Enhancing the Chemical Mixture Methodology: Incorporating 20 Health Code Numbers
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Introduction
The Chemical Mixture Methodology (CMM) is used by the Department of Energy (DOE), its contractors, and other private and public organizations for emergency response planning and to assess the potential health impacts on individuals that would result from exposure to an airborne mixture of chemicals.

Hazard Indices (HIs)
The potential adverse health effects are estimated by summing the Hazard Indices (HIs) for each chemical present in the mixture. To calculate the HI for a given chemical, the concentration at a given receptor point is divided by the chemical’s protective action criteria (PAC) value.

Health Code Numbers (HCNs)
Health Code Numbers (HCNs) are assigned to each chemical based on the human organs targeted by exposure. In the current CMM, only the top 10 HCNs ranked by severity are included in each CMM analysis. This project focuses on assessing what happens when doubling the potential number of HCNs for each chemical that could be used in each CMM analysis.

Methods
A total of 361 chemicals were used in testing (the entire CMM database contains over 3000 chemicals).

<table>
<thead>
<tr>
<th>Rank</th>
<th>HCN</th>
<th>Target Organ Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>17.00</td>
<td>Asphyxiants, anoxics - acute effect</td>
</tr>
<tr>
<td>2</td>
<td>18.00</td>
<td>Explosive, flammable safety hazard (no adverse effects with good housekeeping)</td>
</tr>
<tr>
<td>3</td>
<td>13.00</td>
<td>Blood toxin, methemoglobinemia - acute effect</td>
</tr>
<tr>
<td>4</td>
<td>6.00</td>
<td>Cholinesterase toxin - acute effect</td>
</tr>
<tr>
<td>5</td>
<td>14.01</td>
<td>Eye irritant - severe</td>
</tr>
<tr>
<td>6</td>
<td>14.00</td>
<td>Severe irritant</td>
</tr>
<tr>
<td>7</td>
<td>15.01</td>
<td>Eye irritant - moderate</td>
</tr>
<tr>
<td>8</td>
<td>15.00</td>
<td>Moderate irritant</td>
</tr>
<tr>
<td>9</td>
<td>4.01</td>
<td>Eye - acute, other than irritation</td>
</tr>
<tr>
<td>10</td>
<td>11.01</td>
<td>Respiratory irritant - acute severe or moderate but not mild irritant effects</td>
</tr>
</tbody>
</table>

Table 1. Health Code Numbers (HCNs) used to classify toxic effects by organ system. Only 10 out of 60 HCNs are listed.

A set of 127 representative mixtures were prepared for our analysis. Three different concentration distributions (called “ideal,” “realistic,” and “same”) were used for each test mixture, providing a total of 381 test cases. For “ideal” concentrations, all chemicals in a mixture had the same HI. “Realistic” concentrations were derived using true-to-life chemical inventories from laboratory facilities. The “same” concentrations were defined by assuming each chemical in the mixture was present in the same concentration.

To show the difference between the 10 HCN and 20 HCN approach, Benefit was calculated using the equation below, where “∑ HI_{simple}” is the simple sum of HIs and “∑ HI_{HCN}” is the maximum sum of HIs using the HCN approach.

\[ \text{Benefit (\%)} = \left( \frac{\Sigma HI_{simple} - \Sigma HI_{HCN}}{\Sigma HI_{simple}} \right) \times 100 \]

![Ideal Scenario](image1)

In 92% of the “ideal” test cases, the benefit was identical for both the 10-HCN and 20-HCN CMM. The average benefit for 10-HCN CMM was 27.4%, and the average benefit for 20-HCN CMM was 19.9%.

![Realistic Scenario](image2)

In 84% of the “realistic” test cases, the benefit was identical for both the 10-HCN and 20-HCN CMM. The average benefit for 10-HCN CMM was 11.4%, and the average benefit for 20-HCN CMM was 3.3%.

Results

In 85% of the “same” test cases, the benefit was identical for both the 10-HCN and 20-HCN CMM. The average benefit for 10-HCN CMM was 8.2%, and the average benefit for 20-HCN CMM was 6.1%.

Conclusions & Future Directions
CMM results were compared for all 361 test cases using both the 10-HCN approach and the 20-HCN approach. Only a slight difference was observed between the 10-HCN and 20-HCN approaches. This slight difference suggests that the top 10 HCNs give good representation of the potential toxic health effects. This also indicates that it is impractical to incorporate the 20-HCN approach in a future version of the CMM. Therefore, effort should be directed to other aspects of the CMM development such as refining the nervous system effects or respiratory irritant effects in the near future.

Acknowledgments
Xiao-Ying Yu and Clifford Glantz (Mentors) Juan Yao (Post Masters Research Associate), Kolyne De Jesus (STAR Intern), Jewel Datiri and Rachel Komorek (DHS-STEM Interns), STAR Program, Bechtel, Pacific Northwest National Laboratory

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References: