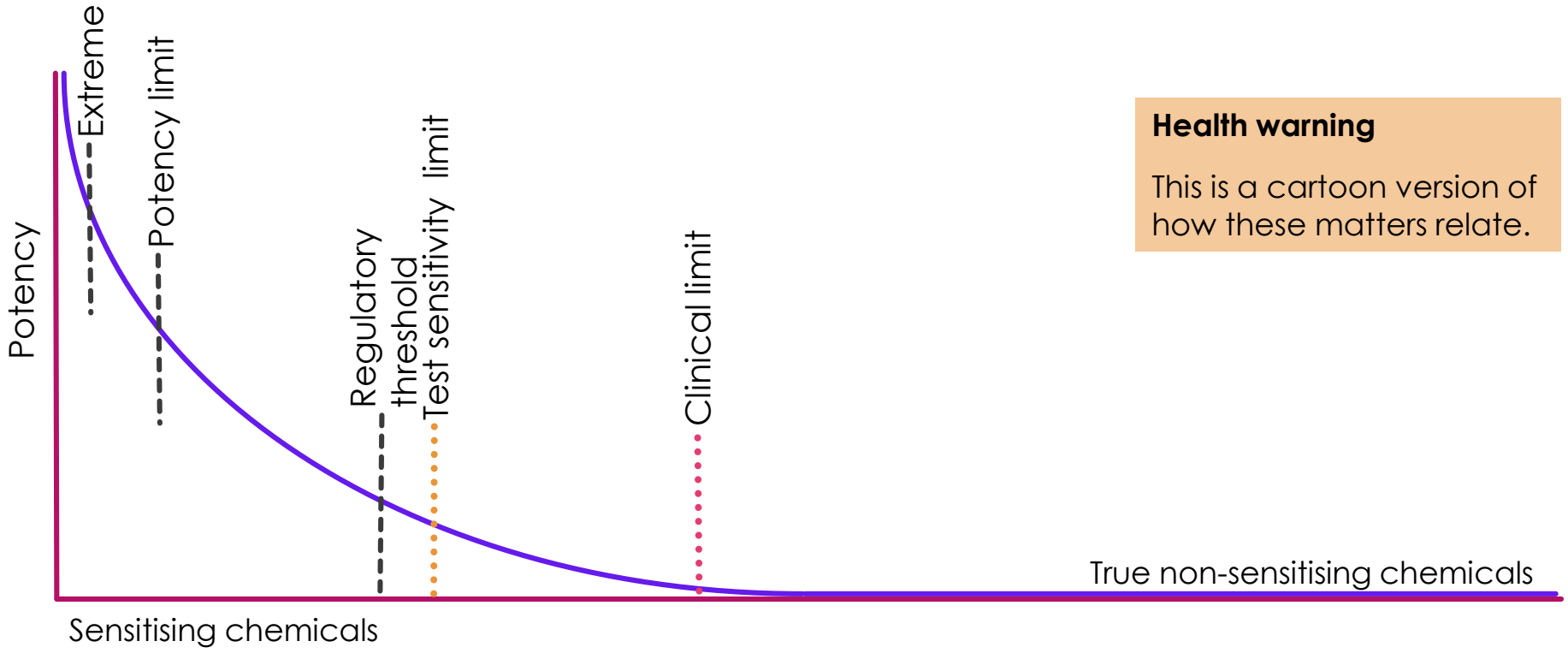
Exploiting current test methods individually or in combination for potency characterisation

What is potency?

- An intrinsic property of a sensitizing substance
- A chemical/biological continuum, ie not discrete steps
- Something that varies very widely
- …but is only 1 of multiple factors that govern sensitisation induction

Sensitisers, hazard, potency and regulations



Health warning

This is a cartoon version of how these matters relate.

28th ERGECD– *Preliminary Program*

November 7 – 9, 2018 at Coty, Darmstadt, Germany

Wednesday, 7th November 2018
17.30-19.30 **Get together**

Thursday, 8th November 2018
Morning session 8.45 – approx.12.00

Welcome

I. Skin sensitization risk assessment

a) *Non-animal concepts*

Andreas Natsch (Dübendorf, CH)
Quantitative risk assessment without animal testing - a scheme for fragrance molecules supported by case studies

Donna Macmillan (Leeds, UK)
A defined approach for skin sensitisation hazard and potency based on the guided integration of in silico, in chemico and in vitro data using exclusion criteria

Annette Mehling (Düsseldorf, DE)
Evaluation of 3D skin model-based assays using difficult to test substances: an EPAA multi-sector project

Susanne Kolle (Ludwigshafen, DE)
The kinetic DPRA to assess skin sensitization potency sub-categories

