does not represent best sampling methods, protocols, or guidelines for the chemical and media of interest (*e.g.*, outdated (but still valid) sampling equipment or procedures, long storage durations). **AND/OR** There are some inconsistencies in the reporting of sampling information (*e.g.*, differences between text and tables in data source, differences between standard method and actual procedures reported to have been used, etc.) which led to a low confidence in the sampling methodology used.
Critically deficient	The sampling methodology is not discussed in the data source or companion source. **AND/OR** Sampling methodology is not scientifically sound or is not consistent with widely accepted methods/approaches for the chemical and media being analyzed (*e.g.*, inappropriate sampling equipment, improper storage conditions). **AND/OR** There are numerous inconsistencies in the reporting of sampling information, resulting in high uncertainty in the sampling methods used.
Not rated/not applicable	
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 2. Analytical methodology	
High	Samples were analyzed according to publicly available analytical methods that are scientifically sound and widely accepted (*i.e.*, from a source generally using sound methods and/or approaches) and are appropriate for the chemical and media of interest. Examples include EPA SW-846 Methods, NIOSH Manual of Analytical Methods 5th Edition, etc. **OR** The analytical method used was not a publicly available method from a source generally known to use sound methods and/or approaches, but the methodology is clear and appropriate (*i.e.*, scientifically sound) and similar to widely accepted protocols for the chemical and media of interest. All pertinent analytical ~~sampling~~ information is provided in the data source or companion source. Examples include: • extraction method • analytical instrumentation (required) • instrument calibration • LOQ, LOD, detection limits, and/or reporting limits • recovery samples • biomarker used (if applicable) • matrix-adjustment method (*i.e.*, creatinine, lipid, moisture)
Medium	Analytical methodology is discussed in detail and is clear and appropriate (*i.e.*, scientifically sound) for the chemical and media of interest; however, one or more pieces of analytical

Data Quality Rating	Metric Description
	information is not described. The missing information is unlikely to have a substantial impact on results. **AND/OR** The analytical method may not be standard/widely accepted, but a method validation study was conducted prior to sample analysis and is expected to be consistent with sound scientific theory and/or accepted approaches. **AND/OR** Samples were collected at a site and immediately analyzed using an on-site mobile laboratory, rather than shipped to a stationary laboratory.
Low	Analytical methodology is only briefly discussed. Analytical instrumentation is provided and consistent with accepted analytical instrumentation/methods. However, most analytical information is missing and likely to have a substantial impact on results. **AND/OR** Analytical method is not standard/widely accepted, and method validation is limited or not available. **AND/OR** Samples were analyzed using field screening techniques. **AND/OR** LOQ, LOD, detection limits, and/or reporting limits not reported. **AND/OR** There are some inconsistencies or possible errors in the reporting of analytical information (*e.g.*, differences between text and tables in data source, differences between standard method and actual procedures reported to have been used, etc.) which leads to a lower confidence in the method used.
Critically deficient	Analytical methodology is not described, including analytical instrumentation (*i.e.*, HPLC, GC). **AND/OR** Analytical methodology is not scientifically appropriate for the chemical and media being analyzed (*e.g.*, method not sensitive enough, not specific to the chemical, out of date). **AND/OR** There are numerous inconsistencies in the reporting of analytical information, resulting in high uncertainty in the analytical methods used.
Not rated/not applicable	
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
<u>Metric 3</u>. Selection of biomarker of exposure	
High	Biomarker in a specified matrix is known to have an accurate and precise quantitative relationship with external exposure, internal dose, or target dose (*e.g.*, previous studies (or the current study) have indicated the biomarker of interest reflects external exposures). **AND** Biomarker (parent chemical or metabolite) is derived from exposure to the chemical of interest.

Data Quality Rating	Metric Description
Medium	Biomarker in a specified matrix has accurate and precise quantitative relationship with external exposure, internal dose, or target dose. **AND** Biomarker is derived from multiple parent chemicals, not only the chemical of interest, **but** there is a stated method to apportion the estimate to only the chemical of interest
Low	Biomarker in a specified matrix has accurate and precise quantitative relationship with external exposure, internal dose, or target dose. **AND** Biomarker is derived from multiple parent chemicals, not only the chemical of interest, **and** there is NOT a stated method to apportion the estimate to only the chemical of interest. **OR** Biomarker in a specified matrix is a poor surrogate (low accuracy and precision) for exposure/dose.
Critically deficient	Not applicable. A study will not be deemed critically deficient based on the use of biomarker of exposure. ~~Biomarker in a specified matrix is a poor surrogate (low accuracy and precision) for exposure/dose.~~
Not rated/not applicable	Metric is not applicable to the data source.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Domain 2. Representative	
Metric 4. Testing scenario	
High	Testing conditions closely represent relevant exposure scenarios (*i.e.*, population/scenario/media of interest). Examples include: • amount and type of chemical/product used • source of exposure/test substance • method of application or by-stander exposure • use of exposure controls • microenvironment (location, time, climate, temperature, humidity, pressure, airflow) **AND** Testing conducted under a broad range of conditions for factors such as temperature, humidity, pressure, airflow, and chemical mass/weight fraction (if appropriate).
Medium	The data likely represent the relevant exposure scenario (*i.e.*, population/scenario/media of interest). One or more key pieces of information may not be described but the deficiencies are unlikely to have a substantial impact on the characterization of the exposure scenario. **AND/OR** If surrogate data, activities seem similar to the activities within scope.
Low	The data lack multiple key pieces of information and the deficiencies are likely to have a substantial impact on the characterization of the exposure scenario. **AND/OR**

Data Quality Rating	Metric Description
	There are some inconsistencies or possible errors in the reporting of scenario information (*e.g.*, differences between text and tables in data source, differences between standard method and actual procedures reported to have been used, etc.) which leads to a lower confidence in the scenario assessed. **AND/OR** If surrogate data, activities have lesser similarity but are still potentially applicable to the activities within scope. **AND/OR** Testing conducted under a single set of conditions, except for experiments to determine a weight fraction or concentration in a product.
Critically deficient	Testing conditions are not relevant to the exposure scenario of interest for the chemical.
Not rated/not applicable	
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 5. Sample size and variability	
High	Sample size is reported and large enough (*i.e.*, ≥ 10 samples) to be reasonably assured that the samples represent the scenario of interest. **AND** Replicate tests performed and variability across tests is characterized (if appropriate).
Medium	Sample size is moderate (*i.e.*, 5 to ~~10~~ <10 samples), thus the data are likely to represent the scenario of interest. **AND** Replicate tests performed and variability across tests is characterized (if appropriate).
Low	Sample size is small (*i.e.*, <5 samples), thus the data are likely to poorly represent the scenario of interest. **AND/OR** Replicate tests were not performed.
Critically deficient	Sample size is not reported, **AND/OR** Single sample collected per data set, except for experiments to determine a weight fraction or concentration in a product. **AND/OR** For biomonitoring studies, the timing of sample collected is not appropriate based on chemical properties (*e.g.*, half-life), the pharmacokinetics of the chemical (*e.g.*, rate of uptake and elimination), and when the exposure event occurred.
Not rated/not applicable	

Data Quality Rating	Metric Description
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 6. Temporality	
High	Source(s) of tested items appears to be current (within 5 years).
Medium	Source(s) of tested items is less consistent with when current or recent exposures (>5 to 15 years) are expected.
Low	Source(s) of tested items is not consistent with when current or recent exposures (>15 years) are expected or is not identified.
Critically deficient	Temporality of tested items is not reported, discussed, or referenced.
Not rated/not applicable	
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Domain 3. Accessibility/clarity	
Metric 7. Reporting of results	
High	Supplementary or raw data (*i.e.*, individual data points) are reported, allowing summary statistics to be calculated or reproduced. **AND** Summary statistics are detailed and complete. Example parameters include: • Description of data set summarized (*i.e.*, location, population, dates, etc.) • Range of concentrations or percentiles • Number of samples in data set • Frequency of detection • Measure of variation (CV, standard deviation) • Measure of central tendency (mean, geometric mean, median) • Test for outliers (if applicable) **AND** Both adjusted and unadjusted results are provided (*i.e.*, correction for void completeness in urine biomonitoring, whole-volume or lipid adjusted for blood biomonitoring) (only if applicable)
Medium	Supplementary or raw data (*i.e.*, individual data points) are not reported, and therefore summary statistics cannot be reproduced. **AND/OR** Summary statistics are reported but are missing one or more parameters (see description for high). **AND/OR** Only adjusted or unadjusted results are provided, but not both (only if applicable)
Low	Supplementary data are not provided, and summary statistics are missing most parameters (see description for high).

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

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

5.4.1.3 Data Evaluation Criteria for Databases, as Revised

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

Data Quality Rating	Description
Domain 1. Reliability	
Metric 1. Sampling methodology	
High	Widely accepted sampling methodologies (*i.e.,* from a source generally known to use ~~using~~ sound methods and/or approaches) were used to generate the data presented in the database. Example SOPs include USGS's "National Field Manual for the Collection of Water-Quality Data," EPA's "Ambient Air Sampling" (SESDPROC-303-R5), etc.
Medium	One or more pieces of sampling methodology information is not described, but missing information is unlikely to have a substantial impact on results. **OR** The sampling methodologies were consistent with sound scientific theory and/or accepted approaches based on the reported sampling information but may not have followed published procedures from a source generally known to use sound methods and/or approaches.
Low	The sampling methodology was not reported in data source or readily available companion data source.
Critically deficient	The sampling methodologies used were not appropriate for the chemical/media of interest in the database (*e.g.*, inappropriate sampling equipment, improper storage conditions).
Not rated/not applicable	
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 2. Analytical methodology	
High	Widely accepted analytical methodologies (*i.e.,* from a source generally using sound methods and/or approaches) were used to generate the data presented in the database. Example SOPs include EPA SW-846 Methods, NIOSH Manual of Analytical Methods 5th Edition, etc.
Medium	The analytical methodologies were consistent with sound scientific theory and/or accepted approaches based on the reported analytical information but may not have followed published procedures from a source generally known to use sound methods and/or approaches.
Low	The analytical methodology was not reported in data source or companion data source.
Critically deficient	The analytical methodologies used were not appropriate for the chemical/media of interest in the database (*e.g.*, method not sensitive enough, not specific to the chemical, out of date).
Not rated/not applicable	

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

Data Quality Rating	Description
	• Method of application or by-stander exposure • Use of exposure controls • Microenvironment (location, time, climate)
Medium	The data likely represent the relevant exposure scenario (*i.e.*, population/scenario/media of interest). **One or more key pieces of information may not be described** but the deficiencies are unlikely to have a substantial impact on the characterization of the exposure scenario. **AND/OR** If surrogate data, activities seem similar to the activities within scope.
Low	The data lack multiple key pieces of information, and the deficiencies are likely to have a substantial impact on the characterization of the exposure scenario. **AND/OR** There are **some inconsistencies or possible errors** in the reporting of scenario information (*e.g.*, differences between text and tables in data source, differences between standard method and actual procedures reported to have been used, etc.) which leads to a lower confidence in the scenario assessed. **AND/OR** If surrogate data, activities have lesser similarity but are still potentially applicable to the activities within scope.
Critically deficient	If reported, the exposure scenario discussed in the monitored study does not represent the exposure scenario of interest for the chemical.
Not rated/not applicable	
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Domain 3. Accessibility/clarity	
Metric 6. Availability of database and supporting documents	
High	Database is widely accepted and/or from a source generally known to use sound methods and/or approaches (*e.g.*, raw data from NHANES, STORET).
Medium	The database may not be widely known or accepted (*e.g.*, state-maintained databases), but the database is adequately documented with most or all of the following information: 1. Within the database, metadata is present (sample identifiers, annotations, flags, units, matrix descriptions, etc.) and-data fields are generally clear and defined. 2. A user manual and other supporting documentation is available, or there is sufficient documentation in the data source or companion source. Database quality assurance and data quality control measures are defined and/or a QA/QC protocol was followed.
Low	The database may not be widely known or accepted, and only limited database documentation is available (see the medium rating).

Data Quality Rating	Description
Critically deficient	No information is provided on the database source or availability to the public.
Not rated/not applicable	
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 7. Reporting of results	
High	The database or information source reporting the analysis of the database data is well organized and understandable by the target audience. **AND** Summary statistics in the data source are detailed and complete. Example parameters include: • Description of data set summarized (*i.e.*, location, population, dates, etc.) • Range of concentrations or percentiles • Number of samples in data set • Frequency of detection • Measure of variation (CV, standard deviation) • Measure of central tendency (mean, geometric mean, median) • Test for outliers (if applicable)
Medium	The database or information source reporting the analysis of the database data is well organized and understandable by the target audience. **AND/OR** Summary statistics are missing one or more parameters (see description for high).
Low	The database or information source reporting the analysis of the database data is unclear or not well organized. **AND/OR** Summary statistics are missing most parameters (see description for high) **AND/OR** There are some inconsistencies or errors in the results reported, resulting in low confidence in the results reported (*e.g.*, differences between text and tables in data source, less appropriate statistical methods).
Critically deficient	There are numerous inconsistencies or errors in the calculation and/or reporting of results, resulting in highly uncertain reported results. **AND/OR** The information source reporting the analysis of the database data is missing key sections or lacks enough organization and clarity to locate and extract necessary information.
Not rated/not applicable	
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*

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

5.5 Environmental and Human Health Hazard

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

- *Data Quality Evaluation Information for Environmental Hazard Risk Evaluation for Asbestos Part 2 - Supplemental Including Legacy Uses and Associated Disposal of Asbestos - Systematic Review Support Document for the Risk Evaluation* (U.S. EPA, 2024f)

- *Data Quality Evaluation Information for Human Health Hazard Epidemiology Risk Evaluation for Asbestos Part 2 - Supplemental Including Legacy Uses and Associated Disposal of Asbestos - Systematic Review Support Document for the Risk Evaluation:* (U.S. EPA, 2024h)
- *Data Extraction Information for Environmental Hazard and Human Health Hazard Animal Toxicology and Epidemiology Risk Evaluation for Asbestos Part 2 - Supplemental Including Legacy Uses and Associated Disposal of Asbestos - Systematic Review Support Document for the Risk Evaluation* (U.S. EPA, 2024a)

5.5.1 Environmental Hazard

As described in Appendix R and Section 6.4.1 of the 2021 Draft Systematic Review Protocol, references that met PECO screening criteria at full text screening underwent data quality evaluation (U.S. EPA, 2021). One clarification regarding the extraction of environmental hazard data is that all of the extracted data, except those with confidential business information claims, will also be available in the ECOTOX Knowledgebase, which also contains the extracted publicly available information.

