METHYL N-METHYLANTHRANILATE

CAS N°: 85-91-6 **Empirical formula:** $C_9H_{11}NO_2$

Synonyms: **Benzoic acid, 2-(methylamino)-, methyl ester** (CAS)
Dimethyl anthranilate
2-Methylamino methyl benzoate
N-Methylanthranilic acid, methyl ester
Methyl 2-methylaminobenzoate
Methyl *o*-methylaminobenzoate

History: Initial reviews: October 1978, April 2001

Current revision date: January 2002

Implementation date: for new submissions*: Not applicable
for existing fragrance compounds*: Not applicable

Next review date: 2007

* 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:

Skin-contact products:

Leave-on products: 0.1% Rinse-off products: No restriction
including household cleaning products

Non skin-contact products: No restriction

Note box: The Standard is set due to the phototoxic effects of the material. The limit only applies to applications on skin, excluding rinse-off products.

If combinations of phototoxic fragrance ingredients are used, the use levels have to be reduced accordingly. The sum of the concentrations of all phototoxic ingredients, expressed in % of their recommended maximum level in the consumer product shall not exceed 100.

The level set for Methyl N-methylanthranilate comprises the fragrance ingredient added as such, as well as contributions from Petitgrain Mandarin oil (see Annex I).

Fragrance material specification: Not applicable

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Contribution from other sources: see Note box and Annex 1.

Critical effect: **Phototoxicity**

RIFM summaries:

A human phototoxicity study at 0.5% in 75% ethanol/25% diethyl phthalate (DEP) resulted in 0/26 reactions (RIFM, 2001). Another human phototoxicity study with concentrations of 0.1, 0.3, and 0.5% resulted in 0/29 reactions (RIFM, 1998). Several other phototoxicity studies showed phototoxic reactions at 1% and 5% (Kaidbey and Kligman, 1980; Letizia and Api, 2003; RIFM, 1999).

A human photosensitization study at 0.5% in 75% ethanol/25% DEP resulted in 0/26 reactions (RIFM, 2001). Another human photosensitization study at 5.0% resulted in no photoallergic reactions. However, 14/18 phototoxic reactions were observed (RIFM, 1978a).

A phototoxicity study at 50% in methanol and 100% on hairless mice produced reactions at both dose levels (RIFM, 1978b).

An *in vitro* phototoxicity assay using a human skin model (Skin$^{2®}$) with concentrations of methyl N-methylanthranilate ranging from 0.05% to 25% in corn oil showed that the material was phototoxic at dose levels above 5% (Api, 1997).

Rexpan Rationale / Conclusion:

The RIFM Expert Panel reviewed the critical effect data for methyl n-methyl anthranilate and recommended no change to the Standard (January 2002).

References:

Api A.M. (1997). *In vitro* assessment of phototoxicity. *In Vitro* Toxicology: Journal of Molec. Cell. Toxicol., 10(3), 339-350.

Kaidbey K.H. and Kligman A.M. (1980). Identification of contact photosensitizers by human assay. In Current Concepts In Cutaneous Toxicity, Academic Press, New York, pages 55-68.

Letizia C.S. and Api A.M. (2003). Evaluation of the phototoxic and photoallergenic potential of methyl n-methyl anthranilate. The Toxicologist, 72(S1), 378-379.

Research Institute for Fragrance Materials, Inc. (1978a). Phototoxicity and contact photoallergy testing in human subjects. RIFM report number 1788, 18 January.

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Research Institute for Fragrance Materials, Inc. (1978b). Phototoxicity and irritation studies of mice and pigs with fragrance materials. RIFM report number 2042, 13 April.

Research Institute for Fragrance Materials, Inc. (1998). Evaluation of phototoxicity of dimethyl anthranilate in humans. RIFM report number 34768, 8 December.

Research Institute for Fragrance Materials, Inc. (1999). Evaluation of phototoxicity of dimethyl anthranilate in humans. RIFM report number 34769, 20 July.

Research Institute for Fragrance Materials, Inc. (2001) Evaluation of human photoallergy by repeated insult patch test. RIFM report number 36789, 1 March.