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# Evidence Integration of Physical-Chemical and Fate Properties under 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 evidence integration process for physical-chemical and environmental fate property data.

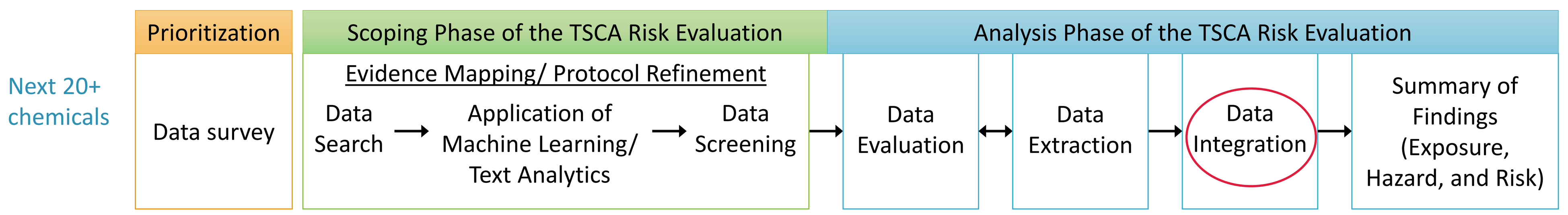


*Figure 1. Systematic Review Overview*

**Key Terms in Evidence Integration**

**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.

**Weight of the Scientific Evidence** – A systematic review method that uses a preestablished 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.

## Physical-Chemical and Fate Property Assessments

| Physical and Chemical Properties Assessed | |
|---|---|
| Physical Form (Solid, Liquid, Gas) | Physical Properties (Color, Scent) |
| Melting Point | Water Solubility |
| Boiling Point | Henry's Law Constant |
| Vapor Pressure | Octanol-Water Partition Coefficient (log $K_{OW}$) |
| Vapor Density | Flash Point |
| Viscosity | Autoflammability |
| Density | Dielectric Constant |
| Refractive Index | |

Physical and chemical properties influence the environmental behavior and the toxic properties of a chemical, thereby informing the potential conditions of use, exposure pathways and routes, and hazards that EPA evaluates.

Physical and chemical properties are used in quantitative and qualitative assessments such as:

- Modeling concentrations in environmental media,
- Estimating degree of exposure via inhalation of vapors,
- Determining potential for exposure via absorption through the skin,
- Assessing safety concerns in occupational settings (e.g., autoignition in industrial processes), and
- Evaluating whether study methods were appropriate for the test chemical.

Environmental fate and transport properties inform the determination of the specific exposure pathways and potential human and environmental receptors which EPA evaluates in its TSCA risk evaluations.

Fate properties are used in quantitative and qualitative assessments including:

- Modeling concentrations in and partitioning among environmental media,
- Identifying environmental media which are likely or unlikely to be significant exposure pathways,
- Evaluating the exposures of environmental organisms and humans (including potentially exposed and susceptible subpopulations [PESS]) via consumption of species in which the chemical bioaccumulates, and
- Determining whether the chemical is persistent, bioaccumulative, and toxic (PBT).

| Fate and Transport Properties Assessed | |
|---|---|
| Bioconcentration Potential<br>• Bioconcentration factor<br>• Bioaccumulation factor<br>• Trophic magnification factor<br>• Biota-sediment accumulation factor | Abiotic Degradation Rates<br>• Abiotic reduction<br>• Hydrolysis<br>• Incineration<br>• Photolysis (aqueous, atmospheric)<br>• Other abiotic processes |
| Sorption Information<br>• Organic carbon-water partitioning (log $K_{OC}$) | Biodegradation Rates<br>• Aerobic biodegradation<br>• Anaerobic biodegradation |
| Wastewater Treatment Removal | Degradation and Transformation Products |

## Physical-Chemical and Fate Evidence Integration Considerations

After data extraction and evaluation are complete for all data sources (i.e. peer-reviewed literature, gray literature, TSCA submissions, and other reasonably available information), the physical-chemical and fate information must be synthesized to develop the environmental fate assessment. Further, values or ranges of values for physical-chemical and fate properties must be selected for use in models and other quantitative and qualitative assessments throughout the risk evaluation.

