

Introduction

All medical devices need to be evaluated for the endpoint skin sensitization according to the Biological Evaluation of Medical Devices (ISO 10993-1:2018), today commonly involving *in vivo* assays. Here, we show that the *in vitro* assay, **GARD®skin Medical Device** can classify leachables as either skin sensitizers or non-sensitizers in polar and non-polar extraction vehicles of Medical Device.

Conclusions

GARD®skin Medical Device

- is an *in vitro* alternative for assessment of skin sensitization of Medical Devices
- is compatible with the extraction vehicles, saline, olive oil and sesame oil

GARD®skin Medical Device

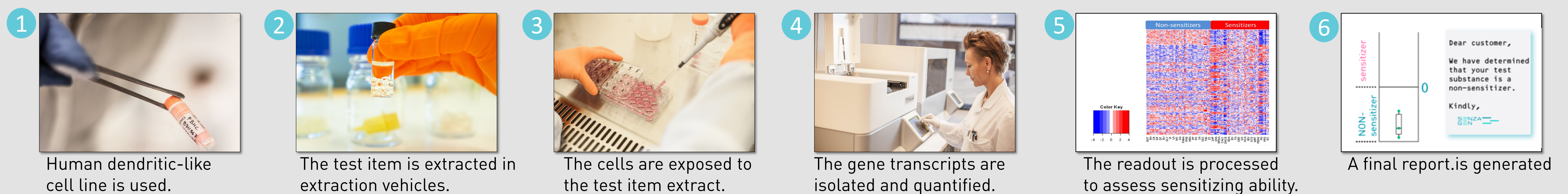


Figure 1. A brief description of The Genomic Allergen Rapid Detection (GARD®) assay, for full description see Johansson et al. Toxicological Science 2019

Results

In the in-house validation of GARD®skin Medical Device we used model materials, spiked with strong, moderate and weak sensitizers and an unspiked control material. Three additional medical grade materials were used as control materials. Extracts from the materials were prepared in saline, Sesame oil and Super Refined Olive Oil and analysed using GARD®skin

prediction model. All the model materials were correctly classified, the spiked materials as sensitizers, and the non-spiked materials as non-sensitizers. The three additional medical grade materials were all classified as non-sensitizers. The results are presented in Table 1.

Table 1. Summary of the results from the in-house validation of GARD®skin Medical Device compared with LLNA (as listed in the CE STTF database) and Human potency classification (HP) for the chemicals (Basketter et al. 2014).

Test material	Chemical	Sensitizing potential		GARD®skin Medical Device Prediction		
		LLNA	HP	Saline	Olive Oil	Sesame oil
Silicone	None	N/A	N/A	Non-sensitizer	Non-sensitizer	Non-sensitizer
	2-aminophenol	Strong	Cat 2	Sensitizer	Sensitizer	Sensitizer
	Cinnamic aldehyde	Moderate	Cat 2	Sensitizer	Sensitizer	Sensitizer
	Propyl gallate	Strong	Cat 2	Sensitizer	Sensitizer	Sensitizer
	Phenyl benzoate	Weak	Cat 3	Sensitizer	Sensitizer	Sensitizer
TPU	None	N/A	N/A	Non-sensitizer	Non-sensitizer	Not tested
	2-aminophenol	Strong	Cat 2	Sensitizer	Sensitizer	Not tested
	Cinnamic aldehyde	Moderate	Cat 2	Sensitizer	Sensitizer	Not tested
Silicone tube	-	N/A	N/A	Non-sensitizer	Non-sensitizer	Non-sensitizer
TPU tube	-	N/A	N/A	Non-sensitizer	Non-sensitizer	Non-sensitizer
PVC tube	-	N/A	N/A	Non-sensitizer	Non-sensitizer	Non-sensitizer
Vehicle control	-	Neg		Non-sensitizer	Non-sensitizer	Non-sensitizer
Positive control	p-Phenylenediamine	Pos		Sensitizer	Sensitizer	Sensitizer

Material and Methods

Specific for this in-house validation study, Research Institutes of Sweden (RISE), produced model materials: Silicone, spiked with four sensitizers of different sensitizing potency (2-aminophenol, cinnamic aldehyde, propyl gallate and phenyl benzoate) and thermo-plastic polyurethane (TPU), spiked with two different sensitizers (2-aminophenol, cinnamic aldehyde). In addition three materials: Silicone tube, Polyvinyl chloride (PVC) tube and TPU tube, supplied by Medizintechnik Promedt, were analysed.

Extracts from the materials were prepared according to ISO 10993-12:2012;

0.2 g/ml of the material were incubated in Saline (0.9% NaCl, G-Biosciences), Super Refined Olive Oil (CRODA) or Super Refined Sesame Oil Ph Eur (Sigma) at 37° C (± 1°C) for 72 h (± 2 h) in borosilicate tubes with PTFE lined lids. The extracts were added to the SenzaCells™ at a maximum concentration of 10%. (in 10% of final concentration).

After cell stimulation, RNA were isolated and the gene expression were analysed using pattern recognition.

References

- Johansson H. et al. Validation of the GARD™skin Assay for Assessment of Chemical Skin Sensitizers: Ring Trial Results of Predictive Performance and Reproducibility. *Toxicological Science*. 2019
- Basketter et al. Categorization of Chemicals According to Their Relative Human Skin Sensitizing Potency. *Dermatitis*. 2014

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