# Using Alternatives Assessment Approaches to Inform the Ranking of TRI-Listed Solvent Chemicals

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# Overview

- Background
- Overview of Pilot Project
  - Method
  - Results
- Lessons Learned & Takeaways
- Potential Project Impact

# Background

- There are hundreds of chemicals on the TRI list which vary in regard to their basis for being listed.
- These chemicals are “data-rich” in regards to the amount of information available regarding their toxicity.
- Is there was a way to rank TRI-listed chemicals, based on the available data related to their hazard?
- **Goal of the project**: Develop a method to rank TRI-listed chemicals against one another based on hazard and implement the method in a pilot project to assess its value

# Background

- Use methods and principles based in the field of alternatives assessments
- Alternatives assessments consist of a framework to inform chemical, product or process substitution decisions
  - U.S. EPA Design for the Environment *Alternatives Assessment Criteria for Hazard Evaluation*
  - National Academy of Sciences *A Framework to Guide Selection of Chemical Alternatives* (October, 2014)
  - Washington State *Quick Chemical Assessment Tool (QCAT)*

# Background

- Alternatives assessment frameworks provides a methodology to assess a variety of human health and ecological health hazard endpoints and directly compare a chemical's hazard profile.
- The methodologies put forward criteria to rank a chemical's hazard in for a certain endpoint as high medium or low.

| Chemical | Human Health Effects | | | | | Aquatic Toxicity | | Environmental Fate | | Grade/Benchmark | Average Score | Rank |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Acute Toxicity | Carcinogenicity | Genotoxicity | Reproductive | Developmental | Acute | Chronic | Persistence | Bioaccumulation | | | |
| Methanol | H | L | L | H | H | M | L | VL | *ND* | F | 3.25 | 1 |
| N-Hexane | L | L | M | H | H | H | M | *VL* | M | F | 3.11 | 2 |
| Toluene | L | L | M | H | H | H | H | M | L | F | 2.89 | 3 |
| N,N-Dimethylformamide | M | M | H | H | H | L | M | M | L | F | 2.89 | 3 |
| N,N-Dimethylaniline | H | H | M | *H* | L | H | H | H | L | F | 2.56 | 5 |
| Xylenes (mixed isomers) | M | L | L | H | H | H | H | VH | M | F | 2.56 | 5 |
| Nitromethane | H | H | M | *H* | *H* | M | *M* | *M* | M | F | 2.33 | 7 |
| Dibutyl phthalate | VH | M | M | H | H | VH | H | L | VH | F | 2.11 | 8 |
| Carbon tetrachloride | H | VH | M | H | H | VH | M | VH | M | F | 2.00 | 9 |
| Chloroform | H | VH | H | H | H | H | VH | VH | M | F | 1.78 | 10 |

VL = Very Low hazard L = Low hazard M = Moderate hazard H = High hazard VH = Very High hazard — Endpoints in colored text (VL, L, M, H, and VH) were assigned based on empirical data. Endpoints in black italics (*VL, L, M, H,* and *VH*) were assigned using values from estimation software and professional judgment. *ND = No data located*

# Method for Ranking TRI-Listed Chemicals

1) Develop List of Chemicals

2) Gather Hazard Data

3) Evaluate and Interpret Data

4) Summarize Results

# 1) Develop a List of Chemicals

- Develop a list of chemicals for a set of functionally similar chemicals for which hazard will be assessed
- TRI solvent chemicals were used as the example functional class of chemicals for this pilot assessment
- 33 solvents were identified in initial scoping step
- 10 of the 33 solvents were reviewed for pilot assessment
- Subset included those with relative high, medium, and low quantities of production-related waste reported to TRI

# 1) Develop a List of Chemicals

| Chemical | CASRN | Production-Related Waste (pounds) |
|---|---|---|
| METHANOL | 67-56-1 | 2,348,971,369 |
| TOLUENE | 108-88-3 | 1,533,848,455 |
| N-HEXANE | 110-54-3 | 1,061,632,515 |
| XYLENE (MIXED ISOMERS) | 1330-20-7 | 568,343,510 |
| N,N-DIMETHYLFORMAMIDE | 68-12-2 | 46,639,295 |
| CHLOROFORM | 67-66-3 | 42,940,969 |
| CARBON TETRACHLORIDE | 56-23-5 | 31,049,846 |
| DIBUTYL PHTHALATE | 84-74-2 | 1,687,077 |
| NITROMETHANE | 75-52-5 | 1,031,473 |
| N,N-DIMETHYLANILINE | 121-69-7 | 507,572 |

