METHYL ACETATE
(CAS #79-20-9)
GREENSCREEN® FOR SAFER CHEMICALS (GREENSCREEN®) ASSESSMENT

Prepared by:
ToxServices LLC
Assessment Date: May 2, 2017
Expiration Date: May 2, 2020
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GreenScreen® Executive Summary for Methyl Acetate (CAS #79-20-9)

Methyl acetate is primarily used as a solvent in adhesives, paint systems, cosmetic agents, and cleaning products. It is also used as a chemical intermediate for plant protection products, vitamins and sweeteners.

Methyl acetate was assigned a GreenScreen Benchmark™ Score of 2 (“Use but Search for Safer Substitutes”). This score is based on the following hazard score combinations:

- Benchmark 2e (“Moderate T (Group I Human)"
  - Moderate Group I Human Health Hazard (developmental toxicity (D) and endocrine activity (E))
- Benchmark 2g (“High Flammability or High Reactivity")"
  - High Flammability (F)

There are no data gaps (DG). Therefore, methyl acetate meets the requirements for a GreenScreen® Benchmark Score of 2.

GreenScreen® Benchmark Score for Relevant Route of Exposure:
As a standard approach for GreenScreen® evaluations, all exposure routes (oral, dermal, and inhalation) were evaluated together, so the GreenScreen® Benchmark Score of 2 (“Use but Search for Safer Substitutes”) is applicable for all routes of exposure.

<table>
<thead>
<tr>
<th>Group I Human</th>
<th>Group II and II* Human</th>
<th>Ecotox</th>
<th>Fate</th>
<th>Physical</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>M</td>
<td>R</td>
<td>D</td>
<td>E</td>
</tr>
<tr>
<td>L</td>
<td>L</td>
<td>M</td>
<td>M</td>
<td>M</td>
</tr>
</tbody>
</table>

Note: Hazard levels (Very High (vH), High (H), Moderate (M), Low (L), Very Low (vL)) in italics reflect estimated values, authoritative B lists, screening lists, weak analogues, and lower confidence. Hazard levels in BOLD font are used with good quality data, authoritative A lists, or strong analogues. Group II Human Health endpoints differ from Group II* Human Health endpoints in that they have four hazard scores (i.e., vH, H, M, and L) instead of three (i.e., H, M, and L), and are based on single exposures instead of repeated exposures. Please see Appendix A for a glossary of hazard acronyms.
**GreenScreen® Assessment for Methyl Acetate (CAS #79-20-9)**

**Method Version:** GreenScreen® Version 1.3

**Assessment Type:** Certified

**Assessor Type:** Licensed GreenScreen® Profiler

**GreenScreen® Assessment Prepared By:**
Name: Sara Ciotti, Ph.D.
Title: Toxicologist
Organization: ToxServices LLC
Date: November 14, 2016
Expiration Date: November 14, 2019

**Quality Control Performed By:**
Name: Bingxuan Wang, Ph.D., D.A.B.T.
Title: Toxicologist
Organization: ToxServices LLC
Date: November 14, 2016

**GreenScreen® Assessment Updated By:**
Name: Zach Guerrette, Ph.D., D.A.B.T.
Title: Toxicologist
Organization: ToxServices LLC
Date: March 30, 2017
Expiration Date: May 2, 2020

**Update Quality Control Performed By:**
Name: Bingxuan Wang, Ph.D., D.A.B.T.
Title: Senior Toxicologist
Organization: ToxServices LLC
Date: May 2, 2017

**Confirm application of the Disclosure and Assessment Rules and Best Practice:**
(List disclosure threshold and any deviations)
Commercially available pure methyl acetate is > 99% pure (ECB 2003).
No impurities were identified.

**Notes related to production specific attributes:**
No relevant information is available. The screen is performed on the theoretical pure substance.

**Chemical Name:** Methyl Acetate

**CAS Number:** 79-20-9

**Chemical Structure(s):**

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1 Use GreenScreen® Hazard Assessment Guidance (Guidance) v1.3
2 GreenScreen reports are either “UNACCREDITED” (by unaccredited person), “AUTHORIZED” (by Authorized GreenScreen® Practitioner), “CERTIFIED” (by Licensed GreenScreen® Profiler or equivalent) or “CERTIFIED WITH VERIFICATION” (Certified or Authorized assessment that has passed GreenScreen® Verification Program)
3 Assessments expire three years from the date of completion.
4 Assessments expire three years from the date of completion.
5 Every chemical in a material or formulation should be assessed if it is:
   1. intentionally added and/or
   2. present at greater than or equal to 100 ppm
6 Note any composition or hazard attributes of the chemical product relevant to how it is manufactured. For example, certain synthetic pathways or processes result in typical contaminants, by-products or transformation products. Explain any differences between the manufactured chemical product and the GreenScreen assessment of the generic chemical by CAS #.
Also called: Acetic acid, methyl ester; CCRIS 5846; Devoton; EC 201-185-2; EINECS 201-185-2; Ethyl ester of monoacetic acid; FEMA No. 2676; FEMA Number 2676; HSDB 95; Methyl acetate (natural); Methyl acetic ester; Methyl ethanoate; NSC 405071; RTECS AJ7224000; Tereton; UNII-W684QT396F; Methyl acetate [UN1231] (Flammable liquid); UN1231 (ChemIDplus 2017)

Suitable analogs or moieties of chemicals used in this assessment (CAS #’s):
No cancer, reproductive toxicity, or developmental toxicity data were available for methyl acetate (CAS #79-20-9). Methyl acetate is rapidly hydrolyzed to methanol and acetic acid by non-specific esterases in the blood, respiratory tract, liver, and small intestine (HCN 2004). Therefore, methyl acetate’s immediate metabolites methanol (CAS #67-56-1) and acetic acid (CAS #64-19-7) were used as analogs to address the data gaps for these endpoints. These analogs were also used by the European Union in the risk assessment of methyl acetate (ECB 2003).

HO — CH₃
Analog: Methanol (CAS #67-56-1)

O
\[ \text{H}_3\text{C} \text{CH}_{\text{COOH}} \]
Analog: Acetic acid (CAS #64-19-7)

Identify Applications/Functional Uses (EC 2003):
1. Solvent in adhesives, paint systems, cosmetics and cleaning products (70%)
2. Chemical intermediate for plant protection products and vitamins (10%) and for the production of sweeteners (20%)

GreenScreen® Summary Rating for Methyl Acetate: Methyl acetate was assigned a GreenScreen Benchmark™ Score of 2 (“Use but Search for Safer Substitutes”) (CPA 2017a). This score is based on the following hazard score combinations:
- Benchmark 2e (“Moderate T (Group I Human)”)  
  o Moderate Group I Human Health Hazard (developmental toxicity (D) and endocrine activity (E))

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7 For inorganic chemicals with low human and ecotoxicity across all hazard endpoints and low bioaccumulation potential, persistence alone will not be deemed problematic. Inorganic chemicals that are only persistent will be evaluated under the criteria for Benchmark 4.
8 See Appendix A for a glossary of hazard endpoint acronyms
9 For inorganic chemicals only, see GreenScreen® Guidance v1.3 Section 13 (Exceptions for Persistence).
10 For Systemic Toxicity and Neurotoxicity, repeated exposure data are preferred. Lack of single exposure data is not a Data Gap when repeated exposure data are available. In that case, lack of single exposure data may be represented as NA instead of DG. See GreenScreen Guidance v1.3 Section 8.2.1.

GreenScreen® Version 1.3 Assessment Template – February 2017
Limited license provided to University of Massachusetts Lowell for public distribution through the University of Massachusetts Lowell website, publications, presentations and for no other purpose whatsoever. Further copying, resale, and distribution are expressly prohibited.
- Benchmark 2g (“High Flammability or High Reactivity”)
  - High Flammability (F)

There are no data gaps (DG). Therefore, methyl acetate meets the requirements for a GreenScreen® Benchmark Score of 2.

