Usefulness and Limitations of the Cytosensor® Microphysiometer (CM) Test Method for Ocular Safety Testing

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Introduction

- The Cytosensor® microphysiometer (CM) test method evaluates damage to corneal and conjunctival epithelium.
- Use of CM is restricted to water soluble substances.
- CM evaluates interference with keratocyte, fibroblast, and conjunctival epithelial cell function, by monitoring the rate of acidification in a chamber containing a multi-well plate of cells.
- Rate of pH change per well is taken as a relative measure of cell function and lower values are indicative of presence of irritation.

Figure 1. Diagram of the Operating Components of CM

Figure 2. ICCVAM-Recommended Protocol for CM

Figure 3. Example of CM Data and MRD_{50} Calculation

Table 1. Decision Criteria for the EPA and GHS Classification Systems Used for CM Evaluation

<table>
<thead>
<tr>
<th>Substance</th>
<th>EPA Classification</th>
<th>GHS Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>Category IV</td>
<td>Category 1</td>
</tr>
<tr>
<td>≤ 12</td>
<td>Category II-III</td>
<td>Category 2</td>
</tr>
<tr>
<td>&gt; 12</td>
<td>Category I</td>
<td>Category 3</td>
</tr>
</tbody>
</table>

Table 2. Accuracy for Surfactant-Containing Substances

<table>
<thead>
<tr>
<th>Classification System</th>
<th>Accuracy</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>False Positive Rate</th>
<th>False Negative Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPA</td>
<td>52</td>
<td>66</td>
<td>19/29</td>
<td>67</td>
<td>16/24</td>
</tr>
<tr>
<td>GHS</td>
<td>50</td>
<td>44</td>
<td>23/25</td>
<td>71</td>
<td>5/7</td>
</tr>
</tbody>
</table>

Table 3. Accuracy for Nonsurfactant Substances

<table>
<thead>
<tr>
<th>Classification System</th>
<th>Accuracy</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>False Positive Rate</th>
<th>False Negative Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPA</td>
<td>92</td>
<td>92</td>
<td>23/25</td>
<td>71</td>
<td>5/7</td>
</tr>
<tr>
<td>GHS</td>
<td>90</td>
<td>90</td>
<td>23/25</td>
<td>71</td>
<td>5/7</td>
</tr>
</tbody>
</table>

Test Method Accuracy

Distinguishing Ocular Corrosives and Severe Irritants from All Other Ocular Hazard Categories
- For these studies, select from the list of ICCVAM-recommended reference substances for the CM test method.
- Use the CM test method to identify corrosives/severe irritants and substances not labeled as irritants.

ICCVAM Recommendations: Usefulness and Limitations

- Valid across different chemical structures and test results may be compared across testing laboratories.
- Test results may be compared with other irritant severity classification systems.
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References


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