

June 2<sup>nd</sup>, 2020

## Comments from the University of California, San Francisco's Program on Reproductive Health and the Environment on the EPA Draft TSCA Risk Evaluation for Asbestos

Submitted online via *Regulations.gov* to docket EPA-HQ-OPPT-2019-0501

These comments are submitted on behalf of the University of California, San Francisco's Program on Reproductive Health and the Environment the signer's institutional affiliations are included for identification purposes only and do not imply institutional endorsement or support unless indicated otherwise.

We appreciate the opportunity to provide written comments on the draft risk evaluation for Asbestos, issued under EPA's Toxic Substances Control Act (TSCA), as amended by the Frank R. Lautenberg Chemical Safety for the 21<sup>st</sup> Century Act ("amended TSCA").<sup>1</sup> The first medical article on the hazards of asbestos dust appeared in the *British Medical Journal* in 1924.<sup>2</sup> Asbestos is used in building materials or for heat-resistant clothing, and has been linked to several cancers and diseases. Of EPA's First 10 Chemicals to consider under amended TSCA, Asbestos is the most well-known by the public and is currently the subject of legislative action.<sup>3</sup>

We have previously commented on the inadequate scientific methods EPA has implemented in the completed draft risk evaluations, and many of the methodological issues which undercut the science

<sup>1</sup>US EPA. (2020). Asbestos; Draft Toxic Substances Control Act (TSCA) Risk Evaluation and TSCA Science Advisory Committee on Chemicals (SACC) Meetings; Notice of Availability, Public Meetings, and Request for Comment. Available: <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0501-0001>

<sup>2</sup> Bartrip P. W. (2004). History of asbestos related disease. *Postgraduate medical journal*, 80(940), 72–76. <https://doi.org/10.1136/pmj.2003.012526>

<sup>3</sup> Alan Reinstein Ban Asbestos Now Act of 2019, S. 717, 116th Cong., 1st Sess. (2019).

and underestimate risk are present in this evaluation.<sup>4,5,6, 7,8,9,10</sup> EPA also fails to assess the legacy uses of Asbestos, which is in direct conflict with the U.S. Court of Appeals for the Ninth Circuit which ruled in November 2019 that EPA’s exclusion of legacy activities was a violation of the plain language of TSCA, finding its rationale for the exclusion “without merit.”<sup>11</sup> EPA states in the draft risk evaluation that it “...intends to consider legacy uses and associated disposal in a supplemental scope document and supplemental risk evaluation.”<sup>12</sup> However, while EPA has signaled their acknowledgement that they need to address legacy use, it needs to be in the draft risk evaluation to ensure that it has been adequately accounted for. Until that time, it is essentially missing from the risk evaluation, and thus will be counted as zero. We again identify multiple flaws in EPA’s systematic review methodology, including; its incomplete and non-transparent literature review practice and that it fails to use a protocol that outlines the pre-established methods to be used throughout the systematic review process as required by EPA regulation under TSCA.

Our comments address the following main points:

- 1. EPA fails to document how every reference identified in the literature search was used in the draft risk evaluation.**
- 2. EPA fails to transparently apply a predefined eligibility criteria to the references in the literature search.**

<sup>4</sup> US EPA. (2019). Toxic Substances Control Act (TSCA) Science Advisory Committee on Chemicals Review of Risk Evaluation for Pigment Violet 29 (PV 29). Comment submitted by Hanna Vesterinen, Research Consultant to UCSF PRHE et al. Available: <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2018-0604-0043>

<sup>5</sup> US EPA. (2019). Draft Toxic Substances Control Act (TSCA) Risk Evaluations and TSCA Science Advisory Committee on Chemicals (SACC) Meetings; Cyclic Aliphatic Bromide Cluster (HBCD) and 1,4-Dioxane; Notice of Availability and Public Meetings. Comment submitted by Swati Rayasam, Science Associate, Program on Reproductive Health and the Environment, Department of Obstetrics, Gynecology and Reproductive Sciences, University of California, San Francisco et al. Available: <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0237-0059> and <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0238-0056>

<sup>6</sup> US EPA. (2019). Toxic Substances Control Act (TSCA) Science Advisory Committee on Chemicals Review of Risk Evaluation for 1-Bromopropane. Comment submitted by Swati Rayasam, Science Associate, Program on Reproductive Health and the Environment, Department of Obstetrics, Gynecology and Reproductive Sciences, University of California, San Francisco et al. Available: <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0235-0053>

