VANILLIN

CAS N°: 121-33-5 **Empirical formula:** $C_8H_8O_3$

Synonyms: Benzaldehyde, 4-hydroxy-3-methoxy-
4-Hydroxy-3-methoxybenzaldehyde
2-Methoxy-4-formylphenol
3-Methoxy-4-hydroxybenzaldehyde
Methylprotocatechuic aldehyde
Protocatechualdehyde-3-methyl ether
Vanillaldehyde
Vanillic aldehyde

History: Initial reviews: New Standard

Current revision date: 2009

Implementation date: for new submissions*: August 7, 2009

for existing fragrance compounds*: August 7, 2011

Next review date: 2014

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

Standard: **RESTRICTED**

RESTRICTIONS:

Limits in the finished product:
For a description of the categories, refer to the QRA Information Booklet.

Category 1 - See Note box (1)	0.03 %	Category 7	0.08 %
Category 2	0.04 %	Category 8	1.10 %
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 - See Note box (1)	0.80 %		

Note box:

(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 negligible skin contact the concentration of a fragrance ingredient should not exceed the usual concentration of the fragrance compound in the finished product.

Fragrance material specification: N/A

VANILLIN

Contribution from other sources: See **Annex I**

Critical effect: **Sensitization**

RIFM Summaries:

LLNA weighted mean EC3 values (µg/cm^2) [no. studies])	Potency Classification Based on Animal Data[1]	Human Data			WoE NESIL[3] (µg/cm^2)
		NOEL – HRIPT (induction) (µg/cm^2)	NOEL – HMT (induction) (µg/cm^2)	LOEL[2] (induction) (µg/cm^2)	
> 12500 [1][4]	Weak	1181	3450	NA	1100

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

REXPAN Rationale / Conclusion:

The RIFM Expert Panel reviewed the critical effect data for Vanillin and, based on the weight of evidence, established the No Expected Sensitization Induction Level (NESIL) as 1100 µg/cm^2. They recommend the limits for the 11 different product categories, which are the acceptable use levels of Vanillin 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 June 22, 2006.

References:

Basketter, D.A., Wright, Z.M., Warbrick, E.V., Dearman, R.J., Kimber, I., Ryan, C.A., Gerberick, G.F., White, I.R., 2001. Human potency predictions for aldehydes using the local lymph node assay. Contact Dermatitis, 45, 89-94.

RIFM (Research Institute for Fragrance Materials, Inc.), 1970. Maximization study with vanillin. RIFM report number 1760, October 7. (RIFM, Woodcliff Lake, NJ, USA).

RIFM (Research Institute for Fragrance Materials, Inc.), 2009. Human repeated insult patch test. RIFM report number 57359. (RIFM, Woodcliff Lake, NJ, USA).