2-Methoxy-4-methylphenol

CAS N°: 93-51-6 **Empirical formula:** $C_8H_{10}O_2$

Synonyms: Creosol
p-Creosol
p-Cresol, 2-methoxy-
Homoguaiacol
1-Hydroxy-2-methoxy-4-methylbenzene
4-Hydroxy-3-methoxytoluene
2-Methoxy-p-cresol
3-Methoxy-4-hydroxytoluene
4-Methylguaiacol
p-Methylguaiacol
4-Methyl-2-methoxyphenol
Phenol, 2-methoxy-4-methyl-
Valspice

History:

Initial reviews:	January 1999, April 2005 (39th Amendment, new format only), May 2007 (42nd Amendment)	
Current revision date:	2008	
Implementation date:	For new submissions*:	August 16, 2008
	For existing fragrance compounds*:	August 16, 2010
Next review date:	2013	

* 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 Informational Booklet.

Category 1: See Note box (1)	0.003 %	Category 7:	0.009 %
Category 2:	0.004 %	Category 8:	0.01 %
Category 3:	0.01 %	Category 9:	0.01 %
Category 4:	0.01 %	Category 10:	0.01 %
Category 5:	0.01 %	Category 11: Not Restricted (2)	
Category 6: See Note box (1)	0.09 %		

Note box:
For this material, for pragmatic reasons, restrictive levels allowed by the QRA for certain categories but actually being higher than those already in place before applying the QRA, will temporarily not be implemented until the end of a 5 year monitoring phase. At the end of the 5 years the position will be reevaluated again.
(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.

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(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 specification: N/A

Contribution from other sources: None to consider (see also the note on contributions from other sources in the Introduction to the IFRA Standards).

Critical effect: Sensitization

RIFM Summaries:

2-Methoxy-4-methylphenol - Sensitization Potency Estimation Based on Weight of Evidence

LLNA weighted mean EC3 values ($\mu g/cm^2$) [no. studies]	Human Data			Potency Classification[2]	WOE NESIL[3] ($\mu g/cm^2$)
	NOEL – HRIPT (induction) ($\mu g/cm^2$)	NOEL – MAX (induction) ($\mu g/cm^2$)	LOEL[1] (induction) ($\mu g/cm^2$)		
1450	118	NA	NA	Weak	118

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 2-methoxy-4-methylphenol and, based on the weight of evidence, established the No Expected Sensitization Induction Level (NESIL) as 118 $\mu g/cm^2$. They recommend the limits for the 11 different product categories, which are the acceptable use levels of 2-methoxy-4-methylphenol 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., Gilmour, N., Dearman, R. J., Kimber, I., Ryan, C. A., Gerberick, E., 2003. Classification of skin sensitisation potency using the Local Lymph Node Assay. The Toxicologist, 72(S-1), 101.

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.

RIFM (Research Institute for Fragrance Materials, Inc.), 1998. Repeated insult patch test of 2-methoxy-4-methylphenol in human subjects. RIFM report number 33100, June 15.

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(RIFM, Woodcliff Lake, NJ, USA).