



# Derek Nexus And The Prediction Of Human Skin Sensitisation Potential - An Evaluation

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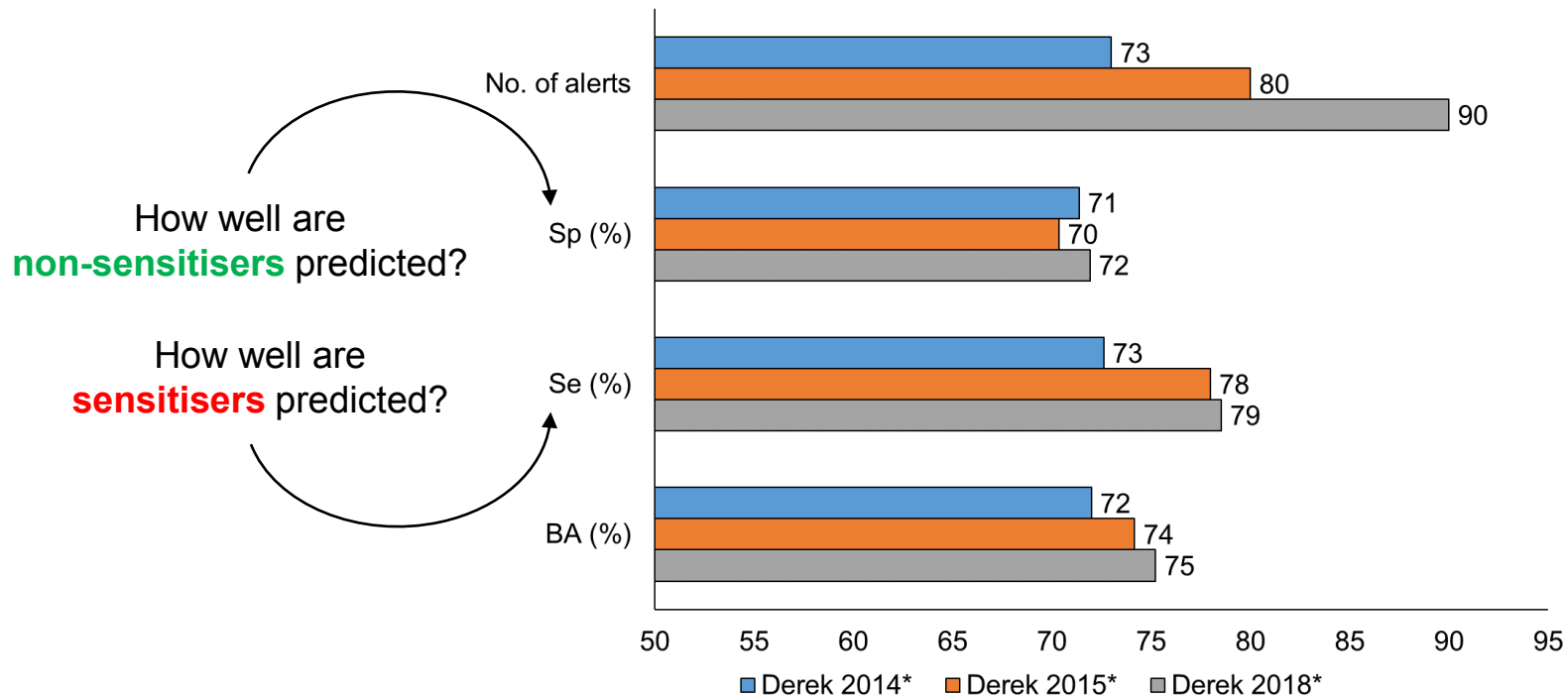
# Agenda

- Derek Nexus alerts
- Compiling a human dataset
- How well does Derek Nexus predict human skin sensitisation?
- Mispredicted chemical classes of interest
- Conclusions.



# Derek Nexus alerts

- 90 skin sensitisation alerts in Derek Nexus
- Built using mainly animal data



- How well does Derek predict for human data?

