Database Search and Systematic Evidence Map (SEM)

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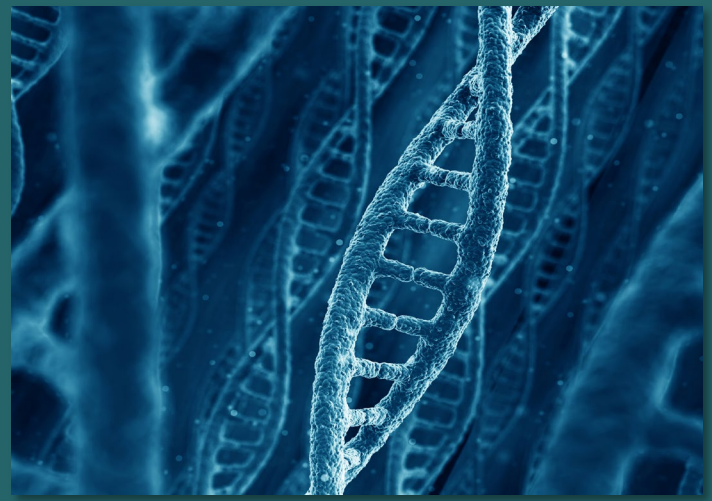

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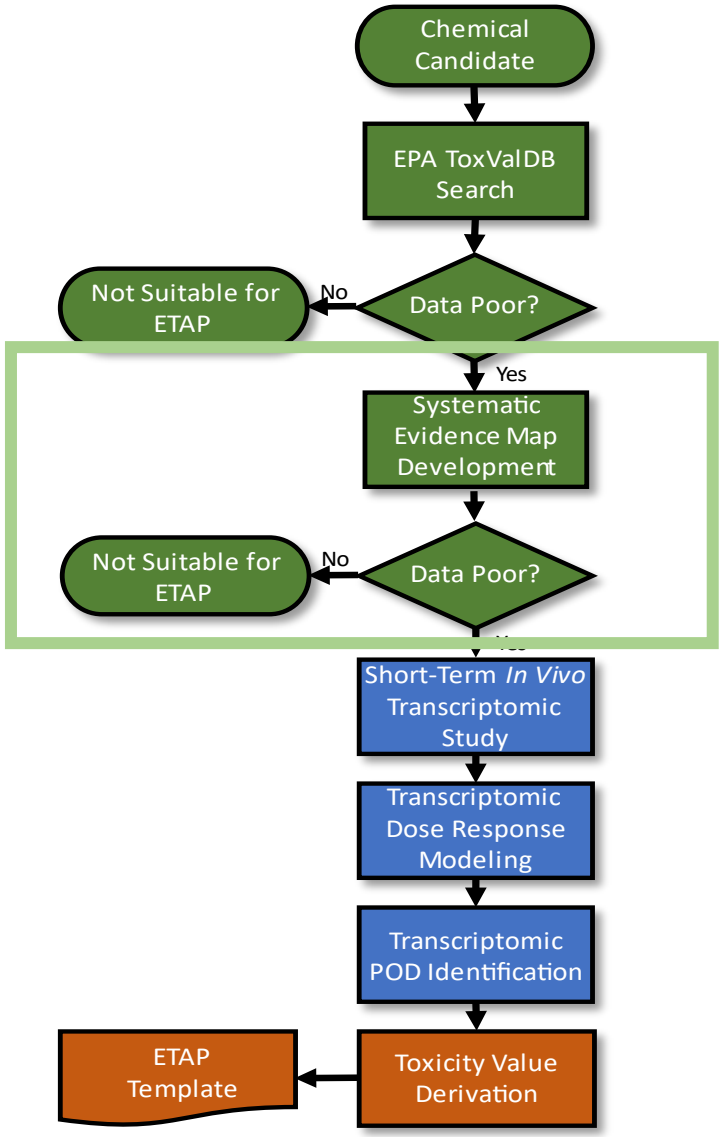
Outline



