OBJECTIVES

- Establish a clear path for Read-Across based on use cases
  - Attributes: structures, molecular, physicochemical, ADE (absorption distribution elimination) and/or biological properties
- Develop a clear / well-defined data template to compare various attributes
- To demonstrate the reproducible process in a software tool
  - Capture the complex steps
  - Save, export and report the results set
  - Share the results set with others

USE CASE

<table>
<thead>
<tr>
<th>Compound Properties</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAS RN</td>
<td>121552-61-2</td>
</tr>
<tr>
<td>NAME</td>
<td>Cyprophenidin: 4-cyclopropyl-6-methyl-N-phenyl-pyrimidin-2-amine</td>
</tr>
<tr>
<td>Target endpoints</td>
<td>Reproductive-developmental toxicity</td>
</tr>
<tr>
<td>Physicochemical and ADE properties</td>
<td>logD (logP/pKa), Water solubility, Absorption, Distribution, Elimination</td>
</tr>
<tr>
<td>Molecular properties</td>
<td>Complexity, TPSA, H-bond donors/acceptors, Dipole moment, Polarizability</td>
</tr>
<tr>
<td>Biological assays</td>
<td>Clastogenicity (in vitro chromosome aberration)</td>
</tr>
</tbody>
</table>

Property Similarity

- Calculated properties were normalized to -1 and 1 (min/max) and centered at zero
- Physicochemical and ADE properties from Percepta (ACD/Labs)
- Molecular properties are from CORINA Symphony (MN-AM)
- Biological assay: clastogenicity assay (in vitro chromosome aberration) is from ToxGPS (MN-AM)

Read-Across Data Matrix Template

Individual Evidences

<table>
<thead>
<tr>
<th>T</th>
<th>A1-T</th>
<th>A2-T</th>
<th>M1-T</th>
</tr>
</thead>
<tbody>
<tr>
<td>Structure</td>
<td>Cyanimid</td>
<td>Pyrimethane</td>
<td>Mepanipyrim</td>
</tr>
</tbody>
</table>

Analog similarity: structure(s) skyline plot correlation

1.0

Analog profile: skyline plot

0.82

Experimental data: Repro Tox reliability

Target data not used NA

Experimental data: Dev Tox - offspring reliability

Target data not used NA

In Silico data: Repro Tox QSAR reliability

No effects, Klimisch 2

In Silico data: DART alerts total hits

No hits

Values

-0.53

-0.60

-0.64

-0.70

-0.79

-0.87

-0.90

-0.92

-0.95

-0.98

-1.00

Belief Function: combining evidence from multiple sources

Uncertainty

Combining in vivo experimental data for Analog A1

Combining in vivo experimental data for Analog A2

Combining evidences of in silico prediction results for T

Combining all evidences for T

SUMMARY AND FUTURE

- A Read-Across (RA) process is validated through conducting a case study with known result
- Storage of workflow and results set to be reproduced or shared with others is demonstrated from a software tool
- A consistent data matrix template is developed to transparently combine various pieces of evidence during the RA process
- Demonstrated the power of "similarity profile" by leveraging two tools to obtain wide array of molecular, physicochemical and biological assay profiles

REFERENCES

1. Percepta at ACD/Labs: http://www.acdlabs.com/products/percepta/
2. CORINA Symphony at MN AM: https://www.mn-am.com/products/corinasymphony
3. ChemTunes/ToxGPS: https://www.mn-am.com/products/toxgps
4. EFSA Scientific Report (2005) 51, 1-78, Conclusion on the peer review of pyrimethane