5.5.2 Human Health Hazard

5.5.2.1 Epidemiology Studies

As described above in Section 4.6.2, to better identify dose-response information for the Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2024i), all references containing epidemiological information that met PECO screening criteria during full-text screening were grouped by cohort and underwent an additional further filtering screening step. Individual references or cohort groups of references that met the further filtering screening criteria then proceeded to data quality evaluation. Data quality evaluation includes consideration of 22 different metrics that are rated as high, medium, low, or critically deficient based on pre-defined criteria presented below in Table 5-4 and Table 5-5 below. The assessment of each of the metrics contributes to an overall quality determination (OQD) of high, medium, low, or critically deficient. Cohorts with an OQD of medium or high proceeded to data extraction and were further considered for dose-response assessment.

One update to the data quality evaluation process used for data sources containing epidemiological data as described in Appendix R of the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021) is that for the Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2024i) the data quality evaluation criteria were based on the data quality evaluation criteria used for epidemiological information in the Risk Evaluation Asbestos Part 1 (U.S. EPA, 2020). The epidemiology data quality evaluation criteria described in Appendix R of the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021) serves as a general template for data quality evaluation criteria for epidemiological studies, but those used for Risk Evaluation Asbestos Part 1 (U.S. EPA, 2020) contained several asbestos-specific modifications, including the use of separate data quality evaluation forms to specifically address mesothelioma and lung cancer-related considerations (*e.g.*, mesothelioma has a longer latency period and therefore more stringent criteria for Metric 6: Temporality, because a longer study follow-up time is required to detect mesothelioma cases. Therefore, it was more appropriate and efficient to update the data quality evaluation criteria used for the Risk Evaluation Asbestos Part 1 (U.S. EPA, 2020) to conduct data quality evaluation for references containing epidemiological data for the Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2024i).

The data quality evaluation criteria used for the consideration of epidemiological data considered for the Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2024i) are described below in Table 5-4 and Table 5-5. Specifically, the Mesothelioma Data Quality Evaluation Form used in the Risk Evaluation Asbestos Part 1 (U.S. EPA, 2020) was appropriate for the evaluation of mesothelioma for the Risk Evaluation for

Asbestos Part 2 (U.S. EPA, 2024i) because the form includes criteria that address mesothelioma-specific characteristics (*e.g.*, rare disease with a long latency period and few known causes other than asbestos and thus few potential confounders). The Lung Cancer Data Quality Evaluation Form from the Risk Evaluation Asbestos Part 1 (U.S. EPA, 2020) was used as a template and modified to develop the Other Outcomes Data Quality Evaluation Form (Table 5-5) for the Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2024i), which addresses all non-cancer outcomes and all cancer outcomes other than mesothelioma, because many of the data quality evaluation criteria are applicable to all health outcomes. For aspects of the criteria from the Risk Evaluation Asbestos Part 1 (U.S. EPA, 2020) that were lung-cancer specific, modifications were made to address the additional cancer and non-cancer outcomes, including deleting the term "lung cancer" from the criteria for high and low for Metric 8. For Metric 6: Temporality, the latency period of other outcomes was considered, and although there is variation in latency within and between outcomes, the criteria from the lung cancer form were maintained for other outcomes because the latencies for lung cancer and other outcomes are generally shorter than for mesothelioma. Metric 7 (Outcome measurement or characterization) was substantially expanded to address the specific measurement methods for different outcomes such that each of the following outcome categories had their own distinct Metric 7 criteria: lung cancer, ovarian cancer, laryngeal cancer, other cancer(s), asbestosis, pulmonary function/spirometry results, pleural plaques, and other non-cancer outcomes. The criteria for each of those outcomes were developed specifically as new additions for Asbestos the Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2024i).

To clarify the interpretation of metric language and ensure consistency between reviewers, on both the Mesothelioma and Other Outcomes forms, minor wording changes were made on the criteria for low for Metric 1, the criteria for medium for Metric 11, the criteria for medium for Metric 14, and the criteria for low for Metric 15; and a note was added under Domain 4 (the Potential confounding/Variable control Domain) to clarify which aspects of confounding fit into each of the metrics (Metrics 9, 10, and 11) within Domain 4. Also, for clarification of metric language, on the Other Outcomes Form minor wording changes were made to the criteria for low for Metric 6 and the criteria for high for Metric 10; and on the Mesothelioma form minor wording changes were made to Metrics 3, 4, 13, 14, and 15. Additionally, during calibration trainings, data quality evaluation criteria were updated in both the Mesothelioma and the Other Outcomes forms to ensure consistency between assessors in interpreting the criteria. For Metric 2, in the criteria for high the "AND" was changed to an "OR" for the bullet point about imputation because imputation is one of several methods that can be used to adequately address missing data or subject attrition as described in the "NOTE for all study types" under the criteria for high. For Metric 3, "OR If there is substantial potential for healthy worker effect" was added to the criteria for medium to address the healthy worker effect, which occurs due to differences between groups and may bias study results towards the null hypothesis of no association between exposure and outcome. For Metric 4, "OR The method of quantifying/counting fibers was not specified (PCM, TEM, or other method not specified)" was added to the criteria for low to address situations when there are insufficient details reported within a reference (including within cited methods papers) regarding exposure methods. For Metric 9, during calibration reviewers were unclear on the decreasing stringency between the criteria for high, medium, and low, so the wording of the criteria for medium and low were changed so that the criteria for high, medium, and low require appropriate adjustment, stratification, or consideration of three, two, or one demographic variables, respectively. A note was added under Metric 10 stating that "for occupational studies, it can be assumed that personnel records were used to obtain covariate data if not otherwise specified" because the consensus among reviewers was that this was a reasonable assumption. In Metric 12, the "AND" in the criteria for medium was changed to an "OR" to make the medium category more inclusive because the only options that may be selected for Metric 12 are medium and critically deficient.

Additionally, on the Mesothelioma form, for Metric 5, the criteria for Not Rated/Not Applicable were deleted and changed to "Do not select for this metric," ensuring this metric would have a rating for all references. On the mesothelioma form, "For mesothelioma studies, evaluations of potential confounders are not required as there are few other causes of mesothelioma (zeolites, viruses, therapeutic or diagnostic radiation) and none that are likely to be correlated in a dose-dependent manner with asbestos. Evaluation of potential confounding in mesothelioma studies should be labeled as 'Not rated/applicable'" was moved from the criteria for Not Applicable for Metric 9 to the criteria for Not Applicable for Metric 11, and the clause "unless there is substantial information to indicate otherwise" was added, because Metric 11 addresses co-exposures such as zeolites, viruses, radiation, etc. whereas Metric 9 addresses covariates other than co-exposures. The criteria for Not Applicable (NA) for Metric 9 were replaced with "Rate this metric as NA if no analyses of the association between exposure and outcome were performed or if there are no potential confounders" because in some studies there might be potential confounders; although there are few other known causes of mesothelioma, substantial differences in some covariates such as demographic variables still could be associated with differences in exposure to asbestos as well as differences in risk of mesothelioma due to differences in known or unknown susceptibility or exposure (*e.g.*, zeolites, viruses, radiation) factors.

Some references contain multiple health outcomes, therefore, a given reference may have multiple data quality evaluation forms and respective overall quality determinations (OQDs). The data evaluation criteria for mesothelioma and other health outcomes are presented below in Table 5-4 and Table 5-5, respectively. To make it easier for the reader to see changes made to the data quality evaluation criteria from the Risk Evaluation Asbestos Part 1 (U.S. EPA, 2020) to the Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2024i), the following conventions are used: text inserted is underlined, and text deleted is in ~~strikethrough~~. Finally, another update from the data extraction process described in Section 6.4 of the 2021 Draft Systematic Review Protocol is that for data sources containing epidemiological data, data extraction was only performed for cohorts with an OQD of medium or high (U.S. EPA, 2021).

Table 5-4. Data Quality Evaluation Criteria for Mesothelioma for Asbestos Part 2

Data Quality Rating	Description
Domain 1. Study participation	
Metric 1. Participant selection (selection, performance biases)	
High	***For all study types*:** All key elements of the study design are reported (*e.g.*, setting, participation rate described at all steps of the study, inclusion and exclusion criteria, and methods of participant selection or case ascertainment). **AND** The reported information indicates that selection in or out of the study (or analysis sample) and participation was not likely to be biased (*i.e.*, the exposure-outcome distribution of the participants is likely representative of the exposure-outcome distributions in the population of persons eligible for inclusion in the study).
Medium	***For all study types:*** Some key elements of the study design were not present but available information indicates a low risk of selection bias (*i.e.*, the exposure-outcome distribution of the participants is likely representative of the exposure outcome distributions in the population of persons eligible for inclusion in the study).

Data Quality Rating	Description
Low	***For all study types:*** Key elements of the study design and information on the population (*e.g.*, setting, participation rate described at most steps of the study, inclusion and exclusion criteria, and methods of participant selection or case ascertainment) are not reported (Strengthening the reporting of observational studies in epidemiology [STROBE] checklist 4, 5 and 6 (Von Elm et al., 2008)). If the study provides little to no information about selection criteria, then rate this metric as Low.
Critically deficient	***For all study types:*** The reported information indicates that selection in or out of the study (or analysis sample) and participation was likely to be significantly biased (*i.e.*, the exposure-outcome distribution of the participants is likely not representative of the exposure-outcome distributions of the population of persons eligible for inclusion in the study).
Not rated/not applicable	Do not select for this metric
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 2. Attrition (missing data/attrition/exclusion, reporting biases)	
High	***For cohort studies:*** There was minimal subject loss to follow up during the study (or exclusion from the analysis sample) and outcome and exposure data were largely complete. **OR** Loss of subjects (*e.g.*, incomplete outcome data) or missing exposure and outcome data was adequately addressed (as described below) and reasons were documented when human subjects were removed from a study (NTP, 2015). **OR** ~~**AND**~~ Missing data have been imputed using appropriate methods (*e.g.*, multiple imputation methods), and characteristics of subjects lost to follow up or with unavailable records are not significantly different from those of the study participants (NTP, 2015). ***For case-control studies and cross-sectional studies:*** There was minimal subject withdrawal from the study (or exclusion from the analysis sample) and outcome data and exposure were largely complete. **OR** Any exclusion of subjects from analyses was adequately addressed (as described below), and reasons were documented when subjects were removed from the study or excluded from analyses (NTP, 2015). ***NOTE for all study types:*** Adequate handling of subject attrition can include: Use of imputation methods for missing outcome and exposure data; reasons for missing subjects unlikely to be related to outcome (for survival data, censoring was unlikely to introduce bias); missing outcome data balanced in numbers across study groups, with similar reasons for missing data across groups.

Data Quality Rating	Description
Medium	***For cohort studies:*** There was moderate subject loss to follow up during the study (or exclusion from the analysis sample) or outcome and exposure data were nearly complete. **AND** Any loss or exclusion of subjects was adequately addressed (as described in the acceptable handling of subject attrition in the high confidence category) and reasons were documented when human subjects were removed from a study. ***For case-control studies and cross-sectional studies:*** There was moderate subject withdrawal from the study (or exclusion from the analysis sample), but outcome and exposure data were largely complete. **AND** Any exclusion of subjects from analyses was adequately addressed (as described above), and reasons were documented when subjects were removed from the study or excluded from analyses (NTP, 2015).
Low	***For cohort studies:*** The loss of subjects (*e.g.*, loss to follow up, incomplete outcome or exposure data) was moderate and unacceptably handled (as described below in the unacceptable confidence category) (Source: OHAT). **OR** Numbers of individuals were not reported at important stages of study (*e.g.*, numbers of eligible participants included in the study or analysis sample, completing follow-up, and analyzed). Reasons were not provided for non-participation at each stage (STROBE Checklist Item 13 (Von Elm et al., 2008)). ***For case-control and cross-sectional studies:*** The exclusion of subjects from analyses was moderate and unacceptably handled (as described below in the unacceptable confidence category). **OR** Numbers of individuals were not reported at important stages of study (*e.g.*, numbers of eligible participants included in the study or analysis sample, completing follow-up, and analyzed). Reasons were not provided for non-participation at each stage (STROBE Checklist Item 13 (Von Elm et al., 2008)).
Critically deficient	***For cohort studies:*** There was large subject attrition during the study (or exclusion from the analysis sample). **OR** Unacceptable handling of subject attrition: reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across study groups; or potentially inappropriate application of imputation (Source: OHAT). ***For case-control and cross-sectional studies:*** There was large subject withdrawal from the study (or exclusion from the analysis sample). **OR** Unacceptable handling of subject attrition: reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across study groups; or potentially inappropriate application of imputation.