- Systematic evidence map (SEM) overview
- Use of SEMs in context of ETAP
- Specific methods
  - Search strategy
  - Information sources
  - Screening processes
  - Dissemination

Systematic Evidence Map

- Pre-decisional analysis that uses systematic review methods to compile and summarize evidence but does not reach assessment hazard or toxicity value conclusions
  - Front end compilation of evidence
- Used for:
  - Prioritization
  - Problem formulation and scoping
  - Identifying data gaps
  - Determining the need for assessment update

Systematic Evidence Map Methods

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Short communication

Use of systematic evidence maps within the US environmental protection agency (EPA) integrated risk information system (IRIS) program: Advancements to date and looking ahead

Kristina A. Thayer [a,*], Rachel M. Shaffer [a], Michelle Angrish [a], Xabier Arzuaga [a], Laura M. Carlson [b], Allen Davis [a], Laura Dishaw [a], Ingrid Druwe [a], Catherine Gibbons [a], Barbara Glenn [a], Ryan Jones [b], J. Phillip Kaiser [a], Channa Keshava [a], Nagalakshmi Keshava [b], Andrew Kraft [a], Lucina Lizarraga [a], Kristan Markey [a], Amanda Persad [a], Elizabeth G Radke [a], Glenn Rice [a], Brittany Schulz [c], Teresa Shannon [a], Andrew Shapiro [b], Shane Thacker [b], Suryanarayana Vulimiri [a], George Woodall [b], Erin Yost [a]

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ABSTRACT

Systematic evidence maps (SEMs) are increasingly used to inform decision-making and risk management priority-setting and to serve as problem formulation tools to refine the focus of questions that get addressed in

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Full length article

Systematic evidence map (SEM) template: Report format and methods used for the US EPA integrated risk information system (IRIS) program, provisional peer reviewed toxicity value (PPRTV) program, and other "fit for purpose" literature-based human health analyses

Kristina A. Thayer [a,*], Michelle Angrish [a], Xabier Arzuaga [a], Laura M. Carlson [b], Allen Davis [a], Laura Dishaw [a], Ingrid Druwe [a], Catherine Gibbons [a], Barbara Glenn [a], Ryan Jones [b], J. Phillip Kaiser [a], Channa Keshava [a], Nagalakshmi Keshava [a], Andrew Kraft [a], Lucina Lizarraga [a], Amanda Persad [a], Elizabeth G. Radke [a], Glenn Rice [a], Brittany Schulz [c], Rachel M. Shaffer [a], Teresa Shannon [a], Andrew Shapiro [b], Shane Thacker [b], Suryanarayana V. Vulimiri [a], Antony J. Williams [d], George Woodall [b], Erin Yost [a], Robyn Blain [e], Katherine Duke [e], Alexandra E. Goldstone [e], Pam Hartman [e], Kevin Hobbie [e], Brandall Ingle [e], Courtney Lemeris [e], Cynthia Lin [e], Alex Lindahl [e], Kristen McKinley [e], Parnian Soleymani [e], Nicole Vetter [e]

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Use of SEMs for ETAP

- Assess availability of repeated dose animal toxicity data if no suitable studies are identified in EPA ToxVal database (ToxValDB)
  - ToxValDB collates publicly available toxicity dose–effect related summary values (e.g., REACH data submissions, ToxRefDB, IRIS, PPRTV)
  - ToxValDB may miss recent studies, assessments and pertinent reviews in open literature
- ETAP considered if no repeated dose toxicity studies are available from ToxValDB or the SEM
  - Other options also considered (viability of read-across analogue approach)

