ESCD CONGRESS 2022

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Assessment of the skin sensitization potential of fragrance ingredients using the U-SENS™ assay

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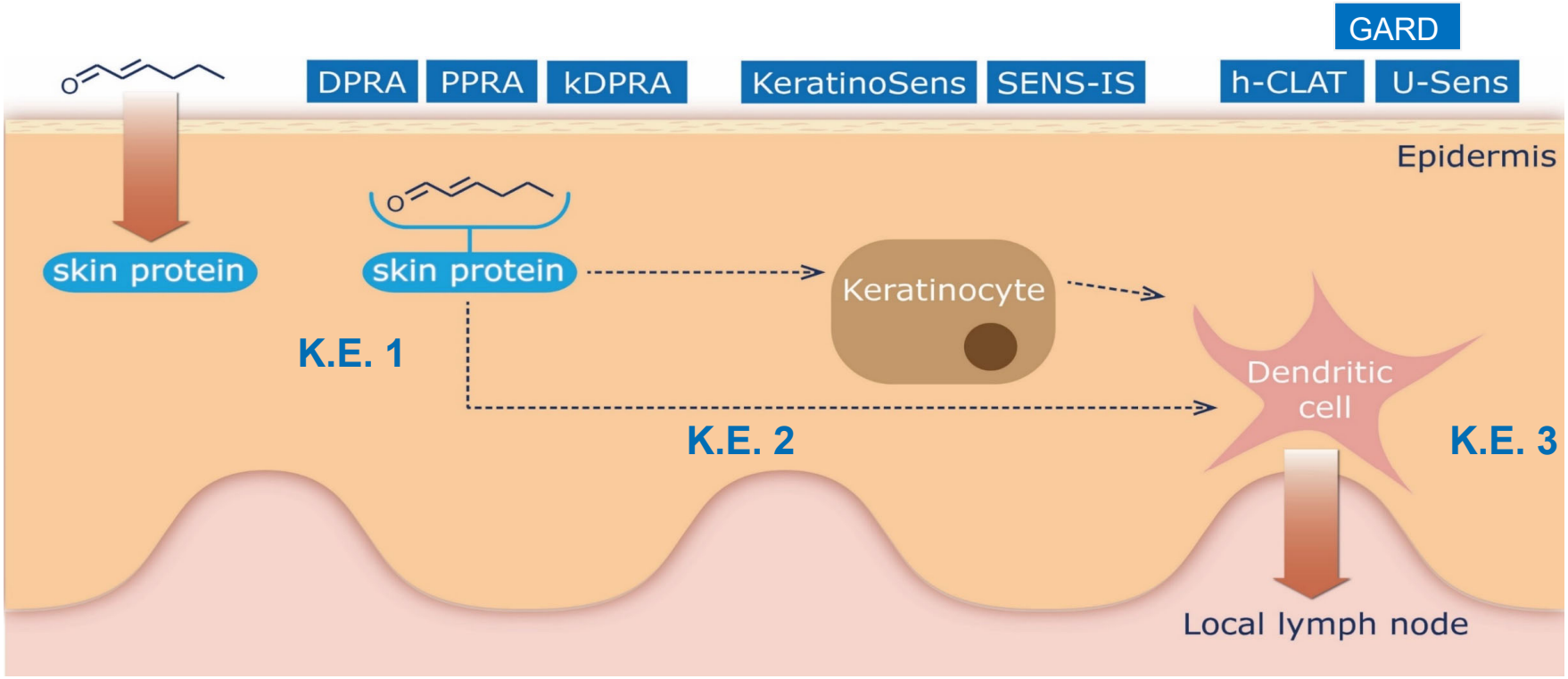
In-vitro assays address key events of the skin sensitization adverse outcome pathway (AOP)