Data Quality Rating	Description
Not rated/not applicable	Do not select for this metric.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 3. Comparison group (selection, performance biases) (see special instructions for mesothelioma studies in "Not rated/applicable")	
High	***For ALL study types:*** Any differences in baseline characteristics of groups were considered as potential confounding or stratification variables and were thereby controlled by statistical analysis (Source: OHAT). **OR** ***For cohort and cross-sectional studies:*** Key elements of the study design are reported (*i.e.*, setting, inclusion and exclusion criteria, and methods of participant selection), and indicate that groups were similar (*e.g.*, recruited from the same eligible population with the same method of ascertainment and within the same time frame using the same inclusion and exclusion criteria, and were of similar age and health status) (NTP, 2015). ***For case-control studies:*** Key elements of the study design are reported indicate that cases and controls were similar (*e.g.*, recruited from the same eligible population with the number of controls described, and eligibility criteria and are recruited within the same time frame (NTP, 2015). ***For studies reporting Standardized Mortality Ratios (SMRs) or Standardized Incidence Ratios (SIRs):*** Age, sex (if applicable), race (if applicable), and calendar time adjustment or stratification is described and choice of reference population (*e.g.*, general population) is reported.
Medium	***For cohort studies and cross-sectional studies:*** There is only indirect evidence (*e.g.*, stated by the authors without providing a description of methods) that groups are similar (as described above for the high confidence rating). **OR** If there is substantial potential for healthy worker effect. ***For case-control studies:*** There is indirect evidence (*i.e.*, stated by the authors without providing a description of methods) that cases and controls are similar (as described above for the high confidence rating). ***For studies reporting SMRs or SIRs:*** Age, sex (if applicable), race (if applicable), and calendar time adjustment or stratification is not specifically described (*i.e.*, indirect evidence) in the text, but results tables are stratified by age, sex (if applicable), race (if applicable); choice of reference population (*e.g.*, general population) is reported.
Low	***For cohort and cross-sectional studies:*** There is indirect evidence (*i.e.*, stated by the authors without providing a description of methods) that groups were not similar (as described above for the high confidence rating). **AND**

Data Quality Rating	Description
	Differences between the exposure groups are not adequately controlled for in the statistical analysis. ***For case-control studies:*** There is indirect evidence (*i.e.*, stated by the authors without providing a description of methods) that cases and controls were not similar (as described above for the high confidence rating). **AND** The characteristics of cases and controls are not reported (Source: (NTP, 2015)). **AND** Differences in groups is not adequately controlled for in the statistical analysis. ***For studies reporting SMRs or SIRs:*** Indirect evidence of a lack of adjustment or stratification for age, sex (if applicable), race (if applicable), and calendar time; or indirect evidence that choice of reference population (*e.g.*, general population) is inappropriate.
Critically deficient	***For cohort studies:*** Subjects in all exposure groups were not similar. **OR** Information was not reported to determine if participant groups were similar (STROBE Checklist 6 (Von Elm et al., 2008)). **AND** Potential differences in exposure groups were for a factor that was related to the outcome and not controlled for in the statistical analysis. **OR** Subjects in the exposure groups had very different participation/response rates (NTP, 2015). **AND** Participation rates were related to exposure and outcome. ***For case-control studies:*** Controls were drawn from a very dissimilar population than cases or recruited within very different time frames (NTP, 2015). **AND** Potential differences in the case and control groups were not controlled for in the statistical analysis. **OR** Rationale and/or methods for case and control selection, matching criteria including number of controls per case (if relevant) were not reported (STROBE Checklist 6 (Von Elm et al., 2008). ***For cross-sectional studies:*** Subjects in all exposure groups were not similar, recruited within very different time frames, or had very different participation/response rates (NTP, 2015). **AND** Potential differences in exposure groups were not controlled for in the statistical analysis. **OR** Sources and methods of selection of participants in all exposure groups were not reported (STROBE Checklist 6 (Von Elm et al., 2008)).

Data Quality Rating	Description
	For studies reporting SMRs or SIRs: Lack of adjustment or stratification for both age, sex (if applicable), race (if applicable), and calendar time; or choice of reference population (*e.g.*, general population) is not reported.
Not rated/not applicable	For mesothelioma studies, a comparison population is not required, as EPA's interest is in the absolute risk and not the relative risk. All studies of mesothelioma allowing for evaluation of absolute risk should be labeled as "Not rated / not applicable". Only rate as N/A if there is no mesothelioma comparison group. Otherwise, if the study includes a comparison group, rate this metric High, Medium, Low, or Critically Deficient.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Domain 2. Exposure characterization	
Metric 4. Measurement of exposure (Detection/measurement/information, performance biases) If exposure was estimated solely using professional judgement, then rate this Metric as Low. Even if this metric is rated as Critically Deficient due to a lack of quantitative exposure estimates, please note in the comments field whether the study might be useful qualitatively.	
High	***For all study types:*** Quantitative estimates of exposure were consistently assessed (*i.e.*, using the same method and sampling time-frame) during multiple time periods and using either PCM or TEM. **OR** A combination of methods were used over time (*i.e.*, midget impinger, PCM or TEM), but side by side sampling and analyses were conducted to develop appropriate conversion criteria. **AND** For an occupational population, contains detailed employment records and quantitative estimates of exposure using either PCM or TEM which allows for construction of job-matrix for entire work history of exposure (*i.e.*, cumulative or peak exposures, and time since first exposure).
Medium	***For all study types:*** Exposure was assessed during one time period but this time period is judged to be reasonably representative of the entire study time period. **AND** Exposure was assessed using a combination of midget impingers, PCM and/or TEM measurements, but side by side sampling and analyses were not conducted for all operations and thus there is a lack of confidence in the conversion factors. **OR** For an occupational study population, contains detailed employment records and quantitative estimates of exposure using a combination of midget impingers and PCM or TEM for only a portion of participant's work history of exposure (*i.e.*, only early years or later years), such that extrapolation of the missing years is required.
Low	***For all study types:*** Exposure was estimated solely using professional judgement. **OR** The method of quantifying/counting fibers was not specified.

Data Quality Rating	Description
	OR Exposure was directly measured (*e.g.*, midget impinger) and assessed using a quantitative method other than PCM or TEM and conversion factors were not determined.
Critically deficient	***For all study types:*** There was no quantitative measure or estimate of exposure. **OR** Methods used to quantify the exposure were not well defined, and sources of data and detailed methods of exposure assessment were not reported (STROBE Checklist 7 and 8 (Von Elm et al., 2008)). **OR** There is evidence of substantial exposure misclassification that would significantly bias the results.
Not rated/not applicable	Do not select for this metric.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 5. Exposure levels (Detection/measurement/information biases)	
High	Do not select for this metric.
Medium	***For all study types:*** The range and distribution of exposure is sufficient or adequate to develop an exposure-response estimate (Cooper et al., 2016).
Low	***For all study types:*** The range of exposure in the population is limited.
Critically deficient	Do not select for this metric.
Not rated/not applicable	Do not select for this metric. ~~***For all study types:***~~ ~~The range and distribution of exposure are not sufficient or adequate to determine an exposure-response relationship (Cooper et al., 2016).~~ ~~**OR**~~ ~~No description is provided on the levels or range of exposure.~~
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 6. Temporality	
High	***For all study types:*** The study presents an appropriate temporality between exposure and outcome (*i.e.*, the exposure precedes the disease).

Data Quality Rating	Description
	AND The interval between the exposure (or reconstructed exposure) and the outcome is sufficiently long considering the latency of the disease (*i.e.*, study follow-up is more than 20 years for mesothelioma) (LaKind et al., 2014).
Medium	***For all study types:*** Temporality is established, but it is unclear whether there is adequate follow-up for consideration of latency (*i.e.*, only 15-20 years of follow-up) (LaKind et al., 2014).
Low	***For all study types:*** The temporality of exposure and outcome is uncertain (10-15 years). **OR** There is inadequate follow-up of the cohort considering the latency period.
Critically deficient	***For all study types:*** Study lacks an established time order, such that exposure is not likely to have occurred prior to outcome (LaKind et al., 2014). **OR** There was inadequate follow-up of the cohort for the expected latency period (<10 years). **OR** Sources of data and details of methods of assessment were not sufficiently reported (*e.g.*, duration of follow-up, periods of exposure, dates of outcome ascertainment, etc.) Source: STROBE Checklist 8 (Von Elm et al., 2008).
Not rated/not applicable	Do not select for this metric.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Domain 3. Outcome assessment	
Metric 7. Outcome measurement or characterization (detection/measurement/information, performance, reporting biases)	
High	***For all study types:*** The outcome was assessed using one or a combination of the following well-established methods: o Mesothelioma cases confirmed by histological or cytological means (including subtypes of mesothelioma) and/or o ICD-10 codes (3 digit) C45 or (4 digit) C45.x (C45.0, C45.1, C45.2, C45.7, C45.9) o All fields on the death certificates of cohort searched for 'mesothelioma' o o Appropriate Pre-ICD 10 codes supplemented by additional evidence (*e.g.*, pathology/autopsy) see Table 1 of (Kopylev et al., 2011).
Medium	***For all study types:*** Examined death certificates searched for mesothelioma for pre-ICD-10 codes that include pleura, peritoneum and site unspecified (ICD code 199).
Low	Do not select for this metric.

Data Quality Rating	Description
Critically deficient	***For all study types:*** Numbers of outcome events or summary measures were not reported (Source: STROBE Checklist 15 (Von Elm et al., 2008). **OR** Only pre ICD-10 codes (without additional information) were used for ascertainment of mesothelioma. **OR** Examined death certificates searched for mesothelioma for codes that included only pleura and/or peritoneum. **OR** Study lacks individual assessment of mesothelioma (*i.e*, mesothelioma is assessed as a combination with other cancer types, excluding lung and bronchus or trachea). **OR** Any self-reported information.
Not rated/not applicable	Do not select for this metric.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 8. Reporting Bias	
High	***For all study types:*** Mesothelioma findings are reported in the abstract, results or discussion. Effect estimates are reported with confidence intervals and/or standard errors, number of cases/controls or exposed/unexposed reported for each analysis, to be included in exposure response analysis or fully tabulated during data extraction and analyses (NTP, 2015).
Medium	***For all study types:*** All of the study's findings (primary and secondary) outlined in the abstract, results or discussion (that are relevant for the evaluation) are reported, but not in a way that would allow for detailed extraction (*e.g.*, results were discussed in the text but accompanying data were not shown).
Low	***For all study types:*** Mesothelioma outcomes outlined in the methods, abstract, and/or introduction (that are relevant for the evaluation) have not been reported (NTP, 2015).
Critically deficient	Do not select for this metric.
Not rated/not applicable	Do not select for this metric.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*

Data Quality Rating	Description
Domain 4. Potential confounding/Variable control Notes: • Smoking fits in Metrics 9 and 10, not Metric 11. • Metric 9 addresses whether there was appropriate adjustment or consideration of confounders (such as stratification) (other than co-exposures). • Metric 10 addresses how the potential confounders (other than co-exposures) were measured. • Metric 11 assesses co-exposure confounding.	
Metric 9. Covariate adjustment (confounding) (see special instructions for mesothelioma studies in "Not rated/applicable")	
High	***For all study types:*** Appropriate adjustments or explicit considerations were made for potential confounders (*e.g.*, age, sex, SES, race, etc.) (excluding co-exposures, which are evaluated in metric 11) in the final analyses through the use of statistical models to reduce research-specific bias, including matching, adjustment in multivariate models, stratification, or other methods that were appropriately justified (NTP, 2015). ***For Studies reporting SMRs or SIRs:*** Adjustments are described and results are age-, race-, and sex-adjusted (or stratified) if applicable.
Medium	***For all study types:*** There is indirect evidence that appropriate adjustments were made (*i.e.*, considerations were made for primary covariates (excluding co-exposures) and potential confounders adjustment) without providing a description of methods. **OR** The distribution of potential confounders (excluding co-exposures) did not differ significantly between exposure groups or between cases and controls. **OR** The major potential confounders (excluding co-exposures) were appropriately adjusted and any not adjusted for are considered not to appreciably bias the results (*e.g.*, smoking rates in an occupational cohort are expected to be generally similar in different departments and thus confounding by smoking is unlikely when internal analyses are applied). ***For Studies reporting SMRs or SIRs:*** Results are adjusted (or stratified) for age and sex, unless adjustment or stratification is not necessary because the exposed and control groups are sufficiently similar on the particular demographic variable. ~~Indirect evidence that results are age, sex-, and race-adjusted (or stratified) if applicable.~~
Low	***For all study types:*** There is indirect evidence (*i.e.*, no description is provided in the study) that considerations were not made for potential confounders adjustment in the final analyses (NTP, 2015). **AND** The distribution of primary covariates (excluding co-exposures) and potential confounders was not reported between the exposure groups or between cases and controls (NTP, 2015). ***For Studies reporting SMRs or SIRs:***

Data Quality Rating	Description
	~~Results are age-, race-, OR sex adjusted (or stratified) if applicable (*i.e.*, if 2 or all should have been adjusted).~~ Results are adjusted or stratified for age, race, OR sex (any one of the three), unless adjustment or stratification is not necessary because the exposed and control groups are sufficiently similar on the particular demographic variable.
Critically deficient	***For all study types:*** The distribution of potential confounders differed significantly between the exposure groups. **AND** Confounding was demonstrated and was not appropriately adjusted for in the final analyses (NTP, 2015). ***For Studies reporting SMRs or SIRs:*** No discussion of adjustments. Results are not adjusted for age, sex, and race (or stratified) if applicable.
Not rated/not applicable	Rate this metric as NA if no analyses of the association between exposure and outcome were performed or if there are no potential confounders. ~~For mesothelioma studies, evaluations of potential confounders are not required as there are few other causes of mesothelioma (zeolites, viruses, therapeutic or diagnostic radiation) and none that are likely to be correlated in a dose-dependent manner with asbestos. Evaluation of potential confounding in mesothelioma studies should be labeled as "Not rated/applicable".~~
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 10. Covariate characterization (measurement/information, confounding biases) (see special instructions for mesothelioma studies in "Not rated/applicable") For occupational studies, it can be assumed that personnel records were used to obtain covariate data if not otherwise specified.	
High	***For all study types:*** Potential confounders (*e.g.*, age, sex, SES, race, etc.) were assessed using valid and reliable methodology where appropriate (*e.g.*, validated questionnaires, biomarker).
Medium	***For all study types:*** A less-established method was used to assess confounders (excluding co-exposures) and no method validation was conducted against well-established methods, but there was little to no evidence that that the method had poor validity and little to no evidence of confounding.
Low	***For all study types:*** The confounder assessment method is an insensitive instrument or measure or a method of unknown validity.
Critically deficient	***For all study types:*** Confounders were assessed using a method or instrument known to be invalid.
Not rated/not applicable	Covariates were not assessed. **OR** Metric 9 is rated "Not applicable".

