

OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION

WASHINGTON, D.C. 20460

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MEMORANDUM

SUBJECT: IN-11401; Various Fragrance Components. Human Health Risk Assessment and Ecological Effects Assessment to Support Inert Ingredient Approval for use in Pesticide Formulations

PC Code: Multiple (See Section III) Decision No.: 560320 Petition No.: IN-11401 CAS No.: Multiple (See Section III) Registration No.: N/A Regulatory Action: Addition to inert ingredient list

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1. EXECUTIVE SUMMARY

In February 2020, Innovative Reform Group (IRG), on behalf of The Clorox Company, submitted a petition (IN-11401) to the Environmental Protection Agency (EPA or the Agency) requesting an exemption from the requirement of tolerance for various fragrances (CAS Reg. No. multiple) as inert ingredients for use under 40 CFR § 180.940(a) in antimicrobial pesticide formulations used on food contact surfaces in public eating places, dairy processing equipment, and food processing equipment and utensils with end-use concentration not to exceed 33 ppm.

Although there is generally a lack of chemical-specific animal toxicity data for these fragrances, predictive toxicology indicates low potential for carcinogenicity and the expected use concentration is low. Therefore, the Agency assessed these fragrance components via the Threshold of Toxicological Concern (TTC) approach as outlined by the European Food Safety Authority (EFSA) in their 2019 guidance document on the use of TTC in food safety assessment.

TTCs are derived from a conservative and rigorous approach developed by Munro and Kroes to establish generic threshold values for human exposure at which a very low probability of adverse effects is likely. By comparing a range of compounds by Cramer Class (classes I, II, and III) and NOEL (no-observed-effect-level), fifth percentile NOELs were established for each Cramer Class as "Human Exposure Thresholds". These values were 3, 0.91 and 0.15 mg/kg/day for classes I, II and III, respectively. All fragrances in this document are in Cramer class II; therefore, this assessment uses the NOEL of 0.91 mg/kg/day as the point of departure for all exposure scenarios assessed (chronic dietary, incidental oral, dermal and inhalation exposures).

The dietary assessment for food contact sanitizer solutions calculated the Daily Dietary Dose (DDD) and the Estimated Daily Intake (EDI). The assessment considered: application rates, residual solution or quantity of solution remaining on the treated surface without rinsing with potable water, surface area of the treated surface which comes into contact with food, pesticide migration fraction, and body weight. These assumptions are based on FDA guidelines (1993).

The dietary assessment for food contact sanitizer solutions showed that children 1-2 years old would be the highest exposed subgroup (58% of the cPAD). The general U.S. population resulted in 21% of the cPAD. As these percent cPADs do not exceed 100%, they are not of concern.

Combined short-term aggregated food, water, and residential pesticidal exposures result in MOEs of 455 for both adult males and females and 168 for children. As the level of concern is for MOEs that are lower than 100, these MOEs are not of concern.

Although the proposed use for these fragrances as an inert ingredient in antimicrobial products is expected for residential use, it is possible that these products could be used in commercial

settings. However, exposures in commercial settings have already been incorporated into the FDA model used. Therefore, an additional occupational exposure assessment is not needed.

Environmental fate and ecological effects are expected to be minimal as only indoor exposure scenarios are anticipated.

Taking into consideration all available information for the fragrances listed in this document, EPA has determined that there is a reasonable certainty that no harm to the general population or any population subgroup, including infants and children, will result from aggregate exposure to residues of these fragrances. Therefore, the establishment of an exemption from the requirement of a tolerance under 40 CFR 180.940 for residues of the listed fragrances when used as inert ingredients in pesticide formulations at concentrations not to exceed 33 ppm of the formulation can be considered assessed as safe under section 408 of the FFDCA.

2. BACKGROUND

In February 2020, Innovative Reform Group, on behalf of The Clorox Company, submitted a petition (IN-11401) requesting an exemption from the requirement of a tolerance for various chemicals (CAS Reg. No. multiple, listed in section III) as inert ingredients under 40 CFR § 180.940(a) for use as fragrance components in antimicrobial pesticide formulations for use on food contact surfaces in public eating places, dairy processing equipment, and food processing equipment and utensils at end-use concentrations not to exceed 33 parts per million (ppm). EPA published the notice of filing (NOF) for this petition in the Federal Register on June 2, 2021 (86 FR 29229). No substantive comments were received in response to this notice.

Although there generally is limited animal toxicity data for the listed fragrances, there is a predicted low carcinogenic potential for these substances and these fragrances will be used at low concentrations (≤33ppm) in pesticide formulations. Therefore, the Agency will be assessing these fragrance components via the Threshold of Toxicological Concern (TTC) approach as outlined by the European Food Safety Authority (EFSA) in their 2019 guidance document on the use of TTC in food safety assessment. This approach relies on the most recent evaluation of the literature on TTC as reviewed by EFSA and the World Health Organization (WHO) in 2016. Information regarding the database of studies and chemicals used to derive TTCs are reviewed therein. The TTC approach has been used by the Joint Expert Committee on Food Additives of the U.N.'s Food and Agriculture Organization and the World Health Organization, the former Scientific Committee on Food of the European Commission and by the European Medicines Agency, and EFSA. Details about how the TTC method is applied can be found in section IV of this document.

This document provides an assessment of the risk to human health and the environment for the listed chemicals when used as inert ingredients (fragrance) in food-use antimicrobial

pesticide formulations. Information from the submitter's petition is referenced in this assessment.

3. INERT INGREDIENT PROFILE

The Clorox Company proposes amending the 40 CFR 180.940(a) to include the following fragrance components: For more details, including molecular formulas and simplified molecular-input line-entry system (SMILES) for each of these chemicals, please see Appendix III.

| Chemical Name in EPA Pesticide Databases | CAS Reg. No. | Chemical name Provided in Petition | Current Inert Ingredient Approval Status |
|--|-----------------|--|--|
| Acetoin | 513-86-0 | Acetoin | Fragrance Use |
| 4-acetyl-6-t-butyl-1,1- | | 4-acetyl-6-t-butyl-1,1- | |
| dimethylindan | 13171-00-1 | dimethylindan | Fragrance Use |
| Allyl cinnamate | 1866-31-5 | Allyl cinnamate | Fragrance Use |
| Allyl heptanoate | 142-19-8 | Allyl heptanoate | Fragrance Use |
| Allyl hexanoate | 123-68-2 | Allyl hexanoate | Fragrance Use |
| Allyl propionate | 2408-20-0 | Allyl propionate | Fragrance Use |
| Heptanal, 2-(phenlymethylene)- | 122-40-7 | alpha-Amylcinnamaldehyde | Nonfood Use/Fragrance Use |
| .alphaButylcinnamaldehyde | 7492-44-6 | alpha-Butylcinnamaldehyde | Fragrance Use |
| 2-secButylcyclohexanone | 14765-30-1 | 2-sec-butylcyclohexanone | Fragrance Use |
| Bicyclo[2.2.1]heptan-2-one, 1,7,7- trimethyl-, (1R, 4R)- | 464-49-3 | d-Camphor | Nonfood Use/Fragrance Use |
| Camphor | 21368-68-3 | dl-Camphor | Food (180.920) no more than 5%w/w |
| Cajeput oil (Melaleuca | | Cajeput oil (Melaleuca | |
| leucadendron L.) | 8008-98-8 | leucadendron L.) | Fragrance Use |
| Cardamom (Elettaria | | Cardamom (Elettaria cardamomum | |
| cardamomum (L.) Maton) | 85940-32-5 | (L.) Maton) | Fragrance Use |
| Cardamom seed oil (Elettaria cardamomum (L.) Maton) | 8000-66-6 | Cardamom seed oil (Elettaria cardamomum (L.) Maton) | Fragrance Use |
| 7-Oxabicyclo(2.2.1.)heptane, 1- methyl-4-(1-methylethyl)- | 470-67-7 | 1,4-Cineole | Nonfood Use/Fragrance Use |
| Tetrahydro-6-(3-pentenyl)-2H- pyran-2-one | 32764-98-0 | 8-Decen-5-olide | Fragrance Use |
| 3,4-Dimethyl-1,2-cyclopentadione | 13494-06-9 | 3,4-Dimethyl-1,2-cyclopentadione | Fragrance Use |
| Diisobutyl ketone | 108-83-8 | 2,6-Dimethyl-4-heptanone | Nonfood Use/Fragrance Use |
| 2,5-Dimethylpyrazine | 123-32-0 | 2,5-Dimethylpyrazine | Fragrance Use |
| 2,6-Dimethylpyrazine | 108-50-9 | 2,6-Dimethylpyrazine | Fragrance Use |
| 6,10-Dimethylundeca-5,9-dien-2- | | 6,10-Dimethyl-5,9-undecadien-2- | <u> </u> |
| one | 689-67-8 | one | Fragrance Use |
| | | | Food (180.910 + 180.920 + 180.930)/Nonfood |
| | | | 100.320//10011000 |

| | | | Food (180.910 + |
|-----------------------------------|------------|-------------------------------------|----------------------|
| | | | 180.930)/Nonfood |
| Ethyl maltol | 4940-11-8 | Ethyl maltol | Use/Fragrance Use |
| 2-Ethyl-3-methylpyrazine | 15707-23-0 | 2-Ethyl-3-methylpyrazine | Fragrance Use |
| | | | Nonfood |
| Ethylvanillin | 121-32-4 | Ethyl vanillin | Use/Fragrance Use |
| | | | Nonfood |
| p-Menthane, 1,8-epoxy- | 470-82-6 | Eucalyptol | Use/Fragrance Use |
| | | Eucalyptus oil (Eucalyptus globulus | Nonfood |
| Eucalyptus oil | 8000-48-4 | Labill) | Use/Fragrance Use |
| Fenchone | 4695-62-9 | d-Fenchone | Fragrance Use |
| | | | Food (180.910 + |
| | | | 180.930)/Nonfood |
| Methyl n-amyl ketone | 110-43-0 | 2-Heptanone | Use/Fragrance Use |
| 3-Heptanone | 106-35-4 | 3-Heptanone | Fragrance Use |
| 2,3-Hexanedione | 3848-24-6 | 2,3-Hexanedione | Fragrance Use |
| | | | Nonfood |
| alpha-Hexylcinnamaldehyde | 101-86-0 | alpha-Hexylcinnamaldehyde | Use/Fragrance Use |
| 4-Hydroxy-2,5-dimethyl-3(2H)- | | 4-Hydroxy-2,5-dimethyl-3(2H)- | |
| furanone | 3658-77-3 | furanone | Fragrance Use |
| Phenylethyl isoamyl ether | 56011-02-0 | Isoamyl phenethyl ether | Fragrance Use |
| 2-Isobutyl-3-methoxypyrazine | 24683-00-9 | 2-Isobutyl-3-methoxypyrazine | Fragrance Use |
| alpha-Isobutylphenethyl alcohol | 7779-78-4 | alpha-Isobutylphenethyl alcohol | Fragrance Use |
| Isojasmone | 11050-62-7 | Isojasmone | Fragrance Use |
| d,I-Isomenthone | 491-07-6 | d,l-Isomenthone | Fragrance Use |
| 2-Isopropyl-4-methylthiazole | 15679-13-7 | 2-Isopropyl-4-methylthiazole | Fragrance Use |
| | | | No current pesticide |
| Linalool oxide | 60047-17-8 | Linalool oxide | use |
| | | | No current pesticide |
| (Z)-Linalool oxide | 5989-33-3 | Linalool oxide | use |
| | | | No current pesticide |
| (E)-Linalool oxide | 34995-77-2 | Linalool oxide | use |
| 4H-Pyran-4-one, 3-hydroxy-2- | | | Nonfood |
| methyl- | 118-71-8 | Maltol | Use/Fragrance Use |
| Maltyl isobutyrate | 65416-14-0 | Maltyl isobutyrate | Fragrance Use |
| p-Mentha-8-thiol-3-one | 38462-22-5 | p-Mentha-8-thiol-3-one | Fragrance Use |
| 1-p-Menthene-8-thiol | 71159-90-5 | 1-p-Menthene-8-thiol | Fragrance Use |
| | | | No current pesticide |
| p-Menthan-3-one | 10458-14-7 | Menthone | use |
| 2-Methoxy-3-(1- | | 2-Methoxy-3-(1- | |
| methylpropyl)pyrazine | 24168-70-5 | methylpropyl)pyrazine | Fragrance Use |
| 3-Methyl-1-cyclopentadecanone | 541-91-3 | 3-Methyl-1-cyclopentadecanone | Fragrance Use |
| Methylcyclopentenolone | 80-71-7 | Methylcyclopentenolone | Fragrance Use |
| Cyclopentaneacetai acid, 3-oxo-2- | | | Nonfood |
| pentyl-, methyl ester | 24851-98-7 | Methyl dihydrojasmonate | Use/Fragrance Use |
| 6-Methyl-3,5-heptadien-2-one | 1604-28-0 | 6-Methyl-3,5-heptadien-2-one | Fragrance Use |
| 6-Methyl-5-hepten-2-one | 110-93-0 | 6-Methyl-5-hepten-2-one | Fragrance Use |
| 3-Methyl-2-(n-pentanyl)-2- | | 3-Methyl-2-(n-pentanyl)-2- | |
| cyclopenten-1-one | 1128-08-1 | cyclopenten-1-one | Fragrance Use |

| 3-Methyl-2-(2-pentenyl)-2- | 488-10-8 | 3-Methyl-2-(2-pentenyl)-2- | |
|---|-----------------|---|------------------------------|
| cyclopenten-1-one, (Z)- | | cyclopenten-1-one | Fragrance Use |
| 3-Methyl-2-(2E)-2-penten-1-yl-2- | | 3-Methyl-2-(2-pentenyl)-2- | No current pesticide |
| cyclopenten-1-one | 6261-18-3 | cyclopenten-1-one | use |
| Methyl phenethyl ether | 3558-60-9 | Methyl phenethyl ether | Fragrance Use |
| 5-Methyl-2-phenyl-2-hexenal | 21834-92-4 | 5-Methyl-2-phenyl-2-hexenal | Fragrance Use |
| 2-Methyl-4-propyl-1,3-oxathiane | 67715-80-4 | 2-Methyl-4-propyl-1,3-oxathiane | Fragrance Use |
| 2-Methylpyrazine | 109-08-0 | 2-Methylpyrazine | Fragrance Use |
| 5-Methyl-2- | | 5-Methyl-2- | |
| thiophenecarboxyaldehyde | 13679-70-4 | thiophenecarboxyaldehyde | Fragrance Use |
| Cyclopropanemethanol, 1- methyl-2-[(1,2,2- trimethylbicyclo[3.1.0]hex-3- yl)methyl]- | 198404-98- 7 | (1-Methyl-2-(1,2,2- trimethylbicyclo[3.1.0]hex-3- ylmethyl)cyclopropyl)methanol | Fragrance Use |
| | | 3-Methyl-5-(2,2,3- | |
| 3-Methyl-5-(2,2,3-trimethyl-3- | | trimethylcyclopent-3-en-1-yl)pent- | |
| cyclopenten-1-yl)pent-4-en-2-ol | 67801-20-1 | 4-en-2-ol | Fragrance Use |
| Nerol oxide | 1786-08-9 | Nerol oxide | Fragrance Use |
| 2-Nonanone | 821-55-6 | 2-Nonanone | Fragrance Use |
| Nootkatone | 4674-50-4 | Nootkatone | Fragrance Use |
| 2-Octanone | 111-13-7 | 2-Octanone | Fragrance Use |
| | | | Nonfood |
| Ethyl amyl ketone | 106-68-3 | 3-Octanone | Use/Fragrance Use |
| | | | Nonfood |
| 1-Octen-3-ol | 3391-86-4 | 1-Octen-3-ol | Use/Fragrance Use |
| | | Rosemary oil (Rosemarinus | Nonfood |
| Oils, rosemary | 8000-25-7 | officinalis L.) | Use/Fragrance Use |
| | | Sage oil, Spanish (Salvia | Nonfood |
| Oils, sage | 8022-56-8 | lavandulaefolia Vahl.) | Use/Fragrance Use |
| | | | Nonfood |
| Origanum oil, Spanish | 8007-11-2 | Origanum oil | Use/Fragrance Use |
| 1,3-Benzodioxole-5- | | | Nonfood |
| carboxaldehyde | 120-57-0 | Piperonal | Use/Fragrance Use |
| Piperonyl acetate | 326-61-4 | Piperonyl acetate | Fragrance Use |
| Rue oil (Ruta graveolens L.) | 8014-29-7 | Rue oil (Ruta graveolens L.) | Fragrance Use |
| Tetrahydro-4-methyl-2-(2- | | Tetrahydro-4-methyl-2-(2- | |
| methylpropen-1-yl)pyran | 16409-43-1 | methylpropen-1-yl)pyran | Fragrance Use |
| Theaspirane | 36431-72-8 | Theaspirane | Fragrance Use |
| 2-Tridecanone | 593-08-8 | 2-Tridecanone | Fragrance Use |
| 2-Undecanone | 112-12-9 | 2-Undecanone | Nonfood Use/Fragrance Use |

In the case of the fragrance components listed above, most of these chemicals already have EPA approval for nonfood use in pesticide formulations. Also, many of these substances have been approved for use as a flavoring substance in food under 21 CFR 172.515 or 182.60 by the U.S. Food and Drug Administration (FDA). Additionally, the fragrance components listed above have all been evaluated and approved for use as food flavoring agents by the Joint Food and Agricultural Organization of the United Nations/World Health Organization Expert Committee

on Food Additives (JECFA) as part of their assessment of more than 2,300 food flavoring substances. Toxicological profiles on each are available via the links to the relevant JECFA summary in Appendix II.

4. HAZARD CHARACTERIZATION

4.1. Toxicology Summary

There is limited animal toxicity information available for the fragrances listed in section III. The Joint FAO/WHO Expert Committee on Food Additives (JECFA) reviewed available toxicity information for these chemicals and structurally related compounds in a series of reports, as described in Appendix II. Information from these reports as well as predictive toxicology using the OECD QSAR Toolbox was used to confirm that the fragrances listed in section III have low carcinogenic potential and are thus good candidates for the application of the TTC method. For most chemicals, no alerts were found using the carcinogenicity (genotox and nongenotox) alerts by the ISS tool in the OECD QSAR Toolbox (see Appendix III). For 17 chemicals (CAS Reg. Nos. 120-57-0; 326-61-4; 118-71-8; 3658-77-3; 65416-14-0; 1128-08-1; 488-10-8; 6261-18-3; 11050-62-7; 21834-92-4; 1604-28-0; 4674-50-4; 80-71-7; 13679-70-4; 121-32-4; 67801-20-1; 104-76-7), carcinogenicity alerts were found with the QSAR Toolbox. However, JECFA has concluded in its reports, and EPA concurs, that these 17 chemicals all have a low carcinogenic potential, based on *in vitro* and/or *in vivo* genotoxicity studies available on the chemical or structurally related chemicals (see Appendix II). Therefore, the TTC method can be applied to all fragrances listed in section III.

Munro (1996) developed TTC values for non-cancer effects which were based on analyses of NOAELs from repeated dose toxicity data for chemicals separated into three structural classes using the Cramer (1978) decision scheme. A TTC value was calculated from the respective distribution of NOELs for each of the 3 Cramer structural classes, using a database of 613 chemicals with 2941 NOELs. These substances represent a range of industrial chemicals, pharmaceuticals, food chemicals and environmental, agricultural and consumer chemicals likely to be encountered in commerce with good supporting toxicological data, yielding 137, 28 and 448 chemicals in Cramer class I, II and III, respectively. For each of the 613 chemicals, the most conservative NOEL was selected, based on the most sensitive species, sex and endpoint. The fifth percentile NOEL (in mg/kg bw/day) was calculated for each structural class as "Human Exposure Thresholds". These values were 3, 0.91 and 0.15 mg/kg/day for classes I, II and III, respectively.

The TTC values for Cramer structural classes derived by Munro in 1996 have been supported by all subsequent analyses of additional databases (providing that the 5th percentile NOEL/NOAEL is converted to a TTC value using the same 100-fold safety factor). Blackburn (2005) analyzed a database of 145 chemicals found in personal and household products; Bernauer (2008) analyzed reproductive and developmental toxicity data for 91 chemicals assessed for oral toxicity under REACH; Brown (2009) analyzed data for 100 active pesticides and 15 pesticide

metabolites and concluded that the TTC values are valid; Pinalli (2011) analyzed the TDIs for 232 food contact materials in relation to the TTC and found that the distribution of recalculated NOAELs was similar to that reported by Munro; Tluczkiewicz (2011) analyzed the RepDose database of 521 chemicals, using dose levels expressed on a molar basis making direct comparison difficult, but the distribution of NOAELs, the overlap between Cramer classes and the TTC values were comparable to Munro; van Ravenzwaay (2011) analyzed data for pre-natal toxicity using NOAELs for maternal and developmental toxicity and found 5th percentile values higher (maternal NOAELs = 4 mg/kg/day, developmental NOAELs = 5 mg/kg/day) than those used by Munro (NOEL = 3 mg/kg/day); Kalkhof (2012) analyzed NOAELs from subacute and subchronic studies (with adjustment for duration of study) on 813 different chemicals and found TTC values for Cramer classes I, II and III similar to those of Munro; Laufersweiler (2012) analyzed reproductive and developmental toxicity data for 283 chemicals and generated TTC values 2-3 times higher than those of Munro. Feigenbaum (2015) assessed the reliability of the TTC approach using 328 pesticides that had been fully evaluated by the EU and by EFSA and concluded that the respective TTC values are protective, even for these biologically active substances.

4.2. Toxicity Endpoint Selection

As outlined in section IV, fifth percentile NOELs established by Munro are 3, 0.91 and 0.15 mg/kg/day for Cramer classes I, II and III, respectively. In the case of the fragrance components listed above, they are all in the Cramer Class II category, which is defined as less innocuous than substances in Class I, but no positive indication of toxic potential. Therefore, the 5th percentile NOEL value of 0.91 mg/kg/day is selected as the point of departure (POD) for all exposure scenarios, as described in Table 2 below.

The OECD Toolbox outputs are provided in Appendix III. Multiple of the OECD Toolbox outputs suggested Cramer classes other than "II". However, all chemicals in this document were ultimately classified as Cramer class II. Please see explanations and justifications in Appendix IV.

| Table 2. Summary of Tox Assessments. | icological Doses | and Endpoints for Variou | is Fragrances for Use | e in Human Health Risk | | | | | | |
|---|--|---|--|---|--|--|--|--|--|--|
| Exposure/ Scenario | POD | Uncertainty/FQPA Safety Factors | RfD, PAD, LOC for Risk Assessment | Study and Toxicological Effects | | | | | | |
| Acute Dietary (All Populations) | | Not selected. No appropriate toxicological endpoint attributable to a single exposure was identified. | | | | | | | | |
| Chronic Dietary (All Populations) | 5th percentile NOEL = 0.91 mg/kg/day | UFA =10X UFH =10X FQPA= 1X Total UF=100 | cRfD = 0.0091 mg/kg/day cPAD = 0.0091 mg/kg/day | Munro et al 1996 TTC method using cumulative distribution of NOELs | | | | | | |

| Table 2. Summary of Toxicological Doses and Endpoints for Various Fragrances for Use in Human Health Risk | |
|---|--|
| Assessments. | |

| Assessments. | | | | | |
|--|--|--|---|---|--|
| Exposure/ Scenario POD | | Uncertainty/FQPA Safety Factors | RfD, PAD, LOC for Risk Assessment | Study and Toxicological Effects | |
| Incidental Oral (Short-Term) | 5th percentile NOEL = 0.91 mg/kg/day | UFA =10X UFH =10X FQPA= 1X Total UF=100 | LOC for MOE = 100 | Munro et al 1996 TTC method using cumulative distribution of NOELs | |
| Dermal and Inhalation (Short-Term and Intermediate-Term) | 5th percentile NOEL = 0.91 mg/kg/day | UFA =10X UFH =10X FQPA= 1X Total UF=100 | LOC for MOE = 100 | Munro et al 1996 TTC method using cumulative distribution of NOELs | |

Point of departure (POD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOEL = no-observed-effect level. UF = uncertainty factor. UF_A = extrapolation from animal to human (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies).FQPA SF = FQPA Safety Factor. PAD = population-adjusted dose (a = acute, c = chronic). RfD = reference dose. MOE = margin of exposure. LOC = level of concern.

4.3. Special Considerations for Infants and Children

FFDCA Section 408(b)(2)(C) provides that EPA shall retain an additional tenfold (10X) margin of safety for infants and children in the case of threshold effects to account for prenatal and postnatal toxicity and the completeness of the database on toxicity and exposure unless EPA determines based on reliable data that a different margin of safety will be safe for infants and children. This additional margin of safety is commonly referred to as the FQPA safety factor (SF). In applying this provision, EPA either retains the default value of 10X, or uses a different additional safety factor when reliable data available to EPA support the choice of a different factor. The FQPA SF has been reduced to 1X in this risk assessment because clear NOELs and LOELs were established in the studies analyzed by Munro et al 1996 (which included developmental and reproductive toxicity studies), maternal and developmental-specific 5th percentile NOAELs calculated by van Ravenzwaay et al 2011 indicate low potential for offspring susceptibility, and the conservative assumptions made in the exposure assessment are unlikely to underestimate risk.

5. DIETARY EXPOSURE

Dietary exposure (food and drinking water) may occur from the existing and proposed pesticidal uses of these various fragrances (e.g., eating foods placed on surfaces cleaned with pesticide formulations containing these various fragrances, and drinking water exposures). Dietary exposure may also occur from non-pesticidal uses but no reliable information is available for non-pesticidal exposures. Therefore, EPA assessed dietary exposures from pesticidal uses of these various fragrances only.

The FDA food contact surface sanitizing solution dietary exposure assessment model was used to calculate an Estimated Daily Intake (EDI) and Daily Dietary Dose (DDD) using assumptions described in Appendix I. The original FDA model only derived an exposure amount but did not specifically address population subgroups. Therefore, data from the National Health and Nutrition Examination Survey (NHANES) on food consumption (specifically the 2005-2010 survey data) was used to obtain adjustment factors (AFs). Adjusted DDDs for the US population and various population subgroups were obtained by multiplying the DDDs by the AFs, as described in Table 3. The %cPADs were then calculated by comparing the cPAD to the adjusted DDDs.

<u>Acute Dietary Risk Assessment</u>: No acute dietary effects are anticipated from uses at concentrations ≤ 33 ppm. Therefore, a quantitative acute dietary assessment is not necessary.

<u>Chronic Dietary Risk Assessment</u>: The chronic dietary exposure for food and drinking water utilized 21% and 58% of the cPAD for the U.S. population and children 1-2 years old (the most highly exposed population), respectively (see results in Table 3 and assumptions in Appendix II). These risks were not of concern (i.e. values were below 100% of the cPAD).

<u>Cancer Dietary Risk Assessment</u>: These various fragrances are not expected to be carcinogenic, based on their TTC evaluation. Therefore, a cancer dietary exposure assessment was not performed.

| Table 3: Chronic Dietary Exposure Assessment for Food-contact Surface Sanitizing Uses | | | | | | | | | | | | |
|---|--|---|---|---------|--|--|--|--|--|--|--|--|
| | | Risk Estimates | | | | | | | | | | |
| Population Group | Exposure (DDD ¹ in mg/kg/day) | Adjustment factor ² (Consumption Ratio) | Total Exposure (Adjusted DDD ³ in mg/kg/day) | % cPAD⁴ | | | | | | | | |
| General U.S. Population | 0.0018803 | 1.000000 | 0.001880 | 21 | | | | | | | | |
| Children (1-2 years old) | 0.0104762 | 0.5068493 | 0.005310 | 58 | | | | | | | | |
| Females (13-49 years old) | 0.0018107 | 0.8664384 | 0.001569 | 17 | | | | | | | | |

¹ DDD = Daily Dietary Dose = Estimated Daily Intake/Body weight

² Adjustment factor (AF)= total food consumed by each population/total food consumed by the US population

³ Adjusted DDD = DDD*AF

⁴ %cPAD = (Adjusted DDD/cPAD)*100

6. RESIDENTIAL EXPOSURE ASSESSMENT

The term "residential exposure" is used in this document to refer to non-occupational, nondietary exposure (e.g., for lawn and garden pest control, indoor pest control, termiticides, and flea and tick control on pets). Although there are non-pesticidal uses for these various fragrances, no reliable exposure information is available to EPA on those uses. These various fragrances may be used as an inert ingredient in pesticide products that are registered for specific uses that may result in residential exposure, such as pesticides used in and around the home. Therefore, screening level residential handler and post-application risk assessments have been performed for common residential exposure scenarios, using assumptions detailed in the 2012 Residential SOPs¹.

Residential handler exposure: the Agency assumed handlers may receive short-term and intermediate-term dermal and inhalation exposure to these various fragrances from formulations containing the inert ingredient in outdoor and indoor scenarios. Also, homeowners are assumed to complete all elements of an application without use of any protective equipment. Long-term exposures are not calculated because applications are not expected to occur daily for more than 6 months. As shown in tables 4 below, residential handler MOEs range from 13,000 to 230,000 and are not of concern (i.e., MOEs are >100).

Residential post-application exposure: Residential post-application scenarios include shortand intermediate-term dermal (skin contact with treated surfaces) exposure for adults and children as well as short-term incidental oral exposure for children (hand-to-mouth exposure with treated surfaces). As shown in table 5 below, the lowest residential post-application MOE is 16,000 and is not of concern (i.e., MOEs are >100).

¹ Available at <u>https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedures-residential-pesticide</u>

| Table 4. Short- and | able 4. Short- and Intermediate-Term Residential Handler Exposure and Risk Estimates for Various Fragrances | | | | | | | | | | | | | |
|---------------------|---|---------------|-------------------|-------------------------------|-------------------|--------|-----------|------------------|------------------|--|--|--|--|--|
| | Dermal Unit | Inhalation | Estimated | Area Treated | Derm | al | Inhala | tion | | | | | | |
| Exposure | Exposure | Unit Exposure | Application | or Amount | Dose ³ | | Dose⁵ | | Total | | | | | |
| Scenario | mg/lb ai | mg/lb ai | Rate ¹ | Handled Daily ² | mg/kg/day | MOE⁴ | mg/kg/day | MOE ⁶ | MOE ⁷ | | | | | |
| | Antimicrobial Product Scenarios | | | | | | | | | | | | | |
| Mopping | 71.6 | 2.38 | 4.30031E-06 | 1 | 3.849E-06 | 240000 | 1.279E-07 | 7100000 | 230000 | | | | | |
| Wiping | 2870 | 67.3 | 4.30031E-06 | 0.13 | 2.006E-05 | 45000 | 4.703E-07 | 1900000 | 44000 | | | | | |
| Aerosol | | | | | | | | | | | | | | |
| Spray/Trigger | | | | | | | | | | | | | | |
| Pump | 220 | 2.4 | 0.00027522 | 0.094 | 7.114E-05 | 13000 | 7.761E-07 | 1200000 | 13000 | | | | | |

1. Based on application assumptions described in D364751 (A. LaMay, 2009)

2. Based on HED's 2012 Residential SOPs (https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedure-residential-exposure).

3. Dermal Dose = Dermal Unit Exposure (mg/lb ai) × Application Rate (lb ai/acre or gal) × Area Treated or Amount Handled (A/day or gallons/day) x dermal absorption factor ÷ BW (80 kg). 4. Dermal MOE = Dermal NOAEL (mg/kg/day) ÷ Dermal Dose (mg/kg/day)

5. Inhalation Dose = Inhalation Unit Exposure (mg/lb ai) × Application Rate (lb ai/acre or gal) × Area Treated or Amount Handled (A/day or gallons/day) × inhalation absorption factor ÷ BW (80 kg).

6. Inhalation MOE = Inhalation NOAEL (mg/kg/day) ÷ Inhalation Dose (mg/kg/day)

7. Total MOE = 1/ ((1/dermal MOE)+(1/inhalation MOE))

NA =not applicable due to negligible unit exposure

| Table 5. Residential Post-application Exposure and Risk Estimates for Antimicrobial Uses | | | | | | | | | | | | |
|--|----------------------|---|-------------------------------------|----------------------------------|--------|------------------------------|---------------------------|--|--|--|--|--|
| Lifestage | Route of Exposure | Transferable residue (ug/cm2) ¹ | Exposure (mg/day) ^{2,3} | Dose (mg/kg/day) ⁴ | MOEs⁵ | Combined MOE ⁶ | Combined MOE (rounded) | | | | | |
| Adult | Dermal | 0.000 | 0.00 | 0.000029 | 32000 | NA | NA | | | | | |
| Children 1 | Dermal | 0.000 | 0.00 | 0.000055 | 16000 | | | | | | | |
| to <2 years | Hand to mouth | NA | 0.000 | 0.000004 | 220000 | 14915 | 15000 | | | | | |

1. Transferable residue = deposited residue*fraction transfered where the deposited residue is the application rate in ug/cm2 and the fraction transfered=0.08

2. Exposure assumptions obtained from 2012 Residential SOPs

3. Dermal Exposure =(Transferable residue)(Weight unit conversion factor in mg/ug)(Transfer coefficient in cm2/hr)(exposure time)

Hand to Mouth Exposure =(HR*(FM*SAH)*(exposure time*N_replen)*(1-(1-SE)^(HtM events per hour/N_replen))

4. Dose (mg/kg/day) = Exposure (mg/day) (dermal absorption factor for dermal route only)/ BW (80 kg for adults or 11 kg for children)

5. MOE = POD (mg/kg/day) ÷ Dose (mg/kg/day).

6. Combined MOE = 1 / ((1/Dermal MOE)+ (1/ hand to mouth M

7. AGGREGATE ASSESSMENT

The Federal Food, Drug, and Cosmetic Act (FFDCA) section 408 directs EPA to consider available information concerning exposure from the pesticide residue in food and other non-occupational exposures to determine that "there is a reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue, including all anticipated dietary exposures and all other exposures for which there is reliable information".