**Figure 1: GreenScreen® Hazard Ratings for Methyl Acetate**

<table>
<thead>
<tr>
<th>Group I Human</th>
<th>Group II and II* Human</th>
<th>Ecotox</th>
<th>Fate</th>
<th>Physical</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>M</td>
<td>R</td>
<td>D</td>
<td>E</td>
</tr>
<tr>
<td>L</td>
<td>L</td>
<td>M</td>
<td>M</td>
<td>L</td>
</tr>
</tbody>
</table>

Note: Hazard levels (Very High (vH), High (H), Moderate (M), Low (L), Very Low (vL)) in italics reflect estimated (modeled) values, authoritative B lists, screening lists, weak analogues and lower confidence. Hazard levels in BOLD font are used with good quality data, authoritative A lists, or strong analogues. Group II Human Health endpoints differ from Group II* Human Health endpoints in that they have four hazard scores (i.e. vH, H, M, and L) instead of three (i.e. H, M, and L), and are based on single exposures instead of repeated exposures. Please see Appendix A for a glossary of hazard acronyms.

**Transformation Products and Ratings**

Identify feasible and relevant fate and transformation products (i.e., dissociation products, transformation products, valence states) and/or moieties of concern

No feasible and relevant transformation products were identified for methyl acetate. As methyl acetate is readily biodegradable (see the persistence section below), no feasible environmental transformation products are expected to form that are persistent enough to be of any concern.

**Introduction**

Methyl acetate is primarily used as a solvent in adhesives, paint systems, cosmetic agents, and cleaning products. It is also used as a chemical intermediate (ECB 2003).

ToxServices assessed methyl acetate against GreenScreen® Version 1.3 (CPA 2017b) following procedures outlined in ToxServices’ SOPs (GreenScreen® Hazard Assessment) (ToxServices 2016).

**U.S. EPA Safer Choice Program’s Safer Chemical Ingredients List (SCIL)**

The SCIL is a list of chemicals that meet the Safer Choice standard (U.S. EPA 2017). It can be accessed at: [http://www2.epa.gov/saferchoice/safer-ingredients](http://www2.epa.gov/saferchoice/safer-ingredients). Chemicals on the SCIL have been assessed for compliance with the Safer Choice Standard and Criteria for Safer Chemical Ingredients (U.S. EPA 2015).

Methyl acetate is not listed on the SCP SCIL.

**GreenScreen® List Translator Screening Results**

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11 See GreenScreen® Guidance v1.3 Section 12.
12 A moiety is a discrete chemical entity that is a constituent part or component of a substance. A moiety of concern is often the parent substance itself for organic compounds. For inorganic compounds, the moiety of concern is typically a dissociated component of the substance or a transformation product.
The GreenScreen® List Translator identifies specific authoritative or screening lists that should be searched to identify GreenScreen® benchmark 1 chemicals (CPA 2017b,c). Pharos (Pharos 2017) is an online list-searching tool that is used to screen chemicals against the List Translator electronically. It checks all of the lists in the List Translator with the exception of the U.S. Department of Transportation (U.S. DOT) lists (U.S. DOT 2008a,b) and these should be checked separately in conjunction with running the Pharos query. The output indicates benchmark or possible benchmark scores for each human health and environmental endpoint. The output for methyl acetate can be found in Appendix C.

- Methyl acetate is an LT-P1 chemical when screened using Pharos, and therefore a full GreenScreen® is required.

**Hazard Statement and Occupational Control**

The harmonized H-Statements for methyl acetate are presented in Table 1 below. Available occupational exposure limits and recommended personal protective equipment are presented in Table 2 below.

<table>
<thead>
<tr>
<th>H Statement</th>
<th>H Statement Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>H225</td>
<td>Highly flammable liquid and vapor</td>
</tr>
<tr>
<td>H336</td>
<td>May cause drowsiness or dizziness</td>
</tr>
<tr>
<td>H319</td>
<td>Causes serious eye irritation</td>
</tr>
</tbody>
</table>

**Table 2: Occupational Exposure Limits and Recommended Personal Protective Equipment for Methyl Acetate (CAS #79-20-9)**

<table>
<thead>
<tr>
<th>Personal Protective Equipment (PPE)</th>
<th>Reference</th>
<th>Occupational Exposure Limits (OEL)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Face shield and safety glasses; gloves; impervious clothing; full-face respirator if threshold values are exceeded</td>
<td>Sigma-Aldrich 2016</td>
<td>TWA = 200 ppm ST = 250 ppm IDLH = 3100 ppm TLV = 200 ppm</td>
<td>NIOSH 1997</td>
</tr>
</tbody>
</table>

TWA: Time-weighted average; ST: Short-term exposure limit; IDLH: Immediately dangerous to life or health value; TLV: Threshold limit value

**Physicochemical Properties of Methyl Acetate**

Methyl acetate is a colorless liquid at room temperature. It is freely soluble in water. Its high vapor pressure (162.75 mm Hg) indicates it is highly volatile and exists mostly as a gas. Its partition coefficient (log K<sub>ow</sub> = 0.18) indicates it is highly soluble in water and is not expected to bioaccumulate in aquatic biota.

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular formula</td>
<td>C3-H6-O2</td>
<td>ChemIDplus 2017</td>
</tr>
<tr>
<td>SMILES Notation</td>
<td>C(OC)(C)=O</td>
<td>ChemIDplus 2017</td>
</tr>
</tbody>
</table>

13 DOT lists are not required lists for GreenScreen List Translator v1.3. They are reference lists only.
### Table 3: Physical and Chemical Properties of Methyl Acetate (CAS #79-20-9)

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight</td>
<td>74.0784</td>
<td>ChemIDplus 2017</td>
</tr>
<tr>
<td>Physical state</td>
<td>Liquid</td>
<td>ECHA 2017b</td>
</tr>
<tr>
<td>Appearance</td>
<td>Colorless liquid</td>
<td>ECHA 2017b</td>
</tr>
<tr>
<td>Melting point</td>
<td>-98°C</td>
<td>ECHA 2017b</td>
</tr>
<tr>
<td>Vapor pressure</td>
<td>217 hPa @ 20°C (equivalent to 162.75 mm Hg)¹¹⁴</td>
<td>ECB 2003</td>
</tr>
<tr>
<td>Water solubility</td>
<td>243.5 g/L @ 20°C</td>
<td>ECHA 2017b</td>
</tr>
<tr>
<td>Dissociation constant</td>
<td>n/a</td>
<td>ECHA 2017b</td>
</tr>
<tr>
<td>Density/specific gravity</td>
<td>0.93 g/cm³ @ 20°C</td>
<td>ECHA 2017b</td>
</tr>
<tr>
<td>Partition coefficient</td>
<td>Log K&lt;sub&gt;ow&lt;/sub&gt; = 0.18</td>
<td>ECHA 2017b</td>
</tr>
</tbody>
</table>

