Botanical Source

Synonyms Benzyl alcohol;

PHENYLMETHYL ALCOHOL; alpha-HYDROXYTOLUENE; BENZENEMETHANOL

IUPAC Name BENZYL ALCOHOL

CAS Reference 100-51-6

E Number

Food Legislation

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

US Food and Drug Administration				
Number	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				
25	16000	ADI 0-5.0 mg/kg bw		

FEMA		
FEMA No.	Comment	
2137	Generally recognised as safe as a flavour ingredient:GRAS List Number 3	

Natural Occurrence and Use in Food

Found in apricot, beer, almonds, apple, apple juice, asparagus, bananas, blackcurrants, blackberries; used in chewing gum, candy, baked goods.

Estimated Intake from Food and Drink			
Daily Intake mg/kg/day	FEMA Possible Average Daily Intake mg		
0.2	41.87		

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

Smoke Chemistry			
Published Source	Level Tested %	Comment	
BAT	0.17000	At maximum application level this ingredient is not associated with significant increases in levels of Hoffmann analytes in smoke.	
Philip Morris	0.14260	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				
system the Ames activity of the cigarette		smoke condensate was not increased by the		
Philip Morris	0.14260	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	
ВАТ	0.17000	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	0.17000	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	0.14260	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	0.17000	The results indicate that the addition of the ingredient had no discernible effect on the inhalation toxicity of mainstream smoke.		
Lorillard	0.36740	The results indicate that the addition of the ingredient had no discernible effect on the inhalation toxicity of mainstream smoke.		
Philip Morris 0.14260		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	0.36740	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.

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.

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, ddY, 6 males/ group	Bone marrow micronucleus assay in mice administered a single intraperitoneal injection at 0, 50, 100 or 200 mg/kg bw; evaluated 24 hours after dosing.	Chromosome damage	-ve High quality study.	Hayashi et al. 1988
Mouse; ddY; 6 males/ group	Bone marrow micronucleus assay in mice injected intraperitoneally at 0 or 100 mg/kg bw/day for 4 days; evaluation 24 hours after final dose.	Chromosome damage	-ve High quality study.	Hayashi et al. 1988
Drosophila melanogaster	Adult flies fed 0 or 5000 ppm solution for 3 days, or injected with 0 or 8000 ppm solution. Three successive matings with broods monitored for appearance of sex-linked recessive lethal mutations.	Germ cell mutations	-ve High quality study	NTP
Drosophila melanogaster	SMART (somatic mutation and recombination test). Larvae treated with up to 50 mM and wings of adults scored for mutant spots.	Mutation	+ve	Demir et al. 2008

In vitro

Test system	Test conditions	Endpoint	Activation status	Results	Reference
Mouse lymphoma L5178Y cells	Gene mutation assay in cells exposed at up to 5 mg/ml; 4 tests without S9, 2 tests with S9.	Mutation	With and without S9	Equivocal without S9 (1/4 tests +ve) High quality study	McGregor et al. 1988; NTP, 1989
Chinese hamster ovary (CHO) cells	Chromosome aberration assay in cells exposed at up to 5 mg/ml for 12-18 hours; 4 tests both with and without S9	Chromosome damage	With and without S9	+ve (3/4 tests +ve with S9; 1/4 test +ve without S9) High quality study	Anderson, 1990; NTP, 1989; Zeiger et al. 1990
Chinese hamster ovary (CHO) cells	Sister chromatid exchange assay in cells exposed at up to 5 mg/ml for 12-18 hours; 4 tests both with and without S9	Chromosome effects	With and without S9	Weak +ve (or equivocal) High quality study	Anderson, 1990; NTP, 1989; Zeiger et al. 1990
Human alveolar tumour cells	Cells exposed at up to 0.5 mmol/litre [54 mg/ml] [no further details in citing source]	DNA damage	Not known	-ve	Waters et al. 1982
Rat hepatocytes	Alkaline elution assay with cells exposed at up to 10 mmol/litre [1080 mg/ml]	DNA damage	Not applicable	-ve	Storer et al. 1996

Salmonella typhimurium strains TA92, TA94, TA97, TA98, TA100, TA102, TA1535 and TA1537	Ames tests, some with up to 10 mg/plate	Mutation	With and without S9	-ve	Ball et al. 1984; Florin et al. 1980; Fujita et al. 1992; Ishidate et al. 1984; Milvy & Garro, 1976; Mortelmans et al. 1986; NTP, 1989; Rogan et al. 1986; Wiessler et al. 1983; Zeiger et al. 1990
Escherichia coli polA deficient	Bacterial mutation assay with up to 50 µl [~50 mg]/plate	Mutation	With and without S9	-ve	Fluck et al. 1976
Escherichia coli strain WP2 uvrA	Bacterial mutation assay with up to 8 mg/plate	Mutation	Without	-ve	Kuroda et al. 1984; Yoo, 1986
Salmonella typhimurium strain TA1535/ pSK1002	Umu test with up to 5 mg/ml	DNA damage	With and without S9	-ve	Yasunaga et al. 2004
Bacillus subtilis strains H17 and M45	Rec assay (measuring differential killing) with up to 20 µl [~20 mg]/disc	DNA damage [indicative test]	Without	+ve	Kuroda et al. 1984; Yoo, 1986

References

Adams T M et al. (2005). The FEMA GRAS assessment of benzyl derivatives used as flavour ingredients. Food and Chemical Toxicology 43, 1207-1240.

