

# THE IDEA NAMs PROJECT

*Purpose, Objectives and Challenges  
and  
Development of the Reference  
Chemicals Potency List (RPCL)*

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# The Objective

***Work with others(\*) to develop a platform of New Approach Methodologies (NAMs) that provide accurate measurements of skin sensitising potency such that reliable risk assessments can be conducted without recourse to data derived from animals***  
***(\* RIFM, SenzaGen, Givaudan represented here)***

# The Challenges (1)

***Markers of potency should be causally  
AND quantitatively associated with the  
relevant end-point***

***(acquisition of skin sensitisation)***

# The Challenges (2)

***How to determine whether a NAM provides an accurate measurement of skin sensitising potency***

**One approach**

***The RCPL***

***An integration of best available  
human data and animal data***



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# Reference Chemical Potency List (RCPL): A new tool for evaluating the accuracy of skin sensitisation potency measurements by New Approach Methodologies (NAMs)

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### ABSTRACT

Considerable progress has been made in the design of New Approach Methodologies (NAMs) for the hazard identification of skin sensitising chemicals. However, effective risk assessment requires accurate measurement of sensitising potency, and this has proven more difficult to achieve without recourse to animal tests.

One important requirement for the development and adoption of novel approaches for this purpose is the availability of reliable databases for determining the accuracy with which sensitising potency can be predicted. Some previous approaches have relied on comparisons with potency estimates based on either human or animal (local lymph node assay) data. In contrast, we here describe the development of a carefully curated Reference Chemical Potency List (RCPL) which is based on consideration of the best available human and animal data.

The RCPL is comprised of 33 readily available chemicals that span a wide range of chemistry and sensitising potency, and contain examples of both direct and indirect (pre- and pro-) haptens. For each chemical a potency

# RCPL Characteristics

- *33 readily available chemicals comprising a wide range of chemistry, and skin sensitising potency*
- *Includes direct haptens and indirect [both pre- and pro-] haptens*
- *Potency expressed as a Potency Value (PV) derived from the best available human and animal (LLNA) data*
- *PVs do not include consideration of in vitro or in silico data*
- *Chemicals ranked according to PV without the use of potency categories*

## **PV: a definition**

***The PV provides an estimate of the lowest concentration of chemical (measured as  $\mu\text{g}/\text{cm}^2$  of skin) that is necessary to initiate the development of skin sensitisation***

***(an inflection point for the initiation of skin sensitisation)***



# Potency Values

Name	Pre / Pro - Hapten	Potency Value [µg/cm <sup>2</sup> ]
5-Chloro-2-methyl-4-isothiazolin-one (CMIT)		2.3
2,4-Dinitrochlorobenzene (DCNB)		3.4
1,4-Phenylenediamine (PPD)	Pre	3.9
Glutaraldehyde		20.0
trans-2-Hexenal		39.3
1,4-Dihydroquinone	Pre	47.5
Benzyl bromide		50.0
1,1,3-Trimethyl-2-formylcyclohexa-2,4-diene (Safranal)		106
Methyl 2-nonynoate (Methyl octine carbonate)		109
Methyl 2-octynoate (Methyl heptine carbonate)		125
Isoeugenol	Pre	325
Phenylacetaldehyde		750
Allyl phenoxyacetate		775
Cinnamic aldehyde		885
3-Propylideneophthalide	Pre	925
4-Hydroxy-2,5-dimethyl-3(2H)-furanone (Furaneol)		1181

Name	Pre / Pro - Hapten	Potency Value [µg/cm <sup>2</sup> ]
Citral		1450
p-Mentha-1,8-dien-7-al (Perillaldehyde)		2175
Benzaldehyde		4094
Lylal (HICC)		4275
Hydroxycitronellal		5275
Cinnamic alcohol	Pre / Pro	5775
Eugenol	Pre / Pro	7357
Geraniol	Pre / Pro	9197
Coumarin		11792
Carvone		17573
Benzyl salicylate		17715
Hexyl cinnamic aldehyde		23620
Benzyl Alcohol	Pro	>25000
Benzyl benzoate		>25000
Isomethylionone (α-)		>25000
Methyl salicylate		No PV derived - very weak/non-sensitiser
Vanillin		No PV derived - very weak/non-sensitiser

# Next Steps

- ***Promote the use of the RCPL among stakeholders and the relevant scientific community***
- ***Encourage the use of the RCPL for the evaluation of candidate methods for skin sensitisation potency assessment***
- ***In due course provide a review of the value of the RCPL in practice and of the need for any modifications or extensions***

# Applications/Challenges

- *Use of the RCPL for evaluation of NAMs for measurement of skin sensitisation potency (Peter Griem presentation)*
- *Extension and possible modification of the RCPL (Amaia Irizar presentation)*
- *Considerations of uncertainty (Andreas Natsch presentation)*
- *Case of weak sensitisers (benzyl alcohol)*