Towards a meaningful system for characterisation and categorisation of allergens

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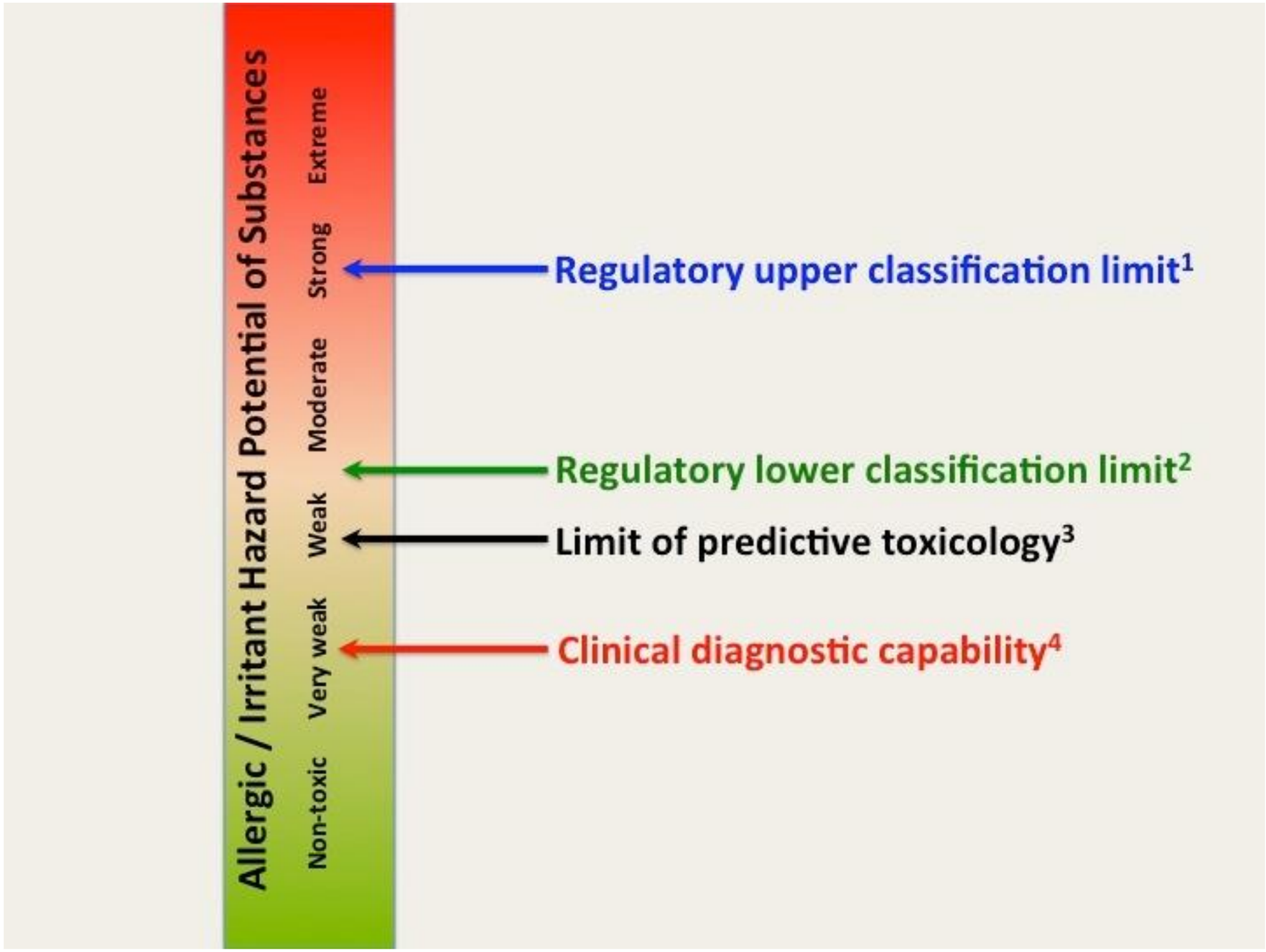
First words