<sup>7</sup> US EPA. (2019). Toxic Substances Control Act (TSCA) Science Advisory Committee on Chemicals Review of Risk Evaluation for Methylene Chloride. Comment submitted by Swati Rayasam, Science Associate, Program on Reproductive Health and the Environment, University of California, San Francisco (UCSF PRHE) et al. Available: <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0437-0069>

<sup>8</sup> US EPA. (2020). Meetings: N-Methylpyrrolidone; Draft Toxic Substances Control Act (TSCA) Risk Evaluation and TSCA Science Advisory Committee on Chemicals. Comment submitted by Veena Singla, Associate Director, Program on Reproductive Health and the Environment, School of Medicine, University of California, San Francisco. Available: <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0236-0040>

<sup>9</sup> US EPA. (2020). Toxic Substances Control Act (TSCA) Science Advisory Committee on Chemicals Review of Risk Evaluation for Carbon Tetrachloride. Comment submitted by Swati Rayasam, Science Associate, Program on Reproductive Health and the Environment, Department of Obstetrics, Gynecology and Reproductive Sciences, University of California, San Francisco et al. Available: <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0499-0041>

<sup>10</sup> US EPA. (2020). Trichloroethylene; Draft Toxic Substances Control Act (TSCA) Risk Evaluation and TSCA Science Advisory Committee on Chemicals (SACC) Meetings; Notice of Availability, Public Meetings, and Request for Comment. Comment submitted by Swati Rayasam et al., Science Associate, Program on Reproductive Health and the Environment, Department of Obstetrics, Gynecology and Reproductive Sciences, University of California, San Francisco (UCSF PRHE). Available: <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0500-0106>

<sup>11</sup> *Safer Chemicals, Healthy Families v USEPA* (2019). No. 17-72260 (9th Cir. Nov. 14, 2019). Pg. 53. “EPA’s contention that TSCA can reasonably be read to refer to the future use of a product, and disposals associated with such use, only when the product will also be manufactured in the future for that use—and not when the product is no longer manufactured for the relevant use—is without merit. TSCA’s “conditions of use” definition plainly addresses conditions of use of chemical substances that will be used or disposed of in the future, regardless of whether the substances are still manufactured for the particular use.”

<sup>12</sup> US EPA. (2020). Asbestos; Draft Toxic Substances Control Act (TSCA) Risk Evaluation and TSCA Science Advisory Committee on Chemicals (SACC) Meetings; Notice of Availability, Public Meetings, and Request for Comment. Pg 29. Available: <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0501-0001>

**3. EPA fails to use a protocol that outlines the pre-established methods to be used throughout the systematic review process as required by EPA regulation under TSCA.**

We appreciate the opportunity to provide public input. Please do not hesitate to contact us with any questions regarding these comments.

Sincerely,

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**DETAILED COMMENTS**

**1. EPA fails to document how every reference identified in the literature search was used in the draft risk evaluation.**

We have commented previously on the issues with the literature review step present in EPA's draft risk evaluations for Carbon Tetrachloride<sup>13</sup> and Trichloroethylene<sup>14</sup> and these same issues carry through in both similar and different ways in the draft risk evaluation for Asbestos. For example, '1.5.1 Data and Information Collection' of the Asbestos draft risk evaluation it states that:

*"The literature and screening strategy as specifically applied to asbestos is described in the Strategy for Conducting Literature Searches for Asbestos: Supplemental Document to the TSCA Scope Document (EPA-HQ-OPPT-2016-0736), and the results of the title and abstract screening*

<sup>13</sup> US EPA. (2020). Draft Toxic Substances Control Act Risk Evaluations: Carbon Tetrachloride. Comment submitted by Swati Rayasam, Science Associate, Program on Reproductive Health and the Environment, University of California, San Francisco et al. Available: <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0499-0041>

