

# Methyl pyrazine (2-)

## Botanical Source

**Synonyms** METHYL PYRAZINE;  
METHYL-1,4-DIAZINE (2-)

## IUPAC Name

**CAS Reference** 109-08-0

## E Number

## Food Legislation

### Council of Europe (CoE)

| Number | Comment                                                                        |
|--------|--------------------------------------------------------------------------------|
| 2270   | Listed by the Council of Europe as acceptable for use in food at up to 10 ppm. |

### US Food and Drug Administration

| Number | Comment |
|--------|---------|
| -      | -       |

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

| Number | ADI | Comment                                                                        |
|--------|-----|--------------------------------------------------------------------------------|
| 761    | 20  | No safety concern at current levels of intake when used as a flavouring agent. |

### FEMA

| FEMA No. | Comment                                                                 |
|----------|-------------------------------------------------------------------------|
| 3309     | Generally recognised as safe as a flavour ingredient:GRAS List Number 3 |

### Natural Occurrence and Use in Food

|                                                                                      |
|--------------------------------------------------------------------------------------|
| Found in peppermint oil, tomato, popcorn, used in milk products, baked goods, candy. |
|--------------------------------------------------------------------------------------|

### Estimated Intake from Food and Drink

| Daily Intake mg/kg/day | FEMA Possible Average Daily Intake mg |
|------------------------|---------------------------------------|
| 0.0001836              | 4.709                                 |

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### Tobacco Product Related Chemical and Biological Studies

| Smoke Chemistry  |                |                                                                                                                                    |
|------------------|----------------|------------------------------------------------------------------------------------------------------------------------------------|
| Published Source | Level Tested % | Comment                                                                                                                            |
| BAT              | 0.00250        | At maximum application level this ingredient is not associated with significant increases in levels of Hoffmann analytes in smoke. |

| Ames Activity    |                |                                                                                                                                                               |
|------------------|----------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Published Source | Level Tested % | Comment                                                                                                                                                       |
| BAT              | 0.00250        | 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. |

| Micronucleus     |                |                                                                                                                                                               |
|------------------|----------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Published Source | Level Tested % | Comment                                                                                                                                                       |
| BAT              | 0.00250        | 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              | 0.00250        | 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. |

| Inhalation       |                |                                                                                                                                    |
|------------------|----------------|------------------------------------------------------------------------------------------------------------------------------------|
| Published Source | Level Tested % | Comment                                                                                                                            |
| BAT              | 0.00250        | The results indicate that the addition of the ingredient had no discernible effect on the inhalation toxicity of mainstream smoke. |
| Lorillard        | 0.00007        | The results indicate that the addition of the ingredient had no discernible effect on the                                          |

|  |  |                                          |
|--|--|------------------------------------------|
|  |  | inhalation toxicity of mainstream smoke. |
|--|--|------------------------------------------|

| Mouse Skin Painting |                |                                                                                                                                                                                                                                                                                        |
|---------------------|----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Published Source    | Level Tested % | Comment                                                                                                                                                                                                                                                                                |
| Lorillard           | 0.00007        | 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.                                                                                     |
| 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                                                                                             |
|--------------------------------------------------------------------------------------------------------|
| 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                                                                           | Reference                       |
|--------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|---------------------|----------------------------------------------------------------------------------|---------------------------------|
| Chinese hamster ovary cells                      | Incubated for 3 hr at several concentrations up to 40 mg/ml. Metaphase cells (100-200 per sample) examined 20 hr later for chromosome aberrations.<br><br>(single test concentration of 30 mg/ml recorded in Stich <i>et al.</i> 1981) | Chromosome damage | With and without S9 | +ve                                                                              | Stich <i>et al.</i> 1980 & 1981 |
| <i>Salmonella typhimurium</i> TA98, TA100, TA102 | Ames test on “methylpyrazine” at up to 1 mmol/plate [up to 94 mg/plate].                                                                                                                                                               | Mutation          | With and without S9 | -ve<br><br>(limited assay, testing in 4 strains is usually recommended )         | Aeschbacher <i>et al.</i> 1989  |
| <i>Salmonella typhimurium</i> TA98, TA100        | Ames test, tested amounts were not disclosed.                                                                                                                                                                                          | Mutation          | With and without S9 | -ve<br><br>(limited study, only 2 strains used, revertant numbers not presented) | Lee <i>et al.</i> 1994          |

|                                                           |                                                                                                                                                                                                                                                                                                                                                                  |                              |                     |                                                                                                                    |                           |
|-----------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|---------------------|--------------------------------------------------------------------------------------------------------------------|---------------------------|
| <i>Salmonella typhimurium</i> TA98, TA100, TA1537         | Ames, tested at up to 100 mg/plate (included toxic levels).                                                                                                                                                                                                                                                                                                      | Mutation                     | With and without S9 | -ve<br><br>(limited assay, only 3 strains used)                                                                    | Stich <i>et al.</i> 1980  |
| <i>Salmonella typhimurium</i> TA98, TA100, TA1535, TA1537 | Ames, tested at up to 3 umol/plate [0.28 mg/plate].<br><br>Then tested at 0, 0.03, 0.3 and 30 umol/plate [up to 2.8 mg/plate] in TA100 only.                                                                                                                                                                                                                     | Mutation                     | With and without S9 | -ve<br><br>(the detailed test in TA100 was carried out due to an uncertain result in this strain in the spot test) | Florin <i>et al.</i> 1980 |
| <i>Saccharomyces cerevisiae</i> D5                        | White colonies treated at up to 67.5 mg/ml for 4 hr, cells plated and scored 7 days later for colonies containing pink or red pigment, indicative of one of several types of gene mutation, including gene conversion, point mutations, chromosome deletions and aneuploidy. Colonies containing both pink and red pigments were scored as mitotic recombinants. | Gene mutation, various types | Without             | +ve for mutations<br><br>-ve for recombinants                                                                      | Stich <i>et al.</i> 1980  |

## References

Aeschbacher H U *et al* (1989). Contribution of coffee aroma constituents to the mutagenicity of coffee. *Food and Chemical Toxicology*, 27, 227-232.

Florin I *et al* (1980). Screening of tobacco smoke constituents for mutagenicity

using the Ames test. *Toxicology*, 15, 219-232.

Lee H *et al* (1994). Genotoxicity of 1,3-dithiane and 1,4-dithiane in the CHO/SCE assay and the *Salmonella*/microsomal test. *Mutation Research*, 321, 213–218.

Stich H F *et al* (1980). Mutagenic activity of pyrazine derivatives: A comparative study with *Salmonella typhimurium*, *Saccharomyces cerevisiae* and Chinese hamster ovary cells. *Food and Cosmetics Toxicology*, 18, 581–584.

Stich H F *et al* (1981). Intake, formation and release of mutagens by man. Banbury Report, 7, 247-266.