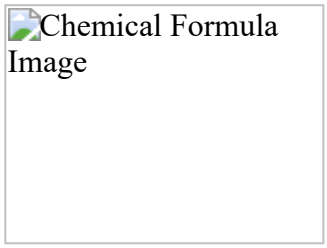
Ingredient synonym names

IDENTIFIER DETAILS

CAS Number	FEMA Number	Additive Number	Ingredient EC Number	Ingredient chemical structure
557-48-2			209-178-6	

CAS Additional Number	FL Number	CoE Number

Chemical formula	C9H14O

Ingredient CLP Classification

Ingredient REACH Registration Number
-

Acute Oral Toxicity	Eye Damage/Irritation	Carcinogenity
		Not Checked

Acute Dermal Toxicity	Respiratory Sensitisation	Reproductive Toxicity
	Not Checked	Not Checked

Acute Inhalation Toxicity	Skin Sensitisation	Aspiration Toxicity
	1B	

Skin Corrosive/Irritant	Mutagenicity/ Genotoxicity	Specific Target Organ Toxicity
2	Not Checked	

SPECIFICATIONS

Melting Point	-	Boiling Point	94C

STATUS IN FOOD AND DRUG LAWS

Acceptable Daily Intake (ADI, mg/kg)	ACCEPTABLE
Acceptable Daily Intake (ADI) comments	No safety concern at current levels of intake when used as a flavouring agent

FDA Status					
CoE limits - Beverages(mg/kg)	-	CoE limits - Food (mg/kg)	-	CoE limits - Exceptions (mg/kg)	-

HUMAN EXPOSURE

Ingredient Natural Occurence (if applicable)

Nonadienal is found in nature in the following violet leaves and flowers, cucumber, sweet and sour cherry, guava, peas, tomato, potato, bell pepper, wheat bread, rye bread, milk, milk powder, fish an d fish oil, roast chicken, guinea hen, beef, beer, coffee, tea, oats, mango, prickly pear, malt, dried b onito, endive, oysters, clam and mate. [Fenaroli, 2005].

References - Ingredient Natural Occurence

Fenaroli, (2005). Fenaroli's Handbook of flavour ingredients Volume 2 5th Edition CRC Press Lon don

Ingredient Reported Uses

Nonadienal is reportedly used in condiments and relishes at 0.10 ppm, frozen dairy at 0.10 ppm, so ft candy at 0.10 ppm [Fenaroli, 2005].

References - Ingredient Reported Uses

Fenaroli, (2005). Fenaroli's Handbook of flavour ingredients Volume 2 5th Edition CRC Press Lon don

TOXICITY DATA

In Vivo Data

Acute Toxicity Data

LD50, Rat, Oral, > 5000 mg/kg
LD50, Rabbit, Dermal, LD50 > 5000 mg/kg

Food and Chemical Toxicology. Vol. 20, Pg. 769, 1982.

In Vivo Carcinogenicity/Mutagenicity

In a study an in vivo Comet assay was conducted in compliance with GLP regulations. The test material was administered in corn oil via oral gavage to groups of male Han Wistar rats (6/sex/dose) with doses of 175, 350, or 700 mg/ kg body weight. Rats from each dose level were euthanized at the end of the study, and liver tissue was analyzed for tail intensity and tail migration in the Comet assay. No increases in the group mean tail intensity and tail moment values were observed when compared to the vehicle control group. Under the conditions of the study, the authors considered nona-2-trans-6-cis-dienal to be non-mutagenic in the Comet assay in vivo. In another study the clastogenic activity of nona-2-trans-6-cis-dienal was evaluated in an in vivo micronucleus test conducted in compliance with GLP regulations and in accordance with OECD TG474. The test material was administered in corn oil via oral gavage to groups of male and female Han Wistar mice (6/sex/dose). Doses of 175, 350, or 700 mg/kg were administered at 0, 24, and 45 h. Mice from each dose level were euthanized at 48 h; the bone marrow was extracted and examined for polychromatic erythrocytes. The test material did not induce statistically significant increases in the incidence of micronucleated polychromatic erythrocytes in the bone marrow. Under the conditions of the study, the authors considered nona-2-trans-6-cis-dienal to be not clastogenic in the in vivo micronucleus test (Api et al., 2022)