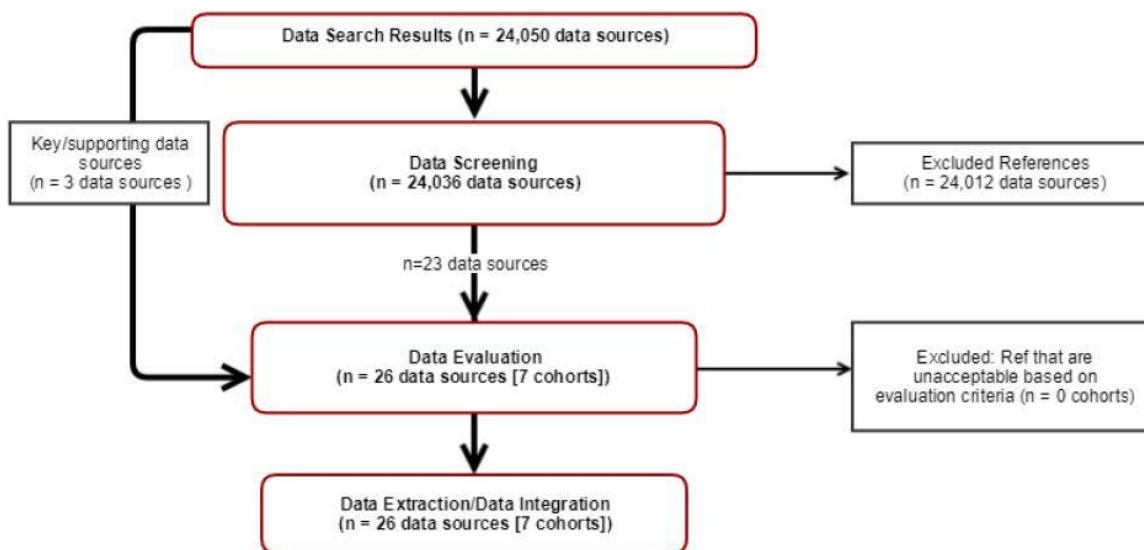
<sup>14</sup> US EPA. (2020). Draft Toxic Substances Control Act Risk Evaluations: Trichloroethylene. Comment submitted by Swati Rayasam, Science Associate, Program on Reproductive Health and the Environment, University of California, San Francisco et al. Available: <https://www.regulations.gov/docket?D=EPA-HQ-OPPT-2019-0500>

process were published in the Asbestos (CASRN 1332-21-4) Bibliography: Supplemental File for the TSCA Scope Document, EPA-HQ-OPPT-2016-0736) (U.S. 1510 EPA, 2017b). **For studies determined to be on-topic (or relevant) after title and abstract screening, EPA conducted a full text screening to further exclude references that were not relevant to the risk evaluation.**"<sup>15</sup>

In 'Asbestos Bibliography: Supplemental File for the TSCA Scope Document'<sup>16</sup> there are 344 pages (Pg. 783-1127) of "on Topic" studies following title and abstract screening for the 'Human health Hazard Literature Search Results' with approximately 30 studies per page, totaling approximately 10,320 studies. However, in the Asbestos draft risk evaluation, 'Figure 1-8 Key Supporting Data Sources for Human Health Hazards'<sup>17</sup> (shown below) EPA has excluded this step and failed to show how many "on topic" studies went through full text screening. The Agency has also failed to provide a rationale as to why those studies that were excluded at this step.

**Figure 1-8. Key/Supporting Data Sources for Human Health Hazard**

**Note:** Studies were restricted to only mesothelioma and lung cancer as health outcomes, and further restricted to studies containing information specific to chrysotile asbestos only. The data evaluation and data extraction files are provided as separate files (See Appendix B in this draft RE).



In a systematic review, studies that make it to 'Full text screening' but are excluded thereafter should only be excluded with an explicit justification. The Institute of Medicine (IOM) report 'Finding What Works in Health Care: Standards for Systematic Review' has 21 standards covering the entire systematic

<sup>15</sup>US EPA. (2020). Asbestos; Draft Toxic Substances Control Act (TSCA) Risk Evaluation. Pg. 43-44. Available: [https://www.epa.gov/sites/production/files/2020-03/documents/1\\_draft\\_risk\\_evaluation\\_for\\_asbestos\\_pub.pdf](https://www.epa.gov/sites/production/files/2020-03/documents/1_draft_risk_evaluation_for_asbestos_pub.pdf)

<sup>16</sup> US EPA. (2017). Asbestos (CASRN: 1332-21-4) Bibliography: Supplemental File for the TSCA Scope Document: [https://www.epa.gov/sites/production/files/2017-06/documents/abestos\\_comp\\_bib.pdf](https://www.epa.gov/sites/production/files/2017-06/documents/abestos_comp_bib.pdf) Supplemental File for the TSCA Scope Document. Available: [https://www.epa.gov/sites/production/files/2017-06/documents/ccl4\\_comp\\_bib\\_0.pdf](https://www.epa.gov/sites/production/files/2017-06/documents/ccl4_comp_bib_0.pdf)

