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RIFM fragrance ingredient safety assessment, *o*-(Methylthio)-phenol, CAS Registry Number 1073-29-6

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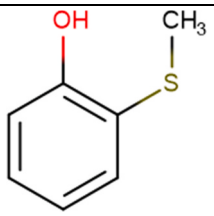

Name: o-(Methylthio)-phenol
CAS Registry Number: 1073-29-6

Abbreviation/Definition List:

2-Box Model - A RIFM, Inc. proprietary *in silico* tool used to calculate fragrance air exposure concentration
AF - Assessment Factor
BCF - Bioconcentration Factor
CNIH – Confirmation of No Induction in Humans test. A human repeat insult patch test that is performed to confirm an already determined safe use level for fragrance ingredients (Na et al., 2021)
Creme RIFM Model - The Creme RIFM Model uses probabilistic (Monte Carlo) simulations to allow full distributions of data sets, providing a more realistic estimate of aggregate exposure to individuals across a population (Comiskey et al., 2015, 2017; Safford et al., 2015a, 2017) compared to a deterministic aggregate approach
DEREK - Derek Nexus is an *in silico* tool used to identify structural alerts
DRF - Dose Range Finding
DST - Dermal Sensitization Threshold
ECHA - European Chemicals Agency
ECOSAR - Ecological Structure-Activity Relationships Predictive Model
EU - Europe/European Union
GLP - Good Laboratory Practice
IFRA - The International Fragrance Association
LOEL - Lowest Observed Effect Level
MOE - Margin of Exposure
MPPD - Multiple-Path Particle Dosimetry. An *in silico* model for inhaled vapors used to simulate fragrance lung deposition
NA - North America
NESIL - No Expected Sensitization Induction Level
NOAEC - No Observed Adverse Effect Concentration
NOAEL - No Observed Adverse Effect Level
NOEC - No Observed Effect Concentration
NOEL - No Observed Effect Level
OECD - Organisation for Economic Co-operation and Development
OECD TG - Organisation for Economic Co-operation and Development Testing Guidelines
PBT - Persistent, Bioaccumulative, and Toxic
PEC/PNEC - Predicted Environmental Concentration/Predicted No Effect Concentration
Perfumery - In this safety assessment, perfumery refers to fragrances made by a perfumer used in consumer products only. The exposures reported in the safety assessment include consumer product use but do not include occupational exposures.
QRA - Quantitative Risk Assessment
QSAR - Quantitative Structure-Activity Relationship
REACH - Registration, Evaluation, Authorisation, and Restriction of Chemicals
RfD - Reference Dose
RIFM - Research Institute for Fragrance Materials
RQ - Risk Quotient
Statistically Significant - Statistically significant difference in reported results as compared to controls with a $p < 0.05$ using appropriate statistical test
TTC - Threshold of Toxicological Concern
UV/Vis spectra - Ultraviolet/Visible spectra
VCF - Volatile Compounds in Food
VoU - Volume of Use
vPvB - (very) Persistent, (very) Bioaccumulative
WoE - Weight of Evidence

The Expert Panel for Fragrance Safety* concludes that this material is safe as described in this safety assessment.

This safety assessment is based on the RIFM Criteria Document (Api et al., 2015), which should be referred to for clarifications.

Each endpoint discussed in this safety assessment includes the relevant data that were available at the time of writing (version number in the top box is indicative of the date of approval based on a 2-digit month/day/year), both in the RIFM Database (consisting of publicly available and proprietary data) and through publicly available information sources (e.g., SciFinder and PubMed). Studies selected for this safety assessment were based on appropriate test criteria, such as acceptable guidelines, sample size, study duration, route of exposure, relevant animal species, most relevant testing endpoints, etc. A key study for each endpoint was selected

(*continued on next column*)

(*continued*)

based on the most conservative endpoint value (e.g., PNEC, NOAEL, LOEL, and NESIL).

*The Expert Panel for Fragrance Safety is an independent body that selects its own members and establishes its own operating procedures. The Expert Panel is comprised of internationally known scientists that provide RIFM with guidance relevant to human health and environmental protection.