# 2) Gather Data

| Hazard Endpoint | Tier 1 Assessment | Tier 2 Assessment |
|---|---|---|
| Acute Mammalian Toxicity | X | X |
| Bioaccumulation | X | X |
| Carcinogenicity | X | X |
| Developmental Toxicity (including developmental neurotoxicity) | X | X |
| Mutagenicity and Genotoxicity | X | X |
| Persistence | X | X |
| Reproductive Toxicity | X | X |
| Acute Aquatic Toxicity | X | X |
| Chronic Aquatic Toxicity | X | X |
| Dermal Irritation | | X |
| Eye Irritation | | X |
| Neurotoxicity | | X |
| Respiratory Sensitization | | X |
| Skin Sensitization | | X |

- *Tier 1 was used for pilot assessment*

# 2) Gather Data

- Data-gathering and assessment approaches developed to align with the DfE *Alternatives Assessment Criteria for Hazard Evaluation.*

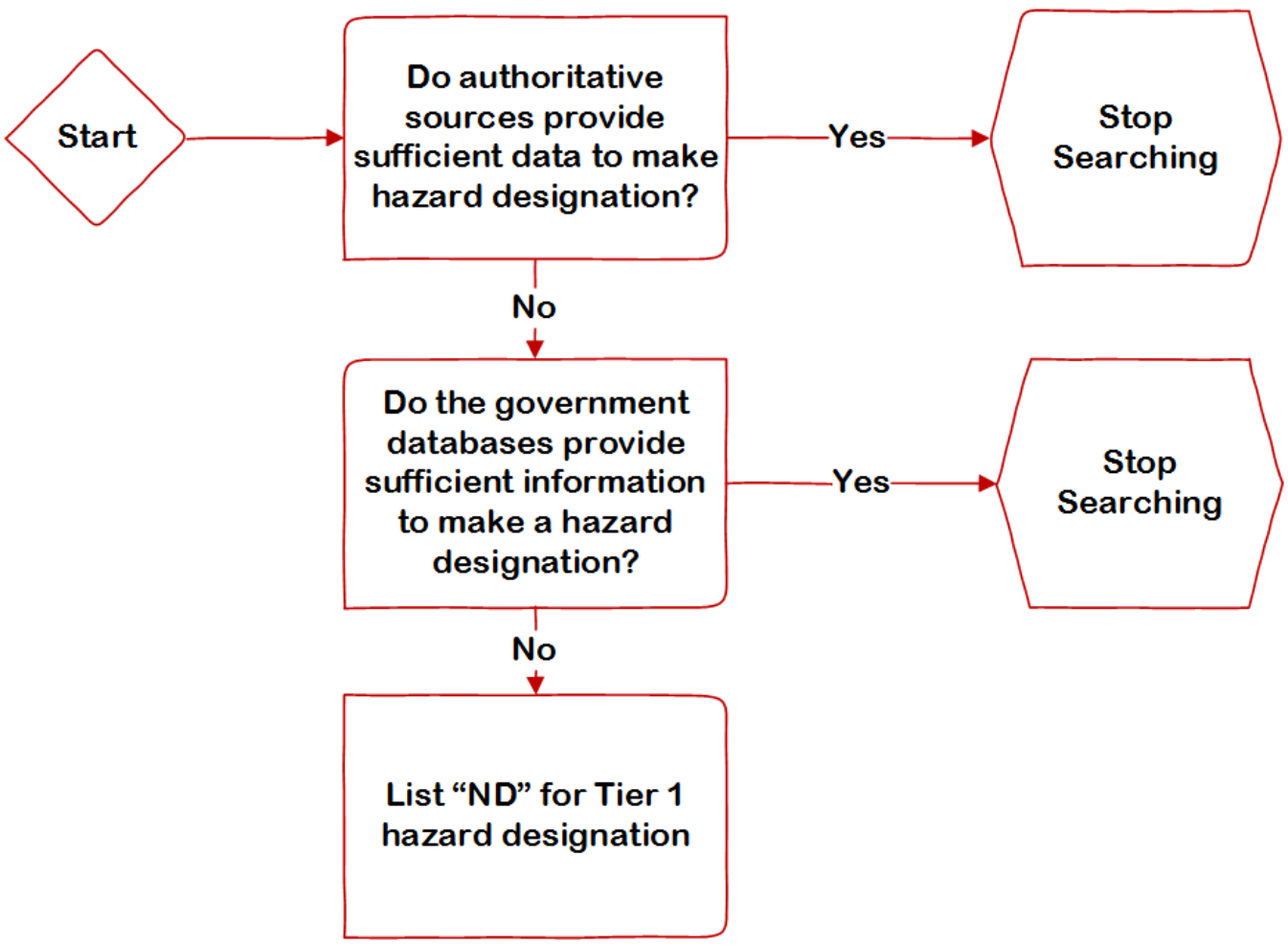
| Reproductive and Developmental Toxicity | High | Moderate | Low | Very Low |
|---|---|---|---|---|
| **Authoritative Lists** | | | | |
| EU Classification, Labeling and Packaging | H362: May cause harm to breast-fed children | | | |
| Cal Prop 65 | Chemicals known to the State of California to cause reproductive toxicity | | | |
| **Criteria based on primary literature** | | | | |
| Oral NOAEL or LOAEL (mg/kg/day) | < 50 | 50 - 250 | > 250 - 1000 | > 1000 |
| Dermal NOAEL or LOAEL (mg/kg/day) | < 100 | 100 - 500 | > 500 - 2000 | > 2000 |
| Inhalation NOAEL or LOAEL (vapor/gas) (mg/L/day) | < 1 | 1 - 2.5 | > 2.5 - 20 | > 20 |
| Inhalation NOAEL or LOAEL (dust/mist/fume) (mg/L/day) | < 0.1 | 0.1 - 0.5 | > 0.5 - 5 | > 5 |