<sup>17</sup>US EPA. (2020). Asbestos; Draft Toxic Substances Control Act (TSCA) Risk Evaluation. Pg. 50. Available: [https://www.epa.gov/sites/production/files/2020-03/documents/1\\_draft\\_risk\\_evaluation\\_for\\_asbestos\\_pub.pdf](https://www.epa.gov/sites/production/files/2020-03/documents/1_draft_risk_evaluation_for_asbestos_pub.pdf)

review process that, if adhered to, result in a scientifically valid, transparent, and reproducible systematic review.<sup>18</sup> The IOM report that:

*“In light of the subjective nature of study selection and the large volume of possible citations, the importance of **maintaining a detailed account of study selection cannot be understated**... The SR final report should include a flow chart that shows the number of studies that remain after each stage of the selection process.... **The flow chart documents the number of records identified through electronic databases searched, whether additional records were identified through other sources, and the reasons for excluding articles.** Maintaining a record of excluded as well as selected articles is important.”<sup>19</sup>(Emphasis ours)*

The critical importance of stating the rationale for excluding studies throughout the systematic review process is highlighted in *IOM Standard 3.4.2 “Document the disposition of each report identified including reasons for their exclusion if appropriate.”*<sup>20</sup>

EPA has failed to appropriately document the disposition of each of these 10,320 “on topic” references following title and abstract screening for the ‘Human health Hazard Literature Search Results’ or offer an explicit justification for their exclusion at the full text screening step. This lack of transparency in documenting the disposition of each report identified, including reasons for their exclusion in the Asbestos draft risk evaluation, could lead to bias in the draft risk evaluation, especially as EPA may have excluded studies that are scientifically relevant.

Further, the numbers shown in ‘*Figure 1-8 Key Supporting Data Sources for Human Health Hazards*’ do not accurately reflect the numbers at each step and do not account for all of the references that go through *Data Quality Evaluation* as cited in the ‘*Systematic Review Supplemental File: Data Quality Evaluation of Human Health Hazard Studies: Mesothelioma and Lung Cancer Studies March 2020.*’<sup>21</sup> These issues include:

- In the ‘Data Search Results’, there are 24,050 data sources. 3 sources are later incorporated as ‘key/supporting data’ in the Data evaluation step. Mathematically then, 24,047 data sources should move to the ‘Data Screening’ step, yet only 24,036 move to this step, leaving **11** studies EPA has excluded without justification.
- In the ‘Data Screening’ step, EPA states there are 24,036 data sources, with 24,012 excluded. Therefore, there should be 24 data sources that move to the ‘Data Evaluation’ step, yet only 23 move to this step. Therefore, there is **1** study EPA has not accounted for at this step.
- In the ‘Data Evaluation’ step, EPA states that it evaluated 26 data sources. However, in the “Systematic Review Supplemental File: Data Quality Evaluation of Human Health Hazard Studies” Table 2.1<sup>22</sup> EPA has evaluated **44** data sources for asbestos exposure and lung cancer

<sup>18</sup> Institute of Medicine. (2011). *Finding What Works in Health Care: Standards for Systematic Reviews*. Washington, DC: The National Academies Press

<sup>19</sup> Institute of Medicine. (2011). *Finding What Works in Health Care: Standards for Systematic Reviews*. 3. Standards for Finding and Assessing Individual Studies. Washington, DC: The National Academies Press

<sup>20</sup> Institute of Medicine. (2011). *Finding What Works in Health Care: Standards for Systematic Reviews*. 3. Standards for Finding and Assessing Individual Studies. Washington, DC: The National Academies Press

<sup>21</sup> US EPA. (2020). *Draft Risk Evaluation for Asbestos Systematic Review Supplemental File: Data Quality Evaluation of Human Health Hazard Studies: Mesothelioma and Lung Cancer Studies March 2020*. Available: [https://www.epa.gov/sites/production/files/2020-03/documents/10\\_asbestos\\_data\\_quality\\_evaluation\\_of\\_human\\_health\\_hazard\\_studies\\_public.pdf](https://www.epa.gov/sites/production/files/2020-03/documents/10_asbestos_data_quality_evaluation_of_human_health_hazard_studies_public.pdf)

