GARD®skin Dose-Response

In vitro skin sensitization potency assessment

GARD®skin Dose-Response is an *in vitro* assay designed to predict skin sensitization potency of chemicals.

The assay provides a Point-of-Departure (POD) for risk assessment, enabling potency ranking and subclassification of candidate ingredients. This makes it a valuable tool for both product development and regulatory decision-making.

By estimating the threshold concentration at which a test substance induces skin sensitization, the assay allows for potency assessment, where lower concentrations indicate higher potency. These data support the prediction of LLNA EC3 values, human skin sensitizing potency NOEL/NESIL, and UN GHS/CLP classification 1A or 1B, all with high statistical significance.

GARD®skin Dose-Response is adapted from GARD®skin (OECD TG 442E) and is currently included in the OECD Test Guideline Program (TGP 4.106).

Potency Prediction

- **LLNA EC3 value**
- **Human potency**
- **GHS/CLP classification**

Features and Benefits

Test system
- Human dendritic-like cell line: SenzaCell®.

Solvents
- Standard: DMSO and H_2O.
- Other available solvents: Acetone, DMF, Isopropanol, Ethanol, Glycerol, Olive oil, Sesame oil.

What it measures
- Response values in a titrated range of multiple concentrations in GARD®skin.

Readout and prediction
- Hazard readout: Skin sensitizer or Non-sensitizer.
- Potency readout: cDV_0.*
- Potency prediction: LLNA EC3 value; Human potency NOEL/NESIL; GHS/CLP classification 1A or 1B.
- Dose-response curve.

High performance
- 94% accuracy in predicting skin sensitizing hazard.**
- Readouts significantly correlate with LLNA EC3 values and human potency.

Short turnaround time
- 6-8 weeks for standard studies.

Low sample requirement
- 0.5g (solid) or 1ml (liquid).

Compliance
- Included in the OECD Test Guideline Program (TGP 4.106).
- GLP or non-GLP.

*cDV_0 is the threshold concentration for the test substance to induce a positive response in GARD®skin.
**Johansson et al., Validation of the GARD®skin assay for assessment of chemical skin sensitizers – ring trial results of predictive performance and reproducibility. Toxicological Sciences. May 17, 2019.

How it works

The GARD®skin Dose-Response investigates the GARD®skin response values in a titrated range of multiple concentrations in a dose-response manner to find the threshold concentration required to induce a positive decision value.

This threshold concentration, cDV_0, is used to estimate the inherent sensitizing potency of a chemical. A low value indicates a high inherent skin sensitizing potency, and a high value indicates a low inherent skin sensitizing potency (Figure 1).

cDV_0 can also be used to predict the traditional EC3 value from Local Lymph Node Assay, the human skin sensitizing potency NOEL/NESIL (Figure 2), and UN GHS/CLP classification 1A or 1B depending on the need.

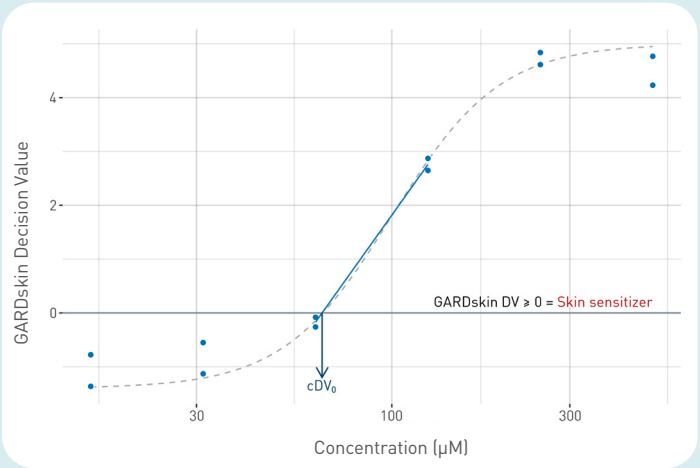

Figure 1. Illustration of the dose-response curve from testing a single chemical with GARD®skin Dose-Response. The readout, cDV_0, represents the estimated skin sensitization potency and corresponds to the lowest dose required to elicit a positive response in GARD®skin.

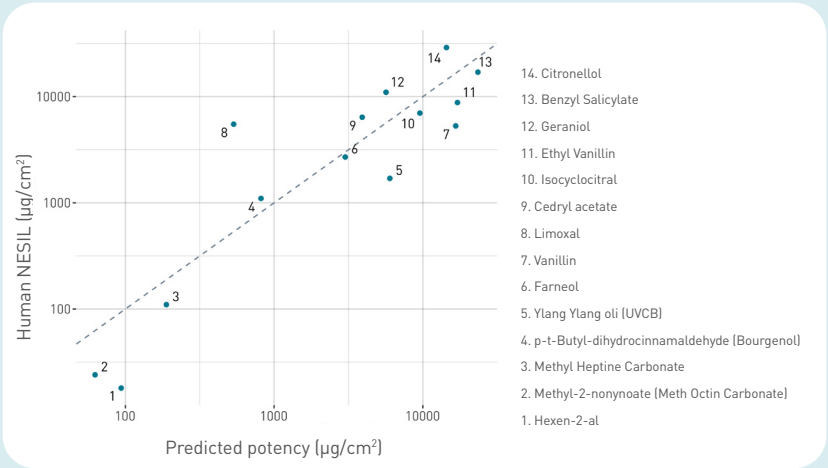

Figure 2. Comparison of GARD®skin Dose-Response predicted human NESIL values with benchmark reference NESIL values for 14 fragrance materials (Donthamsetty et al., 2024). The predicted NESIL values showed strong correlation with reference values (Pearson correlation = 0.906, R^2 = 0.821). The dashed line represents the identity line (y = x).

Scientific publications

- SenzaGen, RIFM and IFF*: Lee et al., *Determining a Point of Departure for Skin Sensitization Potency and Quantitative Risk Assessment of Fragrance Ingredients Using the GARD®skin Dose-Response Assay, ALTEX 2025.*
- SenzaGen and L'Oréal: Gradin et al., *In Vitro Prediction of Skin-Sensitizing Potency Using the GARD®skin Dose-Response Assay: A Simple Regression Approach, Toxics 2024.*
- SenzaGen, RIFM and IFF*: Donthamsetty et al., *GARD®skin Dose-Response Assay and its Application in Conducting Quantitative Risk Assessment (QRA) for Fragrance Materials Using a Next Generation Risk Assessment (NGRA) Framework, Regulatory Toxicology and Pharmacology 2024.*
- SenzaGen proof of concept study: Gradin et al., *Quantitative Assessment of Sensitizing Potency Using a Dose-Response Adaptation of GARD®skin, Nature Scientific Reports 2021.*

** RIFM: Research Institute of Fragrance Materials; IFF: International Flavors & Fragrances.*