Nadège Ade (Lyon, FR)
U-SENS™: New perspective for chemicals interfering with fluorescence by flow cytometry

Brunhilde Blömeke (Trier, DE)
Prediction of skin sensitization potency with the COCAT model

otency

NED

networks

an methods

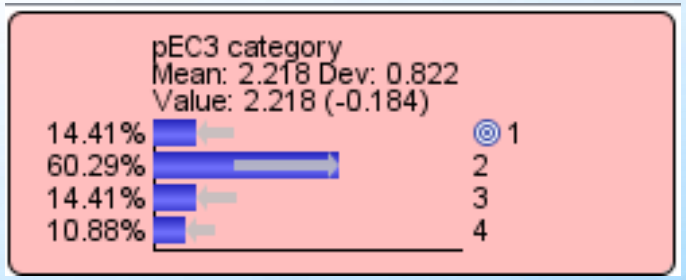
8 + EC50

....

It is well worth reading the recent Cosmetics Europe papers that have appeared in Critical Reviews in Toxicology this year.

Bayesian Net ITS3- Skin Sensitization

- Predicts a skin sensitization potency (even when data are missing)
- Expressed as probability distribution of LLNA pEC3, 4 potency classes: nonsensitizers (NS), weak (W), moderate (M), and combined strong and extreme (S) sensitizers.



P(LLNA=NS, W, M, S| evidence)

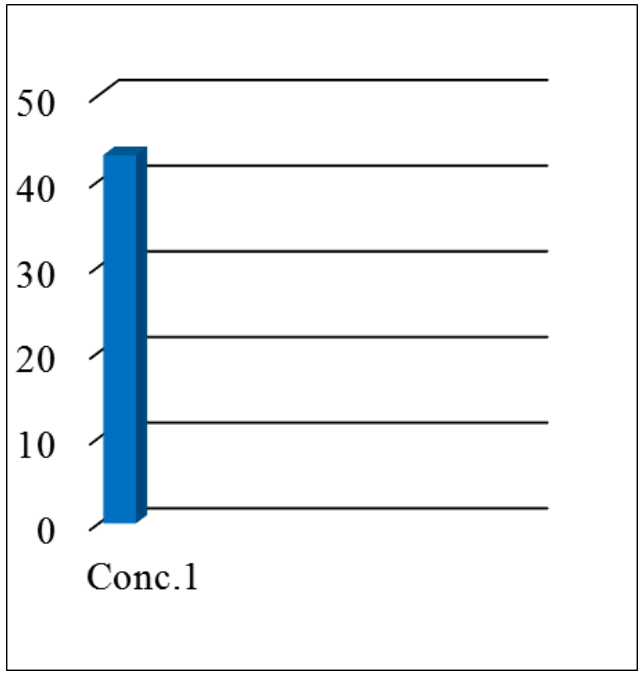
↓

EC3% (50th or any other percentile)

- Could be used:
  - For classification and labeling under the GHS C&L scheme
  - To set NESILs for QRA
  - For the development of testing strategy if data are missing. Measures progress by uncertainty reduction. Resolves data conflicts.

Global Product Stewardship
Safety • Sustainability • Regulatory • Technical Relations

…and from BASF

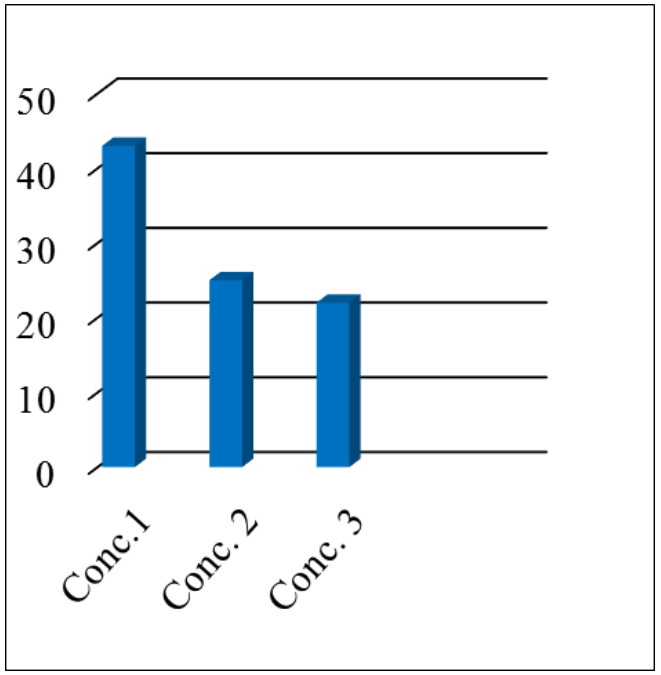


Standard DPRA

Accuracy GHS Cat 1A vs. 1B

56% (vs. LLNA, n = 124)

