# Glycerol

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| **Botanical Source** | |
| **Synonyms** | GLYCERINE;<br>PROPANETRIOL (1,2,3-) |
| **IUPAC Name** | GLYCEROL |
| **CAS Reference** | 56-81-5 |
| **E Number** | E422 |

## Food Legislation

| **Council of Europe (CoE)** | |
|---|---|
| Number | Comment |
| - | - |

| **US Food and Drug Administration** | |
|---|---|
| Number | Comment |
| 182.1320 | Approved by the US FDA. FDA 21 CFR 182.1320 |

| **Joint FAO/WHO Expert Committee on Food Additives (JECFA)** | | |
|---|---|---|
| Number | ADI | Comment |
| 909 | 17000 | Evaluation not finalized, pending definition of "flavouring agent". On the basis of the available data, the total daily intake arising from use levels necessary to achieve the desired effect does not represent a hazard to health |

| **FEMA** | |
|---|---|
| FEMA No. | Comment |
| 2525 | Generally recognised as safe as a flavour ingredient:GRAS List Number 3 |

| **Natural Occurrence and Use in Food** |
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| Found in beer, cherry, wine; used in milk products, baked goods, meat products. |

| **Estimated Intake from Food and Drink** | |
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| Daily Intake mg/kg/day | FEMA Possible Average Daily Intake mg |

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| 24.435 | 7.279 |

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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 | 7.00000 | At maximum application level this ingredient is not associated with significant increases in levels of Hoffmann analytes in smoke. |
| Philip Morris | 4.20480 | 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 | 7.00000 | 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 | 4.20480 | 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 | 7.00000 | 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 | 7.00000 | 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 | 4.20480 | 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 | 7.00000 | The results indicate that the addition of the ingredient had no discernible effect on the inhalation toxicity of mainstream smoke. |
| Lorillard | 5.10000 | The results indicate that the addition of the ingredient had no discernible effect on the inhalation toxicity of mainstream smoke. |
| Philip Morris | 4.20480 | 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 | 2.40000 | 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.

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## Tobacco Product Related Chemical and Biological Studies for Ingredients Tested Singly


| References |
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| Baker RR, Bishop LJ. The pyrolysis of tobacco ingredients. J. Anal. Appl. Pyrolysis 2004, 71, 223-311. |
| Carmines EL, Gaworski CL. Toxicological evaluation of glycerin as a cigarette ingredient. Food Chem Toxicol. 2005; 43(10):1521-1539 |
| Heck JD, Gaworski CL, Rajendran N, Morrissey RL. Toxicologic evaluation of humectants added to cigarette tobacco: 13-week smoke inhalation study of glycerin and propylene glycol in Fischer 344 rats. Inhal Toxicol. 2002, 14(11):1135-52. |

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## 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 |
|---|---|---|---|---|
| Rats, males | Gavage administration of 1 g/kg bw, bone marrow cells examined for chromosome aberrations | Chromosome damage | Equivocal<br><br>Weak activity was reported in this Soviet study (but see comment below) | Barilyak and Kozachuk, 1985 |
| Rats, males | Administration [probably by gavage] of 0.01, 0.1 and 1 g/kg bw. After 2 weeks [the period of treatment is unclear], the males were mated with untreated females, and the incidence of early foetal deaths was monitored | Dominant lethal effect (germ cell mutations/chromosome damage) | Equivocal<br><br>Though a dose-related effect was reported in this Soviet study, none of the other compounds reported as positive would have be expected to possess mutagenic activity, so the validity of the study is questionable | Barilyak and Kozachuk, 1985 |

In vitro

| Test system | Test conditions | Endpoint | Activation | Results | References |
|---|---|---|---|---|---|
| Human lymphocytes or whole blood | Cells incubated with glycerol at 0.17 or 0.68 mg/ml, and | Chromosome damage | Without | -ve<br><br>Limited study, not | Greenrod and Fenech, 2003 |