References - In Vivo Carcinogenicity/Mutagenicity

Api AM, Belsito D, Botelho D, Bruze M, Burton GA Jr, Cancellieri MA, Chon H, Dagli ML, Date M, Dekant W, Deodhar C, Fryer AD, Jones L, Joshi K, Kumar M, Lapczynski A, Lavelle M, Lee I, Liebler DC, Moustakas H, Na M, Penning TM, Ritacco G, Romine J, Sadekar N, Schultz TW, Selechnik D, Siddiqi F, Sipes IG, Sullivan G, Thakkar Y, Tokura Y. RIFM fragrance ingredient

safety assessment, nona-2-trans-6-cis-dienal, CAS registry number 557-48-2. Food Chem Toxicol. 2022 Jun;164 Suppl 1:113098. doi: 10.1016/j.fct.2022.113098. Epub 2022 Apr 30. PMID: 35504458.

Dermal Toxicity

No Data Identified

References - Dermal Toxicity

No Data Identified

Reproductive/ Developmental Toxicity

A search was performed on 15/12/2022 on PubMed (https://pubmed.ncbi.nlm.nih.gov/) regarding nona-2-trans,6-cis-Dienal, using the following search terms;

- ((ingredient name [Text Word]) OR (IUPAC name [Text Word]) OR (Cas No [Text Word]) OR (Additional Cas No [Text Word])) AND ((repro*[Text Word]) OR (spermatogenesis[Text Word]) OR (fertility[Text Word]) OR (pregnancy [Text Word]) OR (libido [Text Word])

- ((ingredient name [Text Word]) OR (IUPAC name [Text Word]) OR (Cas No [Text Word]) OR (Additional Cas No [Text Word])) AND ((teratogen*[Text Word]) OR (embryotox* [Text Word]) OR (fertility[Text Word]) OR (foetus effect*[Text Word]) OR (developmental)

The search, as detailed above, did not show any toxicologically relevant articles. Additionally, a search performed in the ECHA REACh dossier database (https://www.echa.europa.eu/) using the ingredient name or CAS No. or additional CAS No. did not show any relevant data for this toxicological endpoint of interest.

The following sources were also checked on 15/12/2022 using the ingredient name or CAS No. or additional CAS No. and no relevant information specific to this toxicological endpoint was identified.

- EPA: https://www.epa.gov/
- WHO Inchem: https://inchem.org/#/
- Joint FAO/ WHO Expert Committee on Food Additives (JECFA): https://apps.who.int/food-additives-contaminants-jecfa-database/
- International Agency for Research on Cancer (IARC): https://monographs.iarc.who.int/list-of-classification
- National Toxicology Program (NTP): https://ntp.niehs.nih.gov/whatwestudy/assessments/cancer/roc/index.html#toc1
- European Food Safety Authority (EFSA): https://www.efsa.europa.eu/en
- European Medicines Agency (EMA): https://www.ema.europa.eu/en
- EU Cosmetic Ingredients (CosIng): https://ec.europa.eu/growth/tools-databases/cosing/index.cfm?fuseaction=search.simple
- IFRA: https://ifrafragrance.org/safe-use/library
- RIFM: https://rifmdatabase.rifm.org/rifmweb/home/home-page
- GESTIS: https://limitvalue.ifa.dguv.de/
- NIOSH: https://www.cdc.gov/niosh/npg/default.html

- Haz-Map: https://haz-map.com/
- Health and Safety Executive (HSE): https://www.hse.gov.uk/pubns/books/eh40.htm
- MAK: https://onlinelibrary.wiley.com/doi/book/10.1002/3527600418
- Agency for Toxic Substances and Disease Registry (ATSDR) - https://www.atsdr.cdc.gov/

These searches are monitored and reviewed on a regular basis.

QSAR models are widely accepted mathematical tools used to predict the biological outcome of an untested compound. Some flavour ingredients had limited toxicological information available in databases, and computational modelling provided important predictions regarding potential hazards.