Data Quality Rating	Description
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 11. Co-exposure reliability (measurement/information, confounding biases) (see special instructions for mesothelioma studies in "Not rated/applicable")	
High	Do not select for this metric.
Medium	***For all study types:*** Any co-exposures to pollutants that are not the target exposure that would likely bias the results were not likely to be present. **OR** Co-exposures to pollutants were appropriately measured or either directly or indirectly adjusted for. Example: There is confirmation of the likely absence of known co-exposures via mechanisms such as engineering controls (closed systems) for co-pollutants or confirmation of the absence of co-pollutants through monitoring.
Low	***For cohort and cross-sectional studies:*** There is direct evidence that there was an unbalanced provision of additional co-exposures across the primary study groups, which were not appropriately adjusted for. ***For case-control studies:*** There is direct evidence that there was an unbalanced provision of additional co-exposures across cases and controls, which were not appropriately adjusted for, and significant indication a biased exposure-outcome association. **OR** ***For all study types:*** In an occupational setting, potential co-exposures are not discussed.
Critically deficient	Do not select for this metric.
Not rated/not applicable	For mesothelioma studies, evaluations of potential confounders are not required as there are few other causes of mesothelioma (zeolites, viruses, therapeutic or diagnostic radiation) and none that are likely to be correlated in a dose-dependent manner with asbestos. Evaluation of potential confounding in mesothelioma studies should be labeled as "Not rated/applicable" unless there is substantial information to indicate otherwise. ~~For mesothelioma, there are no established risk factors other than exposure to asbestos, therefore no known co-exposures are of concern. Enter 'NA' and do not score this metric.~~
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Domain 5. Analysis	
Metric 12. Study design and methods	
High	Do not select for this metric.

Data Quality Rating	Description
Medium	***For all study types:*** The study design chosen was appropriate for the research question. ~~**AND**~~ **OR** The study uses an appropriate statistical method to address the research question(s) (*e.g.*, Cox and Poisson regression for cohort studies, logistic regression analysis for case-control studies.
Low	Do not select for this metric.
Critically deficient	***For all study types:*** The study design chosen was not appropriate for the research question.
Not rated/not applicable	Do not select for this metric.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 13. Statistical power (sensitivity) (see special instructions for mesothelioma studies in "Not rated/applicable")	
High	Do not select for this metric.
Medium	***For cohort and cross-sectional studies:*** The number of participants is adequate to detect an effect in the exposed population and/or subgroups of the total population. **OR** The paper reported statistical power high is enough (≥ 80%) to detect an effect in the exposure population and/or subgroups of the total population. ***For case-control studies:*** The number of cases and controls are adequate to detect an effect in the exposed population and/or subgroups of the total population. **OR** The paper reported statistical power was high enough (≥ 80%) to detect an effect in the exposure population and/or subgroups of the total population.
Low	Do not select for this metric.
Critically deficient	***For cohort and cross-sectional studies:*** The number of participants is inadequate to detect an effect in the exposed population and/or subgroups of the total population and the study was negative. ***For case-control studies:*** The number of cases and controls are inadequate to detect an effect in the exposed population and/or subgroups of the total population and the study was negative.
Not rated/not applicable	For mesothelioma, EPA is primarily interested in the presentation of data collected in the study, rather than the statistical analysis. EPA will pool data across asbestos studies to conduct for the analysis of mesothelioma risk. Therefore, the power of individual studies will not be considered. This metric may be marked as not rated/applicable.

Data Quality Rating	Description
	Mark as N/A if there were no statistical analyses or models for mesothelioma. If no analyses were performed because (whether stated or implied) there wasn't sufficient statistical power to do analyses, be sure to note this in the comments.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 14. Reproducibility of analyses (adapted from (Blettner et al., 2001)) (see special instructions for mesothelioma studies in "Not rated/applicable")	
High	Do not select for this metric.
Medium	***For all study types:*** The description of the analysis is sufficient to understand how to conceptually reproduce the analysis with access to the analytic data. ~~The description of the analysis is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.~~
Low	***For all study types:*** The description of the analysis is insufficient to understand what has been done and to be reproducible OR a description of analyses are not present (*e.g.*, statistical tests and estimation procedures were not described, variables used in the analysis were not listed, transformations of continuous variables (*e.g.*, logarithmic) were not explained, rules for categorization of continuous variables were not presented, exclusion of outliers was not elucidated and how missing values are dealt with was not mentioned).
Critically deficient	Do not select for this metric.
Not rated/not applicable	For mesothelioma, EPA is primarily interested in the presentation of data collected in the study, rather than the statistical analysis. If individual data elements (*e.g.*, time since first exposure, number of person-years, etc.) are present in the study that will allow EPA to conduct its own analysis, this metric may be marked as not rated/applicable. Mark as N/A if there were no statistical analyses or models for mesothelioma.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 15. Statistical models (confounding bias) (see special instructions for mesothelioma studies in "Not rated/applicable")	
High	Do not select for this metric.
Medium	***For all study types:*** The model or method for calculating the risk estimates (*e.g.*, odds ratios, SMRs, SIRs) is transparent (it is stated how/why variables were included or excluded).
Low	***For all study types:*** The statistical model building process is not fully appropriate OR model assumptions were not met OR a description of analyses and assumptions are not present (STROBE Checklist 12e (Von Elm et al., 2008)).

Data Quality Rating	Description
Critically deficient	Do not select for this metric.
Not rated/not applicable	For mesothelioma, EPA is primarily interested in the presentation of data collected in the study, rather than the statistical analysis. If individual data elements (*e.g.*, time since first exposure, number of person-years, etc.) are present in the study that will allow EPA to conduct its own analysis, this metric may be marked as not rated/applicable. Mark as N/A if there were no statistical analyses or models for mesothelioma.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Domain 6. Other (if applicable) considerations for biomarker selection and measurement (LaKind et al., 2014)	
Metric 16. Use of biomarker of exposure (detection/measurement/information biases)	
High	Biomarker in a specified matrix has accurate and precise quantitative relationship with external exposure, internal dose, or target dose. **AND** Biomarker is derived from exposure to one parent chemical.
Medium	Biomarker in a specified matrix has accurate and precise quantitative relationship with external exposure, internal dose, or target dose. **AND** Biomarker is derived from multiple parent chemicals.
Low	Evidence exists for a relationship between biomarker in a specified matrix and external exposure, internal dose or target dose, but there has been no assessment of accuracy and precision or none was reported.
Critically deficient	Biomarker in a specified matrix is a poor surrogate (low accuracy, specificity, and precision) for exposure/dose.
Not rated/not applicable	Select "NA" if no human biological samples were assessed or if the only biomarkers assessed were biomarkers of effect or biomarkers of susceptibility.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 17. Effect biomarker (detection/measurement/information biases)	
High	Effect biomarker measured is an indicator of a key event in an adverse outcome pathway (AOP).
Medium	Biomarkers of effect shown to have a relationship to health outcomes using well validated methods, but the mechanism of action is not understood.
Low	Biomarkers of effect shown to have a relationship to health outcomes, but the method is not well validated, and mechanism of action is not understood.

Data Quality Rating	Description
Critically deficient	Biomarker has undetermined consequences (*e.g.*, biomarker is not specific to a health outcome).
Not rated/not applicable	Select "NA" if no human biological samples were assessed or if the only biomarkers assessed were biomarkers of exposure or biomarkers of susceptibility.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 18. Method sensitivity (detection/measurement/information biases)	
High	Do not select for this metric.
Medium	Limits of detection are low enough to detect chemicals in a sufficient percentage of the samples to address the research question. Analytical methods measuring biomarker are adequately reported. The limit of detection (LOD) and limit of quantification (LOQ) (value or %) are reported.
Low	Frequency of detection too low to address the research hypothesis. **OR** LOD/LOQ (value or %) are not stated.
Critically deficient	Do not select for this metric.
Not rated/not applicable	Do not select "NA" for this metric if the study assessed biomarkers. If LOD/LOQ are not stated, then select Low. If the study did not assess biomarkers, then this metric is automatically not rated.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 19. Biomarker stability (detection/measurement/information biases)	
High	Samples with a known storage history and documented stability data or those using real-time measurements.
Medium	Samples have known losses during storage, but the difference between low and high exposures can be qualitatively assessed.
Low	Samples with either unknown storage history and/or no stability data for target analytes and high likelihood of instability for the biomarker under consideration.
Critically deficient	Do not select for this metric.
Not rated/not applicable	Do not select "NA" for this metric if the study assessed biomarkers. If the study did not assess biomarkers, then this metric is automatically not rated.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance).*

Data Quality Rating	Description
Metric 20. Sample contamination (detection/measurement/information biases)	
High	Samples are contamination-free from the time of collection to the time of measurement (*e.g.*, by use of certified analyte free collection supplies and reference materials, and appropriate use of blanks both in the field and lab). **AND** Documentation of the steps taken to provide the necessary assurance that the study data are reliable is included.
Medium	Samples are stated to be contamination-free from the time of collection to the time of measurement. **AND** There is incomplete documentation of the steps taken to provide the necessary assurance that the study data are reliable. **OR** Samples are known to have contamination issues, but steps have been taken to address and correct contamination issues. **OR** There is no information included about contamination (only allowed for biomarker samples not susceptible to contamination).
Low	Samples are known to have contamination issues, but steps have been taken to address and correct contamination issues. **OR** Samples are stated to be contamination-free from the time of collection to the time of measurement, but there is no use or documentation of the steps taken to provide the necessary assurance that the study data are reliable.
Critically deficient	There are known contamination issues (*e.g.*, phthalate study that used plastic sample collection vials) and no documentation that the issues were addressed.
Not rated/not applicable	Do not select "NA" for this metric if the study assessed biomarkers. (If the study did not assess biomarkers, then this metric is automatically not rated).
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 21. Method requirements (detection/measurement/information biases)	
High	Instrumentation that provides unambiguous identification and quantitation of the biomarker at the required sensitivity (*e.g.*, gas chromatography/high-resolution mass spectrometry [GC–HRMS]; gas chromatography with tandem mass spectrometry [GC–MS/MS]; liquid chromatography with tandem mass spectrometry [LC–MS/MS]).
Medium	Instrumentation that allows for identification of the biomarker with a high degree of confidence and the required sensitivity (*e.g.*, gas chromatography mass spectrometry (GC–MS), gas chromatography with electron capture detector [GC–ECD]).

Data Quality Rating	Description
Low	Instrumentation that only allows for possible quantification of the biomarker, but the method has known interferants (*e.g.*, gas chromatography with flame-ionization detection [GC–FID], spectroscopy).
Critically deficient	Do not select for this metric.
Not rated/not applicable	Do not select "NA" for this metric if the study assessed biomarkers. If the study did not assess biomarkers, then this metric is automatically not rated.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 22. Matrix adjustment (detection/measurement/information biases)	
High	If applicable for the biomarker under consideration, study provides results, either in the main publication or as a supplement, for both adjusted and unadjusted matrix concentrations (*e.g.*, creatinine-adjusted or specific gravity-adjusted and non-adjusted urine concentrations) and reasons are given for adjustment approach.
Medium	If applicable for the biomarker under consideration, study only provides results using one method (matrix-adjusted or not).
Low	If applicable for the biomarker under consideration, no established method for matrix adjustment was conducted.
Critically deficient	Do not select for this metric.
Not rated/not applicable	Select "NA" if matrix adjustment is not required for assessment of the biomarker.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*

Table 5-5. Data Quality Evaluation Criteria for All Other Outcomes for Asbestos Part 2 (Based on the Lung Cancer Form From the Risk Evaluation Asbestos Part 1)

Data Quality Rating	Description
Domain 1. Study participation	
Metric 1. Participant selection (selection, performance biases)	
High	***For all study types:*** All key elements of the study design are reported (*e.g.*, setting, participation rate described at all steps of the study, inclusion and exclusion criteria, and methods of participant selection or case ascertainment) **AND** The reported information indicates that selection in or out of the study (or analysis sample) and participation was not likely to be biased (*i.e.*, the exposure-outcome distribution of the

Data Quality Rating	Description
	participants is likely representative of the exposure-outcome distributions in the population of persons eligible for inclusion in the study).
Medium	***For all study types:*** Some key elements of the study design were not present but available information indicates a low risk of selection bias (*i.e.*, the exposure-outcome distribution of the participants is likely representative of the exposure-outcome distributions in the population of persons eligible for inclusion in the study).
Low	***For all study types:*** Key elements of the study design and information on the population (*e.g.*, setting, participation rate described at most steps of the study, inclusion and exclusion criteria, and methods of participant selection or case ascertainment) are not reported (Strengthening the reporting of observational studies in epidemiology [STROBE] checklist 4, 5 and 6 (Von Elm et al., 2008)). If the study provides little to no information about selection criteria, then rate this metric as Low.
Critically deficient	***For all study types*:** The reported information indicates that selection in or out of the study (or analysis sample) and participation was likely to be significantly biased (*i.e.*, the exposure-outcome distribution of the participants is likely not representative of the exposure-outcome distributions of the population of persons eligible for inclusion in the study).
Not rated/not applicable	Do not select for this metric.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 2. Attrition (missing data/attrition/exclusion, reporting biases)	
High	***For cohort studies:*** There was minimal subject loss to follow up during the study (or exclusion from the analysis sample), and outcome and exposure data were largely complete. **OR** Loss of subjects (*e.g.*, incomplete outcome data) or missing exposure and outcome data was adequately addressed (as described below) and reasons were documented when human subjects were removed from a study (NTP, 2015). **OR** ~~**AND**~~ Missing data have been imputed using appropriate methods (*e.g.*, multiple imputation methods), and characteristics of subjects lost to follow up or with unavailable records are not significantly different from those of the study participants (NTP, 2015). ***For case-control studies and cross-sectional studies:*** There was minimal subject withdrawal from the study (or exclusion from the analysis sample) and outcome data and exposure were largely complete. **OR**