In an aggregate assessment, exposures from relevant sources are added together and compared to quantitative estimates of hazard (e.g., a NOAEL or PAD), or the risks themselves can be aggregated. When aggregating exposures and risks from various sources, EPA considers both the route and duration of exposure.

Acute aggregate risk:

There is no acute dietary endpoint therefore an acute aggregate risk is not assessed.

<u>Short-term aggregate risk</u>: Short-term aggregate exposure takes into account short-term residential (dermal and inhalation) exposure plus chronic dietary exposure (food and drinking water). As shown in table 6 below, no short-term aggregate risks of concern were identified (i.e., MOEs are >100).

| Table 6. Short-Te | rm and/or Int | ermediate | | gate Risk Calcul or Intermediate | | 0 | |
|-------------------|-------------------|-----------|---|-------------------------------------|---|---------------------------------|--|
| Population | NOEL mg/kg/day | | Max Allowable Exposure ² mg/kg/day Average Food and Water Exposure mg/kg/day | | Residential Exposure mg/kg/day ³ | Total Exposure mg/kg/day⁴ | Aggregate MOE (food, water, and residential) ⁵ |
| Adults | 0.91 | 100 | 0.0091 | 0.0019 | 0.0001 | 0.0020 | 455 |
| Children | 0.91 | 100 | 0.0091 | 0.0053 | 0.0001 | 0.0054 | 168 |

¹ Indicate in this footnote the basis for the LOC (include the standard inter- and intra- species uncertainty factors totaling 100). ² Maximum Allowable Exposure (mg/kg/day) = NOEL/LOC.

³Residential Exposure = [Oral exposure + Dermal exposure + Inhalation Exposure]. Residential exposure values used in aggregate assessment (Table # 4 & 5).

⁴ Total Exposure = Avg Food & Water Exposure + Residential Exposure.

⁵ Aggregate MOE = [NOEL/(Avg Food & Water Exposure + Residential Exposure)].

Intermediate-term aggregate risk: Intermediate-term aggregate exposure takes into account intermediate-term residential (dermal and inhalation) exposure plus chronic dietary exposure (food and drinking water). As the same endpoints were selected for short-term and intermediate-term exposures, intermediate-term aggregate risk is equal to the short-term aggregate risk and it is not of concern (see table 6 above).

<u>Chronic aggregate risk</u>: A chronic aggregate risk assessment considers exposure estimates from chronic dietary consumption of food and drinking water. Therefore, the chronic aggregate risk is equal to the chronic dietary risk, and it is not of concern (see section 5 above).

<u>Aggregate Cancer Risk</u>: The EPA has not identified any concerns for carcinogenicity relating to these various fragrances. Therefore, these various fragrances are not expected to pose a cancer aggregate risk.

8. OCCUPATIONAL EXPOSURE ASSESSMENT

The occupational handler MOEs ranged from 200 to 14,000 (LOC is for MOEs<100) for the assumed maximum applications rates when a double layer of clothing and gloves are worn by workers (see Table 7 below). Therefore, no occupational risks of concern were identified.

| | | Dermal Unit | Level of PPE or | Inhalatio n | Leve l of | Maximum | Арр | Area Treated | Area | Dermal | | Inhalation | | Tot | tal |
|--|--|----------------------------|---------------------------------|--------------------------------|-----------------|----------------------|---------------------------------|-----------------------------------|------------------------------------|--------------------------------------|-------|--------------------------------------|------------------|------|---------|
| Exposure Scenario | Crop or Target | Exposur e (µg/lb ai) | Engineerin g control (EC) | Unit Exposure (µg/lb ai) | PPE or EC | Applicatio n Rate | Rate Unit | or Amount Handle d Daily | Treated/Amoun t Handled Unit | Dose ¹ (mg/kg/day) | MOE 2 | Dose ³ (mg/kg/day) | MOE ⁴ | MOE | AR I |
| | • | | | | | Mi | xer/Loader | | | | | | | • | |
| Wettable Powder, Mechanically -pressurized Handgun, Broadcast | Rights-of-way (e.g., utilities, railroad, roadways) | 32.8 | DL/G | 2.75 | No-R | 0.01 | lb ai/gallo n solution | 1000 | gallons solution | 0.0041 | 220 | 0.000344 | 2600 | 200 | 2 |
| Liquid, Mechanically -pressurized Handgun, Broadcast | Rights-of-way (e.g., utilities, railroad, roadways) | 29.1 | DL/G | 0.219 | No-R | 0.01 | lb ai/gallo n solution | 1000 | gallons solution | 0.00364 | 250 | 2.74E-05 | 33000 | 250 | 2.5 |
| Liquid, Aerial, Broadcast | Field crop, high- acreage | 29.1 | DL/G | 0.219 | No-R | 0.01 | lb ai/acre | 1200 | acres | 0.00436 | 210 | 3.29E-05 | 28000 | 210 | 2.1 |
| Liquid, Airblast, Broadcast | Orchard/Vineyar d | 29.1 | DL/G | 0.219 | No-R | 0.01 | lb ai/acre | 40 | acres | 0.000145 | 6300 | 1.1E-06 | 83000 0 | 6300 | 63 |
| Liquid, Groundboom, Broadcast | Golf course (fairways, tees, greens) | 29.1 | DL/G | 0.219 | No-R | 0.01 | lb ai/acre | 40 | acres | 0.000145 | 6300 | 1.1E-06 | 83000 0 | 6300 | 63 |
| Liquid, Groundboom, Broadcast | Field crop, high- acreage | 29.1 | DL/G | 0.219 | No-R | 0.01 | lb ai/acre | 200 | acres | 0.000728 | 1300 | 5.48E-06 | 17000 0 | 1300 | 13 |
| Wettable Powder, Airblast, Broadcast | Orchard/Vineyar d | 32.8 | DL/G | 2.75 | No-R | 0.01 | lb ai/acre | 40 | acres | 0.000164 | 5500 | 1.38E-05 | 66000 | 5100 | 51 |
| Wettable Powder, Groundboom, Broadcast | Golf course (fairways, tees, greens) | 32.8 | DL/G | 2.75 | No-R | 0.01 | lb ai/acre | 40 | acres | 0.000164 | 5500 | 1.38E-05 | 66000 | 5100 | 51 |
| Wettable Powder, Groundboom, Broadcast | Field crop, high- acreage | 32.8 | DL/G | 2.75 | No-R | 0.01 | lb ai/acre | 200 | acres | 0.00082 | 1100 | 6.88E-05 | 13000 | 1000 | 10 |

| Spray (all starting formulations), Airblast, Broadcast | Orchard/Vineyar d | 1480 | DL/G | 4.71 | No-R | 0.01 | lb ai/acre | 40 | acres | 0.0074 | 120 | 2.35E-05 | 39000 | 120 | 1.2 |
|---|--|------|------|-------|------|----------|---------------------------------|-------|------------------|----------|-------|----------|------------|-----------|-----|
| Spray (all starting formulations), Groundboom, Broadcast | Golf course (fairways, tees, greens) | 12.6 | DL/G | 0.34 | No-R | 0.01 | lb ai/acre | 40 | acres | 0.000063 | 14000 | 1.7E-06 | 54000 0 | 1400 0 | 140 |
| Spray (all starting formulations), Groundboom, Broadcast | Field crop, high- acreage | 12.6 | DL/G | 0.34 | No-R | 0.01 | lb ai/acre | 200 | acres | 0.000315 | 2900 | 8.5E-06 | 11000 0 | 2800 | 28 |
| | | | | | | | Flagger | | | | | | | | |
| Spray (all starting formulations), Aerial, Broadcast | Field crop, high- acreage | 10.6 | DL/G | 0.202 | No-R | 0.01 | lb ai/acre | 350 | acres | 0.000464 | 2000 | 8.84E-06 | 10000 0 | 2000 | 20 |
| | | | | | | Mixer/Lo | oader/Appli | cator | | | | | | | |
| Liquid, Manually- pressurized Handwand, Broadcast (foliar) | Nursery (ornamentals, vegetables, trees, container stock) | 365 | DL/G | 23.6 | No-R | 0.01 | lb ai/gallo n solution | 15 | gallons solution | 0.000685 | 1300 | 4.43E-05 | 21000 | 1200 | 12 |
| Wettable Powder, Manually- pressurized Handwand, Broadcast (foliar) | Nursery (ornamentals, vegetables, trees, container stock) | 365 | DL/G | 23.6 | No-R | 0.01 | lb ai/gallo n solution | 15 | gallons solution | 0.000685 | 1300 | 4.43E-05 | 21000 | 1200 | 12 |
| Wettable Powder, Mechanically -pressurized Handgun, Broadcast | Landscaping, turf (lawns, athletic fields, parks, etc.) | 630 | DL/G | 250 | No-R | 0.01 | lb ai/acre | 5 | acres | 0.000394 | 2300 | 0.000156 | 5800 | 1600 | 16 |

1. Dermal dose = Dermal unit exposure/1000*Application rate*area treated or amount handled daily

2. Dermal MOE = Dermal POD/Dermal dose

3. Inhalation dose = Inhalation unit exposure/1000*Application rate*area treated or amount handled daily

4. Inhalation MOE = Inhalation POD/Dermal dose

9. CUMULATIVE EXPOSURE

Section 408(b)(2)(D)(v) of FFDCA requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity."

EPA has not found these various fragrances to share a common mechanism of toxicity with any other substances, and these various fragrances do not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance exemption, therefore, EPA has assumed that these various fragrances do not have a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/cumulative-assessment-risk-pesticides.

10. ECOTOXICITY AND ENVIRONMENTAL FATE

Environmental fate and effects are expected to be limited and not of concern as the exposure scenarios for 40 CFR 180.940(a) are expected to be on indoor surfaces and a low limitation of 33 ppm is being set for all fragrances listed in this document

11. RISK CHARACTERIZATION

Based on a quantitative human health risk assessment, no risks of concern were identified for the U.S. population, including infants and children following exposure to these various fragrances. Exposures assessed included the oral, dermal and inhalation routes.

Based on the use pattern and anticipated low use concentration, there is low concern for environmental toxicity.

Taking into consideration all available information, EPA concludes that there is a reasonable certainty that no harm to any population subgroup will result from exposure to these various fragrances when considering sources of pesticide exposure for which there is reliable information. Therefore, the use of these various fragrances as inert ingredients under 40 CFR 180.940(a) in antimicrobial pesticide formulations used on food contact surfaces in public eating places, dairy processing equipment, and food processing equipment and utensils with Page **19** of **111**

end-use concentration not to exceed 33 ppm of the finished product can be considered assessed as safe.

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Appendix I.

FDA Food Contact Surface Sanitizing Solution Dietary Exposure Assessment Model

| EDI (mg/p/day) = AR x RS x SA x F x 10-6 | (1) |
|--|-----|
| | |

| DDD (mg/kg/day) = AR x RS x SA x F x 10-6/BW | (2) |
|--|-----|
|--|-----|

Where:

| AR | = | Application rate (ppm) |
|---------|------|--|
| RS | = | Residual solution (mg/cm2) |
| SA | = | Surface area of the treated surface which comes into contact with |
| food (d | cm2) | |
| F | = | Fraction of the pesticide transferred or migrated to food (unitless) |
| BW | = | Body weight (kg) |

Appendix II. Summary of Genotoxicity Information for Chemicals with Carcinogenicity Alerts found Using the OECD QSAR Toolbox (Carcinogenicity Alerts by ISS Profiler)

| CAS Number | InertFinder/ ChemID Plus Chemical Name | JECFA Number | JECFA Meeting | 21 US CFR | DT Class | JECFA Group/Addi tional Notes | Links to JECFA Summary | Flavis No. | EFSA/JECFA Opinion on Genotoxicity Concern |
|---------------|---|-----------------|------------------|-----------------|-------------|---|---|---------------|---|
| 120-57-0 | 1,3- Benzodioxole- 5- carboxaldehyd e | 896 | 48 | 21CFR18 2.60 | Ш | Hydroxy- and alkoxy- substituted benzyl derivatives | Safety evaluation of certain food additives and contaminants prepared by the fifty-seventh meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). WHO Food Additives Series No. 48, 2002 http://www.inchem.org/do cuments/jecfa/jecmono/v4 8je15.htm | 05.016 | Based on combined evidence from <i>in vitro</i> assays (including Ames tests, paper disk mutation assay, DNA repair tests, mutation assay, mitotic recombination assay, chromosomal aberration tests, sister chromatid exchange assay, unscheduled DNA synthesis, micronucleus assay, rec assays, and mammalian cell gene mutation tests) as well as <i>in vivo</i> genotoxicity studies (including sex-linked recessive lethal mutations (SLRL), micronucleus tests, replicative DNA synthesis tests, sister chromatid exchange assays, chromosomal aberrations tests, micronucleus tests, unscheduled DNA synthesis tests, DNA damage tests, Comet assays, Basc tests, Medium-term rat liver bioassays, spot tests, and dominant lethal assay) for 1,3-benzodioxole-5-carboxaldehyde [Fl-no: 05.016], the material 1,3-benzodioxole-5-carboxaldehyde [Fl-no: 05.016] was cleared of genotoxicity concern (EFSA, 2008, 2009, 2012). EFSA Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food, 2008. Flavouring Group Evaluation 52 (FGE.52): Consideration of hydroxy- and alkoxy-substituted benzyl derivatives evaluated by JECFA (57th meeting) structurally related to benzyl alcohols, benzaldehydes, a related acetal, benzoic acids, and related esters evaluated by EFSA in FGE.20 (2005) (Commission Regulation (EC) No 1565/2000 of 18 July 2000) - Opinion of the Scientific Panel on Food Additives, Flavouring, Processing Aids and Materials, Enzymes, Flavourings and Processing Aids, 2009. Flavouring Group Evaluation 54, Revision 1 (FGE. 54Rev1): Consideration of benzyl derivatives evaluated by JECFA (57th meeting) and Processing Aids, 2009. Flavouring Group Evaluation 54, Revision 1 (FGE. 54Rev1): Consideration of benzyl derivatives evaluated by JECFA (57th meeting) structurally related to benzyl alcohols, benzaldehydes, a related acetal, benzoic acids and related esters evaluated by EFSA in FGE. |

| CAS Number | InertFinder/ ChemID Plus Chemical Name | JECFA Number | JECFA Meeting | 21 US CFR | DT Class | JECFA Group/Addi tional Notes | Links to JECFA Summary | Flavis No. | EFSA/JECFA Opinion on Genotoxicity Concern |
|---------------|---|-----------------|------------------|------------------|-------------|---|---|---------------|---|
| | | | | | | | | | 20Rev1 (2009). EFSA Journal 2009; 7(5):1025, 73 pp. doi:10.2903/j.efsa.2009.1025 EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF); Scientific Opinion on Flavouring Group Evaluation 20, Revision 4 (FGE.20Rev4): Benzyl alcohols, benzaldehydes, a related acetal, benzoic acids, and related esters from chemical groups 23 and 30. EFSA Journal 2012; 10(12):2994. [140 pp.]. doi:10.2903/j.efsa.2012.2994. |
| 326-61-4 | Piperonyl acetate | 894 | 48 | 21CFR17 2.515 | III | Hydroxy- and alkoxy- substituted benzyl derivatives | Safety evaluation of certain food additives and contaminants prepared by the fifty-seventh meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). WHO Food Additives Series No. 48, 2002 http://www.inchem.org/do cuments/jecfa/jecmono/v4 8je15.htm | 09.220 | Based on combined evidence from <i>in vitro</i> assays (including Ames tests, paper disk mutation assay, DNA repair tests, mutation assay, mitotic recombination assay, chromosomal aberration tests, sister chromatid exchange assay, unscheduled DNA synthesis, micronucleus assay, rec assays, and mammalian cell gene mutation tests) as well as <i>in vivo</i> genotoxicity studies (including sex-linked recessive lethal mutations (SLRL), micronucleus tests, replicative DNA synthesis tests, sister chromatid exchange assays, chromosomal aberrations tests, micronucleus tests, unscheduled DNA synthesis tests, DNA damage tests, Comet assays, Basc tests, Medium-term rat liver bioassays, spot tests, and dominant lethal assay) for Piperonyl acetate [Fl-no: 09.220] and materials similar to Piperonyl acetate [Fl-no: 09.220], the material Piperonyl acetate [Fl-no: 09.220] was cleared of genotoxicity concern (EFSA, 2008, 2009, 2012). EFSA Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food, 2008. Flavouring Group Evaluation 52 (FGE.52): Consideration of hydroxy- and alkoxy-substituted benzyl derivatives evaluated by JECFA (57th meeting) structurally related to benzyl alcohols, benzaldehydes, a related acetal, benzoic acids, and related esters evaluated by EFSA in FGE.20 (2005) (Commission Regulation (EC) No 1565/2000 of 18 July 2000) - Opinion of the Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in contact with Food (AFC), EFSA Journal 2008; 6(3):637, 69 pp. doi: 10.2903/j.efsa.2008.637 EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids, 2009. Flavouring |

| CAS Number | InertFinder/ ChemID Plus Chemical Name | JECFA Number | JECFA Meeting | 21 US CFR | DT Class | JECFA Group/Addi tional Notes | Links to JECFA Summary | Flavis No. | EFSA/JECFA Opinion on Genotoxicity Concern |
|---------------|---|-----------------|------------------|------------------|-------------|--|---|---------------|---|
| | | | | | | | | | Group Evaluation 54, Revision 1 (FGE. 54Rev1): Consideration of benzyl derivatives evaluated by JECFA (57th meeting) structurally related to benzyl alcohols, benzaldehydes, a related acetal, benzoic acids and related esters evaluated by EFSA in FGE. 20Rev1 (2009). EFSA Journal 2009; 7(5):1025, 73 pp. doi:10.2903/j.efsa.2009.1025 Suggested citation: EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF); Scientific Opinion on Flavouring Group Evaluation 20, Revision 4 (FGE.20Rev4): Benzyl alcohols, benzaldehydes, a related acetal, benzoic acids, and related esters from chemical groups 23 and 30. EFSA Journal 2012; 10(12):2994. [140 pp.]. |
| 118-71-8 | 4H-Pyran-4- one, 3- hydroxy-2- methyl- | 1480 | 56 | 21CFR17 2.515 | Ш | Maltol and related substances | Safety evaluation of certain food additives and contaminants prepared by the sixty-fifth meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). WHO Food Additives Series No. 56, 2006 http://www.inchem.org/do cuments/jecfa/jecmono/v5 6je07.pdf | 07.014 | doi:10.2903/j.efsa.2012.2994. On the basis of combined evidence from <i>in vitro</i> assays (including reverse mutation assay, micronucleus assays, chromosomal aberration tests, sex-linked recessive lethal mutation, DNA damage tests, and sister chromatid exchange) as well as <i>in vivo</i> genotoxicity studies (including micronucleus assays, and comment assays) for 4H-Pyran-4-one, 3-hydroxy-2- methyl- [Fl-no: 07.014], the material 4H-Pyran-4-one, 3- hydroxy-2-methyl [Fl-no: 07.014] was cleared of genotoxicity concern (EFSA, 2015). EFSA CEF Panel (EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids), 2015. Scientific Opinion on Flavouring Group Evaluation 213, Revision 2 (FGE.213Rev2): Consideration of genotoxic potential for α , β - unsaturated alicyclic ketones and precursors from chemical subgroup 2.7 of FGE.19. EFSA Journal 2015; 13 (9):4244, 49 pp. doi:10.2903/j.efsa.2015.4244 |
| 3658-77-3 | 4-Hydroxy- 2,5-dimethyl- 3(2H)- furanone | 1446 | 54 | N/A | III | Tetrahydrofu ran and furanone derivatives | Safety evaluation of certain food additives prepared by the sixty-third meeting of the Joint FAO/WHO Expert Committee on Food Additives (JEFCA). WHO Food Additives Series No. | 13.010 | Based on combined evidence from <i>in vitro</i> assays (reversed mutation assay, DNA damage assays, DNA strand breaks assay, and mouse lymphoma tests), <i>in vivo</i> genotoxicity studies (including dominate lethal assay) and a 2-year carcinogenic study for 4-Hydroxy-2,5-dimethyl-3(2H)-furanone [FL-no: 13.010] the material 4-Hydroxy-2,5-dimethyl-3(2H)-furanone |

| CAS Number | InertFinder/ ChemID Plus Chemical Name | JECFA Number | JECFA Meeting | 21 US CFR | DT Class | JECFA Group/Addi tional Notes | Links to JECFA Summary | Flavis No. | EFSA/JECFA Opinion on Genotoxicity Concern |
|---------------|---|-----------------|------------------|--------------|-------------|--|---|---------------|--|
| | | | | | | | 54, 2006 http://www.inchem.org/do cuments/jecfa/jecmono/v5 4je01.pdf | | [Fl-no: 13.010] was cleared of genotoxicity concern (EFSA, 2015a, 2015b). EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids, 2015. Scientific Opinion on Flavouring Group Evaluation 99 Revision 1 (FGE.99Rev1): Consideration of furanone derivatives evaluated by the JECFA (63rd, 65th and 69th meetings). EFSA Journal 2015; 13(11):4286, 31 pp. doi:10.2903/j.efsa.2015.4286 EFSA CEF Panel (EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids), 2015. Scientific Opinion on Flavouring Group Evaluation 220 Revision 3 (FGE.220Rev3): Consideration of genotoxic potential for \$aL,\$bT-unsaturated 3(2H)-Furanones from subgroup 4.4 of FGE.19. EFSA Journal 2015; 13(5):4117, 37 pp. doi:10.2903/j.efsa.2015.4117 |
| 65416-14-0 | Maltyl isobutyrate | 1482 | 56 | N/A | ш | Maltol and related substances | Safety evaluation of certain food additives and contaminants prepared by the sixty-fifth meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). WHO Food Additives Series No. 56, 2006 http://www.inchem.org/do cuments/jecfa/jecmono/v5 6je07.pdf | 09.525 | On the basis of combined evidence from <i>in vitro</i> assays (including reverse mutation assay, micronucleus assays, chromosomal aberration tests, sex-linked recessive lethal mutation, DNA damage tests, and sister chromatid exchange) as well as <i>in vivo</i> genotoxicity studies (including micronucleus assays, and comment assays) for 4H-Pyran-4-one, 3-hydroxy-2- methyl- [Fl-no: 07.014], the material Maltyl isobutyrate [Fl-no: 09.525] was cleared of genotoxicity concern (EFSA, 2015). EFSA CEF Panel (EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids), 2015. Scientific Opinion on Flavouring Group Evaluation 213, Revision 2 (FGE.213Rev2): Consideration of genotoxic potential for α,β - unsaturated alicyclic ketones and precursors from chemical subgroup 2.7 of FGE.19. EFSA Journal 2015; 13 (9):4244, 49 pp. doi: <u>10.2903/j.efsa.2015.4244</u> |
| 1128-08-1 | 3-Methyl-2- (n-pentanyl)- 2- cyclopenten- 1-one | 1406 | 54 | N/A | II | Monocyclic and bicyclic secondary alcohols, | Safety evaluation of certain food additives prepared by the sixty-third meeting of the Joint FAO/WHO Expert Committee on Food | 07.140 | Based on combined evidence from <i>in vitro</i> assays (including reverse mutation assays and micronucleus assays) as for the close structural relative 3-methyl-2-cyclopenten-1-one [Fl-no: 07.112], the material 3-Methyl-2-(2-pentenyl)-2-cyclopenten-1- |

| CAS Number | InertFinder/ ChemID Plus Chemical Name | JECFA Number | JECFA Meeting | 21 US CFR | DT Class | JECFA Group/Addi tional Notes | Links to JECFA Summary | Flavis No. | EFSA/JECFA Opinion on Genotoxicity Concern |
|------------------------|---|-----------------|------------------|------------------|-------------|--|---|---------------|---|
| | | | | | | ketones, and related esters | Additives (JEFCA). WHO Food Additives Series No. 54, 2006 http://www.inchem.org/do cuments/jecfa/jecmono/v5 4je01.pdf | | one [Fl-no: 07.140] was cleared of genotoxicity concern (EFSA, 2015, 2016) EFSA CEF Panel (EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids), 2015. Scientific Opinion on Flavouring Group Evaluation 212 Revision 3 (FGE.212Rev3): \$aL,\$bT- Unsaturated alicyclic ketones and precursors from chemical subgroup 2.6 of FGE.19. EFSA Journal 2015; 13(5):4116, 39 pp. doi:10.2903/j.efsa.2015.4116 EFSA CEF Panel (EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids), 2016. Scientific Opinion on Flavouring Group Evaluation 51, Revision 2 (FGE.51Rev2): Consideration of alicyclic ketones and secondary alcohols and related esters evaluated by the JECFA (59th meeting) structurally related to alicyclic ketones secondary alcohols and related esters in FGE.09Rev6 (2015b). EFSA Journal 2016; 14(1):4338, 57 pp. doi:10.2903/j.efsa.2016.4338 |
| 488-10-8; 6261-18-3 | 3-Methyl-2- (2-pentenyl)- 2- cyclopenten- 1-one | 1114 | 50 | 21CFR17 2.515 | П | Alicyclic ketones, secondary alcohols and related esters | Safety evaluation of certain food additives and contaminants prepared by the fifty-ninth meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). WHO Food Additives Series No. 50, 2003 http://www.inchem.org/do cuments/jecfa/jecmono/v5 0je12.htm | 07.094 | Based on combined evidence from <i>in vitro</i> assays (including reverse mutation assays and micronucleus assays) as for the close structural relative 3-methyl-2-cyclopenten-1-one [Fl-no: 07.112], the material 3-Methyl-2-(2-pentenyl)-2-cyclopenten-1- one [Fl-no: 07.094] was cleared of genotoxicity concern (EFSA, 2015)EFSA CEF Panel (EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids), 2015. Scientific Opinion on Flavouring Group Evaluation 212 Revision 3 (FGE.212Rev3): \$aL,\$bT- Unsaturated alicyclic ketones and precursors from chemical subgroup 2.6 of FGE.19. EFSA Journal 2015; 13(5):4116, 39 pp. doi: https://doi.org/10.2903/j.efsa.2015.4116 |
| 11050-62-7 | Isojasmone | 1115 | 50 | 21CFR17 2.515 | п | Alicyclic ketones, secondary alcohols and related esters | Safety evaluation of certain food additives and contaminants prepared by the fifty-ninth meeting of the Joint FAO/WHO | 07.033 | Based on combined evidence from <i>in vitro</i> assays (including reverse mutation assays and micronucleus assays) for the close structural relative 3-methyl-2-cyclopenten-1-one [Fl-no: 07.112], the material Isojasmone [Fl-no: 07.033] was cleared of genotoxicity concern (EFSA, 2015) |

| CAS Number | InertFinder/ ChemID Plus Chemical Name | JECFA Number | JECFA Meeting | 21 US CFR | DT Class | JECFA Group/Addi tional Notes | Links to JECFA Summary | Flavis No. | EFSA/JECFA Opinion on Genotoxicity Concern |
|---------------|---|-----------------|------------------|------------------|-------------|---|---|---------------|---|
| | | | | | | | Expert Committee on Food Additives (JECFA). WHO Food Additives Series No. 50, 2003 <u>http://www.inchem.org/do</u> <u>cuments/jecfa/jecmono/v5</u> <u>0je14.htm</u> | | EFSA CEF Panel (EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids), 2015. Scientific Opinion on Flavouring Group Evaluation 212 Revision 3 (FGE.212Rev3): \$aL,\$bT- Unsaturated alicyclic ketones and precursors from chemical subgroup 2.6 of FGE.19. EFSA Journal 2015; 13(5):4116, 39 pp. doi: <u>10.2903/j.efsa.2015.4116</u> |
| 21834-92-4 | 5-Methyl-2- phenyl-2- hexenal | 1472 | 54 | N/A | П | Phenyl- substituted aliphatic alcohols and related aldehydes and esters | Safety evaluation of certain food additives prepared by the sixty-third meeting of the Joint FAO/WHO Expert Committee on Food Additives (JEFCA). WHO Food Additives Series No. 54, 2006 http://www.inchem.org/do cuments/jecfa/jecmono/v5 4je01.pdf | 05.099 | Based on combined evidence from <i>in vitro</i> assays (including Ames tests, paper disk mutation assay, DNA repair tests, mutation assay, mitotic recombination assay, chromosomal aberration tests, sister chromatid exchange assay, unscheduled DNA synthesis, micronucleus assay, rec assays, and mammalian cell gene mutation tests) as well as <i>in vivo</i> genotoxicity studies (including sex-linked recessive lethal mutations (SLRL), micronucleus tests, replicative DNA synthesis tests, sister chromatid exchange assays, chromosomal aberrations tests, micronucleus tests, unscheduled DNA synthesis tests, DNA damage tests, Comet assays, Basc tests, Medium-term rat liver bioassays, spot tests, and dominant lethal assays) for materials similar to 1,3-benzodioxole-5-carboxaldehyde [JECFA no. 1472], the material 1,3-benzodioxole-5-carboxaldehyde [JECFA no. 1472] was cleared of genotoxicity concern (Sips and Hattan, 2006) Sipes, I. G., and D. G. Hattan. "PHENYL- SUBSTITUTED ALIPHATIC ALCOHOLS AND <u>RELATED ALDEHYDES AND ESTERS." Safety evaluation of certain food additives (2006): 525.</u> |
| 1604-28-0 | 6-Methyl-3,5- heptadien-2- one | 1134 | 50 | 21CFR17 2.515 | Ι | Aliphatic secondary alcohols, ketones and related esters | Safety evaluation of certain food additives and contaminants prepared by the fifty-ninth meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). WHO Food Additives Series No. 50, 2003 http://www.inchem.org/do cuments/jecfa/jecmono/v5 0je15.htm | 07.099 | Based on combined evidence from <i>in vitro</i> assays (reverse mutation assays and micronucleus induction assays) for 6- Methyl-3,5-heptadien-2-one [Fl-no: 07.099], the material 6- Methyl-3,5-heptadien-2-one [Fl-no: 07.099] was cleared of genotoxicity concern (EFSA, 2011, 2017a, 2017b). EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF); Scientific Opinion on Flavouring Group Evaluation 206 (FGE.206): Consideration of genotoxicity data on representatives for 12 alpha, beta-unsaturated ketones and precursors from chemical subgroup 1.2.3 of |

| CAS Number | InertFinder/ ChemID Plus Chemical Name | JECFA Number | JECFA Meeting | 21 US CFR | DT Class | JECFA Group/Addi tional Notes | Links to JECFA Summary | Flavis No. | EFSA/JECFA Opinion on Genotoxicity Concern |
|---------------|---|-----------------|------------------|------------------|-------------|--|---|---------------|---|
| | | | | | | | | | FGE.19 by EFSA. EFSA Journal 2011; 9(3):1922. [16 pp.]. doi:10.2903/j.efsa.2011.1922. EFSA CEF Panel (EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids), Silano V, Bolognesi C, Castle L, Cravedi J-P, Engel K-H, Fowler P, Franz R, Grob K, Gürtler R, Husøy T, Kärenlampi S, Milana MR, Penninks A, Tavares Poças MF, Smith A, Tlustos C, Wölfle D, Zorn H, Zugravu C-A, Beckman Sundh U, Brimer L, Mulder G, Binderup M-L, Crebelli R, Marcon F, Marzin D, Mosesso P, Kovalkovičová N and Mennes W, 2016. Scientific Opinion on Flavouring Group Evaluation 63, Revision 3 (FGE.63Rev3): aliphatic secondary alcohols, ketones and related esters evaluated by JECFA (59th and 69th meetings) structurally related to saturated and unsaturated aliphatic secondary alcohols, ketones and esters of secondary alcohols and saturated linear or branched- chain carboxylic acids evaluated by EFSA in FGE.07Rev4. EFSA Journal 2017; 15(1):4662, 41 pp. doi:10.2903/j.efsa.2017.4662 EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF), Silano V, Bolognesi C, Castle L, Cravedi J-P, Engel K-H, Fowler P, Franz R, Grob K, Gürtler R, Husøy T, Kärenlampi S, Milana MR, Penninks A, Tavares Poças MF, Smith A, Tlustos C, Wölfle D, Zorn H, Zugravu C-A, Beckman Sundh U, Brimer L, Mosesso P, Mulder G, Anastassiadou M and Mennes W, 2017. Scientific Opinion on Flavouring Group Evaluation 7, Revision 5 (FGE.07Rev5): saturated and unsaturated aliphatic secondary alcohols, ketones and esters of secondary alcohols and saturated linear or branched- chain carboxylic acids from chemical group 5. EFSA Journal 2017; 15(3):4725, 81 pp. |
| 4674-50-4 | Nootkatone | 1398 | 54 | 21CFR17 2.515 | П | Monocyclic and bicyclic secondary alcohols, ketones, and related esters | Safety evaluation of certain food additives prepared by the sixty-third meeting of the Joint FAO/WHO Expert Committee on Food Additives (JEFCA). WHO | 07.089 | doi:10.2903/j.efsa.2017.4725 Based on combined evidence from <i>in vitro</i> assays (including reverse mutation assays and micronucleus assays) for Nootkatone [Fl-no: 07.089], the material Nootkatone [Fl-no: 07.089] was cleared of genotoxicity concern (EFSA, 2014, 2015). |