Summary: The existing information supports the use of this material as described in this safety assessment.

o-(Methylthio)-phenol was evaluated for genotoxicity, repeated dose toxicity, reproductive toxicity, local respiratory toxicity, phototoxicity/photoallergenicity, skin sensitization, and environmental safety. The genotoxicity, repeated dose, reproductive, and local respiratory toxicity endpoints were evaluated using the Threshold of Toxicological Concern (TTC) for a Cramer Class III material, and the exposure to *o*-(methylthio)-phenol is below the TTC (0.0025 μg/kg/day, 0.0015 mg/kg/day, 0.0015 mg/kg/day, and 0.47 mg/day, respectively). The skin sensitization endpoint was completed using the Dermal Sensitization Threshold (DST) for reactive materials (64 μg/cm^2); exposure is below the DST. Based on study data, the material is phototoxic; however, it is not a concern under the current declared levels of use. Based on ultraviolet/visible (UV/Vis) absorbance spectra, the material is not photoallergenic. The environmental endpoints were evaluated; for the hazard assessment based on the screening data, *o*-(methylthio)-phenol is not Persistent, Bioaccumulative, and Toxic (PBT) as per the International Fragrance Association (IFRA) Environmental Standards. For the risk assessment, *o*-(methylthio)-phenol was not able to be risk screened as there were no reported volumes of use for either North America or Europe in the 2015 IFRA Survey.

Human Health Safety Assessment

Genotoxicity: Exposure is below genotoxicity TTC.
Repeated Dose Toxicity: No NOAEL available. Exposure is below TTC.
Reproductive Toxicity: No NOAEL available. Exposure is below TTC.
Skin Sensitization: Not a concern for skin sensitization under the declared use levels; exposure is below the DST.
Phototoxicity/Photoallergenicity: Phototoxic but not a concern under declared levels of use/not expected to be photoallergenic. (UV/Vis Spectra; RIFM Database; RIFM, 2021)
Local Respiratory Toxicity: No NOAEC available. Exposure is below the TTC.

Environmental Safety Assessment

Hazard Assessment:
Persistence: Screening-level: 2.95 (BIOWIN 3) (EPI Suite v4.11; US EPA, 2012a)
Bioaccumulation: Screening-level: 11.52 L/kg (EPI Suite v4.11; US EPA, 2012a)
Ecotoxicity: Screening-level: Not applicable
Conclusion: Not PBT or vPvB as per IFRA Environmental Standards
Risk Assessment:
- **Revised PEC/PNECs (2015 IFRA VoU):** North America and Europe: Not applicable; no Volume of Use in 2015 reported for Europe and North America

1. Identification

1. **Chemical Name:** *o*-(Methylthio)-phenol
2. **CAS Registry Number:** 1073-29-6
3. **Synonyms:** 1-Hydroxy-2-methylmercaptobenzene; Methyl(2-hydroxyphenyl) sulfide; 2-Methylmercaptophenol; 2-(Methylthio) phenol; Phenol, 2-(methylthio)-; 2-(Methylsulfanyl)phenol; *o*-(Methylthio)-phenol
4. **Molecular Formula:** C_7H_8OS
5. **Molecular Weight:** 140.2 g/mol
6. **RIFM Number:** 6686
7. **Stereochemistry:** No stereocenter present and no stereoisomer possible.

2. Physical data

1. **Boiling Point:** 245.35 °C (EPI Suite)
2. **Flash Point:** Not Available
3. **Log K_{OW}:** 2.11 (EPI Suite)
4. **Melting Point**: 48.81 °C (EPI Suite)
5. **Water Solubility:** 4978 mg/L (EPI Suite)
6. **Specific Gravity:** Not Available

7. **Vapor Pressure:** 0.00482 mm Hg at 20 °C (EPI Suite v4.0), 0.06 mm Hg 20 °C (Fragrance Materials Association), 0.00872 mm Hg at 25 °C (EPI Suite)
8. **UV Spectra:** Minor absorbance between 290 and 700 nm. Molar absorption coefficients under the biologically relevant neutral condition (698 L mol^{-1} • cm^{-1}) and under the acidic condition (179 L mol^{-1} • cm^{-1}) are below the benchmark (1000 L mol^{-1} • cm^{-1}). The molar absorption coefficient under the basic condition (1208 L mol^{-1} • cm^{-1}) is above the benchmark.
9. **Appearance/Organoleptic:** Not available

3. Volume of use (Worldwide band)

1. <0.1 metric ton per year (IFRA, 2015)

Table 1
Maximum acceptable concentrations for *o*-(methylthio)-phenol that present no appreciable risk for skin sensitization based on reactive DST.