### Toxicokinetics

- Methyl Acetate (CAS #79-20-2)
  - ECB 2003
    - **In vitro:** The hydrolysis of methyl acetate has a half-life of 2-3 hours and 4 hours in rat blood and human blood, respectively, and the reaction followed first-order kinetics.
    - **Oral:** Rabbits (strain not specified) were administered oral gavage doses of 5% methyl acetate (purity not specified) in water at 1,000 mg/kg. Blood samples were collected from 30 minutes to 5 hours after dosing. Methyl acetate was not detected in blood samples, but methanol was detected in blood and urine samples as early as 30 minutes after dosing. A peak methanol concentration of 0.573 mg/mL in the blood was reached 3 hours after dosing. The results indicate that methyl acetate undergoes hydrolysis in the gastrointestinal tract prior to reaching systemic circulation.
      - Following hydrolysis of methyl acetate to methanol and acetic acid, methanol may be further metabolized to formaldehyde via alcohol dehydrogenase. Formaldehyde is subsequently metabolized to formic acid. The deprotonated form of formic acid, formate, is considered to be the toxic metabolite of methanol. Humans are more sensitive to methanol toxicity than rodents as they have lower levels of tetrahydrofolate, a requirement for formate metabolism, in their livers.
  - ECB 2003, ECHA 2017b
    - **Inhalation:** A GLP-compliant subacute inhalation test was performed with rats (10/sex, strain not specified) administered inhalation exposures to methyl acetate (greater than 99.5% purity) at 2,000 ppm (equivalent to 6.04 mg/L) for 6 hours per day 5 days/week. Blood samples were collected immediately after the last exposure period and at 30, 60, and 120 minutes and 18 hours later. Blood levels of methyl acetate were all less than the limit of detection (5 ppm v/v). The study authors concluded that the results of this study are indicative of rapid clearance of methyl acetate from the blood.
  - ECHA 2017b
    - **Inhalation:** Tracheotomized rabbits (number, sex, and strain not specified) were exposed to methyl acetate (purity not specified) at up to 20 mg/L for up to 3 hours. Shortly after the start of the exposure, exhaled air was collected and analyzed for

¹¹⁴ 217 hPa * 0.75 mm Hg/hPa = 162.75 mm Hg
methyl acetate. Methyl acetate was present in exhaled air at up to 30-50% of the inhaled concentration. No methyl acetate was detected in exhaled air once the exposure ceased. At the end of the exposure period, blood samples were collected for analysis of methyl acetate. No detectable levels of methyl acetate were measured in the blood, indicating rapid hydrolysis of methyl acetate according to the study authors.

- **In vitro**: Methyl acetate (purity not specified) was incubated with blood samples (species not specified but likely human) at 36°C for 2-8 hours. The concentration of methyl acetate and methanol were measured via gas chromatography (GC) and gas chromatography mass spectrometry (GC-MS). In two hours, 60% of the methyl acetate was converted to methanol, and methyl acetate was exhausted at the end of 8 hours.

- **Inhalation**: F344/N rats, New Zealand White rabbits and Syrian hamsters were administered inhalation exposures to methyl acetate (purity, exposure concentration, and exposure duration not specified). The lung, nasal, and liver tissues were removed and analyzed for methyl acetate via ion chromatography and an unspecified enzymatic technique. Methyl acetate was rapidly hydrolyzed to acetic acid and methanol, and the hydrolysis rate exhibited tissue and species differences. The hydrolysis rate of methyl acetate was 15 nmol/mg S-9 protein/min with rat ethmoturbinates. No further details were provided.

- **Inhalation**: Four human males were administered inhalation exposures to methyl acetate (purity not specified) at 0.3 mg/L for 10 minutes. Exhaled air was collected and analyzed for methyl acetate. The percentage of methyl acetate in end-exhaled and mixed-exhaled air increased following the start of the exposure and reached a quasi-steady state level after a few minutes. The mean respiratory uptake of methyl acetate during the last 5 minutes of the exposure period was 60.4%. Methanol, one of the products of methyl acetate hydrolysis, was measured in exhaled air at 1.3 ppm at the first minute of reaching the quasi-steady state level. The study authors suggest that methyl acetate hydrolysis may be performed by the respiratory tract tissues.

- **Inhalation**: Human volunteers (2 total, sex not specified) were administered 2-hour inhalation exposures to methyl acetate (purity not specified) at 200 ppm (equivalent to approximately 610 mg/m³) twice a day for 3-4 days. Urine samples were collected at regular intervals for analysis of methanol. Peak urine concentrations (greater than 10 mg/L urine) of methanol were achieved within 4 hours of the second exposure on each exposure day. The following morning, methanol concentrations were “restored to normal” (less than 5 mg/L urine).

- In summary, methyl acetate is rapidly absorbed after inhalation and oral exposure. It is rapidly and completely hydrolyzed to methanol and acetic acid by esterases of the gastric mucosa, blood and respiratory epithelium. Methyl acetate is excreted in exhaled air and urine as methanol.

**Hazard Classification Summary Section:**

**Group I Human Health Effects (Group I Human)**

**Carcinogenicity (C) Score (H, M, or L): L**
Methyl acetate was assigned a score of Low for carcinogenicity based on negative findings in studies using methanol and acetic acid. GreenScreen® criteria classify chemicals as a Low hazard for carcinogenicity when adequate data are available and negative, there are no structural alerts, and they
are not classified under GHS (CPA 2017c). Confidence in this classification is high because it is based on experimental data.

- Authoritative and Screening Lists
  - Authoritative: Not listed on any authoritative lists for this endpoint.
  - Screening: Not listed on any authoritative lists for this endpoint.
- Methyl Acetate (CAS #79-20-2)
  - No data were identified for this endpoint.
- Analog: Acetic Acid (CAS #64-19-7)
  - EC 2012
    - Application of acetic acid to the skin of mice was reported to stimulate the occurrence of epidermal hyperplasia, indicating very weak tumor promoting activity.
  - ECB 2000
    - Rabbits received acetic acid at 100 – 700 mg/kg/day in drinking water for 13 months and no tumors were found. No further details were provided for the study (GLP status not reported).
    - In a 5-month gavage study in rabbits (GLP status not reported), animals received 100 – 200 mg/kg acetic acid twice daily. No tumors were found. No further details were provided.
    - In a 135-day study in rats, animals received 350 mg/kg acetic acid orally (unspecified) 3 times per week for 63 days and then 140 mg/kg for 72 days. No histological evidence of tumors was found. No further details were provided.
    - In a tumor promotion study in CD-1 mice (20 – 30/group), beta-propiolactone- or DMBA-initiated animals received acetic acid on the skin at the doses of 17, 33, 167, 333, 500, or 667 µmol for 1 – 3 times/week for 32 weeks. Animals in the highest dose group had an average of 0.73 papillomas/mouse, and these papillomas were noted in 41% of the high dose animals. Single dermal applications of 500 – 833 µmol acetic acid stimulated RNA, protein and DNA synthesis followed by epidermal hyperplasia. The study authors concluded that acetic acid is a weak tumor promoter.
    - In another tumor promotion study using the multistage mouse-skin model, mice were initiated with a topical dose of 7,12-dimethylbenzanthracene and two weeks later promoted with 12-O-tetradecanoylphosbol-13-acetate twice weekly for 16 weeks. Four weeks later, mice received topical treatment of 40 mg glacial acetic acid in 200 µl acetone twice weekly for 30 weeks. Prior to acetic acid administration, each group of mice had roughly the same number of papillomas at the site of exposure. After treatment of acetic acid, mice treated with the chemical had 55% more conversion of skin papillomas to carcinomas compared to control mice. Selective cytotoxicity to certain cells within the papilloma with a compensatory increase in cell proliferation was considered to be the most probably mechanism of tumor promotion for acetic acid.
  - JECFA 1974
    - About 1g/day of acetic acid has been consumed by humans in vinegar and other items of food and drinks without known adverse effects at these consumption levels. However, continued ingestion of large doses has been regarded as a contributory factor in the development of Laennec type of liver cirrhosis.
- Analog: Methanol (CAS #67-56-1)
  - ECB 2003
    - In an 18-month inhalation study, mice were exposed to 0, 10, 100, or 1,000 ppm methanol and no increase in tumor rate was found. No further details were provided.
In a 24-month inhalation study, rats were exposed to 0, 10, 100, or 1,000 ppm methanol and a dose-dependent increase of papillary lung adenoma or adenomatosis in males which gained significance at the 1,000 ppm dose group. No further details were provided.

