Ethyl isovalerate

Botanical Source	
Synonyms	ETHYL ISOVALERIANATE; ETHYL beta-METHYL BUTYRATE; ETHYL-3-METHYL BUTANOATE; ETHYL ISOPENTANOATE; METHYL BUTANOIC ACID (3-), ETHYL ESTER
IUPAC Name	ETHYL ISO VALERATE
CAS Reference	108-64-5
E Number	

Food Legislation

Council of Europe (CoE)	
Number	Comment
442	Listed by the Council of Europe as acceptable for use in food at up to 30 ppm.

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
196	760	No safety concern at current levels of intake when used as a flavouring agent.

FEMA	
FEMA No.	Comment
2463	Generally recognised as safe as a flavour ingredient:GRAS List Number 3

Natural Occurrence and Use in Food
Found in banana, celery, apple, beer, brandy, cantaloupes, cashew apple, parmesan cheese; used in condiments, ice cream, baked goods.

Estimated Intake from Food and Drink

Daily Intake mg/kg/day	FEMA Possible Average Daily Intake mg
0.008855	2.489

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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	0.00300	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	0.00300	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	0.00300	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	0.00010	The results indicate that the addition of the ingredient had no discernible effect on the inhalation toxicity of mainstream smoke.
Philip Morris	0.00300	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	0.00010	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

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LH, Morrissey R. Toxicologic evaluation of flavor ingredients added to cigarette tobacco: 13 week inhalation exposures in rats. Inhal. Toxicol. 1998; 10:357-381

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Tobacco Product Related Chemical and Biological Studies for Ingredients Tested Singly

References
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Toxicological Data on the Unburnt Ingredient

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

In vitro

Test system	Test conditions	Endpoint	Activation	Result	References
Hamster lung fibroblast cells	Up to 2 mg/ml (the highest non-toxic concentration) for 48 hr, cells examined for chromosome aberrations and polyploidy.	Chromosome damage	Without	-ve limited study as not tested in presence of activation	Ishidate *et al* 1984
Salmonella typhimurium, strains TA92, TA94, TA98, TA100, TA1535 and TA1537	Up to 10 mg/plate (the highest non-toxic concentration)	Mutation	With and without S9	-ve good quality study	Ishidate *et al* 1984
Salmonella typhimurium, TA97, TA102	Concentrations up to 1 mg/plate using the preincubation method.	Mutation	Without	-ve limited study	Fujita & Sasaki 1987.
Bacillus subtilis H17 (rec+) and M45 (rec-)	Tested in a rec assay at up to 17 µg/disc. Toxicity was not achieved in either strain.	DNA damage (as indicated by differential toxicity)	Without	No test (as toxicity was not seen in either strain)	Oda *et al* 1978

Bacillus subtilis ('Rec' assay) in H17 (rec+) and M45 (rec-)	Tested at up to 20 μL/disc in a rec assay. Toxicity was not achieved in either strain.	DNA damage (as indicated by differential toxicity)	Without?	No test (as toxicity was not seen in either strain)	Yoo, 1986
Escherichia coli PQ37	Up to 0.5 mg/ml, assessed effect on induction of SOS by UV light	DNA damage	Without	-ve	Ohta *et al* 1986

References

Fujita H & Sasaki M (1987). Mutagenicity test of food additives with Salmonella typhimurium TA97 and TA102. II. Kenkyu Nenpo – Tokyo-Toritsu Eisei Kenkyusho 38, 423-430 (cited in CCRIS, 2003).

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