Flow Chart

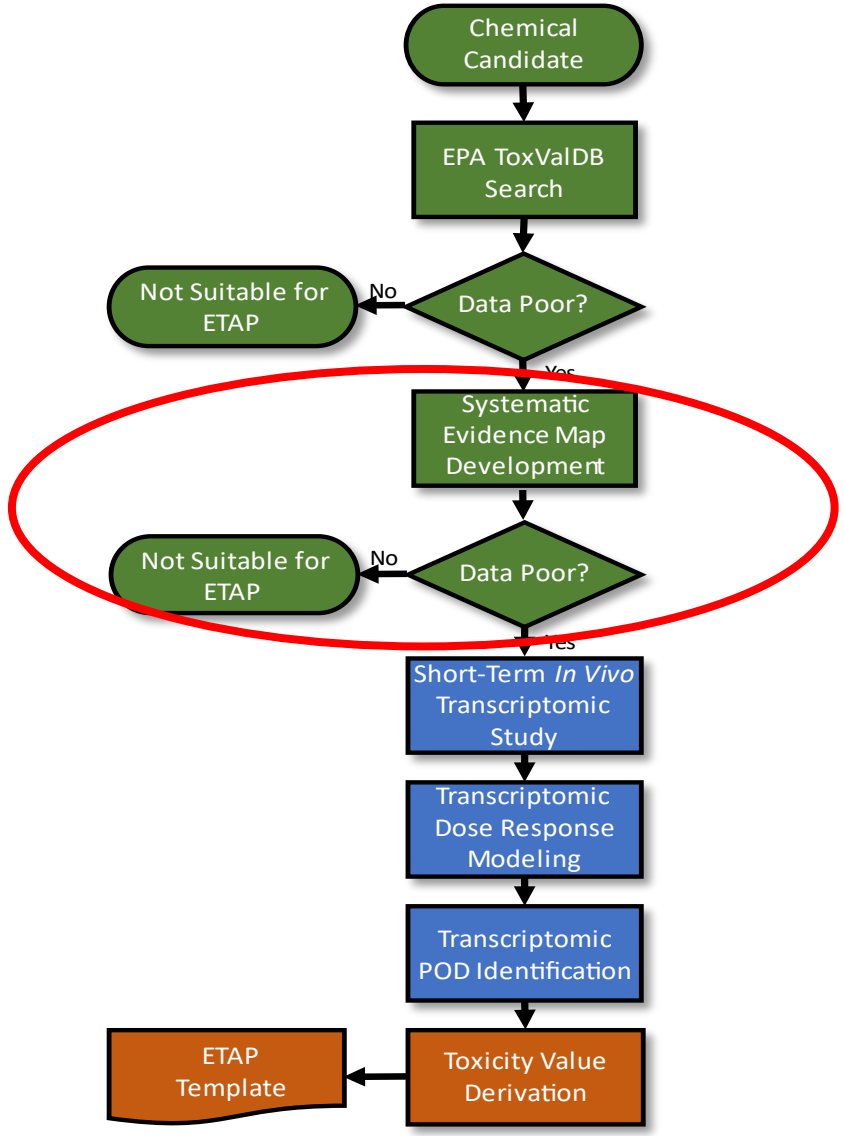


Figure 2-1 From Standard Methods for Development of EPA Transcriptomic Assessment Products (ETAPs)

Search Strategy

- Literature search has no date or language restriction
- Preferred chemical name, CASRN, DTXSID, and synonyms used as foundation of search
  - Synonyms identified from CompTox Chemicals Dashboard indicated as “valid” or “good”
  - If number of records retrieved are few (i.e., <200), no further filtering undertaken
  - Otherwise, pre-set literature search strategies (“filters”) in SWIFT Review software used to identify human health content (i.e, human, animal models for human health, and *in vitro* studies).