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| | examined for micronuclei. | | | tested with S9. | |
| Chinese hamster lung fibroblasts | Incubated for 48 hr at up to 1 mg/ml, cells examined for chromosome aberrations and polyploidy. Highest concentration chosen on basis of either toxicity or osmotic pressure | Chromosome damage. Changes in chromosome number. | Without | -ve<br><br>(limited study as no S9 was used) | Ishidate et al. 1984 |
| Chinese hamster ovary WBL cells | Cells were incubated for 4 hr with glycerol at up to 1 M, which was not toxic. Cells were examined for chromosome aberrations | Chromosome damage | Without | -ve<br><br>(limited study as no S9 was used) | Galloway et al. 1987 |
| Chinese hamster ovary WBL cells | Tested at six concentrations up to 1 mg/ml. Cells were treated for 2 hr with activation and 10 or 14 hr without activation. Cells were examined for chromosome aberrations | Chromosome damage | With and without S9 | -ve<br><br>good quality study | Doolittle et al. 1988; Lee et al. 1988 |
| Human peripheral blood cells | Incubated at unspecified concentrations | Chromosome effects | Without | ? Small increase in SCE | Tucker et al. 1984 |

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| (lymphocytes) | for 75 hr, cells assessed for sister-chromatid exchanges (SCEs) | | | frequency reported, data not shown in paper.<br><br>Minimal data were presented | |
| Chinese hamster ovary WBL cells | Tested at five concentrations up to 1 mg/ml. Cells were treated for 2 hr with activation and 25.5 hr without activation. Cells were examined for sister chromatid exchanges (SCEs) | Chromosome effects | With and without S9 | -ve<br><br>good quality study | Doolittle et al. 1988; Lee et al. 1988 |
| Chinese hamster ovary K1-BH4 cells | Tested at six concentrations up to 1 mg/ml. Cells were treated for 5 hr and examined for HGPRT mutations | Somatic cell mutation | With and without S9 | -ve<br><br>[significant increases at top two doses without S9, but not dose-related and considered to be of no biological relevance]<br><br>good quality study | Doolittle et al. 1988; Lee et al. 1988 |
| Rat hepatocytes | Tested at eight separate laboratories, at | DNA damage | Not applicable | -ve<br><br>good quality | Fautz et al. 1991 |

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| | concentrations ranging from 0.01-3.2 mg/ml up to 1-126 mg/ml. Both single strand breaks and unscheduled DNA synthesis (UDS) were monitored | | | study | |
| Rat hepatocytes | Tested at five concentrations up to 1 mg/ml. Tested in duplicate using cells from two male rats, net nuclear grain counts were monitored | DNA damage | Not applicable | -ve<br><br>good quality study | Doolittle et al. 1988; Lee et al. 1988 |
| *Salmonella typhimurium* strains TA92, TA94, TA98, TA100, TA1535 and TA1537 (possibly also TA2637) | Tested at up to 50 mg/plate | Mutation | With and without S9 | -ve<br><br>good quality study | Ishidate et al. 1984 |
| *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 | Tested at five concentrations up to 1 mg/plate (with a repeat in TA100 at "slightly higher" concentrations [not disclosed]) | Mutation | With and without S9 | -ve<br><br>good quality study | Doolittle et al. 1988; Lee et al. 1988 |
| *Salmonella typhimurium* strains TA98, | Tested at up to 10 mg/plate, in three separate | Mutation | With and without S9 | -ve<br><br>good quality | Haworth et al. 1983 |

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| TA100, TA1535 and TA1537 | laboratories | | | study | |
| *Salmonella typhimurium* (various strains) | Several Ames tests. Some were of high quality. | Mutation | With and without S9 | -ve | Clark et al. 1979; Ishidate et al. 1988; Litton Bionetics, 1975; Shimizu et al. 1985; Stolzenberg and Hine, 1979; Yamaguchi, 1982 (all cited in Bibra, 2004); Fujita et al. 1994; Haresaku et al. 1985; MacPhee, 1985 |
| *Escherichia coli* bacteria | No details given in secondary source | Mutation | With and without S9 | -ve | Shimizu et al. 1985 |
| *Bacillus subtilis* bacteria, strains H17 and M45 | A rec assay measuring differential killing, which reflects DNA damage. No details given except the incubation time (0.5 hr) | DNA damage | Without | +ve<br><br>[the relevance of this result is unclear, because all 25 tested compounds were reported to have an effect and no mention was | Nonaka, 1989 |

