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Data Quality Evaluation of Epidemiologic Studies under Amended TSCA

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Systematic Review Process

Systematic Review is a comprehensive, 'unbiased', transparent and reproducible way to identify relevant literature on a topic.

On June 22, 2016, the Frank R. Lautenberg Chemical Safety for the 21st Century Act was signed into law, amending the Toxic Substance Control Act (TSCA), the Nation's primary chemicals management law. The U.S. EPA's Office of Pollution Prevention and Toxics (EPA/OPPT) intends to apply systematic review in developing risk evaluations under TSCA.

This involves implementing a structured process to identify, evaluate, and integrate evidence for the hazard and exposure assessments developed for risk evaluation. This poster describes the data evaluation process assessing the quality of the epidemiologic data types supporting the human health hazard assessment and exposure assessment.

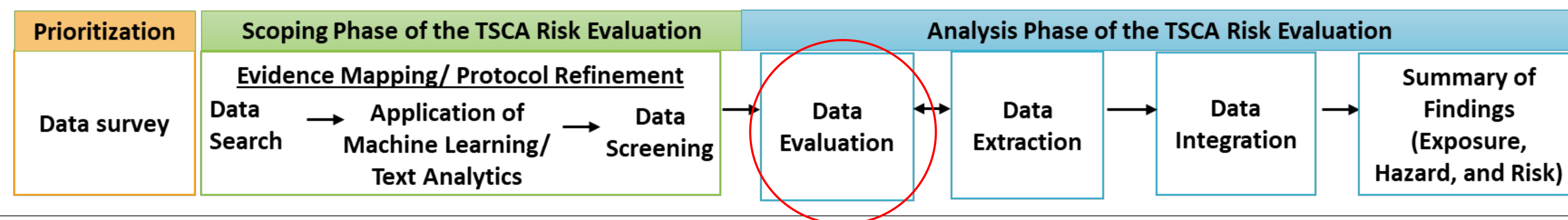
Background

EPA designed an evaluation tool to review epidemiologic data on exposure and health. Epidemiologic studies can contain information both on chemical exposure and human health hazards, and as such will be assessed independently to support the exposure and hazard assessments. EPA used elements of evaluation procedures implemented in past TSCA risk assessments and adapted and supplemented with elements from other established evaluation tools in order to design epidemiologic evaluation criteria that are fit-for-purpose and fulfill the scientific standards requirements under amended TSCA.

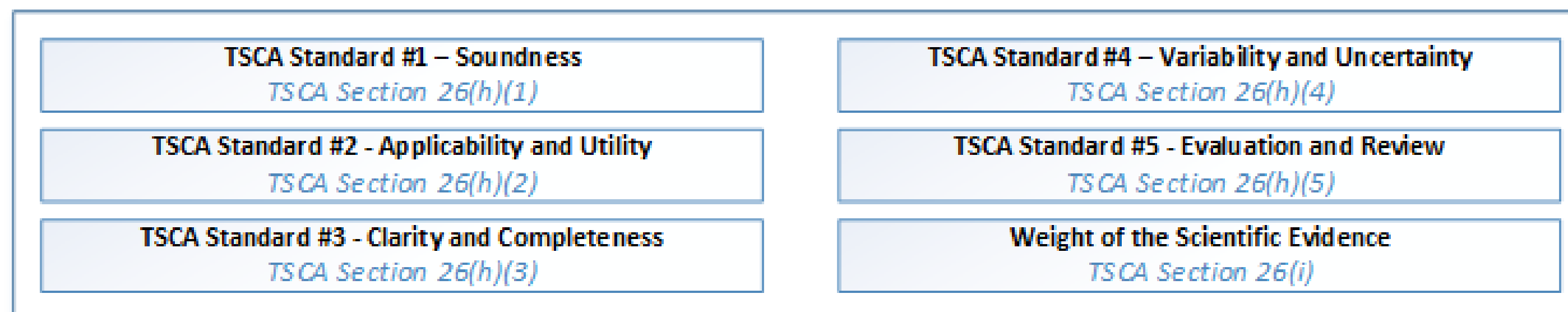
Systematic Review Process for Epi Data and General Structure of Epi Strategies