CASRN = Chemical Abstracts Service Registry Number; DTXSID = Distributed Structure-Searchable Toxicity (DSSTox) database substance identifier

Information Sources

- Database searches
  - PubMed
  - Web of Science
  - ProQuest
- Other resources (“grey literature”)
  - Manual review of reference lists in publicly available draft assessments
  - Manual review of reference list from studies meeting inclusion criteria
  - ECHA registration dossiers, EPA ChemView, NTP, OECD Chemicals Database and eChemPortal, EPA ECOTOX database
  - Searches of databases for Confidential Business Information (CBI)

ECHA= European Chemicals Agency; NTP = National Toxicology Program, OECD = Organisation for Economic Cooperation and Development

Inclusion Criteria

PECO element	Evidence
Populations	**Human**: Any population and lifestage (occupational or general population, including children and other sensitive populations). **Animal:** Non-human mammalian animal species (whole organism) of any lifestage (including fetal, early postnatal, adolescents and adults).
Exposures	**Relevant forms:** [substance X] (CAS number) Other forms of [chemical X] that readily dissociate (*e.g.*, list any salts, etc.). Known metabolites of interest, including metabolites used to estimate exposures to [chemical X]. **Human:** Any exposure to [chemical X] via [oral or inhalation] route[s]. Studies will also be included if biomarkers of exposure are evaluated (*e.g.*, measured chemical or metabolite levels in tissues or bodily fluids), but the exposure route is unclear or likely from multiple routes. Other exposure routes, such as those that are clearly dermal, are tracked during title and abstract screening and tagged as "potentially relevant supplemental material." **Animal:** Any exposure to [chemical X] via [oral or inhalation] route[s] of >1 day duration, or any duration assessing exposure during reproduction or development. Studies involving exposures to mixtures will be included only if they include an experimental arm with exposure to [chemical X] alone. Other exposure routes, including [dermal or injection], are tracked during title and abstract as "potentially relevant supplemental material."
Comparators	**Human:** A comparison or referent population exposed to lower levels (or no exposure/exposure below detection limits), or exposure for shorter periods of time, or cases versus controls, or a repeated measures design. However, worker surveillance studies are considered to meet PECO criteria even if no statistical analyses using a referent group is presented. Case reports or case series of > 3 people will be considered to meet PECO criteria, while case reports describing findings in 1–3 people will be tracked as "potentially relevant supplemental material." **Animal:** A concurrent control group exposed to vehicle-only and/or untreated control (control could be a baseline measurement, *e.g.*, acute toxicity studies of mortality, or a repeated measure design).
Outcomes	All health outcomes (cancer and non-cancer). In general, endpoints related to clinical diagnostic criteria, disease outcomes, biochemical, histopathological examination, or other apical/phenotypic outcomes are considered to meet PECO criteria.

Screening Process

- Each record reviewed independently by 2 screeners at title and abstract (TIAB) and full-text levels
  - PECO criteria guide screening decisions
- Conflicts tracked for resolution
- TIAB screening
  - Include, exclude, or unclear
- “Include” or “unclear” records advance to full-text
- Specialized systematic review software used to save time and keep track of screening decisions

Example:
Perfluoro-3-Methoxypropanoic Acid (MOPA)