- Towards (i.e. we are not there yet)
- Meaningful (suggests that we can measure it)
- Characterisation (dose response/potency)
- Categorisation (use of characterisation data)
- Skin allergens (chemicals)

Current systems (as per GHS)



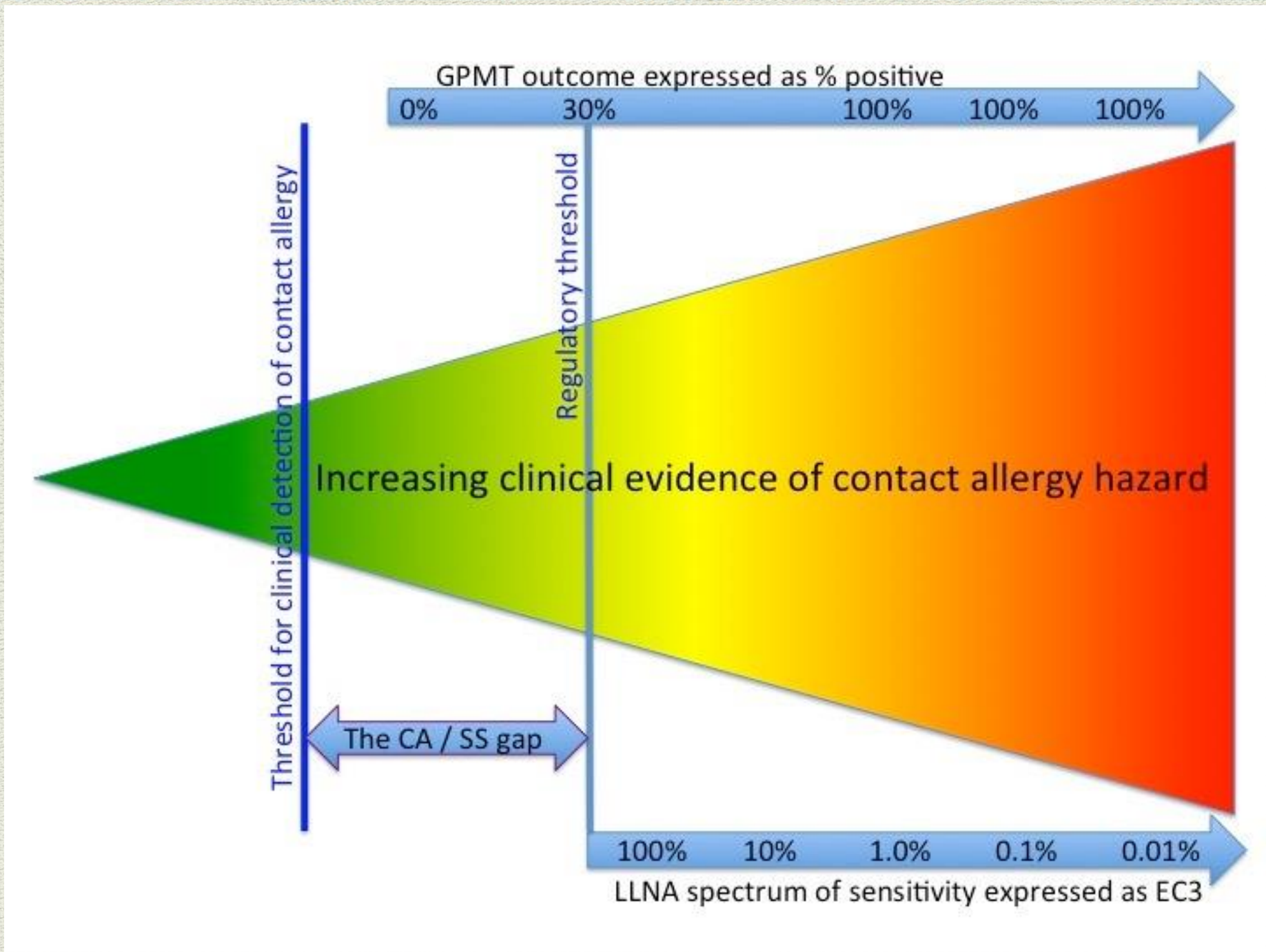
Characterisation

- After a hazard has been identified, the next step is to examine the dose response and use it to characterise the relative potency of the substance
- For the LLNA, this is well recognised as the EC3 value, now widely used as a potency marker
- For in vitro methods, some methods or IATA seem to inform on potency, but they do not achieve the graded response of the LLNA
- Human data can play a role