<sup>22</sup> US EPA. (2020). *Draft Risk Evaluation for Asbestos Systematic Review Supplemental File: Data Quality Evaluation of Human Health Hazard Studies: Mesothelioma and Lung Cancer Studies March 2020*. Pp 28-29. Available: [https://www.epa.gov/sites/production/files/2020-03/documents/10\\_asbestos\\_data\\_quality\\_evaluation\\_of\\_human\\_health\\_hazard\\_studies\\_public.pdf](https://www.epa.gov/sites/production/files/2020-03/documents/10_asbestos_data_quality_evaluation_of_human_health_hazard_studies_public.pdf)

incidence (which also includes the studies on asbestos exposure and mesothelioma incidence). Therefore, there are **18** data sources EPA has not accounted for in the draft risk evaluation without any explanation for their exclusion.

This is a small portion of the overall study database and it raises the larger issue with EPA's ability to accurately identify the science and evaluate it. We have previously commented on the literature review step of EPA's TSCA systematic review method that incorporates select best practices, but also falls short of, or is unclear about, many other best practices for conducting a systematic and transparent literature review.<sup>23</sup> This includes two key features of EPA's framework that are clearly inconsistent with IOM's best practices. EPA fails to:

1. Include or exclude studies based on the protocol's pre-specified criteria, a practice that is critical to avoiding results-based decisions (IOM 3.3.1);<sup>24</sup> and
2. Use two or more members of the review team, working independently, to screen and select studies, which is an essential quality-assurance measure (IOM 3.3.3).<sup>25</sup>

If EPA had complied with this standard (IOM standard 3.3.3) of having two or more members of the review team, working independently, to screen and select studies, such exclusions would be reduced. We therefore recommended EPA immediately comply with this standard for all future evaluations.

Additionally, EPA's method to account for included studies in each step of the literature flow diagram for Human Health Hazards (shown above) is inconsistent with its flow diagram for Environmental Hazards as shown below in *'Figure 1-7. Key/Supporting Data Sources for Environmental Hazards'*, despite that these diagrams are only one page apart in the Asbestos draft risk evaluation.<sup>26</sup> *'Figure 1-7'* below includes the appropriate additional step of reporting the number of studies that are screened at the *'Title/Abstract'* stage and the number at the *'Full Text Screening'* stage while *'Figure 1-8'* does not.

<sup>23</sup> US EPA (2018) The Application of Systematic Review in TSCA Risk Evaluations. Available: EPA-HQ-OPPT-2018-0210

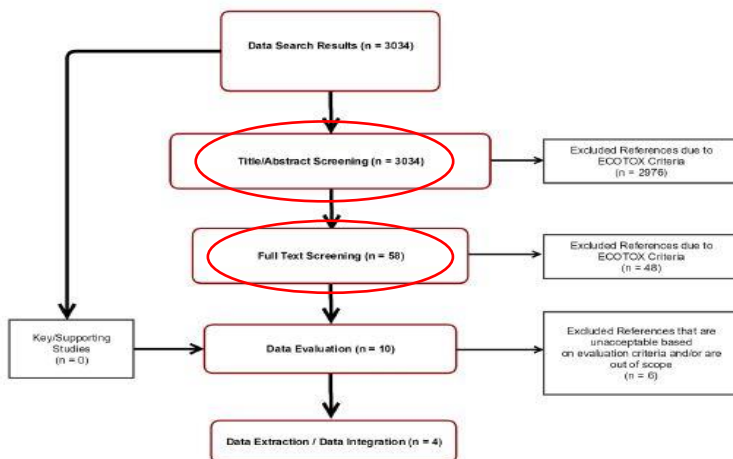
<sup>24</sup> Institute of Medicine. (2011). Finding What Works in Health Care: Standards for Systematic Reviews. 3. Standards for Finding and Assessing Individual Studies. Washington, DC: The National Academies Press

<sup>25</sup> Institute of Medicine. (2011). Finding What Works in Health Care: Standards for Systematic Reviews. 3. Standards for Finding and Assessing Individual Studies. Washington, DC: The National Academies Press

<sup>26</sup> US EPA. (2020). Asbestos; Draft Toxic Substances Control Act (TSCA) Risk Evaluation. Pg. 49. Available: [https://www.epa.gov/sites/production/files/2020-03/documents/1\\_draft\\_risk\\_evaluation\\_for\\_asbestos\\_pub.pdf](https://www.epa.gov/sites/production/files/2020-03/documents/1_draft_risk_evaluation_for_asbestos_pub.pdf)