Physical-chemical and fate property evidence is weighed based on tiered considerations. In Tier 1, the studies are sorted based on data quality and whether the information was measured (experimentally derived, e.g. in a laboratory or monitoring study) or estimated via models (e.g. quantitative structure-activity relationships [QSAR]) or read-across from structural analogues. Values for each property are selected for use in the risk evaluation from the highest occupied Tier 1 category based on the overall weight of the evidence as determined by Tier 2 considerations, including chemical- and endpoint-specific considerations (e.g., physical-chemical property values should align with values calculated from other properties). Studies determined to be unacceptable in the data evaluation phase are not included in evidence integration.

<u>*Tier 1*</u>

| Category | |
|---|---|
| *Category 1* | High-Quality Measured Data |
| *Category 2* | Medium-Quality Measured Data and/or High-Quality Estimated Data |
| *Category 3* | Low-Quality Measured Data and/or Medium-Quality Estimated Data |
| *Category 4* | Low-Quality Estimated Data |

<u>*Tier 2*</u>

| | Factors that Increase Strength | Factors that Decrease Strength |
|---|---|---|
| Consistency | • Consistency and replication within and across studies<br>• Multiple studies or several data points which indicate similar findings<br>• Results align with other reported physical-chemical and fate properties for the target chemical and/or structural analogues | • Unexplained inconsistency in values<br>• Limited number of studies or data points<br>• Studies with inexplicable contradictory findings, or other evidence demonstrating implausibility<br>• Results conflict with other reported physical-chemical or fate properties |
| Study Design | • Experimental design or model has been peer-reviewed and is being applied in a manner appropriate to its design and objective<br>  ○ Standard test guidelines, e.g. OECD or OCSPP protocols<br>  ○ Non-guideline studies conducted according to sound scientific principles and sufficiently documented<br>  ○ Peer-reviewed models, e.g. EPI Suite™[a] or OPERA[b]<br>• (For physical-chemical properties) Results are reported in established physical-chemical property databases which have been expert- or peer-reviewed | • Experimental design or model has not been peer-reviewed<br>• Experimental design, model, or model parameterization is not well described or is poorly documented |
| Study Conditions | • Studies conducted using high-purity test substances<br>• Studies conducted at environmentally-relevant temperature and pressure<br>  ○ Standard temperature (20-25°C) and pressure (760 mmHg) preferred | • Studies conducted using low-purity test substances<br>• Studies conducted at extreme temperature and pressure or conditions that are otherwise not environmentally-relevant |
| Uncertainty | • Uncertainties and limitations are well documented, fully described and explained<br>• Variability is presented, described, and explained | • Imprecision or inaccuracy in results |

[a]Estimation Programs Interface (EPI) Suite™. https://www.epa.gov/tsca-screening-tools/epi-suitetm-estimation-program-interface
[b]OPEn (quantitative) structure-activity Relationship Application (OPERA). https://github.com/kmansouri/OPERA

## Examples

In the systematic review currently underway for the second set of existing chemicals being assessed under amended TSCA ("Next 20"), 17 melting point values have been collected for trans-1,2-dichloroethylene. The values were all measured and obtained from expert-reviewed databases and indexes. Figure 2 illustrates these data, with the high- and medium-quality data indicated by open green and yellow diamonds, respectively. Although the values span more than 30°C, 11 of the 17 collected values lie at approximately -50°C. The preliminarily-selected value is near the mean of this cluster, at -49.8°C, as indicated by the solid, light-green diamond.