\*Analysis based on an in-house dataset of 1167 sensitisers and 1282 non-sensitisers based on results from the LLNA and/or GPMT. Conflicting and equivocal results have been removed.

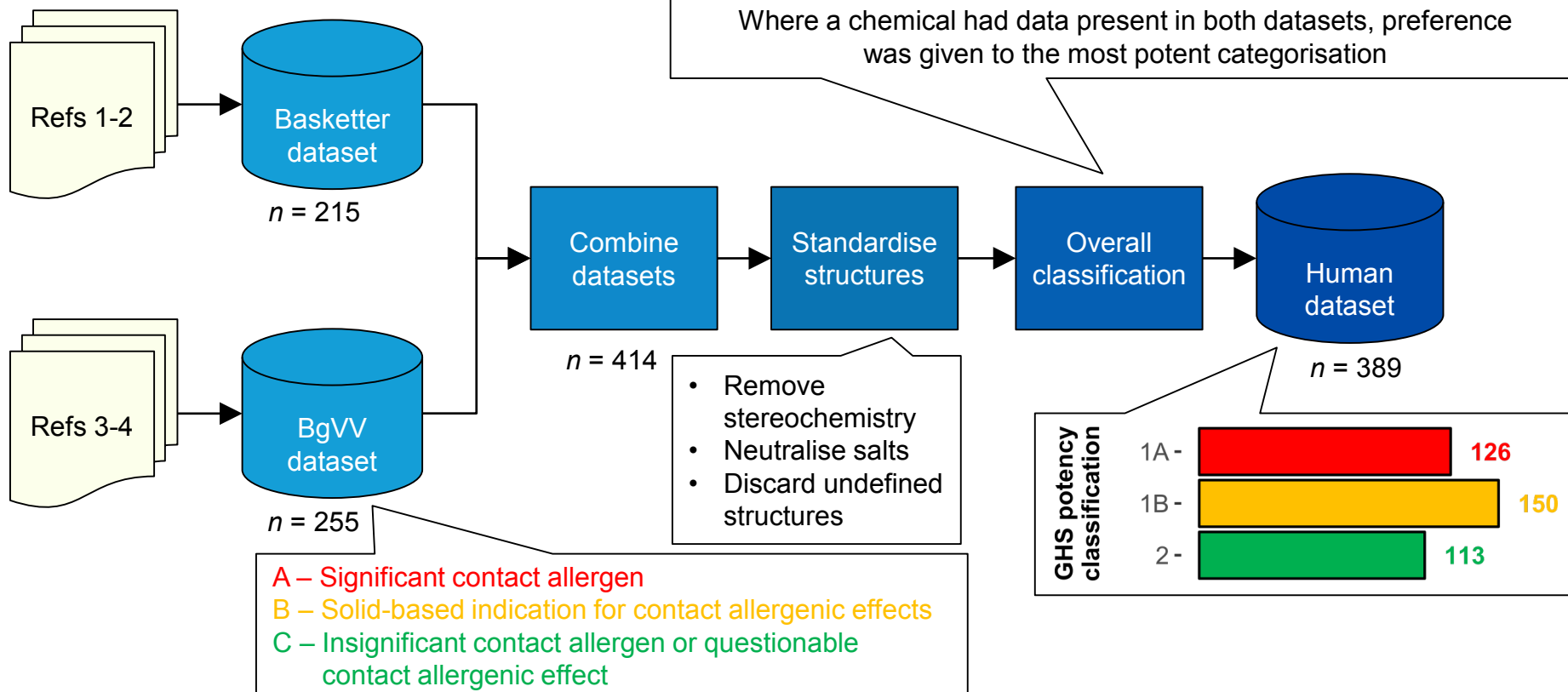
\*against an in-house dataset of >2500 chemicals with murine Local Lymph Node Assay (LLNA) and/or Guinea Pig Maximisation Test (GPMT) data