Figure 1

Next 20+ chemicals

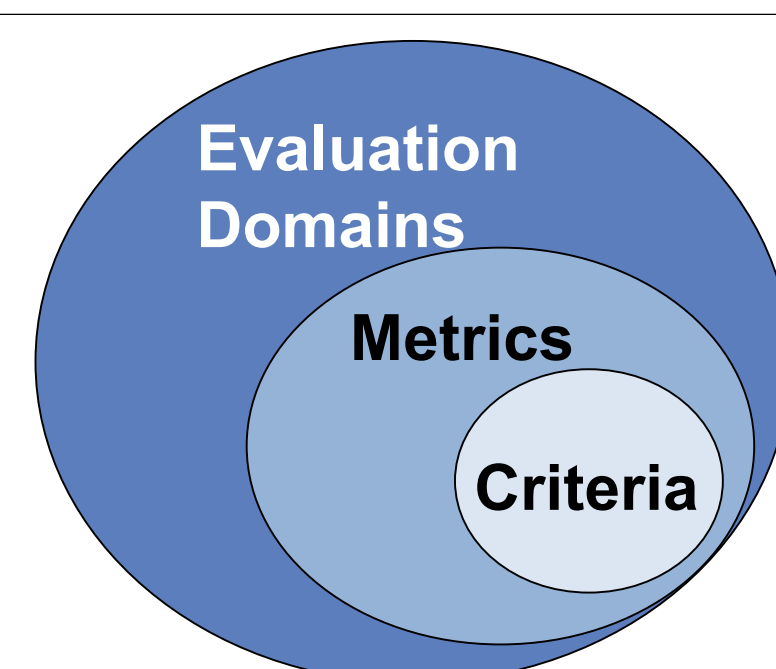


- Data relevancy issues are considered during the Data Screening, Data Evaluation, and Data Integration
- Literature screening partially assesses TSCA section 26(h)(5) standard by identifying peer-reviewed publications. Most of the independent verification of the study results (e.g., study replicability) will be assessed during the Data Integration step.



Key Terms in Data Evaluation

- Domain** - the general categories of data/information attributes intended to assess methodological conduct and risk of bias
- Metric** - the sub-categories of domain attributes
- Criterion** - specific criteria are developed for each metric, which express conditions of the quality level assigned to the metric (high, medium, low, or unacceptable)
- Data Quality Score** - quantitative score calculated following evaluation of discipline-specific and data type-specific data evaluation domains and metrics according to predefined scoring criteria and accounting for metric weighting factors.



Quality Domains for Human Health and Exposure Strategies

Quality Metrics for Human Health Domains

Human Health Epi			
Study Participation	M1-M3	Potential Confounding	M9-M11
Exposure Characterization	M4-M6	Analysis	M12-M15
Outcome Assessment	M7-M8	Other/Consideration for Biomarkers	M16-M22

Exposure Epi
Reliability
Representativeness
Accessibility/Clarity
Variability and Uncertainty

M1: Participant Selection
M2: Attrition
M3: Comparison Group
M4: Measurement of Exposure
M5: Exposure Levels
M6: Temporality
M7: Outcome Measurement or Characterization
M8: Reporting Bias
M9: Covariate Adjustment
M10: Covariate Characterization
M11: Co-exposure Moderation
M12: Study Design and Methods
M13: Statistical Power
M14: Reproducibility of Analyses
M15: Statistical Models

Quality Metrics – 2 Examples: General Epi and Asbestos Epi Strategies

Quality Metrics consist of criteria reviewers used to evaluate the data. Each metric is assigned a score/rating based on the criteria bin that best fits the data.