**Figure 1-7. Key /Supporting Data Sources for Environmental Hazard**

Note: The environmental hazard data sources were identified through literature searches and screening strategies using the ECOTOX Standing Operating Procedures. Additional details can be found in the *Strategy for Conducting Literature Searches for Asbestos: Supplemental Document to the TSCA Scope Document*, (EPA-HQ-OPPT-2016-0736). During PF, EPA made refinements to the conceptual models resulting in the elimination of the terrestrial exposure pathways. Thus, environmental hazard data sources on terrestrial organisms were determined to be out of scope and excluded from data quality evaluation. The data evaluation file is provided as a separate file (See Appendix B in this draft RE).



We strongly recommend that EPA includes **both** of these steps in **every** literature flow diagram it uses in the Asbestos draft risk evaluation, and every future risk evaluation it conducts.

**2. EPA fails to transparently apply a predefined eligibility criteria to the references in the literature search.**

The method in which EPA has developed and applied the eligibility criteria for the identified references throughout the Asbestos draft risk evaluation is deeply concerning. EPA states that:

*“For studies determined to be on-topic (or relevant) after title and abstract screening, EPA conducted a full text screening to further exclude references that were not relevant to the risk evaluation. Screening decisions were made based on eligibility criteria documented in the form of the populations, exposures, comparators, and outcomes (PECO) framework or a modified framework. Data sources that met the criteria were carried forward to the data evaluation stage. The inclusion and exclusion criteria for full text screening for asbestos are available in Appendix D of the Problem Formulation of the Risk Evaluation for Asbestos (U.S. EPA, 2018d).”<sup>27</sup>*

However, the literature and screening strategy as specifically applied to the Asbestos draft risk evaluation is described in ‘*Strategy for Conducting Literature Searches for Asbestos: Supplemental Document to the TSCA Scope Document*’ which was published in June of 2017.<sup>28</sup> The results of the screening of literature search were published in ‘*Asbestos (CASRN 1332-21-4) Bibliography: Supplemental File for the TSCA Scope Document*’ (no date is given in this document although the

<sup>27</sup>US EPA. (2020). Asbestos; Draft Toxic Substances Control Act (TSCA) Risk Evaluation. Pg. 43-44. Available: [https://www.epa.gov/sites/production/files/2020-03/documents/1\\_draft\\_risk\\_evaluation\\_for\\_asbestos\\_pub.pdf](https://www.epa.gov/sites/production/files/2020-03/documents/1_draft_risk_evaluation_for_asbestos_pub.pdf)

<sup>28</sup> US EPA. (2017). Strategy for Conducting Literature Searches for Asbestos: Supplemental Document to the TSCA Scope Document CASRN: 1332-21-4. Available: [https://www.epa.gov/sites/production/files/2017-06/documents/asbestos\\_lit\\_search\\_strategy\\_053017.pdf](https://www.epa.gov/sites/production/files/2017-06/documents/asbestos_lit_search_strategy_053017.pdf)

webpage on which this document is made available says ‘last updated on June 22, 2017’).<sup>29</sup> However, as highlighted by EPA in the Asbestos draft risk evaluation, for studies determined to be ‘on-topic’ (or relevant) after title and abstract screening, EPA conducted a full text screening to further exclude references that were not relevant to the risk evaluation:

***“Screening decisions were made based on eligibility criteria documented in the form of the populations, exposures, comparators, and outcomes (PECO) framework or a modified framework. Data sources that met the criteria were carried forward to the data evaluation stage. The inclusion and exclusion criteria for full text screening for asbestos are available in Appendix D of the Problem Formulation of the Risk Evaluation for Asbestos (U.S. EPA, 2018d).”***<sup>30</sup>

However, the ‘Problem Formulation of the Risk Evaluation for Asbestos’ that outlined this PECO framework was published in May 2018, **after** the searches and initial screening had been completed.<sup>31</sup> The PECO statement (framework) should shape the entire review process, including the search strategy to be used, the study eligibility criteria to be applied, how the data will be extracted from the included studies, the strategy for synthesizing the evidence and how the results will be reported.<sup>32</sup> The IOM states that:

***‘Using prespecified inclusion and exclusion criteria to choose studies is the best way to minimize the risk of researcher biases influencing the ultimate results of the SR. The SR research protocol should make explicit which studies to include or exclude based on the patient population and patient outcomes of interest, the healthcare intervention and comparators, clinical settings (if relevant), and study designs (e.g., randomized vs. observational research) that are appropriate for the research question.’***<sup>33</sup>

While the IOM use PICO (population, intervention, comparator, outcomes) and not PECO statements as their standards relate to systematic reviews applied in the clinical sciences, these principles are the same, as they are designed ‘*minimize the risk of researcher biases influencing the ultimate results of the SR*’. The critical importance of this is again further reinforced in *IOM standard 3.3.1 “Include or exclude studies based on the protocol’s pre-specified criteria.”*<sup>34</sup> The fact that the PECO framework was published after the studies had already been identified in the literature search and screened at the title and abstract stage, means that the PECO could be adjusted based on what literature had been included rather than using a more agnostic approach to literature selection. The possible consequence of this could be that the eligibility criteria was adjusted to support a pre-expected health hazard conclusion and thus contribute to bias in the evaluation if studies were subsequently excluded or included that may support a pre-expected hazard conclusion.

<sup>29</sup> US EPA. (2017). Asbestos (CASRN: 1332-21-4) Bibliography: Supplemental File for the TSCA Scope Document. Available: [https://www.epa.gov/sites/production/files/2017-06/documents/asbestos\\_comp\\_bib.pdf](https://www.epa.gov/sites/production/files/2017-06/documents/asbestos_comp_bib.pdf)

<sup>30</sup>US EPA. (2020). Asbestos; Draft Toxic Substances Control Act (TSCA) Risk Evaluation. Pg. 43-44. Available: [https://www.epa.gov/sites/production/files/2020-03/documents/1\\_draft\\_risk\\_evaluation\\_for\\_asbestos\\_pub.pdf](https://www.epa.gov/sites/production/files/2020-03/documents/1_draft_risk_evaluation_for_asbestos_pub.pdf)

<sup>31</sup> US EPA. (2018). Problem Formulation of the Risk Evaluation for Asbestos. Available: [https://www.epa.gov/sites/production/files/2018-06/documents/asbestos\\_problem\\_formulation\\_05-31-18.pdf](https://www.epa.gov/sites/production/files/2018-06/documents/asbestos_problem_formulation_05-31-18.pdf)

<sup>32</sup> NTP. (2015). Handbook for conducting a literature-based health assessment using OHAT approach for systematic review and evidence integration. U.S. Dept. of Health and Human Services, National Toxicology Program.

<sup>33</sup> Institute of Medicine. (2011). Finding What Works in Health Care: Standards for Systematic Reviews. 3. Standards for Finding and Assessing Individual Studies. Washington, DC: The National Academies Press

<sup>34</sup> Institute of Medicine. (2011). Finding What Works in Health Care: Standards for Systematic Reviews. 3. Standards for Finding and Assessing Individual Studies. Washington, DC: The National Academies Press



Therefore, EPA's failure to predefine the study eligibility criteria applied to the 'on topic' references in the Asbestos draft risk evaluation has the opportunity to introduce bias that may have impacted the results of the draft risk evaluation.

**3. EPA fails to use a protocol that outlines the pre-established methods to be used throughout the systematic review process as required by EPA regulation under TSCA.**

In order for EPA to adequately address these issues relating to its lack of transparency in accounting for all references identified in the literature search and applying a pre-defined eligibility criteria to references in the literature search, EPA must immediately implement protocols for all future draft risk evaluations. The use of pre-established protocols minimizes such biases in the evidence base by explicitly pre-defining how: the questions will be formulated, the searches will be conducted, the eligibility criteria will be applied, and the quality of the included studies will be assessed.<sup>35</sup> Most importantly, it allows greater transparency in the decision-making process throughout the systematic review and is a fundamental element to ensure the integrity of evidence-based evaluations; it is also a critical methodological step absent in the Asbestos draft risk evaluation. Further, not using predefined protocols directly contradicts the EPA's 2017 framework rules mandating that the agency use "a pre-established protocol" to conduct risk assessments.<sup>36</sup> We again urge EPA to immediately implement the use of pre-established protocols to enhance transparency in the decision-making process and consistency in their draft risk evaluations.

<sup>35</sup> National Research Council. (2014). Review of EPA's Integrated Risk Information System (IRIS) Process. Washington, DC: National Academies Press.

<sup>36</sup> 40 CFR 702 Pg. 33733