IFRA Category[a]	Description of Product Type	Maximum Acceptable Concentrations in Finished Products Based on Reactive DST	Reported 95th Percentile Use Concentrations in Finished Products
1	Products applied to the lips	0.0049%	NRU[b]
2	Products applied to the axillae	0.0015%	NRU[b]
3	Products applied to the face using fingertips	0.029%	3.8×10^{-8}%
4	Fine fragrance products	0.027%	NRU[b]
5	Products applied to the face and body using the hands (palms), primarily leave-on	0.0070%	4.8×10^{-8}%
6	Products with oral and lip exposure	0.016%	2.1×10^{-7}%
7	Products applied to the hair with some hand contact	0.056%	NRU[b]
8	Products with significant ano-genital exposure	0.0029%	No Data[c]
9	Products with body and hand exposure, primarily rinse-off	0.054%	1.9×10^{-7}%
10	Household care products with mostly hand contact	0.19%	NRU[b]
11	Products with intended skin contact but minimal transfer of fragrance to skin from inert substrate	0.11%	No Data[c]
12	Products not intended for direct skin contact, minimal or insignificant transfer to skin	Not restricted	8.5×10^{-4}%

Note: [a]For a description of the categories, refer to the IFRA/RIFM Information Booklet.
bNo reported use.
cFragrance exposure from these products is very low. These products are not currently in the Creme RIFM Aggregate Exposure Model.

4. Exposure to fragrance ingredient (Creme RIFM aggregate exposure model v3.1.4)

1. **95**th **Percentile Concentration in Toothpaste:** 0.00000021% (No reported use in Fine Fragrance)	RIFM (2021)
2. **Inhalation Exposure*:** <0.0001 mg/kg/day or <0.0001 mg/day	RIFM (2021)
3. **Total Systemic Exposure**:** 0.0000001 mg/kg/day	RIFM (2021)

*95th percentile calculated exposure derived from concentration survey data in the Creme RIFM Aggregate Exposure Model (Comiskey et al., 2015; Safford et al., 2015a; Safford et al., 2017; and Comiskey et al., 2017).

95th percentile calculatedcentile Concentration in Toothpa** exposure; assumes 100% absorption unless modified by dermal absorption data as reported in Section V. It is derived from concentration survey data in the Creme RIFM Aggregate Exposure Model and includes exposure via dermal, oral, and inhalation routes whenever the fragrance ingredient is used in products that include these routes of exposure (Comiskey et al., 2015; Safford et al., 2015a; Safford et al., 2017; and Comiskey et al., 2017).

5. Derivation of systemic absorption

1. **Dermal:** Assumed 100%
2. **Oral:** Assumed 100%
3. **Inhalation:** Assumed 100%

6. Computational toxicology evaluation

1. **Cramer Classification:** Class III, High* (Expert Judgment)

Expert Judgment	Toxtree v3.1	OECD QSAR Toolbox v4.2
III	III	II

*See Appendix for details.

2. Analogs Selected:
   a. **Genotoxicity:** None
   b. **Repeated Dose Toxicity:** None
   c. **Reproductive Toxicity:** None
   d. **Skin Sensitization:** None
   e. **Phototoxicity/Photoallergenicity:** None
   f. **Local Respiratory Toxicity:** None
   g. **Environmental Toxicity:** None
3. **Read-across Justification:** None

7. Metabolism

No relevant data is available for inclusion in this safety assessment.

7.1. Additional References

None.

8. Natural occurrence

o-(Methylthio)-phenol is reported to occur in the following foods by the VCF*:
Coffee.
*VCF (Volatile Compounds in Food): Database/Nijssen, L.M.; Ingen-Visscher, C.A. van; Donders, J.J.H. (eds). – Version 15.1 – Zeist (The Netherlands): TNO Triskelion, 1963–2014. A continually updated database containing information on published volatile compounds that have been found in natural (processed) food products. Includes FEMA GRAS and EU-Flavis data.

9. REACH dossier

Pre-registered for 2010. No dossier available as of 02/17/22.

10. Conclusion

The existing information supports the use of this material as described in this safety assessment.

Summary

Human health endpoint summaries

Genotoxicity

Based on the current existing data, *o*-(methylthio)-phenol does not present a concern for genotoxicity.

Risk assessment. *o*-(Methylthio)-phenol was assessed in the BlueScreen assay and found positive for both cytotoxicity (positive: <80% relative cell density) and genotoxicity, with and without metabolic activation (RIFM, 2014). BlueScreen is a human cell-based assay for measuring the genotoxicity and cytotoxicity of chemical compounds and mixtures.