Data Quality Rating	Description
	Any exclusion of subjects from analyses was adequately addressed (as described below), and reasons were documented when subjects were removed from the study or excluded from analyses (NTP, 2015). ***NOTE for all study types:*** Adequate handling of subject attrition can include: use of imputation methods for missing outcome and exposure data; reasons for missing subjects unlikely to be related to outcome (for survival data, censoring was unlikely to introduce bias); missing outcome data balanced in numbers across study groups, with similar reasons for missing data across groups.
Medium	***For cohort studies:*** There was moderate subject loss to follow up during the study (or exclusion from the analysis sample) or outcome and exposure data were nearly complete. **AND** Any loss or exclusion of subjects was adequately addressed (as described in the acceptable handling of subject attrition in the high confidence category) and reasons were documented when human subjects were removed from a study. ***For case-control studies and cross-sectional studies:*** There was moderate subject withdrawal from the study (or exclusion from the analysis sample), but outcome and exposure data were largely complete. **AND** Any exclusion of subjects from analyses was adequately addressed (as described above), and reasons were documented when subjects were removed from the study or excluded from analyses (NTP, 2015).
Low	***For cohort studies:*** The loss of subjects (*e.g.*, loss to follow up, incomplete outcome or exposure data) was moderate and unacceptably handled (as described below in the unacceptable confidence category) (Source: OHAT). **OR** Numbers of individuals were not reported at important stages of study (*e.g.*, numbers of eligible participants included in the study or analysis sample, completing follow-up, and analyzed). Reasons were not provided for nonparticipation at each stage (STROBE Checklist Item 13 (Von Elm et al., 2008)). ***For case-control and cross-sectional studies:*** The exclusion of subjects from analyses was moderate and unacceptably handled (as described below in the unacceptable confidence category). **OR** Numbers of individuals were not reported at important stages of study (*e.g.*, numbers of eligible participants included in the study or analysis sample, completing follow-up, and analyzed). Reasons were not provided for nonparticipation at each stage (STROBE Checklist Item 13 (Von Elm et al., 2008)).
Critically deficient	***For cohort studies:*** There was large subject attrition during the study (or exclusion from the analysis sample). **OR**

Data Quality Rating	Description
	Unacceptable handling of subject attrition: reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across study groups; or potentially inappropriate application of imputation (Source: OHAT). ***For case-control and cross-sectional studies:*** There was large subject withdrawal from the study (or exclusion from the analysis sample). **OR** Unacceptable handling of subject attrition: reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across study groups; or potentially inappropriate application of imputation.
Not rated/not applicable	Do not select for this metric.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 3. Comparison group (selection, performance biases)	
High	***For ALL study types:*** Any differences in baseline characteristics of groups were considered as potential confounding or stratification variables and were thereby controlled by statistical analysis (Source: OHAT). **OR** ***For cohort and cross-sectional studies:*** Key elements of the study design are reported (*i.e.*, setting, inclusion and exclusion criteria, and methods of participant selection), and indicate that groups were similar (*e.g.*, recruited from the same eligible population with the same method of ascertainment and within the same time frame using the same inclusion and exclusion criteria, and were of similar age and health status) (NTP, 2015). ***For case-control studies:*** Key elements of the study design are reported indicate that that cases and controls were similar (*e.g.*, recruited from the same eligible population with the number of controls described, and eligibility criteria and are recruited within the same time frame (NTP, 2015). ***For studies reporting Standardized Mortality Ratios (SMRs) or Standardized Incidence Ratios (SIRs):*** Age, sex (if applicable), and race (if applicable) adjustment or stratification is described and choice of reference population (*e.g.*, general population) is reported.
Medium	***For cohort studies and cross-sectional studies:*** There is only indirect evidence (*e.g.*, stated by the authors without providing a description of methods) that groups are similar (as described above for the high confidence rating). **OR** If there is substantial potential for healthy worker effect. ***For case-control studies:*** There is indirect evidence (*i.e.*, stated by the authors without providing a description of methods) that cases and controls are similar (as described above for the high confidence rating).

Data Quality Rating	Description
	For studies reporting SMRs or SIRs: Age, sex (if applicable), and race (if applicable) adjustment or stratification is not specifically described in the text, but results tables are stratified by age and/or sex (*i.e.*, indirect evidence); choice of reference population (*e.g.*, general population) is reported.
Low	***For cohort and cross-sectional studies:*** There is indirect evidence (*i.e.,* stated by the authors without providing a description of methods) that groups were not similar (as described above for the high confidence rating). **AND** Differences between the exposure groups are not adequately controlled for in the statistical analysis. ***For case-control studies:*** There is indirect evidence (*i.e.*, stated by the authors without providing a description of methods) that cases and controls were not similar (as described above for the high confidence rating). **AND** The characteristics of cases and controls are not reported (Source: (NTP, 2015)). **AND** Differences in groups is not adequately controlled for in the statistical analysis. ***For studies reporting SMRs or SIRs:*** Indirect evidence of a lack of adjustment or stratification for age or sex (if applicable); indirect evidence that choice of reference population (*e.g.*, general population) is inappropriate.
Critically deficient	***For cohort studies:*** Subjects in all exposure groups were not similar. **OR** (Information was not reported to determine if participant groups were similar (STROBE Checklist 6 (Von Elm et al., 2008)) **AND** Potential differences in exposure groups were for a factor that was related to the outcome and not controlled for in the statistical analysis.) **OR** (Subjects in the exposure groups had very different participation/response rates (NTP, 2015). **AND** Participation rates were related to exposure and outcome) ***For case-control studies:*** (Controls were drawn from a very dissimilar population than cases or recruited within very different time frames (NTP, 2015). **AND** Potential differences in the case and control groups were not controlled for in the statistical analysis). **OR** Rationale and/or methods for case and control selection, matching criteria including number of controls per case (if relevant) were not reported (STROBE Checklist 6 (Von Elm et al., 2008)).

Data Quality Rating	Description
	For cross-sectional studies: (Subjects in all exposure groups were not similar, recruited within very different time frames, or had very different participation/response rates (NTP, 2015). **AND** Potential differences in exposure groups were not controlled for in the statistical analysis). **OR** Sources and methods of selection of participants in all exposure groups were not reported (STROBE Checklist 6 (Von Elm et al., 2008)). ***For studies reporting SMRs or SIRs:*** Lack of adjustment or stratification for both age and sex (if applicable), race (if applicable), and calendar time or choice of reference population (*e.g.*, general population) is not reported.
Not rated/not applicable	Do not select for this metric.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Domain 2. Exposure characterization	
Metric 4. Measurement of exposure (Detection/measurement/information, performance biases) If exposure was estimated solely using professional judgement, then rate this Metric as Low. Even if this metric is rated as Critically Deficient due to a lack of quantitative exposure estimates, please note in the comments field whether the study might be useful qualitatively.	
High	***For all study types:*** Quantitative estimates of exposure were consistently assessed (*i.e.*, using the same method and sampling time-frame) during multiple time periods and using either PCM or TEM. **OR** A combination of methods were used over time (*i.e.*, midget impinger, PCM or TEM), but side by side sampling and analyses were conducted to develop appropriate conversion criteria. **AND** For an occupational population, contains detailed employment records and quantitative estimates of exposure using either PCM or TEM which allows for construction of job-matrix for entire work history of exposure (*i.e.*, cumulative or peak exposures, and time since first exposure).
Medium	***For all study types:*** (Exposure was assessed during one time period but this time period is judged to be reasonably representative of the entire study time period. **AND** Exposure was assessed using a combination of midget impingers, PCM, and/or TEM measurements, but side by side sampling and analyses were not conducted for all operations and thus there is a lack of confidence in the conversion factors.) **OR** For an occupational study population, contains detailed employment records and quantitative estimates of exposure using a combination of midget impingers and PCM or TEM

Data Quality Rating	Description
	measurements for only a portion of participant's work history of exposure (*i.e.*, only early years or later years), such that extrapolation of the missing years is required.
Low	***For all study types:*** Exposure was estimated solely using professional judgement. **OR** Exposure was directly measured and assessed using a quantitative method other than PCM or TEM and conversion factors were not determined. **OR** The method of quantifying/counting fibers was not specified (PCM, TEM, or other method not specified).
Critically deficient	***For all study types:*** There was no quantitative measure or estimate of exposure. **OR** Methods used to quantify the exposure were not well defined, and sources of data and detailed methods of exposure assessment were not reported (STROBE Checklist 7 and 8 (Von Elm et al., 2008)). **OR** There is evidence of substantial exposure misclassification that would significantly bias the results.
Not rated/not applicable	Do not select for this metric.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 5. Exposure levels (Detection/measurement/information biases)	
High	Do not select for this metric.
Medium	***For all study types:*** The range and distribution of exposure is sufficient or adequate to develop an exposure-response estimate (Cooper et al., 2016). **AND** Reports 3 or more levels of exposure (referent group + 2 or more) or an exposure-response model using a continuous measure of exposure.
Low	***For all study types:*** The range of exposure in the population is limited. **OR** Reports 2 levels of exposure (*e.g.*, exposed/unexposed)) (Cooper et al., 2016) (Source: IRIS).
Critically deficient	***For all study types:*** The range and distribution of exposure are not adequate to determine an exposure-response relationship (Cooper et al., 2016). **OR**

Data Quality Rating	Description
	No description is provided on the levels or range of exposure.
Not rated/not applicable	Do not select for this metric.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 6. Temporality	
High	***For all study types:*** The study presents an appropriate temporality between exposure and outcome (*i.e.*, the exposure precedes the disease). **AND** The interval between the exposure (or reconstructed exposure) and the outcome is sufficiently long considering the latency of the disease (*i.e.*, study follow-up is more than 15 years for lung cancer) (LaKind et al., 2014).
Medium	***For all study types:*** Temporality is established, but it is unclear whether there is adequate follow-up for consideration of latency (*i.e.*, only 10 years of follow-up) (LaKind et al., 2014).
Low	***For all study types:*** The temporality of exposure and outcome is uncertain. ~~(5-10 years).~~ **OR** There is inadequate follow-up of the cohort considering the latency period (5-10 years of follow-up).
Critically deficient	***For all study types:*** Study lacks an established time order, such that exposure is not likely to have occurred prior to outcome (LaKind et al., 2014). **OR** There was inadequate follow-up of the cohort for the expected latency period (<5 years). **OR** Sources of data and details of methods of assessment were not sufficiently reported (*e.g.*, duration of follow-up, periods of exposure, dates of outcome ascertainment, etc.) Source: STROBE Checklist 8 (Von Elm et al., 2008)).
Not rated/not applicable	Do not select for this metric.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*

Data Quality Rating	Description
Domain 3. Outcome Assessment	
Each of the following outcomes has separate criteria for Metric 7: Lung Cancer, Ovarian Cancer, Laryngeal Cancer, Other Cancer(s), Asbestosis, Pulmonary Function/Spirometry Results, Pleural Plaques, and Other Non-cancer Outcomes (Mesothelioma criteria are on the Mesothelioma Form)	
Metric 7. Outcome Measurement or Characterization (detection/measurement/information, performance, reporting biases): **Lung Cancer**	
High	***For all study types:*** The outcome was assessed using one or a combination of the following well-established methods: o Lung cancer cases confirmed by histological or cytological means (including subtypes of lung cancer) o ICD-10 C34 (lung and bronchus with or without C33 (trachea) o ICD-9 (5-digit code) 162.2-162.9 or o ICD-8 (4-digit code) 162.1 or o ICD-7 (4-digit code) 162.1 and 163 o ICD-9 (3-digit code) 162 o ICD-8 (3-digit code) 162 o o ICD-7 (3-digit code) 162 and 163
Medium	***For all study types:*** Although authors state they identified lung cancer cases they did not use or report the ICD codes or cases were not confirmed by histological or cytological means. ~~Although authors state they identified lung cancer cases they did not report the ICD codes.~~
Low	Do not select for this metric.
Critically deficient	***For all study types:*** Any self-reported information. **OR** Study lacks individual assessment of lung cancer (*i.e.*, lung cancer is assessed as a combination of cancer types, excluding lung and bronchus or trachea).
Not rated/not applicable	Do not select for this metric
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 7. Outcome Measurement or Characterization (detection/measurement/information, performance, reporting biases): **Ovarian Cancer**	
High	***For all study types:*** The outcome was assessed using one or a combination of the following well-established methods: o Ovarian cancer cases confirmed by tissue biopsy o ICD-11 2C73 Malignant neoplasm of ovary o ICD-10 C56 Malignant neoplasm of ovary

Data Quality Rating	Description
	○ ICD-9 183 Malignant neoplasm of ovary ○ ICD-8 183 Malignant neoplasm of ovary, fallopian tube and broad ligament, supplemented by additional information to validate a diagnosis of ovarian cancer. ○ Pre-ICD-8 codes supplemented by additional information to validate a diagnosis of ovarian cancer. All fields on the death certificate were searched for a diagnosis of ovarian cancer.
Medium	***For all study types:*** Other diagnostic methods such as imaging tests (ultrasound or CT scan) or CA-125 blood tests were used without confirmation by tissue biopsy. **OR** The study reports a doctor diagnosis without additional details or validation.
Low	Do not select for this metric
Not rated/not applicable	The study did not assess ovarian cancer.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 7. Outcome Measurement or Characterization (detection/measurement/information, performance, reporting biases): **Laryngeal Cancer**	
High	***For all study types:*** The outcome was assessed using one or a combination of the following well-established methods: ○ Laryngeal cancer cases confirmed by tissue biopsy. ○ ICD-11 2C23 Malignant neoplasm of larynx ○ ICD-10 C32 Malignant neoplasm of larynx ○ ICD-9 161 Malignant neoplasm of larynx ○ ICD-8 132 Malignant neoplasm of larynx ○ ICD-7 161 Malignant neoplasm of larynx ○ Pre-ICD-7 codes supplemented by additional information to validate a diagnosis of laryngeal cancer. All fields on the death certificate were searched for a diagnosis of laryngeal cancer.
Medium	***For all study types:*** Other diagnostic methods were used without confirmation by tissue biopsy. **OR** Doctor diagnosis without additional details or validation.
Low	Do not select for this metric
Critically deficient	***For all study types:*** The only included information is a self-reported diagnosis of laryngeal cancer without any additional validation.

