Nonalactone (gamma-)

Botanical Source

Synonyms
ALDEHYDE C-18
AMYL BUTYROLACTONE (gamma-n-)
HYDROXY NONANOIC ACID LACTONE (4-)
COCONUT ALDEHYDE
PRUNOLIDE
ABRICOLIN
NONAN-4-OLIDE
NONANOLACTONE (1,4-)

IUPAC Name

CAS Reference 104-61-0

E Number

Food Legislation

Council of Europe (CoE)	
Number	Comment
178	Listed by the Council of Europe as acceptable for use in food.

US Food and Drug Administration	
Number	Comment
172.515	Approved by the US FDA. FDA 21 CFR 172.515

Joint FAO/WHO Expert Committee on Food Additives (JECFA)		
Number	ADI	Comment
229	ADI 0-1.25 MG/KG BW	No safety concern at current levels of intake when used as a flavouring agent.

FEMA	
FEMA No.	Comment
2781	Generally recognised as safe as a flavour ingredient:GRAS List Number 3

Natural Occurrence and Use in Food
Found in beer, wheat bread, capers, cherry, chicken, clam; used in candy, baked goods, ice cream.

Estimated Intake from Food and Drink	
Daily Intake mg/kg/day	FEMA Possible Average Daily Intake mg
0.007655	5.518

Nonalactone (gamma-)

Tobacco Product Related Chemical and Biological Studies for Ingredients Added in a Mixture

Smoke Chemistry		
Published Source	Level Tested %	Comment
BAT	0.01200	At maximum application level this ingredient is not associated with significant increases in levels of Hoffmann analytes in smoke.
Philip Morris	0.00060	An overall assessment of the data suggests that this ingredient did not add to the toxicity of smoke.

Ames Activity		
Published Source	Level Tested %	Comment
BAT	0.01200	Within the sensitivity and specificity of the system the Ames activity of the cigarette smoke condensate was not increased by the addition of the ingredient.
Philip Morris	0.00060	Within the sensitivity and specificity of the system the Ames activity of the cigarette smoke was not increased by the addition of the ingredient.

Micronucleus		
Published Source	Level Tested %	Comment
BAT	0.01200	Within the sensitivity of the in vitro micronucleus assay the activity of the cigarette smoke condensate was not increased by the addition of the ingredient.

Neutral Red		
Published Source	Level Tested %	Comment
BAT	0.01200	Within the sensitivity of the test system the in vitro cytotoxicity of the cigarette smoke condensate was not increased by the addition of the ingredient.
Philip Morris	0.00060	Within the sensitivity of the test system the in vitro cytotoxicity of the cigarette smoke was not increased by the addition of the ingredient.

Inhalation		
Published Source	Level Tested %	Comment
BAT	0.01200	The results indicate that the addition of the ingredient had no discernible effect on the inhalation toxicity of mainstream smoke.
Lorillard	0.00007	The results indicate that the addition of the ingredient had no discernible effect on the inhalation toxicity of mainstream smoke.
Philip Morris	0.00060	The data indicate that the addition of the ingredient, when added with one of three groups, did not increase the inhalation toxicity of the smoke.

Mouse Skin Painting		
Published Source	Level Tested %	Comment
Lorillard	0.00007	None of the changes appeared to be substantial enough to conclude that the tumour promotion capacity of the condensate was discernibly different between condensate produced from cigarettes with the ingredient in comparison with condensate from cigarettes without the ingredient.

References

Baker RR, Pereira da Silva JR, Smith G. The effect of tobacco ingredients on smoke chemistry. Part I: Flavourings and additives. Food Chem Toxicol. 2004; 42 Suppl:S3-37.

Baker RR, Pereira da Silva JR, Smith G. The effect of tobacco ingredients on smoke chemistry. Part II: casing ingredients. Food Chem Toxicol. 2004; 42 Suppl:S39-52.

Baker RR, Massey ED, Smith G. An overview of the effects of tobacco ingredients on smoke chemistry and toxicity. Food Chem Toxicol. 2004; 42 Suppl:S53-83.

Carmines EL. Evaluation of the potential effects of ingredients added to cigarettes. Part 1: cigarette design, testing approach, and review of results. Food Chem Toxicol. 2002; 40(1): 77-91.

Rustemeier K, Stabbert R, Haussmann HJ, Roemer E, Carmines EL. Evaluation of the potential effects of ingredients added to cigarettes. Part 2: chemical composition of mainstream smoke. Food Chem Toxicol. 2002; 40(1): 93-104.