# Compiling a human dataset

- 1 – Extreme sensitiser
- 2 – Strong sensitiser
- 3 – Moderate sensitiser
- 4 – Weak sensitiser
- 5 – Very weak sensitiser
- 6 – Non-sensitiser

Basketter category	BgVV category	Hazard classification	GHS potency classification
1 or 2	A	Sensitiser	1A
3 or 4	B	Sensitiser	1B
5 or 6	C	Non-sensitiser	2

Where a chemical had data present in both datasets, preference was given to the most potent categorisation

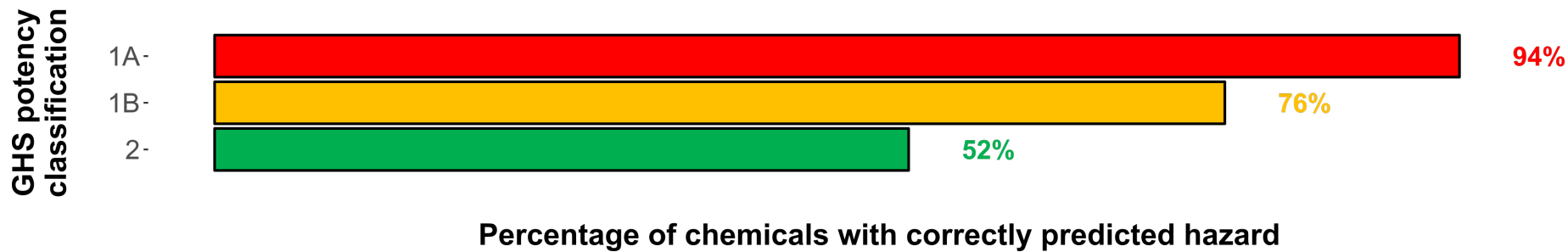


# Hazard performance

- Predicting sensitisers / non-sensitiser (hazard)



- Predicting GHS classifications



# Mispredictions

False positives	Comments	False negatives	Comments
<p>R = H, Me, CN</p>	<ul style="list-style-type: none"> <li>• 16 acrylate esters</li> <li>• All in GHS category 2</li> <li>• 11 have +ve GPMT data, 1 is –ve</li> <li>• Chemicals with this substructure are known to be weak sensitizers in mice, and can sensitize humans given prolonged exposure<sup>1-2</sup></li> <li>• As such, these predictions could be considered to be true positives</li> <li>• Updated performance would be: sensitivity = 85%, specificity = 61%</li> </ul>		<ul style="list-style-type: none"> <li>• 5 terpenoids with an allylic H atom</li> <li>• All in GHS category 1B</li> <li>• 1 has +ve LLNA data, 1 is –ve</li> <li>• Suspected prehapten<sup>3</sup></li> <li>• Possible candidates for inclusion in equivocal terpenoid alert 712</li> </ul>
			<ul style="list-style-type: none"> <li>• 3 substituted aromatic aldehydes</li> <li>• All in GHS category 1B</li> <li>• 2 have +ve animal data, 1 is –ve</li> <li>• Excluded from aldehyde alert 419</li> <li>• Data are conflicting for this class</li> </ul>

1. Kimber, M. A. Pemberton, *Regul. Toxicol. Pharmacol.*, **2014**, *70*, 24-32.

2. A. Lazarov, *J. Eur. Acad. Dermatol. Venereol.*, **2006**, *21*, 169-171.

3. A.-T. Karlberg et al., *Contact Dermatitis*, 2013, *69*, 323-334.

# Conclusions

- Derek predicts human sensitisation well – 75% accuracy for this dataset
- High sensitivity – 84%
  - 94% when only considering strong sensitisers (GHS 1A)
- Lower specificity indicates tendency to over-predict the sensitising ability of human non-sensitisers
  - Indicates animal data over-predicts as Derek alerts mainly made up of this data
- Future work will focus on using this human data to improve Derek alerts