Data Quality Rating	Description
Not rated/not applicable	The study did not assess laryngeal cancer.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 7. Outcome Measurement or Characterization (detection/measurement/information, performance, reporting biases): **Other Cancer Outcomes**	
High	***For all study types:*** The cancer was assessed using well-established methods, such as one or a combination of the following: specific ICD Codes cases confirmed using histological or cytological methods, other lab tests, or diagnostic imaging. **OR** All fields on the death certificate were searched for the specific diagnosis.
Medium	***For all study types:*** The authors state that they identified a specific health outcome, but less-established methods were used and they did not conduct method validation. **AND** There is little to no evidence that the method had poor validity and little to no evidence of outcome misclassification. **OR** There was a doctor's report or diagnosis, but no ICD code and no additional confirmation or validation of the diagnosis.
Low	Do not select for this metric
Critically deficient	***For all study types:*** The study lacks individual assessment of specific cancer types (*i.e.*, the specific cancer is assessed as a combination with other cancer types). **OR** Only self-reported information was included, without any validation.
Not rated/not applicable	The study did not assess other cancer outcomes.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 7. Outcome Measurement or Characterization (detection/measurement/information, performance, reporting biases): **Asbestosis**	
High	***For all study types:*** The outcome was assessed using one or a combination of the following well-established methods: Diagnostic imaging tests (such as chest x-rays or computed tomography (CT) scans) showing pulmonary fibrosis or scarring of the lung tissue. ICD-11 code CA60.2 Pneumoconiosis due to mineral fibers including asbestos o ICD-10 Code J61 Pneumoconiosis due to asbestos and other mineral fibers o ICD-9 Code 501 Asbestosis

Data Quality Rating	Description
	○ ICD-8 515.2 Asbestosis ○ Pre-ICD-8 codes supplemented by additional information to validate a diagnosis of asbestosis All fields on the death certificate were searched for a diagnosis of asbestosis.
Medium	***For all study types:*** The authors report doctor-diagnosed asbestosis but do not report specific evidence of lung tissue scarring or ICD codes.
Low	A less valid method was used to diagnose asbestosis without confirmation using imaging tests.
Critically deficient	***For all study types:*** The only included information is a self-reported diagnosis of asbestosis without any additional validation.
Not rated/not applicable	The study did not assess asbestosis.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 7. Outcome Measurement or Characterization (detection/measurement/information, performance, reporting biases): **Pulmonary Function/Spirometry Testing Results**	
High	***For all study types:*** The outcome was assessed using well established methods that include standardized spirometric measurements (FEV1, FVC) and/or diffusing capacity of the lungs for carbon monoxide (DLCO) measurements. Forced expiratory Volume in 1s (FEV1) and Forced Vital Capacity (FVC)) (FIOH, 2014).
Medium	***For all study types:*** Use of less sensitive and standard methods such as low scanning electron microscopy (SEM), which lacks sensitivity and standardization as it relates to pulmonary function. There is little to no evidence that the method had poor validity and little to no evidence of outcome misclassification.
Low	Do not select for this metric.
Critically deficient	***For all study types:*** Any self-reported information without additional validation. Study lacks individual assessment of pulmonary function and does not use spirometry testing.
Not rated/not applicable	The study did not assess pulmonary function.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*

Data Quality Rating	Description
Metric 7. Outcome Measurement or Characterization (detection/measurement/information, performance, reporting biases): **Pleural Abnormalities, Pleural Plaques, or Parenchymal Opacities**	
High	***For all study types:*** The outcome was assessed using well-established methods such as x-rays or high-resolution computed tomography (HRCT), with cases defined based on consensus of two or more B-readers* (blinded) for any pleural abnormality or parenchymal opacities (ILO, 2000). **OR** ○ ICD-11 Code CB20 Pleural Plaque ○ ICD-10 Code CM J92 Pleural Plaque **OR** All fields on the death certificate were searched for the specific diagnosis.
Medium	**For all study types:** The outcome was assessed using x-rays or HRCT methods: cases defined as one B-reader assessment (with either blinding reported or not) for any pleural abnormality or parenchymal opacities. **OR** There was a doctor's report or diagnosis but using other less-established methods.
Low	Do not select for this metric.
Critically deficient	***For all study types:*** The study lacks assessment of any of the specific pleural abnormality types (*i.e.*, costophrenic angle obliteration or diffuse pleural thickening) or parenchymal opacities *(i.e.*, small opacities or large opacities). **OR** Only self-reported information without any validation.
Not rated/not applicable	The study did not assess pleural abnormalities, pleural plaques, or parenchymal opacities.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 7. Outcome Measurement or Characterization (detection/measurement/information, performance, reporting biases): **Other Non-cancer Outcomes**	
High	***For all study types:*** The outcome was assessed using well-established methods, such as one or a combination of the following: specific ICD Codes, cases confirmed using histological or cytological methods, other lab tests, or diagnostic imaging. **OR** All fields on the death certificate were searched for the specific diagnosis.
Medium	***For all study types:*** The authors state that they identified a specific health outcome, but less-established methods were used and they did not conduct method validation. **AND** There is little to no evidence that the method had poor validity and little to no evidence of outcome misclassification.

Data Quality Rating	Description
	OR There was a doctor's report or diagnosis, but no ICD code and no additional confirmation or validation of the diagnosis.
Low	Do not select for this metric.
Critically deficient	***For all study types:*** Only self-reported information was included, without any validation.
Not rated/not applicable	The study did not assess other non-cancer outcomes.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 8. Reporting bias	
High	***For all study types:*** ~~Lung cancer f~~ Findings are reported in the abstract, results or discussion. Effect estimates are reported with confidence intervals and/or standard errors, number of cases/controls or exposed/unexposed reported for each analysis, to be included in exposure-response analysis or fully tabulated during data extraction and analyses (NTP, 2015).
Medium	***For all study types:*** All of the study's findings (primary and secondary) outlined in the abstract, results or discussion (that are relevant for the evaluation) are reported but not in a way that would allow for detailed extraction (*e.g.*, results were discussed in the text but accompanying data were not shown).
Low	***For all study types:*** ~~Lung cancer o~~ Outcomes outlined in the methods, abstract, and/or introduction (that are relevant for the evaluation) have not been reported (NTP, 2015).
Critically deficient	Do not select for this metric.
Not rated/not applicable	Do not select for this metric.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Domain 4. Potential confounding/Variable control Notes: • Smoking fits in Metrics 9 and 10, not Metric 11. • Metric 9 addresses whether there was appropriate adjustment or consideration of confounders (such as stratification) (other than co-exposures). • Metric 10 addresses how the potential confounders (other than co-exposures) were measured. • Metric 11 assesses co-exposure confounding.	
Metric 9. Covariate adjustment (confounding)	

Data Quality Rating	Description
High	***For all study types:*** Appropriate adjustments or explicit considerations were made for potential confounders (*e.g.*, age, sex, SES, race, etc.) (excluding co-exposures, which are evaluated in metric 11) in the final analyses through the use of statistical models to reduce research-specific bias, including matching, adjustment in multivariate models, stratification, or other methods that were appropriately justified (NTP, 2015). ***For Studies reporting SMRs or SIRs:*** Adjustments are described and results are age-, race-, and sex-adjusted (or stratified) if applicable.
Medium	***For all study types:*** There is indirect evidence that appropriate adjustments were made (*i.e.*, considerations were made for primary covariates (excluding co-exposures) and potential confounders adjustment) without providing a description of methods. **OR** The distribution of potential confounders (excluding co-exposures) did not differ significantly between exposure groups or between cases and controls. **OR** The major potential confounders (excluding co-exposures) were appropriately adjusted (*e.g.*, SMRs, SIRs, etc.) and any not adjusted for are considered not to appreciably bias the results (*e.g.*, smoking rates in an occupational cohort are expected to be generally similar in different departments and thus confounding by smoking is unlikely when internal analyses are applied). ***For Studies reporting SMRs or SIRs:*** ~~Indirect evidence that results are age-, sex-, and race-adjusted (or stratified) if applicable.~~ Results are adjusted (or stratified) for age and sex, unless adjustment or stratification is not necessary because the exposed and control groups are sufficiently similar on the particular demographic variable.
Low	***For all study types:*** There is indirect evidence (*i.e.*, no description is provided in the study) that considerations were not made for potential confounders adjustment in the final analyses (NTP, 2015). **AND** The distribution of primary covariates (excluding co-exposures) and potential confounders was not reported between the exposure groups or between cases and controls (NTP, 2015). ***For Studies reporting SMRs or SIRs:*** ~~Results are age-, race-, OR sex-adjusted (or stratified) if applicable (*i.e.*, if 2 or all should have been adjusted).~~ Results are adjusted or stratified for age, race, OR sex (any one of the three), unless adjustment or stratification is not necessary because the exposed and control groups are sufficiently similar on the particular demographic variable.
Critically deficient	***For all study types:*** The distribution of potential confounders differed significantly between the exposure groups. **AND** Confounding was demonstrated and was not appropriately adjusted for in the final analyses (NTP, 2015).

Data Quality Rating	Description
	For Studies reporting SMRs or SIRs: No discussion of adjustments. Results are not adjusted for age, sex, and race (or stratified) if applicable.
Not rated/not applicable	Do not select for this metric.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 10. Covariate characterization (measurement/information, confounding biases) For occupational studies, it can be assumed that personnel records were used to obtain covariate data if not otherwise specified.	
High	***For all study types:*** Potential confounders (*e.g.*, age, sex, SES), excluding co-exposures, ~~Potential confounders (*e.g.*, age, sex, SES, race, etc.) and~~ were assessed using valid and reliable methodology where appropriate (*e.g.*, validated questionnaires, biomarker).
Medium	***For all study types:*** A less-established method was used to assess confounders (excluding co-exposures) and no method validation was conducted against well-established methods, but there was little to no evidence that that the method had poor validity and little to no evidence of confounding.
Low	***For all study types:*** The confounder assessment method is an insensitive instrument or measure or a method of unknown validity.
Critically deficient	***For all study types:*** Confounders were assessed using a method or instrument known to be invalid.
Not rated/not applicable	Covariates were not assessed.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 11. Co-exposure confounding (measurement/information, confounding biases)	
High	Do not select for this metric.
Medium	***For all study types:*** Any co-exposures to pollutants that are not the target exposure that would likely bias the results were not likely to be present. **OR** Co-exposures to pollutants were appropriately measured and ~~or~~ either directly or indirectly adjusted for.

Data Quality Rating	Description
	There is confirmation of the likely absence of known co-exposures via mechanisms such as engineering controls (closed systems) for co-pollutants or confirmation of the absence of co-pollutants through monitoring.
Low	***For cohort and cross-sectional studies:*** There is direct evidence that there was an unbalanced provision of additional co-exposures across the primary study groups, which were not appropriately adjusted for. ***For case-control studies:*** There is direct evidence that there was an unbalanced provision of additional co-exposures across cases and controls, which were not appropriately adjusted for, and significant indication a biased exposure-outcome association. **OR** ***For all study types:*** In an occupational setting, potential co-exposures are not discussed.
Critically deficient	Do not select for this metric.
Not rated/not applicable	Enter 'NA' and do not score this metric.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Domain 5. Analysis	
Metric 12. Study design and methods	
High	Do not select for this metric.
Medium	***For all study types:*** The study design chosen was appropriate for the research question. **OR** ~~**AND**~~ The study uses an appropriate statistical method to address the research question(s) (*e.g.*, Cox and Poisson regression for cohort studies and logistic regression analysis for case-control studies.
Low	Do not select for this metric.
Critically deficient	***For all study types:*** The study design chosen was not appropriate for the research question. **OR** Inappropriate statistical analyses were applied to assess the research questions.
Not rated/not applicable	Do not select for this metric.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*

Data Quality Rating	Description
Metric 13. Statistical power (sensitivity)	
High	Do not select for this metric.
Medium	***For cohort and cross-sectional studies:*** The number of participants are adequate to detect an effect in the exposed population and/or subgroups of the total population. **OR** The paper reported statistical power high is enough (≥ 80%) to detect an effect in the exposure population and/or subgroups of the total population. ***For case-control studies:*** The number of cases and controls are adequate to detect an effect in the exposed population and/or subgroups of the total population. **OR** The paper reported statistical power was high enough (≥ 80%) to detect an effect in the exposure population and/or subgroups of the total population.
Low	Do not select for this metric.
Critically deficient	***For cohort and cross-sectional studies:*** The number of participants is inadequate to detect an effect in the exposed population and/or subgroups of the total population and the study was negative. ***For case-control studies:*** The number of cases and controls are inadequate to detect an effect in the exposed population and/or subgroups of the total population and the study was negative.
Not rated/not applicable	Do not select for this metric.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 14. Reproducibility of analyses (adapted from (Blettner et al., 2001))	
High	Do not select for this metric.
Medium	***For all study types:*** The description of the analysis is sufficient to understand how to conceptually reproduce the analysis with access to the analytic data. ~~The description of the analysis is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.~~
Low	***For all study types:*** The description of the analysis is insufficient to understand what has been done and to be reproducible OR a description of analyses are not present (*e.g.*, statistical tests and estimation procedures were not described, variables used in the analysis were not listed, transformations of continuous variables (*e.g.* logarithmic) were not explained, rules for categorization of continuous variables were not presented, exclusion of outliers was not elucidated and how missing values are dealt with was not mentioned).

Data Quality Rating	Description
Critically deficient	Do not select for this metric.
Not rated/not applicable	Do not select for this metric.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 15. Statistical models (confounding bias)	
High	Do not select for this metric.
Medium	***For all study types:*** The model or method for calculating the risk estimates (*e.g.*, odds ratios, SMRs, SIRs) is transparent (it is stated how/why variables were included or excluded) **AND** Model assumptions were met.
Low	***For all study types:*** The statistical model building process is not fully appropriate OR model assumptions were not met OR a description of analyses and assumptions are not present. ~~The statistical model building process is not fully appropriate.~~ ~~**OR**~~ ~~Model assumptions were not met.~~ ~~**OR**~~ ~~A description of analyses is not present~~ (STROBE Checklist 12e (Von Elm et al., 2008)).
Critically deficient	Do not select for this metric.
Not rated/not applicable	Enter 'NA' if the study did not use a statistical model.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Domain 6. Other (if applicable) considerations for biomarker selection and measurement (LaKind et al., 2014)	
Metric 16. Use of biomarker of exposure (detection/measurement/information biases)	
High	Biomarker in a specified matrix has accurate and precise quantitative relationship with external exposure, internal dose, or target dose. **AND** Biomarker is derived from exposure to one parent chemical.
Medium	Biomarker in a specified matrix has accurate and precise quantitative relationship with external exposure, internal dose, or target dose.