| CAS Number | InertFinder/ ChemID Plus Chemical Name | JECFA Number | JECFA Meeting | 21 US CFR | DT Class | JECFA Group/Addi tional Notes | Links to JECFA Summary | Flavis No. | EFSA/JECFA Opinion on Genotoxicity Concern |
|---------------|---|-----------------|------------------|------------------|-------------|-------------------------------------|---|---------------|---|
| | | | | | | | Food Additives Series No. 54, 2006 http://www.inchem.org/do cuments/jecfa/jecmono/v5 4je01.pdf | | EFSA CEF Panel (EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids), 2014. Scientific Opinion on Flavouring Group Evaluation 87, Revision 2 (FGE.87Rev2): Consideration of bicyclic secondary alcohols, ketones and related esters evaluated by JECFA (63rd meeting) structurally related to bicyclic secondary alcohols, ketones and related esters evaluated by EFSA in FGE.47Rev1 (2008). EFSA Journal 2014; 12(10):3864, 41 pp. doi:<u>10.2903/j.efsa.2014.3864</u> EFSA CEF Panel (EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids), 2015. Scientific Opinion on Flavouring Group Evaluation 213, Revision 2 (FGE.213Rev2): Consideration of genotoxic potential for α,β- unsaturated alicyclic ketones and precursors from chemical subgroup 2.7 of FGE.19. EFSA Journal 2015; 13 (9):4244, 49 pp. doi:<u>10.2903/j.efsa.2015.4244</u> |
| 4940-11-8 | Ethyl maltol | 1481 | 56 | 21CFR17 2.515 | П | Maltol and related substances | Safety evaluation of certain food additives and contaminants prepared by the sixty-fifth meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). WHO Food Additives Series No. 56, 2006 http://www.inchem.org/do cuments/jecfa/jecmono/v5 6je07.pdf | 07.047 | Based on combined evidence from <i>in vitro</i> assays (including reverse mutation assays), <i>in vivo</i> genotoxicity studies (including micronucleus formation tests and Base tests), and a 2-year carcinogenicity study for Ethyl maltol [Fl-no: 07.047], the material Ethyl maltol [Fl-no: 07.047] was cleared of genotoxicity concern (EFSA, 2010, 2015).EFSA; Scientific Opinion on Flavouring Group Evaluation 83, Revision 1 (FGE.83Rev1): EFSA Journal 2010; 8(2):1409. [22 pp.]. doi:10.2903/j.efsa.2010.1409.EFSA CEF Panel (EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids), 2015. Scientific Opinion on Flavouring Group Evaluation 213, Revision 2 (FGE.213Rev2): Consideration of genotoxic potential for α,β- unsaturated alicyclic ketones and precursors from chemical subgroup 2.7 of FGE.19. EFSA Journal 2015; 13 (9):4244, 49 pp. doi:10.2903/j.efsa.2015.4244 |
| 80-71-7 | Methylcyclop entenolone | 418 | 42 | 21CFR17 2.515 | III | Aliphatic acyclic and | Safety evaluation of certain food additives and | 07.056 | Based on combined evidence from <i>in vitro</i> assays (including reverse mutation assays and unscheduled DNA synthesis tests) |

| CAS Number | InertFinder/ ChemID Plus Chemical Name | JECFA Number | JECFA Meeting | 21 US CFR | DT Class | JECFA Group/Addi tional Notes | Links to JECFA Summary | Flavis No. | EFSA/JECFA Opinion on Genotoxicity Concern |
|---------------|---|-----------------|------------------|------------------|-------------|---|---|---------------|--|
| | | | | | | alicyclic alpha- diketones and related alpha- hydroxyketo nes | contaminants prepared by the fifty-first meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). WHO Food Additives Series No. 42, 1999 <u>http://www.inchem.org/do</u> <u>cuments/jecfa/jecmono/v0</u> <u>42je20.htm</u> | | for Methylcyclopentenolone [Fl-no: 07.056] and a 2-year carcinogenicity study for a related substance, 3- Ethylcyclopentan-1,2-dione [Fl-no: 07.057], the material Methylcyclopentenolone [Fl-no: 07.056] was cleared of genotoxicity concern (EFSA, 2015). EFSA CEF Panel (EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids), 2015. Scientific Opinion on Flavouring Group Evaluation 213, Revision 2 (FGE.213Rev2): Consideration of genotoxic potential for α ,β- unsaturated alicyclic ketones and precursors from chemical subgroup 2.7 of FGE.19. EFSA Journal 2015; 13 (9):4244, 49 pp. doi:10.2903/j.efsa.2015.4244 |
| 13679-70-4 | 5-Methyl-2- thiophenecarb oxaldehyde | 1050 | 50 | N/A | III | Sulfur- containing heterocyclic compounds | Safety evaluation of certain food additives and contaminants prepared by the fifty-ninth meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). WHO Food Additives Series No. 50, 2003 http://www.inchem.org/do cuments/jecfa/jecmono/v5 0je12.htm | 15.004 | Based on combined evidence from <i>in vitro</i> assays (including Ames assays and micronucleus assays) as well as <i>in vivo</i> genotoxicity studies (including micronucleus assay and comet assays) for 5-Methyl-2-thiophenecarboxaldehyde [Fl-no: 15.004], the material Methyl-2-thiophenecarboxaldehyde [Fl-no: 15.004] was cleared of genotoxicity concern (EFSA, 2013a, 2013b) EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF); Scientific Opinion on Flavouring Group Evaluation 224 (FGE.224): Consideration of genotoxic potential for two α,β -unsaturated thiophenes from subgroup 5.2 of FGE.19 by EFSA. EFSA Journal 2013; 11 (2):3093. [18 pp.] doi: <u>10.2903/j.efsa.2013.3093</u> . EFSA CEF Panel (EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids), 2013. Scientific Opinion on Flavouring Group Evaluation 76, Revision 1 (FGE.76Rev1): Consideration of sulphur-containing heterocyclic compounds evaluated by JECFA (59th meeting) structurally related to thiazoles, thiophene, thiazoline and thienyl derivatives from chemical group 30 evaluated by EFSA. IFSA Journal 2013; 11(11):3455, 52 pp. doi:10.2903/j.efsa.2013.3455 |
| 121-32-4 | Ethylvanillin | 893 | 48 | 21CFR18 2.60; | II | Hydroxy- and alkoxy- | Safety evaluation of certain food additives and | 05.019 | Based on combined evidence from <i>in vitro</i> assays (including Ames tests, paper disk mutation assay, DNA repair tests, |

| CAS Number | InertFinder/ ChemID Plus Chemical Name | JECFA Number | JECFA Meeting | 21 US CFR | DT Class | JECFA Group/Addi tional Notes | Links to JECFA Summary | Flavis No. | EFSA/JECFA Opinion on Genotoxicity Concern |
|---------------|---|-----------------|------------------|-----------------|-------------|--|---|---------------|---|
| | | | | 21CFR18 2.90 | | substituted benzyl derivatives | contaminants prepared by the fifty-seventh meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). WHO Food Additives Series No. 48, 2002 http://www.inchem.org/do cuments/jecfa/jecmono/v4 8je15.htm | | mutation assay, mitotic recombination assay, chromosomal aberration tests, sister chromatid exchange assay, unscheduled DNA synthesis, micronucleus assay, rec assays, and mammalian cell gene mutation tests) as well as <i>in vivo</i> genotoxicity studies (including sex-linked recessive lethal mutations (SLRL), micronucleus tests, replicative DNA synthesis tests, sister chromatid exchange assays, chromosomal aberrations tests, micronucleus tests, unscheduled DNA synthesis tests, DNA damage tests, Comet assays, Basc tests, Medium-term rat liver bioassays, spot tests, and dominant lethal assays) for Ethylvanillin [Fl-no: 05.019] and materials similar to Ethylvanillin [Fl-no: 05.019], the material Ethylvanillin [Fl-no: 05.019] was cleared of genotoxicity concern (EFSA, 2008, 2009). EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids, 2009. Flavouring Group Evaluation 54, Revision 1 (FGE. 54Rev1): Consideration of benzyl derivatives evaluated by JECFA (57th meeting) structurally related to benzyl alcohols, benzaldehydes, a related acetal, benzoic acids and related esters evaluated by EFSA in FGE. 20Rev1 (2009). EFSA Journal 2009; 7(5):1025, 73 pp. doi:10.2903/j.efsa.2009.1025 EFSA Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food, 2008. Flavouring Group Evaluated by JECFA (57th meeting) structurally related to benzyl derivatives evaluated by JECFA (57th meeting) structurally related sters evaluated by Decreation of hydroxy- and alkoxy-substituted benzyl derivatives evaluated by JECFA (57th meeting) structurally related is and related esters evaluated by JECFA (57th meeting) structurally related to benzyl alcohols, benzaldehydes, a related acetal, benzoic acids, and related esters evaluated by JECFA (57th meeting) structurally related to benzyl derivatives evaluated by JECFA (57th meeting) structurally related to benzyl derivatives evaluated by JECFA (57th meeting) structurally related to benzyl alcohols, benzaldehydes, |
| 67801-20-1 | 3-Methyl-5- (2,2,3- trimethyl-3- cyclopenten- 1-yl)pent-4- en-2-ol | 2220 | 73 | N/A | Ι | Aliphatic secondary alcohols, ketones and related esters | Safety Evaluation of Certain Food Additives. Prepared by the 82nd meeting of the Joint FAO/WHO Expert Committee on Food | N/A | Based on combined evidence from <i>in vitro</i> assays (including reverse mutation assay, forward mutation assay, and chromosome aberration) for 3-Methyl-5-(2,2,3-trimethyl-3-cyclopenten-1-yl)pent-4-en-2-ol [JECFA 2220], the material 3-Methyl-5-(2,2,3-trimethyl-3-cyclopenten-1-yl)pent-4-en-2-ol |

| CAS Number | InertFinder/ ChemID Plus Chemical Name | JECFA Number | JECFA Meeting | 21 US CFR | DT Class | JECFA Group/Addi tional Notes | Links to JECFA Summary | Flavis No. | EFSA/JECFA Opinion on Genotoxicity Concern |
|---------------|---|-----------------|------------------|--------------|-------------|--|---|---------------|--|
| | | | | | | | Additives (JECFA). Who Food Additives Series 73. 2017. http://apps.who.int/iris/bits tream/handle/10665/25893 4/9789241660730- eng.pdf;jsessionid=3AD1C CCA38A3AEBA4162A4D 51490168E?sequence=1 | | [JECFA 2220] was cleared of genotoxicity concern (WHO, 2017) <u>World Health Organization. "Safety evaluation of</u> <u>certain food additives: prepared by the Eighty-second</u> <u>meeting of the Joint FAO/WHO Expert Committee</u> <u>on Food Additives (JECFA)." (2017).</u> |
| 104-76-7 | 1-Hexanol, 2- ethyl- | 267 | 40 | N/A | I | Saturated aliphatic acyclic branched- chain primary alcohols, aldehydes, and acids | Safety evaluation of certain food additives and contaminants prepared by the forty-ninth meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). WHO Food Additives Series No. 40, 1998 <u>http://www.inchem.org/do</u> cuments/jecfa/jecmono/v0 40je11.htm | -02.082 | Based on combined evidence from <i>in vitro</i> assays (including an Ames assay and a chromosome aberration assay) for 1-hexanol, 2-ethyl- [Fl-no: 02.082], the material 1-hexanol, 2-ethyl- [Fl-no: 02.082], was cleared of genotoxicity concern. (Api et al., 2016). A.M. Api, D. Belsito, S. Bhatia, M. Bruze, P. Calow, M.L. Dagli, W. Dekant, A.D. Fryer, L. Kromidas, S. La Cava, J.F. Lalko, A. Lapczynski, D.C. Liebler, T.M. Penning, V.T. Politano, G. Ritacco, D. Salvito, T.W. Schultz, J. Shen, I.G. Sipes, B. Wall, D.K. Wilcox, RIFM fragrance ingredient safety assessment, 2-ethyl-1-hexanol, CAS registry number 104-76-7, Food and Chemical Toxicology, Volume 97, Supplement, 2016, Pages S147-S156, ISSN 0278-6915, https://doi.org/10.1016/j.fct.2016.09.001. (https://www.sciencedirect.com/science/article/pii/S0 278691516303155) |

Appendix III. Results from QSAR Toolbox Analysis Using QSAR Toolbox 4.5 (<u>http://www.qsartoolbox.org/home</u>)

| InertFinder/ChemID | (+)-Fenchone | Camphor | Linalyl | p- Menthan- 3- | .alpha | 1,3-Benzodioxole- 5- | 1- Hexanol, | 1-Octen-3- ol |
|---|---|---|---|---|--|---|---|--|
| Plus Name | | | oxide | one | Butylcinnamaldehyde | carboxaldehyde | 2-ethyl- | |
| CAS | 4695-62-9 | 21368-68-3 | 60047-17-8; 5989-33-3; 34995-77-2 | 10458-14-7 | 7492-44-6 | 120-57-0 | 104-76-7 | 3391-86-4 |
| SMILES | CC1(C)[C@@ H]2CC[C@@](C)(C2)C1=O | CC1(C)C2 CCC1(C)C(=O)C2 | CC1(CCC(O1)C(C)(C)O)C=C | CC(C)C1C CC(C)CC1 =O | CCCC\C(C=O)=C/c1cc ccc1 | O=Cc1ccc2OCOc 2c1 | CCCCC(CC)CO | CCCCCC(O)C=C |
| Ionization at pH = 1 | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) No pKb value | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) |
| Biodegradation ultimate (Biowin 3) | Weeks to months | Weeks to months | Weeks to months | Weeks | Weeks | Weeks | Days to weeks | Days to weeks |
| Estrogen Receptor Binding | without OH or NH2 group | Non binder, without OH or NH2 group | Non binder, without OH or NH2 group | Non binder, without OH or NH2 group | Non binder, without OH or NH2 group | Non binder, without OH or NH2 group | Non binder, non cyclic structure | Non binder, non cyclic structure |
| Biodeg BioHC half- life (Biowin) | No value | No value | No value | No value | No value | No value | No value | No value |
| Hydrolysis half-life (pH 6.5-7.4) | No value | No value | No value | No value | No value | No value | No value | No value |
| Biodegradation probability (Biowin 5) | Does NOT Biodegrade Fast | Does NOT Biodegrade Fast | Does NOT Biodegrade Fast | Does NOT Biodegrade Fast | Biodegrades Fast | Biodegrades Fast | Biodegrades Fast | Biodegrades Fast |
| Toxic hazard classification by Cramer | Intermediate (Class II) | Intermediate (Class II) | High (Class III) | Intermediate (Class II) | Low (Class I) | High (Class III) | Low (Class I) | Intermediate (Class II) |

| InertFinder/ChemID | (+)-Fenchone | Camphor | Linalyl | p- Menthan- 3- | .alpha | 1,3-Benzodioxole- 5- | 1- Hexanol, | 1-Octen-3- o |
|----------------------|----------------|---------------|------------|----------------|---------------------|-------------------------|----------------|---------------|
| Plus Name | | | oxide | one | Butylcinnamaldehyde | carboxaldehyde | 2-ethyl- | |
| Biodegradation | Does NOT | Does NOT | Does NOT | Biodegrades | Biodegrades Fast | Biodegrades Fast | Biodegrades | Biodegrades |
| probability (Biowin | Biodegrade | Biodegrade | Biodegrade | Fast | | | Fast | Fast |
| 2) | Fast | Fast | Fast | | | | | |
| Ionization at pH = 4 | Acidic [0.000, | Acidic | Acidic | Acidic | Acidic [0.000, | Acidic [0.000, | Acidic [0.000, | Acidic |
| | 10.000) | [0.000, | [0.000, | [0.000, | 10.000) | 10.000) | 10.000) | [0.000, |
| | Basic [0.000, | 10.000) | 10.000) | 10.000) | No pKb value | Basic [0.000, | Basic [0.000, | 10.000) |
| | 10.000) | Basic [0.000, | Basic | Basic [0.000, | | 10.000) | 10.000) | Basic [0.000, |
| | | 10.000) | [0.000, | 10.000) | | | | 10.000) |
| | | | 10.000) | | | | | |
| Protein binding | DPRA less | DPRA less | DPRA less | DPRA less | Out of mechanistic | DPRA less than 9% | DPRA less than | DPRA less |
| potency Lys (DPRA | than 9% | than 9% | than 9% | than 9% | domain | (DPRA 13%) | 9% (DPRA | than 9% |
| 13%) | (DPRA 13%) | (DPRA 13%) | (DPRA | (DPRA 13%) | | DPRA less than 9% | 13%) | (DPRA 13%) |
| | DPRA less | DPRA less | 13%) | DPRA less | | (DPRA 13%) | DPRA less than | DPRA less |
| | than 9% | than 9% | DPRA less | than 9% | | >> Vaniline derivatives | 9% (DPRA | than 9% |
| | (DPRA 13%) | (DPRA 13%) | than 9% | (DPRA 13%) | | | 13%) >> | (DPRA 13%) |
| | >> Non- | >> | (DPRA | >> | | | Alcohols | >> |
| | conjugated | Non- | 13%) >> | Non- | | | | Alcohols |
| | mono- and | conjugate d | Alcohols | conjugate d | | | | |
| | diketones | mono- and | | mono- and | | | | |
| | (non reactive) | diketones | | diketones | | | | |
| | | (non | | (non | | | | |
| | | reactive) | | reactive) | | | | |
| Protein binding | Out of | Out of | DPRA less | Out of | DPRA less than 9% | DPRA less than 9% | DPRA less than | DPRA less |
| potency Cys (DPRA | mechanistic | mechanistic | than 9% | mechanistic | (DPRA 13%) | (DPRA 13%) | 9% (DPRA | than 9% |
| 13%) | domain | domain | (DPRA | domain | DPRA less than 9% | DPRA less than 9% | 13%) | (DPRA 13%) |
| | | | 13%) | | (DPRA 13%) >> alpha | (DPRA 13%) | DPRA less than | DPRA less |
| | | | DPRA less | | alkyl | >> Non- Conjugated | 9% (DPRA | than 9% |
| | | | than 9% | | cinnamaldehydes | monoaldehydes (non | 13%) >> | (DPRA 13%) |
| | | | (DPRA | | | reactive) DPRA less | Alcohols | >> |
| | | | 13%) >> | | | than 9% (DPRA 13%) | | Alcohols |
| | | | Alcohols | | | >> Vaniline derivatives | | |

| InertFinder/ChemID | (+)-Fenchone | Camphor | Linalyl | p- Menthan- 3- | .alpha | 1,3-Benzodioxole- 5- | 1- Hexanol, | 1-Octen-3- ol |
|----------------------|----------------|--------------------|------------|--------------------|----------------------|----------------------|----------------|--------------------|
| Plus Name | | | oxide | one | Butylcinnamaldehyde | carboxaldehyde | 2-ethyl- | |
| Hydrolysis half-life | No value | No value | No value | No value | No value | No value | No value | No value |
| (Kb, pH 8) | | | | | | | | |
| (Hydrowin) | | | | | | | | |
| Hydrolysis half-life | No value | No value | No value | No value | No value | No value | No value | No value |
| (Kb, pH 7) | | | | | | | | |
| (Hydrowin) | | | | | | | | |
| Biodegradation | Does NOT | Does NOT | Does NOT | Biodegrades | Does NOT | Biodegrades Fast | Biodegrades | Biodegrades |
| probability (Biowin | Biodegrade | Biodegrade | Biodegrade | Fast | Biodegrade Fast | | Fast | Fast |
| 6) | Fast | Fast | Fast | | | | | |
| Protein binding by | No alert | No alert | No alert | No alert | Michael addition | No alert found | No alert found | No alert |
| OECD | found | found | found | found | Michael addition >> | | | found |
| | | | | | Polarised Alkenes | | | |
| | | | | | Michael addition >> | | | |
| | | | | | Polarised Alkenes >> | | | |
| | | | | | Polarised alkene - | | | |
| | | | | | aldehydes | | | |
| | | | | | Schiff Base Formers | | | |
| | | | | | Schiff Base Formers | | | |
| | | | | | >> Direct Acting | | | |
| | | | | | Schiff Base Formers | | | |
| | | | | | Schiff Base Formers | | | |
| | | | | | >> Direct Acting | | | |
| | | | | | Schiff Base Formers | | | |
| | | | | | >> Mono-carbonyls | | | |
| Ultimate biodeg | 10 to 100 | 1 to 10 days | 10 to 100 | 10 to 100 | No data | 1 to 10 days | 0 to 1 day | 1 to 10 days |
| | days | 10 to 100 | days | days | | 10 to 100 days | 1 to 10 days | 10 to 100 |
| | | days | | | | | | days |
| Ionization at pH = 9 | Acidic [0.000, | Acidic | Acidic | Acidic | Acidic [10.000, | Acidic [90.000, | Acidic [0.000, | Acidic |
| - | 10.000) | [0.000, | [0.000, | [0.000, | 20.000) | 100.000] | 10.000) | [0.000, |
| | • | 10.000) | 10.000) | 10.000) | No pKb value | Basic [0.000, | Basic [0.000, | 10.000) |
| | | , Basic [0.000, | Basic | , Basic [0.000, | | 10.000) | 10.000) | , Basic [0.000, |

| InertFinder/ChemID | (+)-Fenchone | Camphor | Linalyl | p- Menthan- 3- | .alpha | 1,3-Benzodioxole- 5- | 1- Hexanol, | 1-Octen-3- o |
|--|--------------------------------|--------------------------------|--------------------------------|--------------------------------|--|----------------------------|--------------------------------|--------------------------------|
| Plus Name | | | oxide | one | Butylcinnamaldehyde | carboxaldehyde | 2-ethyl- | |
| | | 10.000) | [0.000 <i>,</i> 10.000) | 10.000) | | | | 10.000) |
| Hydrolysis half-life (Ka, pH 7) (Hydrowin) | No value | No value | No value | No value |
| Toxic hazard classification by Cramer (extended) | Intermediate (Class II) | Intermediate (Class II) | High (Class III) | Intermediate (Class II) | Low (Class I) | High (Class III) | Low (Class I) | High (Class III) |
| Biodegradation | Does NOT Biodegrade Fast | Does NOT Biodegrade Fast | Does NOT Biodegrade Fast | Does NOT Biodegrade Fast | Does NOT Biodegrade Fast | Biodegrades Fast | Does NOT Biodegrade Fast | Does NOT Biodegrade Fast |
| DNA binding by OASIS | No alert found | No alert found | No alert found | No alert found | AN2 AN2 >> Nucleophilic addition to alpha, beta-unsaturated carbonyl compounds AN2 >> Nucleophilic addition to alpha, beta-unsaturated carbonyl compounds >> Alpha, Beta- Unsaturated Aldehydes AN2 >> Schiff base formation AN2 >> Schiff base formation >> Alpha, Beta- Unsaturated Aldehydes | No alert found | No alert found | No alert found |
| lonization at pH = 7.4 | Acidic [0.000, 10.000) | Acidic [0.000, | Acidic [0.000 <i>,</i> | Acidic [0.000 <i>,</i> | Acidic [0.000, 10.000) | Acidic [10.000, 20.000) | Acidic [0.000, 10.000) | Acidic [0.000, |

| InertFinder/ChemID Plus Name | (+)-Fenchone | Camphor | Linalyl oxide | p- Menthan- 3- one | .alpha Butylcinnamaldehyde | 1,3-Benzodioxole- 5- carboxaldehyde | 1- Hexanol, 2-ethyl- | 1-Octen-3- ol |
|--|--------------------------|-------------------------------------|--|-------------------------------------|--|--|--------------------------|-------------------------------------|
| | Basic [0.000, 10.000) | 10.000) Basic [0.000, 10.000) | 10.000) Basic [0.000, 10.000) | 10.000) Basic [0.000, 10.000) | No pKb value | Basic [0.000, 10.000) | Basic [0.000, 10.000) | 10.000) Basic [0.000, 10.000) |
| Hydrolysis half-life (Ka, pH 8) (Hydrowin) | No value | No value | No value | No value | No value | No value | No value | No value |
| • • • | No alert found | No alert found | No alert found | No alert found | Michael addition Michael addition >> Michael addition on alpha, beta- Unsaturated carbonyl compounds Michael addition >> Michael addition on alpha, beta- Unsaturated carbonyl compounds >> alpha, beta- Aldehydes Schiff base formation Schiff base formation >> Schiff base formation with carbonyl compounds Schiff base formation >> Schiff base formation with carbonyl compounds Schiff base | | No alert found | No alert found |
| DNA binding by | No alert | No alert | No alert | No alert | No alert found | Michael addition | No alert found | No alert |

| InertFinder/ChemID | (+)-Fenchone | Camphor | Linalyl | p- Menthan- 3- | | 1,3-Benzodioxole- 5- | 1- Hexanol, | 1-Octen-3- ol |
|---|--------------------|--------------------|--------------------|-------------------|---------------------|---|---|-------------------|
| Plus Name | | | oxide | one | Butylcinnamaldehyde | • | 2-ethyl- | |
| OECD | found | found | found | found | | Michael addition >> P450 Mediated Activation to Quinones and Quinone-type Chemicals Michael addition >> P450 Mediated Activation to Quinones and Quinone-type | Y | found |
| Biodegradation | Does NOT | Does NOT | Does NOT | Biodegrades | Biodegrades Fast | Chemicals >> Methylenedioxyphenyl Biodegrades Fast | Biodegrades | Biodegrades |
| probability (Biowin 1) | Biodegrade Fast | Biodegrade Fast | Biodegrade Fast | Fast | | | Fast | Fast |
| Biodegradation primary (Biowin 4) | Days to weeks | Days to weeks | Days to weeks | Days to weeks | Days | Days | Days | Days |
| Carcinogenicity (genotox and nongenotox) alerts by ISS | No alert found | No alert found | No alert found | No alert found | No alert found | 1,3- Benzodioxoles (Nongenotox) Simple aldehyde (Genotox) Structural alerts for both genotoxic and nongenotoxic carcinogenicity | Structural alert for nongenotoxic carcinogenicity Substitute d n- alkylcarboxylic acids (Nongenotox) | No alert found |
| in vitro mutagenicity (Ames test) alerts by ISS | No alert found | No alert found | No alert found | No alert found | No alert found | Simple aldehyde | No alert found | No alert found |
| in vivo | No alert | No alert | H- | No alert | No alert found | H-acceptor-path3 H- | No alert found | No alert |

| InertFinder/ChemID | (+)-Fenchone | Camphor | Linalyl | p- Menthan- 3- | .alpha | 1,3-Benzodioxole- 5- | 1- Hexanol, | 1-Octen-3- o |
|---|---|--|-----------------------------------|--|--|---|-------------------------------|-------------------------------|
| Plus Name | | | oxide | one | Butylcinnamaldehyde | carboxaldehyde | 2-ethyl- | |
| mutagenicity (Micronucleus) alerts by ISS | found | found | acceptor- path3-H- acceptor | found | | acceptor Simple aldehyde | | found |
| - | | | Oxolane | | | | | |
| Protein Binding | No alert | No alert | No alert | No alert | alpha, beta- | No alert found | No alert found | No alert |
| Potency h-CLAT | found | found | found | found | Unsaturated aldehydes | | | found |
| Skin irritation/corrosion Inclusion rules by BfR | Ketones | Ketones | Inclusion rules not met | Ketones | Aldehydes | Aldehydes | Inclusion rules not met | Inclusion rules not met |
| DNA alerts for | No alert | No alert | No alert | No alert | No alert found | No alert found | No alert found | No alert |
| AMES, CA and MNT | | found | found | found | No alert Touriu | | NO alert Tourio | found |
| by OASIS | lound | Iounu | lound | lound | | | | lound |
| Protein binding | Nucleophilic | Nucleophilic | No alert | Nucleophilic | Michael Addition | Schiff base formation | No alert found | No alert |
| alerts for skin | addition | addition | found | addition | Michael Addition >> | Schiff base formation | | found |
| sensitization by | Nucleophilic | Nucleophilic | | Nucleophilic | Michael addition on | >> Schiff base | | |
| OASIS | addition >> Addition to carbon- hetero | addition >> Addition to carbon- | | addition >> Addition to carbon- | alpha, beta- Unsaturated carbonyl compounds Michael Addition >> | formation with carbonyl compounds Schiff base formation >> Schiff base | | |
| | double bonds Nucleophilic addition >> | | | hetero double bonds | Michael addition on alpha, beta- Unsaturated | formation with carbonyl compounds >> Aldehydes | | |
| | Addition to carbon- | Nucleophilic addition | | Nucleophilic addition | carbonyl compounds >> alpha, beta- | | | |
| | hetero double bonds >> Ketones | >> Addition to carbon- hetero double | | >> Addition to carbon- hetero double | Aldehydes | | | |

| InertFinder/ChemID | (+)-Fenchone | Camphor | Linalyl | p-Menthan- 3- | .alpha | 1,3-Benzodioxole- 5- | 1- Hexanol, | 1-Octen-3- o |
|----------------------|--------------|-----------|-----------|---------------|-----------------------|-----------------------|----------------|--------------|
| Plus Name | | | oxide | one | Butylcinnamaldehyde | carboxaldehyde | 2-ethyl- | |
| | | bonds >> | | bonds >> | | | | |
| | | Ketones | | Ketones | | | | |
| rtER Expert System | No alert | No alert | No alert | No alert | No alert found | No alert found | No alert | No alert |
| - | found | found | found | found | | | found | found |
| USEPA | | | | | | | | |
| Skin | Undefined | Undefined | Undefined | Undefined | Undefined | Group C Melting Point | Undefined | Undefined |
| irritation/corrosion | | | | | | > 55 C Undefined | | |
| Exclusion rules by | | | | | | | | |
| BfR | | | | | | | | |
| Protein binding | No alert | No alert | No alert | No alert | AN2 | No alert found | No alert found | No alert |
| alerts for | found | found | found | found | AN2 >> Michael | | | found |
| Chromosomal | | | | | addition to activated | | | |
| aberration by | | | | | double bonds | | | |
| OASIS | | | | | AN2 >> Michael | | | |
| | | | | | addition to activated | | | |
| | | | | | double bonds >> | | | |
| | | | | | alpha, beta- | | | |
| | | | | | Unsaturated | | | |
| | | | | | Carbonyls and | | | |
| | | | | | Related Compounds | | | |

| InertFinder/ChemI | 1-p-Menthene- | 2,3- | 2,5- | 2,6- | 2-Ethyl-3- | 2-Isobutyl- 3- | 2- | 2- | 2-Methyl- 4- |
|---------------------|----------------|------------------|----------------|----------------|----------------|------------------|----------------|----------------|---------------|
| D Plus Name | 8 thiol | Hexanedione | Dimethyl | Dimethyl | methylpyrazin | methoxypyrazin | Isopropyl- 4- | Methoxy- 3- | propyl- 1,3- |
| | | | pyrazine | pyrazine | е | e | methylthiazol | (1- | oxathiane |
| | | | | | | | e | methylpropyl | |
| | | | | | | | |) pyrazine | |
| CAS | 71159-90-5 | 3848-24-6 | 123-32-0 | 108-50-9 | 15707-23-0 | 24683-00-9 | 15679-13-7 | 24168-70-5 | 67715-80-4 |
| SMILES | CC1=CCC(CC1) | CCCC(=O)C(C)= | Cc1cnc(C) cn1 | Cc1cncc(C | CCc1nccn c1C | COc1nccn | CC(C)c1sc | CCC(C)c1 | CCCC1CC |
| | C(C)(C)S | 0 | |)n1 | | c1CC(C)C | c(C)n1 | nccnc1OC | OC(C)S1 |
| Ionization at pH = | Acidic [0.000, | Acidic [0.000, | Acidic [0.000, | Acidic [0.000, | Acidic [0.000, | Acidic [0.000, | Acidic [0.000, | Acidic [0.000, | Acidic |
| 1 | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) | [0.000, |
| | No pKb value | Basic [0.000, | Basic [70.000, | • | Basic [70.000, | Basic [40.000, | | Basic [40.000, | 10.000) |
| | | 10.000) | 80.000) | 100.000] | 80.000) | 50.000) | 100.000] | 50.000) | Basic [0.000, |
| | | | | | | | | | 10.000) |
| | | | | | | | | | |
| Biodegradation | Weeks to | Weeks | Weeks | Weeks | Weeks | Weeks to | Weeks to | Weeks to | Weeks |
| ultimate (Biowin 3) | | | | | | months | months | months | |
| Estrogen Receptor | Non binder, | Non binder, | Non binder, | Non | Non binder, | Non binder, | Non | Non binder, | Non |
| Binding | | non cyclic | without OH | binder, | without OH | without OH | binder, | without OH | binder, |
| | NH2 group | structure | or NH2 | | or NH2 | or NH2 | without | or NH2 | without |
| | | | group | | group | group | OH or NH2 | group | OH or |
| | | | | group | | | group | | NH2 |
| | | | | | | | | | group |
| Biodeg BioHC | No value | No value | No value | No value | No value | No value | No value | No value | No value |
| half-life (Biowin) | | | | | | | | | |
| Hydrolysis half- | No value | No value | No value | No value | No value | No value | No value | No value | No value |
| life (pH 6.5-7.4) | | | | | | | | | |
| Biodegradation | Does NOT | Biodegrades | Does NOT | Does NOT | Does NOT | Does NOT | Does NOT | Does NOT | Does NOT |
| probability | Biodegrade | Fast | Biodegrade | | Biodegrade | Biodegrade | Biodegrade | Biodegrade | Biodegrad |
| (Biowin 5) | Fast | | Fast | Fast | Fast | Fast | Fast | Fast | e Fast |
| Toxic hazard | Low (Class I) | High (Class III) | Intermediat | High (Class | High (Class | High (Class III) | High (Class | High (Class | High |
| classification by | | | e (Class II) | III) | III) | | 111) | 111) | (Class III) |
| Cramer | | | | | | | | | |
| Biodegradation | Does NOT | Biodegrades | Biodegrade | Biodegrade | Biodegrades | Biodegrades | Biodegrade | Biodegrade | Does NOT |