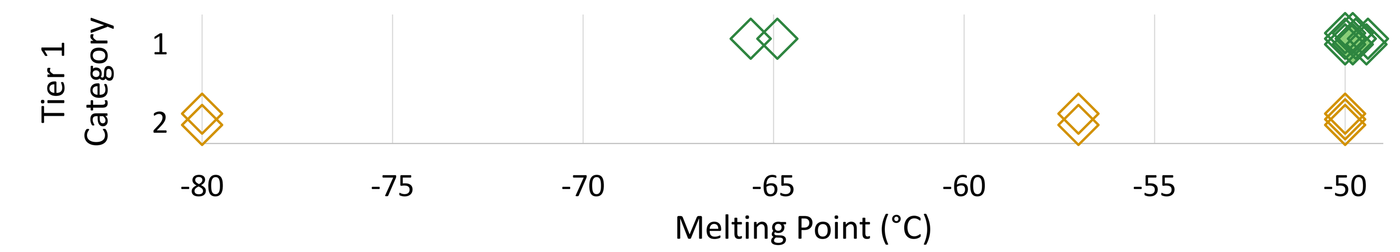


*Figure 2. Reported Melting Point Values for Trans-1,2-Dichloroethylene*

Thus far, 12 log $K_{OW}$ values have been collected for dibutyl phthalate. The values were obtained from expert-reviewed databases and indexes and peer-reviewed journal articles. Figure 3 illustrates these data, with measured and estimated values indicated by diamonds and circles, respectively. The preliminary-selected value (4.53), marked by the solid, light-green diamond, was determined using 99% pure substance in triple replicates using a standard shake-flask method and thus carries more weight in Tier 2. In contrast, one study used concentrations higher than recommended by the guideline (◌).

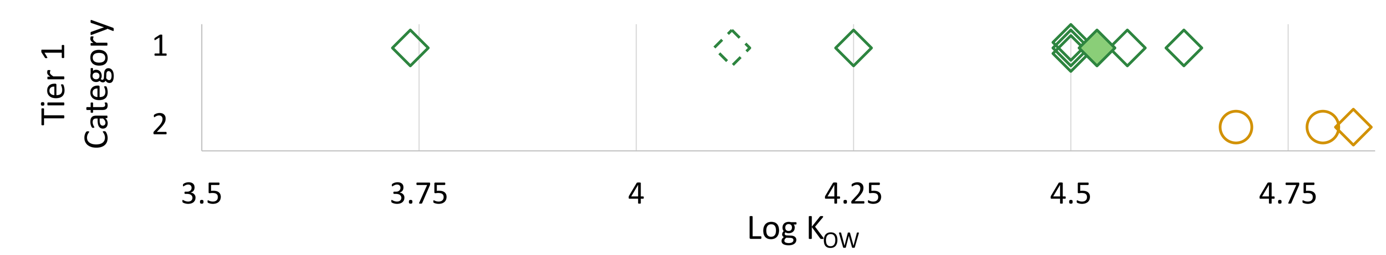


*Figure 3. Reported Log $K_{OW}$ Values for Dibutyl Phthalate*

## Evidence Integration Results

As illustrated in the "Evidence Integration Considerations" section, EPA prefers high-quality measured data for physical-chemical and fate properties to minimize uncertainty in the assessment. For endpoints where there is no measured data of sufficient quality or other uncertainties determined during evidence integration, EPA may rely on models or read-across from structural analogues to resolve the data gap or may issue test orders under the authority of TSCA Section 4 to obtain measured values. Although preliminary evidence integration can occur once systematic review of peer-reviewed literature, gray literature, and TSCA submissions is completed, information later obtained via models, read-across, test orders, or other data submissions will be incorporated in the final evidence integration.

Once all data are collected and evaluated, evidence integration will be finalized. The outcomes of physical-chemical and fate property evidence integration may include:

- Judgment regarding whether there is sufficient evidence to describe the physical-chemical properties and environmental fate and transport of the target chemical;
- Summary of the information, including the range of reported values, mean, and other statistics of the data, upon which the judgment is primarily made;
- Description of the coherence or comparison of the measured and modeled values and possible explanations of the reasons for any disagreements in the data;
- Description of the strengths, limitations, and uncertainties in the information; and
- Final selected values or ranges of values to be used in qualitative and quantitative assessments across the risk evaluation.





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*NASEM Review of the Environmental Protection Agency's Toxic Substance Control Act Systematic Review Guidance Document*
*Webinar 2.3, August 24, 2020*