Dimethylcyclohex-3-ene-1-carbaldehyde (mixed isomers)

CAS N°:	68737-61-1 (mixed isomers) 68039-49-6 68039-48-5 27939-60-2 67801-65-4 36635-35-5 68084-52-6 35145-02-9	**Empirical formula:**	$C_9H_{14}O$
Synonyms:	Dimethylcyclohex-3-ene-1-carbaldehyde (isomer mixture) (68737-61-1) 2,4-Dimethyl-3-cyclohexen-1-carboxaldehyde (68039-49-6) 3,5-Dimethylcyclohex-3-ene-1-carbaldehyde (68039-48-5) Dimethylcyclohex-3-ene-1-carbaldehyde (isomer unspecified) (27939-60-2) 3,6-Dimethyl-3-cyclohexene-1-carboxaldehyde (67801-65-4) 3-Cyclohexene-1-carboxaldehyde, dimethyl- (isomer mixture) 2,4-Dimethyltetrahydrobenzaldehyde Dimethyltetrahydrobenzaldehyde (isomer mixture) Triplal, Vertocitral, Vertoliff, Tricyclal, Hivertal, Agrumen Aldehyde, Cyclovertal, Ligustral, Aldehyde AA (commercial names)		

History:	Initial reviews:	June 11, 2010	
	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 See Note box (1)	0.17 %	Category 7	0.45 %
Category 2	0.22 %	Category 8	2.0 %
Category 3	0.89 %	Category 9	5.0 %
Category 4	2.7 %	Category 10	2.5 %
Category 5	1.4 %	Category 11	See Note box (2)
Category 6	4.3 %		

Note box:

The above limits apply to Dimethylcyclohexen-3-ene-1-carbaldehyde (mixed isomers) used individually or in combination.
(1) IFRA would recommend that any material used to impart perfume or flavour in products intended for human ingestion should consist of ingredients that are in compliance with appropriate regulations for foods and food flavourings in the countries of planned distribution and, where these are lacking, with the recommendations laid down in the Code of Practice of IOFI (International Organisation of the Flavor Industry - www.iofiorg.org)
(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.

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Fragrance material specifications:	N/A

CONTRIBUTION FROM OTHER SOURCES:

See **Annex II**

CRITICAL EFFECT:	SENSITIZATION

RIFM SUMMARIES:

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) ($\mu g/cm^2$)	
2500-5875 [7][4]	Weak	5905[5]	1380-6900[6]	N/A	5900

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]A range of values and not the weighted mean was provided because the seven studies were performed on 7 different materials – all are isomers but the isomeric mixtures were different. There are currently 4 isomers of this material in the RIFM Database. Each material is typically a mixture of two or more isomers. In order to confirm the potency and characterization of these materials, a set of LLNAs was conducted on different commercial samples provided by individual suppliers with isomer ratios specified. The LLNA data showed all materials with similar dermal sensitization potency.
[5]MT-NOEL = Maximum Tested No Effect Level. No sensitization was observed in human predictive studies. Doses reported reflect the highest concentration tested, not necessarily the highest achievable NOEL. The HRIPT MT-NOEL reported is for the fragrance material with the highest reported use in perfumery (IFRA Survey, 2004); the LLNA data showed all materials with similar dermal sensitization potency.
[6]A range of values was provided; three human maximization studies were conducted. No dermal sensitization was observed in any of the tests. The 3 studies were performed on 3 different isomer mixtures

REXPAN RATIONALE / CONCLUSION:

The RIFM Expert Panel reviewed the critical effect data for dimethylcyclohex-3-ene-1-carbaldehyde and, based on the weight of evidence, established the No Expected Sensitization Induction Level (NESIL) as 5900 $\mu g/cm^2$. They recommend the limits for the 11 different product categories, which are the acceptable use levels of dimethylcyclohex-3-ene-1-carbaldehyde 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 GF, et al. Dermal Sensitization Quantitative Risk Assessment (QRA) For Fragrance Ingredients. *Regulatory Toxicology and Pharmacology* 2008;52(1): 3-23.

RIFM (Research Institute for Fragrance Materials, Inc.), 2010a. Local Lymph Node Assay. RIFM report number 58108, Draft Report. (RIFM, Woodcliff Lake, NJ, USA).

RIFM (Research Institute for Fragrance Materials, Inc.), 2010b. Local Lymph Node Assay. RIFM report number 58112, Draft Report. (RIFM, Woodcliff Lake, NJ, USA).

RIFM (Research Institute for Fragrance Materials, Inc.), 2010c. Local Lymph Node Assay. RIFM report number 58113, Draft Report. (RIFM, Woodcliff Lake, NJ, USA).

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RIFM (Research Institute for Fragrance Materials, Inc.), 2009. Human repeated insult patch test. RIFM report number 58150, December 14. (RIFM, Woodcliff Lake, NJ, USA).

RIFM (Research Institute for Fragrance Materials, Inc.), 1982. Maximization study. RIFM report number 1643, October 5. (RIFM, Woodcliff Lake, NJ, USA).

RIFM (Research Institute for Fragrance Materials, Inc.), 1978. Maximization study. RIFM report number 1698, February 27b. (RIFM, Woodcliff Lake, NJ, USA).

RIFM (Research Institute for Fragrance Materials, Inc.), 1977. Maximization study. RIFM report number 1702, May 4c. (RIFM, Woodcliff Lake, NJ, USA).