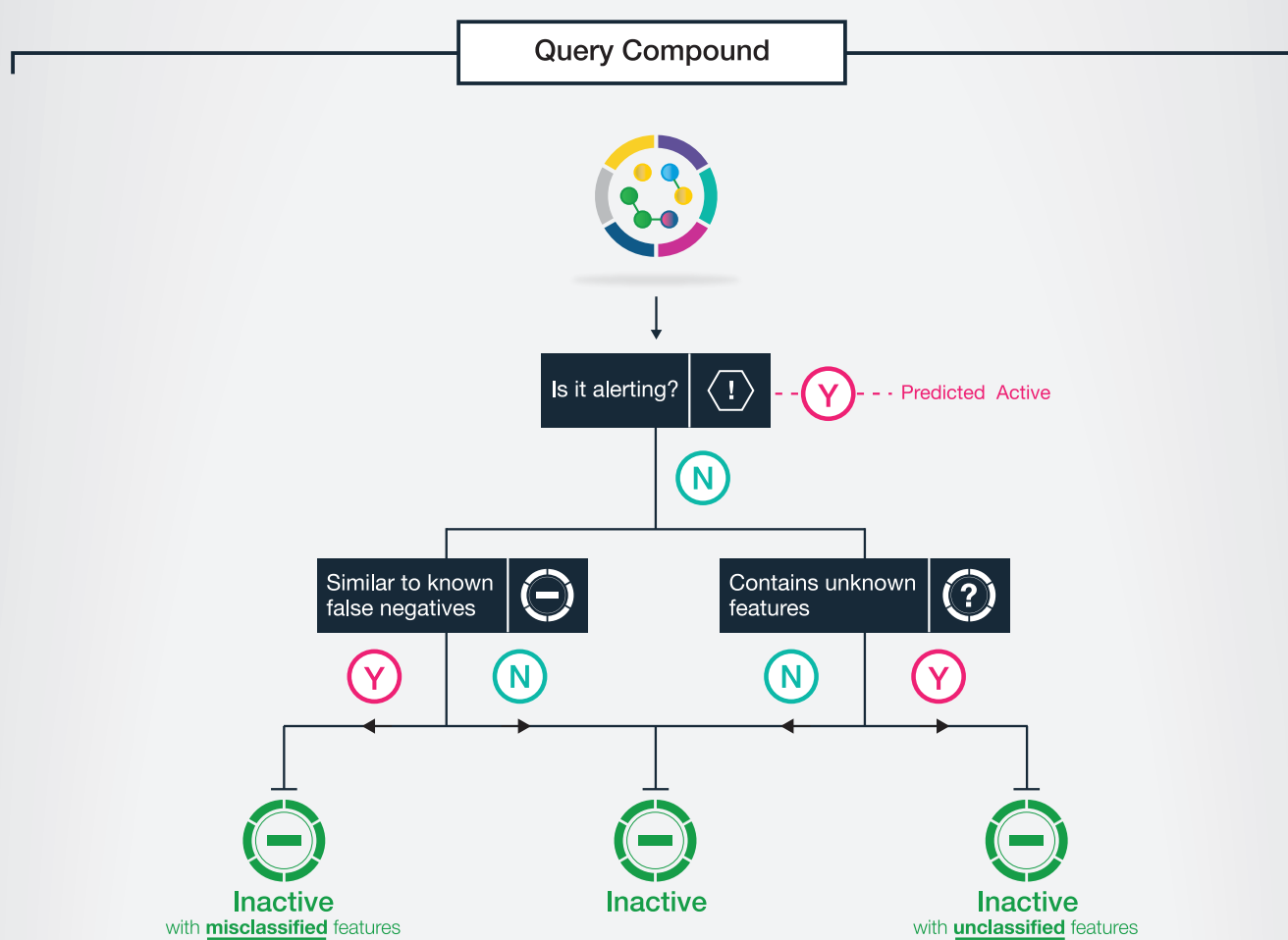# Understanding Negative Predictions in

Derek
nexus

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

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

Four potential outcomes are then possible*:

Query Compound

Is it alerting? **!** - - Y - - - Predicted Active

N

Similar to known false negatives **⊖**   Contains unknown features **?**

Y   N   N   Y

Inactive
with **misclassified** features

Inactive

Inactive
with **unclassified** features

A negative prediction could also potentially contain both mis- and unclassified features.

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

Workflow

| Query | Derek Nexus Knowledge Base | Derek Nexus Prediction | Expert Review by user | Expert Decision |
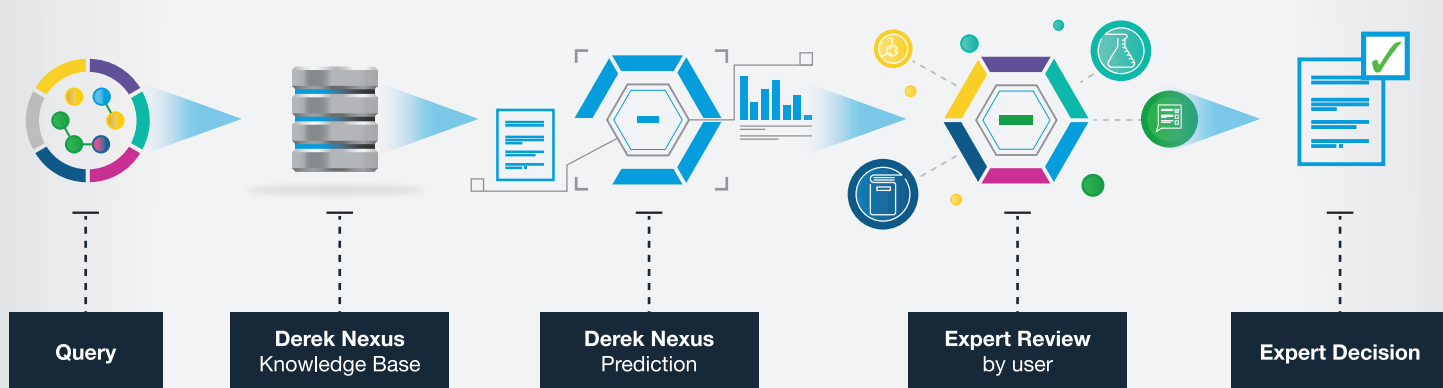
For a detailed version of this workflow please **click here**