Table 1. Example of Criteria for a Human Health Epidemiology Metric (General Epi Criteria for 1st 10 existing chemical assessments)

Domain 3. Outcome Assessment Metric 7. Outcome Measurement or Characterization	High (score = 1)	For cohort studies and cross-sectional studies: The outcome was assessed using well-established methods (e.g., the "gold standard"). For case-control studies: The outcome was assessed in cases (i.e., case definition) and controls using well-established methods (the gold standard). Subjects had been followed for the same length of time in all study groups *Note: Acceptable assessment methods will depend on the outcome, but examples of such methods may include: objectively measured with diagnostic methods, measured by trained interviewers, obtained from registries
	Medium (score = 2)	For all study types: A less-established method was used, 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 outcome misclassification (e.g., differential reporting of outcome by exposure status).
	Low (score = 3)	For cohort studies and cross-sectional studies: The outcome assessment method is an insensitive instrument or measure. OR The length of follow up differed by study group. For case-control studies: The outcome was assessed in cases (i.e., case definition) using an insensitive instrument or measure. OR Any self-reported information
	Unacceptable (score = 4)	For all study types: Diagnostic criteria were not defined or reported

Assigning Overall Study Quality Rating

- Strengths and limitations are considered when assigning a quality rating for each relevant metric
- With proper justification, a reviewer may adjust the overall quality rating to capture professional judgment not originally captured in metric criteria.

Table 3. Definitions of Overall Quality Levels and Corresponding Quality Scores

Overall Quality Level	Definition	Overall Quality Score
High	No notable deficiencies or concerns are identified, and the data therefore could be used in the assessment with a high degree of confidence.	≥ 1 and < 1.7
Medium	Possible deficiencies or concerns are noted, and the data therefore could be used in the assessment with a medium degree of confidence.	≥ 1.7 and < 2.3
Low	Deficiencies or concerns are noted, and the data therefore could be used in the assessment with a low degree of confidence.	≥ 2.3 and ≤ 3
Unacceptable	Serious flaw(s) are identified and therefore, the data cannot be used for the assessment.	4

Next Steps

- EPA is in the process of further refinement of TSCA epi criteria based on feedback from reviewers who conducted the quality evaluations for the 1st 10 TSCA chemicals, as well as comments from the public and the SACC peer reviews on the 1st 10 chemicals.
- Application of these criteria to epidemiologic data sources identified as relevant for the next 20 chemicals being evaluated under amended TSCA will begin this year.

Table 2. Example of Criteria for a Human Health Epidemiology Metric (Asbestos Exposure and Mesothelioma Health Outcome)

Domain 3. Outcome Assessment Metric 7. Outcome Measurement or Characterization	High (score = 1)	For all study types: The outcome was assessed using one or a combination of the following well-established methods: - Mesothelioma cases confirmed by histological or cytological means (including subtypes of mesothelioma) and/or - ICD-10 codes (3 digit) C45 or (4 digit) C45.x (C45.0, C45.1, C45.2, C45.7, C45.9) - All fields on the death certificates of cohort searched for 'mesothelioma' - Appropriate Pre-ICD 10 codes supplemented by additional evidence (e.g. pathology/autopsy)
	Medium (score = 2)	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 (score = 3)	For all study types: Do not select for this metric.
	Unacceptable (score = 4)	For all study types: Numbers of outcome events or summary measures were not reported 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

Assigning Weights in Human Health Epi Strategy

- Unlike other discipline evaluation strategies, the weighting strategy in the human health epi criteria assumes that each domain carries an equal amount of weight of 1.
- Key or critical metrics *within* a given domain are given 2x greater weights than others in the same domain.

Table 4: Example of Domain and Metric Weighting in Human Health Epi Criteria

Domain	Metric	Range of Metric Scores	Metric Weighting Factors	Domain Weight	Range of Weighted Metric Scores
Potential Confounding	Covariate Adjustment	1 to 3	0.50	1	0.50 to 1.50
	Covariate Characterization	1 to 3	0.25		0.25 to 0.75
	Co-exposure	1 to 3	0.25		0.25 to 0.75