50% (vs. human, n = 14)

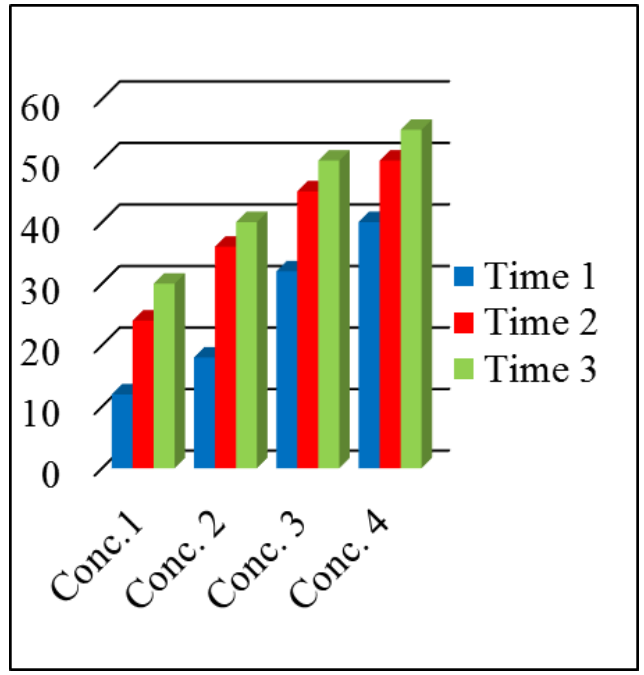


qDPRA

Accuracy GHS Cat 1A vs. 1B

81% (vs. LLNA, n = 36)

57% (vs. human, n = 14)