| InertFinder/ChemI | 1-p-Menthene- | 2,3- | 2,5- | 2,6- | 2-Ethyl-3- | 2-Isobutyl- 3- | 2- | 2- | 2-Methyl- 4- |
|--------------------|-----------------|----------------|------------|------------|---------------|----------------|---------------|--------------|--------------|
| D Plus Name | 8 thiol | Hexanedione | Dimethyl | Dimethyl | methylpyrazin | methoxypyrazin | Isopropyl- 4- | Methoxy- 3- | propyl- 1,3- |
| | | | pyrazine | pyrazine | е | e | methylthiazol | (1- | oxathiane |
| | | | | | | | е | methylpropyl | |
| | | | | | | | |) pyrazine | |
| probability | Biodegrade | Fast | s Fast | s Fast | Fast | Fast | s Fast | s Fast | Biodegrad |
| (Biowin 2) | Fast | | | | | | | | e Fast |
| Ionization at pH = | Acidic [0.000, | Acidic [0.000, | Acidic | Acidic | Acidic | Acidic [0.000, | Acidic | Acidic | Acidic |
| 4 | 10.000) | 10.000) | [0.000, | [0.000, | [0.000, | 10.000) | [0.000, | [0.000, | [30.000, |
| | No pKb value | Basic [0.000, | 10.000) | 10.000) | 10.000) | Basic [0.000, | 10.000) | 10.000) | 40.000) |
| | | 10.000) | Basic | Basic | Basic [0.000, | 10.000) | Basic | Basic | Basic |
| | | | [0.000, | [0.000, | 10.000) | | [10.000, | [0.000, | [0.000, |
| | | | 10.000) | 10.000) | | | 20.000) | 10.000) | 10.000) |
| Protein binding | DPRA less than | Out of | DPRA less | DPRA less | DPRA less | DPRA less | DPRA less | DPRA less | DPRA less |
| potency Lys | 9% (DPRA | mechanistic | than 9% | than 9% | than 9% | than 9% | than 9% | than 9% | than 9% |
| (DPRA 13%) | 13%) | domain | (DPRA 13%) | (DPRA | (DPRA 13%) | (DPRA 13%) | (DPRA | (DPRA 13%) | (DPRA |
| | DPRA less than | | DPRA less | 13%) | DPRA less | DPRA less | 13%) | DPRA less | 13%) |
| | 9% (DPRA | | than 9% | DPRA less | than 9% | than 9% | DPRA less | than 9% | DPRA less |
| | 13%) | | (DPRA 13%) | than 9% | (DPRA 13%) | (DPRA 13%) | than 9% | (DPRA 13%) | than 9% |
| | >> Thiols and | | >> | (DPRA | >> | >> | (DPRA | >> | (DPRA |
| | disulfides (non | | No protein | 13%) >> | No protein | No protein | 13%) >> | No protein | 13%) >> |
| | reactive) | | binding | No protein | binding alert | binding alert | No protein | binding | No |
| | | | alert | binding | | | binding | alert | protein |
| | | | | alert | | | alert | | binding |
| | | | | | | | | | alert |
| Protein binding | DPRA above | DPRA above | DPRA less | DPRA less | DPRA less | DPRA less | DPRA less | DPRA less | DPRA less |
| potency Cys | 21% (DPRA | 21% | than 9% | than 9% | than 9% | than 9% | than 9% | than 9% | than 9% |
| (DPRA 13%) | 13%) | (DPRA 13%) | (DPRA 13%) | (DPRA | (DPRA 13%) | (DPRA 13%) | (DPRA | (DPRA 13%) | (DPRA |
| | DPRA above | DPRA above | DPRA less | 13%) | DPRA less | DPRA less | 13%) | DPRA less | 13%) |
| | 21% (DPRA | 21% | than 9% | DPRA less | than 9% | than 9% | DPRA less | than 9% | DPRA less |
| | 13%) >> Thiols | (DPRA 13%) | (DPRA 13%) | than 9% | (DPRA 13%) | (DPRA 13%) | than 9% | (DPRA 13%) | than 9% |
| | (reactive) | >> 1,2- | >> | (DPRA | >> | >> | (DPRA | >> | (DPRA |
| | | and 1,3- | No protein | 13%) >> | No protein | No protein | 13%) >> | No protein | 13%) >> |

| InertFinder/ChemI | | | 2,5- | 2,6- | 2-Ethyl-3- | , | 2- | 2- | 2-Methyl- 4- |
|---|---|--|----------------------|--------------------------------|--------------------|---------------------|--------------------------------|----------------------------|-----------------------------------|
| D Plus Name | 8 thiol | Hexanedione | Dimethyl pyrazine | Dimethyl pyrazine | methylpyrazin e | methoxypyrazin e | methylthiazol e | methylpropyl) pyrazine | propyl- 1,3- oxathiane |
| | | Diketones (reactive) | binding alert | No protein binding alert | binding alert | binding alert | No protein binding alert | binding alert | No protein binding alert |
| Hydrolysis half- life (Kb, pH 8) (Hydrowin) | No value | No value | No value | No value | No value | No value | No value | No value | No value |
| Hydrolysis half- life (Kb, pH 7) (Hydrowin) | No value | No value | No value | No value | No value | No value | No value | No value | No value |
| Biodegradation | Does NOT | Biodegrades | Does NOT | Does NOT | Does NOT | Does NOT | Does NOT | Does NOT | Does NOT |
| probability | Biodegrade | Fast | Biodegrade | Biodegrade | Biodegrade | Biodegrade | Biodegrade | Biodegrade | Biodegrad |
| (Biowin 6) | Fast | | Fast | Fast | Fast | Fast | Fast | Fast | e Fast |
| Protein binding by | SN2 | Schiff Base | No alert | No alert | No alert | No alert | No alert | No alert | No alert |
| OECD | SN2 >> SN2 reaction at a sulphur atom SN2 >> SN2 reaction at a sulphur atom >> Thiols | Formers Schiff Base Formers >> Direct Acting Schiff Base Formers Schiff Base Formers >> Direct Acting Schiff Base Formers >> 1-2- Dicarbonyls | found | found | found | found | found | found | found |

| InertFinder/ChemI | 1-p-Menthene- | 2,3- | 2,5- | 2,6- | 2-Ethyl-3- | 2-Isobutyl- 3- | 2- | 2- | 2-Methyl- 4- |
|--------------------|----------------------|------------------|--------------|-------------|---------------|------------------|---------------|--------------|--------------|
| D Plus Name | 8 thiol | Hexanedione | Dimethyl | Dimethyl | methylpyrazin | methoxypyrazin | Isopropyl- 4- | Methoxy- 3- | propyl- 1,3- |
| | | | pyrazine | pyrazine | е | e | methylthiazol | (1- | oxathiane |
| | | | | | | | e | methylpropyl | |
| | | | | | | | |) pyrazine | |
| Ultimate biodeg | No data | No data | No data | No data | > 100 | No data | No data | No data | No data |
| | | | | | days | | | | |
| Ionization at pH = | | Acidic [0.000, | Acidic | Acidic | Acidic | Acidic | Acidic | Acidic | Acidic |
| 9 | 10.000) | 10.000) | [60.000, | [60.000, | [60.000, | [60.000, | [0.000, | [60.000, | [90.000, |
| | No pKb value | Basic [0.000, | 70.000) | 70.000) | 70.000) | 70.000) | 10.000) | 70.000) | 100.000] |
| | | 10.000) | Basic | Basic | Basic [0.000, | Basic [0.000, | Basic | Basic | Basic |
| | | | [0.000, | [0.000, | 10.000) | 10.000) | [0.000, | [0.000, | [0.000, |
| | | | 10.000) | 10.000) | | | 10.000) | 10.000) | 10.000) |
| Hydrolysis half- | No value | No value | No value | No value | No value | No value | No value | No value | No value |
| life (Ka, pH 7) | | | | | | | | | |
| (Hydrowin) | | | | | | | | | |
| Toxic hazard | Low (Class I) | High (Class III) | Intermediat | High (Class | High (Class | High (Class III) | High (Class | High (Class | High |
| classification by | | | e (Class II) | III) | III) | | III) | III) | (Class III) |
| Cramer | | | | | | | | | |
| (extended) | | | | | | | | | |
| Biodegradation | Does NOT | Biodegrades | Does NOT | Does NOT | Does NOT | Does NOT | Does NOT | Biodegrade | Does NOT |
| probability | Biodegrade | Fast | Biodegrade | Biodegrade | Biodegrade | Biodegrade | Biodegrade | s Fast | Biodegrad |
| (Biowin 7) | Fast | | Fast | Fast | Fast | Fast | Fast | | e Fast |
| DNA binding by | Radical Radical | No alert found | No alert | No alert | No alert | No alert | No alert | No alert | No alert |
| OASIS | >> | | found | found | found | found | found | found | found |
| | Radical | | | | | | | | |
| | mechanism via | | | | | | | | |
| | ROS formation | | | | | | | | |
| | (indirect) | | | | | | | | |
| | Radical >> | | | | | | | | |
| | Radical | | | | | | | | |
| | mechanism via | | | | | | | | |
| | ROS formation | | | | | | | | |

| InertFinder/ChemI | 1-p-Menthene- | 2,3- | 2,5- | 2,6- | 2-Ethyl-3- | 2-Isobutyl- 3- | 2- | 2- | 2-Methyl- 4- |
|-----------------------------|-------------------------|----------------|----------------------|----------------------|-------------------------|---------------------|-------------------------------------|---|---------------------------|
| | 8 thiol | Hexanedione | Dimethyl pyrazine | Dimethyl pyrazine | , methylpyrazin e | methoxypyrazin e | lsopropyl- 4- methylthiazol e | Methoxy- 3- (1- methylpropyl | propyl- 1,3- oxathiane |
| | | | | | | | C |) pyrazine | |
| | (indirect) >> Thiols | | | | | | | , | |
| Ionization at pH = | Acidic [0.000, | Acidic [0.000, | Acidic | Acidic | Acidic | Acidic [0.000, | Acidic | Acidic | Acidic |
| 7.4 | 10.000) | 10.000) | [0.000, | [0.000, | [0.000, | 10.000) | [0.000, | [0.000, | [90.000, |
| | No pKb value | Basic [0.000, | 10.000) | 10.000) | 10.000) | Basic [0.000, | 10.000) | 10.000) | 100.000] |
| | | 10.000) | Basic | Basic | Basic [0.000, | 10.000) | | Basic | Basic |
| | | | [0.000, | [0.000, | 10.000) | | [0.000, | [0.000, | [0.000, |
| | | | 10.000) | 10.000) | | | | 10.000) | 10.000) |
| Hydrolysis half- | No value | No value | No value | No value | No value | No value | No value | No value | No value |
| life (Ka, pH 8) | | | | | | | | | |
| (Hydrowin) | SN2 SN2 >> | Schiff base | No alert | No alert | No alert | No alert | No alert | No alert | No alert |
| Protein binding by OASIS | Interchange | formation | found | found | found | found | | found | found |
| UA313 | • | Schiff base | Touriu | lound | lound | Iounu | Iouna | Iouna | Touriu |
| | sulphur | formation | | | | | | | |
| | containing | >> Direct | | | | | | | |
| | compounds | acting Schiff | | | | | | | |
| | SN2 >> | base formers | | | | | | | |
| | Interchange | Schiff base | | | | | | | |
| | reaction with | formation | | | | | | | |
| | sulphur | >> Direct | | | | | | | |
| | containing | acting Schiff | | | | | | | |
| | compounds >> | base formers | | | | | | | |
| | Thiols | >> 1,2- | | | | | | | |
| | | Dicarbonyls | | | | | | | |

| InertFinder/ChemI D Plus Name | 1-p-Menthene- 8 thiol | Hexanedione and 1,3- | 2,5- Dimethyl pyrazine | 2,6- Dimethyl pyrazine | 2-Ethyl-3- methylpyrazin e | 2-Isobutyl- 3- methoxypyrazin e | 2- Isopropyl- 4- methylthiazol e | 2- Methoxy- 3- (1- methylpropyl) pyrazine | 2-Methyl- 4- propyl- 1,3- oxathiane |
|---|--------------------------------|--|------------------------------|------------------------------|----------------------------------|---------------------------------------|---|--|---|
| DNA binding by OECD | No alert found | Dicarbonyls Schiff base formers Schiff base formers >> Direct Acting Schiff Base Formers Schiff base formers >> Direct Acting Schiff Base Formers >> Alpha- beta- dicarbonyl | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found |
| Biodegradation probability (Biowin 1) | Does NOT Biodegrade Fast | Biodegrades Fast | Biodegrade s Fast | Biodegrade s Fast | Biodegrades Fast | Biodegrades Fast | Biodegrade s Fast | Biodegrade s Fast | Does NOT Biodegrad e Fast |
| Biodegradation primary (Biowin 4) | Days to weeks | Days to weeks | Days to weeks | Days to weeks | Days to weeks | Days to weeks | Days to weeks | Days to weeks | Days to weeks |
| Carcinogenicity (genotox and nongenotox) alerts by ISS | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found |
| in vitro mutagenicity | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found |

| InertFinder/ChemI | | | 2,5- | 2,6- | 2-Ethyl-3- | 2-Isobutyl- 3- | 2- | 2- | 2-Methyl- 4- |
|---------------------|-----------------|----------------|-----------|-----------|---------------|----------------|---------------|--------------|--------------|
| D Plus Name | 8 thiol | Hexanedione | Dimethyl | Dimethyl | methylpyrazin | methoxypyrazin | Isopropyl- 4- | Methoxy- 3- | propyl- 1,3- |
| | | | pyrazine | pyrazine | e | e | methylthiazol | (1- | oxathiane |
| | | | | | | | е | methylpropyl | |
| | | | | | | | |) pyrazine | |
| (Ames test) alerts | | | | | | | | | |
| by ISS | | | | | | | | | |
| in vivo | No alert found | H-acceptor- | H- | H- | H- | Н- | No alert | Н- | No alert |
| mutagenicity | | path3-H- | acceptor- | acceptor- | acceptor- | acceptor- | found | acceptor- | found |
| (Micronucleus) | | acceptor | path3-H- | path3-H- | path3-H- | path3-H- | | path3-H- | |
| alerts by ISS | | | acceptor | acceptor | acceptor | acceptor | | acceptor | |
| Protein Binding | Thiols and | 1,2- and 1,3- | No alert | No alert | No alert | No alert | No alert | No alert | No alert |
| Potency h-CLAT | disulfides | Dicarbonyls | found | found | found | found | found | found | found |
| Skin | Inclusion rules | Ketones | Inclusion | Inclusion | Inclusion | Inclusion | Inclusion | Inclusion | Inclusion |
| irritation/corrosio | not met | | rules not | rules not | rules not | rules not | rules not | rules not | rules not |
| n Inclusion rules | | | met | met | met | met | met | met | met |
| by BfR | | | | | | | | | |
| DNA alerts for | No alert found | No alert found | No alert | No alert | No alert | No alert | No alert | No alert | No alert |
| AMES, CA and | | | found | found | found | found | found | found | found |
| MNT by OASIS | | | | | | | | | |
| Protein binding | SN2 SN2 >> | Schiff base | No alert | No alert | No alert | No alert | No alert | No alert | No alert |
| alerts for skin | Interchange | formation | found | found | found | found | found | found | found |
| sensitization by | reaction with | Schiff base | | | | | | | |
| OASIS | sulphur | formation | | | | | | | |
| | Ŭ | >> Direct | | | | | | | |
| | • | acting Schiff | | | | | | | |
| | SN2 >> | base formers | | | | | | | |
| | Interchange | Schiff base | | | | | | | |
| | | formation | | | | | | | |
| | • | >> Direct | | | | | | | |
| | U U | acting Schiff | | | | | | | |
| | compounds >> | | | | | | | | |
| | Thiols and | >> 1,2- | | | | | | | |

| InertFinder/ChemI | 1-p-Menthene- | 2,3- | 2,5- | 2,6- | 2-Ethyl-3- | 2-Isobutyl- 3- | 2- | 2- | 2-Methyl- 4- |
|---------------------|----------------|----------------|-----------|-----------|---------------|----------------|---------------|--------------|--------------|
| D Plus Name | 8 thiol | Hexanedione | Dimethyl | Dimethyl | methylpyrazin | methoxypyrazin | Isopropyl- 4- | Methoxy- 3- | propyl- 1,3- |
| | | | pyrazine | pyrazine | e | e | methylthiazol | (1- | oxathiane |
| | | | | | | | е | methylpropyl | |
| | | | | | | | |) pyrazine | |
| | disulfide | Dicarbonyls | | | | | | | |
| | compounds | and 1,3- | | | | | | | |
| | | Dicarbonyls | | | | | | | |
| rtER Expert | No alert found | No alert found | No alert | No alert | No alert | No alert | No alert | No alert | No alert |
| System - | | | found | found | found | found | found | found | found |
| USEPA | | | | | | | | | |
| Skin | Undefined | Undefined | Undefined | Undefined | Undefined | Undefined | Undefined | Undefined | Undefined |
| irritation/corrosio | | | | | | | | | |
| n Exclusion rules | | | | | | | | | |
| by BfR | | | | | | | | | |
| Protein binding | No alert found | No alert found | No alert | No alert | No alert | No alert | No alert | No alert | No alert |
| alerts for | | | found | found | found | found | found | found | found |
| Chromosomal | | | | | | | | | |
| aberration by | | | | | | | | | |
| OASIS | | | | | | | | | |

| InertFinder/Che | 2- | 2- | 2- | 2- | 2- | 3,4- | 3- | 3-Methyl- | 3-Methyl- 2- | 3-Methyl- 2- | 3-Methyl- 5- |
|-------------------|-------------|------------|------------|------------|------------|--------------|------------|---------------|----------------|----------------|----------------|
| mID Plus Name | Methylpyraz | Nonanon | Octanone | Tridecano | Undecano | Dimethyl- | Heptanon | 1- | (2- | (n- pentanyl)- | (2,2,3- |
| | ine | e | | ne | ne | 1,2- | e | cyclopentad | pentenyl)- 2- | 2- cyclopent | trimethyl- 3- |
| | | | | | | cyclopentadi | | ecanone | cyclopenten- | en-1-one | cyclopent en- |
| | | | | | | one | | | 1-one | | 1- yl) pent-4- |
| | | | | | | | | | | | en-2-ol |
| CAS | 109-08-0 | 821-55-6 | 111-13-7 | 593-08-8 | 112-12-9 | 13494-06-9 | 106-35-4 | 541-91-3 | 488-10-8; | 1128-08-1 | 67801-20-1 |
| | | | | | | | | | 6261-18-3 | | |
| SMILES | Cc1cnccn 1 | 2222222 |)000000 | 2222222 | 2222222 | | | CC1CCCC | CCC=CCC | CCCCCC1 | CC(O)C(C) |
| | | C(C)=O | C)=O | CCCCC(C) | CCC(C)=O | =O |)CC | CCCCCCC | 1=C(CCC1 | =C(C)CCC 1=O | \C=C/C1C |
| | | | | =O | |)C1C | | CC(=O)C1 | =O)C | | C=C(C)C1(C)C |
| Ionization at pH | Acidic | Acidic | Acidic | Acidic | Acidic | Acidic | Acidic | Acidic | Acidic [0.000, | Acidic [0.000, | Acidic [0.000, |
| = 1 | [0.000, | [0.000, | [0.000, | [0.000, | [0.000, | [0.000, | [0.000, | [0.000, | 10.000) | 10.000) | 10.000) |
| | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) | Basic [0.000, | Basic [0.000, | Basic [0.000, |
| | Basic | Basic | Basic | Basic | Basic | No pKb | Basic | Basic [0.000, | 10.000) | 10.000) | 10.000) |
| | [70.000, | [0.000, | [0.000, | [0.000, | [0.000, | value | [0.000, | 10.000) | | | |
| | 80.000) | 10.000) | 10.000) | 10.000) | 10.000) | | 10.000) | | | | |
| Biodegradation | Weeks | Weeks | Weeks | Weeks | Weeks | Weeks | Weeks | Weeks to | Weeks | Weeks | Weeks to |
| ultimate (Biowin | | | | | | | | months | | | months |
| 3) | | | | | | | | | | | |
| Estrogen | Non | Non | Non | Non | Non | Non binder, | Non | Non | Non | Non | Non |
| Receptor | binder, | binder, | binder, | binder, | binder, | without OH | binder, | binder, | binder, | binder, | binder, |
| Binding | without | non cyclic | non cyclic | non cyclic | non cyclic | or NH2 | non cyclic | without | without OH | without OH | without OH |
| | OH or | structure | structure | structure | structure | group | structure | OH or | or NH2 | or NH2 | or NH2 |
| | NH2 | | | | | | | NH2 | group | group | group |
| | group | | | | | | | group | | | |
| Biodeg BioHC | No value | No value | No value | No value | No value | No value | No value | No value | No value | No value | No value |
| half-life | | | | | | | | | | | |
| (Biowin) | | | | | | | | | | | |
| Hydrolysis half- | No value | No value | No value | No value | No value | No value | No value | No value | No value | No value | No value |
| life (pH 6.5-7.4) | | | | | | | | | | | |
| Biodegradation | Does NOT | Biodegrad | Biodegrad | Biodegrad | Biodegrad | Does NOT | Biodegrad | Does NOT | Does NOT | Biodegrade | Does NOT |
| probability | Biodegrad | es Fast | es Fast | es Fast | es Fast | Biodegrade | es Fast | Biodegrad | Biodegrade | s Fast | Biodegrade |

| InertFinder/Che | 2- | 2- | 2- | 2- | 2- | 3,4- | 3- | 3-Methyl- | 3-Methyl- 2- | 3-Methyl- 2- | 3-Methyl- 5- |
|-------------------|-------------|------------|------------|------------|------------|--------------|------------|-------------|---------------|----------------|----------------|
| mID Plus Name | Methylpyraz | Nonanon | Octanone | Tridecano | Undecano | Dimethyl- | Heptanon | 1- | (2- | (n- pentanyl)- | (2,2,3- |
| | ine | e | | ne | ne | 1,2- | e | cyclopentad | pentenyl)- 2- | 2- cyclopent | trimethyl- 3- |
| | | | | | | cyclopentadi | | ecanone | cyclopenten- | en-1-one | cyclopent en- |
| | | | | | | one | | | 1-one | | 1- yl) pent-4- |
| | | | | | | | | | | | en-2-ol |
| (Biowin 5) | e Fast | | | | | Fast | | e Fast | Fast | | Fast |
| Toxic hazard | Intermedi | Intermedi | Intermedi | Intermedi | Intermedi | Intermediat | Intermedi | Intermedi | Intermediat | Intermediat | Low (Class |
| classification by | ate (Class | ate (Class | ate (Class | ate (Class | ate (Class | e (Class II) | ate (Class | ate (Class | e (Class II) | e (Class II) | I) |
| Cramer | II) | II) | II) | II) | II) | | II) | II) | | | |
| Biodegradation | Biodegrad | Biodegrad | Biodegrad | Biodegrad | Biodegrad | Biodegrades | Biodegrad | Does NOT | Biodegrade | Biodegrade | Does NOT |
| probability | es Fast | es Fast | es Fast | es Fast | es Fast | Fast | es Fast | Biodegrad | s Fast | s Fast | Biodegrade |
| (Biowin 2) | | | | | | | | e Fast | | | Fast |
| Ionization at pH | Acidic | Acidic | Acidic | Acidic | Acidic | Acidic | Acidic | Acidic | Acidic | Acidic | Acidic |
| = 4 | [0.000, | [0.000, | [0.000, | [0.000, | [0.000, | [0.000, | [0.000, | [0.000, | [0.000, | [0.000, | [0.000, |
| | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) |
| | Basic | Basic | Basic | Basic | Basic | No рКb | Basic | Basic | Basic | Basic | Basic |
| | [0.000, | [0.000, | [0.000, | [0.000, | [0.000, | value | [0.000, | [0.000, | [0.000, | [0.000, | [0.000, |
| | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) | | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) |
| Protein binding | DPRA less | Out of | Out of | Out of | DPRA less | DPRA less | DPRA less |
| potency Lys | than 9% | mechanist | mechanist | mechanist | mechanist | mechanistic | mechanist | mechanist | than 9% | than 9% | than 9% |
| (DPRA 13%) | (DPRA | ic domain | ic domain | ic domain | ic domain | domain | ic domain | ic domain | (DPRA 13%) | (DPRA 13%) | (DPRA 13%) |
| | 13%) | | | | | | | | DPRA less | DPRA less | DPRA less |
| | DPRA less | | | | | | | | than 9% | than 9% | than 9% |
| | than 9% | | | | | | | | (DPRA 13%) | (DPRA 13%) | (DPRA 13%) |
| | (DPRA | | | | | | | | >> | >> | >> |
| | 13%) >> | | | | | | | | Conjugate d | Conjugate d | Alcohols |
| | No | | | | | | | | alpha, beta- | alpha, beta- | |
| | protein | | | | | | | | unsaturate | unsaturate | |
| | binding | | | | | | | | d ketones | d ketones | |
| | alert | | | | | | | | (non | (non | |
| | | | | | | | | | reactive) | reactive) | |
| Protein binding | DPRA less | Out of | Out of | Out of | DPRA less | DPRA less | DPRA less |

| InertFinder/Che | 2- | 2- | 2- | 2- | 2- | 3,4- | 3- | 3-Methyl- | 3-Methyl- 2- | 3-Methyl- 2- | 3-Methyl- 5- |
|-----------------------|--------------|--------------|--------------|--------------|--------------|------------------------|--------------|-------------|---------------|----------------|----------------|
| mID Plus Name | Methylpyraz | Nonanon | Octanone | Tridecano | Undecano | Dimethyl- | Heptanon | 1- | (2- | (n- pentanyl)- | (2,2,3- |
| | ine | е | | ne | ne | 1,2- | e | cyclopentad | pentenyl)- 2- | 2- cyclopent | trimethyl- 3- |
| | | | | | | cyclopentadi | | ecanone | cyclopenten- | en-1-one | cyclopent en- |
| | | | | | | one | | | 1-one | | 1- yl) pent-4- |
| | | | | | | | | | | | en-2-ol |
| potency Cys | than 9% | mechanist | mechanist | mechanist | mechanist | mechanistic | mechanist | mechanist | than 9% | than 9% | than 9% |
| (DPRA 13%) | (DPRA | ic domain | ic domain | ic domain | ic domain | domain | ic domain | ic domain | (DPRA 13%) | (DPRA 13%) | (DPRA 13%) |
| | 13%) | | | | | | | | DPRA less | DPRA less | DPRA less |
| | DPRA less | | | | | | | | than 9% | than 9% | than 9% |
| | than 9% | | | | | | | | (DPRA 13%) | (DPRA 13%) | (DPRA 13%) |
| | (DPRA | | | | | | | | >> | >> | >> |
| | 13%) >> | | | | | | | | No protein | No protein | Alcohols |
| | No | | | | | | | | binding | binding | |
| | protein | | | | | | | | alert | alert | |
| | binding | | | | | | | | | | |
| | alert | | | | | | - | | | | - |
| | No value | No value | No value | No value | No value | No value |
| life (Kb, | | | | | | | | | | | |
| pH 8) | | | | | | | | | | | |
| (Hydrowin) | | | | | | | | | | | |
| , , | No value | No value | No value | No value | No value | No value |
| life (Kb, | | | | | | | | | | | |
| pH 7) | | | | | | | | | | | |
| (Hydrowin) | Die de sue d | Die de sus de s | Die de eve d | | Die de sue de | Diadaanada | |
| Biodegradation | Biodegrad | 0 | 0 | - | - | Biodegrades | - | | Biodegrade | Biodegrade | Does NOT |
| probability | es Fast | Fast | es Fast | Biodegrad | s Fast | s Fast | Biodegrade |
| (Biowin 6) | N1 | | NL L I | N a slast | | | NL L L | e Fast | | N | Fast |
| Protein binding | No alert | Schiff Base | No alert | No alert | No alert | No alert | No alert |
| by OECD | found | found | found | found | found | Formers Schiff Base | found | found | found | found | found |
| | | | | | | Formers >> | | | | | |
| | | | | | | | | | | | |
| | | | | | | Direct | | | | | |

| InertFinder/Che | 2- | 2- | 2- | 2- | 2- | 3,4- | 3- | 3-Methyl- | 3-Methyl- 2- | 3-Methyl- 2- | 3-Methyl- 5- |
|-------------------|-------------|----------|-----------|-----------|-----------|---------------|----------|-------------|---------------|----------------|----------------|
| mID Plus Name | Methylpyraz | Nonanon | Octanone | Tridecano | Undecano | Dimethyl- | Heptanon | 1- | (2- | (n- pentanyl)- | (2,2,3- |
| | ine | е | | ne | ne | 1,2- | е | cyclopentad | pentenyl)- 2- | 2- cyclopent | trimethyl- 3- |
| | | | | | | cyclopentadi | | ecanone | cyclopenten- | en-1-one | cyclopent en- |
| | | | | | | one | | | 1-one | | 1- yl) pent-4- |
| | | | | | | | | | | | en-2-ol |
| | | | | | | Acting Schiff | | | | | |
| | | | | | | Base | | | | | |
| | | | | | | Formers | | | | | |
| | | | | | | Schiff Base | | | | | |
| | | | | | | Formers >> | | | | | |
| | | | | | | Direct | | | | | |
| | | | | | | Acting Schiff | | | | | |
| | | | | | | Base | | | | | |
| | | | | | | Formers >> | | | | | |
| | | | | | | 1-2- | | | | | |
| | | | | | | Dicarbonyls | | | | | |
| | No data | No data | 1 to 10 | No data | 10 to 100 | No data | No data | 10 to 100 | No data | No data | 10 to 100 |
| biodeg | | | days | | days | | | days | | | days |
| | | | 10 to 100 | | | | | | | | |
| | | | days | | | | | | | | |
| | | | > 100 | | | | | | | | |
| | | | days | | | | | | | | |
| Ionization at pH | | Acidic | Acidic | Acidic | Acidic | Acidic | Acidic | Acidic | Acidic | Acidic | Acidic |
| = 9 | [60.000, | [0.000, | [0.000, | [0.000, | [0.000, | [0.000, | [0.000, | [0.000, | [0.000, | [0.000, | [0.000, |
| | 70.000) | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) |
| | Basic | Basic | Basic | Basic | Basic | No pKb | Basic | Basic | Basic | Basic | Basic |
| | [0.000, | | [0.000, | [0.000, | [0.000, | value | [0.000, | [0.000, | [0.000, | [0.000, | [0.000, |
| | 10.000) | 10.000) | 10.000) | , | 10.000) | Nevelue | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) |
| | No value | No value | No value | No value | No value | No value | No value | No value | No value | No value | No value |
| life (Ka, pH7) | | | | | | | | | | | |
| • • | | | | | | | | | | | |
| (Hydrowin) | | | | | | | | | | | |

| InertFinder/Che | 2- | 2- | 2- | 2- | 2- | 3,4- | 3- | 3-Methyl- | 3-Methyl- 2- | 3-Methyl- 2- | 3-Methyl- 5- |
|-------------------|-------------|------------|------------|------------|------------|--------------|------------|-------------|---------------|----------------|----------------|
| mID Plus Name | Methylpyraz | Nonanon | Octanone | Tridecano | Undecano | Dimethyl- | Heptanon | 1- | (2- | (n- pentanyl)- | (2,2,3- |
| | ine | е | | ne | ne | 1,2- | е | cyclopentad | pentenyl)- 2- | 2- cyclopent | trimethyl- 3- |
| | | | | | | cyclopentadi | | ecanone | cyclopenten- | en-1-one | cyclopent en- |
| | | | | | | one | | | 1-one | | 1- yl) pent-4- |
| | | | | | | | | | | | en-2-ol |
| Toxic hazard | Intermedi | Intermedi | Intermedi | Intermedi | Intermedi | Intermediat | Intermedi | Intermedi | Intermediat | Intermediat | Low (Class |
| classification by | ate (Class | ate (Class | ate (Class | ate (Class | ate (Class | e (Class II) | ate (Class | ate (Class | e (Class II) | e (Class II) | I) |
| Cramer | II) | II) | II) | II) | II) | | II) | 11) | | | |
| (extended) | | | | | | | | | | | |
| Biodegradation | Does NOT | Does NOT | Does NOT | Does NOT | Does NOT | Biodegrades | Does NOT | Does NOT | Does NOT | Does NOT | Does NOT |
| probability | Biodegrad | Biodegrad | Biodegrad | Biodegrad | Biodegrad | Fast | Biodegrad | Biodegrad | Biodegrade | Biodegrade | Biodegrade |
| (Biowin 7) | e Fast | e Fast | e Fast | e Fast | e Fast | | e Fast | e Fast | Fast | Fast | Fast |
| DNA binding by | No alert | No alert | No alert | No alert | No alert | AN2 | No alert | No alert | No alert | No alert | No alert |
| OASIS | found | found | found | found | found | AN2 >> | found | found | found | found | found |
| | | | | | | Schiff base | | | | | |
| | | | | | | formation | | | | | |
| | | | | | | AN2 >> | | | | | |
| | | | | | | Schiff base | | | | | |
| | | | | | | formation | | | | | |
| | | | | | | >> | | | | | |
| | | | | | | Dicarbonyl | | | | | |
| | | | | | | compounds | | | | | |
| Ionization at pH | | Acidic | Acidic | Acidic | Acidic | Acidic | Acidic | Acidic | Acidic | Acidic | Acidic |
| = 7.4 | [0.000, | [0.000, | [0.000, | [0.000, | [0.000, | [0.000, | [0.000, | [0.000, | [0.000, | [0.000, | [0.000, |
| | 10.000) | | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) |
| | Basic | | Basic | Basic | Basic | No pKb | Basic | Basic | Basic | Basic | Basic |
| | [0.000, | | [0.000, | [0.000, | [0.000, | value | [0.000, | [0.000, | [0.000, | [0.000, | [0.000, |
| | 10.000) | | 10.000) | 10.000) | 10.000) | | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) |
| | No value | No value | No value | No value | No value | No value | No value | No value | No value | No value | No value |
| life (Ka, | | | | | | | | | | | |
| рН 8) | | | | | | | | | | | |
| (Hydrowin) | | | | | | | | | | | |

| InertFinder/Che mID Plus Name | 2- Methylpyraz ine | | | 2- Tridecano ne | | 3,4- Dimethyl- 1,2- cyclopentadi one | Heptanon e | 1- cyclopentad ecanone | 3-Methyl- 2- (2- pentenyl)- 2- cyclopenten- 1-one | 3-Methyl- 2- (n- pentanyl)- 2- cyclopent en-1-one | 3-Methyl- 5- (2,2,3- trimethyl- 3- cyclopent en- 1- yl) pent-4- en-2-ol |
|----------------------------------|--------------------------|-------------------|-------------------|-----------------------|-------------------|---|-------------------|------------------------------|---|--|--|
| Protein binding by OASIS | No alert found | No alert found | No alert found | No alert found | No alert found | Schiff base formation Schiff base formation >> Direct acting Schiff base formers Schiff base formation >> Direct acting Schiff base formers >> 1,2- Dicarbonyls and 1,3- Dicarbonyls | No alert found | No alert found | No alert found | No alert found | No alert found |
| DNA binding by OECD | No alert found | No alert found | No alert found | No alert found | No alert found | Schiff base formers Schiff base formers >> Direct Acting Schiff Base Formers Schiff base formers >> | No alert found | No alert found | No alert found | No alert found | No alert found |

