Potency classification of skin sensitizers  
(EC WG on Sensitization)

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- Occupational and environmental dermatology
- Clinical, experimental and epidemiological research
- Risk assessment tasks
  - SCCP member (2004-2009); SCCS external expert (2009-2012)
  - OECD Test Guideline: skin sensitization (1992)
  - ECHA CLP: guidance on application of the CLP criteria (2012-2013)
- Funding
  - Karolinska Institutet and Stockholm County Council
  - Swedish Research Council for Health, Working Life and Welfare
The clinical disease: allergic contact dermatitis

Clinical tests

- Diagnostic patch test
- Baseline series
- Special series, serial dilutions
- Repeated open application (ROAT)

Species | Induction / sensitization | Elicitation / allergic reaction / disease
---|---|---
Human | Skin exposure (products, mixtures, articles, etc) | Disease: 
- allergic contact dermatitis 
Clinical tests: 
- diagnostic patch test 
- dose-response (ROAT etc)

- Guinea pig | GPMT, Buehler (subst) | Challenge testing
- Mouse | LLNA (subst) | -
- Human | HRIPT etc | Challenge testing (not clinical tests)
**Guinea pig: GPMT, Buehler**

**OECD GUIDELINE FOR TESTING OF CHEMICALS**

Adopted by the Council on 17th July 1992

Skin Sensitisation

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**Mouse: LLNA**

**OECD/OCDE**

**OECD GUIDELINE FOR THE TESTING OF CHEMICALS**

Skin Sensitisation: Local Lymph Node Assay

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**WG sensitization 2002-2003**

- TC on classification and labelling, harmonized classification
- First question:
  
  Propose how to use the existing methods in order to grade allergen potency, providing detailed guidance for current predictive test methods
- The approach has been introduced in GHS and CLP
Potency categorization of classified skin sensitizers based on LLNA

<table>
<thead>
<tr>
<th>EC3 value (%)</th>
<th>EC WG sens &amp; SCCP</th>
<th>CLP &amp; GHS (H317 former R43)</th>
<th>EC3 value (%)</th>
<th>ECETOC</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤0.2</td>
<td>extreme</td>
<td>1A</td>
<td>&lt;0.1</td>
<td>extreme</td>
</tr>
<tr>
<td>&gt;0.2 - ≤2</td>
<td>strong</td>
<td>1A</td>
<td>≥0.1 - &lt;1</td>
<td>strong</td>
</tr>
<tr>
<td>&gt;2</td>
<td>moderate</td>
<td>1B</td>
<td>≥1 - &lt;10</td>
<td>moderate</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>≥10 - ≤100</td>
<td>weak</td>
</tr>
</tbody>
</table>

**EC3 value**: the amount of a chemical that is required to elicit a three-fold increase in lymph node cell proliferative activity (SI ≥ 3)


Potency categorization based on GPMT or Buehler Test

- Categorization is based on
  - intradermal induction concentration in the GPMT
  - topical induction concentration in the Buehler test
- Methods designed for assessment of sensitization potential (yes or no), not potency
How to deal with discrepancies

- When EC3 values are available from more than 1 study, the lowest value should normally be used.
- Where multiple animal data sets lead to different categorization of the same substance, the higher potency category should apply.
- Human data may indicate the need to change the potency categorization derived from animal experiments. Normally, only for re-categorization into a higher potency category.

Baskett et al 2005

Submissions to SCCP often insufficient

- LLNA
  - Conc: too low, too high, too narrow span
  - Vehicle: inadequate, not prio
- GPMT
  - Conc: too low for induction, challenge
  - Often no dose-range-finding test
- SCCP conclusions often inconsistent
- SCCP memorandum
  - OECD TG requirements
  - Potency categories
- Memorandum on hair dye substances and their skin sensitising properties. SCCP 19 December 2006
- Memorandum on hair dye chemical sensitisation. SCCS 26 February 2013
- Opinion on fragrance allergens in cosmetic products. SCCS 26-27 June 2012
- Other SCCP and SCCS opinions
Conclusions

- The categorization in the SCCP memorandum was recently implemented in GHS and CLP

- Animal tests will continue to be important for SCCS
  - LLNA and GPMT. Modifications may give more information

- Human data on elicitation
  - Elicitation thresholds are much lower and correlate poorly with induction potency
  - Essential basis for prevention of clinical disease