Documentation

Search	Search Strategy	Date and Results
WOS	TS="2,2,3,3-Tetrafluoro-3-(trifluoromethoxy)propanoic acid" OR TS="377-73-1" OR TS="O=C(O)C(F)(F)C(F)(F)OC(F)(F)F" OR TS="Perfluoro-3-methoxypropanoic acid" OR TS="Perfluoro-4-oxapentanoic acid" OR TS="Propanoic acid, 2, 2, 3, 3- tetrafluoro-3- (trifluoromethoxy) -" OR TS="BRN 1795024" OR TS="Perfluoromethoxypropionic acid" OR TS="PERFLUORO PFMPA" OR TS="PF4OPeA" OR TS="PF-4O-PeA" OR TS="PFMOPrA" OR TS="PFMPA" OR TS="PFPE-2" OR TS="Propionic acid, 2,2,3,3-tetrafluoro-3-(trifluoromethoxy)-"	12/19/2022 5 results
PubMed	"2,2,3,3-Tetrafluoro-3-(trifluoromethoxy)propanoic acid"[tw] OR "377-73-1"[tw] OR "377-73-1"[rn] OR "O=C(O)C(F)(F)C(F)(F)OC(F)(F)F"[tw] OR "Perfluoro-3-methoxypropanoic acid"[tw] OR "Perfluoro-4-oxapentanoic acid"[tw] OR "Propanoic acid, 2, 2, 3, 3- tetrafluoro- 3- (trifluoromethoxy) -"[tw] OR "BRN 1795024"[tw] OR "Perfluoromethoxypropionic acid"[tw] OR "PERFLUORO PFMPA"[tw] OR "PF4OPeA"[tw] OR "PF-4O-PeA"[tw] OR "PFMOPrA"[tw] OR "PFMPA"[tw] OR "PFPE-2"[tw] OR "Propionic acid, 2,2,3,3-tetrafluoro-3-(trifluoromethoxy)-"[tw]	12/19/2022 4 results
ProQuest	ABSTRACT,TITLE("2,2,3,3-Tetrafluoro-3-(trifluoromethoxy)propanoic acid") OR ABSTRACT,TITLE("377-73-1") OR ABSTRACT,TITLE("O=C(O)C(F)(F)C(F)(F)OC(F)(F)F") OR ABSTRACT,TITLE("Perfluoro-3-methoxypropanoic acid") OR ABSTRACT,TITLE("Perfluoro-4-oxapentanoic acid") OR ABSTRACT,TITLE("Propanoic acid, 2, 2, 3, 3- tetrafluoro- 3-(trifluoromethoxy) -") OR ABSTRACT,TITLE("BRN 1795024") OR ABSTRACT,TITLE("Perfluoromethoxypropionic acid") OR ABSTRACT,TITLE("PERFLUORO PFMPA") OR ABSTRACT,TITLE("PF4OPeA") OR ABSTRACT,TITLE("PF-4O-PeA") OR ABSTRACT,TITLE("PFMOPrA") OR ABSTRACT,TITLE("PFMPA") OR ABSTRACT,TITLE("PFPE-2") OR ABSTRACT,TITLE("Propionic acid, 2,2,3,3-tetrafluoro-3-(trifluoromethoxy)-")	12/19/2022 3 results
	Total unique references found	**5**

Appendix 1 From EPA Transcriptomic Assessment Product (ETAP) for Perfluoro-3-Methoxypropanoic Acid

