Isophorone

CAS-No.:	78-59-1 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:	2-Cyclohexen-1-one, 3,5,5-trimethyl- Isoacetophorone 3,5,5-Trimethyl-2-cyclohexen-1-one

History:	Publication date:	2020 (Amendment 49)	Previous Publications:	2008

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:	**PROHIBITION / RESTRICTION**

FRAGRANCE INGREDIENT PROHIBITION:	Isophorone as such should not be used as fragrance ingredient. Natural extracts containing Isophorone should not be used as substitutes for this substance.

MAXIMUM ACCEPTABLE CONCENTRATIONS IN THE FINISHED PRODUCT (%):			
Category 1	See notebox	Category 7A	See notebox
Category 2	See notebox	Category 7B	See notebox
Category 3	See notebox	Category 8	See notebox
Category 4	See notebox	Category 9	See notebox
Category 5A	See notebox	Category 10A	See notebox
Category 5B	See notebox	Category 10B	See notebox
Category 5C	See notebox	Category 11A	See notebox
Category 5D	See notebox	Category 11B	See notebox

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Category 6	See notebox	Category 12	See notebox

Fragrance ingredient restriction - Note box
On the basis of established maximum concentration levels of this substance in commercially available natural sources (like essential oils and extracts), exposure to this substance from the use of these oils and extracts is not significant and the use of these oils is authorized as long as the level of Isophorone in the finished product does not exceed 0.0013%.

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 ON CONTRIBUTIONS FROM OTHER SOURCES**

INTRINSIC PROPERTY DRIVING RISK MANAGEMENT:	**INSUFFICIENT DATA**

RIFM SUMMARIES:

The dose response for preputial gland carcinoma was identified as the critical effect for deriving an oral exposure threshold. Thus the NOAEL for preputial gland carcinoma from the 2-year US-NTP carcinogenicity study was determined to be 250 mg/kg/day.

The U.S. Environmental Protection Agency (EPA) reported that over a life-time, an individual could consume 40 µg/l (0.04 mg/l) Isophorone and would have no more than a one-in-a-million increased chance of developing cancer as a direct result of ingesting water containing this chemical. According to the EPA, drinking water consumption is 2 l/day. As such, 40 µg/l X 2l/day consumption = 80 µg/person/day. Using a 60 kg bodyweight/person the Reference Dose (RfD) can be derived for humans as, 80/60 = 1.33 µg/kg/day.
This dose was used in the Creme RIFM Model to derive the acceptable safe use of 0.0013% in the final product.

EXPERT PANEL FOR FRAGRANCE SAFETY RATIONALE / CONCLUSION:

The Expert Panel for Fragrance Safety reviewed all the available data for Isophorone and recommends not to use Isophorone as or in fragrance ingredients in any finished product application.
However, the presence of Isophorone in natural extracts used as ingredients in finished consumer products is tolerated only according to the upper concentration level mentioned in the Notebox if the natural extracts are not being used to provide an alternative, indirect source of the banned substance.

REFERENCES:

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The IFRA Standard on Isophorone is based on at least one of the following publications:

• The RIFM Safety Assessment on Isophorone if available at the RIFM Fragrance Material Safety Assessment Center: 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 (http://fragrancematerialsafetyresource.elsevier.com/sites/default/files/Criteria_Document_Final.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).

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