# Substance Information Document

# 4-(para-Hydroxyphenyl)-2-butanone

## 1. Substance identity

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| Name | 4-(para-Hydroxyphenyl)-2-butanone |
| Synonyms | Raspberry ketone<br>4-(4-Hydroxyphenyl)-2-butanone<br>4-(*p*-Hydroxyphenyl)-2-butanone<br>1-(4-Hydroxyphenyl)-3-butanone |
| IUPAC Name | 4-(4-hydroxyphenyl)butan-2-one |
| CAS | 5471-51-2 |

## 2. Toxicological information

4-(para-Hydroxyphenyl)-2-butanone, probably undiluted, caused evidence of skin irritation in nine of 13 workers, but skin irritation was not observed when a 12% concentration was applied to the skin of 25 subjects for 48 hours. In OECD Guideline 439 in vitro skin irritation test was not irritating. In OECD Guideline 437 in vitro eye irritation, an unspecified concentration of 4-(para-hydroxyphenyl)-2-butanone was not irritating when instilled into one eye of each rabbit. No respiratory tract irritation data were identified.

No evidence of skin sensitisation was seen in a human maximization test (using a 12% test material) or a mouse local lymph node assay (at up to 50%).

No acute or repeated-dose inhalation toxicity data were identified. 4-(para-Hydroxyphenyl)-2-butanone was of low to moderate acute oral systemic toxicity in rodents (LD50 values of about 640 to >2000 mg/kg bw) and very low acute dermal systemic toxicity in rabbits (LD50 of >5000 mg/kg bw). In a guideline-compliant study, rats were fed diets containing 4-(para-hydroxyphenyl)-2-butanone for 90 days. Liver weight (both sexes) and clinical chemistry changes (females only) were statistically significantly increased at 275 mg/kg bw/day and above. Based on these effects, the NOAEL was considered to be 70 mg/kg bw/day. Evaluation included gross and microscopic examination of a wide range of tissues (including the heart, lung, and reproductive organs).

4-(para-hydroxyphenyl)-2-butanone is considered no genotoxic. No concerns for bacterial or mammalian cell mutagenicity (in vitro) were observed. Conflicting results were obtained in chromosome aberration tests in vitro, but 4-(para-hydroxyphenyl)-2-butanone did not increase the incidence of micronuclei in the bone marrow of mice in an oral test. No standard reproductive, developmental, or carcinogenicity studies were identified.

Existing expert-group health-based guidance values were not identified, but JECFA and EFSA have raised no human health concerns over the use of 4-(para-hydroxyphenyl)-2-butanone as a flavouring in the diet.

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| JECFA | PHENOL AND PHENOL DERIVATIVES (inchem.org) |

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| FEMA | 0320 FEMA GRAS 29 (femaflavor.org) |
| EFSA | Scientific Opinion on Flavouring Group Evaluation 22, Revision 1 (FGE.22Rev1): Ring-substituted phenolic substances from chemical groups 21 and 25 (wiley.com) |
| ECHA – REACH dossier | Registration Dossier - ECHA (europa.eu) |
| PUBCHEM | 4-(4-Hydroxyphenyl)-2-butanone \| C10H12O2 - PubChem (nih.gov) |
| CIR | - |
| OSHA | - |

## 3. Addictiveness and attractiveness

No substance-specific addictiveness data were identified.

In an investigation into the most common flavouring ingredients added to e-liquids on the Dutch market, 4-(para-hydroxyphenyl)-2-butanone was identified in 9.43% of e-liquid samples. The investigators noted that such flavourings increase e-cigarette attractiveness and use and thereby exposure to potentially toxic ingredients.

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| SCENIHR | - |
| EMA | - |
| PUBMED | Comprehensive overview of common e-liquid ingredients and how they can be used to predict an e-liquid's flavour category - PubMed (nih.gov) |