Derek Nexus is an expert, knowledge-based toxicology software which gives predictions for a variety of endpoints that provides a comparison to Lhasa's chemical structure knowledge base for prediction of carcinogenicity, mutagenicity/genotoxicity, reproductive toxicity, as well as skin and respiratory sensitization. The Derek Nexus version used was 6.2.1. The predictions setup used was:

- Derek Database: Derek KB 2022 1.0
- Derek Perception: Perceive Tautomers; Perceive mixtures
- Derek Endpoints: Carcinogenicity; Genotoxicity; Irritation; Miscellaneous; Neurotoxicity; Organ toxicity; Reproductive toxicity; Respiratory sensitisation; Skin sensitisation.
- Derek Species: Escherichia coli; Salmonella Typhimurium; Dog; human; monkey; rabbit; guinea pig; hamster; mouse; rat.

A search for the ingredient by CAS number, IUPAC name and synonyms, was performed on https://pubchem.ncbi.nlm.nih.gov/. From the 'canonical SMILES' or 'Isomeric SMILES' section of the ingredient PubChem page, the SMILES code was retrieved and used the in silico tools.

The Derek prediction fired no alerts for reproductive and developmental toxicity under all conditions tested.

References - Reproductive/ Developmental Toxicity

No Data Identified

Inhalation Toxicity

No Data Identified

References - Inhalation Toxicity

No Data Identified

Cardiac Toxicity

No Data Identified

References - Cardiac Toxicity

No Data Identified

Addictive Data

No Data Identified

References - Addictive Data

No Data Identified

Behavioral data

No Data Identified

References - Behavioral data

No Data Identified

In Vivo - Other Relevant Studies

No Data Identified

References - In Vivo - Other Relevant Studies

No Data Identified

In Vitro Data

In Vitro Carcinogenicity/Mutagenicity

No mutagenicity was detected in a bacterial reverse mutation (Ames) assay with Nonadienal (CAS RN 557-48-2) at 0.05-
0.2ul/plate in DMSO in Salmonella typhimurium strain TA100. (Eder et al, 1992).

In a study, nona-2-trans-6-cis-dienal was assessed in the BlueScreen assay and the authors found nona-2-trans-6-cis-dienal positive for cytotoxicity and negative for genotoxicity, with and without metabolic activation. In another test the clastogenic activity of nona-2-trans-6-cis-dienal was evaluated in an in vitro micronucleus test conducted in compliance with GLP regulations and equivalent with OECD TG 487. Human peripheral blood lymphocytes were treated with nona-2-trans-6-cis-dienal in dimethyl sulfoxide (DMSO) at concentrations up to 60 µg/mL in the presence and absence of metabolic activation (S9) at the 4-h and 24-htime pointss. Nona-2-trans-6-cis-dienal induced increases in binucleated cells with micronuclei when tested up to cytotoxic levels in either non-activated or S9-activated test systems at all time points. The authors concluded that under the conditions of the study, nona-2-trans-6-cis-dienal was clastogenic in the in vitro micronucleus test. (Api et al., 2022)

References - In Vitro Carcinogenicity/Mutagenicity

[EDER,E, DEININGER,C, NEUDECKER,T AND DEININGER,D; MUTAGENICITY OF BETA-ALKYL SUBSTITUTED ACROLEIN CONGENERS IN THE SALMONELLA TYPHIMURIUM STRAIN TA100 AND GENOTOXICTY TESTING IN THE SOS CHROMOTEST; ENVIRON. MOL. MUTAGEN. 19(4):338-345, 1992]

Api AM, Belsito D, Botelho D, Bruze M, Burton GA Jr, Cancellieri MA, Chon H, Dagli ML, Date M, Dekant W, Deodhar C, Fryer AD, Jones L, Joshi K, Kumar M, Lapczynski A, Lavelle M, Lee I, Liebler DC, Moustakas H, Na M, Penning TM, Ritacco G, Romine J, Sadekar N, Schultz TW, Selechnik D, Siddiqi F, Sipes IG, Sullivan G, Thakkar Y, Tokura Y. RIFM fragrance ingredient safety assessment, nona-2-trans-6-cis-dienal, CAS registry number 557-48-2. Food Chem Toxicol. 2022 Jun;164 Suppl 1:113098. doi: 10.1016/j.fct.2022.113098. Epub 2022 Apr 30. PMID: 35504458.

In Vitro - Other Relevant Studies

No Data Identified

References - In Vitro - Other Relevant Studies

No Data Identified

Emissions and Associated Toxicity Data

No Data Identified

References - Emissions and Associated Toxicity Data

No Data Identified