Categorisation

- For nearly 50 years, we have had two categories: *sensitiser/not classified*
- Recent "progress" advanced this to three: *strong sensitiser/moderate sensitiser/not classified*
- ECHA Guidelines have taken a step further: *extreme/strong/moderate/not classified*
- The SCCS have also made category suggestions
- A recent proposal has proposed 6 categories: *extreme/strong/moderate/weak/very weak/non-sensitiser*

Regulatory classification: in vivo



Regulatory classification: human

- **Annex I: 3.4.2.2.2.1.** Human evidence for sub-category 1A can include:
  - positive responses at ≤ 500 µg/cm^2 (HRIPT, HMT – induction threshold);
  - diagnostic patch test data where there is a relatively high and substantial incidence of reactions in a defined population in relation to relatively low exposure;
  - other epidemiological evidence where there is a relatively high and substantial incidence of allergic contact dermatitis in relation to relatively low exposure.

- **Annex I: 3.4.2.2.2.2.** Human evidence for sub-category 1B can include:
  - positive responses at > 500 µg/cm^2 (HRIPT, HMT – induction threshold);
  - diagnostic patch test data where there is a relatively low but substantial incidence of reactions in a defined population in relation to relatively high exposure;
  - other epidemiological evidence where there is a relatively low but substantial incidence of allergic contact dermatitis in relation to relatively high exposure.

Further guidance - 1

Human diagnostic patch test data	**High frequency**	**Low/moderate frequency**
General population studies	≥ 0.2%	< 0.2%
Dermatitis patients (unselected, consecutive)	≥ 1.0%	< 1.0%
Selected dermatitis patients (aimed testing, usually special test series	≥ 2.0%	< 2.0%
Work place studies 1: all or randomly selected workers 2: selected workers with known exposure or dermatitis	 ≥ 0.4% ≥ 1.0%	 < 0.4% < 1.0%
Number of published cases	≥ 100 cases	< 100 cases

Further guidance - 2

Exposure data (weighting)	**Relatively low exposure**	**Relatively high exposure**
Concentration/dose	< 1.0% < 500 µg/cm^2 (*score 0*)	≥ 1.0% ≥ 500 µg/cm^2 (*score 2*)
Repeated exposure	< once daily (*score 1*)	≥ once daily (*score 2*)
Number of exposures (irrespective of concentration)	< 100 exposures (*score 0*)	≥ 100 exposures (*score 2*)

