

Methyl N-formylanthranilate

CAS-No.:	41270-80-8 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.
Synonyms:	Benzoic acid, 2-(formylamino)-, methyl ester Methyl 2-(formylamino)benzoate Methyl 2-formamidobenzoate Methyl o-formamidobenzoate N-Formylanthranilic acid, methyl ester

History:	Publication date:	2020 (Amendment 49)	Previous Publications:	Not applicable.
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Implementation dates:	For new creation*:	February 10, 2021
	For existing creation*:	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
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MAXIMUM ACCEPTABLE CONCENTRATIONS 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 %
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

Methyl N-formylanthranilate

The Standard is set due to the phototoxic effects of Methyl N-formylanthranilate. 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.
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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.
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CONTRIBUTIONS FROM OTHER SOURCES:	SEE ANNEX ON CONTRIBUTIONS FROM OTHER SOURCES
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INTRINSIC PROPERTY DRIVING RISK MANAGEMENT:	PHOTOTOXICITY, POTENTIAL OF NITROSAMINE FORMATION
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RIFM SUMMARIES:

Phototoxicity effects of Methyl N-formylanthranilate have been assessed by read-across from Methyl N-methylantranilate. The following studies have been considered for the determination of the phototoxicity potential of Methyl N-methylantranilate:

- 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-formylanthranilate and recommends the concentrations for the 12 different product categories, which are the maximum acceptable concentrations of Methyl N-formylanthranilate in the various product categories.

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In addition, they recommend to use Methyl N-formylanthranilate according to the specification above mentioned.

REFERENCES:

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

- The RIFM Safety Assessment on Methyl N-formylanthranilate 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.

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