# Isophorone

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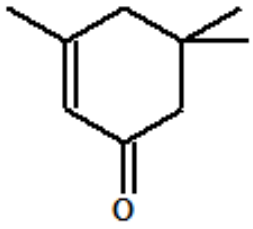
| **CAS-No.:** | 78-59-1<br>The scope of this Standard includes, but is not limited to the CAS number(s) indicated above; any other CAS number(s) used to identify this fragrance ingredient should be considered in scope as well. | **Molecular formula:** | $C_9H_{14}O$ |
| | | **Structure:** |  |
| **Synonyms**: | 2-Cyclohexen-1-one, 3,5,5-trimethyl-<br>Isoacetophorone<br>3,5,5-Trimethyl-2-cyclohexen-1-one | | |

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

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| **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. | |

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| **RECOMMENDATION:** | **PROHIBITION / RESTRICTION** |

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

| **RESTRICTION LIMITS IN THE FINISHED PRODUCT (%):** | | | |
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| Category 1 | See notebox | Category 7A | See notebox |
| Category 2 | See notebox | Category 7B | See notebox |
| Category 3 | See notebox | Category 8 | See notebox |

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| 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 |
| 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%.

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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 I** |

**ANNEX I**

**Natural Complex Substances (NCS) containing Isophorone**

| Concentration in NCS (%) | CAS number of ingredient | Name of NCS | Botanical name | CAS number of NCS | Essential oil category |
|---|---|---|---|---|---|
| 0.2 | 78-59-1 | Saffron | Crocus sativus L. | 8022-19-3 | F2.19 |
| 0.2 | 78-59-1 | Cistus oil | Cistus ladaniferus L. | 8016-26-0 | E2.12 |

This is a non-exhaustive indicative list of typical natural presence for Isophorone 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.

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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: | INSUFFICIENT DATA |
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## 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:

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 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 (http://fragrancematerialsafetyresource.elsevier.com/sites/default/files/Criteria_Document_Final.pdf).

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• 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).

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.