4-METHYLACETOPHENONE

MODULE 1

SUBSTANCE INFORMATION SHEET

4-METHYLACETOPHENONE

CAS number	122-00-9
Natural Origin	Occurs sour cherry, guava, peach, fresh blackberry, stalks of celery, baked potato, and in essential oils from the wood of Myrocarpus and bois de rose.
Chemical Formula	C9-H10-O
Synonymes	p-Methylacetophenone; Methyl p-tolyl ketone; 1-Acetyl-4-methylbenzene; 1-methyl-4-acetyl benzene
E number	N/A
FEMA GRAS number	2677

General Information

Council of Europe (CoE)

Number	Comment
156	N/A

US Food & Drug Administration (FDA)

Number	Comment
21 CFR 172.515	Approved by U.S. FDA as Food Additives.

Joint FAO/WHO Expert Committee on Food Additives (JECFA)

Number	ADI	Comment
807	ACCEPTABLE	No safety concern at current levels of intake when used as a flavouring agent

European Food Safety Authority (EFSA)

Number	Comment
07.022	Aromatic ketones, secondary alcohols and related esters.

Flavors & Extracts Manufacturers Association (FEMA)

Number	Comment
2677	Generally Recognized as Safe as a flavor ingredient - GRAS 3

Uses and Exposure

4'-Methoxyacetophenone is used as an intermediate for pharmaceuticals, agrochemicals and other organic compounds. It also has been used as a drug to induce sleep. It is used as solvent for plastics, resins, cellulose ethers, and esters. It is also used as a component of perfumes and as chemical intermediate in the manufacture of resins and flavouring agents.

Estimated Intake from Food and Drink

Daily Intake
The average person is estimated to consume as much as 0.0001412 mg/kg/day of 4-methylacetophenone. Based on FEMA reported disappearance data, 4-methylacetophenone consumption is 0.00089 mg/kg/day. Consumption of 4-methylacetophenone from natural sources (0.01114 mg/kg/day) is very high compared to the estimated intake as an added ingredient (0.00014 mg/kg/day). The FDA estimate of consumption based on disappearance data is much lower than the FEMA PADI value of 0.033 mg/kg/day[1,2,3,4]

Summary of the Toxicological Investigations on the Use of the Substance in Tobacco Products

Smoke Chemistry

Internal Studies	Level Tested ppm	Comment
Carmines for Philip Morris	12, 13, 37, 39	The effect of the addition of 4-methylacetophenone as part of a mixture at concentrations up to 39 ppm on the composition of the cigarette smoke was investigated.

Neutral Red Uptake Assay (NRU)

Internal Studies	Level Tested ppm	Comment
Carmines for Philip Morris	12, 13, 37, 39	The effect of the addition of 4-methylacetophenone as part of a mixture at concentrations up to 39 ppm on the cytotoxicity, as measured by the Neutral Red Uptake assay, was investigated.

AMES Assay

Internal Studies	Level Tested ppm	Comment
Carmines for Philip Morris	12, 13, 37, 39	The effect of the addition of 4-methylacetophenone as part of a mixture at concentrations up to 39 ppm on the mutagenic response, as measured by the Salmonella reverse mutation assay, was investigated.

Mouse Lymphoma Assay (MLA)

Internal Studies	Level Tested ppm	Comment
N/A	N/A	N/A

In vivo Micronucleus

Internal Studies	Level Tested ppm	Comment
N/A	N/A	N/A

Inhalation studies

Internal Studies	Level Tested ppm	Comment
Carmines for Philip Morris	12, 13, 37, 39	The effect of the addition of 4-methylacetophenone as part of a mixture at concentrations up to 39 ppm on the toxicity of cigarette smoke, as suggested in a 90-day inhalation study, was investigated.

References

1. NAS (1989) National Academy of Sciences. 1987 Poundage and Technical Effects Update of Substances Added to Food. CFSAN, FDA, 200 C Street S.W., Washington, D.C. 20204. p. 117, 370.

2. Lucas, C. D.; Putnam, J. M. and Hallagan, J. B. (1999) 5-Ethyl-3-hydroxy-4-methyl-2(5H)-furanone. In 1995 Poundage and Technical Effects Update Survey. Flavor and Extract Manufacturers' Association of the United States, Washington, DC. p. 106.

3. Stofberg, J. and Grundschober, F. (1987) Consumption ratio and food predominance of flavoring materials: Third cumulative series. Perfumer & Flavorist 12:1-27.

4. USDA (2000) Continuing Survey of Food Intakes by Individuals (CSFII) 1994-96, 1998. Agricultural Research Service, Beltsville Human Nutrition Research Center, NTIS PB2000-500027 (CD-ROM).