# 2) Gather Data

## Overview of Data Sources Used for Tier 1 Hazard Assessments

| Databases with Authoritative Source information | Other Government Databases |
|---|---|
| • Japanese Government National of Technology and Evaluation<br>• ECHA Substances of Very High Concern<br>• CalEPA Prop 65 Chemicals<br>• NIH NTP Report on Carcinogens<br>• EPA IRIS<br>• IARC Monograph<br>• NIOSH Carcinogen List<br>• NIH NTP Office of Health Assessment and Translation<br>• ECHA Registered Substances Database | • eChemPortal<br>- EnviChem (Finnish Database of Environmental Chemicals)<br>- EPA HPVIS<br>- IPCS collection of chemical safety reports<br>- OECD SIDS IUCLID<br>- SIDS UNEP<br>• TRI-CHIP<br>• ATSDR Toxic Substances Portal<br>• EPA ChemView<br>• EPA ECOTOX<br>• TOXNET Hazardous Substances Database<br>• ECHA Registered Substances Database |

# 2) Gather Data



# 3) Evaluate and Interpret Data

- Consists of two sub-steps:
  - (a) Evaluating the hazard data against hazard criteria
  - (b) Ranking/grading chemicals based on hazard evaluation results

# 3a) Evaluate the Compiled Data Against Hazard Criteria

- Also based on DfE Alternatives Assessment Criteria
  - Outlines how measured data (e.g., NOAELs, LOAELs, $EC_{50}$, or $LC_{50}$) map to High, Medium or Low (and in some instances Very High or Very Low) designations
  - Hazard designations assigned based on most conservative data to maximize human health and environmental protection

| Reproductive and Developmental Toxicity | High | Moderate | Low | Very Low |
|---|---|---|---|---|
| **Authoritative Lists** | | | | |
| EU Classification, Labeling and Packaging | H362: May cause harm to breast-fed children | | | |
| Cal Prop 65 | Chemicals known to the State of California to cause reproductive toxicity | | | |
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| Inhalation NOAEL or LOAEL (vapor/gas) (mg/L/day) | < 1 | 1 - 2.5 | > 2.5 - 20 | > 20 |
| Inhalation NOAEL or LOAEL (dust/mist/fume) (mg/L/day) | < 0.1 | 0.1 - 0.5 | > 0.5 - 5 | > 5 |

# 3b) Ranking/Grading Chemicals Based on Hazard Evaluation Results

- There are multiple ways to compare chemicals hazard profiles. Two approaches were evaluated in this pilot.