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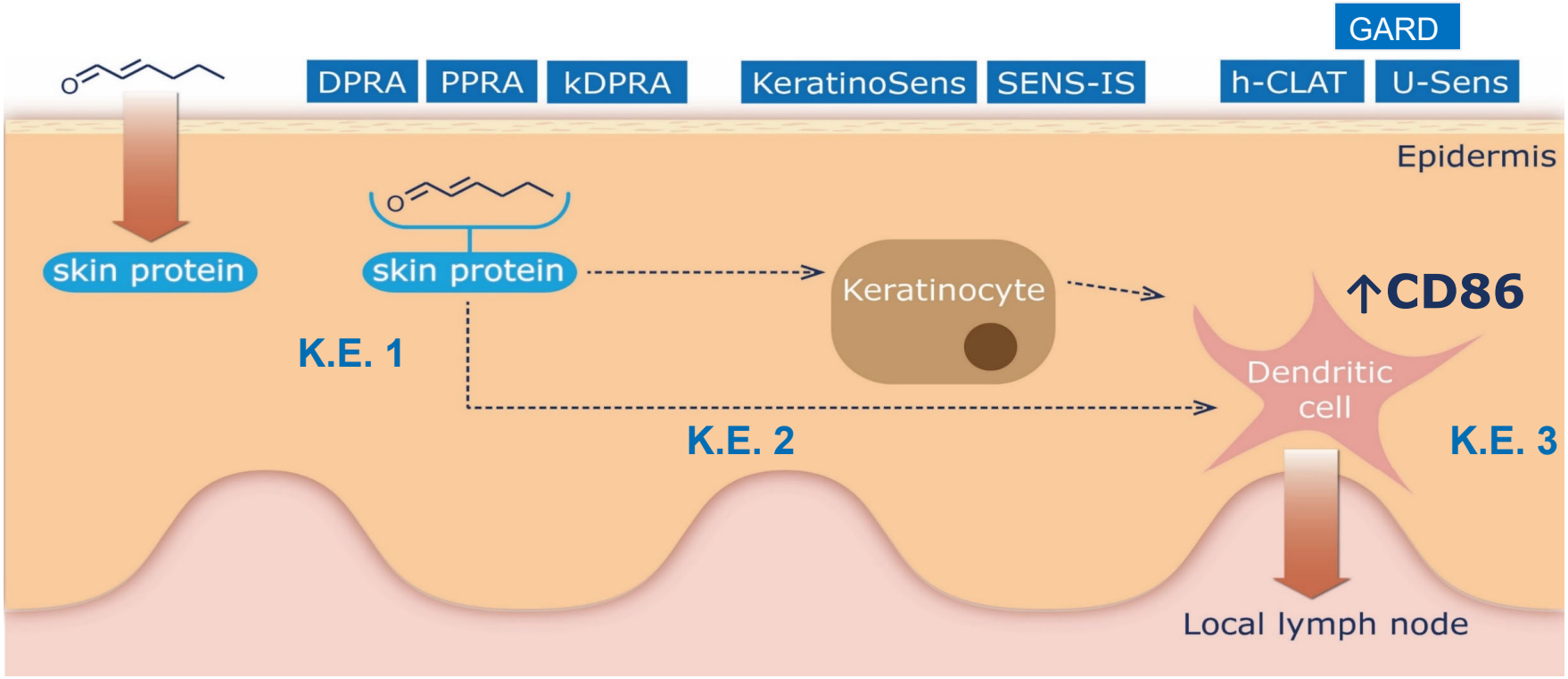
U-SENS™ was developed to address KE3 of the skin sensitization AOP



