

Methyl phenylacetate

Botanical Source

Synonyms

IUPAC Name

CAS Reference 101-41-7

E Number

Food Legislation

Council of Europe (CoE)	
Number	Comment
2155	Listed by the Council of Europe as acceptable for use in food at up to 50 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
-	-	No safety concern at current levels of intake when used as a flavouring agent.

FEMA	
FEMA No.	Comment
2733	Generally recognised as safe as a flavour ingredient:GRAS List Number 3

Natural Occurrence and Use in Food
Found in coffee, cocoa; used in candy, syrups, baked goods.

Estimated Intake from Food and Drink	
Daily Intake mg/kg/day	FEMA Possible Average Daily Intake mg
0.0002118	12.72

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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	0.06720	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	0.06720	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	0.06720	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.
Philip Morris	0.06720	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

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.

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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.

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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
Mouse lymphoma cells L5178Y Tk ^{+/-}	Phenylacetic acid, cells examined for mutations. No further details were given in the original source, which is an abstract. JECFA (who presumably contacted the investigators) reported that the test was carried out at a maximum concentration of 1500 mg [which is not a concentration].	Mutation	With and without S9	-ve	Heck <i>et al.</i> 1989

<p>Rat liver cells (hepatocytes)</p>	<p>Phenylacetic acid tested, unscheduled DNA synthesis measured.</p> <p>No further details were given in the original source, which is an abstract. JECFA (who presumably contacted the investigators) reported that the test was carried out at a maximum concentration of 500 mg [which is not a concentration].</p>	<p>DNA damage</p>	<p>Not applicable</p>	<p>-ve</p>	<p>Heck <i>et al.</i> 1989</p>
<p><i>Salmonella typhimurium</i> TA98, TA100, TA1535, TA1537, TA1538</p>	<p>Phenylacetic acid, Ames test.</p> <p>No further details were given in the original source, which is an abstract. JECFA (who presumably contacted the investigators) reported that up to 1000 mg/plate was tested. This is presumably incorrect, as the maximum amount is usually 5-10 mg/plate.</p>	<p>Mutation</p>	<p>With and without S9</p>	<p>-ve</p>	<p>Heck <i>et al.</i> 1989</p>

Chinese hamster lung fibroblasts	Ethyl phenylacetate, incubated at up to 1 mg/ml for 48 hr, cells examined for chromosome aberrations and polyploidy.	Chromosome damage and changes in chromosome number.	Without	-ve for damage ? for number changes [limited assay, no S9 used]	Ishidate <i>et al.</i> 1984
<i>Salmonella typhimurium</i> TA92, TA94, TA98, TA100, TA1535, TA1537 (and possibly TA2637)	Ethyl phenylacetate, Ames test at up to 5 mg/plate.	Mutation	With and without S9	-ve (good quality study)	Ishidate <i>et al.</i> 1984
<i>Bacillus subtilis</i> strains H17 and M45	Ethyl phenylacetate, tested at up to 20 ul/disk [about 20 mg/disk] in a rec assay measuring differential toxicity.	DNA damage (indicative test)	Probably without (the paper is in Japanese)	+ve	Yoo, 1986
<i>Bacillus subtilis</i> strains H17 and M45	Ethyl phenylacetate, tested at up to 21 ug/disk in a rec assay measuring differential toxicity.	DNA damage (indicative test)	Probably without (the paper is in Japanese)	-ve	Oda <i>et al.</i> 1978

<i>Escherichia coli</i> WP2uvrA	Ethyl phenylacetate, tested at up to 1.6 mg/plate.	Mutation	Apparently without (the paper is in Japanese)	-ve	Yoo, 1986
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References

Heck J D *et al* (1989). An evaluation of food flavouring ingredients in a genetic toxicity screening battery. *Toxicologist*, 9, 257 (additional data taken from JECFA, 2003).

Ishidate M *et al* (1984). Primary mutagenicity screening of food additives currently used in Japan. *Food and Chemical Toxicology*, 22, 623-636.

Oda Y *et al* (1979). Mutagenicity of food flavours in bacteria (1st report). *Shokuhin Eisei Hen*, 9, 177-181 (in Japanese, some data in English).

Yoo Y S (1986). Mutagenic and antimutagenic activities of flavouring agents used in foodstuffs. *Journal of the Osaka City Medical Centre*, 34, 267-288 (in Japanese, some data in English).