A study report which possibly presents the same data as above reports rats (F344/DuCrj) and mice (Crj:B6C3F1) were exposed to 0, 10, 100, or 1,000 ppm methanol via whole body exposure. A higher incidence of lung adenomas was found in males (1/52, 5/52, 2/2, and 6/52 in control, 10, 100, and 1,000 ppm males only), but it was not related to methanol concentrations. The incidence of adenomas was within the range of historical data. Animals with either adenoma or adenomatoid lesions was increased in a dose-dependent manner, but it was not significantly different from controls (5/52, 6/52, 7/52, and 10/52). Additionally, a higher incidence of phaeochromocytomas was found in 1,000 ppm females (2/50, 3/51, 2/49, and 7/51 in control, 10, 100, and 1,000 ppm groups), but it was not significantly different from controls.

Authors of the risk assessment concluded methanol is not carcinogenic in inhalation studies of rats and mice.

- The weight of evidence indicates that methyl acetate is not carcinogenic. No carcinogenicity studies were identified for methyl acetate; therefore, data for methanol and acetic acid were evaluated. Methanol was not carcinogenic in studies in mice and rats, and the weight of evidence indicates that acetic acid is not carcinogenic by itself. Based on the long history of safe use of acetic acid as a food additive, it is unlikely to be carcinogenic in humans. Therefore, methyl acetate is not expected to be carcinogenic and a score of Low was assigned.

**Mutagenicity/Genotoxicity (M) Score (H, M, or L): L**
Methyl acetate was assigned a score of Low for mutagenicity/genotoxicity based on negative results in bacterial mutagenicity assays, and an in vivo bone micronucleus assay. GreenScreen® criteria classify chemicals as a Low hazard for mutagenicity/genotoxicity when adequate data are available and negative for both chromosomal aberrations and gene mutations (CPA 2017c). Confidence in this classification is high because it is based on well-conducted studies.

- Authoritative and Screening Lists
  - **Authoritative:** Not listed on any authoritative lists for this endpoint.
  - **Screening:** Not listed on any authoritative lists for this endpoint.

- Methyl Acetate (CAS #79-20-9)
  - ECB 2003, ECHA 2017b
    - **In vitro:** Methyl acetate (purity not specified) was not mutagenic in a GLP-compliant bacterial reverse mutation assay conducted according to OECD Guideline 471 and performed in *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537, and TA1538, and *Escherichia coli* WP2uvrA, in the presence and absence of metabolic activation at 4-5,000 µg/plate in dimethyl sulfoxide (DMSO).
    - **In vitro:** Methyl acetate (greater than 99% purity) was not mutagenic in a bacterial reverse mutation assay conducted in a manner similar to OECD Guideline 471 and performed in *S. typhimurium* strains TA97, TA98, TA100, TA1535, and TA1538 in the presence and absence of metabolic activation at 100-10,000 µg/plate in water. This study included a 20 minute pre-incubation period.
    - **In vitro:** Methyl acetate (greater than 97% purity) was positive in an aneuploidy study in the yeast strain D 61.M. The lowest dose with an observable effect was 33,800 µg/mL or 456 mmol/L. The EU RAR authors note that this finding has low
relevance for the in vivo situation, and the REACH dossier lists this study with a Klimisch score of 3 (not reliable) based on the high concentrations not being relevant to the in vivo situation.

- In vivo: Methyl acetate (greater than 99.5% purity) was negative in a rat bone marrow micronucleus test. Rats (5/sex/group) were administered nose-only inhalation exposures of 2,000 or 75,350 ppm methyl acetate for 6 hours per day, 5 days per week, for 28 days. Cells were sampled 24 hours after the last treatment and polychromatic and normochromatic erythrocytes were analyzed. No local cytotoxicity (PCE/NCE) was observed.

- Based on the weight of evidence, a score of Low was assigned. Methyl acetate was negative in bacterial mutagenicity assays and an in vivo bone micronucleus assay. Although it was positive in an aneuploidy study in yeast, the study authors noted that positive results only occurred at high doses and it was not relevant to the in vivo situation. Additionally, authors of the methyl acetate risk assessment (EC 2003) note that the hydrolysis products, methanol and acetic acid, are not mutagenic. Therefore, a score of Low was assigned.

**Reproductive Toxicity (R) Score (H, M, or L): L**

Methyl acetate was assigned a score of Low for reproductive toxicity based on acetic acid/s long history of safe use in foods, and negative results in a two-generation study in rats with methanol. GreenScreen® criteria classify chemicals as a Low hazard for reproductive toxicity when adequate data are available and negative, there are no structural alerts, and they are not classified under GHS (CPA 2016b). The confidence in the score was reduced as no standard reproductive toxicity data were available for acetic acid.

- Authoritative and Screening Lists
  - Authoritative: Not listed on any authoritative lists for this endpoint.
  - Screening: Not listed on any authoritative lists for this endpoint.
- Methyl Acetate (CAS #79-20-9)
  - No data were identified.
- Analog: Acetic Acid (CAS #64-19-7)
  - EC 2008
    - Although no reproductive toxicity studies were identified for acetic acid, a new multi-generation study is not required based on its long history of safe use in various foods in humans without any indication of adverse effects on fertility.
- Analog: Methanol (CAS #67-56-1)
  - ECB 2003
    - In a two-generation study in Sprague-Dawley rats, male and female rats (30/sex/dose) were exposed to 10, 100, or 1,000 ppm methanol (purity not specified) vapor continuously via whole body exposure (from 8 weeks through the end of mating (males) or through mating and gestation to the end of lactation (females) for F0; from birth through the end of mating (males) or from birth through weaning of their pups (females) for F1; from birth to postnatal day (PND) 21 for F2). Treatment had no effect on reproductive parameters (sexual cycle, days needed for insemination, insemination rate, pregnancy rate) in F0 or F1 animals. Authors identified a fertility NOAEC of 1,000 ppm (1,300 mg/m³, or 1.3 mg/L).
Developmental Toxicity incl. Developmental Neurotoxicity (D) Score (H, M, or L): M

Methyl acetate was assigned a score of Moderate for developmental toxicity because ToxServices considered the hydrolysis product, methanol, a GHS Category 2 developmental toxicant. GreenScreen® criteria classify chemicals as a Moderate hazard for developmental toxicity when they are classified as GHS Category 2 (CPA 2017c). Confidence in this score is reduced due to the uncertainty regarding the relevance of the available rodent data to humans and mechanistic data indicating that methanol-induced developmental toxicity may be secondary to systemic toxicity.