Roemer E, Tewes FJ, Meisgen TJ, Veltel DJ, Carmines EL. Evaluation of the potential effects of ingredients added to cigarettes. Part 3: in vitro genotoxicity and cytotoxicity. Food Chem Toxicol. 2002; 40(1): 105-111.

Vanscheeuwijck PM, Teredesai A, Terpstra PM, Verbeeck J, Kuhl P, Gerstenberg B, Gebel S, Carmines EL. Evaluation of the potential effects of ingredients added to

cigarettes. Part 4: subchronic inhalation toxicity. Food Chem Toxicol. 2002; 40(1): 113-131.

Gaworski CL, Dozier MM, Heck JD, Gerhart JM, Rajendran N, David RM. Brennecke LH, Morrissey R. Toxicologic evaluation of flavor ingredients added to cigarette tobacco: 13 week inhalation exposures in rats. Inhal. Toxicol. 1998; 10:357-381

Gaworski CL, Heck JD, Bennett MB, Wenk ML. Toxicologic evaluation of flavor ingredients added to cigarette tobacco: skin painting bioassay of cigarette smoke condensate in SENCAR mice. Toxicology. 1999; 139(1-2):1-17.

Nonalactone (gamma-)

Tobacco Product Related Chemical and Biological Studies for Ingredients Tested Singly

References
Baker RR, Bishop LJ. The pyrolysis of tobacco ingredients. J. Anal. Appl. Pyrolysis 2004, 71, 223-311.

Nonalactone (gamma-)

Toxicological Data on the Unburnt Ingredient

[+ve, positive; -ve, negative; ?, equivocal; with, with metabolic activation; without, without metabolic activation]

In vivo

Species	Test conditions	Endpoint	Result	Reference
Mouse	STRUCTURALLY RELATED LACTONES Negative findings were reported in 5 studies on gama-butyrolactone and gamma-undecalactone (micronucleus and sperm head abnormality) in which the test materials were given by i.p. (≤ 2 g/kg bw/day, ≤5 days).	Chromosome damage Germ cell mutation	-ve	JECFA, 1998 (citing various reports)

In vitro

Test system	Test conditions	Endpoint	Activation	Result	References
Human leucocytes	0.7 mM [*ca.* 109 mg/l]. 4/50 abnormal metaphases (presence of chromosome aberrations)/spreads counted. Said to be significant compared to [undisclosed] control values. Limited study	Chromosome damage	without	+ve	Withers, 1966

Mouse lymphoma	Positive results obtained in the presence of activation. [The test concentrations are not given in this brief abstract, although a review citing this abstract (JECFA, 1998) includes the values 400 and 1000 μg/ml]. Another review, (which claims mutation in the absence rather than the presence of activation) notes that the positive results may be artefact, due to changes in the culture pH or osmolality (Adams *et al.* 1998).]	Mutation	with and without S9	+ve	Heck *et al.* 1989 JECFA, 1998 Adams *et al.* 1998
Salmonella typhimurium strains TA98, TA100, 1535, TA1537, TA1538	Ames test. The test concentrations are not given in this brief abstract, although a review citing this abstract refers to 37.5 mg/plate (JECFA, 1998).	Mutation	with and without S9	-ve	Heck *et al.* 1989 JECFA, 1998
Rat hepatocytes	UDS. [The test concentrations are not given in this brief abstract, although a review citing this abstract refers to 500 μg/ml (JECFA, 1998).]	DNA damage (indicativ etest)	not applicable	-ve	Heck *et al.* 1989 JECFA, 1998
Bacillus subtilis	Rec assay, 20 μl/disk.	DNA damage	without	+ve	Yoo, 1986
Escherichia coli	Rec assay ≤1.6 mg/plate	DNA damage	without	-ve	Yoo, 1986

Various	STRUCTURALLY RELATED LACTONES Reviews also reports a mixture of positive and negative findings in many studies on 7 related materials, although numerically negatives greatly outweigh positives.	various	not reported in review		JECFA, 1998 Adams *et al.* 1998

References

Adams T.B. *et al.* (1998). Fd Chem. Toxic. 36, 249.

Heck J.D. *et al.* (1989). Toxicologist 9, 257. [Abstract only]

JECFA (1998). Safety evaluation of certain food additives and contaminants. Prepared by the forty-ninth meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). WHO Fd Add. Ser. 40, 1.

Withers R.F.J. (1966). Mechanisms of Mutation and Inducing Factors. Landa Z. (Ed.). The action of some lactones and related compounds on human chromosomes, 359.

Yoo Y.S. (1986). J. Osaka Cy med. Cent. 34, 267.