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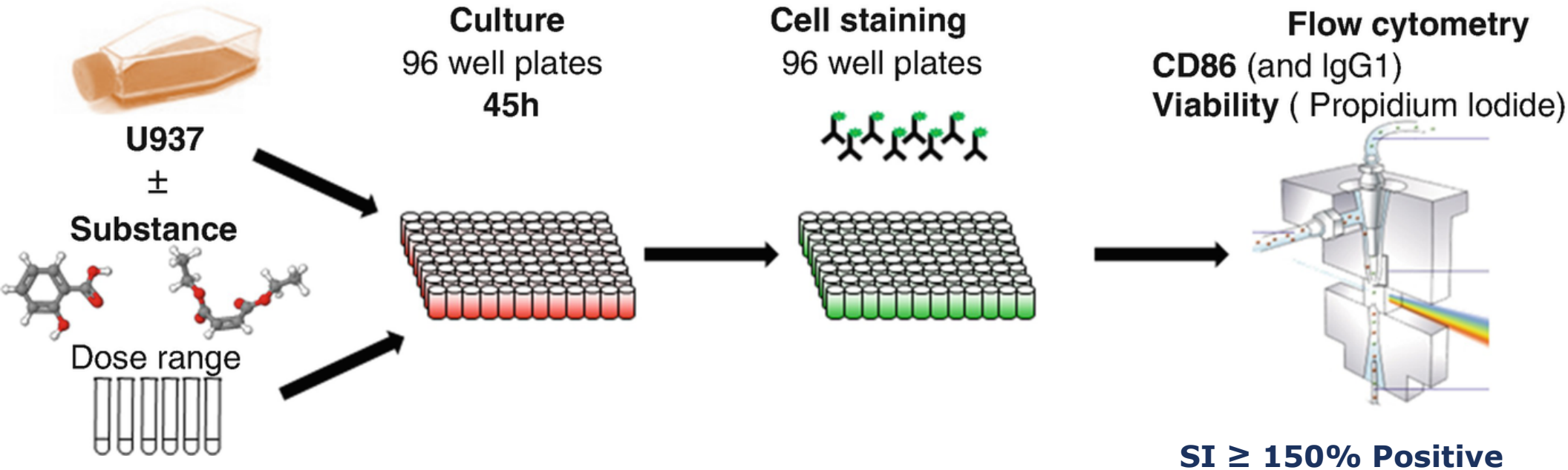
U-SENS™ detects an increase in a cell surface marker, CD86



SI ≥ 150% Positive

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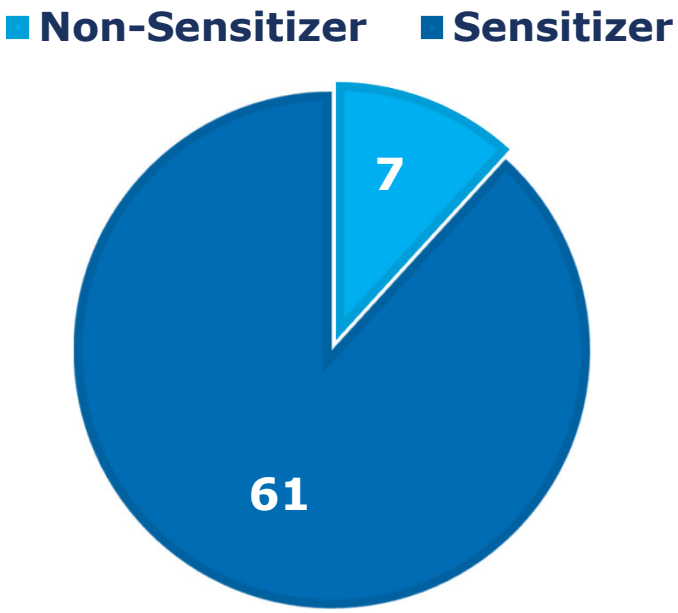
Alépée N., Piroird C., Nardelli L. (2017) U-SENS™: A U937 Cell Line Activation Test for Skin Sensitization. In: Eskes C., van Vliet E., Maibach H. (eds) Alternatives for Dermal Toxicity Testing. Springer, Cham

Sufficient historical human and animal data were available for 68 materials tested in U-SENS™



Historical data for WoE assessment:

- Confirmation of no induction in humans (CNIH) tests
- Human maximization tests
- Local lymph node assays
- Guinea pig maximization tests
- Buehler tests