- Authoritative and Screening Lists
  - Authoritative:
    - MAK - Pregnancy Risk Group C (“There is no reason to fear damage to the embryo or fetus when MAK and BAT values are observed”)
  - Screening: Not listed on any authoritative lists for this endpoint.
- Methyl Acetate (CAS #79-20-9)
  - No data were identified.
- Acetic Acid (CAS #64-19-7)
  - ECHA 2017c
    - In a study similar to EU method B.31 (Prenatal Developmental Toxicity Study) (GLP status unknown), acetic acid (table strength 5%) in the form of apple cider vinegar (table strength 5%) was administered to female Wistar rats (25/dose) via daily gavage at doses up to 1,600 mg/kg during gestation days (GD) 6-15. Body weights, appearance and behavior of the animals were monitored throughout the study. On gestation day 20, all dams were subjected to C-section and the numbers of implantation sites, resorption sites, and live and dead fetus were recorded. The urogenital tract of each dam was examined for anatomical normality. Body weights of the live pups were recorded and all fetuses were examined grossly for the presence of external congenital abnormalities. One-third of the fetuses of each litter were examined using Wilson technique and the rest of the fetuses were examined for skeletal defects. No clearly discernible effect was noted on fetal survival and soft or skeletal tissue abnormalities. Therefore, an NOAEL of 1,600 mg/kg/day (highest dose tested) was established for developmental toxicity.
    - In a study similar to EU method B.31 (Prenatal Developmental Toxicity Study) (GLP status unknown), acetic acid in the form of apple cider vinegar (table strength 5%) was administered to female CD-1 mice (25/dose) via daily gavage at doses of 0, 16, 76.3, 345, or 1,600 mg/kg during GD 6-15. Body weights, appearance and behavior of the animals were monitored throughout the study. On gestation day 17, all dams were subjected to C-section and the numbers of implantation sites, resorption sites, and live and dead fetus were recorded. The urogenital tract of each dam was examined for anatomical normality. Body weights of the live pups were recorded and all fetuses were examined grossly for the presence of external congenital abnormalities. One-third of the fetuses of each litter were examined using Wilson technique and the rest of the fetuses were examined for skeletal defects. No clearly discernible effect was noted on fetal survival and soft or skeletal tissue abnormalities. Therefore, an NOAEL of 1,600 mg/kg/day (highest dose tested) was established for developmental toxicity.
    - In a study similar to EU method B.31 (Prenatal Developmental Toxicity Study) (GLP status unknown), acetic acid in the form of apple cider vinegar (table strength 5%) was administered to female Dutch rabbits (approx. 12/dose) via daily gavage at doses of 0, 16, 76.3, 345, or 1,600 mg/kg during GD 6-18. Body weights,
appearance and behavior of the animals were monitored throughout the study. On gestation day 29, all dams were subjected to C-section and the numbers of corpora lutea, implantation sites, resorption sites, and live and dead fetus were recorded. The urogenital tract of each dam was examined for anatomical normality. Life fetuses of each litter were placed in an incubator for 24 hours to evaluate neonatal survival. Then all were sacrificed and examined for visceral abnormalities and skeletal defects. No clearly discernible effect was noted on fetal survival and soft or skeletal tissue abnormalities. Therefore, an NOAEL of 1,600 mg/kg/day (highest dose tested) was established for developmental toxicity.

- ECB 2000
  - Male offspring from dams treated with acetic acid were exposed to acetic acid from parturition until 17 days of age. These animals had above normal pre-weaning body weights and were significantly less active than control rats in an open field by the age of 44 days old. No further details were provided for the study.

- Methanol (CAS #67-56-1)
  - Pharos 2017
    - Methanol is a known developmental toxicant and is associated with the following authoritative lists which warrant a High score.
      - US NIH – Reproductive & Developmental Monographs – Clear Evidence of Adverse Effects – Developmental Toxicity
      - CA EPA – Prop 65 – Developmental Toxicity
      - MAK Pregnancy Risk Group C
  - Numerous developmental toxicity studies have been conducted using methanol. These studies are described in detail in the U.S. EPA Integrated Risk Information System (IRIS) Chemical Assessment Summary (U.S. EPA 2013). Only the key study used to derive the oral reference dose (RfD) is described below.
  - U.S. EPA 2013
    - In a developmental toxicity study, pregnant female CD-1 mice were exposed to air, 1,000, 2,000, 5,000, 7,500, 10,000, or 15,000 ppm (0, 1,310, 2,620, 6,552, 9,894, 13,104, and 19,656 mg/m3 or 0, 1.310, 2,620, 6,552, 9,894, 13,104, and 19.656 mg/L) methanol vapors (at least 99.9% purity) in a chamber for 7 hours per day on GD 6-15. There were no overt signs of maternal toxicity and no methanol-related reductions in maternal body weight gain. A NOEC of 1,000 ppm (1.31 mg/L) was identified based on an increased incidence of abnormal cervical ribs, exencephaly, and cleft palate.

- Based on the weight of evidence, a score of Moderate was assigned. While no data were available for methyl acetate, the EU Risk Assessment Committee (RAC) (ECB 2003) used data on the immediate hydrolysis products acetic acid and methanol as surrogates. Acetic acid is not a developmental toxicant, whereas methanol is a known developmental toxicant. EU RAR identified a NOAEC of 1,000 ppm (1.3 mg/L methanol, equivalent to 3 mg/L methyl acetate) for developmental toxicity for methyl acetate based on methanol data (specifically, a prenatal developmental toxicity study each in rats and mice by inhalation (ECB 2003)). The EU RAC compared methyl acetate exposure under various occupational and consumer scenarios and concluded that there is a need for limiting developmental toxicity risk by inhalation for occupational exposure scenarios of flooring works and building trade. The European Commission’s Scientific Committee on Toxicity, Ecotoxicity and Environment (CSTEE) noted that blood methanol concentrations in humans are much less than those in mice at the same external exposure
concentration, based on PBPK modeling for methanol. Hence, the internal dose of methanol differs greatly between mice and humans. CSTEE believed that the true NOAEC for methyl acetate’s developmental toxicity in humans may be higher than the 1,000 ppm NOAEC selected by EU RAC. The CSTEE concluded that there is no developmental toxicity risk for workers in the flooring works and building trade in terms of occupational exposure to methyl acetate (EC 2002). ToxServices notes that the GreenScreen® is a hazard based tool that does not takes exposure into consideration. Further, the GHS criteria for developmental toxicity are not based on doses, but on severity of effects. While methanol is classified as a high concern developmental toxicant by many authoritative bodies (Prop 65¹⁵, US NIH), methyl acetate is not classified as a developmental toxicant by these authoritative bodies. Only Germany classified methyl acetate to MAK Pregnancy Group C, which corresponds to a GreenScreen® score of Low to Moderate. Germany also classified methanol to the same pregnancy risk category. The EU did not classify either methyl acetate or methanol as a developmental toxicant. The EU RAC acknowledged that there are clear positive data in rodents that support GHS Category 1B classification, but the RAC also noted that there are vast differences in metabolism of methanol between rodents and humans, and very high doses/concentrations (the lowest LOAELs/LOAECs were 1,000 mg/kg and 2,000 ppm via oral and inhalation exposure, respectively) were used in the positive rodent studies. Further, the EU RAC noted that as an acute toxicant, methanol would trigger acute toxicity in mothers (acidosis, blindness, lethality) before exerting developmental toxicity in humans (EC 2014a,b). For these reasons, the EU RAC concluded that classification of methanol to GHS Category 1B is not appropriate (EC 2014a,b). This is in contrast to the US NIH’s classification of methanol as a developmental toxicant in humans if exposures are sufficiently high (NTP 2003). The US NIH reported similar concerns as the EU RAC; they discussed the species specificity of methanol metabolism and also noted that the blood methanol concentrations that are associated with developmental toxicity in rodents are within the range of formate (toxic metabolite of methanol) accumulation in humans which causes metabolic acidosis, as well as other signs of acute toxicity in humans. Data from in vitro mechanistic studies suggest that acidosis contributes to the developmental effects of formate (NTP 2003), suggesting that developmental toxicity in humans may be at least partially a secondary effect of systemic toxicity. GHS Guidance indicates that chemicals should be classified as Category 1B when “data from animal studies provide clear evidence of an adverse effect on sexual function and fertility or on development in the absence of other toxic effects, or if occurring together with other toxic effects the adverse effect on reproduction is considered not to be a secondary no-specific consequence of other toxic effects. However, when there is mechanistic information that raises doubt about the relevance of the effect for humans, classification in Category 2 may be more appropriate” (UN 2015). As relevance of the available rodent data to humans is unclear and mechanistic data suggest that methanol-induced developmental toxicity may be a secondary effect to systemic toxicity, ToxServices considered methanol to be GHS Category 2, which warrants a Moderate score. This is a more conservative approach than not classifying methanol for developmental toxicity, which is the approach taken by the EU RAC (EC 2014b), but is consistent with the MAK Pregnancy Group C authoritative list. Therefore, methyl acetate was assigned a Moderate score.

¹⁵ Methanol was listed on California’s Proposition 65 based on the US NIH classification, via the authoritative bodies listing mechanism (OEHHA 2012).

