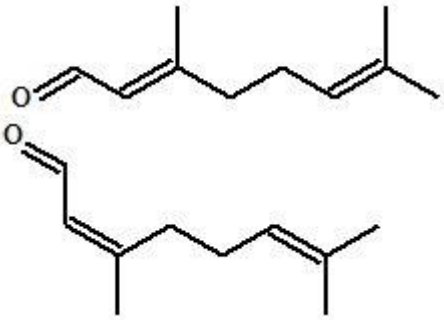
Citral

CAS N°:	5392-40-5 141-27-5 106-26-3	**Empirical formula:** **Structure:**	$C_{10}H_{16}O$ 
Synonyms:	3,7-Dimethyl-2,6-octadienal Geranial (trans-citral) Lemarome, Neral, Geranial (commercial names)		

History:	Initial reviews:	March 2002 (36th Amendment), June 2008	
	Current revision date:	June 2013	
	Implementation date:	For new submissions*:	August 10, 2013
		For existing fragrance compounds*:	August 10, 2014
	Next review date	2018	

* This date applies to the supply of fragrance compounds (formulas) only, not to the finished products in the marketplace.

RECOMMENDATION:	**RESTRICTED**

RESTRICTIONS:

Limits in the finished product:			
Category 1	0.04 %	Category 7	0.1 %
Category 2	0.05 %	Category 8	1.4 %
Category 3	0.2 %	Category 9	5.0 %
Category 4	0.6 %	Category 10	2.5 %
Category 5	0.3 %	Category 11	See Note Box
Category 6	1.0 %		

Note box:

Category 11 includes all non-skin contact or incidental skin contact products. Due to the negligible skin contact from these types of products there is no justification for a restriction of the concentration of this fragrance ingredient in the finished product.

This Standard cancels and replaces the existing one on citral, which was based on the no longer supported 'quenching' phenomenon.

Fragrance material specifications:	N/A

CONTRIBUTION FROM OTHER SOURCES:

See **Annex I** and **Annex II**

Citral

CRITICAL EFFECT:	SENSITIZATION

RIFM SUMMARIES:

Citral - Sensitization Potency Estimation Based on Weight of Evidence

LLNA weighted mean EC3 values ($\mu g/cm^2$) [no. studies]	Potency Classification Based on Animal Data[2]	Human Data			WoE NESIL[3] ($\mu g/cm^2$)
		NOEL – HRIPT (induction) ($\mu g/cm^2$)	NOEL – HMT (induction) ($\mu g/cm^2$)	LOEL[1] (induction) ($\mu g/cm^2$)	
1414 [11]	Weak	1400	NA	3876	1400 $\mu g/cm^2$

NOEL = No observed effect level; HRIPT = Human Repeat Insult Patch Test; MAX = Human Maximization Test;
LOEL = lowest observed effect level; NA = Not Available

[1] Data derived from HRIPT or Human Max Tests
[2] Gerberick *et al*., 2001
[3] WoE NESIL limited to two significant figures

REXPAN RATIONALE / CONCLUSION:

The RIFM Expert Panel reviewed the critical effect data for citral and based on the weight of evidence established the No Expected Sensitization Induction Level (NESIL) as 1400 µg/cm².They recommend the limits for the 11 different product categories, which are the acceptable use levels of citral in the various product categories. These were derived from the application of the exposure-based quantitative risk assessment approach for fragrance ingredients, which is detailed in the QRA Expert Group Technical Dossier of March 15, 2006.

REFERENCES:

Basketter, D. A., Wright, Z., Gilmour, N. J., Ryan, C. A., Gerberick, G. F., Robinson, M. K., Dearman, R. J., Kimber, I., 2002a. Prediction of human sensitization potency using local lymph node assay EC3 values. The Toxicologist, 66(1-S), 240.

Gerberick, GF. et. al. (2001) Contact allergenic potency: Correlation of human and local lymph node assay data. American Journal of Contact Dermatitis, 12(3), 156-161.

QRA Expert Group (AM Api, DA Basketter, PA Cadby, M-F Cano, G Ellis, GF Gerberick, P Griem, PM McNamee, CA Ryan and R Safford), Dermal Sensitization Quantitative Risk Assessment (QRA) for Fragrance Ingredients, Technical Dossier, March 15, 2006, http://www.rifm.org/pub/publications.asp.

Research Institute for Fragrance Materials, Inc (1964). Repeated insult patch test of citral in human subjects. Unpublished report from International Flavors and Fragrances Inc., Report number 14576 (RIFM, Woodcliff Lake, NJ USA).
Research Institute for Fragrance Materials, Inc (2004). Repeated insult patch test in human subjects with citral. RIFM report number 47157 (RIFM, Woodcliff Lake, NJ USA).

Research Institute for Fragrance Materials, Inc (2004). Local Lymph Node Assay on Citral. RIFM report number 45126 (RIFM, Woodcliff Lake, NJ USA).