Page **56** of **111**

| InertFinder/Che | | | 2- | 2- | 2- | 3,4- | 3- | 3-Methyl- | 3-Methyl- 2- | 3-Methyl- 2- | 3-Methyl- 5- |
|-----------------|-------------|----------|----------|-----------|----------|---------------|----------|-------------|-------------------------|-------------------------|---------------------|
| mID Plus Name | Methylpyraz | Nonanon | Octanone | Tridecano | Undecano | Dimethyl- | Heptanon | 1- | (2- | (n- pentanyl)- | (2,2,3- |
| | ine | е | | ne | ne | 1,2- | е | cyclopentad | pentenyl)- 2- | 2- cyclopent | trimethyl- 3- |
| | | | | | | cyclopentadi | | ecanone | cyclopenten- | en-1-one | cyclopent en- |
| | | | | | | one | | | 1-one | | 1- yl) pent-4- |
| | | | | | | | | | | | en-2-ol |
| | | | | | | Direct | | | | | |
| | | | | | | Acting Schiff | | | | | |
| | | | | | | Base | | | | | |
| | | | | | | Formers >> | | | | | |
| | | | | | | Alpha-beta- | | | | | |
| | | | | | | dicarbonyl | | | | | |
| • | Biodegrad | - | - | - | - | Biodegrades | - | - | Biodegrade | Biodegrade | Biodegrade |
| • • | es Fast | es Fast | es Fast | es Fast | es Fast | Fast | es Fast | es Fast | s Fast | s Fast | s Fast |
| (Biowin 1) | _ | _ | _ | _ | _ | _ | _ | _ | | | |
| | Days to | Days | Days | Days | Days | Days to | Days | Days to | Days | Days | Days to |
| primary (Biowin | weeks | | | | | weeks | | weeks | | | weeks |
| 4) | | | | | | | | | | | - |
| • • | No alert | No alert | No alert | No alert | No alert | No alert | No alert | No alert | alpha, beta- | alpha, beta- | Structural |
| (genotox and | found | found | found | found | found | found | found | found | unsaturate | unsaturate | alert for |
| nongenotox) | | | | | | | | | d carbonyls | d carbonyls | nongenoto |
| alerts by ISS | | | | | | | | | (Genotox) | (Genotox) | xic |
| | | | | | | | | | Structural alert for | Structural alert for | carcinogeni city |
| | | | | | | | | | genotoxic | genotoxic | Substitute |
| | | | | | | | | | carcinogeni | carcinogeni | d n- |
| | | | | | | | | | city | city | alkylcarbox |
| | | | | | | | | | city | City | ylic acids |
| | | | | | | | | | | | (Nongeno |
| | | | | | | | | | | | tox) |
| in vitro | No alert | No alert | No alert | No alert | No alert | No alert | No alert | No alert | alpha, bet | alpha, bet | No alert |
| | found | | found | found | found | found | found | found | a- | а- | found |
| (Ames test) | | | | | | | | | unsaturate | unsaturate | |

| InertFinder/Che | 2- | 2- | 2- | 2- | 2- | 3,4- | 3- | 3-Methyl- | 3-Methyl- 2- | 3-Methyl- 2- | 3-Methyl- 5- |
|------------------|-------------|----------|----------|-----------|----------|--------------|----------|-------------|---------------|----------------|----------------|
| mID Plus Name | Methylpyraz | Nonanon | Octanone | Tridecano | Undecano | Dimethyl- | Heptanon | 1- | (2- | (n- pentanyl)- | (2,2,3- |
| | ine | е | | ne | ne | 1,2- | e | cyclopentad | pentenyl)- 2- | 2- cyclopent | trimethyl- 3- |
| | | | | | | cyclopentadi | | ecanone | cyclopenten- | en-1-one | cyclopent en- |
| | | | | | | one | | | 1-one | | 1- yl) pent-4- |
| | | | | | | | | | | | en-2-ol |
| alerts by ISS | | | | | | | | | d carbonyls | d carbonyls | |
| in vivo | H- | No alert | No alert | No alert | No alert | H-acceptor- | No alert | No alert | alpha, beta- | alpha, beta- | No alert |
| mutagenicity | acceptor- | found | found | found | found | path3-H- | found | found | unsaturate | unsaturate | found |
| (Micronucleus) | path3-H- | | | | | acceptor | | | d carbonyls | d carbonyls | |
| alerts by ISS | acceptor | | | | | | | | | | |
| Protein Binding | No alert | No alert | No alert | No alert | No alert | 1,2- and | No alert | No alert | alpha, beta- | alpha, beta- | No alert |
| Potency h-CLAT | found | found | found | found | found | 1,3- | found | found | Unsaturted | Unsaturted | found |
| | | | | | | Dicarbonyls | | | ketones | ketones | |
| Skin | Inclusion | Ketones | Ketones | Ketones | Ketones | Ketones | Ketones | Ketones | Ketones | Ketones | Inclusion |
| irritation/corro | rules not | | | | | | | | | | rules not |
| sion Inclusion | met | | | | | | | | | | met |
| rules by BfR | | | | | | | | | | | |
| DNA alerts for | No alert | No alert | No alert | No alert | No alert | AN2 | No alert | No alert | No alert | No alert | No alert |
| AMES, CA and | found | found | found | found | found | AN2 >> | found | found | found | found | found |
| MNT by OASIS | | | | | | Schiff base | | | | | |
| | | | | | | formation | | | | | |
| | | | | | | AN2 >> | | | | | |
| | | | | | | Schiff base | | | | | |
| | | | | | | formation | | | | | |
| | | | | | | >> | | | | | |
| | | | | | | Dicarbonyl | | | | | |
| | | | | | | compounds | | | | | |

| InertFinder/Che | 2- | 2- | 2- | 2- | 2- | 3,4- | 3- | 3-Methyl- | 3-Methyl- 2- | 3-Methyl- 2- | 3-Methyl- 5- |
|------------------|-------------|-------------|-------------|-------------|-------------|---------------|-------------|-------------|---------------|----------------|----------------|
| mID Plus Name | Methylpyraz | Nonanon | Octanone | Tridecano | Undecano | Dimethyl- | Heptanon | 1- | (2- | (n- pentanyl)- | (2,2,3- |
| | ine | e | | ne | ne | 1,2- | е | cyclopentad | pentenyl)- 2- | 2- cyclopent | trimethyl- 3- |
| | | | | | | cyclopentadi | | ecanone | cyclopenten- | en-1-one | cyclopent en- |
| | | | | | | one | | | 1-one | | 1- yl) pent-4- |
| | | | | | | | | | | | en-2-ol |
| Protein binding | No alert | | • | • | • | Schiff base | • | Nucleophi | No alert | No alert | No alert |
| alerts for skin | found | ic addition | ic addition | ic addition | ic addition | formation | ic addition | lic | found | found | found |
| sensitization by | | Nucleophil | Nucleophil | Nucleophil | Nucleophil | Schiff base | Nucleophil | addition | | | |
| OASIS | | ic addition | ic addition | ic addition | ic addition | formation | ic addition | Nucleophi | | | |
| | | >> | >> | >> | >> | >> Direct | >> | lic | | | |
| | | Addition | Addition | Addition | Addition | acting Schiff | Addition | addition | | | |
| | | to carbon- | to carbon- | to carbon- | to carbon- | base | to carbon- | >> | | | |
| | | hetero | hetero | hetero | hetero | formers | hetero | Addition | | | |
| | | double | double | double | double | Schiff base | double | to carbon- | | | |
| | | bonds | bonds | bonds | bonds | formation | bonds | hetero | | | |
| | | Nucleophil | Nucleophil | Nucleophil | Nucleophil | >> Direct | Nucleophil | double | | | |
| | | ic addition | ic addition | ic addition | ic addition | acting Schiff | ic addition | bonds | | | |
| | | >> | >> | >> | >> | base | >> | Nucleophi | | | |
| | | Addition | Addition | Addition | Addition | formers >> | Addition | lic | | | |
| | | to carbon- | to carbon- | to carbon- | to carbon- | 1,2- | to carbon- | addition | | | |
| | | hetero | hetero | hetero | hetero | Dicarbonyls | hetero | >> | | | |
| | | double | double | double | double | and 1,3- | double | Addition | | | |
| | | bonds >> | bonds >> | bonds >> | bonds >> | Dicarbonyls | bonds >> | to carbon- | | | |
| | | Ketones | Ketones | Ketones | Ketones | | Ketones | hetero | | | |
| | | | | | | | | double | | | |
| | | | | | | | | bonds >> | | | |
| | | | | | | | | Ketones | | | |
| rtER Expert | No alert | No alert | No alert | No alert | No alert | No alert |
| System - USEPA | found | found | found | found | found | found | found | found | found | found | found |
| Skin | Undefine | Undefined | Undefined | Undefined | Undefined | Undefined | Undefined | Group C | Undefined | Undefined | Undefined |
| irritation/corro | d | | | | | | | Melting | | | |
| sion Exclusion | | | | | | | | Point > 55 | | | |
| rules by BfR | | | | | | | | С | | | |

| InertFinder/Che | 2- | 2- | 2- | 2- | 2- | 3,4- | 3- | 3-Methyl- | 3-Methyl- 2- | 3-Methyl- 2- | 3-Methyl- 5- |
|-----------------|-------------|----------|----------|-----------|----------|--------------|----------|-------------|---------------|----------------|----------------|
| mID Plus Name | Methylpyraz | Nonanon | Octanone | Tridecano | Undecano | Dimethyl- | Heptanon | 1- | (2- | (n- pentanyl)- | (2,2,3- |
| | ine | е | | ne | ne | 1,2- | e | cyclopentad | pentenyl)- 2- | 2- cyclopent | trimethyl- 3- |
| | | | | | | cyclopentadi | | ecanone | cyclopenten- | en-1-one | cyclopent en- |
| | | | | | | one | | | 1-one | | 1- yl) pent-4- |
| | | | | | | | | | | | en-2-ol |
| | | | | | | | | Undefine | | | |
| | | | | | | | | d | | | |
| Protein binding | No alert | No alert | No alert | No alert | No alert | No alert | No alert | No alert | No alert | No alert | No alert |
| alerts for | found | found | found | found | found | found | found | found | found | found | found |
| Chromosomal | | | | | | | | | | | |
| aberration by | | | | | | | | | | | |
| OASIS | | | | | | | | | | | |

| InertFinder/ChemID Plus Name | 4-Acetyl-6 t- butyl- 1,1- dimethylindan | 4H-Pyran-4-one, 3- hydroxy-2- methyl- 118-71-8 | 4-Hydroxy-2,5- dimethyl-3(2H)- furanone 3658-77-3 | 5-Methyl-2-phenyl-2-hexenal | 5-Methyl-2- thiophenecarboxaldehyde | 6,10- Dimethyl undeca- 5,9-dien- 2- one |
|---|---|---|--|---|---|---|
| CAS SMILES | 13171-00-1 CC(=O)c1 | CC1=C(0)C(=0)C=CO1 | CC1OC(=C(O)C1= | CC(C)C\C=C(C=O)/c1ccccc1 | 13679-70-4 Cc1sc(C=O)cc1 | 689-67-8 CC(C)=CC |
| Siviles | cc(cc2c1C CC2(C)C)C (C)(C)C | | 0)C | | | C\C(C)=C\ C\C(C)=C\ CCC(C)=O |
| Ionization at pH = 1 | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) |
| Biodegradation ultimate (Biowin 3) | Months | Weeks | Weeks | Weeks | Weeks | Weeks to months |
| Estrogen Receptor | Non binder, | Non binder, impaired OH | Non binder, | Non binder, without OH or | Non binder, without OH or | Non binder, |
| Binding | without OH or NH2 group | or NH2 group | impaired OH or NH2 group | NH2 group | NH2 group | non cyclic structure |
| Biodeg BioHC half- life (Biowin) | No value | No value | No value | No value | No value | No value |
| Hydrolysis half-life (pH 6.5-7.4) | No value | No value | No value | No value | No value | No value |
| Biodegradation probability (Biowin 5) | Does NOT Biodegrade Fast | Biodegrades Fast | Biodegrades Fast | Biodegrades Fast | Biodegrades Fast | Biodegrades Fast |
| Toxic hazard classification by Cramer | Intermediate (Class II) | Intermediate (Class II) | High (Class III) | Intermediate (Class II) | High (Class III) | Low (Class I) |
| Biodegradation | Does NOT | Does NOT Biodegrade | Does NOT | Biodegrades Fast | Biodegrades Fast | Does NOT |

| InertFinder/ChemID | 4-Acetyl-6 t- | 4H-Pyran-4-one, | 4-Hydroxy-2,5- | 5-Methyl-2-phenyl-2-hexenal | 5-Methyl-2- | 6,10- |
|----------------------|---------------|-------------------------|-----------------|-----------------------------|-------------------------|----------------|
| Plus Name | butyl- 1,1- | 3- hydroxy-2- | dimethyl-3(2H)- | | thiophenecarboxaldehyde | Dimethyl |
| | dimethylindan | methyl- | furanone | | | undeca- |
| | | | | | | 5,9-dien- 2- |
| | | | | | | one |
| probability (Biowin | Biodegrade | Fast | Biodegrade Fast | | | Biodegrade |
| 2) | Fast | | | | | Fast |
| Ionization at pH = 4 | Acidic | Acidic [0.000, 10.000) | Acidic [0.000, | Acidic [0.000, 10.000) | Acidic [0.000, 10.000) | Acidic [0.000, |
| | [0.000, | Basic [0.000, 10.000) | 10.000) | Basic [0.000, 10.000) | Basic [0.000, 10.000) | 10.000) |
| | 10.000) | | Basic [0.000, | | | Basic [0.000, |
| | Basic [0.000, | | 10.000) | | | 10.000) |
| | 10.000) | | | | | |
| Protein binding | DPRA less | DPRA less than 9% | DPRA less than | Out of mechanistic domain | Out of mechanistic | Out of |
| potency Lys (DPRA | than 9% | (DPRA 13%) | 9% (DPRA 13%) | | domain | mechanistic |
| 13%) | (DPRA 13%) | DPRA less than 9% | DPRA less than | | | domain |
| | DPRA less | (DPRA 13%) >> | 9% (DPRA 13%) | | | |
| | than 9% | Conjugated alpha, beta- | >> Conjugated | | | |
| | (DPRA 13%) | unsaturated ketones | alpha, beta- | | | |
| | >> | (non reactive) | unsaturated | | | |
| | Non- | | ketones (non | | | |
| | conjugate d | | reactive) | | | |
| | mono- and | | | | | |
| | diketones | | | | | |
| | (non | | | | | |
| | reactive) | | | | | |
| Protein binding | DPRA less | Out of mechanistic | DPRA less than | Out of mechanistic domain | DPRA less than 9% (DPRA | Out of |
| potency Cys (DPRA | than 9% | domain | 9% (DPRA 13%) | | 13%) | mechanistic |
| 13%) | (DPRA 13%) | | DPRA less than | | DPRA less than 9% (DPRA | domain |
| | DPRA less | | 9% (DPRA 13%) | | 13%) >> Non- | |
| | than 9% | | >> No protein | | Conjugated | |
| | (DPRA 13%) | | binding alert | | monoaldehydes (non | |
| | >> | | | | reactive) | |
| | No protein | | | | | |

| InertFinder/ChemID Plus Name | 4-Acetyl-6 t- butyl- 1,1- dimethylindan | 4H-Pyran-4-one, 3- hydroxy-2- methyl- | 4-Hydroxy-2,5- dimethyl-3(2H)- furanone | 5-Methyl-2-phenyl-2- hexenal | 5-Methyl-2- thiophenecarboxaldehyde | 6,10- Dimethyl undeca- 5,9-dien- 2- one |
|--|---|--|---|--|--|---|
| | binding alert | | | | | |
| Hydrolysis half-life (Kb, pH 8) (Hydrowin) | No value | No value | No value | No value | No value | No value |
| Hydrolysis half-life (Kb, pH 7) (Hydrowin) | No value | No value | No value | No value | No value | No value |
| Biodegradation probability (Biowin 6) | Does NOT Biodegrad e Fast | Biodegrades Fast | Biodegrades Fast | Does NOT Biodegrade Fast | Biodegrades Fast | Biodegrades Fast |
| Protein binding by OECD | No alert found | Michael addition Michael addition >> Quinones and Quinone- type Chemicals Michael addition >> Quinones and Quinone- type Chemicals >> Pyranones (and related nitrogen chemicals) | No alert found | Michael addition Michael addition >> Polarised Alkenes Michael addition >> Polarised Alkenes >> Polarised alkene - aldehydes Schiff Base Formers Schiff Base Formers >> Direct Acting Schiff Base Formers Schiff Base Formers >> Direct Acting Schiff Base Formers >> Mono-carbonyls | No alert found | No alert found |
| Ultimate biodeg | > 100 days | (N/A) | No data | No data | No data | No data |

| InertFinder/ChemID Plus Name | butyl- 1,1- dimethylindan | | 4-Hydroxy-2,5- dimethyl-3(2H)- furanone | 5-Methyl-2-phenyl-2- hexenal | 5-Methyl-2- thiophenecarboxaldehyde | 6,10- Dimethyl undeca- 5,9-dien- 2- one |
|--|--|---|---|--|--|---|
| Ionization at pH = 9 | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [90.000, 100.000] Basic [0.000, 10.000) | Acidic [90.000, 100.000] Basic [0.000, 10.000) | Acidic [30.000, 40.000) Basic [0.000, 10.000) | Acidic [90.000, 100.000] Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) |
| Hydrolysis half-life (Ka, pH 7) (Hydrowin) | No value | No value | No value | No value | No value | No value |
| Toxic hazard classification by Cramer (extended) | Intermediate (Class II) | Intermediate (Class II) | High (Class III) | Intermediate (Class II) | High (Class III) | Low (Class I) |
| Biodegradation probability (Biowin 7) | Does NOT Biodegrade Fast | Does NOT Biodegrade Fast | Does NOT Biodegrade Fast | Does NOT Biodegrade Fast | Does NOT Biodegrade Fast | Does NOT Biodegrade Fast |
| DNA binding by OASIS | No alert found | No alert found | No alert found | AN2 AN2 >> Nucleophilic addition to alpha, beta-unsaturated carbonyl compounds AN2 >> Nucleophilic addition to alpha, beta-unsaturated carbonyl compounds >> Alpha, Beta-Unsaturated Aldehydes AN2 >> Schiff base formation AN2 >> Schiff base formation >> Alpha, Beta- Unsaturated Aldehydes | No alert found | No alert found |

| InertFinder/ChemID Plus Name Ionization at pH = 7.4 | 4-Acetyl-6 t- butyl- 1,1- dimethylindan Acidic [0.000, 10.000) | | 4-Hydroxy-2,5- dimethyl-3(2H)- furanone Acidic [90.000, 100.000] Basic [0.000, | 5-Methyl-2-phenyl-2- hexenal Acidic [0.000, 10.000) Basic [0.000, 10.000) | 5-Methyl-2- thiophenecarboxaldehyde Acidic [30.000, 40.000) Basic [0.000, 10.000) | 6,10- Dimethyl undeca- 5,9-dien- 2- one Acidic [0.000, 10.000) Basic [0.000, |
|--|---|--|---|---|---|---|
| Hydrolysis half-life (Ka, | Basic [0.000, 10.000) No value | No value | 10.000) No value | No value | No value | 10.000) No value |
| pH 8)(Hydrowin) Protein binding by OASIS | No alert found | Michael addition Michael addition >> Michael addition on quinoid type compounds Michael addition >> Michael addition on quinoid type compounds >> Pyranones, Pyridones (and related nitrogen chemicals) | | Michael addition Michael addition >> Michael addition on alpha, beta- Unsaturated carbonyl compounds Michael addition >> Michael addition on alpha, beta- Unsaturated carbonyl compounds >> alpha, beta- Aldehydes Schiff base formation Schiff base formation >> Schiff base formation with carbonyl compounds Schiff base formation >> Schiff base formation with carbonyl compounds >> Aldehydes | Schiff base formation Schiff base formation >> Schiff base formation with carbonyl compounds Schiff base formation >> Schiff base formation with carbonyl compounds >> Aldehydes | No alert found |
| DNA binding by OECD | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found |

| InertFinder/ChemID Plus Name Biodegradation | 4-Acetyl-6 t- butyl- 1,1- dimethylindan Does NOT | 4H-Pyran-4-one, 3- hydroxy-2- methyl- Biodegrades Fast | 4-Hydroxy-2,5- dimethyl-3(2H)- furanone Biodegrades Fast | 5-Methyl-2-phenyl-2-hexenal Biodegrades Fast | 5-Methyl-2- thiophenecarboxaldehyde Biodegrades Fast | 6,10- Dimethyl undeca- 5,9-dien- 2- one Biodegrades |
|---|---|--|---|---|---|--|
| probability (Biowin 1) | Biodegrade Fast | | | | | Fast |
| Biodegradation primary (Biowin 4) | Weeks | Days | Days | Days | Days | Days to weeks |
| Carcinogenicity (genotox and nongenotox) alerts by ISS | No alert found | alpha, beta-unsaturated carbonyls (Genotox) Structural alert for genotoxic carcinogenicity | alpha, beta- unsaturated carbonyls (Genotox) Structural alert for genotoxic carcinogenicity | alpha, beta-unsaturated carbonyls (Genotox) Structural alert for genotoxic carcinogenicity | Simple aldehyde (Genotox) Structural alert for genotoxic carcinogenicity | No alert found |
| in vitro mutagenicity (Ames test) alerts by ISS | | alpha, beta-unsaturated carbonyls | alpha, beta- unsaturated carbonyls | alpha, beta-unsaturated carbonyls | Simple aldehyde | No alert found |
| in vivo mutagenicity (Micronucleus) alerts by ISS | No alert found | alpha, beta-unsaturated carbonyls H-acceptor-path3-H- acceptor | alpha, beta- unsaturated carbonyls H-acceptor- path3-H- acceptor | alpha, beta-unsaturated carbonyls | Simple aldehyde | No alert found |
| Protein Binding Potency h-CLAT | No alert found | Pyranones, Pyridones and related chemicals | No alert found | alpha, beta-Unsaturated aldehydes | No alert found | No alert found |
| Skin irritation/corrosion Inclusion rules by BfR | Ketones | Ketones | Ketones | Aldehydes | Aldehydes | Ketones |
| DNA alerts for | No alert | No alert found | No alert found | No alert found | No alert found | No alert |

| Plus Name | 4-Acetyl-6 t- butyl- 1,1- dimethylindan found | 4H-Pyran-4-one, 3- hydroxy-2- methyl- | 4-Hydroxy-2,5- dimethyl-3(2H)- furanone | 5-Methyl-2-phenyl-2- hexenal | 5-Methyl-2- thiophenecarboxaldehyde | 6,10- Dimethyl undeca- 5,9-dien- 2- one found |
|---|--|--|---|---|---|--|
| by OASIS | | | | | | |
| Protein binding alerts for skin sensitization by OASIS | No alert found | Michael Addition Michael Addition >> Michael addition on quinoid type compounds Michael Addition >> Michael addition on quinoid type compounds >> Pyranones, Pyridones (and related nitrogen chemicals) | No alert found | Michael Addition Michael Addition >> Michael addition on alpha, beta- Unsaturated carbonyl compounds Michael Addition >> Michael addition on alpha, beta- Unsaturated carbonyl compounds >> alpha, beta- Aldehydes | Schiff base formation Schiff base formation >> Schiff base formation with carbonyl compounds Schiff base formation >> Schiff base formation with carbonyl compounds >> Aldehydes | Nucleophilic addition Nucleophilic addition >> Addition to carbon- hetero double bonds Nucleophilic addition >> Addition to carbon- hetero double bonds >> Ketones |
| rtER Expert System - USEPA | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found |
| Skin irritation/corrosion Exclusion rules by BfR | Group C Melting Point > 55 C Undefine d | Group C Melting Point > 55 C Undefined | Group C Melting Point > 55 C Group C Surface Tension > 62 mN/m Undefined | Undefined | Undefined | Undefined |

| InertFinder/ChemID | 4-Acetyl-6 t- | 4H-Pyran-4-one, | 4-Hydroxy-2,5- | 5-Methyl-2-phenyl-2-hexenal | 5-Methyl-2- | 6,10- |
|---------------------|---------------|-------------------------|-----------------|-----------------------------|-------------------------|--------------|
| Plus Name | butyl- 1,1- | 3- hydroxy-2- | dimethyl-3(2H)- | | thiophenecarboxaldehyde | Dimethyl |
| | dimethylindan | methyl- | furanone | | | undeca- |
| | | | | | | 5,9-dien- 2- |
| | | | | | | one |
| Protein binding | No alert | AN2 | No alert found | No alert found | No alert found | No alert |
| alerts for | found | AN2 >> Michael addition | | | | found |
| Chromosomal | | to activated double | | | | |
| aberration by OASIS | | bonds AN2 >> Michael | | | | |
| | | addition to activated | | | | |
| | | double bonds | | | | |
| | | >> alpha, beta- | | | | |
| | | Unsaturated Carbonyls | | | | |
| | | and Related Compounds | | | | |

| InertFinder/ChemID | 6-Methyl-3,5- | 6-Methyl- 5- | 7- | Acetoin | Allyl cinnamate | Allyl | Allyl | Allyl |
|---|---|---|---|---|---|---|---|---|
| Plus Name | heptadien-2-one | one | Oxabicyclo(2.2.1.) heptane, 1- methyl-4- (1- methylethyl)- | | | heptanoate | hexanoate | propionate |
| CAS | 1604-28-0 | 110-93-0 | 470-67-7 | 513-86-0 | 1866-31-5 | 142-19-8 | 123-68-2 | 2408-20-0 |
| SMILES | CC(C)=C/C=C/C(C)= O | CC(C)=CC CC(C)=O | CC(C)C12 CCC(C)(CC 1)O2 | CC(O)C(C) =O | C=CCOC(=O)\C=C \c1ccccc1 | CCCCCCC(=0)OCC= C | CCCCCC(= 0)0CC=C | CCC(=O)O CC=C |
| Ionization at pH = 1 | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) |
| Biodegradation ultimate (Biowin 3) | Weeks | Weeks | Weeks to months | Weeks | Weeks | Days to weeks | Days to weeks | Weeks |
| Estrogen Receptor Binding | Non binder, non cyclic structure | Non binder, non cyclic structure | Non binder, without OH or NH2 group | Non binder, non cyclic structure | Non binder, without OH or NH2 group | Non binder, non cyclic structure | Non binder, non cyclic structure | Non binder, non cyclic structure |
| Biodeg BioHC half- life (Biowin) | No value | No value | No value | No value | No value | No value | No value | No value |
| Hydrolysis half-life (pH 6.5-7.4) | No value | No value | No value | No value | Very slow | Moderate | Moderate | Moderate |
| Biodegradation probability (Biowin 5) | Biodegrades Fast | Biodegrades Fast | Does NOT Biodegrade Fast | Biodegrades Fast | Does NOT Biodegrade Fast | Biodegrades Fast | Biodegrades Fast | Biodegrades Fast |
| Toxic hazard classification by Cramer | Low (Class I) | Low (Class I) | High (Class III) | Low (Class I) | High (Class III) Intermediate (Class II) | Intermediate (Class II) | Intermediate (Class II) | Intermediate (Class II) |
| Biodegradation probability (Biowin 2) | Biodegrades Fast | Biodegrades Fast | Does NOT Biodegrade Fast | Biodegrades Fast | Biodegrades Fast | Biodegrades Fast | Biodegrades Fast | Biodegrades Fast |

| InertFinder/ChemID | 6-Methyl-3,5- | 6-Methyl- 5- | 7- | Acetoin | Allyl cinnamate | Allyl | Allyl | Allyl |
|--|--|---|---|--|---|--|--|--|
| Plus Name | heptadien-2-one | hepten- 2- one | Oxabicyclo(2.2.1.) heptane, 1- methyl-4- (1- methylethyl)- | | | heptanoate | hexanoate | propionate |
| Ionization at pH = 4 | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) |
| Protein binding potency Lys (DPRA 13%) | DPRA less than 9% (DPRA 13%) DPRA less than 9% (DPRA 13%) >> Conjugated alpha, beta- unsaturated ketones (non reactive) | Out of mechanistic domain | DPRA less than 9% (DPRA 13%) DPRA less than 9% (DPRA 13%) >> No protein binding alert | DPRA less than 9% (DPRA 13%) DPRA less than 9% (DPRA 13%) >> Alcohols | Out of mechanistic domain | DPRA less than 9% (DPRA 13%) DPRA less than 9% (DPRA 13%) >> Non- Conjugate d carboxylic acids and esters (non reactive) | DPRA less than 9% (DPRA 13%) DPRA less than 9% (DPRA 13%) >> Non- Conjugate d carboxylic acids and esters (non reactive) | DPRA less than 9% (DPRA 13%) DPRA less than 9% (DPRA 13%) >> Non- Conjugate d carboxylic acids and esters (non reactive) |
| Protein binding potency Cys (DPRA 13%) | Grey zone 9-21% (DPRA 13%) Grey zone 9-21% (DPRA 13%) >> Conjugated alpha, beta-unsaturated ketones (Grey zone) | Out of mechanistic domain | DPRA less than 9% (DPRA 13%) DPRA less than 9% (DPRA 13%) >> No protein binding alert | DPRA less than 9% (DPRA 13%) DPRA less than 9% (DPRA 13%) >> Alcohols | (DPRA 13%) | DPRA less than 9% (DPRA 13%) DPRA less than 9% (DPRA 13%) >> Non- Conjugate d carboxylic | DPRA less than 9% (DPRA 13%) DPRA less than 9% (DPRA 13%) >> Non- Conjugate d carboxylic | DPRA less than 9% (DPRA 13%) DPRA less than 9% (DPRA 13%) >> Non- Conjugate d carboxylic |