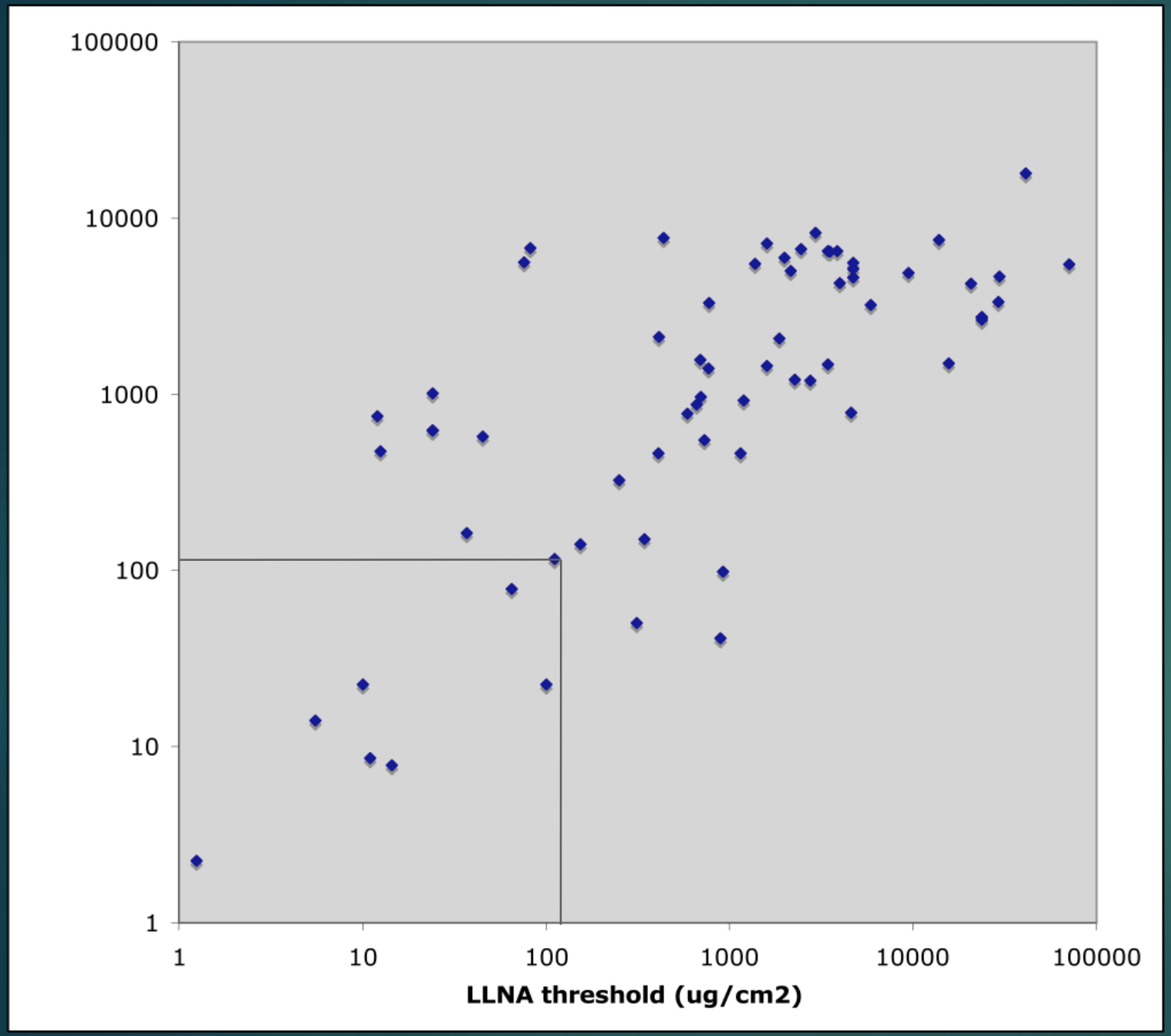
Kinetic DPRA

Accuracy GHS Cat 1A vs. 1B

92% (vs. LLNA, n = 38)

93% (vs. human, n = 14)

BASF
We create chemistry



…but we cannot estimate potency without some reliable basis for comparison

Please treat human potency categorisation with at least the same level of disrespect that you would give to the LLNA EC3 value as a predictor of human potency!

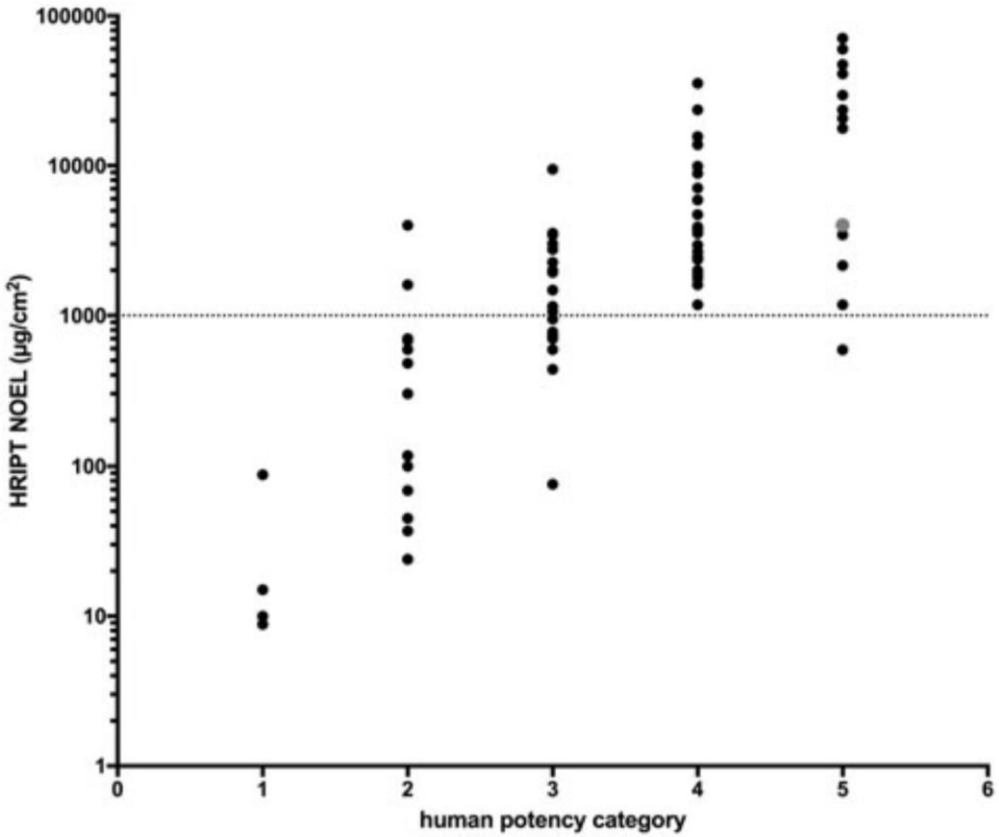


Figure 1. HRIPT no observed effect levels (NOEL) as µg/cm^2 for the human potency categories for 79 substances, for which Basketter et al. (2014) or Api et al. (2017) reported NOEL.

Perhaps an urgent task is to agree on a definitive and substantial list of chemicals whose relative potency is well characterised - using **ALL** of the available data.

Is the CE 128 substances dataset fit for this purpose? If it is, can a final ranking of relative potency be agreed?