There are no studies assessing the mutagenicity or clastogenicity of *o*-(methylthio)-phenol to support the genotoxicity endpoint. The total systemic exposure for *o*-(methylthio)-phenol (0.0001 μg/kg/day) is below the TTC for genotoxicity (0.0025 μg/kg/day; Kroes et al., 2004) at the current level of use and therefore does not present a concern for genotoxicity.

Additional References: None.

Literature Search and Risk Assessment Completed On: 07/30/21.

Repeated dose toxicity

There are insufficient repeated dose toxicity data on *o*-(methylthio)-phenol or any read-across materials. The total systemic exposure to *o*-(methylthio)-phenol is below the TTC for the repeated dose toxicity endpoint of a Cramer Class III material at the current level of use.

Risk assessment. There are no repeated dose toxicity data on *o*-(methylthio)-phenol or any read-across materials that can be used to support the repeated dose toxicity endpoint. The total systemic exposure (0.0001 μg/kg/day) is below the TTC for *o*-(methylthio)-phenol (1.5 μg/kg/day; Kroes et al., 2007).

Additional References: None.

Literature Search and Risk Assessment Completed On: 06/14/21.

Reproductive toxicity

There are insufficient reproductive toxicity data on *o*-(methylthio)-phenol or any read-across materials. The total systemic exposure to *o*-(methylthio)-phenol is below the TTC for the reproductive toxicity endpoint of a Cramer Class III material at the current level of use.

11.1.3.1. Risk assessment. There are no reproductive toxicity data on *o*-(methylthio)-phenol or any read-across materials that can be used to support the reproductive toxicity endpoint. The total systemic exposure (0.0001 μg/kg/day) is below the TTC for *o*-(methylthio)-phenol (1.5 μg/kg/day; Kroes et al., 2007; Laufersweiler et al., 2012).

Additional References: None.

Literature Search and Risk Assessment Completed On: 06/14/21.

Skin sensitization

Based on the application of DST, *o*-(methylthio)-phenol does not present a safety concern for skin sensitization under the current, declared levels of use.

Risk assessment. No skin sensitization studies are available for *o*-(methylthio)-phenol. No protein binding alerts were detected by *in silico* tools (Roberts et al., 2007; Toxtree v3.1.0; OECD Toolbox v4.2); however, the chemical possesses a phenol substructure, which could react with skin proteins. Acting conservatively due to the lack of data, the reported exposure was benchmarked utilizing the reactive DST of 64 μg/cm^2 (Safford, 2008; Safford et al., 2011; Roberts et al., 2015; Safford et al., 2015b). The current exposure from the 95th percentile concentration is below the DST for reactive materials when evaluated in all QRA categories. Table 1 provides the maximum acceptable concentrations for *o*-(methylthio)-phenol that present no appreciable risk for skin sensitization based on the reactive DST. These levels represent maximum acceptable concentrations based on the DST approach. However, additional studies may show it could be used at higher levels.

Additional References: None.

Literature Search and Risk Assessment Completed On: 07/26/21.

Phototoxicity/photoallergenicity

Based on *in vitro* study data, *o*-(methylthio)-phenol is phototoxic. However, based on the highest dermal 95th percentile concentration data, *o*-(methylthio)-phenol would not be expected to present a concern for phototoxicity under the current, declared levels of use. Based on the available UV/Vis absorption spectra, *o*-(methylthio)-phenol does not present a concern for photoallergenicity.

Risk assessment. UV/Vis absorption spectra indicate minor absorption between 290 and 700 nm under both the biologically relevant neutral condition and the acidic condition. The corresponding molar absorption coefficients are below the benchmark of concern for phototoxicity and photoallergenicity (Henry et al., 2009). Absorbance under the basic condition between 290 and 700 nm was demonstrated, and the corresponding molar absorption coefficient was above the benchmark of concern. However, the basic condition in this assay is defined as pH 10 or greater and may not be biologically relevant for our purposes, where the route of exposure is topical. Furthermore, per the ICH S10 guidance of photosafety Evaluation of Pharmaceuticals, some chromophores, including those with phenolic structures, are considered pH-sensitive. The pKa of the phenol group is expected to be around 10, hence a phenolate anion would be present and would account for the absorbance. In an *in vitro* neutral red uptake phototoxicity test, *o*-(methylthio)-phenol was predicted to have phototoxic potential in 2 of 3 trials conducted (RIFM, 2016). In a multidose reconstructed human epidermis (RhE) phototoxicity assay, 0.3% *o*-(methylthio)-phenol was not phototoxic, but 1% *o*-(methylthio)-phenol was phototoxic; 3% *o*-(methylthio)-phenol could not be assessed for phototoxic potential, due to high cytotoxicity (RIFM, 2017). The prediction model states that a significant difference in viability (>30%) at any dose shall be considered evidence of phototoxicity. It should be noted, however, that the concentration of *o*-(methylthio)-phenol where phototoxicity was observed in the RhE assay (1%) is orders of magnitude higher than current dermal exposure levels. The highest 95th percentile dermal concentration among all phototoxicity-applicable product categories was found in Category 4 and was 0.0000011%. This level is below the maximum acceptable concentration for leave-on cosmetics (0.0005%) set for furocoumarins, a potent class of phototoxicants; this value is used as an exposure limit, below which it is unlikely that any type of phototoxic potential exists (Api et al., 2015). Based on *in vitro* study data, *o*-(methylthio)-Phenol is phototoxic at concentrations of 1% or greater. However, based on the highest dermal 95th percentile concentration data, *o*-(methylthio)-phenol does not present a concern for phototoxicity under the current declared levels of use. Based on lack of absorbance under neutral conditions, *o*-(methylthio)-phenol does not present a concern for