Data Quality Rating	Description
	AND Biomarker is derived from multiple parent chemicals.
Low	Evidence exists for a relationship between biomarker in a specified matrix and external exposure, internal dose or target dose, but there has been no assessment of accuracy and precision, or none was reported.
Critically deficient	Biomarker in a specified matrix is a poor surrogate (low accuracy, specificity, and precision) for exposure/dose.
Not rated/not applicable	Select "NA" if no human biological samples were assessed or if the only biomarkers assessed were biomarkers of effect or biomarkers of susceptibility.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 17. Effect biomarker (detection/measurement/information biases)	
High	Effect biomarker measured is an indicator of a key event in an adverse outcome pathway (AOP).
Medium	Biomarkers of effect shown to have a relationship to health outcomes using well validated methods, but the mechanism of action is not understood.
Low	Biomarkers of effect shown to have a relationship to health outcomes, but the method is not well validated, and mechanism of action is not understood.
Critically deficient	Biomarker has undetermined consequences (*e.g.*, biomarker is not specific to a health outcome).
Not rated/not applicable	Select "NA" if no human biological samples were assessed or if the only biomarkers assessed were biomarkers of exposure or biomarkers of susceptibility.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 18. Method sensitivity (detection/measurement/information biases)	
High	Do not select for this metric.
Medium	Limits of detection are low enough to detect chemicals in a sufficient percentage of the samples to address the research question. Analytical methods measuring biomarker are adequately reported. The limit of detection (LOD) and limit of quantification (LOQ) (value or %) are reported.
Low	Frequency of detection too low to address the research hypothesis. **OR** LOD/LOQ (value or %) are not stated.
Critically deficient	Do not select for this metric.

Data Quality Rating	Description
Not rated/not applicable	Do not select "NA" for this metric if the study assessed biomarkers. If LOD/LOQ is not stated, then select Low. If the study did not assess biomarkers, then this metric is automatically not rated.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 19. Biomarker stability (detection/measurement/information biases)	
High	Samples with a known storage history and documented stability data or those using real-time measurements.
Medium	Samples have known losses during storage, but the difference between low and high exposures can be qualitatively assessed.
Low	Samples with either unknown storage history and/or no stability data for target analytes and high likelihood of instability for the biomarker under consideration.
Critically deficient	Do not select for this metric.
Not rated/not applicable	Do not select "NA" for this metric if the study assessed biomarkers. If the study did not assess biomarkers, then this metric is automatically not rated.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 20. Sample contamination (detection/measurement/information biases)	
High	Samples are contamination-free from the time of collection to the time of measurement (*e.g.*, by use of certified analyte free collection supplies and reference materials, and appropriate use of blanks both in the field and lab). **AND** Documentation of the steps taken to provide the necessary assurance that the study data are reliable is included.
Medium	Samples are stated to be contamination-free from the time of collection to the time of measurement. **AND** There is incomplete documentation of the steps taken to provide the necessary assurance that the study data are reliable. **OR** Samples are known to have contamination issues, but steps have been taken to address and correct contamination issues. **OR** There is no information included about contamination (only allowed for biomarker samples not susceptible to contamination).
Low	Samples are known to have contamination issues, but steps have been taken to address and correct contamination issues. **OR**

Data Quality Rating	Description
	Samples are stated to be contamination-free from the time of collection to the time of measurement, but there is no use or documentation of the steps taken to provide the necessary assurance that the study data are reliable.
Critically deficient	There are known contamination issues (*e.g.*, phthalate study that used plastic sample collection vials) and no documentation that the issues were addressed.
Not rated/not applicable	Do not select "NA" for this metric if the study assessed biomarkers. If the study did not assess biomarkers, then this metric is automatically not rated.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 21. Method requirements (detection/measurement/information biases)	
High	Instrumentation that provides unambiguous identification and quantitation of the biomarker at the required sensitivity (*e.g.*, gas chromatography/high-resolution mass spectrometry [GC–HRMS]; gas chromatography with tandem mass spectrometry [GC–MS/MS]; liquid chromatography with tandem mass spectrometry [LC–MS/MS]).
Medium	Instrumentation that allows for identification of the biomarker with a high degree of confidence and the required sensitivity (*e.g.*, gas chromatography mass spectrometry [GC–MS], gas chromatography with electron capture detector [GC–ECD]).
Low	Instrumentation that only allows for possible quantification of the biomarker, but the method has known interferants (*e.g.*, gas chromatography with flame-ionization detection [GC–FID], spectroscopy).
Critically deficient	Do not select for this metric.
Not rated/not applicable	Do not select "NA" for this metric if the study assessed biomarkers. If the study did not assess biomarkers, then this metric is automatically not rated.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*
Metric 22. Matrix adjustment (detection/measurement/information biases)	
High	If applicable for the biomarker under consideration, study provides results, either in the main publication or as a supplement, for both adjusted and unadjusted matrix concentrations (*e.g.*, creatinine-adjusted or specific gravity-adjusted and non-adjusted urine concentrations) and reasons are given for adjustment approach.
Medium	If applicable for the biomarker under consideration, study only provides results using one method (matrix-adjusted or not).
Low	If applicable for the biomarker under consideration, no established method for matrix adjustment was conducted.
Critically deficient	Do not select for this metric.

Data Quality Rating	Description
Not rated/not applicable	Select "NA" if matrix adjustment is not required for assessment of the biomarker.
Reviewer's comments	*(Document concerns, uncertainties, limitations, and deficiencies and any additional comments that may highlight study strengths or important elements such as relevance)*

6 EVIDENCE INTEGRATION

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

6.1 Physical and Chemical Properties

EPA gathered and evaluated physical and chemical property data and information according to the process described in Section 7.1 in the 2021 Draft Systematic Review Protocol Application of Systematic Review in TSCA Risk Evaluations (U.S. EPA, 2021). Section 7.1 describes how information from data sources that undergo systematic review are integrated for use in risk evaluations under TSCA for physical and chemical property data. Appendix F.1 in the Risk Evaluation for Asbestos Part 2 provides the rationale for selecting data values from systematic review (U.S. EPA, 2024i).

During the evaluation of asbestos, EPA considered both measured and estimated property data and information set forth in Table 2-1 of the Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2024i). Most values were taken from the *Final Scope of the Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos* (U.S. EPA, 2022) except for the surface area (anthophyllite and tremolite), individual fiber diameter (anthophyllite), particle dimensions (crocidolite, amosite, actinolite, and LAA), density (anthophyllite, tremolite, and actinolite), refractive index (actinolite), tensile strength (crocidolite, amosite and tremolite), and zeta potential (anthophyllite and tremolite).

6.2 Environmental Fate and Transport

EPA gathered and evaluated environmental fate and transport data and information according to the process described in Sections 7.2 – 7.2.3.1 in the 2021 Draft Systematic Review Protocol Application of Systematic Review in TSCA Risk Evaluations (U.S. EPA, 2021). Sections 7.2 – 7.2.3.1 describes how information from data sources that undergo systematic review are integrated for use in risk evaluations under TSCA for environmental fate and transport data and information. Appendix F.2 in the Risk Evaluation for Asbestos Part 2 provides the rationale for selecting data values from systematic review (U.S. EPA, 2024i). In some cases, multiple high-quality data values or a range of values may be given.

Including multiple data values or a range of values provides some transparency on how asbestos occurs in real world scenarios and to highlight the variability and/or potential uncertainties in any individual value. A determination of confidence in the range of fate endpoint(s) are also made based on the study quality of contributing data values. The main purpose of this determination is to evaluate how consistent the conclusions are for studies of congruent ratings. Interpretations regarding the strength of a study, model, or data point contribute to how these are individually judged and then considered together. This process culminates in a final judgment about the extent to which an endpoint is supported by the available evidence.

During the evaluation of asbestos, EPA considered both measured and estimated environmental fate and transport data and information set forth in Table 2-2 of the Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2024i). EPA conducted a Tier I assessment to identify the environmental compartments (*i.e.*, water, sediment, biosolids, soil, groundwater, air) of major and minor relevance to the fate and transport of asbestos. EPA then conducted a Tier II assessment to identify the fate pathways and media most likely to cause exposure from environmental releases as described in Section 2.2.2 of the Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2024i). Media-specific fate analyses were performed as described in Sections F.2.2, F.2.3, and F.2.4 of the Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2024i). Fate and transport approaches typically used for discrete organic chemicals, such as the use of EPI Suite™ models or the LRTP screening tool were not used, as they are not applicable for asbestos fibers. However, EPA used AERMOD to estimate air deposition of asbestos fibers as described in Section 3.3.4 of the Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2024i).

6.3 Environmental Release and Occupational Exposure

For evaluating environmental releases and occupational exposures of the various conditions of use (COUs), EPA first developed a map of COUs to broader occupational exposure scenario (OES) categories as shown in Table 3-1 of the Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2024i). Specifically, EPA developed OES categories to group processes or applications with similar sources of release and occupational exposures that occur at industrial and commercial workplaces within the scope of the risk evaluation. For each OES, occupational exposure and environmental release results are expected to be representative of the entire population of workers and sites involved for the given OES in the United States.

Regarding environmental release assessment, EPA identified useful release data for asbestos in three programmatic databases: TRI, NEI, and NRC. As described in Section 3.1 of the Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2024i), EPA estimated OES-specific releases using TRI and NEI for air release estimates, NRC and TRI for water release estimates, and TRI for land release estimates. Where available, EPA used literature search data for estimation of associated release days. To estimate the number of sites using asbestos within a condition of use, EPA relied mainly on U.S. Census Bureau data. However, for two OES categories (*i.e.*, Handling Asbestos-Containing Building Materials During Maintenance, Renovation, and Demolition Activities; and Handling Asbestos-Containing Building Materials During Firefighting or Other Disaster Response Activities), programmatic and systematic review literature search data were insufficient to assess average daily land releases, release frequency, or number of release sites on a national level. Therefore, EPA conducted supplemental searches to collect the data needed to quantify each release parameter on a national level for these two OES categories. The sources used in release assessment for these cases, as well as the approach for estimating releases, are described in detail in Appendix G of the Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2024i).

Regarding occupational exposure assessment, EPA assessed OES-specific exposures to workers and ONUs based on monitoring data, surrogate monitoring data, modeling approaches, and worker activity

information from standard engineering sources and systematic review as described in Section 5.1.1 of the Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2024i). Specifically, inhalation monitoring data for relevant asbestos uses were identified in NIOSH Health Hazard Evaluations (HHE's), OSHA Chemical Exposure Health Data (CEHD), industry submissions, and published and peer-reviewed literature. Where available, EPA used literature search data for estimation of associated exposure days. To estimate the number of workers and ONUs potentially exposed to asbestos within a condition of use, EPA relied mainly on U.S. Census Bureau data. However, for one OES (*i.e.*, Handling Asbestos-Containing Building Materials During Firefighting or Other Disaster Response Activities), U.S. Census Bureau data and systematic review literature search data were not sufficient in characterizing the number of workers. Instead, the number of workers (*i.e.*, career and volunteer firefighters) were determined from a supplemental search of National Fire Protection Agency (NFPA) literature (see Appendix G of the Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2024i) for details).

6.4 General Population, Consumer, and Environmental Exposure

EPA evaluated environmental releases based on reported release data, modeling approaches, and industry sector information from standard engineering sources such as TRI and NEI. As described in Appendix E of the Risk Evaluation for Asbestos Part 2, EPA estimated COU-specific releases where supporting data existed and documented uncertainties where an absence of such data required a broader application of release estimates (U.S. EPA, 2024i). EPA used COU-specific assessment approaches where supporting data existed and documented uncertainties where supporting data were only applicable for broader assessment approaches.

6.4.1 General Population Exposure: Surface and Drinking Water

As described in Section 3.3.2 of the Risk Evaluation for Asbestos Part 2 to evaluate the surface water pathway, EPA relied on measured surface water concentrations (U.S. EPA, 2024i). Measured surface water concentrations were obtained from EPA's Water Quality Exchange (WQX) using the Water Quality Portal (WQP). EPA identified ambient surface water monitoring data through the systematic review process mainly from asbestos waste handling sites and mining related studies to compare these high asbestos concentrations with lower concentrations sources. Drinking water monitoring data from the STORET and Six-Year Review database (Section 3.3.2 of the Risk Evaluation of Asbestos Part 2 (U.S. EPA, 2024i)) were used to discuss asbestos fibers removal or deposition processes before water reaches the general population. EPA used data from 2008 forward and only U.S.-based studies to obtain a current representation of asbestos concentrations in water from legacy uses, disposal, and possibly from natural sources.

6.4.2 General Population Exposure Air Pathway: Ambient Air

EPA identified outdoor air monitoring data for asbestos fibers through systematic review and via modeling environmental releases and dispersion and transport from the source. The data used to evaluate environmental and general population exposures from available studies that have measured asbestos in ambient air as described in Section 3.3.1.1 of the Risk Evaluation for Asbestos Part 2 are studies are from the year 2000 and after to evaluate asbestos exposure concentrations using data that best represents current asbestos fiber releases in the U.S (U.S. EPA, 2024i). The data used in ambient air modeling efforts from environmental releases from occupational activity-based scenarios (Section 3.3.1.2 of the Risk Evaluation of Asbestos Part 2 (U.S. EPA, 2024i)) relied on modeled air concentrations based on industrial releases reported to TRI and NEI databases. Ambient air modeled releases were done for specific and generic facilities.

6.4.3 General Population Exposure Land Pathway: Soil

EPA modeled releases to ambient air from activities that are likely to result in subsequent deposition to soil, as described in Section 3.3.4 of the Risk Evaluation for Asbestos Part 2 from TRI and NEI databases (U.S. EPA, 2024i). EPA used AERMOD to estimate air deposition from facility releases to calculate deposition concentrations near specific and generic facilities. EPA identified measured asbestos concentrations from studies; however, the literature search did not identify studies that had sampled U.S. soils after the year 2000 and without mining influences to obtain representative concentrations for current conditions.

6.4.4 General Population Exposure to Indoor Air

No studies were identified which met all criteria for needed measured indoor air data in residential, public, or school buildings that was COU specific. The general population indoor air exposure assessment focuses only on asbestos levels in buildings that have known or unknown asbestos-containing materials in the building structure, which are not associated with the activity-based consumer and take-home scenarios. EPA searched the systematic review extraction results for representative data to use in a quantitative assessment in which indoor air or suspended dust was sampled after the year 2000 and was from the U.S. or Canada. Additionally, data were excluded in which monitoring samples were collected after disasters (*e.g.,* fallout from the World Trade Center [WTC] terrorist attack) or were influenced by legacy activities not under assessment in the Risk Evaluation for Asbestos Part 2, such as mining (U.S. EPA, 2024i).