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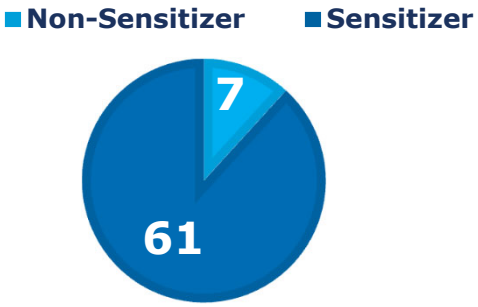
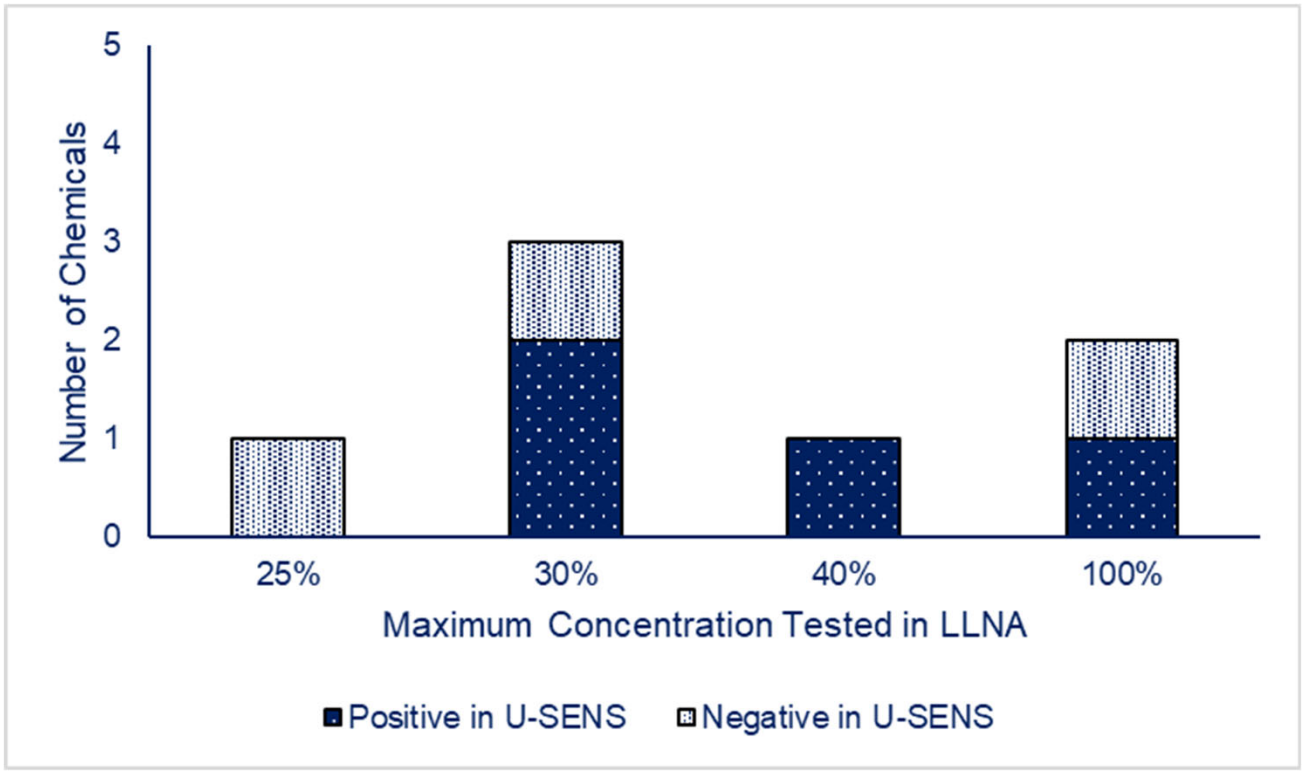
Of the 7 non-sensitizers, 3 were negative in U-SENS™