| InertFinder/ChemID | 6-Methyl-3,5- | 6-Methyl- 5- | 7- | Acetoin | Allyl cinnamate | Allyl | Allyl | Allyl |
|--|---|---------------------|---|---------------------|---|--|--|--|
| Plus Name | heptadien-2-one | hepten- 2- one | Oxabicyclo(2.2.1.) heptane, 1- methyl-4- (1- methylethyl)- | | | heptanoate | hexanoate | propionate |
| | | | | | | acids and esters (non reactive) | acids and esters (non reactive) | acids and esters (non reactive) |
| Hydrolysis half-life (Kb, pH 8) (Hydrowin) | No value | No value | No value | No value | > 100 days | 10 to 100 days | 10 to 100 days | 10 to 100 days |
| Hydrolysis half-life (Kb, pH 7) (Hydrowin) | No value | No value | No value | No value | > 100 days | > 100 days | > 100 days | > 100 days |
| Biodegradation probability (Biowin 6) | Biodegrades Fast | Biodegrades Fast | Does NOT Biodegrade Fast | Biodegrades Fast | Does NOT Biodegrade Fast | Biodegrades Fast | Biodegrades Fast | Biodegrades Fast |
| Protein binding by OECD | Michael addition Michael addition >> Polarised Alkenes Michael addition >> Polarised Alkenes >> Polarised alkene - ketones | No alert found | No alert found | No alert found | Michael addition Michael addition >> Polarised Alkenes Michael addition >> Polarised Alkenes >> Polarised alkene - esters SN2 SN2 >> SN2 reaction at sp3 carbon atom SN2 >> SN2 reaction at sp3 carbon at sp3 carbon at sp3 | SN2 SN2 >> SN2 reaction at sp3 carbon atom SN2 >> SN2 reaction at sp3 carbon atom >> Allyl acetates and related chemicals | SN2 SN2 >> SN2 reaction at sp3 carbon atom SN2 >> SN2 reaction at sp3 carbon atom >> Allyl acetates and related chemicals | SN2 SN2 >> SN2 reaction at sp3 carbon atom SN2 >> SN2 reaction at sp3 carbon atom >> Allyl acetates and related chemicals |

| InertFinder/ChemID | 6-Methyl-3,5- | 6-Methyl- 5- | 7- | Acetoin | Allyl cinnamate | Allyl | Allyl | Allyl |
|--|---|---|---|---|---|---|---|---|
| Plus Name | heptadien-2-one | hepten- 2- one | Oxabicyclo(2.2.1.) heptane, 1- methyl-4- (1- methylethyl)- | | | heptanoate | hexanoate | propionate |
| | | | | | Allyl acetates and related chemicals | | | |
| Ultimate biodeg | No data | 1 to 10 days 10 to 100 days | No data | 10 to 100 days | 1 to 10 days | 1 to 10 days 10 to 100 days | 1 to 10 days 10 to 100 days | 0 to 1 day 1 to 10 days 10 to 100 days |
| Ionization at pH = 9 | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) |
| Hydrolysis half-life (Ka, pH 7) (Hydrowin) | No value | No value | No value | No value | No value | No value | No value | No value |
| Toxic hazard classification by Cramer (extended) | Low (Class I) | Low (Class I) | High (Class III) | Low (Class I) | High (Class III) Intermediate (Class II) | High (Class III) | High (Class III) | High (Class III) |
| Biodegradation probability (Biowin 7) | Does NOT Biodegrade Fast | Does NOT Biodegrade Fast | Does NOT Biodegrade Fast | Does NOT Biodegrade Fast | Does NOT Biodegrade Fast | Biodegrades Fast | Biodegrades Fast | Biodegrades Fast |
| DNA binding by OASIS | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found |

| InertFinder/ChemID | 6-Methyl-3,5- | 6-Methyl- 5- | 7- | Acetoin | Allyl cinnamate | Allyl | Allyl | Allyl |
|----------------------|--------------------|---------------|--------------------|---------------|-------------------|----------------|----------------|----------------|
| Plus Name | heptadien-2-one | hepten- 2- | Oxabicyclo(2.2.1.) | | | heptanoate | hexanoate | propionate |
| | | one | heptane, 1- | | | | | |
| | | | methyl-4- (1- | | | | | |
| | | | methylethyl)- | | | | | |
| Ionization at pH = | Acidic [0.000, | | Acidic [0.000, | | Acidic [0.000, | | Acidic [0.000, | Acidic [0.000, |
| 7.4 | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) |
| | Basic [0.000, | Basic [0.000, | Basic [0.000, | Basic [0.000, | Basic [0.000, | Basic [0.000, | Basic [0.000, | Basic [0.000, |
| | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) |
| Hydrolysis half-life | No value | No value | No value | No value | No value | No value | No value | No value |
| (Ka, pH 8) | | | | | | | | |
| (Hydrowin) | | | | | | | | |
| Protein binding by | Michael addition | No alert | No alert found | No alert | Michael addition | SN2 SN2 >> | SN2 SN2 >> | SN2 SN2 >> |
| OASIS | Michael addition | found | | found | Michael addition | SN2 | SN2 | SN2 |
| | >> Michael | | | | >> Michael | Reaction at a | Reaction at a | Reaction at a |
| | addition on | | | | addition on | sp3 carbon | sp3 carbon | sp3 carbon |
| | conjugated systems | | | | conjugated | atom SN2 >> | atom SN2 >> | atom SN2 >> |
| | with electron | | | | systems with | SN2 | SN2 | SN2 |
| | withdrawing group | | | | electron | Reaction at a | Reaction at a | Reaction at a |
| | Michael addition | | | | withdrawing group | sp3 carbon | sp3 carbon | sp3 carbon |
| | >> Michael | | | | Michael addition | atom >> | atom >> | atom >> |
| | addition on | | | | >> Michael | Activated | Activated | Activated |
| | conjugated systems | | | | addition on | alkyl esters | alkyl esters | alkyl esters |
| | with electron | | | | conjugated | and thioesters | and thioesters | and thioesters |
| | withdrawing group | | | | systems with | | | |
| | >> alpha, beta- | | | | electron | | | |
| | Carbonyl | | | | withdrawing group | | | |
| | compounds with | | | | >> alpha, beta- | | | |
| | polarized double | | | | Carbonyl | | | |
| | bonds | | | | compounds with | | | |
| | | | | | polarized double | | | |
| | | | | | bonds | | | |

| InertFinder/ChemID | 6-Methyl-3,5- | 6-Methyl- 5- | 7- | Acetoin | Allyl cinnamate | Allyl | Allyl | Allyl |
|---|--|---------------------|---|---------------------|------------------|---------------------|---------------------|---------------------|
| Plus Name | heptadien-2-one | hepten- 2- one | Oxabicyclo(2.2.1.) heptane, 1- methyl-4- (1- methylethyl)- | | | heptanoate | hexanoate | propionate |
| DNA binding by OECD | Michael addition Michael addition >> Polarised Alkenes- Michael addition Michael addition >> Polarised Alkenes- Michael addition >> Alpha, beta- unsaturated ketones | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found |
| Biodegradation probability (Biowin 1) | Biodegrades Fast | Biodegrades Fast | Does NOT Biodegrade Fast | Biodegrades Fast | Biodegrades Fast | Biodegrades Fast | Biodegrades Fast | Biodegrades Fast |
| Biodegradation primary (Biowin 4) | Days to weeks | Days to weeks | Days to weeks | Days | Days | Days | Days | Days |
| Carcinogenicity (genotox and nongenotox) alerts by ISS | alpha, beta- unsaturated carbonyls (Genotox) Structural alert for genotoxic carcinogenicity | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found |
| in vitro mutagenicity (Ames test) alerts by ISS | alpha, beta- unsaturated carbonyls | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found |
| in vivo mutagenicity (Micronucleus) | alpha, beta- unsaturated | No alert found | Oxolane | H- acceptor- | No alert found | No alert found | No alert found | No alert found |

| InertFinder/ChemID | 6-Methyl-3,5- | 6-Methyl- 5- | 7- | Acetoin | Allyl cinnamate | Allyl | Allyl | Allyl |
|---|--|-------------------|---|----------------------|------------------------------------|-------------------------------|-------------------------------|-------------------------------|
| Plus Name | heptadien-2-one | hepten- 2- one | Oxabicyclo(2.2.1.) heptane, 1- methyl-4- (1- methylethyl)- | | | heptanoate | hexanoate | propionate |
| alerts by ISS | carbonyls | | | path3-H- acceptor | | | | |
| Protein Binding Potency h-CLAT | alpha, beta- Unsaturated ketones | No alert found | No alert found | No alert found | alpha, beta- Unsaturated esters | No alert found | No alert found | No alert found |
| Skin irritation/corrosion Inclusion rules by BfR | Ketones | Ketones | Inclusion rules not met | Ketones | Inclusion rules not met | Inclusion rules not met | Inclusion rules not met | Inclusion rules not met |
| DNA alerts for AMES, CA and MNT by OASIS | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found |
| Protein binding | Michael Addition | Nucleophilic | No alert found | Nucleophilic | Michael Addition | SN2 SN2 >> | SN2 SN2 >> | No alert |
| alerts for skin | Michael Addition | addition | | addition | Michael Addition | SN2 | SN2 | found |
| sensitization by | >> Michael | Nucleophilic | | Nucleophilic | >> Michael | Reaction at a | Reaction at a | |
| OASIS | addition on | addition | | addition | addition on | sp3 carbon | sp3 carbon | |
| | conjugated systems | >> | | >> | conjugated | atom SN2 >> | atom SN2 >> | |
| | with electron | Addition to | | Addition to | systems with | SN2 | SN2 | |
| | withdrawing group | carbon- | | carbon- | electron | Reaction at a | Reaction at a | |
| | Michael Addition | hetero | | hetero | withdrawing group | sp3 carbon | sp3 carbon | |
| | >> Michael | double | | double | Michael Addition | atom >> | atom >> | |
| | addition on | bonds | | bonds | >> Michael | Activated | Activated | |
| | conjugated systems | Nucleophilic | | Nucleophilic | addition on | alkyl esters | alkyl esters | |
| | with electron | addition | | addition | conjugated | and thioesters | and thioesters | |
| | withdrawing group | >> | | >> | systems with | | | |
| | >> alpha, beta- | Addition to | | Addition to | electron | | | |
| | Carbonyl | carbon- | | carbon- | withdrawing group | | | |
| | compounds with | hetero | | hetero | >> alpha, beta- | | | |

| InertFinder/ChemID | 6-Methyl-3,5- | 6-Methyl- 5- | 7- | Acetoin | Allyl cinnamate | Allyl | Allyl | Allyl |
|----------------------|------------------|--------------|--------------------|-----------|------------------|------------|-----------|------------|
| Plus Name | heptadien-2-one | hepten- 2- | Oxabicyclo(2.2.1.) | | | heptanoate | hexanoate | propionate |
| | | one | heptane, 1- | | | | | |
| | | | methyl-4- (1- | | | | | |
| | | | methylethyl)- | | | | | |
| | polarized double | double | | double | Carbonyl | | | |
| | bonds | bonds >> | | bonds >> | compounds with | | | |
| | | Ketones | | Ketones | polarized double | | | |
| | | | | | bonds | | | |
| rtER Expert System - | No alert found | No alert | No alert | No alert | No alert found | No alert | No alert | No alert |
| USEPA | | found | found | found | | found | found | found |
| Skin | Undefined | Undefined | Undefined | Undefined | Undefined | Undefined | Undefined | Undefined |
| irritation/corrosion | | | | | | | | |
| Exclusion rules by | | | | | | | | |
| BfR | | | | | | | | |
| Protein binding | No alert found | No alert | No alert found | No alert | No alert found | No alert | No alert | No alert |
| alerts for | | found | | found | | found | found | found |
| Chromosomal | | | | | | | | |
| aberration by OASIS | | | | | | | | |

| InertFinder/ChemI | alpha- | alpha- | Bicyclo[2. | Cyclohexa | Cyclopentan | Cycloprop | d,l- | Diisobutyl | Ethyl |
|--|---|---|---|---|--|---|---|---|---|
| D Plus Name | Hexylcinnamaldehyde | • | | none, 2- (1- methylpropyl)- | e acetai acid, 3- oxo-2- pentyl- | anemethano l, 1- methyl- 2- [(1,2,2- trimethyl bicyclo[3. 1.0]hex-3- yl)methyl] | Isomenthone | ketone | amyl ketone |
| CAS | 101-86-0 | 7779-78-4 | 464-49-3 | 14765-30-1 | 24851-98-7 | 198404-98-7 | 491-07-6 | 108-83-8 | 106-68-3 |
| SMILES | CCCCCC\C(C=O)=C/c1 cc ccc1 | CC(C)CC(O)Cc1cc cc c1 | CC1(C)[C @H]2CC[C@@]1(C)C(=O)C2 | CCC(C)C1 CCCCC1= O | CCCCCC1C(C C C1=0)CC(=0) OC | 2C1(C2)C) | CC(C)C1C CC(C)CC1 =0 | CC(C)CC(= O)CC(C)C | CCCCCC(= O)CC |
| Ionization at pH = 1 | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) |
| Biodegradation ultimate (Biowin 3) | Weeks | Weeks | Weeks to months | Weeks | Weeks | Months | Weeks | Weeks | Weeks |
| Estrogen Receptor Binding | Non binder, without OH or NH2 group | Non binder, without OH or NH2 group | Non binder, without OH or NH2 group | Non binder, without OH or NH2 group | Non binder, without OH or NH2 group | Non binder, without OH or NH2 group | Non binder, without OH or NH2 group | Non binder, non cyclic structure | Non binder, non cyclic structure |
| Biodeg BioHC half-life (Biowin) | No value | No value | No value | No value | No value | No value | No value | No value | No value |
| Hydrolysis half- life (pH 6.5-7.4) | No value | No value | No value | No value | Slow | No value | No value | No value | No value |
| Biodegradation | Biodegrades Fast | Does NOT | Does NOT | Does NOT | Biodegrade | Does NOT | Does NOT | Does NOT | Biodegrade |

| InertFinder/ChemI | alpha- | alpha- | Bicyclo[2. | Cyclohexa | Cyclopentan | Cycloprop | d,l- | Diisobutyl | Ethyl |
|-------------------|-----------------------------|------------------|---------------------|---------------|--------------------------|------------------|--------------|--------------|--------------|
| D Plus Name | Hexylcinnamaldehyde | Isobutylphenethy | 2.1]hepta n- | none, 2- | e acetai acid, | anemethano | Isomenthone | ketone | amyl |
| | | l alcohol | 2-one, | (1- | 3- oxo-2- | l, 1- methyl- | | | ketone |
| | | | 1,7,7- | methylpropyl | pentyl- | 2- [(1,2,2- | | | |
| | | | trimethyl- |)- | , methyl | trimethyl | | | |
| | | | , (1R,4R)- | | ester | bicyclo[3. | | | |
| | | | | | | 1.0]hex-3- | | | |
| | | | | | | yl)methyl] | | | |
| probability | | Biodegrade Fast | Biodegrade | Biodegrade | s Fast | Biodegrad | Biodegrade | Biodegrade | s Fast |
| (Biowin 5) | | | Fast | Fast | | e Fast | Fast | Fast | |
| Toxic hazard | Intermediate (Class | Intermediate | Intermediat | Intermediat | High (Class | Low (Class | Intermediat | Intermediat | Intermediat |
| classification by | II) | (Class II) | e (Class II) | e (Class II) | 111) | I) | e (Class II) | e (Class II) | e (Class II) |
| Cramer | | | | | | | | | |
| • | Biodegrades Fast | Biodegrades Fast | | Biodegrades | Biodegrade | Does NOT | Biodegrade | Biodegrade | • |
| probability | | | Biodegrade | Fast | s Fast | Biodegrad | s Fast | s Fast | s Fast |
| (Biowin 2) | | | Fast | | | e Fast | | | |
| - | Acidic [0.000, 10.000) | | Acidic | Acidic | Acidic | Acidic | Acidic | Acidic | Acidic |
| 4 | Basic [0.000, 10.000) | , | [0.000, | [0.000, | [0.000, | [0.000, | [0.000, | [0.000, | [0.000, |
| | | Basic [0.000, | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) | - | 10.000) |
| | | 10.000) | Basic | Basic [0.000, | Basic | Basic | Basic | Basic | Basic |
| | | | [0.000, | 10.000) | [0.000, | [0.000, | [0.000, | [0.000, | [0.000, |
| | | | 10.000) | | 10.000) | 10.000) | 10.000) | | 10.000) |
| U | DPRA less than 9% | | DPRA less | DPRA less | DPRA less | DPRA less | DPRA less | | Out of |
| potency Lys | (DPRA 13%) | 9% (DPRA 13%) | than 9% | than 9% | than 9% | than 9% | than 9% | | mechanistic |
| (DPRA 13%) | DPRA less than 9% | DPRA less than | (DPRA 13%) | (DPRA 13%) | (DPRA 13%) | (DPRA | (DPRA 13%) | domain | domain |
| | (DPRA 13%) >> | 9% (DPRA 13%) | DPRA less | DPRA less | DPRA less | 13%) | DPRA less | | |
| | Conjugated alpha, | >> | than 9% | than 9% | than 9% | DPRA less | than 9% | | |
| | beta- unsaturated | Alcohols | (DPRA 13%) | (DPRA 13%) | (DPRA 13%) | than 9% | (DPRA 13%) | | |
| | aldehydes (non reactive) | | >> Non- | >> Non- | >> Non- | (DPRA 13%) >> | >> Non- | | |
| | ieallive) | | non- conjugate d | conjugate d | Conjugated carboxylic | Alcohols | conjugate d | | |
| | | | mono- and | mono- and | acids and | AICOHOIS | mono- and | | |
| | | | diketones | diketones | esters (non | | diketones | | |
| | | | uikelühes | uiketones | esters (non | | uikelühes | | |

| InertFinder/ChemI | alpha- | alpha- | Bicyclo[2. | | Cyclohexa | Cyclopentan | Cycloprop | d,l- | Diisobutyl | Ethyl |
|---|---|---|---------------------------------|----|---------------------------------|---|---|---------------------------------|-------------|---------------------------------|
| D Plus Name | Hexylcinnamaldehyde | • | • - | n- | - | e acetai acid, 3- oxo-2- pentyl- | | • | ketone | amyl ketone |
| | | | (non reactive) | | (non reactive) | reactive) DPRA less than 9% (DPRA 13%) >> Non- conjugated mono- and diketones (non | yl)methyl] | (non reactive) | | |
| Protein binding potency Cys (DPRA 13%) | DPRA less than 9% (DPRA 13%) DPRA less than 9% (DPRA 13%) >> alpha alkyl cinnamaldehydes | DPRA less than 9% (DPRA 13%) DPRA less than 9% (DPRA 13%) >> Alcohols | Out of mechanistic domain | | Out of mechanistic domain | reactive) DPRA less than 9% (DPRA 13%) DPRA less than 9% (DPRA 13%) >> Non- Conjugated carboxylic acids and esters (non reactive) | DPRA less than 9% (DPRA 13%) DPRA less than 9% (DPRA 13%) >> Alcohols | Out of mechanistic domain | mechanistic | Out of mechanistic domain |
| Hydrolysis half- life (Kb, pH 8) (Hydrowin) | No value | No value | No value | | No value | > 100 days | No value | No value | No value | No value |

| InertFinder/ChemI | alpha- | alpha- | Bicyclo[2. | Cyclohexa | Cyclopentan | Cycloprop | d,l- | Diisobutyl | Ethyl |
|-------------------|----------------------------------|------------------|--------------|--------------|----------------|---------------|-------------|--------------|--------------|
| D Plus Name | Hexylcinnamaldehyde | Isobutylphenethy | 2.1]hepta n- | none, 2- | e acetai acid, | anemethano | Isomenthone | ketone | amyl |
| | | l alcohol | 2-one, | (1- | 3- oxo-2- | l, 1- methyl- | | | ketone |
| | | | 1,7,7- | methylpropyl | pentyl- | 2- [(1,2,2- | | | |
| | | | trimethyl- |)- | | trimethyl | | | |
| | | | , (1R,4R)- | | ester | bicyclo[3. | | | |
| | | | | | | 1.0]hex-3- | | | |
| | | | | | | yl)methyl] | | | |
| , , | No value | No value | No value | No value | > 100 days | No value | No value | No value | No value |
| life (Kb, pH 7) | | | | | | | | | |
| (Hydrowin) | | | | | | | | | |
| - | Biodegrades Fast | Does NOT | Does NOT | Biodegrades | Biodegrade | Does NOT | Biodegrade | Biodegrade | - |
| probability | | Biodegrade Fast | • | Fast | s Fast | Biodegrde | s Fast | s Fast | s Fast |
| (Biowin 6) | | | Fast | | | Fast | | | |
| U | Michael addition | No alert found | No alert | No alert | No alert | No alert | No alert | No alert | No alert |
| ' | Michael addition >> | | found | found | found | found | found | found | found |
| | Polarised Alkenes | | | | | | | | |
| | Michael addition >> | | | | | | | | |
| | Polarised Alkenes >> | | | | | | | | |
| | Polarised alkene - | | | | | | | | |
| | aldehydes Schiff Base Formers | | | | | | | | |
| | Schiff Base Formers | | | | | | | | |
| | >> Direct Acting | | | | | | | | |
| | Schiff Base Formers | | | | | | | | |
| | Schiff Base Formers | | | | | | | | |
| | >> Direct Acting | | | | | | | | |
| | Schiff Base Formers | | | | | | | | |
| | >> Mono- carbonyls | | | | | | | | |
| | No data | No data | 1 to 10 | 10 to 100 | 1 to 10 days | > 100 | 10 to 100 | 1 to 10 davs | 1 to 10 days |
| -0 | | | days | days | 10 to 100 | days | days | 10 to 100 | 10 to 100 |
| | | | 10 to 100 | | days | , | | days | days |
| | | | days | | , | | | , | , |

| InertFinder/ChemI | alpha- | alpha- | Bicyclo[2. | Cyclohexa | Cyclopentan | Cycloprop | d,l- | Diisobutyl | Ethyl |
|-------------------------------------|-----------------------|------------------|--------------|---------------|----------------|---------------|----------------------------|--------------|---------------------|
| D Plus Name | Hexylcinnamaldehyde | Isobutylphenethy | 2.1]hepta n- | none, 2- | e acetai acid, | anemethano | Isomenthone | ketone | amyl |
| | | l alcohol | 2-one, | (1- | 3- oxo-2- | l, 1- methyl- | | | ketone |
| | | | 1,7,7- | methylpropyl | pentyl- | 2- [(1,2,2- | | | |
| | | | trimethyl- |)- | | trimethyl | | | |
| | | | , (1R,4R)- | | ester | bicyclo[3. | | | |
| | | | | | | 1.0]hex-3- | | | |
| | | | | | | yl)methyl] | | - | |
| Ionization at pH = | | Acidic [0.000, | Acidic | Acidic | Acidic | Acidic | Acidic | Acidic | Acidic |
| 9 | 50.000) | 10.000) | [0.000, | [0.000, | [0.000, | [0.000, | [0.000, | [0.000, | [0.000, |
| | Basic [0.000, 10.000) | Basic [0.000, | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) | 10.000) |
| | | 10.000) | Basic | Basic [0.000, | Basic | Basic | Basic | Basic | Basic |
| | | | [0.000, | 10.000) | [0.000, | [0.000, | [0.000 <i>,</i> 10.000) | [0.000, | [0.000, |
| | Nevelue | No value | 10.000) | Nevelue | 10.000) | 10.000) | No value | 10.000) | 10.000) No value |
| Hydrolysis half- life (Ka, pH 7) | No value | No value | No value | No value | No value | No value | No value | No value | No value |
| (Hydrowin) | | | | | | | | | |
| Toxic hazard | Intermediate (Class | Intermediate | Intermediat | Intermediat | High (Class | Low (Class | Intermediat | Intermediat | Intermediat |
| classification by | II) | (Class II) | e (Class II) | e (Class II) | | 1) | e (Class II) | e (Class II) | e (Class II) |
| Cramer | , | | | | , | ', | | | |
| (extended) | | | | | | | | | |
| Biodegradation | Does NOT | Does NOT | Does NOT | Does NOT | Does NOT | Does NOT | Does NOT | Does NOT | Does NOT |
| probability | Biodegrade Fast | Biodegrade Fast | Biodegrade | Biodegrade | Biodegrade | Biodegrde | Biodegrade | Biodegrade | Biodegrade |
| (Biowin 7) | | | Fast | Fast | Fast | Fast | Fast | Fast | Fast |
| DNA binding by | AN2 | No alert found | No alert | No alert | No alert | No alert | No alert | No alert | No alert |
| OASIS | AN2 >> Nucleophilic | | found | found | found | found | found | found | found |
| | addition to alpha, | | | | | | | | |
| | beta- unsaturated | | | | | | | | |
| | carbonyl compounds | | | | | | | | |
| | AN2 >> Nucleophilic | | | | | | | | |
| | addition to alpha, | | | | | | | | |
| | beta- unsaturated | | | | | | | | |
| | carbonyl compounds | | | | | | | | |

| InertFinder/ChemI | alpha- | alpha- | Bicyclo[2. | Cyclohexa | Cyclopentan | Cycloprop | d,l- | Diisobutyl | Ethyl |
|---|--|-------------------------------|--|--|---|---|---|---|---|
| D Plus Name | Hexylcinnamaldehyde | Isobutylphenethy I alcohol | 2.1]hepta n- 2-one, 1,7,7- trimethyl- , (1R,4R)- | none, 2- (1- methylpropyl)- | 3- oxo-2- pentyl- | anemethano l, 1- methyl- 2- [(1,2,2- l trimethyl bicyclo[3. 1.0]hex-3- yl)methyl] | Isomenthone | ketone | amyl ketone |
| | >> Alpha, Beta- Unsaturated Aldehydes AN2 >> Schiff base formation AN2 >> Schiff base formation >> Alpha, Beta-Unsaturated Aldehydes | | | | | | | | |
| Ionization at pH = 7.4 | Acidic [0.000, 10.000) Basic [0.000, 10.000) | | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) |
| Hydrolysis half- life (Ka, pH 8) (Hydrowin) | No value | No value | No value | No value | No value | No value | No value | No value | No value |
| Protein binding by OASIS | Michael addition Michael addition >> Michael addition on alpha, beta- Unsaturated carbonyl compounds Michael addition >> | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found |

| InertFinder/ChemI | alpha- | alpha- | Bicyclo[2. | Cyclohexa | Cyclopentan | Cycloprop | d,l- | Diisobutyl | Ethyl |
|-------------------|-----------------------|------------------|--------------|--------------|----------------|---------------|-------------|------------|----------|
| D Plus Name | Hexylcinnamaldehyde | Isobutylphenethy | 2.1]hepta n- | none, 2- | e acetai acid, | anemethano | Isomenthone | ketone | amyl |
| | | l alcohol | 2-one, | (1- | 3- oxo-2- | l, 1- methyl- | | | ketone |
| | | | 1,7,7- | methylpropyl | pentyl- | 2- [(1,2,2- | | | |
| | | | trimethyl- |)- | | trimethyl | | | |
| | | | , (1R,4R)- | | ester | bicyclo[3. | | | |
| | | | | | | 1.0]hex-3- | | | |
| | | | | | | yl)methyl] | | | |
| | Michael addition on | | | | | | | | |
| | alpha, beta- | | | | | | | | |
| | Unsaturated | | | | | | | | |
| | carbonyl compounds | | | | | | | | |
| | >> alpha, beta- | | | | | | | | |
| | Aldehydes Schiff | | | | | | | | |
| | base formation Schiff | | | | | | | | |
| | base formation | | | | | | | | |
| | >> Schiff base | | | | | | | | |
| | formation with | | | | | | | | |
| | carbonyl compounds | | | | | | | | |
| | Schiff base formation | | | | | | | | |
| | >> Schiff base | | | | | | | | |
| | formation with | | | | | | | | |
| | carbonyl compounds | | | | | | | | |
| | >> Aldehydes | | | | | | | | |
| DNA binding by | No alert found | Michael addition | | No alert | No alert | No alert | No alert | No alert | No alert |
| OECD | | Michael addition | found | found | found | found | found | found | found |
| | | >> P450 | | | | | | | |
| | | Mediated | | | | | | | |
| | | Activation to | | | | | | | |
| | | Quinones and | | | | | | | |
| | | Quinone-type | | | | | | | |
| | | Chemicals | | | | | | | |
| | | Michael addition | | | | | | | |
| | | >> P450 | | | | | | | |

| InertFinder/ChemI | alpha- | alpha- | Bicyclo[2. | Cyclohexa | Cyclopentan | Cycloprop | d,l- | Diisobutyl | Ethyl |
|---|---------------------|---|--------------------------------|---------------------|--|-------------------------------|----------------------|----------------------|----------------------|
| D Plus Name | Hexylcinnamaldehyde | Isobutylphenethy I alcohol | • - | | e acetai acid, 3- oxo-2- pentyl- | | | ketone | amyl ketone |
| | | Mediated Activation to Quinones and Quinone-type Chemicals >> Arenes | | | | yıjınetnyıj | | | |
| Biodegradation probability (Biowin 1) | Biodegrades Fast | Biodegrades Fast | Does NOT Biodegrade Fast | Biodegrades Fast | Biodegrade s Fast | Does NOT Biodegrde Fast | Biodegrade s Fast | Biodegrade s Fast | Biodegrade s Fast |
| Biodegradation primary (Biowin 4) | Days | Days to weeks | Days to weeks | Days to weeks | Days | Weeks | Days to weeks | Days to weeks | Days |
| Carcinogenicity (genotox and nongenotox) alerts by ISS | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found |
| in vitro mutagenicity (Ames test) alerts by ISS | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found |
| in vivo mutagenicity (Micronucleus) alerts by ISS | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found |
| Protein Binding | No alert found | No alert found | No alert | No alert | No alert | No alert | No alert | No alert | No alert |

| InertFinder/ChemI | alpha- | alpha- | Bicyclo[2. | Cyclohexa | Cyclopentan | Cycloprop | d,l- | Diisobutyl | Ethyl |
|---------------------|---------------------|------------------|-------------|--------------|----------------|---------------|-------------|-------------|-------------|
| D Plus Name | Hexylcinnamaldehyde | Isobutylphenethy | 2.1]hepta n | none, 2- | e acetai acid, | anemethano | Isomenthone | ketone | amyl |
| | | l alcohol | 2-one, | (1- | 3- oxo-2- | l, 1- methyl- | | | ketone |
| | | | 1,7,7- | methylpropyl | pentyl- | 2- [(1,2,2- | | | |
| | | | trimethyl- |)- | , methyl | trimethyl | | | |
| | | | , (1R,4R)- | | ester | bicyclo[3. | | | |
| | | | | | | 1.0]hex-3- | | | |
| | | | | | | yl)methyl] | | | |
| Potency h-CLAT | | | found | found | found | found | found | found | found |
| Skin | Aldehydes | Inclusion rules | Ketones | Ketones | Ketones | Inclusion | Ketones | Ketones | Ketones |
| irritation/corrosio | | not met | | | | rules not | | | |
| n Inclusion rules | | | | | | met | | | |
| by BfR | | | | | | | | | |
| DNA alerts for | No alert found | No alert found | No alert | No alert | No alert | No alert | No alert | No alert | No alert |
| AMES, CA and | | | found | found | found | found | found | found | found |
| MNT by OASIS | | | | | | | | | |
| Protein binding | Michael Addition | No alert found | Nucleophili | Nucleophilic | Nucleophilic | | Nucleophili | Nucleophili | Nucleophili |
| alerts for skin | Michael Addition >> | | c addition | addition | addition | found | c addition | c addition | c addition |
| sensitization by | Michael addition on | | Nucleophili | Nucleophilic | Nucleophilic | | Nucleophili | Nucleophili | Nucleophili |
| OASIS | alpha, beta- | | c addition | addition | addition >> | | c addition | c addition | c addition |
| | Unsaturated | | >> | >> | Addition to | | >> | >> | >> |
| | carbonyl compounds | | Addition to | Addition to | carbon- | | Addition to | Addition to | Addition to |
| | Michael Addition >> | | carbon- | carbon- | hetero | | carbon- | carbon- | carbon- |
| | Michael addition on | | hetero | hetero | double | | hetero | hetero | hetero |
| | alpha, beta- | | double | double | bonds | | double | double | double |
| | Unsaturated | | bonds | bonds | Nucleophilic | | bonds | bonds | bonds |
| | carbonyl compounds | | Nucleophili | Nucleophilic | addition >> | | Nucleophili | Nucleophili | Nucleophili |
| | >> alpha, beta- | | c addition | addition | Addition to | | c addition | c addition | c addition |
| | Aldehydes | | >> | >> | carbon- | | >> | >> | >> |
| | | | Addition to | Addition to | hetero | | Addition to | Addition to | Addition to |
| | | | carbon- | carbon- | double | | carbon- | carbon- | carbon- |
| | | | hetero | hetero | bonds | | hetero | hetero | hetero |
| | | | double | double | >> Ketones | | double | double | double |