Anderson B E (1990). Chromosome aberrations and sister chromatid exchange test results with 42 chemicals. Environmental and Molecular Mutagenesis 16, 55-137.

Ball J C et al. (1984). Mutagenicity studies of *p*-substituted benzyl derivatives in the Ames *Salmonella* plate-incorporation assay. Mutation Research 138,145-151 (cited in IUCLID, 2000).

CCRIS (2008). Chemical Carcinogenesis Research Information System. Record for Benzyl alcohol, 100-51-6. http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?CCRIS.

Demir E et al. (2008). Genotoxicity testing of four benzyl derivatives in the *Drosophila* wing spot test. Food and Chemical Toxicology 46, 1034-1041.

Florin I et al. (1980). Screening of tobacco smoke constituents for mutagenicity using the Ames test. Toxicology 15, 219-232.

Fluck E R et al. (1976). Evaluation of a DNA polymerase-deficient mutant of *E. coli* for the rapid detection of carcinogens. Chemico-Biological Interactions 15, 219-231.

Fujita H et al. (1992). Mutagenicity test of food additives with *Salmonella typhimurium* TA97 and TA102. VII. Annual Report of Tokyo Metropolitan Research Laboratory of Public Health 43, 219-227 (cited in CCRIS, 2008).

Hayashi M et al. (1988). Micronucleus tests in mice on 39 food additives and eight miscellaneous chemicals. Food and Chemical Toxicology 26, 487-500.

IUCLID (2000). Dataset for Benzyl alcohol, 100-51-6. http://ecb.jrc.it/IUCLID-DataSheets/100516.pdf.

Ishidate M et al. (1984). Primary mutagenicity screening of food additives currently used in Japan. Food and Chemical Toxicology 22, 623-636 (cited in IUCLID, 2000)

Kuroda K et al. (1984). Antimutagenic activity of food additives. Mutation Research, 130, 369 [abstract].

McGregor D B et al. (1988). Response of the L5178Y tk+/tk- lymphoma cell forward mutation assay. III. 72 coded chemicals. Environmental and Molecular Mutagenesis 12, 85-154.

Milvy P & Garro A J (1976). Mutagenic activity of styrene oxide (1,2-epoxyethylbenzene), a presumed styrene metabolite. Mutation Research 40, 15-18.

Mortelmans K et al (1986). *Salmonella* mutagenicity tests II. Results from the testing of 270 compounds. Environmental Mutagenesis 8, 1-119.

NTP (1989). US National Toxicology Program. Toxicology and carcinogenesis studies of benzyl alcohol (CAS No. 100-51-6) in F344/N rats and B6C3F₁ mice (gavage studies). Report no. 343. http://ntp.niehs.nih.gov/ntp/htdocs/LT_rpts/tr343.pdf.

NTp (undated). Study 419402. Sex-linked recessive lethal study on benzyl alcohol. Available at http://ntp-apps.niehs.nih.gov/ntp_tox/index.cfm

.

Rogan E G et al. (1986). Mutagenicity of benzylic acetates, sulphates and bromides of polycyclic aromatic hydrocarbons. Chemico-Biological Interactions 58, 253-275. Storer R D et al. (1996). Revalidation of the *in vitro* alkaline elution/rat hepatocyte assay for DNA damage: improved criteria for assessment of cytotoxicity and genotoxicity and results for 81 compounds. Mutation Research 368, 59-101.

Waters et al. (1982). Correlations in mammalian cells between types of DNA damage, rates of DNA repair and the biological consequence. Progress in Mutation Research (DNA Repair, Chromosome Alterations Chromatin Structure) 4, 247-259 (cited in Adams et al. 2005)

Wiessler M et al. (1983). Biological activity of benzylating N-nitroso compounds. Models of activated N-nitrosomethyl-benzylamine. Carcinogenesis 4, 867-871 (cited in IUCLID, 2000).

Yasunaga K et al. (2004). Evaluation of the *Salmonella* umu test with 83 NTP chemicals. Environmental and Molecular Mutagenesis 44, 329-345.

Yoo H S (1986). Mutagenic and antimutagenic activities of flavouring agents used in foodstuffs. Journal of the Osaka City Medical Centre 34, 267-288.

Zeiger E et al. (1990). Evaluation of four *in vitro* genetic toxicity tests for predicting rodent carcinogenicity: confirmation of earlier results with 41 additional chemicals. Environmental and Molecular Mutagenesis 16, 1-14.