(1) Equal weighting of hazard endpoints

- Assumes that "each end point is considered to have equivalent importance, and the trade-off is resolved by assigning a relative weight to the high, medium, and low categories and then adding up the score. The total would indicate the preference ordering of alternatives" (National Research Council, 2014, p. 153).

- Requires no ordering of hazard endpoints

- Assessor can make own scoring scheme (Ex: Very Low = 5; Very High = 1)

- To account for potential missing data, we averaged the score per chemical based on the sum of the scores divided by the number of endpoints with designations.

# 3b) Ranking/Grading Chemicals Based on Hazard Evaluation Results

(2) Rule-based ranking

-Uses logical statements to establish preferences and rank alternatives based on Quick Chemical Assessment Tool (QCAT) developed by Washington State

-Ex: Grade B = Moderate Persistence; or Moderate Bioaccumulation; or Moderate Acute Aquatic Toxicity; or Moderate Acute Mammalian Toxicity or ≥1 Human Health endpoints

# 3b) Ranking/Grading Chemicals Based on Hazard Evaluation Results

**Grading Criteria Based on Washington State QCAT**

| | |
|---|---|
| Grade A | Low P + Low T (AA, AT and all HH endpoints). |
| Grade B | Moderate P; or<br>Moderate B; or<br>Moderate AA; or<br>Moderate AT or one or more HH endpoints. |
| Grade C | Moderate P + Moderate B + Moderate T (AA, AT, or any HH endpoint); or<br>High P + Moderate T (AA, AT, or any HH endpoints); or<br>High B + Moderate T (AA, AT, or any HH endpoints); or<br>Very High T (AA or AT) or High T (any HH endpoint). |
| Grade F | PBT = High P + High B + [Very High T (AA or AT) or High T (HH)]; or<br>VpVb = very High P + very High B; or<br>vPT = very High P + [very High T (AA or AT) or High T (HH)]; or<br>vBT = very High B + [very High T (AA or AT) or High T (HH)]; or<br>High T (HH). |

# 4) Summarize Results

- Two main ways to present hazard information under process:

  1) A detailed description of the data used to inform the hazard designation

  2) A table summarizing a chemical's hazard profile based on the designations for each hazard endpoint along with the hazard score, rank and grade Based on DfE Alternatives Assessment Criteria for Hazard Evaluation

# 4) Present Results: Detailed

**Acute Mammalian Toxicity**

**HIGH:** Carbon tetrachloride is categorized as high in regards to acute mammalian toxicity. This is based on authoritative list designations provided by the European Union's Classification, Labeling, and Packaging Regulation (EU CLP) and the EU Risk Phrases. H301, H311, and H331 under the EU CLP and the EU Risk Phrases R23, R24, and R25 are all associated with a high hazard designation as outlined by the criteria.

| Reference | Findings |
|---|---|
| ***Inhalation route of exposure*** | |
| GHS classification (as cited by ECHA) | Acute Tox. 3 H331: Toxic if inhaled |
| EU Risk Phrases (as cited by ECHA) | R23: Toxic by inhalation |
| GHS classification (as cited by NITE) | H332: Harmful if inhaled<br>Based on a $LC_{50}$ (4 hour) value of 8000 ppm for rats (Initial Environmental Risk Assessment of Chemicals (Ministry of Environment) vol. 3 (2004)), the substance was classified into Category 4. Since the $LC_{50}$ value was lower than 90% of saturated vapor pressure concentration (151,316 ppmV), the classification criteria for gas (ppm) was adopted. |
| ***Oral route of exposure*** | |
| GHS classification (as cited by ECHA) | Acute Tox. 3 H301: Toxic if swallowed. |
| EU Risk Phrases (as cited by ECHA) | R25: Toxic if swallowed |
| ***Dermal route of exposure*** | |
| GHS classification (as cited by ECHA) | Acute Tox. 3 H311: Toxic in contact with skin. |
| EU Risk Phrases (as cited by ECHA) | R24: Toxic in contact with skin |

# 4) Summarize Results: Summary Table

## Screening Level Toxicology Hazard Summary for Carbon Tetrachloride

**Screening Level Toxicology Hazard Summary**

This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are not addressed in the hazard profiles.