| InertFinder/ChemI D Plus Name | alpha- Hexylcinnamaldehyde | Isobutylphenethy I alcohol | • - | Cyclohexa none, 2- (1- methylpropyl)- | 3- oxo-2- pentyl- | · · · | | Diisobutyl ketone | Ethyl amyl ketone |
|--|-------------------------------|-------------------------------|---------------------|--|--|--|---------------------|----------------------|-------------------------|
| | | | bonds >> Ketones | bonds >> Ketones | | | bonds >> Ketones | bonds >> Ketones | bonds >> Ketones |
| rtER Expert System - USEPA | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found |
| Skin irritation/corrosio n Exclusion rules by BfR | Undefined | Undefined | Undefined | Undefined | Group C Melting Point > 55 C Undefined | Group C Melting Point > 55 C Undefined | Undefined | Undefined | Undefined |
| Protein binding alerts for Chromosomal aberration by OASIS | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found |

| InertFinder/ChemI D Plus Name | | Ethyl vanillin | Heptanal, 2- (phenylmethylen e)- | Isojasmone | Maltyl isobutyrate | amyl ketone | ether | Methylcyclopentenolo ne |
|---|---|---|--|--|---|---|--|---|
| CAS | 4940-11-8 | 121-32-4 | 122-40-7 | 11050-62-7 | 65416-14-0 | 110-43-0 | 3558-60-9 | 80-71-7 |
| SMILES | CCC1=C(O)C(=O) C =CO1 | CCOc1cc(C= 0)ccc10 | CCCCC/C(C=O)=C/c1 cc ccc1 | CC/C=C/C C1=C(C)C(=O)CC1 | CC(C)C(=O)OC 1 =C(C)OC=CC1= 0 | CCCCCC(C)=O | COCCc1ccccc 1 | CC1=C(O) C(=O)CC1 |
| Ionization at pH = 1 | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) No pKb value | Acidic [0.000, 10.000) No pKb value | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) |
| Biodegradation ultimate (Biowin 3) | Weeks | Weeks | Weeks | Weeks | Weeks | Weeks | Weeks | Weeks |
| Estrogen Receptor Binding | Non binder, impaired OH or NH2 group | Weak binder, OH group | Non binder, without OH or NH2 group | Non binder, without OH or NH2 group | Non binder, without OH or NH2 group | Non binder, non cyclic structure | Non binder, without OH or NH2 group | Non binder, impaired OH or NH2 group |
| Biodeg BioHC half-life (Biowin) | No value | No value | No value | No value | No value | No value | No value | No value |
| Hydrolysis half- life (pH 6.5-7.4) | No value | No value | No value | No value | Fast | No value | No value | No value |
| Biodegradation probability (Biowin 5) | Biodegrades Fast | Biodegrades Fast | Biodegrades Fast | Does NOT Biodegrade Fast | Biodegrades Fast | Biodegrade s Fast | Does NOT Biodegrade Fast | Biodegrades Fast |
| Toxic hazard classification by Cramer | Intermediate (Class II) | Intermediate (Class II) | Intermediate (Class II) | Intermediate (Class II) | High (Class III) | Intermediat e (Class II) | Intermediat e (Class II) | High (Class III) |
| Biodegradation probability (Biowin 2) | Does NOT Biodegrade Fast | Biodegrades Fast | Biodegrades Fast | Biodegrades Fast | Biodegrades Fast | Biodegrade s Fast | Biodegrade s Fast | Biodegrades Fast |

| InertFinder/ChemI D Plus Name | Ethyl maltol | | Heptanal, 2- (phenylmethylen e)- | Isojasmone | Maltyl isobutyrate | Methyl n- amyl ketone | Methyl phenethyl ether | Methylcyclopentenolo ne |
|----------------------------------|---|--|---|--|--|---|---|---|
| Ionization at pH = 4 | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) No pKb value | Acidic [0.000, 10.000) No pKb value | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) |
| Protein binding | DPRA less than | DPRA less | DPRA less than 9% | DPRA less | DPRA less | Out of | DPRA less | DPRA less than 9% |
| (DPRA 13%) | | (DPRA 13%) DPRA less than 9% (DPRA 13%) >> Vaniline derivatives Grey zone 9- 21% (DPRA 13%) Grey zone 9- 21% (DPRA 13%) >> Non- alpha, beta- conjugated monoaldehyd | (DPRA 13%) DPRA less than 9% (DPRA 13%) >> Conjugated alpha, beta- unsaturated aldehydes (non reactive) | than 9% (DPRA 13%) DPRA less than 9% (DPRA 13%) >> Conjugate d alpha, beta- unsaturated ketones (non reactive) | than 9% (DPRA 13%) DPRA less than 9% (DPRA 13%) >> Conjugated alpha, beta- unsaturated ketones (non reactive) | domain | than 9% (DPRA 13%) DPRA less than 9% (DPRA 13%) >> No protein binding alert | (DPRA 13%) DPRA less than 9% (DPRA 13%) >> Conjugate d alpha, beta- unsaturated ketones (non reactive) |
| Duatain hindin - | Out of | es (Grey zone) | DDDA loss then 0% | | Out of | Out of | | DDDA loss than 0% |
| Protein binding potency Cys | Out of mechanistic | DPRA less than 9% | DPRA less than 9% (DPRA 13%) | DPRA less than 9% | Out of mechanistic | Out of mechanistic | DPRA less | DPRA less than 9% (DPRA 13%) |
| (DPRA 13%) | domain | (DPRA 13%) DPRA less than 9% | DPRA less than 9% (DPRA 13%) >> alpha alkyl | (DPRA 13%) DPRA less than 9% | domain | domain | (DPRA 13%) DPRA less than 9% | DPRA less than 9% (DPRA 13%) >> No protein binding |
| | | (DPRA 13%) | cinnamaldehydes | (DPRA 13%) | | | (DPRA 13%) | alert |

| InertFinder/ChemI D Plus Name | Ethyl maltol | Ethyl vanillin | Heptanal, 2- (phenylmethylen e)- | Isojasmone | Maltyl isobutyrate | Methyl n- amyl ketone | | Methylcyclopentenolo ne |
|---|---|--|--|-----------------------------------|---|--------------------------|--------------------------------------|----------------------------|
| | | >> Non- Conjugated monoaldehyd es (non reactive) DPRA less than 9% (DPRA 13%) >> Vaniline derivatives | | >> No protein binding alert | | | >> No protein binding alert | |
| Hydrolysis half- life (Kb, pH 8) (Hydrowin) | No value | No value | No value | No value | > 100 days | No value | No value | No value |
| Hydrolysis half- life (Kb, pH 7) (Hydrowin) | No value | No value | No value | No value | > 100 days | No value | No value | No value |
| Biodegradation probability (Biowin 6) | Biodegrades Fast | Biodegrades Fast | Biodegrades Fast | Biodegrades Fast | Biodegrades Fast | Biodegrade s Fast | Does NOT Biodegrade Fast | Biodegrades Fast |
| Protein binding by OECD | Michael addition Michael addition >> Quinones and Quinone- type Chemicals Michael addition >> Quinones and Quinone- | No alert found | Michael addition Michael addition >> Polarised Alkenes Michael addition >> Polarised Alkenes >> Polarised alkene - aldehydes Schiff Base Formers >> Direct Acting Schiff Base Formers | No alert found | Acylation Acylation >> Direct Acylation Involving a Leaving group Acylation >> Direct Acylation Involving a Leaving group | No alert found | No alert found | No alert found |

| InertFinder/ChemI D Plus Name | Ethyl maltol | Ethyl vanillin | Heptanal, 2- (phenylmethylen e)- | Isojasmone | Maltyl isobutyrate | Methyl n- amyl ketone | Methyl phenethyl ether | Methylcyclopentenolo ne |
|---|--|--|---|---|---|---|---|---|
| | type Chemicals >> Pyranones (and related nitrogen chemicals) | | Schiff Base Formers >> Direct Acting Schiff Base Formers >> Mono-carbonyls | | >> Acetates Michael addition Michael addition >> Quinones and Quinone-type Chemicals Michael addition >> Quinones and Quinones and | | | |
| Ultimate biodeg | (N/A) | 0 to 1 day 1 to 10 days | 10 to 100 days | No data | No data | 10 to 100 days | 10 to 100 days | 10 to 100 days |
| Ionization at pH = 9 | Acidic [90.000, 100.000] Basic [0.000, 10.000) | Acidic [80.000, 90.000) Basic [0.000, 10.000) | Acidic [40.000, 50.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) No pKb value | Acidic [0.000, 10.000) No pKb value | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) |
| Hydrolysis half- life (Ka, pH 7) (Hydrowin) | No value | No value | No value | No value | No value | No value | No value | No value |
| Toxic hazard classification by Cramer (extended) | Intermediate (Class II) | Intermediate (Class II) | Intermediate (Class II) | Intermediate (Class II) | High (Class III) | Intermediat e (Class II) | Intermediat e (Class II) | High (Class III) |

| InertFinder/ChemI D Plus Name | Ethyl maltol | Ethyl vanillin | Heptanal, 2- (phenylmethylen e)- | Isojasmone | Maltyl isobutyrate | Methyl n- amyl ketone | Methyl phenethyl ether | Methylcyclopentenolo ne |
|----------------------------------|-----------------|-----------------|--|----------------|-----------------------|--------------------------|------------------------------|----------------------------|
| Biodegradation | Does NOT | Biodegrades | Does NOT | Does NOT | Does NOT | Does NOT | Does NOT | Does NOT Biodegrade |
| probability | Biodegrade Fast | Fast | Biodegrade Fast | Biodegrade | Biodegrade | Biodegrade | Biodegrade | Fast |
| (Biowin 7) | | | | Fast | Fast | Fast | Fast | |
| DNA binding by | No alert found | No alert found | AN2 | No alert | No alert found | No alert | No alert | No alert found |
| OASIS | | | AN2 >> Nucleophilic | found | | found | found | |
| | | | addition to alpha, | | | | | |
| | | | beta-unsaturated | | | | | |
| | | | carbonyl | | | | | |
| | | | compounds AN2 >> | | | | | |
| | | | Nucleophilic | | | | | |
| | | | addition to alpha, | | | | | |
| | | | beta-unsaturated | | | | | |
| | | | carbonyl | | | | | |
| | | | compounds | | | | | |
| | | | >> Alpha, Beta- | | | | | |
| | | | Unsaturated | | | | | |
| | | | Aldehydes | | | | | |
| | | | AN2 >> Schiff base | | | | | |
| | | | formation | | | | | |
| | | | AN2 >> Schiff base | | | | | |
| | | | formation >> Alpha, | | | | | |
| | | | Beta- Unsaturated | | | | | |
| | | | Aldehydes | | | | | |
| Ionization at pH = | Acidic [90.000, | Acidic [10.000, | Acidic [0.000, | Acidic [0.000, | Acidic [0.000, | Acidic | Acidic | Acidic [0.000, |
| 7.4 | 100.000] | 20.000) | 10.000) | 10.000) | 10.000) | [0.000, | [0.000, | 10.000) |
| | Basic [0.000, | Basic [0.000, | Basic [0.000, | No pKb value | No pKb value | 10.000) | 10.000) | Basic [0.000, |
| | 10.000) | 10.000) | 10.000) | | | Basic | Basic | 10.000) |
| | | | | | | [0.000, | [0.000, | |
| | | | | | | 10.000) | 10.000) | |
| Hydrolysis half- | No value | No value | No value | No value | No value | No value | No value | No value |

| InertFinder/ChemI D Plus Name | Ethyl maltol | Ethyl vanillin | Heptanal, 2- (phenylmethylen e)- | Isojasmone | Maltyl isobutyrate | Methyl n- amyl ketone | Methyl phenethyl ether | Methylcyclopentenolo ne |
|----------------------------------|--|----------------|---|-------------------|---|--------------------------|------------------------------|----------------------------|
| life (Ka, pH 8) (Hydrowin) | | | | | | | | |
| Protein binding by OASIS | Michael addition Michael addition >> Michael addition on quinoid type compounds Michael addition >> Michael addition on quinoid type compounds >> Pyranones, Pyridones (and related nitrogen chemicals) | No alert found | Michael addition Michael addition >> Michael addition on alpha, beta- Unsaturated carbonyl compounds Michael addition >> Michael addition on alpha, beta- Unsaturated carbonyl compounds >> alpha, beta- Aldehydes Schiff base formation Schiff base formation >> Schiff base formation with carbonyl compounds Schiff base formation >> Schiff base formation with carbonyl compounds Schiff base formation >> Schiff base | No alert found | Michael addition Michael addition >> Michael addition on quinoid type compounds Michael addition >> Michael addition on quinoid type compounds >> Pyranones, Pyridones (and related nitrogen chemicals) | No alert found | No alert found | No alert found |

| InertFinder/ChemI D Plus Name | Ethyl maltol | Ethyl vanillin | Heptanal, 2- (phenylmethylen e)- | - | Maltyl isobutyrate | Methyl n- amyl ketone | Methyl phenethyl ether | Methylcyclopentenolo ne |
|---|-----------------------------|---------------------|--|---------------------|--------------------------------|--------------------------|--|----------------------------|
| DNA binding by OECD | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found | Michael addition Michael addition >> P450 Mediated Activation to Quinones and Quinone- type Chemicals Michael addition >> P450 Mediated Activation to Quinones and Quinone- type Chemicals >> Arenes | |
| Biodegradation probability (Biowin 1) | Does NOT Biodegrade Fast | Biodegrades Fast | Biodegrades Fast | Biodegrades Fast | Does NOT Biodegrade Fast | Biodegrade s Fast | Biodegrade s Fast | Biodegrades Fast |
| Biodegradation primary (Biowin 4) | Days to weeks | Days | Days | Days | Days | Days | Days to weeks | Days |

| InertFinder/Cheml D Plus Name | Ethyl maltol | Ethyl vanillin | Heptanal, 2- (phenylmethylen e)- | Isojasmone | Maltyl isobutyrate | amyl ketone | Methyl phenethyl ether | Methylcyclopentenolo ne |
|---|---|--|--|--|--|-------------------|-------------------------------|--|
| Carcinogenicity (genotox and nongenotox) alerts by ISS | alpha, beta- unsaturated carbonyls (Genotox) Structural alert for genotoxic carcinogenicity | Simple aldehyde (Genotox) Structural alert for genotoxic carcinogenicit y | No alert found | alpha, beta- unsaturated carbonyls (Genotox) Structural alert for genotoxic carcinogenici ty | alpha, beta- unsaturated carbonyls (Genotox) Structural alert for genotoxic carcinogenicit Y | No alert found | No alert found | alpha, beta- unsaturated carbonyls (Genotox) Structural alert for genotoxic carcinogeniciy |
| in vitro mutagenicity (Ames test) alerts by ISS | alpha, beta- unsaturated carbonyls | Simple aldehyde | No alert found | alpha, beta- unsaturated carbonyls | alpha, beta- unsaturated carbonyls | No alert found | No alert found | alpha, beta- unsaturated carbonyls |
| in vivo mutagenicity (Micronucleus) alerts by ISS | alpha, beta- unsaturated carbonyls H-acceptor- path3- H- acceptor | H-acceptor- path3-H- acceptor Simple aldehyde | No alert found | alpha, beta- unsaturated carbonyls | alpha, beta- unsaturated carbonyls H-acceptor- path3-H- acceptor | No alert found | No alert found | alpha, beta- unsaturated carbonyls H- acceptor- path3-H- acceptor |
| Protein Binding Potency h-CLAT | Pyranones, Pyridones and related chemicals | No alert found | alpha, beta- Unsaturated aldehydes | alpha, beta- Unsaturated ketones | Pyranones, Pyridones and related chemicals | No alert found | No alert found | No alert found |
| Skin irritation/corrosio n Inclusion rules by BfR | Ketones | Aldehydes Phenols | Aldehydes | Ketones | Ketones | Ketones | Inclusion rules not met | Ketones |
| DNA alerts for AMES, CA and MNT by OASIS | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found |

| D Plus Name Michael Schiff base formation Michael Addition Michael Addition No alert found Michael No alert Addition No alert found No alert found OASIS Michael Schiff base addition on formation Michael Addition on formation Instructed compounds Michael Addition on formation Michael Addition on alpha, beta- Michael Addition on formation Michael Addition on alpha, beta- Michael Michael Nucleophili addition Caddition addition Instructed addition Addition Caddition Instructed addition Addition Instructed addition Addition Instructed addition Instructed addition Instructed addition Instructed addition Instructed addition Instructed addition Instructed addition Instruc | |
|---|--|
| Protein binding alerts for skin sensitization byMichaelSchiff baseMichael Addition formationNo alert Michael Addition >> foundMichaelNucleophili c additionNo alert foundOASISMichaelSchiff baseMichael addition on alpha, beta- Unsaturated carbonylMichaelNucleophili Addition on alpha, beta- Unsaturated compoundsMichaelNucleophili c addition on Addition to quinoid typeNo alert foundNo alert foundNo alert foundOASISMichaelSchiff base formation quinoid type>> Schiff base compoundsUnsaturated compoundsMichael addition >> michael addition on alpha, beta-No alert foundNo alert foundNo alert foundMichaelSchiff base formation compoundsMichael Addition >> compoundsMichael addition on alpha, beta-Michael addition >> MichaelNo alert foundAdditionformation formation alpha, beta-Michael addition on alpha, beta-Michael MichaelNo alert Addition >> Michael>> MichaelSchiff base formation addition on quinoid type compounds >> compounds >> compounds >> compounds >> compounds >> compounds >> AldehydesNo alertNo alert Addition on addition on alpha, beta->> MichaelSchiff base addition on quinoid type compounds >> compounds >> soliff base pyranones, Pyridones (and related nitrogen chemicals)No alertPridones (and related nitrogenSchiff base compounds >> soliff base addit | |
| alerts for skin sensitization by OASISAddition formationformation MichaelMichael Addition >> foundfoundfoundOASISMichael AdditionSchiff baseMichael addition on alpha, beta-MichaelNucleophiliNucleophiliOASISAdditionformationalpha, beta-Addition on addition on formationNucleophiliNucleophiliAddition onformationcarbonyladdition on quinoid typeSchiff baseUnsaturatedAddition on addition >>Addition to carbonylCompoundscompoundscompoundsCompoundscompoundscompoundsIteroMichaelSchiff baseMichael Addition >>CompoundsNucleophiliAdditionformationalpha, beta-CompoundsNucleophiliAdditionformationalpha, beta-MichaeldoubleAddition onformationcarbonylMichaelNucleophiliaddition onformationcarbonylMichaelNucleophiliaddition onformationcarbonylMichaelNucleophiliaddition onformationcarbonyladdition ocadditionquinoid typewith carbonylcompounds >>quinoid type>>compoundscompoundsalpha, beta-compounds >>Addition toPyranones,>> AldehydesAldehydesPyranones,arbon-Pyridones (and related nitrogencarbonylalpha, beta-pyridonesPyridones (and rela | |
| sensitization by OASISMichaelSchiff baseMichael addition on alpha, beta-MichaelNucleophiliAdditionformationalpha, beta-Addition >>caddition>> Michael>>Schiff baseUnsaturatedMichael>>addition onformationcarbonyladdition onAddition toquinoid typewith carbonylcompoundsquinoid typecarbon-compoundscompoundsMichael Addition >>compoundsheteroAdditionformationalpha, beta-MichaeldoubleAdditionformationalpha, beta-MichaelbondsAdditionformationalpha, beta-MichaelNucleophiliAdditionformationalpha, beta-MichaelNucleophiliAdditionformationalpha, beta-MichaelNucleophiliaddition onformationcarbonylcarbonyladdition onquinoid typewith carbonylcompounds >>MichaelNucleophiliaddition onformationcarbonyladdition oncarditionquinoid typewith carbonylcompounds >>quinoid type>pyranones,pyranones,AldehydesPyranones,Addition topyridones (andrelated nitrogenpyridonesAldehydespyridoneshttps://dot.org/licelicelicelicelicelicelicelicelicelice | |
| OASISAdditionformationalpha, beta- UnsaturatedAddition >>c addition>> Michael>> Schiff baseUnsaturatedMichael>>addition onformationcarbonyladdition onAddition toquinoid typewith carbonylcompoundsquinoid typecarbon-compoundscompoundsMichael Addition >>compoundsheteroMichaelSchiff baseMichael addition onMichaeldoubleAdditionformationalpha, beta-Addition >>bonds>> Michael>> Schiff baseUnsaturatedMichaelNucleophiliaddition onformationcarbonylcompounds >>quinoid type>> Michael>> Schiff baseUnsaturatedMichaelNucleophiliaddition onformationcarbonylcompounds >>quinoid type>> Michael>> Schiff baseUnsaturatedMichaelNucleophiliaddition onformationcarbonylcompounds >>quinoid typeyuinoid typewith carbonylcompounds >>quinoid type>>compounds >>compoundsalpha, beta-compounds >>Addition toPyranones,>> AldehydesPyranones,Pyranones,carbon-Pyridones (and related nitrogenif hetero(and relateddoublehetero(and relatednitrogenbonds >>if hetero | |
| >> Michael>> Schiff baseUnsaturatedMichael>>addition onformationcarbonyladdition onAddition toquinoid typewith carbonylcompoundsquinoid typecarbon-compoundscompoundsMichael Addition >>compoundsheteroMichaelSchiff baseMichael addition onMichaeldoubleAdditionformationalpha, beta-Addition >>bonds>> Michael>> Schiff baseUnsaturatedMichaelNucleophiliaddition onformationcarbonyladdition oncadditionquinoid typevith carbonylcompounds >>quinoid type>>compoundscompoundscompounds >>quinoid type>>off baseUnsaturatedMichaelNucleophiliaddition oncarbonyladdition onformationcarbonylcompounds >>quinoid type>>compounds>>compoundsalpha, beta-compounds >>Addition toquinoid typevith carbonylcompounds >>quinoid type>>compounds>>compoundsAldehydesPyranones,carbon-Pyridones (andFaleed nitrogenAldehydesPyridonesheterorelated nitrogenchemicals)into onintrogenbonds >> | |
| addition on quinoid typeformationcarbonyladditionAddition to quinoid typeAddition to carbon-compoundscompoundsMichael Addition >>compoundsketeroMichaelSchiff baseMichael addition on alpha, beta-MichaeldoubleAddition onformationalpha, beta-Addition >>bonds>> Michael>> Schiff baseUnsaturatedMichaelNucleophiliaddition onformationcarbonyladdition oncadditionquinoid typewith carbonylcompounds >>quinoid type>>quinoid typewith carbonylcompounds >>quinoid type>>compoundscompoundsadditon onformationaddition oncaddition onquinoid typewith carbonylcompounds >>quinoid type>pyranones,>> AldehydesAldehydesPyranones,Addition toPyridones (andFelated nitrogenFelated nitrogenformationformationchemicals)Felated nitrogenFelated nitrogenformationformation | |
| quinoid typewith carbonylcompoundscompoundsquinoid typecarbon-compoundsMichael Addition >>compoundsMichael Addition >>compoundsheteroMichaelSchiff baseMichael addition onMichaeldoubledoubleAdditionformationalpha, beta-Addition >>bonds>> Michael>> Schiff baseUnsaturatedMichaelNucleophiliaddition onformationcarbonyladdition onc additionquinoid typewith carbonylcompounds >>quinoid type>>compounds >>compoundsalpha, beta-compounds >>Addition toquinoid typewith carbonylcompounds >>quinoid type>>pyranones,>> AldehydesAldehydesPyranones,Pyranones,Pyridones (andrelated nitrogenFunctionfunctionfunctionchemicals)introgenbonds >>functionfunction | |
| compoundscompoundsMichael Addition >>compoundsheteroMichaelSchiff baseMichael addition onMichaeldoubleAdditionformationalpha, beta-Addition >>bonds>> Michael>> Schiff baseUnsaturatedMichaelNucleophiliaddition onformationcarbonyladdition onc additionquinoid typewith carbonylcompounds >>quinoid type>>compounds >>compoundsalpha, beta-compounds >>Addition toPyranones,>> AldehydesAldehydesPyranones,carbon-Pyridones (and related nitrogen chemicals)Image: Schiff baseImage: Schiff baseSchiff baseImage: Schiff baseImage: Schiff baseImage: Schiff baseSchiff baseSchiff baseImage: Schiff baseImage: Schiff baseImage: Schiff baseImage: Schiff baseSchiff baseaddition onformationcarbonylcompounds >>quinoid typeSchiff baseImage: Schiff basealpha, beta-pyranones,carbon-Pyranones,Pyridones (and related nitrogenImage: Schiff baseAldehydesPyridonesheteroImage: Schiff baseImage: Schiff baseImage: Schiff baseImage: Schiff baseSchiff baseImage: Schiff baseImage: Schiff baseImage: Schiff baseImage: Schiff baseSchiff baseImage: Schiff baseImage: Schiff baseImage: Schiff baseImage: Schiff baseSchiff baseImage: | |
| Michael AdditionSchiff base formationMichael addition on alpha, beta-Michael Addition >>double bonds>> Michael>> Schiff baseUnsaturated carbonylMichaelNucleophili addition on quinoid typeNucleophili addition on with carbonyladdition on compounds >>compounds >>quinoid type>>Pyranones, Pyridones (and related nitroge chemicals)>> AldehydesAldehydesPyranones, (and related nitrogenPyridones (and carbonylAldehydesPyridones (and related nitrogenHetero | |
| Additionformationalpha, beta-Addition >>bonds>> Michael>> Schiff baseUnsaturatedMichaelNucleophiliaddition onformationcarbonyladdition onc additionquinoid typewith carbonylcompounds >>quinoid type>>compounds >>compoundsalpha, beta-compounds >>Addition toPyranones,>> AldehydesAldehydesPyranones,carbon-Pyridones (andrelated nitrogeninto the terointo terointo terochemicals)into terointo terointo terointo tero | |
| >> Michael addition on quinoid type compounds >> Pyranones, Pyridones (and related nitrogen chemicals)>> Schiff base Unsaturated carbonyl compounds >> alpha, beta- AldehydesMichael addition on quinoid type compounds >> AldehydesNucleophili addition on quinoid type compounds >> Addition to Pyranones, Pyridones (and related nitrogen>> Schiff base formation alpha, beta- AldehydesMichael addition on quinoid type compounds >> AldehydesNucleophili addition on quinoid type pyranones, PyridonesNucleophili caddition pyridonesNucleophili addition on compounds >> AldehydesCompounds >> AldehydesNucleophili addition on punoid type compounds >> Addition to PyridonesNucleophili addition on pyrianones, PyridonesNucleophili addition on compounds >> AldehydesNucleophili compounds >> AldehydesNucleophili addition on pyrianones, Pyrianones, PyridonesNucleophili compounds >> AldehydesNucleophili compounds >> AldehydesNucleophili addition on pyrianones, Pyrianones, PyridonesNucleophili compounds >> Pyridones (and chemicals)>> AldehydesNucleophili compounds Pyrianones, <th></th> | |
| addition on quinoid typeformationcarbonyladdition on compounds >>caddition on quinoid typecadditioncompounds >>compounds >>compounds >>alpha, beta-compounds >>Addition toPyranones, | |
| quinoid type compounds >> Compounds >> Pyranones,with carbonyl compoundscompounds >> alpha, beta- Aldehydesquinoid type compounds >> Addition to Pyranones,Pyridones (and related nitrogen chemicals)>AldehydesParanones, alpha, beta- AldehydesPyranones, alpha, beta- AldehydesPyranones, alpha, beta- AldehydesPyranones, alpha, beta- AldehydesPyranones, alpha, beta- alpha, beta- AldehydesPyranones, alpha, beta- alpha, beta- AldehydesPyranones, alpha, beta- alpha, beta- AldehydesPyranones, alpha, beta- alpha, beta- alpha, beta- alpha, beta- alpha, beta- AldehydesPyranones, alpha, beta- alpha, beta- alpha, beta- alpha, beta- AldehydesPyranones, alpha, beta- alpha, bet | |
| compounds >>compoundsalpha, beta-compounds >>Addition toPyranones,>> AldehydesAldehydesPyranones,carbon-Pyridones (andrelated nitrogenchemicals) | |
| Pyranones, Pyridones (and related nitrogen chemicals)>> AldehydesPyranones, PyridonesCarbon- Pyridones, hetero (and related nitrogenPyranones, Pyridones (and related nitrogen>> AldehydesPyranones, Pyridones (and related nitrogenCarbon- Pyridones (and related bonds >> | |
| Pyridones (and related nitrogen chemicals)Pyridones (and related nitrogenhetero double bonds >> | |
| related nitrogen chemicals)(and related nitrogendouble bonds >> | |
| chemicals) nitrogen bonds >> | |
| | |
| chemicals) Ketones | |
| | |
| rtER Expert No alert found No alert No alert found No alert No alert No alert No alert No alert No alert | |
| System - USEPA found found found found found | |
| Skin Group C Undefined Undefined Group C Undefined Undefined | |
| irritation/corrosio Melting Point > Melting Point Melting Point | |
| n Exclusion rules 55 C Undefined > 55 C > 55 C | |
| by BfR Undefined Undefined | |
| Protein bindingAN2No alert foundNo alert foundNo alertAN2No alertNo alertNo alert found | |
| alerts for AN2 >> Michael found AN2 >> found | |
| Chromosomal addition to Michael | |
| aberration by activated addition to | |
| OASIS double bonds activated | |

| InertFinder/ChemI | Ethyl maltol | Ethyl vanillin | Heptanal, 2- | Isojasmone | Maltyl | Methyl n- | Methyl | Methylcyclopentenolo |
|-------------------|-----------------|----------------|-----------------|------------|---------------|-------------|-----------|----------------------|
| D Plus Name | | | (phenylmethylen | | isobutyrate | amyl ketone | phenethyl | ne |
| | | | e)- | | | | ether | |
| | AN2 >> Michael | | | | double bonds | | | |
| | addition to | | | | AN2 >> | | | |
| | activated | | | | Michael | | | |
| | double bonds | | | | addition to | | | |
| | >> alpha, beta- | | | | activated | | | |
| | Unsaturated | | | | double bonds | | | |
| | Carbonyls and | | | | >> alpha, | | | |
| | Related | | | | beta- | | | |
| | Compounds | | | | Unsaturated | | | |
| | | | | | Carbonyls and | | | |
| | | | | | Related | | | |
| | | | | | Compounds | | | |

| InertFinder/ChemID | Nerol | Nootkatone | Phenylethyl isoamyl | Piperonyl acetate | p-Mentha-8-thiol-3-one | p- Menthan | Tetrahydr o-4- |
|---------------------------------------|----------------|--------------------|---------------------|------------------------|-------------------------|--------------------|----------------|
| Plus Name | oxide | | ether | | | e, 1,8- | methyl-2- (2- |
| | | | | | | ероху- | methylpropen- |
| | | | | | | | 1yl) pyran |
| CAS | 1786-08-9 | 4674-50-4 | 56011-02-0 | 326-61-4 | 38462-22-5 | 470-82-6 | 16409-43-1 |
| SMILES | CC(C)=CC | CC1CC(=O | CC(C)CCOCCc1ccccc | CC(=O)OCc1ccc2OCOc2c | CC1CCC(C(=O)C1)C(C)(C)S | CC12CCC(| CC1CCOC(|
| | 1CC(=CCO |)C=C2CCC | 1 | 1 | | CC1)C(C)(| C1)C=C(C) C |
| | 1)C | (CC12C)C(C)=C | | | | C)O2 | |
| Ionization at pH = 1 | Acidic [0.000, | Acidic [0.000, | Acidic [0.000, | Acidic [0.000, 10.000) | Acidic [0.000, 10.000) | Acidic [0.000, | Acidic [0.000, |
| | 10.000) | 10.000) | 10.000) | Basic [0.000, 10.000) | No pKb value | 10.000) | 10.000) |
| | Basic [0.000, | No pKb value | Basic [0.000, | | | Basic [0.000, | Basic [0.000, |
| | 10.000) | | 10.000) | | | 10.000) | 10.000) |
| Biodegradation ultimate (Biowin 3) | Weeks | Weeks to months | Weeks to months | Weeks | Weeks to months | Weeks to months | Weeks |
| Estrogen Receptor | Non | Non binder, | Non binder, | Non binder, without OH | Non binder, without OH | Non | Non binder, |
| Binding | binder, | without OH or | without OH or NH2 | or NH2 group | or NH2 group | binder, | without OH |
| Dinaing | without | NH2 | group | | | without | or NH2 |
| | OH or NH2 | group | Broup | | | OH or NH2 | group |
| | group | Broop | | | | group | Blockb |
| | Broap | | | | | Broap | |
| Biodeg BioHC half- | No value | No value | No value | No value | No value | No value | No value |
| life (Biowin) | | | | | | | |
| Hydrolysis half-life | No value | No value | No value | Very slow | No value | No value | No value |
| (pH 6.5-7.4) | | | | | | | |
| Biodegradation | Does NOT | Does NOT | Does NOT | Biodegrades Fast | Does NOT Biodegrade | Does NOT | Does NOT |
| probability (Biowin | Biodegrade | Biodegrade | Biodegrade Fast | | Fast | Biodegrade | Biodegrade |
| 5) | Fast | Fast | | | | Fast | Fast |
| Toxic hazard | High (Class | Intermediate | Intermediate | High (Class III) | High (Class III) | High (Class | High (Class |
| classification by | III) | (Class II) | (Class II) | | | 111) | III) |
| Cramer | | | | | | | |
| Biodegradation | Does NOT | Does NOT | Does NOT | Biodegrades Fast | Does NOT Biodegrade | Does NOT | Does NOT |
| probability (Biowin | Biodegrade | Biodegrade | Biodegrade Fast | | Fast | Biodegrade | Biodegrade |
| 2) | Fast | Fast | | | | Fast | Fast |