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| | | | | made of negative controls. The study was only published as an abstract] | |
| *Saccharomyces cerevisiae* yeast | No details given in secondary source | Mutation | With and without S9 | -ve | Litton Bionetics, 1975 |
| *Saccharo-myces cerevisiae* yeast | Tested at a very high concentration of 184.2 g/l, cells examined for DNA damage. | DNA damage | Unstated | ? Some evidence, possibly due to the high test concen-tration | Tuite et al. 1981 |

References


Barilyak I R & Kozachuk S Y (1985). Tsitol. Genet. 19, 436 (cited in Bibra, 2004).

Bibra (2004). Toxicity Profile: glycerol (draft update to 1993 Toxicity Profile). Bibra, Sutton, Surrey.

CCRIS (2002). File Locator, ChemIDplus website - http://chem.sis.nlm.nih.gov/chemidplus/cmplxqry.html

Clark C R et al. (1979). Toxicology and Applied Pharmacology, 51, 529 (cited in Bibra, 2004).

Doolittle D J et al. (1988). The genotoxic activity of glycerol in an in vitro test battery. Food and Chemical Toxicology, 26, 631.

Fautz R et al. (1991). Report of a comparative study of DNA damage and repair assays in primary rat hepatocytes with five coded chemicals. Mutation Research, 260, 281-294.

Fujita H et al (1994). Mutagenicity test of food additives with Salmonella typhimurium TA97 and TA102. IX, Tokyo-Toritsu Eisei Kenkyusho Kenkyu Nenpo 45, 191-199 (cited in CCRIS, 2002).

Galloway S M et al. (1987). Effects of high osmotic strength on chromosome aberrations, sister-chromatid exchanges and DNA strand breaks, and the relation to toxicity. Mutation Research, 189, 15.

Greenrod W & Fenech M (2003). The principal phenolic and alcoholic components of wine protect human lymphocytes against hydrogen peroxide- and ionizing radiation-induced DNA damage in vitro. Mutagenesis 18, 119-126.

Haresaku M et al. (1985). Journal of the Society of Cosmetics Chemists 19, 100-104.

Haworth S et al. (1983). Salmonella mutagenicity test results for 250 compounds, Environmental Mutagenesis, 5 (Suppl.1), 3-142.

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

Ishidate M et al. (1988). A comparative analysis of data on the clastogenicity of 951 chemical substances tested in mammalian cell culture. Mutation Research, 195, 151-213.

Lee C K et al. (1988). The genotoxic activity of glycerol in an in vitro test battery. Toxicologist, 8, 103 (cited in Bibra, 2004).

Litton Bionetics (1975). NTIS PB-2435 479 (cited in Bibra, 2004).

MacPhee D G (1985). Indications that mutagenesis in Salmonella may be subject to catabolite repression. Mutation Research 151, 35-41.

Nonaka M (1989). DNA repair tests on food additives. Environmental and Molecular Mutagenesis, 14 (Suppl. 15), 143.

Shimizu H et al. (1985). Japanese Journal of industrial Health, 27, 400 (cited in Bibra, 2004).

Stolzenberg S J & Hine C H (1979). Journal of Toxicological and Environmental Health, 5, 1149 (cited in Bibra, 2004).

Tucker J D et al. (1984). Detection of sister-chromatid exchanges in human peripheral lymphocytes induced by ethylene dibromide vapour. Mutation Research, 138, 93-98.

Tuite M F et al. (1981). Genetics 98, 691.

Yamaguchi T (1982). Agric. Biol. Chemistry, 46, 849 (cited in Bibra, 2004).