Validation

This approach was validated for the mutagenicity *in vitro* endpoint using twelve proprietary data sets containing more than 13,000 compounds [Williams *et al*.]. 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 leads to an increase in variability, though in both cases negative predictivity remains high (i.e. above the background rate of non-mutagens in the external data sets).

	Negative Predictions			
		Inactive	Inactive with misclassified features	Inactive with unclassified features
	% Non - mutagens in test data set	% Correct	% Correct	% Correct
Median	81.0	89.5	84.0	90.3

Table 1: Performance of negative predictions against 12 proprietary data sets, containing 13,096 compounds.

% of non-mutagenic compounds

All Data Set   Inactive   Inactive/W/Mis   Inactive/W/Un
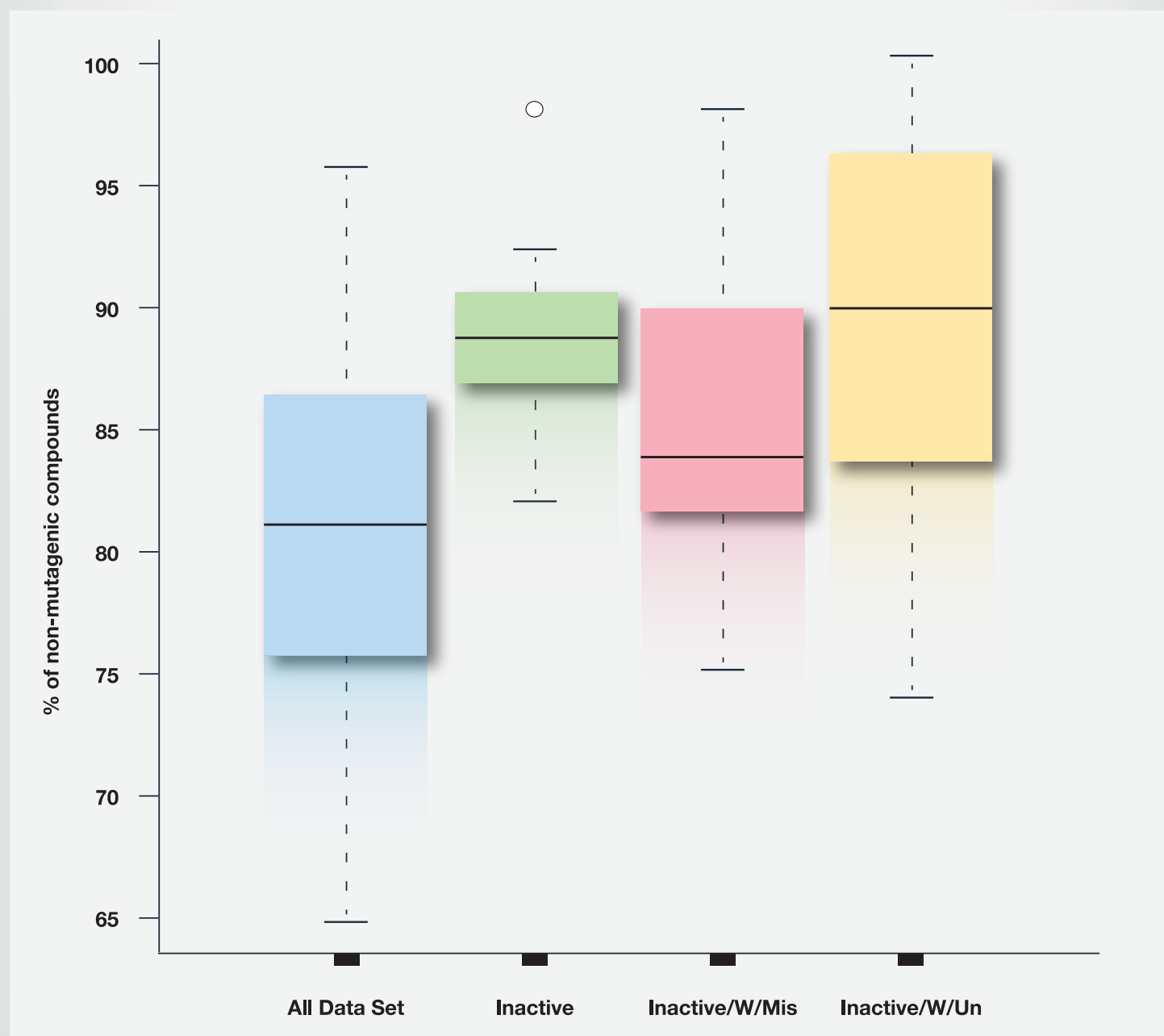
References: Williams et al., (2016), 'It's difficult, but important, to make negative predictions', Regulatory Toxicology and Pharmacology,Volume 76, Pages 79-86, http://dx.doi.org/10.1016/j.yrtph.2016.01.008