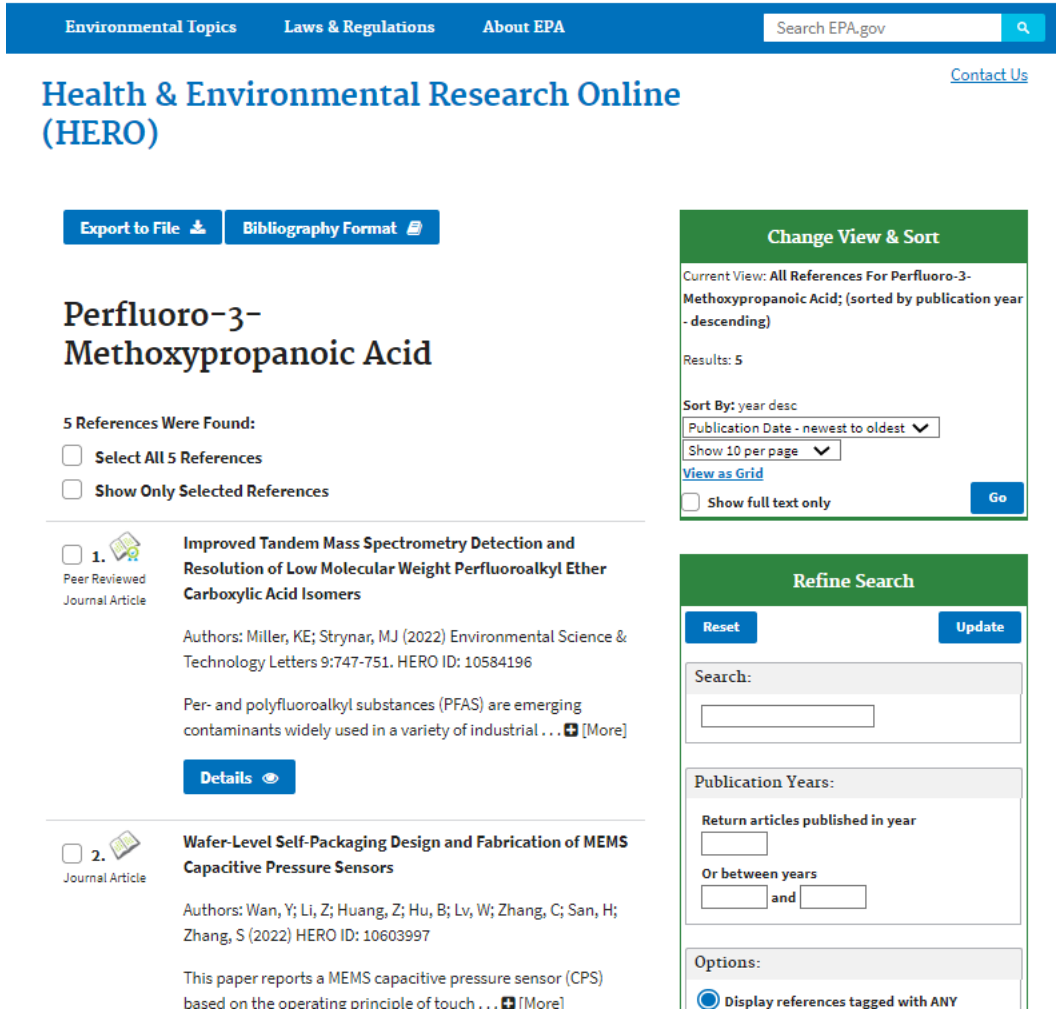
Dissemination

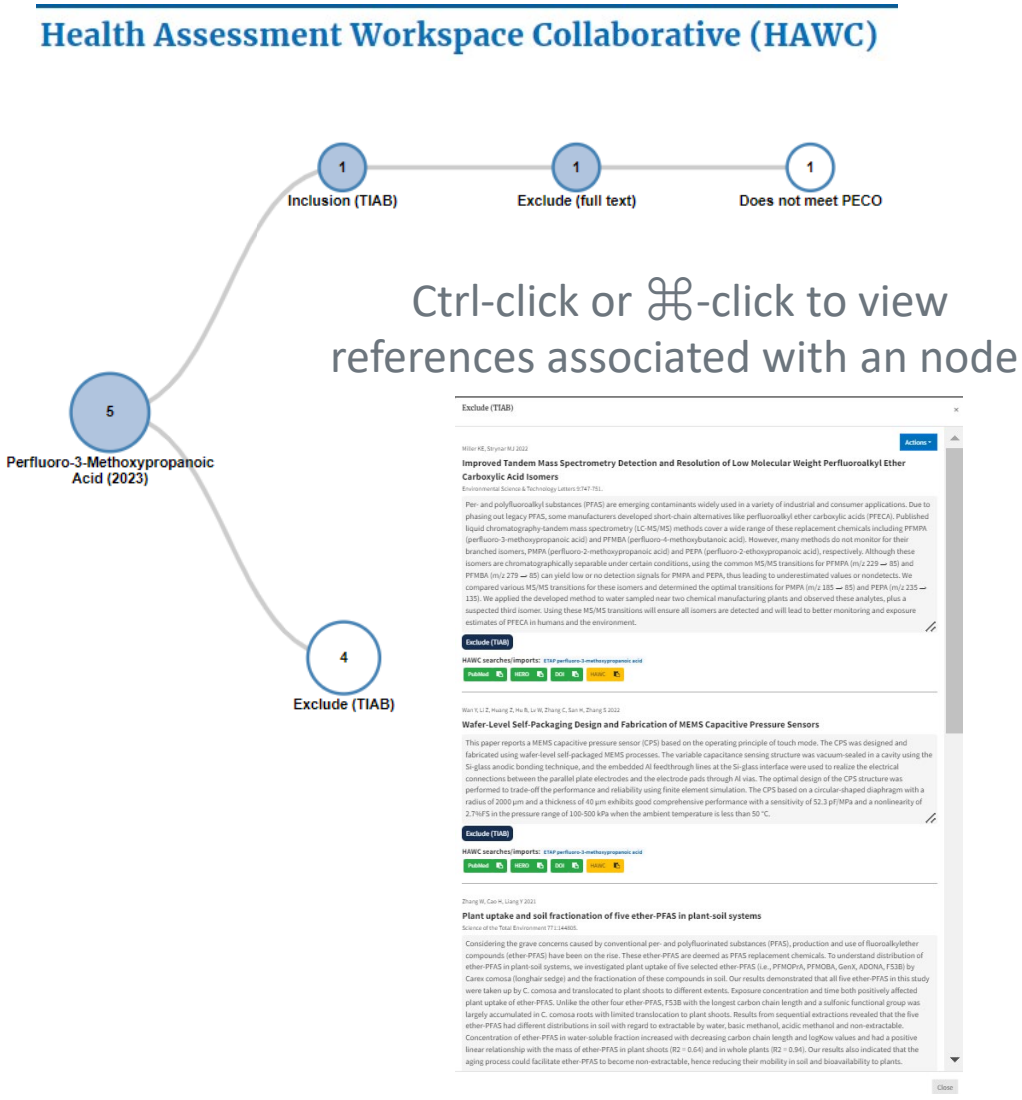
The five unique references identified for perfluoro-3-methoxypropanoic acid are:

1. Miller, KE; Strynar, MJ. (2022). Improved Tandem Mass Spectrometry Detection and Resolution of Low Molecular Weight Perfluoroalkyl Ether Carboxylic Acid Isomers Environmental Science & Technology Letters 9:747-751. http://dx.doi.org/10.1021/acs.estlett.2c00509 HERO ID: 10584196
2. Wan, Y; Li, Z; Huang, Z; Hu, B; Lv, W; Zhang, C; San, H; Zhang, S. (2022). Wafer-Level Self-Packaging Design and Fabrication of MEMS Capacitive Pressure Sensors http://dx.doi.org/10.3390/mi13050738 HERO ID: 10603997
3. Woodlief, T; Vance, S; Hu, Q; Dewitt, J. (2021). Immunotoxicity of per- and polyfluoroalkyl substances: Insights into short-chain PFAS exposure Toxics 9:100. http://dx.doi.org/10.3390/toxics9050100 HERO ID: 9959537
4. Zhang, W; Cao, H; Liang, Y. (2021). Plant uptake and soil fractionation of five ether-PFAS in plant-soil systems Science of the Total Environment 771:144805. http://dx.doi.org/10.1016/j.scitotenv.2020.144805 HERO ID: 9952516
5. Kometani, N; Kaneko, M; Morita, T; Yonezawa, Y. (2008). The formation of photolytic silver clusters in water/supercritical CO2 microemulsions Colloids and Surfaces A: Physicochemical and Engineering Aspects 321:301-307. http://dx.doi.org/10.1016/j.colsurfa.2008.02.005 HERO ID: 5387167

Appendix 1 From EPA Transcriptomic Assessment Product (ETAP) for Perfluoro-3-Methoxypropanoic Acid

Dissemination, continued





https://hero.epa.gov/hero/index.cfm/project/page/project_id/4746

Summary

- SEMs are a comprehensive approach to identifying data using systematic review methods.
- By using the SEM approach, we have a high degree of confidence that no data exist and ETAP is an appropriate next step.