photoallergenicity.

UV spectra analysis. UV/Vis absorption spectra (OECD TG 101) were obtained. The spectra indicate minor absorbance in the range of 290–700 nm under neutral and acidic conditions. The molar absorption coefficients under neutral and acidic conditions (698 and 179 L mol^{-1} • cm^{-1}, respectively) are below the benchmark of concern for phototoxic effects, 1000 L mol^{-1} • cm^{-1} (Henry et al., 2009). Absorbance under the basic condition was greater, and the corresponding molar absorption coefficient (1208 L mol^{-1} • cm^{-1}) was above the benchmark of concern. However, basic conditions for the assay are defined as a pH of 10 or greater and thus do not represent a biologically relevant condition.

Additional References: None.

Literature Search and Risk Assessment Completed On: 12/13/21.

Local Respiratory Toxicity

The margin of exposure could not be calculated due to a lack of appropriate data. The exposure level for *o*-(methylthio)-phenol is below the Cramer Class III TTC value for inhalation exposure local effects.

Risk assessment. There are no inhalation data available on *o*-(methylthio)-phenol. Based on the Creme RIFM Model, the inhalation exposure is < 0.0001 mg/day. This exposure is at least 470 times lower than the Cramer Class III TTC value of 0.47 mg/day (based on human lung weight of 650 g; Carthew et al., 2009); therefore, the exposure at the current level of use is deemed safe.

Additional References: None.

Literature Search and Risk Assessment Completed On: 07/19/21.

Environmental endpoint summary

Screening-level assessment

A screening-level risk assessment of *o*-(methylthio)-phenol was performed following the RIFM Environmental Framework (Salvito et al., 2002), which provides 3 tiered levels of screening for aquatic risk. In Tier 1, only the material's regional VoU, its log K_{OW}, and its molecular weight are needed to estimate a conservative risk quotient (RQ), expressed as the ratio Predicted Environmental Concentration/Predicted No Effect Concentration (PEC/PNEC). A general QSAR with a high uncertainty factor applied is used to predict fish toxicity, as discussed in Salvito et al. (2002). In Tier 2, the RQ is refined by applying a lower uncertainty factor to the PNEC using the ECOSAR model (US EPA, 2012b), which provides chemical class-specific ecotoxicity estimates. Finally, if necessary, Tier 3 is conducted using measured biodegradation and ecotoxicity data to refine the RQ, thus allowing for lower PNEC uncertainty factors. The data for calculating the PEC and PNEC for this safety assessment are provided in the table below. For the PEC, the range from the most recent IFRA Volume of Use Survey is reviewed. The PEC is then calculated using the actual regional tonnage, not the extremes of the range. Following the RIFM Environmental Framework, *o*-(methylthio)-phenol was not able to be risk screened as there were no reported volumes of use for either North America or Europe in the 2015 IFRA Survey.

