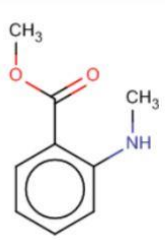
Methyl N-methylanthranilate

CAS N°:	85-91-6	**Empirical formula:** **Structure:**	$C_9H_{11}NO_2$ 
Synonyms:	Benzoic acid, 2-(methylamino)-, methyl ester Dimethyl anthranilate 2-Methylamino methyl benzoate N-Methylanthranilic acid, methyl ester Methyl 2-(methylamino)benzoate Methyl 2-methylaminobenzoate Methyl o-methylaminobenzoate		

History:	Initial reviews:	1978, 2001, 2002, 2006, 2009	
	Current revision date:	2015	
	Implementation date:	For new submissions*:	Not applicable
		For existing fragrance compounds*:	Not applicable
	Next review date	2020	

* 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:			
Skin contact products:			
Leave-on products :	0.1 %	Rinse-off products: *Including household cleaning products*	No restriction
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 exposed to sunshine, excluding rinse-off products (please refer to Table 4 of the QRA booklet for more detailed information). The material has been identified for having the potential of forming nitrosamines in nitrosating systems. Downstream users therefore have to be notified of the presence of the material and its potential to be able to consider adequate protective measures.			
Fragrance material specifications:	N/A		

CONTRIBUTION FROM OTHER SOURCES:

See **Annex I.**

Methyl N-methylanthranilate

CRITICAL EFFECT:	PHOTOTOXICITY, POTENTIAL FOR NITROSAMINE FORMATION

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 (Skin2®) 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:

IFRA measures regarding potential nitrosamine formation noted - REXPAN April 2009.

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.

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.

Nitrosamine policy as contained in the EU Cosmetics Directive 76/768/EEC and its Amendments.