**VL = Very Low hazard L = Low hazard M = Moderate hazard H = High hazard VH = Very High hazard – Endpoints in colored text (VL, L, M, H, and VH) were assigned based on empirical data. Endpoints in black italics (*VL, L, M, H,* and *VH*) were assigned based on values from estimation software and professional judgment [(Quantitative) Structure Activity Relationships "(Q)SAR"] presented in authoritative sources.**

| | | Human Health Effects | | | | | | | | | | | Aquatic Toxicity | | Environmental Fate | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Chemical** | CASRN | Acute Toxicity | Carcinogenicity | Genotoxicity | Reproductive | Developmental | Neurological[ψ] | Repeated Dose[ψ] | Skin Sensitization[ψ] | Respiratory Sensitization[ψ] | Eye Irritation[ψ] | Dermal Irritation[ψ] | Acute | Chronic | Persistence | Bioaccumulation | Grade/Benchmark | Average Score |
| Carbon tetrachloride | 56-23-5 | H | VH | M | H | H | | | | | | | VH | M | VH | M | F | 2.00 |

ψ These endpoints were not evaluated in the Tier 1 assessment

| Chemical | Human Health Effects | | | | | Aquatic Toxicity | | Environmental Fate | | Grade/Benchmark | Average Score | Rank |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Acute Toxicity | Carcinogenicity | Genotoxicity | Reproductive | Developmental | Acute | Chronic | Persistence | Bioaccumulation | | | |
| Methanol | H | L | L | H | H | M | L | VL | *ND* | F | 3.25 | 1 |
| N-Hexane | L | L | M | H | H | H | M | *VL* | M | F | 3.11 | 2 |
| Toluene | L | L | M | H | H | H | H | M | L | F | 2.89 | 3 |
| N,N-Dimethylformamide | M | M | H | H | H | L | M | M | L | F | 2.89 | 3 |
| N,N-Dimethylaniline | H | H | M | *H* | L | H | H | H | L | F | 2.56 | 5 |
| Xylenes (mixed isomers) | M | L | L | H | H | H | H | VH | M | F | 2.56 | 5 |
| Nitromethane | H | H | M | *H* | *H* | M | *M* | *M* | M | F | 2.33 | 7 |
| Dibutyl phthalate | VH | M | M | H | H | VH | H | L | VH | F | 2.11 | 8 |
| Carbon tetrachloride | H | VH | M | H | H | VH | M | VH | M | F | 2.00 | 9 |
| Chloroform | H | VH | H | H | H | H | VH | VH | M | F | 1.78 | 10 |

VL = Very Low hazard L = Low hazard M = Moderate hazard H = High hazard VH = Very High hazard — Endpoints in colored text (VL, L, M, H, and VH) were assigned based on empirical data. Endpoints in black italics (*VL, L, M, H,* and *VH*) were assigned using values from estimation software and professional judgment. *ND = No data located*

# Lessons Learned & Takeaways

- Overall: Using an alternatives assessment based approach to evaluate and rank the toxicity of TRI chemicals is not only feasible but also valuable.
- Data:
  - Only unavailable in only a few instances.
  - Mechanisms exist for filling data gaps (e.g., modeling software, using primary literature), but introduces variability in data quality and may require technical expertise

# Lessons Learned & Takeaways

- Hazard Ranking Approach:
  - Using a rule-based approach is not as helpful in evaluating a spectrum of potential hazards, especially among a group of chemicals that are known to have a toxic attribute, compared to the equal weighting approach (i.e., all solvents assigned Grade F in this pilot assessment)
  - Therefore, using the equal weighting approach to assess the chemicals in comparison to one another, at least for this purpose, is more useful.

# Lessons Learned & Takeaways

- Level of expertise needed:
  - Although the Tier 1 approach is structured to allow non-experts to conduct similar assessments, we found that having expert input was necessary, especially regarding chronic aquatic toxicity, bioaccumulation, and persistence
  - This is due to the fact data available did not always map exactly to the criteria and expert opinion and input was needed.