6.4.5 Activity-Based Do-it-Yourself Consumer Exposure

The systematic review process identified studies that measured asbestos fibers released during activity-based scenarios. Section 3.1.2 of the Risk Evaluation for Asbestos Part 2 summarizes the activity-based do-it-yourself scenarios under consideration, COUs, subcategories, and the systematic review studies used in this analysis (U.S. EPA, 2024i).

6.4.6 Take-Home Exposure

The take-home exposure scenarios include both handlers and bystanders for each of the occupational exposure scenarios in Section 3.1.1 of the Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2024i). EPA identified studies that mentioned “take-home” exposures in title or abstract, measurements of asbestos released from clothing or other items brought home from the work site during routine handling of clothes, U.S.- or Canada-based studies after the year 2000, and indoor air or personal inhalation data. Experimental simulations and monitoring studies of living area or exposure chambers were used.

6.5 Environmental and Human Health Hazard

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

6.5.1 Environmental Hazard

6.5.1.1 Updates and Clarifications

Section 7.1 of the 2021 Draft Systematic Review Protocol describes how environmental hazard integration is organized into different evidence streams. The environmental hazard evidence streams, as described in Table 7-8 of the 2021 Draft Systematic Review Protocol, have been updated to increase the level of clarity and consistency of granularity (U.S. EPA, 2021); those changes are reflected and described below in Section 6.5.1. Specifically, for risk evaluations conducted under TSCA, the

environmental hazard evidence streams were updated (Table 6-1) to reflect how apical and mechanistic hazardous endpoints more clearly (as defined by the PECO screening criteria) resulting from either controlled field, laboratory, or uncontrolled exposure field studies are binned to better consider the relevancy of the data for the respective risk evaluation. Underlined text in Table 6-1 indicates when text was added to indicate updates made to describe evidence stream categories and considerations for environmental hazard data.

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

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

Evidence streams for environmental hazard included empirical data with apical endpoints and mechanistic data from controlled laboratory experiments for aquatic and terrestrial organisms.

6.5.1.2 Data Available for Environmental Hazard Evidence Integration

The PECO screening criteria states that all non-human and plant models are relevant ecotoxicological models, this includes rodents, rabbits, hens, and other small mammals. To narrow the scope of the included non-human studies, the studies were screened by exposure route (*e.g.*, oral, dermal, and inhalation); oral exposure studies were considered for environmental hazard analysis while dermal and inhalation non-human studies were excluded during TIAB screening. The oral exposure route is the most ecologically relevant for environmental hazard. Dermal exposures were not assessed for terrestrial vertebrates due to the physical form of asbestos being a solid/fiber. The fiber size and the lack of solubility of asbestos fibers prevents systemic dermal penetration; while asbestos may deposit on skin, it will not absorb through the protective outer layers and into the organism. Inhalation is not the primary route of exposure for ecological organisms, as described in Section 4.2 of the Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2024i). In the Risk Evaluation Asbestos Part 1 (U.S. EPA, 2020), three terrestrial studies were identified but were eliminated during the Problem Formulation (PF) stage as they were not relevant to the COUs for chrysotile asbestos (U.S. EPA, 2018b).

In the environmental hazard characterization for asbestos, for aquatic organisms EPA integrated environmental hazard data from empirical data described in Section 4.2.2 of the Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2024i). The Risk Evaluation Asbestos Part 1 (U.S. EPA, 2020) identified four aquatic toxicity studies that were used to identify hazard and risk; EPA identified two additional aquatic toxicity studies with an overall data quality determination of high or medium for the Risk Evaluation for Asbestos Part 2 (U.S. EPA, 2024i) that were included in the environmental hazard characterization.

Evaluations of the strength of evidence and weight of scientific evidence for environmental hazard was conducted as described within Section 7.4.2 of the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021). For additional details on the application of this methodology, please see Section 4.2.6 of the Risk Evaluation for Asbestos.

6.5.2 Human Health Hazard

6.5.2.1 Data Available for Human Health Hazard Evidence Integration

Section 7.5 of the 2021 Draft Systematic Review Protocol described how EPA considers individual evidence streams (human/epidemiologic, animal toxicity, and mechanistic/supplemental studies) when integrating human health hazard evidence (U.S. EPA, 2021). However, because of the wealth of human epidemiologic evidence and the existing assessments for asbestos, a modified fit for purpose approach was employed. Rather than evaluating and integrating all evidence examining asbestos exposure and a health outcome, EPA focused on identifying studies that could inform an updated dose response assessment. In doing so as described in the White Paper (U.S. EPA, 2023b), no new hazards were identified for which a dose response assessment could be conducted. In particular, hazards from oral and dermal exposures have previously had more limited considerations than inhalation exposures, although IARC had a thorough examination of oral exposures. In the reasonably available information identified for Asbestos Part 2, no dose-response data of sufficient quality were available to expand upon the conclusions from prior assessments. Overall, the conclusions from existing assessments by EPA, IARC, and ATSDR (U.S. EPA, 2020, 2014; IARC, 2012; ATSDR, 2001; U.S. EPA, 1988; U.S, 1986; IARC, 1977) continue to reflect the best available science.

7 REFERENCES

ATSDR. (2001). Toxicological profile for asbestos (Update, September 2001) [ATSDR Tox Profile]. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. http://www.atsdr.cdc.gov/ToxProfiles/tp61.pdf

Blettner, M; Heuer, C; Razum, O. (2001). Critical reading of epidemiological papers: A guide. Eur J Public Health 11: 97-101. http://dx.doi.org/10.1093/eurpub/11.1.97

Cooper, GS; Lunn, RM; Ågerstrand, M; Glenn, BS; Kraft, AD; Luke, AM; Ratcliffe, JM. (2016). Study sensitivity: Evaluating the ability to detect effects in systematic reviews of chemical exposures. Environ Int 92-93: 605-610. http://dx.doi.org/10.1016/j.envint.2016.03.017

FIOH. (2014). Asbestos, asbestosis, and cancer: Helsinki criteria for diagnosis and attribution 2014. Helsinki, Finland. https://core.ac.uk/download/pdf/84918194.pdf

IARC. (1977). IARC monographs on the evaluation of carcinogenic risk of chemicals to man: Asbestos. Lyon, France: World Health Organization. http://monographs.iarc.fr/ENG/Monographs/vol1-42/mono14.pdf

IARC. (2012). ARC Monographs on the evaluation of carcinogenic risks to humans: Asbestos (Chrysotile, amosite, crocidolite, tremolite, actinolite, and anthophyllite). Geneva, Switzerland: World Health Organization, International Agency for Research on Cancer. http://monographs.iarc.fr/ENG/Monographs/PDFs/index.php

ILO. (2000). Guidelines for the use of the ILO International Classification of Radiographs of Pneumoconioses. In Occupational Safety and Health Series, No 22. Geneva, Switzerland. https://www.ilo.org/wcmsp5/groups/public/@ed_protect/@protrav/@safework/documents/publication/wcms_108568.pdf

Kopylev, L; Sullivan, PA; Vinikoor, LC; Bateson, TF. (2011). Monte Carlo analysis of impact of underascertainment of Mesothelioma cases on underestimation of risk. Open Epidemiol J 4: 45-53.

LaKind, JS; Sobus, J; Goodman, M; Barr, DB; Fuerst, P; Albertini, RJ; Arbuckle, T; Schoeters, G; Tan, Y; Teeguarden, J; Tornero-Velez, R; Weisel, CP. (2014). A proposal for assessing study quality: Biomonitoring, Environmental Epidemiology, and Short-lived Chemicals (BEES-C) instrument. Environ Int 73: 195-207. http://dx.doi.org/10.1016/j.envint.2014.07.011

NTP. (2015). Handbook for conducting a literature-based health assessment using OHAT approach for systematic review and evidence integration. Research Triangle Park, NC: U.S. Deptartment of Health and Human Services, National Toxicology Program, Office of Health Assessment and Translation. https://ntp.niehs.nih.gov/ntp/ohat/pubs/handbookjan2015_508.pdf

U.S, EPA. (1986). Airborne asbestos health assessment update. (EPA/600/8-84/003F). Washington DC: U.S. Environmental Protection Agency, Environmental Criteria and Assessment.

U.S. EPA. (1988). IRIS summary for asbestos (CASRN 1332-21-4). Washington, DC: U.S. Environmental Protection Agency, Integrated Risk Information System. https://www.regulations.gov/document/EPA-HQ-OPPT-2018-0159-5902

U.S. EPA. (2014). Toxicological review of libby amphibole asbestos: In support of summary information on the Integrated Risk Information System (IRIS) [EPA Report]. (EPA/635/R-11/002F). Washington, DC: Integrated Risk Information System, National Center for Environmental Assessment, Office of Research and Development. https://cfpub.epa.gov/ncea/iris/iris_documents/documents/toxreviews/1026tr.pdf

U.S. EPA. (2018a). Application of systematic review in TSCA risk evaluations. (740-P1-8001). Washington, DC: 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

U.S. EPA. (2018b). Problem formulation of the risk evaluation for asbestos [EPA Report]. (EPA-740-

R1-7018). Washington, DC: Office of Chemical Safety and Pollution Prevention. https://www.regulations.gov/document/EPA-HQ-OPPT-2019-0501-0024

U.S. EPA. (2020). Risk evaluation for asbestos, Part I: Chrysotile asbestos [EPA Report]. (EPA-740-R1-8012). Washington, DC: Office of Chemical Safety and Pollution Prevention. https://www.regulations.gov/document/EPA-HQ-OPPT-2019-0501-0117

U.S. EPA. (2021). Draft systematic review protocol supporting TSCA risk evaluations for chemical substances, Version 1.0: A generic TSCA systematic review protocol with chemical-specific methodologies. (EPA Document #EPA-D-20-031). Washington, DC: Office of Chemical Safety and Pollution Prevention. https://www.regulations.gov/document/EPA-HQ-OPPT-2021-0414-0005

U.S. EPA. (2022). Final scope of the risk evaluation for asbestos. Part 2: Supplemental evaluation including legacy uses and associated disposals of asbestos [EPA Report]. (EPA Document# EPA-740-R-21-002). n.p.: U.S. Environmental Protection Agency, Office of Chemical Pollution and Safety Prevention. https://www.epa.gov/system/files/documents/2022-06/Asbestos%20Part%202_FinalScope.pdf

U.S. EPA. (2023a). Draft Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos. Washington, DC: Office of Chemical Safety and Pollution Prevention, Office of Pollution Prevention and Toxics.

U.S. EPA. (2023b). White Paper: Quantitative Human Health Approach to be Applied in the Risk Evaluation for Asbestos Part 2 – Supplemental Evaluation including Legacy Uses and Associated Disposals of Asbestos. (EPA-740-S-23-001). Washington, DC: Office of Chemical Safety and Pollution Prevention, Office of Pollution Prevention and Toxics.

U.S. EPA. (2024a). Risk Evaluation for Asbestos Part 2 – Systematic Review Supplemental File: Data Extraction Information for Environmental Hazard and Human Health Hazard Animal Toxicology and Epidemiology. Washington, DC: Office of Chemical Safety and Pollution Prevention, Office of Pollution Prevention and Toxics.

U.S. EPA. (2024b). Risk Evaluation for Asbestos Part 2 – Systematic Review Supplemental File: Data Extraction Information for General Population, Consumer, and Environmental Exposure. Washington, DC: Office of Chemical Safety and Pollution Prevention, Office of Pollution Prevention and Toxics.

U.S. EPA. (2024c). Risk Evaluation for Asbestos Part 2 – Systematic Review Supplemental File: Data Quality Evaluation and Data Extraction Information for Environmental Fate and Transport. Washington, DC: Office of Chemical Safety and Pollution Prevention, Office of Pollution Prevention and Toxics.

U.S. EPA. (2024d). Risk Evaluation for Asbestos Part 2 – Systematic Review Supplemental File: Data Quality Evaluation and Data Extraction Information for Environmental Release and Occupational Exposure. Washington, DC: Office of Chemical Safety and Pollution Prevention, Office of Pollution Prevention and Toxics.

U.S. EPA. (2024e). Risk Evaluation for Asbestos Part 2 – Systematic Review Supplemental File: Data Quality Evaluation and Data Extraction Information for Physical and Chemical Properties. Washington, DC: Office of Chemical Safety and Pollution Prevention, Office of Pollution Prevention and Toxics.

U.S. EPA. (2024f). Risk Evaluation for Asbestos Part 2 – Systematic Review Supplemental File: Data Quality Evaluation Information for Environmental Hazard. Washington, DC: Office of Chemical Safety and Pollution Prevention, Office of Pollution Prevention and Toxics.

U.S. EPA. (2024g). Risk Evaluation for Asbestos Part 2 – Systematic Review Supplemental File: Data Quality Evaluation Information for General Population, Consumer, and Environmental Exposure. Washington, DC: Office of Chemical Safety and Pollution Prevention, Office of Pollution Prevention and Toxics.

U.S. EPA. (2024h). Risk Evaluation for Asbestos Part 2 – Systematic Review Supplemental File: Data Quality Evaluation Information for Human Health Hazard Epidemiology. Washington, DC: Office of Chemical Safety and Pollution Prevention, Office of Pollution Prevention and Toxics.

U.S. EPA. (2024i). Risk Evaluation for Asbestos Part 2: Supplemental Evaluation Including Legacy Uses and Associated Disposals of Asbestos. (EPA-740-D-24-006). Washington, DC: U.S. Environmental Protection Agency, Office of Chemical Safety and Pollution Prevention, Office of Pollution Prevention and Toxics. https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/risk-evaluation-asbestos-part-2-supplemental-evaluation

Von Elm, E; Altman, DG; Egger, M; Pocock, SJ; Gøtzsche, PC; Vandenbroucke, JP. (2008). The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. J Clin Epidemiol 61: 344-349. http://dx.doi.org/10.1016/j.jclinepi.2007.11.008