Linalool

Botanical Source

Synonyms DIMETHYL-1,6-OCTADIEN-3-OL (3,7-);
LINALOL;
Linalyl alcohol

IUPAC Name

CAS Reference 78-70-6

E Number

Food Legislation

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

US Food and Drug Administration	
Number	Comment
182.60	Approved by the US FDA. FDA 21 CFR 182.60

Joint FAO/WHO Expert Committee on Food Additives (JECFA)		
Number	ADI	Comment
356	2600	Group ADI 0-0.5 mg/kg bw (1979)
		Comments: No safety concern at current levels of intake when used as a flavouring agent. The 1979 group ADI of 0-0.5 mg/kg bw for citral, geranyl acetate, citronellol, linalool, and linalyl acetate, expressed as citral, was maintained at the fifty-first (TRS 891/90, 1998) and sixty-first (TRS for JECFA 61 in press) meetings.

FEMA	
FEMA No.	Comment
2635	Generally recognised as safe as a flavour ingredient:GRAS List Number 3

Natural Occurrence and Use in Food
Found in banana, beer, blackberry, beans, blueberry, apple, apricot, arctic bramble, artichoke, grape brandy, plum brandy; used in meat products.

Estimated Intake from Food and Drink	
Daily Intake mg/kg/day	FEMA Possible Average Daily Intake mg
0.01822	3.885

Linalool

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

Smoke Chemistry		
Published Source	Level Tested %	Comment
BAT	0.00150	At maximum application level this ingredient is not associated with significant increases in levels of Hoffmann analytes in smoke.
Philip Morris	0.00030	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	0.00150	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	0.00030	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	0.00150	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	0.00150	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	0.00030	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	0.00150	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	0.00030	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.

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Linalool

Tobacco Product Related Chemical and Biological Studies for Ingredients Tested Singly

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Linalool

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	Results	Reference
Mouse, CD-1, groups of 5/sex	A citation reports oral administration (by stomach tube) at up to 1.5 g/kg bw (a dose which induced overt toxicity), bone marrow cells scored for micronuclei 24 or 48 hr later.	Chromosome damage	-ve	RIFM, 2001

In vitro

Test system	Test conditions	Endpoint	Activation status	Results	Reference
Chinese hamster lung fibroblasts	Cells incubated at up to 0.25 mg/ml for 48 hr, examined for chromosome aberrations and polyploidy.	Chromosome damage and changes in chromosome number.	Without	-ve (Limited assay, activation was not used)	Ishidate et al. 1984
Rat liver cells	Details of this study are given in FFHPVC, JECFA and NTP reports but not in the cited publication. The citing reviewers presumably	DNA damage	Not applicable	-ve	FFHPVC, 2001; JECFA, 1999; NTPa (citing Heck et al. 1989)

	contacted the investigators for details. Hepatocytes, incubated for 18-20 hr at up to 50 ug/ml, were examined for the induction of unscheduled DNA synthesis. Linalyl acetate (a simple ester) also tested at up to 300 ug/ml in this assay.				
Mouse lymphoma cells L5178Y $tk^{+/-}$	Linalool incubated for 4 hr at up to 150 and 200 ug/ml in the absence and presence of S9, respectively. Cells examined for mutations. These details were not given in the original (abstract) report, but in the various citing reviews.	Mutation	With and without S9	+ve (weak) (in the presence of S9) (It has been suggested that positive results in this assay are commonly observed for polar substances in the presence of S9, associated with changes in physiologic culture conditions	FFHPVC, 2001; JECFA, 1999; NTPa (citing Heck et al. 1989)

				such as pH and osmolality.)	
Mouse lymphoma cells L5178Y $tk^{+/-}$	Linalool tested for ability to induce muations, in an assay "taking account of cytotoxicity, osmolality and pH". Unpublished report.	Mutation	Not disclosed in citing review	-ve	RIFM, 1994
Chinese hamster ovary cells, K-1	Incubation of "linallol" at up to 1000 uM. Cells examined for induction of sister chromatid exchanges.	Chromosome effects	Without	-ve (Limited study as activation was not used)	Sasaki et al. 1989
Salmonella typhimurium strains TA97, TA98, TA100, TA102, TA104, TA1535	Tested at up to 1 mg/plate in good quality studies using S9 derived from both rat and hamster liver. The highest concentration was slightly toxic in all strains.	Mutation	With and without S9	-ve (Good quality study)	NTPb
Salmonella typhimurium strains TA92,TA94, TA98, TA100, TA1535, TA1537,	Ames tests at up to 1, 10 and 100 mg/plate. The urine of rats given 0.5 ml linalool	Mutation	With and without S9	-ve (Including good quality studies)	JECFA, 1999 (citing various studies including Heck et

TA1538 (and possibly TA2367)	orally was also tested in Ames tests.				al. 1989 and Ishidate et al. 1984)
Escherichia coli WP2 uvrA	Linalool was tested at up to 1 mg/plate. This paper also reports that linalool - at up to 1 mg/plate - did not affect the mutagenic activity of a known mutagen - AF2 - in this assay.	Mutation	Probably without (the paper is in Japanese)	-ve	Yoo, 1986
Bacillus subtilis strains H17 and M45	Tested in a rec assay measuring differential repair at 10 ul/disc (about 10 mg/disc).	DNA damage (indicative test)	Presumably without (the paper is in Japanese)	+ve	Yoo, 1986
Bacillus subtilis strains H17 and M45	Linalool was tested at 17 ug/disk.	DNA damage (indicative test)	Presumably without (the paper is in Japanese)	No test (No clear evidence of toxicity in either strain)	Oda et al. 1978

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