GreenScreen® Version 1.3 Assessment Template – February 2017

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**Endocrine Activity (E) Score (H, M, or L): M**

Methyl acetate was assigned a score of Moderate for endocrine activity based on limited evidence of endocrine organ weight (adrenal and thymus) changes in rats following repeated inhalation of methyl acetate. GreenScreen® criteria classify chemicals as a Moderate hazard for endocrine activity when there is evidence of endocrine activity (CPA 2017c). Confidence in this classification is reduced because it is unclear in the reported changes in adrenal and thymus weight alter organ function or hormone synthesis.

- **Authoritative and Screening Lists**
  - **Authoritative:** Not listed on any authoritative lists for this endpoint.
  - **Screening:** Not listed on any authoritative lists for this endpoint.
- Not listed as a potential endocrine disruptor on the EU Priority List of Suspected Endocrine Disruptors.
- Not listed as a potential endocrine disruptor on the OSPAR List of Chemicals of Possible Concern.
- Methyl Acetate (CAS #79-20-9)
  - **ECB 2003**
    - **Inhalation:** A 28-day inhalation study (OECD Guideline 412) was conducted using male and female Sprague Dawley rats. Animals (ten/sex/dose) were exposed to methyl acetate (purity > 99.5%) at concentrations of 75, 350, and 2,500 ppm via nose-only inhalation six hours a day, five days a week, for 28 days. Increased adrenal weights were found in high concentration males and females and decreased thymus weights were found in females of the intermediate concentration. No treatment-related macroscopic changes were found. Study authors considered the changes in adrenal weight to be equivocal because no morphological abnormality of the adrenal was observed; they report it indicates a nonspecific toxic effect due to stress. However, they also note a specific response of the adrenal cortex cannot be excluded because steroid hormone concentrations were not generated. This study is discussed in further detail in the repeated dose toxicity section below.

**Group II and II* Human Health Effects (Group II and II* Human)**

**Note:** Group II and Group II* endpoints are distinguished in the v 1.2 Benchmark system. For Systemic Toxicity and Neurotoxicity, Group II and II* are considered sub-endpoints and test data for single or repeated exposures may be used. If data exist for single OR repeated exposures, then the endpoint is not considered a data gap. If data are available for both single and repeated exposures, then the more conservative value is used.

**Acute Mammalian Toxicity (AT) Group II Score (vH, H, M, or L): L**

Methyl acetate was assigned a score of Low for acute toxicity based on the results of acute toxicity studies in rats. GreenScreen® criteria classify chemicals as a Low hazard for acute toxicity when oral and dermal LD$_{50}$ values are greater than 2,000 mg/kg and inhalation LC$_{50}$ values are greater than 20 mg/L (CPA 2017c). Confidence in this classification is high because it is based on reliable animal studies.

- **Authoritative and Screening Lists**
  - **Authoritative:** Not listed on any authoritative lists for this endpoint.
  - **Screening:**
    - **New Zealand - GHS - 6.1E (oral) - Acutely toxic**
      - Based on an oral LD$_{50}$ of 3,705 mg/kg in rabbits (CCID 2017)
- Methyl Acetate (CAS #79-20-9)
• ECB 2003, ECHA 2017b
  ▪ Oral: LD₅₀ (male Carworth-Wistar rat) = 6,482 mg/kg (non-GLP-compliant, similar to OECD Guideline 401)
  ▪ Dermal: LD₅₀ (Wistar rat) = greater than 2,000 mg/kg (GLP-compliant, OECD Guideline 402)
• ECB 2003
  ▪ Inhalation: 4-hour LC₅₀ (rat) = greater than 49 mg/L
• ECHA 2017b
  ▪ Inhalation: 4-hour whole body vapor LC₅₀ (albino rabbit) = greater than 49.2 mg/L and less than 98.4 mg/L

Systemic Toxicity/Organ Effects incl. Immunotoxicity (ST)

Group II Score (single dose) (vH, H, M, or L): M
Methyl acetate was assigned a score of Moderate for systemic toxicity (single dose) based on evidence of respiratory tract irritation in humans and animals. GreenScreen® criteria classify chemicals as a Moderate hazard for systemic toxicity (single dose) when they are classified as GHS Category 3 (transient target organ effects, respiratory tract irritation) (CPA 2017c). Confidence in this classification is high because it is based on both human and animal data.
  • Authoritative and Screening Lists
    o Authoritative: Not listed on any authoritative lists for this endpoint.
    o Screening:
      ▪ Japan - GHS - Specific target organs/systemic toxicity following single exposure - Category 3 (respiratory tract irritation)
      • Based on human observations recorded in multiple sources.
  • Methyl Acetate (CAS #79-20-9)
    o ECB 2003
      ▪ Exposure to methyl acetate vapor at ≥ 15 mg/L for 5 minutes led to respiratory irritation in humans.
      ▪ Inhalation of methyl acetate vapor causes irritation of the upper respiratory tract in animals.
      ▪ Dermal: No adverse systemic effects were found in rats following occlusive application of 2,000 mg/kg methyl acetate for 24 hours in male and female rats.

Group II® Score (repeated dose) (H, M, or L): M
Methyl acetate was assigned a score of Moderate for systemic toxicity (repeated dose) based on the results of a 28-day inhalation study in rats. GreenScreen® criteria classify chemicals as a Moderate hazard for systemic toxicity (repeated dose) when adverse effects occur at concentrations between 0.2 and 1.0 mg/L/6h/day in a 90-day study (CPA 2017c). Confidence in this classification is reduced because the NOAEC and LOAEC values from the study straddle the GHS guidance values.
  • Authoritative and Screening Lists
    o Authoritative: Not listed on any authoritative lists for this endpoint.
    o Screening:
      ▪ Japan - GHS - Specific target organs/systemic toxicity following repeated exposure - Category 1
      • Based on effects on optic nerve (NITE 2006). No further details were provided. This classification is considered in the repeated dose neurotoxicity
section below.

- Methyl Acetate (CAS #79-20-9)
  - ECB 2003
    - Inhalation: A 28-day inhalation study (OECD Guideline 412) was conducted using male and female Sprague Dawley rats. Animals (ten/sex/dose) were exposed to methyl acetate (purity > 99.5%) at concentrations of 75, 350, and 2,500 ppm via nose-only inhalation six hours a day, five days a week, for 28 days. In the high concentration group, decreased body weight, decreased food consumption, and increased mean values of erythrocyte counts, hemoglobin, and hematocrit were found. Additionally, total counts of leukocytes and lymphocytes were decreased in the high concentration group. Treatment produced a dose-related decrease in cholesterol level, which reached significance at all concentrations in females and in males at the high concentration. A significant increase in alanine aminotransferase activity was seen in high concentration females. High concentration females also had significant increases in urine volume and decreases in specific weight. The authors noted that due to the decreased body weight, several absolute organ weights were decreased and relative organ weights were increased in high concentration males (specific organs were not reported). Increased adrenal weights were found in high concentration males and females and decreased thymus weights were found in females of the intermediate concentration. No treatment-related macroscopic changes were found. Histopathologic examination found slight to moderate degeneration and necrosis of the olfactory epithelium (at level 3 out of 4 sections) of high concentration males and females. Study authors considered the changes in adrenal weight to be equivocal because no morphological abnormality of the adrenal was observed. The authors note it indicates a nonspecific toxic effect due to stress. However, they note a specific response of the adrenal cortex cannot be excluded because steroid hormone concentrations were not generated. A NOAEC of 350 ppm (1,057 mg/m³ or 1.057 mg/L, which is equivalent to 0.75 mg/L after adjustment for treatment frequency) was established, based on impaired body weight gain, decreased food consumption, and pathological changes in the olfactory epithelium. The LOAEC is 2,500 ppm (5.4 mg/L/6h/day). Based on the NOAEC of 0.75 mg/L/6h/day and LOAEC of 5.4 mg/L/6h/day, methyl acetate is at most classified as GHS Category 2.

