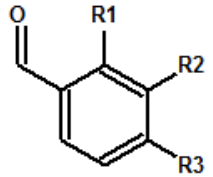
o,m,p-Tolualdehydes and their mixtures

CAS N°:	529-20-4 620-23-5 104-87-0 1334-78-7	**Empirical formula:** **Structure:**	C_8H_8O  With R_1=Me, R_2=H, R_3=H or R_1=H, R_2=Me, R_3=H or R_1=H, R_2=H, R_3=Me
Synonyms:	ortho-Tolualdehyde 2-Methyl-benzaldehyde meta-Tolualdehyde 3-Methyl-benzaldehyde para-Tolualdehyde 4-Methyl-benzaldehyde Tolualdehydes (mixed o,m,p) o,m,p-Methyl-benzaldehydes		

History:	Initial reviews:	New Standard	
	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**

o,m,p-Tolualdehydes and their mixtures

RESTRICTIONS:

Limits in the finished product:			
Category 1 See Note box (1)	0.03 %	Category 7	0.08 %
Category 2	0.04 %	Category 8	1.11 %
Category 3	0.17 %	Category 9	5.00 %
Category 4	0.50 %	Category 10	2.50 %
Category 5	0.26 %	Category 11	See Note box (2)
Category 6	0.80 %		

Note box:

(1) See the IFRA Code of Practice (Appendix 8, Introduction to the IFRA Standards) regarding the Note on Oral Care Products and other products with the potential of ingestion.
(2) 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.

Fragrance material specifications:	N/A

CONTRIBUTION FROM OTHER SOURCES:

None to consider.

CRITICAL EFFECT:	SENSITIZATION

RIFM SUMMARIES:

Cuminaldehyde has been designated as a read across material for the Tolualdehydes for the sensitization endpoint. As such, the data for Cuminaldehyde are below:

LLNA weighted mean EC3 values ($\mu g/cm^2$) [no. studies]	Potency Classification Based on Animal Data[1]	Human Data			WoE NESIL[3] ($\mu g/cm^2$)
		NOEL – HRIPT (induction) ($\mu g/cm^2$)	NOEL – HMT (induction) ($\mu g/cm^2$)	LOEL[2] (induction) ($\mu g/cm^2$)	
> 2500 [1][4]	Weak	1181	2760	NA	1100[5]

All data in this Table are available from RIFM and are listed in the RIFM Database.
NOEL = No observed effect level; HRIPT = Human Repeat Insult Patch Test; HMT = Human Maximization Test; LOEL = lowest observed effect level; NA = Not Available.

[1]Based on animal data using classification defined in ECETOC, Technical Report No. 87, 2003.
[2]Data derived from HRIPT or HMT.
[3]WoE NESIL limited to two significant figures.
[4]EC3 value from one LLNA, not the mean.

o,m,p-Tolualdehydes and their mixtures

REXPAN RATIONALE / CONCLUSION:

The RIFM Expert Panel reviewed the critical effect data for Cuminaldehyde and the Tolualdehydes and, based on the weight of evidence and read-across, established the No Expected Sensitization Induction Level (NESIL) as 1100 µg/cm^2 based on the critical sensitization data on Cuminaldehyde. They recommend the limits for the 11 different product categories, which are the acceptable use levels of Tolualdehydes 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 publication by Api *et al*., 2008.

REFERENCES:

Api AM, Basketter DA, Cadby PA, Cano M-F, Ellis G, Gerberick G, et al. Dermal Sensitization Quantitative Risk Assessment (QRA) For Fragrance Ingredients. Regulatory Toxicology and Pharmacology 2008;52(1): 3-23.

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