Assessment of Toxicity-Normalized Species Sensitivity Distributions (SSDn) for Grouped Chemical Hazard Estimation

Faith Lambert, Sandy Raimondo, and Mace Barron

Office of Research and Development, U.S. Environmental Protection Agency, Gulf Breeze, FL USA

The views expressed in this presentation are those of the authors and do not necessarily represent the views or the policies of the U.S. Environmental Protection Agency. Any mention of trade names, products, or services does not imply an endorsement by the U.S. Government or the EPA.
Introduction

- Increasing number of chemicals in the environment
- Water quality values (WQVs) developed to protect aquatic life
- WQVs often developed using species sensitivity distribution (SSD) approach
SSDs

- SSDs are cumulative probability distributions
- Used to determine a fifth percentile hazard concentration (HC5)
- HC5 used to inform WQV development
Increasing numbers of chemicals in the environment

SSD development requires large amounts of toxicity data for diverse species

Lack of toxicity data due to limited resources (time, funding)

**Issue**

---

Toxicity Normalized Species Sensitivity Distribution (SSDn)

**Solution**

- New approach methodology (NAM): uses computational approach to estimate hazard

- Grouped chemical approach: Combines toxicity data for chemicals with similar characteristics to address information gaps
Toxicity Normalized Species Sensitivity Distribution (SSDn)

- Based on Giddings et al. (2019)
- Grouped chemical method based on species sensitivity distribution (SSD) approach
- Normalizes LC50s and HC5 using common test species LC50

1. Obtain toxicity data for multiple compounds
2. Normalize data to a single common species and combine
3. Build a Normalized SSD and Calculate Normalized HC5 (HC5n)
4. Calculate chemical-specific HC5 values from HC5n
Study Design | Data Selection

- Data sourced from the Web-ICE database
- Highly curated and standardized acute toxicity values for a variety of fish and invertebrates
- Selected 9 transition metals based on:
  - Similar mod of action of acute toxicity to aquatic organisms
  - Presence of *Daphnia magna* toxicity values in all data sets for use in normalization
  - Enough data to develop single-chemical SSD for methods comparison

<table>
<thead>
<tr>
<th>Compound</th>
<th>No. Species</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cadmium</td>
<td>26</td>
</tr>
<tr>
<td>Chromium (VI)</td>
<td>31</td>
</tr>
<tr>
<td>Cobalt</td>
<td>6</td>
</tr>
<tr>
<td>Copper</td>
<td>65</td>
</tr>
<tr>
<td>Lead</td>
<td>12</td>
</tr>
<tr>
<td>Mercury</td>
<td>11</td>
</tr>
<tr>
<td>Nickel</td>
<td>18</td>
</tr>
<tr>
<td>Silver</td>
<td>10</td>
</tr>
<tr>
<td>Zinc</td>
<td>51</td>
</tr>
</tbody>
</table>
Study Design | SSDn Development

1. Random combinations of 3-9 metals were generated and used to develop SSDns
2. Developed SSDns using best-fit method with four potential distributions: log-normal, log-logistic, Weibull, and gamma.

- Single-chemical SSDs were also developed for each metal and used to calculate SSD-based HC5s as a reference.

<table>
<thead>
<tr>
<th>Number of chemicals in SSDn</th>
<th>( n ) (Unique Chemical Combinations)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>80</td>
</tr>
<tr>
<td>4</td>
<td>80</td>
</tr>
<tr>
<td>5</td>
<td>80</td>
</tr>
<tr>
<td>6</td>
<td>80</td>
</tr>
<tr>
<td>7</td>
<td>25</td>
</tr>
<tr>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>9</td>
<td>1</td>
</tr>
</tbody>
</table>
### Single-chemical SSD

**Data Selection**
- Data from a single compound

**Data Processing & Normalization**
- Toxicity values for each species (LC50)

**SSD Development**
- Develop SSD
- Calculate HC5

### SSDn

**Data Selection**
- Data from a group of similar chemicals

**Data Processing & Normalization**
- Individual species toxicity, for each compound X (LC50_X)
  - nSpecies Toxicity for each compound X (LC50_{nSpecies,X})
  - Normalized toxicity values (LC50n)
    \[ LC50n = \frac{LC50_X}{LC50_{nSpecies,X}} \]