Score 5 or 6 = relatively high exposure

Overview of regulatory classification categories

In the EU this is further divided into extreme and strong

GHS 1a

- Extreme
- Strong

ECETOC recommended this sub-division in 2001

GHS 1b

- Moderate
- Weak

Clinically we recognise very weak and true non-allergens

GHS NC

- Very weak
- Non-sensitiser

Basketter et al, 2014; Dermatitis 25; 11-21

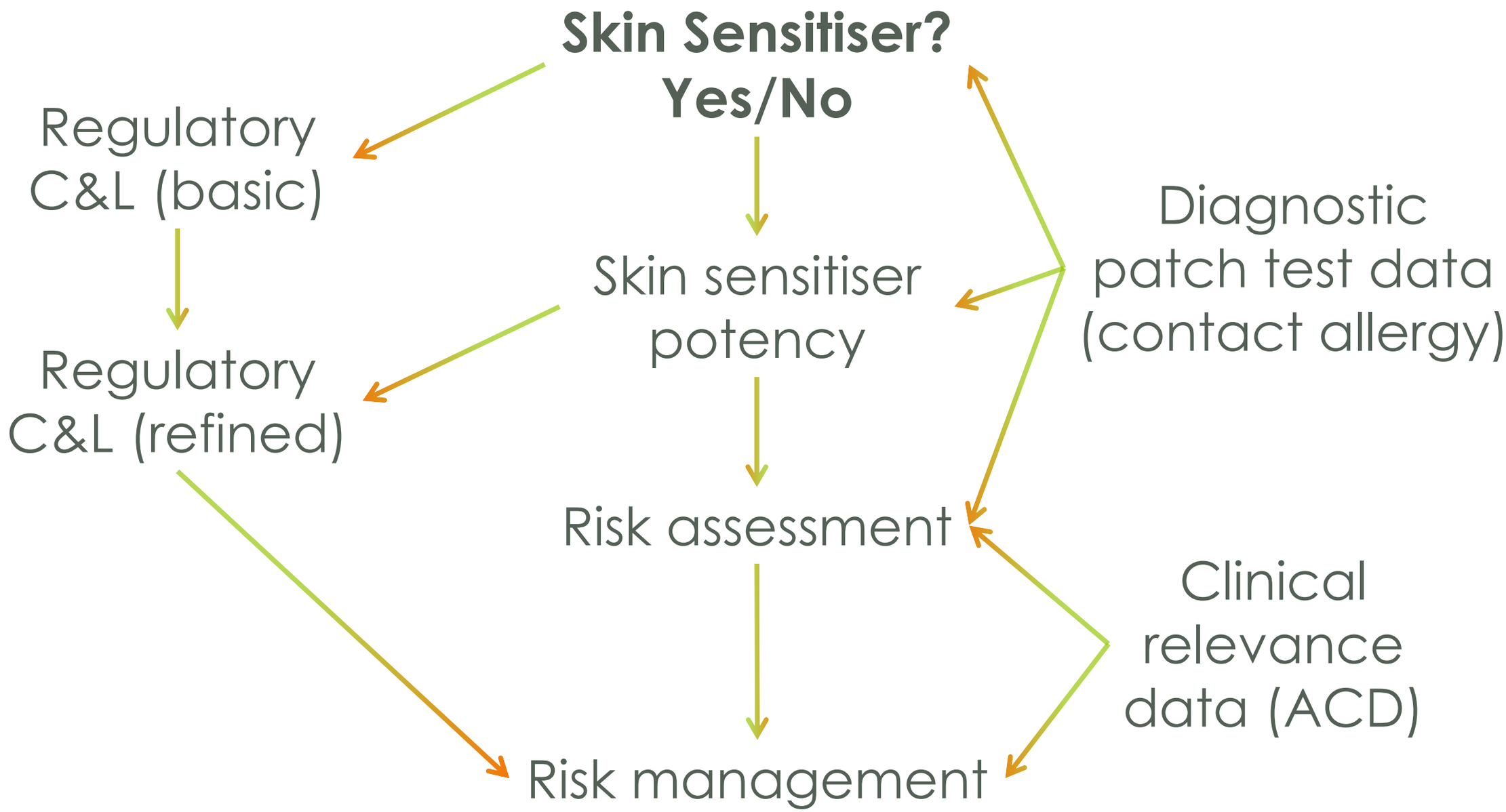
How could this help?

- Each category can be associated with a default NESIL
- Existing substances placed into these six categories assists in the evaluation of in vitro methods for potency prediction
- At the recent WCA, many folk have started to use this information
- Efforts are underway to expand 131 ➔ 200

Is this relevant for fragrances?

- At > 1 tonne per annum, YES, as this is REACH
- ..but also, NO, since REACH does not do (Q)RA
- We should learn from existing regulations, adapt and expand them, but keep the legacy
- To ensure actions are meaningful, there must be measurement: the fragrance industry is well placed to lead this activity

Final words



Consumer?