| Ionization at pH = 4 | Acidic | Acidic [0.000, | Acidic [0.000, | Acidic [0.000, 10.000) | Acidic [0.000, 10.000) | Acidic | Acidic [0.000, |
|------------------------------------|------------|----------------|-------------------|------------------------|------------------------|------------|----------------|
| | [0.000, | 10.000) | 10.000) | Basic [0.000, 10.000) | No pKb value | [0.000, | 10.000) |
| | 10.000) | No pKb value | Basic [0.000, | | | 10.000) | Basic [0.000, |
| | Basic | | 10.000) | | | Basic | 10.000) |
| | [0.000, | | | | | [0.000, | |
| | 10.000) | | | | | 10.000) | |
| Protein binding | DPRA less | DPRA less than | DPRA less than 9% | DPRA less than 9% | DPRA less than 9% | DPRA less | DPRA less |
| potency Lys (DPRA | than 9% | 9% (DPRA | (DPRA 13%) | (DPRA 13%) | (DPRA 13%) | than 9% | than 9% |
| 13%) | (DPRA | 13%) | DPRA less than 9% | DPRA less than 9% | DPRA less than 9% | (DPRA | (DPRA 13%) |
| | 13%) | DPRA less than | (DPRA 13%) >> No | (DPRA 13%) >> Non- | (DPRA 13%) >> Non- | 13%) | DPRA less |
| | DPRA less | 9% (DPRA | protein binding | Conjugated carboxylic | conjugated mono- and | DPRA less | than 9% |
| | than 9% | 13%) >> | alert | acids and esters (non | diketones (non | than 9% | (DPRA 13%) |
| | (DPRA | Conjugated | | reactive) | reactive) | (DPRA | >> |
| | 13%) >> | alpha, beta- | | | DPRA less than 9% | 13%) >> | No protein |
| | No protein | unsaturated | | | (DPRA 13%) >> Thiols | No protein | binding alert |
| | binding | ketones (non | | | and disulfides (non | binding | |
| | alert | reactive) | | | reactive) | alert | |
| Protein binding | DPRA less | Out of | DPRA less than 9% | DPRA less than 9% | DPRA above 21% (DPRA | DPRA less | DPRA less |
| potency Cys (DPRA | than 9% | mechanistic | (DPRA 13%) | (DPRA 13%) | 13%) | than 9% | than 9% |
| 13%) | (DPRA | domain | DPRA less than 9% | DPRA less than 9% | DPRA above 21% (DPRA | (DPRA | (DPRA 13%) |
| | 13%) | | (DPRA 13%) >> No | (DPRA 13%) >> Non- | 13%) >> Thiols | 13%) | DPRA less |
| | DPRA less | | protein binding | Conjugated carboxylic | (reactive) | DPRA less | than 9% |
| | than 9% | | alert | acids and esters (non | | than 9% | (DPRA 13%) |
| | (DPRA | | | reactive) | | (DPRA | >> |
| | 13%) >> | | | | | 13%) >> | No protein |
| | No protein | | | | | No protein | binding alert |
| | binding | | | | | binding | |
| | alert | | | | | alert | |
| Hydrolysis half-life | No value | No value | No value | 10 to 100 days | No value | No value | No value |
| (Kb, pH 8) (Hydrowin) | | | | | | | |
| Hydrolysis half-life (Kb, pH 7) | No value | No value | No value | > 100 days | No value | No value | No value |

| (Hydrowin) | | | | | | | |
|--|--|---|---|---|--|---|---|
| Biodegradation probability (Biowin 6) | Does NOT Biodegrade Fast | Does NOT Biodegrade Fast | Does NOT Biodegrade Fast | Biodegrades Fast | Does NOT Biodegrade Fast | Does NOT Biodegrade Fast | Does NOT Biodegrade Fast |
| Protein binding by OECD | No alert found | No alert found | No alert found | SN2 SN2 >> SN2 reaction at sp3 carbon atom SN2 >> SN2 reaction at sp3 carbon atom >> Allyl acetates and related chemicals | SN2 SN2 >> SN2 reaction at a sulphur atom SN2 >> SN2 reaction at a sulphur atom >> Thiols | No alert found | No alert found |
| Ultimate biodeg | No data | No data | 10 to 100 days | No data | No data | 10 to 100 days | No data |
| Ionization at pH = 9 | Acidic [70.000, 80.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) No pKb value | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [80.000, 90.000) Basic [0.000, 10.000) | Acidic [20.000, 30.000) No pKb value | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [20.000, 30.000) Basic [0.000, 10.000) |
| Hydrolysis half-life (Ka, pH 7) (Hydrowin) | No value | No value | No value | No value | No value | No value | No value |
| Toxic hazard classification by Cramer (extended) | High (Class III) | Intermediate (Class II) | Intermediate (Class II) | High (Class III) | High (Class III) | High (Class III) | High (Class III) |
| Biodegradation | Does NOT Biodegrade Fast | Does NOT Biodegrade Fast | Does NOT Biodegrade Fast | Biodegrades Fast | Does NOT Biodegrade Fast | Does NOT Biodegrade Fast | Does NOT Biodegrade Fast |

| DNA binding by | No alert | No alert found | No alert found | SN1 | Radical | No alert | No alert |
|--|---|---|---|---|--|---|---|
| OASIS | found | | | SN1 >> Nucleophilic attack after carbenium ion formation SN1 >> Nucleophilic attack after carbenium ion formation >> Specific Acetate Esters SN2 SN2 >> Nucleophilic substitution at sp3 Carbon atom SN2 >> Nucleophilic substitution at sp3 Carbon atom >> Specific Acetate Esters | Radical >> Radical mechanism via ROS formation (indirect) Radical >> Radical mechanism via ROS formation (indirect) >> Thiols | found | found |
| Ionization at pH = 7.4 | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) No pKb value | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [10.000, 20.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) No pKb value | Acidic [0.000, 10.000) Basic [0.000, 10.000) | Acidic [0.000, 10.000) Basic [0.000, 10.000) |
| Hydrolysis half-life (Ka, pH 8) (Hydrowin) | No value | No value | No value | No value | No value | No value | No value |
| Protein binding by OASIS | No alert found | Nucleophilic addition Nucleophilic addition >> Addition to carbon- hetero double bonds Nucleophilic addition >> | No alert found | SN2 SN2 >> SN2 Reaction at a sp3 carbon atom SN2 >> SN2 Reaction at a sp3 carbon atom >> Activated alkyl esters and thioesters | SN2 SN2 >> Interchange reaction with sulphur containing compounds SN2 >> Interchange reaction with sulphur containing compounds >> Thiols | No alert found | No alert found |

| | | Addition to carbon- hetero double bonds >> Ketones | | | | | | |
|--|--------------------------------|---|---|---|-----------------------------|--------------------------------|--------------------------------|--|
| DNA binding by OECD | No alert No alert four found | | Michael addition Michael addition >> P450 Mediated Activation to Quinones and Quinone-type Chemicals Michael addition >> P450 Mediated Activation to Quinones and Quinones and Quinone-type Chemicals >> Arenes | Michael addition Michael addition >> P450 Mediated Activation to Quinones and Quinone-type Chemicals Michael addition >> P450 Mediated Activation to Quinones and Quinone-type Chemicals >> Methylenedioxyphenyl | No alert found | No alert found | No alert found | |
| Biodegradation probability (Biowin 1) | Does NOT Biodegrade Fast | Does NOT Biodegrade Fast | Does NOT Biodegrade Fast | Biodegrades Fast | Does NOT Biodegrade Fast | Does NOT Biodegrade Fast | Does NOT Biodegrade Fast | |
| Biodegradation primary | Days to weeks | Days to weeks | Days to weeks | Days | Days to weeks | Days to weeks | Days to weeks | |
| primary (Biowin 4)weeksweeksCarcinogenicity (genotox and nongenotox) alertsNo alert foundalpha,beta- unsaturated carbonylsNo alert found | | 1,3-Benzodioxoles (Nongenotox) Structural alert for nongenotoxic carcinogenicity | No alert found | No alert found | No alert found | | | |
| in vitro mutagenicity | No alert found | alpha,beta- unsaturated | No alert found | No alert found | No alert found | No alert found | No alert found | |

| (Ames test) alerts | | carbonyls | | | | | |
|----------------------|-----------|----------------|---------------------|-------------------------|-----------------------|-----------|-----------|
| by ISS | | | | | | | |
| in vivo | No alert | alpha,beta- | No alert found | H-acceptor-path3-H- | No alert found | No alert | No alert |
| • • | found | unsaturated | | acceptor | | found | found |
| (Micronucleus) | | carbonyls | | | | | |
| alerts by ISS | | | | | | | |
| Protein Binding | No alert | alpha, beta- | No alert found | No alert found | Thiols and disulfides | No alert | No alert |
| Potency h-CLAT | found | Unsaturated | | | | found | found |
| | | ketones | | | | | |
| Skin | Inclusion | Ketones | Inclusion rules not | Inclusion rules not met | Ketones | Inclusion | Inclusion |
| irritation/corrosion | rules not | | met | | | rules not | rules not |
| Inclusion rules by | met | | | | | met | met |
| BfR | | | | | | | |
| DNA alerts for | No alert | No alert found | No alert found | SN1 | No alert found | No alert | No alert |
| AMES, CA and MNT | found | | | SN1 >> Nucleophilic | | found | found |
| by OASIS | | | | attack after carbenium | | | |
| | | | | ion formation | | | |
| | | | | SN1 >> Nucleophilic | | | |
| | | | | attack after carbenium | | | |
| | | | | ion formation >> | | | |
| | | | | Specific Acetate Esters | | | |
| | | | | SN2 | | | |
| | | | | SN2 >> Nucleophilic | | | |
| | | | | substitution at sp3 | | | |
| | | | | Carbon atom | | | |
| | | | | SN2 >> Nucleophilic | | | |
| | | | | substitution at sp3 | | | |
| | | | | Carbon atom >> Specific | | | |
| | | | | Acetate Esters | | | |

| Protein binding | No alert | Nucleophilic | No alert found | SN2 | Nucleophilic addition | No alert | No alert |
|--|-------------------|--|---|--|--|-------------------|-------------------|
| Protein binding alerts for skin sensitization by OASIS | found | Nucleophilic addition Nucleophilic addition >> Addition to carbon- hetero double bonds Nucleophilic addition >> Addition to carbon- hetero double bonds >> Ketones | No alert found | SN2 SN2 >> SN2 Reaction at a sp3 carbon atom SN2 >> SN2 Reaction at a sp3 carbon atom >> Activated alkyl esters and thioesters | Nucleophilic addition Nucleophilic addition >> Addition to carbon- hetero double bonds Nucleophilic addition >> Addition to carbon- hetero double bonds >> Ketones SN2 SN2 >> Interchange reaction with sulphur containing compounds SN2 >> Interchange reaction with sulphur containing compounds >> Thiols and disulfide | found | found |
| rtER Expert System - USEPA | No alert found | No alert found | No alert found | No alert found | compounds No alert found | No alert found | No alert found |
| Skin irritation/corrosion Exclusion rules by BfR | Undefined | Group C Melting Point > 55 C Undefined | Group C Surface Tension > 62 mN/m Undefined | Group C Melting Point > 55 C Undefined | Undefined | Undefined | Undefined |
| Protein binding alerts for Chromosomal aberration by OASIS | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found | No alert found |

| InertFinder/ChemID Plus Name | Tetrahydr o-6-(3- | Theaspira ne |
|---|---|--|
| | pentenyl)- 2H-pyran- 2-one | |
| CAS | 32764-98-0 | 36431-72-8 |
| SMILES | C/C=C/CC C1CCCC(= 0)01 | CC1CCC2(O1)C(=CC CC2(C)C)C |
| Ionization at pH = 1 | Acidic [0.000, 10.000) | Acidic [0.000, 10.000) |
| | Basic [0.000, 10.000) | No pKb value |
| Biodegradation ultimate (Biowin 3) | Days to weeks | Weeks to months |
| Estrogen Receptor Binding | Non binder, without OH or NH2 group | Non binder, without OH or NH2 group |
| Biodeg BioHC half-life (Biowin) | No value | No value |
| Hydrolysis half-life (pH 6.5-7.4) | Moderate | No value |
| Biodegradation probability (Biowin 5) | Biodegrades Fast | Does NOT Biodegrade Fast |
| Toxic hazard classification by Cramer | Low (Class I) | High (Class III) |
| Biodegradation probability (Biowin 2) | Biodegrades Fast | Does NOT Biodegrade Fast |
| Ionization at pH = 4 | Acidic [0.000, 10.000) | Acidic [0.000, 10.000) |
| | Basic [0.000, 10.000) | No pKb value |
| Protein binding potency Lys (DPRA 13%) | DPRA less than 9% (DPRA 13%) | DPRA less than 9% (DPRA |
| | DPRA less than 9% (DPRA 13%) >> | 13%) |
| | Non- Conjugate d carboxylic acids and esters (non reactive) | DPRA less than 9% (DPRA |
| | | 13%) >> |
| | | No protein binding alert |
| Protein binding potency Cys (DPRA 13%) | DPRA less than 9% (DPRA 13%) | DPRA less than 9% (DPRA |
| | DPRA less than 9% (DPRA 13%) >> | 13%) |
| | Non- Conjugate d carboxylic acids and esters (non reactive) | DPRA less than 9% (DPRA |
| | | 13%) >> |
| | | No protein binding alert |
| Hydrolysis half-life (Kb, pH 8)(Hydrowin) | No value | No value |
| Hydrolysis half-life (Kb, pH 7)(Hydrowin) | No value | No value |
| Biodegradation probability (Biowin 6) | Biodegrad es Fast | Does NOT Biodegrad e Fast |
| Protein binding by OECD | Acylation Acylation >> Direct Acylation Involving a Leaving group Acylation | No alert found |
| | >> Direct Acylation Involving a Leaving group >> Acetates | |

| InertFinder/ChemID Plus Name Tet | trahydr o-6-(3- | Theaspira ne |
|---|---|--------------------------|
| per | ntenyl)- 2H-pyran- 2-one | |
| Ultimate biodeg 10 t | to 100 days | No data |
| Ionization at pH = 9 Acid | idic [0.000, 10.000) | Acidic [0.000, 10.000) |
| Bas | sic [0.000, 10.000) | No pKb value |
| Hydrolysis half-life (Ka, pH 7)(Hydrowin) No | value | No value |
| Toxic hazard classification by Cramer Low (extended) | w (Class I) | High (Class III) |
| Biodegradation probability (Biowin 7) | es NOT Biodegrade Fast | Does NOT Biodegrade Fast |
| DNA binding by OASIS No | alert found | No alert found |
| Ionization at pH = 7.4 Acid | idic [0.000, 10.000) | Acidic [0.000, 10.000) |
| Bas | sic [0.000, 10.000) | No pKb value |
| Hydrolysis half-life (Ka, pH 8)(Hydrowin) No | value | No value |
| Protein binding by OASIS Acy | ylation Acylation >> Ring opening acylation Acylation >> Ring opening | No alert found |
| асу | ylation >> Active cyclic agents | |
| DNA binding by OECD No | alert found | No alert found |
| Biodegradation probability (Biowin 1) Biodegradation probability (Biowin 1) | odegrades Fast | Does NOT Biodegrade Fast |
| Biodegradation primary (Biowin 4) Day | γs | Days to weeks |
| Carcinogenicity (genotox and nongenotox) No | alert found | No alert found |
| alerts by ISS | | |
| in vitro mutagenicity (Ames test) alerts by ISS No | alert found | No alert found |
| in vivo mutagenicity (Micronucleus) alerts by No ISS | alert found | Oxolane |
| Protein Binding Potency h-CLAT | ctones | No alert found |
| Skin irritation/corrosion Inclusion rules by BfR Incl | lusion rules not met | Inclusion rules not met |
| DNA alerts for AMES, CA and MNT by OASIS No | alert found | No alert found |
| Protein binding alerts for skin sensitization by Acy | ylation Acylation >> Ring opening acylation Acylation >> Ring opening | No alert found |
| OASIS acy | vlation >> Active cyclic agents | |
| rtER Expert System - USEPA No | alert found | No alert found |
| Skin irritation/corrosion Exclusion rules by BfR Und | defined | Undefined |
| Protein binding alerts for Chromosomal No | alert found | No alert found |
| aberration by OASIS | | |

Appendix IV. Explanation and Justification for OCED Toolbox outputs indicating Cramer classification other than II.

Two outputs regarding Cramer decision tree classification are provided from the OECD Toolbox (Appendix II):

- A. Toxic hazard classification by Cramer (original)
- B. Toxic hazard classification by Cramer (extension)

Outputs (A) and (B) are from the QSAR toolbox (TB) algorithms. Output A represents a programming of the original steps outlined by Cramer and associates based on the scheme published in 1978 (Cramer et al., 1978). The extended algorithm contains 5 additional questions. The QSAR toolbox offers datasheets on each algorithm (see QSAR toxtree accessed 20230905 and QSAR toxtree_extended assessed 20230905).

The Cramer scheme requires expert knowledge or databases on "normal constituents of the body" (Q1), "common terpenes" (Q16) and "common component of food" (Q22). The manner in which these questions, as well as questions regarding hydrolysis of esters and acetals and the interpretation of other questions of the Cramer tree for the purpose of programming the algorithms have differed among the programmers involved (Lapenna and Worth, 2011; Bhatia et al., 2015). The OECD QSAR V.4 Application Manual is using external files with 440 compounds in "Common component of food" and 107 compounds in "Normal constituents of body" from ToxTree v.2.1.0 (https://toxtree.sourceforge.net/).

The approach used by JECFA relied on expert judgement for each compound, following the original Cramer et al., 1978 publication. JECFA experts examined peer-reviewed literature and currated databases (such as Volatile Compounds in Food) to answer questions 16 and 22 on normal constituents of the body, common terpenes and common components in food. In addition, metabolism data was used to predict the hydrolysis of esters and acetals. As the petition cites the JECFA safety determinations, we used the Cramer classifications as assigned by JECFA.

For some materials, the OECD Toolbox output classifies the material as a common terpene based on database knowledge. However, some materials have natural occurrence data relevant to question 22 (common components in food) that have been evaluated by JECFA, but not considered by the OECD QSAR Toolbox. A summary table of the substances with discrepancies between the JECFA assigned decision tree class and the OECD Toolbox "Toxic hazard classification by Cramer (original)" field is listed below.

| CAS | Chemical name in InertFinder/ChemID Plus | JECF A assig ned DT Class | OECD Toolbox Toxic hazard classification by Cramer (original) | Cramer Path for JECFA Assignment | Resol ution |
|-----------------|---|--|--|---|----------------------|
| 19840 4-98-7 | Cyclopropanemethanol, 1-methyl- 2-[(1,2,2- trimethylbicyclo[3.1.0]hex-3- yl)methyl]- | II | I - 1N,2N,3N,5N,6N,7N,16Y | 1N,2N,3N,5N,6N,7N,16N,17N,19 N,23N,24N,25N,26Y | JECFA Class II |

| 71159- 90-5 | 1-p-Menthene-8-thiol | П | l - 1N,2N,3N,5N,6N,7N,16Y | Class II - 1N,2N,3N,5N,6N,7N,16N,17N,19 N,23N,24N,25Y | JECFA Class II |
|---|---|----|--|--|----------------------|
| 104- 76-7 | 1-Hexanol, 2-ethyl- | II | l - 1N,2N,3N,5N,6N,7N,16N,17N,19Y,2 0Y,21N,18N | Class II - 1N,2N,3N,5N,6N,7N,16N,17N,19 Y,20Y,21N,18Y | JECFA Class II |
| 67801- 20-1 | 3-Methyl-5-(2,2,3-trimethyl-3- cyclopenten-1-yl)pent-4-en-2-ol | П | I – 1N,2N,3N,5N,6N,7N,16Y | 1N,2N,3N,5N,6N,7N,16N,17N,19 N,23N,24Y,18N | JECFA Class II |
| 689- 67-8 | 6,10-Dimethylundeca-5,9-dien-2- one | Ш | ا - 1N,2N,3N,5N,6N,7N,16N,17N,19Y,2 0Y,21N,18N | Class II - 1N,2N,3N,5N,6N,7N,16N,17N,19 Y,20Y,21N,18Y | JECFA Class II |
| 1604- 28-0 | 6-Methyl-3,5-heptadien-2-one | 11 | ا - 1N,2N,3N,5N,6N,7N,16N,17N,19Y,2 0Y,21N,18N | Class II - 1N,2N,3N,5N,6N,7N,16N,17N,19 Y,20Y,21N,18Y | JECFA Class II |
| 110- 93-0 | 6-Methyl-5-hepten-2-one | Ш | l - 1N,2N,3N,5N,6N,7N,16N,17N,19Y,2 0Y,21N,18N | Class II - 1N,2N,3N,5N,6N,7N,16N,17N,19 Y,20Y,21N,18Y | JECFA Class II |
| 32764- 98-0 | Tetrahydro-6-(3-pentenyl)-2H- pyran-2-one | II | l – 1N,2N,3N,5N,6N,7Y,8Y,9N,20Y,21N, 18N | Class II – 1N,2N,3N,5N,6N,7Y,8Y,9N,2OY,21 N,18Y | JECFA Class II |
| 513- 86-0 | Acetoin | II | ا 1N,2N,3N,5N,6N,7N,16N,17N,19Y,2 0Y,21N,18N | 1N,2N,3N,5N,6N,7N,16N,17N,19 Y,20Y,21N,18Y | JECFA Class II |
| 7492- 44-6 | .alphaButylcinnamaldehyde | II | ۱ - 1N,2N,3N,5N,6N,7N,16N,17N,19N,2 3Y,27Y,28N,30N,18N | Step 30 – Yes, material contains a ring bearing substituents other than 1-5 carbon aliphatic groups. Class II - 1N,2N,3N,5N,6N,7N,16N,17N,19 N,23Y,27Y,28N,30Y,31N, 32Y | JECFA Class II |
| 60047- 17-8; 5989- 33-3; 34995- 77-2 | Linalyl oxide | 11 | III - 1N,2N,3N,5N,6N,7Y,8N, 10N,11Y,33N | Step 11 – No, other than the heteroatom within the heterocyclic ring, the material does not contain substituents other than simply branched hydrocarbons and an alkyl alcohol. Step 22 – Yes, the material is a common component of food. A consumption ratio of 57 was calculated by JECFA for this | JECFA Class II |
| | | | | material, indicating the natural occurrence of this substance in a variety of foods (JECFA 1454). Class II – 1N,2N,3N,5N,6N,7Y,8N, 10N,11N,12N,22Y Material occurs naturally in beer | |
| 3848- 24-6 | 2,3-Hexanedione | II | III - 1N,2N,3N,5N,6N,7N,16N,17N,19Y,2 0N,22N,33N | (<0.01 ppm); clams (0.02 ppm); and coffee (0.3-3.2 ppm) (VCF, 2024). | JECFA Class II |

| | | | | Class II - 1N,2N,3N,5N,6N,7N,16N,17N,19 Y,20N,22Y | |
|----------------|--|----|---|---|----------------------|
| 108- 50-9 | 2,6-Dimethylpyrazine | II | III - 1N,2N,3N,5N,6N,7Y,8N, 10N,11N,12Y,13Y,14N, 22N,33N | Step 22 – Yes, the material is a common component of food. A consumption ratio of 2,600 was calculated by JECFA for this material in the U.S., indicating the natural occurrence of this substance in a variety of foods (JECFA 767). Class II - 1N,2N,3N,5N,6N,7Y,8N, | JECFA Class II |
| 15707- 23-0 | 2-Ethyl-3-methylpyrazine | 11 | III - 1N,2N,3N,5N,6N,7Y,8N, 10N,11N,12Y,13Y,14N, 22N,33N | 10N,11N,12Y,13Y,14N,22Y Step 22 – Yes, the material is a common component of food. A consumption ratio of 250 was calculated by JECFA for this material in the U.S., indicating the natural occurrence of this substance in a variety of foods (JECFA 768). Class II - 1N,2N,3N,5N,6N,7Y,8N, 10N,11N,12Y,13Y,14N,22Y | JECFA Class II |
| 24683- 00-9 | 2-Isobutyl-3-methoxypyrazine | II | III - 1N,2N,3N,5N,6N,7Y,8N, 10N,11N,12Y,13Y,14N, 22N,33N | Step 22 – Yes, the material is a common component of food. A consumption ratio of 250 was calculated by JECFA for this material in the U.S., indicating the natural occurrence of this substance in a variety of foods (JECFA 792). Class II - 1N,2N,3N,5N,6N,7Y,8N, 10N,11N,12Y,13Y,14N,22Y | JECFA Class II |
| 15679- 13-7 | 2-lsopropyl-4-methylthiazole | 11 | III - 1N,2N,3N,5N,6N,7Y,8N,10N,11N,12 Y,13Y,14N,22N,33N | Step 22 – Yes, JECFA considers this material to be structurally closely related to common constituents of food. Class II – 1N,2N,3N,5N,6N,7Y,8N, 10N,11N,12Y,13Y,14N,22Y | JECFA Class II |
| 24168- 70-5 | 2-Methoxy-3-(1- methylpropyl)pyrazine | II | III - 1N,2N,3N,5N,6N,7Y,8N, 10N,11N,12Y,13Y,14N, 22N,33N | Step 22 – Yes, the material is structurally related to other substances that are common components of foods (<u>see other</u> <u>JECFA materials in group</u>). Class II - 1N,2N,3N,5N,6N,7Y,8N, 10N,11N,12Y,13Y,14N,22Y | JECFA Class II |

| 1786- 08-9 | Methylcyclopentenolone Nerol oxide | | III - 1N,2N,3N,5N,6N,7N,16N,17N,19N,2 3N,24N,25N,26N,22N,33N III - 1N,2N,3N,5N,6N,7Y,8N,10N,11N,12 N,22N,33N | Class II - 1N,2N,3N,5N,6N,7N,16N,17N,19 N,23N,24N,25N,26Y Step 22 – Yes, this material is a common component of food (JECFA 1235). Class II – 1N,2N,3N,5N,6N,7Y,8N,10N,11N, 12N,22Y Step 22 – Yes, this material is | JECFA Class II JECFA Class II |
|----------------|---|----|---|---|--|
| | Methylcyclopentenolone | 11 | 1N,2N,3N,5N,6N,7N,16N,17N,19N,2 | 1N,2N,3N,5N,6N,7N,16N,17N,19 | Class |
| 80-71- 7 | | | | | |
| 65416- 14-0 | Maltyl isobutyrate | 11 | III - 1N,2N,3N,5N,6N,7Y,8N, 10N,11N,12N,22N,33N | Step 22 – Yes, this material is structurally closely related to common constituents of food (see JECFA 1480, maltol). Class II – 1N,2N,3N,5N,6N,7Y,8N, 10N,11N,12N,22Y | JECFA Class II |
| 13679- 70-4 | 5-Methyl-2- thiophenecarboxaldehyde | II | III - 1N,2N,3N,5N,6N,7Y,8N, 10N,11N,12Y,13Y,14N,22N,33N | Step 22 – Yes, the material is a common component of food. A consumption ratio of 9,100 was calculated by JECFA for this material in the U.S., indicating the natural occurrence of this substance in a variety of foods (JECFA 1050). Class II – 1N,2N,3N,5N,6N,7Y,8N, 10N,11N,12Y,13Y,14N,22Y | JECFA Class II |
| 3658- 77-3 | 4-Hydroxy-2,5-dimethyl-3(2H)- furanone | II | lii - 1N,2N,3N,5N,6N,7Y,8N,10N,11N,12 N,22N,33N | Step 22 – Yes, the material is a common component of food. A consumption ratio of 1 was calculated by JECFA for this material in the U.S., indicating the natural occurrence of this substance in a variety of foods (JECFA 1446). Class II – 1N,2N,3N,5N,6N,7Y,8N, 10N,11N,12N,22Y | JECFA Class II |
| 67715- 80-4 | 2-Methyl-4-propyl-1,3-oxathiane | II | III - 1N,2N,3N,5N,6N,7Y,8N, 10N,11N,12N,22N,33N | Step 22 – Yes, the material occurs naturally in food (common component in food) but quantitative data not avaialble for a consumption ratio calculation by JECFA (JECFA 464) Class II – 1N,2N,3N,5N,6N,7Y,8N, 10N,11N,12N,22Y | JECFA Class II |

| | | | | Class II – 1N,2N,3N,5N,6N,7Y,8N,10N,11N, 12N,22Y | |
|----------------|--|----|--|---|----------------------|
| 38462- 22-5 | p-Mentha-8-thiol-3-one | п | III - 1N,2N,3N,5N,6N,7N,16N,17N,19N,2 3N,24N,25N,26N,22N,33N | Step 22 – Yes, this material is a common component of food (JECFA 561). Class II – 1N,2N,3N,5N,6N,7N,16N,17N,19 N,23N,24N,25N,26N,22Y | JECFA Class II |
| 16409- 43-1 | Tetrahydro-4-methyl-2-(2- methylpropen-1-yl)pyran | II | III - 1N,2N,3N,5N,6N,7Y,8N,10N,11N,12 N,22N,33N | Step 22 – Yes, this material is a common component of food (JECFA 1237). Class II – 1N,2N,3N,5N,6N,7Y,8N,10N,11N, 12N,22Y | JECFA Class II |
| 36431- 72-8 | Theaspirane | Ш | III - 1N,2N,3N,5N,6N,7Y,8N,10N,11N,12 N,22N,33N | Step 22 – Yes, this material is a common component of food (JECFA 1238). Class II – 1N,2N,3N,5N,6N,7Y,8N,10N,11N, 12N,22Y | JECFA Class II |
| 470- 67-7 | 7-Oxabicyclo(2.2.1.)heptane, 1- methyl-4-(1-methylethyl)- | П | III - 1N,2N,3N,5N,6N,7Y,8N,10N,11N,12 N,22N,33N | Step 22 – Yes, this material is a common component of food (JECFA 1233). Class II – 1N,2N,3N,5N,6N,7Y,8N,10N,11N, 12N,22Y | JECFA Class II |
| 470- 82-6 | p-Menthane, 1,8-epoxy- | II | III - 1N,2N,3N,5N,6N,7Y,8N,10N,11N,12 N,22N,33N | Step 22 – Yes, the material is a common component of food. A consumption ratio of 23 was calculated by JECFA for this material in the U.S., indicating the natural occurrence of this substance in a variety of foods (JECFA 1234). Class II – 1N,2N,3N,5N,6N,7Y,8N,10N,11N, | JECFA Class II |
| 24851- 98-7 | Cyclopentaneacetai acid, 3-oxo-2- pentyl-, methyl ester | п | III – 1N,2N,3N,5N,6N,7N,16N,17N,19N,2 3N,24N,25N,26N,22N,33N | 12N,22Y Step 22 – Yes, this material is a common component of food (JECFA 1898). Class II – 1N,2N,3N,5N,6N,7N,16N,17N,19 N,23N,24N,25N,26N,22Y 1N,2N,3N,5N,6N,7N,16N,17N,19 N,23N,24N,25N,26Y | JECFA Class II |

| 120- 57-0 | 1,3-Benzodioxole-5-carboxaldehyde | 11 | III - 1N,2N,3N,5N,6N,7Y,8N,10N,11N,12 N,22N,33N | Step 22 – Yes, this material is structurally closely related to common constituents of food. Class II – 1N,2N,3N,5N,6N,7Y,8N,10N,11N, 12N,22Y | JECFA Class II |
|---------------|-----------------------------------|----|---|--|----------------------|
| 1866- 31-5 | Allyl cinnamate | II | II & III – Pathway unavailable | OECD Toolbox provides two outputs for two different predicted metabolic products. Toolbox uses the more conservative class. Class II - 1N,2N,3N,5N,6N,7N,16N,17N,19 N,23Y,27Y,28N,30N,18Y | JECFA Class II |

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