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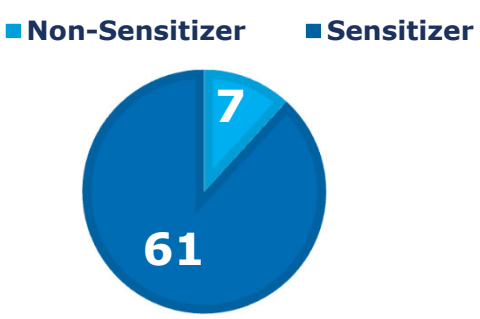
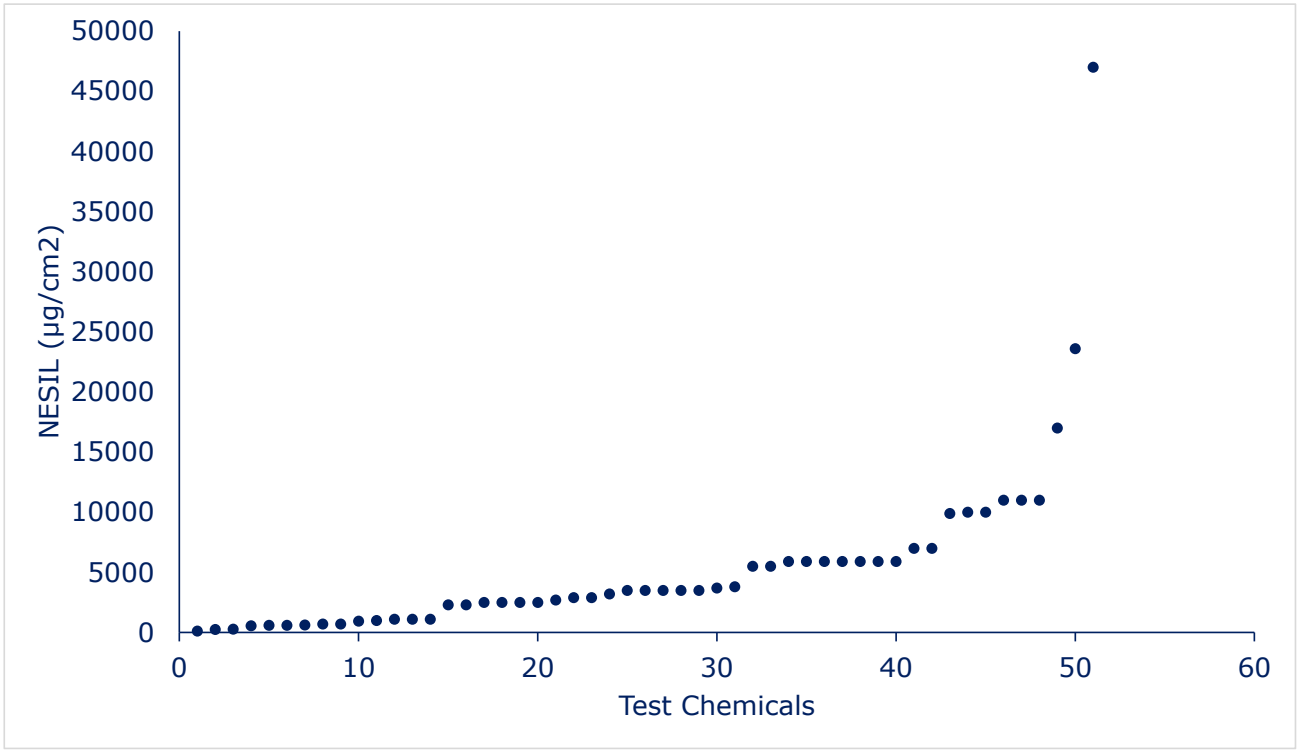
61 materials were skin sensitizers, with WoE NESILs ranging from 110-47000 µg/cm²





