

Methyl N-methylantranilate

CAS-No.:	85-91-6	Molecular formula:	C ₉ H ₁₁ NO ₂
	The scope of this Standard includes, but is not limited to the CAS number(s) indicated above; any other CAS number(s) used to identify this fragrance ingredient should be considered in scope as well.	Structure:	
Synonyms:	Benzoic acid, 2-(methylamino)-, methyl ester Dimethyl anthranilate 2-Methylamino methyl benzoate N-Methylantranilic acid, methyl ester Methyl 2-(methylamino)benzoate Methyl 2-methylaminobenzoate Methyl o-methylaminobenzoate		

History:	Publication date:	2020 (Amendment 49)	Previous Publications:	1978
				2001
				2002
				2006
				2009
				2015

Implementation dates:	For new submissions*:	February 10, 2021
	For existing fragrance compounds*:	February 10, 2022
	*These dates apply to the supply of fragrance mixtures (formulas) only, not to the finished consumer products in the marketplace.	

RECOMMENDATION:
RESTRICTION / SPECIFICATION
RESTRICTION LIMITS IN THE FINISHED PRODUCT (%):

Category 1	0.10 %	Category 7A	No Restriction
Category 2	0.10 %	Category 7B	0.10 %
Category 3	0.10 %	Category 8	0.10 %

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Category 4	0.10 %	Category 9	No Restriction
Category 5A	0.10 %	Category 10A	No Restriction
Category 5B	0.10 %	Category 10B	0.10 %
Category 5C	0.10 %	Category 11A	No Restriction
Category 5D	0.10 %	Category 11B	0.10 %
Category 6	0.10 %	Category 12	No Restriction

Fragrance ingredient restriction - Note box

The Standard is set due to the phototoxic effects of Methyl N-methylantranilate. For more detailed information on the application of this Standard, please refer to the note on phototoxic ingredients in chapter 1 of the Guidance for the use of IFRA Standards.

FRAGRANCE INGREDIENT SPECIFICATION:

This 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.

FLAVOR REQUIREMENTS:

Due to the possible ingestion of small amounts of fragrance ingredients from their use in products in Categories 1 and 6, materials must not only comply with IFRA Standards but must also be recognized as safe as a flavoring ingredient as defined by the IOFI Code of Practice (www.iofi.org). For more details see chapter 1 of the Guidance for the use of IFRA Standards.

CONTRIBUTIONS FROM OTHER SOURCES:
SEE ANNEX I
ANNEX I
Natural Complex Substances (NCS) containing Methyl N-methylantranilate

Concentration in NCS (%)	CAS number of ingredient	Name of NCS	Botanical name	CAS number of NCS	Essential oil category
0.03	85-91-6	Clementine oil	Citrus clementina Hort. Ex Tan	93686-22-7	G2.5
0.34	85-91-6	Genet	Spartium junceum	90131-21-8	E2.1

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0.4	85-91-6	Mandarin oil	Citrus reticulata Blanco	8008-31-9	G2.5
10	85-91-6	Mandarin oil, terpeneless	Citrus reticulata Blanco	68917-20-4	G2.29
48.5	85-91-6	Petitgrain mandarin oil	Citrus reticulata Blanco	8014-17-3	E2.12
80	85-91-6	Petitgrain mandarin oil terpeneless	Citrus reticulata Blanco	84929-38-4	E2.29

This is a non-exhaustive indicative list of typical natural presence for Methyl N-methylantranilate and is intended to be used in the absence of own analytical data. If analysis has shown that the level of the restricted ingredient in a natural complex substance is different from what is provided in this Annex I, then the analytically determined level should be used in place of the indicative level.

It should further be noted that natural complex substances themselves can be restricted by an IFRA Standard.

For a detailed list of natural contributions, please refer to the Annex I of IFRA Standards, publicly available on the IFRA website (www.ifrafragrance.org).

INTRINSIC PROPERTY DRIVING RISK MANAGEMENT:	PHOTOTOXICITY, POTENTIAL OF NITROSAMINE FORMATION
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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-methylantranilate ranging from 0.05% to 25% in corn oil showed that the material was phototoxic at dose levels above 5% (Api, 1997).

EXPERT PANEL FOR FRAGRANCE SAFETY RATIONALE / CONCLUSION:

The Expert Panel for Fragrance Safety reviewed all the available data for Methyl N-methylantranilate and recommends the limits for the 12 different product categories, which are the acceptable use levels of Methyl N-methylantranilate in the various product categories. In addition, they recommend to use Methyl N-methylantranilate according to the specification above mentioned.

Methyl N-methylantranilate**REFERENCES:**

The IFRA Standard on Methyl N-methylantranilate is based on at least one of the following publications:

- The RIFM Safety Assessment on Methyl N-methylantranilate is available at the RIFM Safety Assessment Sheet Database: <http://fragrancematerialsafetyresource.elsevier.com/>.
- Api A.M., Belsito D., Bruze M., Cadby P., Calow P., Dagli M. L., Dekant W., Dent M., Ellis G., Fryer A. D., Fukayama M., Griem P., Hickey C., Kromidas L., Lalko J., Liebler D.C., Miyachi Y., Politano V.T., Renskers K., Ritacco G., Salvito D., Schultz T.W., Sipes I. G., Smith B., Vitale D., Wilcox D.K. (2015). Criteria for the Research Institute for Fragrance Materials, Inc. (RIFM) safety evaluation process for fragrance ingredients. *Food Chem Toxicol.* 2015 Aug;82 Suppl:S1-S19 (doi: 10.1016/j.fct.2014.11.014). (http://fragrancematerialsafetyresource.elsevier.com/sites/default/files/Criteria_Document_Final.pdf).
- IDEA project (International Dialogue for the Evaluation of Allergens) Final Report on the QRA2: Skin Sensitisation Quantitative Risk Assessment for Fragrance Ingredients, September 30, 2016 (<http://www.ideaproject.info/uploads/Modules/Documents/qra2-dossier-final--september-2016.pdf>).
- Salvito D.T., Senna R. J., Federle T.W. (2002). A framework for prioritizing fragrance materials for aquatic risk assessment. *Environ Toxicol Chem.* 2002;21:1301-1308. (<https://www.ncbi.nlm.nih.gov/pubmed/12069318>).
- 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.
- Nitrosamine policy as contained in the EU Cosmetics Directive 76/768/EEC and its Amendments.

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Additional information on the application of IFRA Standards is available in the Guidance to IFRA Standards, publicly available at www.ifrafragrance.org.