Neurotoxicity (N)

**Group II Score (single dose) (vH, H, M, or L): M**

Methyl acetate was assigned a score of Moderate for neurotoxicity (single dose) based on evidence of narcotic effects in humans and animals, and association with the authoritative H336 and R67 lists. GreenScreen® criteria classify chemicals as a Moderate hazard for neurotoxicity (single dose) when they are classified as GHS Category 3 (transient target organ effects, narcotic effects) (CPA 2017c). Confidence in this classification is high because it is based on animal and human data, as well as authoritative lists.

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16 1.057 mg/L * 5 days/7 days = 0.75 mg/L
17 2,500 (ppm) * MW/24,450 * 5 days/7 days = 5.4 (mg/L/6h/day)
• Authoritative and Screening Lists
  o **Authoritative:**
    ▪ EU - GHS (H-Statements) - H336 - May cause drowsiness or dizziness
    ▪ EU - R-phrases - R67 - Vapors may cause drowsiness and dizziness
  o **Screening:**
    ▪ Malaysia - GHS - H336 - May cause drowsiness or dizziness
    ▪ Australia - GHS - H336 - May cause drowsiness or dizziness
    ▪ Boyes - Neurotoxicants – Neurotoxic
    ▪ Japan – GHS – Specific target organ/systemic toxicity following single exposure – Category 1 (nervous system) – based on dizziness, vertigo, headache, unstable walk, vision disappearance of both eyes, withering of optic nerve, scotoma expansion of eyes, tunnel vision, and anesthesia action described in EU’s RAR document (2003) in occupationally exposed humans. – ToxServices noted that the more severe effects than narcotic effects are reported only in a few case reports, and insufficient data were provided regarding co-exposures to other solvents, which may be more neurotoxic.
  • Not classified as a developmental neurotoxicant (Grandjean and Landrigan 2006, 2014).
• Methyl Acetate (CAS #79-20-9)
  o ECB 2003
    ▪ Narcotic effects have been found following inhalation and have a short duration. Narcotic effects start at 34 mg/L in mice and 56 mg/L in cats.
    ▪ In humans, inhalation of methyl acetate for 45min caused severe headache and considerable somnolence which lasted over 6 hours.

**Group II* Score (repeated dose) (H, M, or L): M**
Methyl acetate was assigned a score of Moderate for neurotoxicity (repeated dose) based ToxServices conservatively classifying it as a GHS Category 2 systemic toxicant following repeated dose for neurotoxicity. GreenScreen® criteria classify chemicals as a Low to Moderate hazard for neurotoxicity (repeated dose) when they are classified as GHS Category 2 systemic toxicants following repeated dose for neurotoxicity (CPA 2017c). The confidence in the score is low as there are limited details regarding effects following repeated exposures in humans and a screening list.
• Authoritative and Screening Lists
  o **Authoritative:** Not listed on any authoritative lists for this endpoint.
  o **Screening:**
    ▪ Boyes - Neurotoxicants – Neurotoxic
    ▪ Japan - GHS - Specific target organs/systemic toxicity following repeated exposure - Category 1
      • Based on effects on optic nerve (NITE 2006). No further details were provided.
  • Not classified as a developmental neurotoxicant (Grandjean and Landrigan 2006, 2014).
- **Methyl Acetate (CAS #79-20-9)**
  - ECB 2003
    - Women exposed to a liquid mixture of methylformate, ethylformate, ethyl acetate, and methyl acetate during work in a shoe factory suffered from eye irritation, visual disorders, central nervous system (CNS) symptoms, difficulty breathing, and heart trouble. No further details were provided.
  - HSDB 2015
    - A neurotoxicity study was conducted with a thinner containing 52.8% toluene, 21.7% isopropyl alcohol, 12.6% methyl acetate, 3.4% ethyl acetate, 3.2% butyl acetate, 3.4% isobutyl ketone and 2.9% methanol in rats. Animals were exposed to the vapor mixture twice a day for 10 minutes at 10 minutes intervals, 6 days per week for 12 – 14 months at the concentration of 0 or 10,000 ppm. Treatment caused suppressed body weight gain. Increased abnormal cristae of mitochondria in the neuron and axon and increased number of ER ribosomes and dilated Golgi apparatus in the neuron were observed in the cerebral cortex slices. In addition, there were increased lysosomes and lipid materials in the neuron which suggest a neurodegenerative process.
- **Analog: Methanol (CAS #67-56-1)**
  - U. S. EPA 2013
    - *Inhalation* - Human (inhalation) exposure studies at the threshold limit value (TLV) of 200 ppm (0.26 mg/L) indicate impairment to neurological function (e.g. sensory evoked potentials, memory testing and psychomotor testing) in the absence of measurable formate production.
    - *Inhalation* – In the derivation of an inhalation RfC for methanol, the U.S. EPA selected neurotoxicity as one of the critical effects, and performed benchmark dose modeling to derive a point of departure for neurotoxicity based on decreased male offspring brain weight in a two-generation toxicity inhalation study in rats. The internal dose BMDL was 858 mg-hr/L, which is equivalent to 2 mg/L based on PBPK modeling.
    - *Oral* - In a developmental study in rats, female Wistar albino rats (80/group) were fed folic acid deficient (FAD) or folic acid sufficient (FAS) diets for 14-16 weeks. They were mated and methanol was given in the drinking water at 0, 1, 2, or 4% (0, 480, 960 or 1,920 mg/kg/day) throughout lactation period. Pups were exposed to methanol via lactation from postnatal day (PND) 1 to PND 21. Neurobehavioral parameters and neurochemical parameters were measured at PND 45. Expression of growth-associated protein (GAP 43) was examined using immunohistochemistry and Western blot analysis. For the purpose of this evaluation, only data on the FAS group were summarized below. The authors reported significantly decreased (32%) dopamine levels at 4%. Significant increases in activity (distance traveled in a spontaneous locomotor activity test) were found at 2% and 4%. Dopamine receptor (D2) binding in the hippocampus was significantly increased in the 2 and 4% groups. Increased expression of GAP 43 protein was found at 4%. ToxServices established the NOAEL and LOAEL at 1 and 2% (480 and 960 mg/kg/day), respectively, for this study.
  - *Oral* – In a 90-day gavage study in Sprague-Dawley rats (30/sex/dose), reduced brain weight was found at 2,500 mg/kg/day in both sexes. Increased incidence of colloid in the hypophyseal cleft of the pituitary gland was also found at this dose. Based on these findings, U.S. EPA (2013b) established the NOAEL and LOAEL of 500 and 2,500 mg/kg/day, respectively. **In summary,** very
limited data were identified which found CNS effects in women following occupational exposure to a liquid mixture which contained methyl acetate. A solvent mixture containing methyl acetate led to neurodegenerative changes in the brain of rats after chronic exposure at a high concentration. The Boyes neurotoxic classification does not provide additional resolution as it corresponds to all possible scores for repeated dose neurotoxicity. Methanol is a known neurotoxicant. While effects were observed in humans after methanol exposure, NOAEL/NOAEC values in animal studies by oral and inhalation routes are above the GHS categorization cutoffs. In order to be protective of human health, ToxServices conservatively classified methyl acetate as a GHS Category 2 systemic toxicant following repeated dose for neurotoxicity based on the limited evidence of CNS symptoms observed in humans to a mixture containing methyl acetate and its classification as a Boyes neurotoxicant.

**Skin Sensitization (SnS) Group II* Score (H, M, or L): L**

Methyl acetate was assigned a score of Low for skin sensitization based on negative results in a human maximization test and the absence of skin sensitization following a long history of human exposure. GreenScreen® criteria classify chemicals as a Low hazard for skin sensitization when adequate data are available and negative (CPA 2017c). Confidence in this classification is high because it is based on conclusions drawn by an authoritative body.

- **Authoritative and Screening Lists**
  - **Authoritative:** Not listed on any authoritative lists for this endpoint.
  - **Screening:** Not listed on any authoritative lists for this endpoint.