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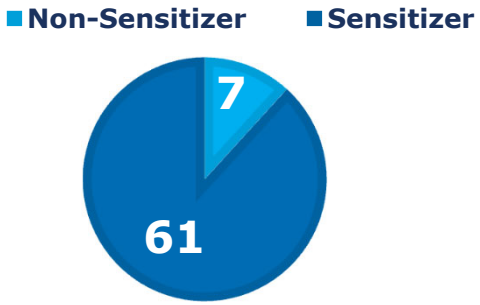
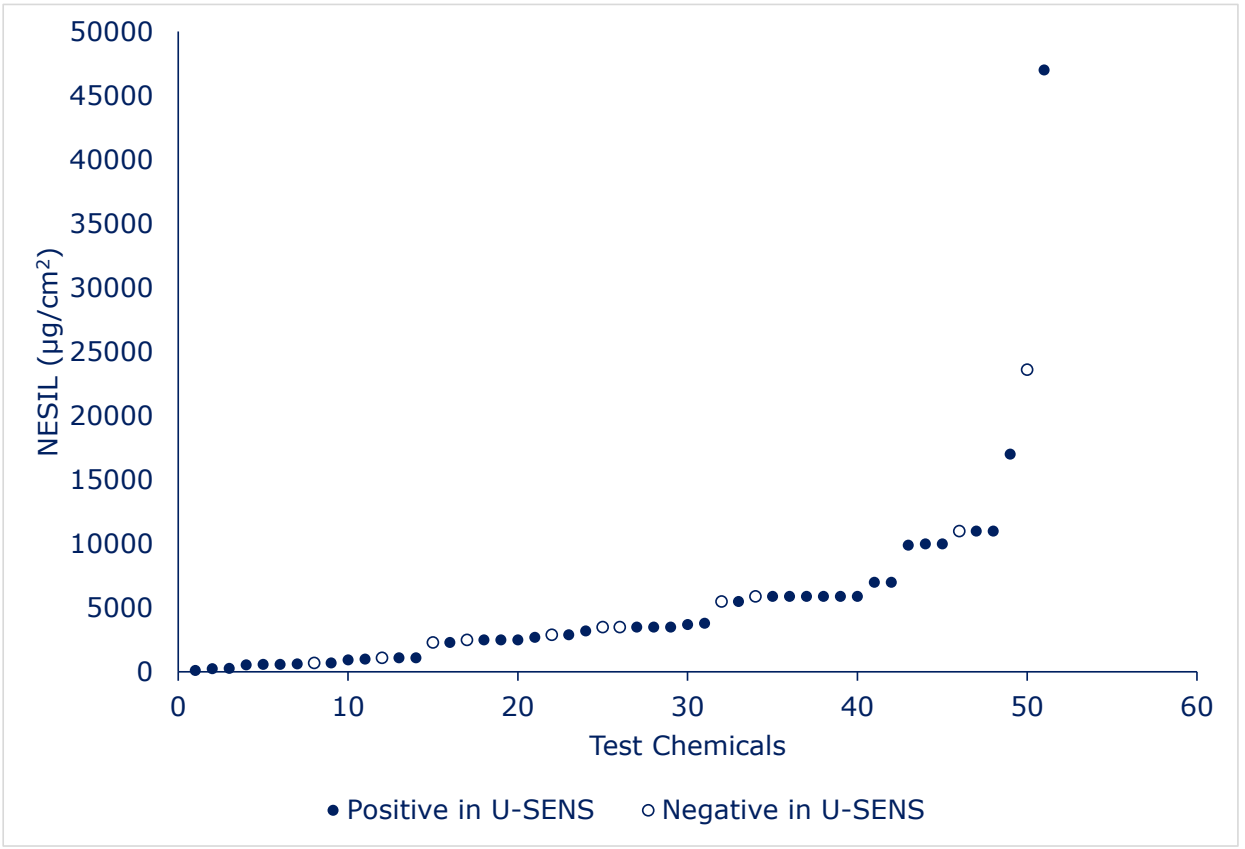
WoE NESIL → Weight of Evidence No Expected Sensitization Induction Level

Of the 61 sensitizers, 50 were positive in U-SENS™





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The performance of U-SENS™ in skin sensitization hazard identification is comparable to that of h-CLAT

82% Match

		U-SENS		h-CLAT	
		Negative	Positive	Negative	Positive
In-vivo assessment	Not a Sensitizer	**3**	**4**	**0**	**7**
	Sensitizer	**11**	**50**	**1**	**57**

Sensitivity:82%
Specificity:42%
PPV:93%
NPV:21%
Accuracy:78%

Sensitivity:98%
Specificity:0%
PPV:89%
NPV:0%
Accuracy:88%

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U-SENS™ should be used in combination with other methods to identify skin sensitization hazard

		U-SENS™		
		Negative	Positive	
DPRA	Negative	**9**	**28**	**52% Match**
	Positive	**2**	**23**	
Keratinosens	Negative	**6**	**28**	**47% Match**
	Positive	**8**	**26**	
h-CLAT	Negative	**1**	**0**	**82% Match**
	Positive	**12**	**52**	

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Skin sensitization hazard predictions improve when U-SENS™ is used in combination with other *in vitro* assays

Positive and negative predictive values: U-SENS™ compared to *in vivo* and *in vitro* data

U-SENS™ comparison with	Positive predictive value (PPV, %)	Negative predictive value (NPV, %)
WoE from all *in vivo* data	91	21
LLNA Only	70	50
In vitro 2 out of 3 call (DPRA, Keratinosens™ and U-SENS™)	97	24

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Thank you!

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Mihwa Na, PhD

Charles River Den Bosch

Walter Westerink, PhD

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Nathalie Alépée, PhD

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Thank you!

Questions/comments?

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