A screening-level hazard assessment using EPI Suite v4.11 (US EPA, 2012a) did not identify *o*-(methylthio)-phenol as possibly persistent or bioaccumulative based on its structure and physical–chemical properties. This screening-level hazard assessment considers the potential for a material to be persistent *and* bioaccumulative *and* toxic, or very persistent *and* very bioaccumulative as defined in the Criteria Document (Api et al., 2015). As noted in the Criteria Document, the screening criteria applied are the same as those used in the EU for REACH (ECHA, 2012). For persistence, if the EPI Suite model BIOWIN 3 predicts a value < 2.2 and either BIOWIN 2 or BIOWIN 6 predicts a value < 0.5, then the material is considered potentially persistent. A material would be considered potentially bioaccumulative if the EPI Suite model BCFBAF predicts a fish BCF ≥2000 L/kg. Ecotoxicity is determined in the above screening-level risk assessment. If, based on these model outputs (Step 1), additional assessment is required, a WoE-based review is then performed (Step 2). This review considers available data on the material's physical–chemical properties, environmental fate (e.g., OECD Guideline biodegradation studies or die-away studies), fish bioaccumulation, and higher-tier model outputs (e.g., US EPA's BIOWIN and BCFBAF found in EPI Suite v4.11).

Risk assessment

Not applicable.

Key studies

Biodegradation. No data available.

Ecotoxicity. No data available.

Other available data

o-(Methylthio)-phenol has been pre-registered with no additional information available at this time.

Risk assessment refinement

Not applicable.

Literature Search and Risk Assessment Completed On: 07/15/21.

Literature Search*

- **RIFM Database:** Target, Fragrance Structure-Activity Group materials, other references, JECFA, CIR, SIDS
- **ECHA:** https://echa.europa.eu/
- **NTP:** https://ntp.niehs.nih.gov/
- **OECD Toolbox:** https://www.oecd.org/chemicalsafety/risk-assessment/oecd-qsar-toolbox.htm
- **SciFinder:** https://scifinder.cas.org/scifinder/view/scifinder/scifinderExplore.jsf
- **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed
- **National Library of Medicine's Toxicology Information Services:** https://toxnet.nlm.nih.gov/
- **IARC:** https://monographs.iarc.fr
- **OECD SIDS:** https://hpvchemicals.oecd.org/ui/Default.aspx
- **EPA ACToR:** https://actor.epa.gov/actor/home.xhtml
- **US EPA HPVIS:** https://ofmpub.epa.gov/oppthpv/public_search.publicdetails?submission_id=24959241&ShowComments=Yes&sqlstr=null&recordcount=0&User_title=DetailQuery%20Results&EndPointRpt=Y#submission
- **Japanese NITE:** https://www.nite.go.jp/en/chem/chrip/chrip_search/systemTop
- **Japan Existing Chemical Data Base (JECDB):** http://dra4.nihs.go.jp/mhlw_data/jsp/SearchPageENG.jsp
- **Google:** https://www.google.com
- **ChemIDplus:** https://chem.nlm.nih.gov/chemidplus/

Search keywords: CAS number and/or material names.

*Information sources outside of RIFM's database are noted as appropriate in the safety assessment. This is not an exhaustive list. The links listed above were active as of 02/17/22.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix

Explanation of Cramer Classification:

Due to potential discrepancies with the current *in silico* tools (Bhatia et al., 2015), the Cramer class of the target material was determined using expert judgment based on the Cramer decision tree (Cramer et al., 1978).

Q1. A normal constituent of the body? No.

Q2. Contains functional groups associated with enhanced toxicity? No.

Q3. Contains elements other than C, H, O, N, and divalent S? No.

Q5. Simply branched aliphatic hydrocarbon or a common carbohydrate? No.

Q6. Benzene derivative with certain substituents? No.

Q7. Heterocyclic? No.

Q16. Common terpene? (see Cramer et al., 1978 for detailed explanation). No.

Q17. Readily hydrolyzed to a common terpene? No.

Q18. One of the list? (see Cramer et al., 1978 for a detailed explanation on the list of categories). No.

Q19. Open chain? No.

Q23. Aromatic? No.

Q27. Rings with substituents? No.

Q28. More than one aromatic ring? No.

Q29. Readily hydrolyzed? No.

Q30. Aromatic ring with complex substituents? No.

Q31. Is the substance an acyclic acetal or ester of substances defined in Q30? No.

Q32. It contains only the functional groups listed in Q30 or Q31 and either a) a single fused non-aromatic carbocyclic ring or b) aliphatic substituent chains longer than 5 carbon atoms or c) a polyoxyethylene ($n \geq 4$) on the aromatic or aliphatic side chain? No. Class III (Class High).

Q33. Has a sufficient number of sulfonate or sulfamate groups for every 20 or fewer carbon atoms, without any free primary amines except those adjacent to the sulphonate or sulphamate? No.

Q41. Possibly harmful of phosphate?

Q42. Possibly harmful analog of benzene?

Q443. Possibly harmful divalent sulfur?

Q44. Free α,β-unsaturated heteroatom? Class III (Class high).

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