# Potential Project Impacts

- By using a comparative approach, one can start to differentiate chemicals based on hazard, even among a group of “known bad” chemicals such as chemicals on the TRI list
- Providing this type of data to TRI reporters, and even the general public, could serve to encourage decision makers to consider hazard more prominently in decision-making
- Information can help to shift industry towards safer chemical substitution (even incremental improvements) wherever possible through a “holistic” approach to chemical risk management

**Thank you!**

**Questions?**

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## 33 TRI-Listed Chemical Solvents[a] and Their Production-Related Waste[b]

| Chemical | CASRN | Production Related Waste (pounds) |
|---|---|---|
| **METHANOL** | 67-56-1 | 2,348,971,369 |
| **TOLUENE** | 108-88-3 | 1,533,848,455 |
| **N HEXANE** | 110-54-3 | 1,061,632,515 |
| **XYLENE (MIXED ISOMERS)** | 1330-20-7 | 568,343,510 |
| **ETHYLENE GLYCOL** | 107-21-1 | 490,399,746 |
| **1,2 DICHLOROETHANE** | 107-06-2 | 436,294,977 |
| **BENZENE** | 71-43-2 | 207,757,143 |
| **TERT BUTYL ALCOHOL** | 75-65-0 | 191,343,495 |
| **DICHLOROMETHANE** | 110-82-7 | 149,518,931 |
| **CYCLOHEXANE** | 110-82-7 | 112,223,458 |
| **ACETONITRILE** | 75-05-8 | 101,825,898 |
| **CARBON DISULFIDE** | 75-15-0 | 84,632,014 |
| **N METHYL 2 PYRROLIDONE** | 872-50-4 | 59,064,440 |
| **N,N DIMETHYLFORMAMIDE** | 68-12-2 | 46,639,295 |
| **CHLOROFORM** | 67-66-3 | 42,940,969 |
| **CARBON TETRACHLORIDE** | 56-23-5 | 31,049,846 |
| **ANILINE** | 62-53-3 | 22,131,896 |
| **CHLOROBENZENE** | 108-90-7 | 18,557,249 |
| **METHYL TERT BUTYL ETHER** | 1634-04-4 | 14,654,626 |
| **CYCLOHEXANOL** | 108-93-0 | 12,815,117 |
| **PYRIDINE** | 110-86-1 | 11,268,855 |
| **ETHYLIDENE DICHLORIDE** | 75-34-3 | 9,804,865 |
| **TRIETHYLAMINE** | 121-44-8 | 9,567,124 |
| **DIMETHYL PHTHALATE** | 108-93-0 | 6,828,573 |
| **O XYLENE** | 95-47-6 | 5,695,227 |
| **SEC BUTYL ALCOHOL** | 78-92-2 | 5,515,979 |
| **P XYLENE** | 106-42-3 | 4,759,983 |
| **1,4 DIOXANE** | 123-91-1 | 4,521,429 |
| **ISOPROPYL ALCOHOL** | 67-63-0 | 3,493,888 |
| **M XYLENE** | 108-38-3 | 3,428,638 |
| **DIBUTYL PHTHALATE** | 84-74-2 | 1,687,077 |
| **NITROMETHANE** | 75-52-5 | 1,031,473 |
| **N,N DIMETHYLANILINE** | 121-69-7 | 507,572 |

[a] Hexamethylphosphoramide was identified as a TRI solvent but not included on this list as zero pounds of production related waste were reported in 2013.

[b] Bolding in the table indicates the chemical was assessed in this pilot project.

Table 9. RSEI Ranking Based on Toxicity Scores

| Rank Based on Pilot Project Table 7 | Chemical | Rank Based on Inhalation Toxicity Score | Rank Based on Oral Toxicity Score |
|---|---|---|---|
| 1 | Methanol | 1 | 1 |
| 2 | N-Hexane | 3 | 6 |
| 3 | Toluene | 2 | 5 |
| 3 | N,N-Dimethylformamide | 6 | 4 |
| 5 | N,N-Dimethylaniline | 7 | 7 |
| 5 | Xylenes (mixed isomers) | 5 | 2 |
| 7 | Nitromethane | n/a | n/a |
| 8 | Dibutyl phthalate | 4 | 3 |
| 9 | Carbon tetrachloride | 8[a] | 9[a] |
| 10 | Chloroform | 9[a] | 8[a] |
| | [a] Toxicity scores for this chemical are based on a cancer endpoint | | |