Acute Oral Systemic Toxicity Modeling – End User Applications

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April 12, 2018
Since 1902

- Subsidiaries in 71 countries
- Sales in nearly 200 countries
- >90,000 employees
- 200+ factories
- Sales: >$30B
- R&D investment: $~2B
- 55,000+ products
- 100,000+ patents
Five Business Groups

- Industrial
- Health Care
- Consumer
- Safety & Graphics
- Electronics & Energy
Toxicology at 3M

Toxicology group resides in the Medical Department
  • Corporate staff group reporting through Research and Development

Approximately 25 individuals
  • Includes division support toxicologists and the Strategic Toxicology Laboratory (STL)

Centralized resource for toxicology
  • Coordinates all global toxicity testing and human health risk assessments
Computational Toxicology Program Development

**Build Internal Capabilities – Acute Toxicity Estimates**
- Estimates of acute toxicity for GHS classifications
- Built software approaches for data collection, (Q)SAR, structural alerts and read-across
- Public and commercial software
- Greatly eased testing burden for acute toxicity studies

**Build Database for Computational Tox Results**
- Stores all results and structures
- Searchable by structural similarity, substructure, etc.
- Greatly improved consistency and speed of estimates
- Database today contains approx. 1000 compounds that have been assessed

**Expand Capabilities for Endpoint Estimates**
- Internal guidance process for other endpoints
- Defines use of computational estimates for classification purposes
- Further refinement of tools for (Q)SAR, structural alerts and read-across

**Build Internal (Q)SAR Models**
- Build (Q)SAR models using historical, internal data
- Difficulty in model building due to differences in test methods
- Acute toxicity - inhalation model is used for starting dose estimation
- New test results are constantly being added to the model
Acute Oral Systemic Toxicity Estimates

Product development and regulatory applications

- Screening estimates
- Internal hazard profiling
- GHS classifications
- Chemical registrations (REACH, etc.)
- Supporting information for regulatory submittals and risk assessments
### Acute Oral Systemic Toxicity Estimates

#### Approaches

<table>
<thead>
<tr>
<th>Combination of (Q)SAR and Read-Across</th>
<th>Applicability domain knowledge is critical</th>
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<tbody>
<tr>
<td>Commercial and Public Software</td>
<td>Most useful on chemistries with low</td>
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<tr>
<td></td>
<td>toxicity potential</td>
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<tr>
<td>Multiple tools – weight of evidence</td>
<td>Add internal data for model building</td>
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<tr>
<td>approach increases confidence</td>
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<tr>
<td>GHS categories – more confidence in</td>
<td>Ability to see analogs used to produce the</td>
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<td>ranges than a single value</td>
<td>estimate is very useful</td>
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Acute Oral Systemic Toxicity Estimates

<table>
<thead>
<tr>
<th>Successes</th>
<th>Challenges</th>
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<tbody>
<tr>
<td>Weight of evidence approach to increases reliability</td>
<td>Regulatory acceptance for submittals</td>
</tr>
<tr>
<td>Minimize reliance on any one tool or approach</td>
<td>Applicability domain issues – no estimates for unique chemistries or unfounded estimates produced</td>
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<tr>
<td>Greatly reduced animal testing on low toxicity chemistries</td>
<td>Limited utility for polymers, inorganic constituents</td>
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<tr>
<td>Experience has helped establish the most useful approaches</td>
<td>Decision making when estimates don’t align</td>
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# Acute Oral Systemic Toxicity Estimates

## Important Considerations for Software

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<th>Ease of use and expertise required</th>
<th>Applicability domain knowledge is critical</th>
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<tr>
<td>Cost and availability – free is best!!</td>
<td>Ability to see analogs used to produce the estimate</td>
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<tr>
<td>Regulator usage and acceptance</td>
<td>Ability to add internal historical data for model building</td>
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Thank you