Understanding Negative Predictions in Derek Nexus

Derek Nexus, Linexa Limited’s expert knowledge-based toxicity prediction software, generates negative predictions for endpoints, such as Ames mutagenicity, to assist with regulatory submissions.

If a query compound does not match any alerts or examples, a negative prediction is given.

Four potential outcomes are then possible:

- **Active**
- **Inactive**
- **Inactive with misclassified features**
- **Inactive with unclassified features**

*Negative predictions cannot currently contain both mis- and unclassified features.

Misclassified and unclassified features are highlighted for expert review, but are not necessarily an indication of activity.

**Workflow**

For a detailed version of this workflow, please [click here](#).

**Validation**

This approach was validated for the mutagenicity in-vivo endpoint using large proprietary data sets containing more than 12,000 compounds (Wilkins et al. 2012). The results, shown in the following table and illustration, show that negative predictivity in the absence of misclassified or unclassified features is very high. The presence of misclassified features reduces negative predictivity, whereas unclassified features lead to an increase in variability, though in both cases negative predictivity remains high.

<table>
<thead>
<tr>
<th>Negative Predictions</th>
<th>Inactive</th>
<th>Inactive with misclassified features</th>
<th>Inactive with unclassified features</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Non-mutagens in test set</td>
<td>91.5</td>
<td>89.5</td>
<td>88.0</td>
</tr>
<tr>
<td>% Correct</td>
<td>99.0</td>
<td>99.0</td>
<td>95.0</td>
</tr>
<tr>
<td>% Correct w/ misclassified features</td>
<td>98.0</td>
<td>98.0</td>
<td>98.0</td>
</tr>
<tr>
<td>% Correct w/ unclassified features</td>
<td>98.0</td>
<td>98.0</td>
<td>98.0</td>
</tr>
</tbody>
</table>

Note: % Predictions of negative predictions against 150 proprietary data sets containing 10,000 compounds.