**SSD Development**
- Combine LC50n values across all compounds
- Develop SSDn
- Estimate chemical-specific HC5
  \[ HC5 = HC5n \times LC50_{nSpecies,X} \]
- Calculate HC5n
### Study Design | Uncertainty Analyses

<table>
<thead>
<tr>
<th>Factor to Consider</th>
<th>SSDn Sizes (# Chemicals)</th>
<th>nSpecies Used for Normalization</th>
<th>Total SSDn Models</th>
<th>Total HC5 Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of chemicals in the SSDn</td>
<td>3-9</td>
<td>$D. magna$</td>
<td>355</td>
<td>1696</td>
</tr>
<tr>
<td>Distribution of chemical data</td>
<td>3-6</td>
<td>$D. magna$</td>
<td>320</td>
<td>1440</td>
</tr>
<tr>
<td>quartiles throughout SSDn quartiles</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chemical representation by number</td>
<td>3-6</td>
<td>$D. magna$</td>
<td>320</td>
<td>1440</td>
</tr>
<tr>
<td>of species contributed to the SSDn</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Choice of nSpecies</td>
<td>3-6</td>
<td>Crustaceans ($D. magna, C. dubia, C. pseudogracilis$), fishes ($O. mykiss, P. promelas$), annelid ($T. tubifex$), amphibian ($E. hexadactylus$)</td>
<td>1022</td>
<td>4337</td>
</tr>
</tbody>
</table>
Uncertainty Analysis

Influence of number of chemicals on HC5 accuracy

- Evaluated whether increasing number of chemicals used for SSDn development affected HC5 accuracy
- HC5 accuracy was similar regardless of the number of chemicals

<table>
<thead>
<tr>
<th>Number of chemicals in SSDn</th>
<th>N</th>
<th>SSDn predictions within 5-fold of SSD HC5</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>240</td>
<td>68.3 %</td>
</tr>
<tr>
<td>4</td>
<td>320</td>
<td>69.1 %</td>
</tr>
<tr>
<td>5</td>
<td>400</td>
<td>68.2 %</td>
</tr>
<tr>
<td>6</td>
<td>480</td>
<td>67.5 %</td>
</tr>
<tr>
<td>7</td>
<td>175</td>
<td>65.7 %</td>
</tr>
<tr>
<td>8</td>
<td>72</td>
<td>65.3 %</td>
</tr>
<tr>
<td>9</td>
<td>9</td>
<td>55.6 %</td>
</tr>
</tbody>
</table>
Uncertainty Analysis

Influence of data distribution on HC5 accuracy

- Evaluated how distribution of chemical data across quartiles of the SSDn affected HC5 accuracy

- Chemicals with data in all four quartiles predicted HC5s within 5-fold of SSD-derived values approximately 75% of the time

- Presence of data within the first quartile (Q1) appeared particularly important

![Graphs showing data distribution and HC5 accuracy](image-url)
Uncertainty Analysis

Influence of Chemical Representation on HC5 accuracy

- Compared the percent of species a chemical contributed to the SSDn and the accuracy of derived HC5 estimate.
- Chemicals with data for >50% of SSDn species had more accurate HC5 estimates.
Uncertainty Analysis
Influence of nSpecies choice on HC5 accuracy

- Evaluated how nSpecies sensitivity in the SSDn and across chemicals affected HC5 accuracy
- Accuracy was best when nSpecies fell in Q1 of the SSDn
- When the nSpecies was similarly sensitive to all compounds, accuracy increased slightly
# SSDn Approach Recommendations

<table>
<thead>
<tr>
<th>Factors to Consider</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Taxonomic contribution of each chemical to the SSDn</td>
<td>✗ Individual chemicals should have data for &gt;50% of the total taxa represented in the SSDn</td>
</tr>
</tbody>
</table>
| Chemical representation throughout the distribution | ✗ Each chemicals should have data represented in the lowest quartile of the SSDn  
 ✗ Data represented across all quartiles of the SSDn reduces HC5 uncertainty |
| nSpecies | ✗ Most sensitive species should be used for normalization.  
 ✗ When possible, using a species with similar sensitivity to all compounds further reduces HC5 uncertainty |
Additional Research Needs

- Evaluate the influence of MOA-based chemical groupings on the accuracy of the SSDn approach
- Evaluate use with non-aquatic organisms and on chronic toxicity endpoints
- Explore potential of HC5n to be used as a single hazard metric for a group of chemicals
Acknowledgements

• Jeff Giddings
• Mike Elias
Thanks for your attention!