- **Methyl Acetate (CAS #79-20-9)**
  - ECB 2003
    - Methyl acetate (10%) was not sensitizing in a maximization test with 25 volunteers.
    - Methyl acetate is not expected to be a skin sensitizer based on its long history of human exposure without instances of skin sensitization. Especially since it is hydrolyzed when in contact with water by non-specific tissue esterases to methanol and acetic acid. Methanol is not a skin sensitizer and the cases of skin sensitization due to acetic acid are limited.

**Respiratory Sensitization (SnR) Group II* Score (H, M, or L): L**

Methyl acetate was assigned a score of Low for respiratory sensitization based on ECHA guidance. GreenScreen® criteria classify chemicals as a Low hazard for respiratory sensitization when they are not GHS classified (CPA 2017c). Confidence in this score is reduced because there are not validated test methods for respiratory sensitization.

- **Authoritative and Screening Lists**
  - **Authoritative:** Not listed on any authoritative lists for this endpoint.
  - **Screening:** Not listed on any authoritative lists for this endpoint.

- **Methyl Acetate (CAS #79-20-9)**
  - No data were identified for this endpoint.

- Based on the weight of evidence and guidance from ECHA regarding assessment of respiratory sensitization potential, a score of Low was assigned. The guidance from ECHA states that the mechanisms leading to respiratory sensitization are essentially similar to those leading to skin sensitization (ECHA 2016). ECHA recommended that if a chemical is not a dermal sensitizer based on high quality data, it is unlikely to be a respiratory sensitizer. ECHA also noted that this rationale does not cover respiratory hypersensitivity caused by non-immunological mechanisms, for which human experience is the main evidence of activity (ECHA 2016). As methyl acetate was not
sensitizing to the skin of human volunteers, and a literature search did not find any human evidence of respiratory sensitization by methyl acetate, and as it does not contain any structural alerts for respiratory sensitization (OECD 2016), it is not expected to be a respiratory sensitizer. Confidence in the score is low as this evaluation does not include non-immunologic mechanisms of respiratory sensitization, and no specific data are available for respiratory sensitization.

**Skin Irritation/Corrosivity (IrS) Group II Score (vH, H, M, or L): L**

Methyl acetate was assigned a score of Low for skin irritation/corrosivity based on the absence of skin irritation in an OECD Guideline study in rabbits. GreenScreen® criteria classify chemicals as a Low hazard for skin irritation/corrosivity when adequate data are available and negative (CPA 2017c). Confidence in this classification is high because it is based on a well-conducted study.

- **Authoritative and Screening Lists**
  - **Authoritative:** Not listed on any authoritative lists for this endpoint.
  - **Screening:**
    - New Zealand - GHS - 6.3A - Irritating to the skin (Cat. 2)
      - Based on moderate skin irritation in rabbits. No study details were provided (CCID 2017).
    - **Other:**
      - EU - R-phrases - R66: Repeated exposure may cause skin dryness or cracking

- **Methyl Acetate (CAS #79-20-9)**
  - ECB 2003, ECHA 2017b
  - Methyl acetate was not irritating in a GLP-compliant, OECD Guideline 404/EU Method B.4 study. New Zealand White rabbits (n=3, sex not reported) were administered topical applications of 0.5 mL undiluted methyl acetate (99.9% purity) to shaved skin under semi-occlusive conditions for 4 hours. An observation period of 72 hours followed the exposure period. No edema was observed but slight erythema (grade 1) was observed in all three animals at the 1-hour time point and in two animals at the 24 hour time point. The mean erythema score at 30-60 minutes, 24, 48, and 72 hours was 0.2 (max score of 0.3). The mean erythema score at 24, 48, and 72 hours was 0.17 (individual scores of 0, 0.3, and 0.2). Erythema was fully reversible within 48 hours. Dry skin was observed at 24, 48, and 72 hours following patch removal.
    - Based on the results of the above test, ToxServices did not classify methyl acetate as a skin irritant under GHS criteria (UN 2015). GHS criteria define skin irritants as chemicals that produce mean erythema and/or edema scores of ≥ 1.5 from gradings in at least 2 of 3 animals from grades at 24, 48, and 72 hours.
    - Repeated exposure to methyl acetate causes skin dryness and roughness in humans.
  - Although New Zealand has classified methyl acetate as a dermal irritant based on moderate irritation effects observed in rabbits, the results of a high quality rabbit dermal irritation test indicate that methyl acetate should not be classified as a dermal irritant under GHS criteria. Therefore, ToxServices relied on data from the high quality animal study to assign a score for this study.

**Eye Irritation/Corrosivity (IrE) Group II Score (vH, H, M, or L): H**

Methyl acetate was assigned a score of High for eye irritation/corrosivity based on association with the authoritative H319 and R36 lists. GreenScreen® criteria classify chemicals as a High hazard for eye
irritation/corrosivity when they are associated with the authoritative H319 and R36 lists (CPA 2017c). Confidence in this score is high because it is based on an authoritative list.

- Authoritative and Screening Lists
  - Authoritative:
    - EU - GHS (H-statements) - H319 - Causes serious eye irritation
    - EU - R-phrases - R36 - Irritating to eyes
  - Screening:
    - New Zealand - GHS - 6.4A - Irritating to the eye (Cat. 2A)
      - Based on moderate eye irritation in rabbits. No study details were provided (CCID 2017).
    - Malaysia - GHS - H319 - Causes serious eye irritation
    - Australia - GHS - H319 - Causes serious eye irritation
    - Japan - GHS - Serious eye damage / eye irritation - Category 2B
      - Based on the studies summarized below (NITE 2006)
  - Methyl Acetate (CAS #79-20-9)
    - ECB 2003, ECHA 2017b
      - Methyl acetate (purity not specified) caused eye irritation in a GLP-compliant OECD Guideline 405/EU Method B.5 study conducted in New Zealand White rabbits (n=3, sex not reported). Undiluted methyl acetate (0.1 mL) was instilled into one eye of each animal and the eyes were rinsed with a sodium chloride solution 24 hours after instillation. An observation period of 7 days followed the instillation. At 24, 48, and 72 hours, the mean opacity score was 1.3 (maximum score of 1.7), the mean iris score was 1 (maximum score of 1), the mean conjunctival score was 2.7 (maximum score of 3), and the mean chemosis score was 1.8 (maximum score of 2). All of the irritation effects cleared within 7 days. The study authors concluded that methyl acetate was irritating to the eyes in this study.
      - Based on the results of the above test, ToxServices classified methyl acetate as a Category 2B eye irritant under GHS criteria (UN 2015). Under GHS criteria, chemicals are classified as Category 2B eye irritants if they produce mean scores ≥ 1 for corneal opacity, ≥ 1 for iritis, ≥ 2 for conjunctival redness, and/or ≥ 2 for chemosis in at least 2 of 3 animals following gradings at 24, 48, and 72 hours, and the irritant effects are fully reversible within 7 days.
    - ECB 2003
      - Exposure to methyl acetate vapor causes eye irritation in humans.
  - Based on the weight of evidence, a score of High was assigned. Methyl acetate is associated with the authoritative H319 and R36 lists which warrant a High and Moderate to High score, respectively. The effects observed in a GLP-compliant, OECD Guideline 405 were sufficient to classify methyl acetate as a GHS Category 2B ocular irritant, which corresponds to a Moderate score for eye irritation. Human data demonstrate that methyl acetate vapor causes eye irritation. Therefore, a score of High was assigned based on association with authoritative lists and evidence of eye irritation in humans.

**Ecotoxicity (Ecotox)**

**Acute Aquatic Toxicity (AA) Score (vH, H, M, or L): L**
Methyl acetate was assigned a score of Low for acute aquatic toxicity based on L(EC50) values of > 120 – 1,027 mg/L. GreenScreen® criteria classify chemicals as a Low hazard for acute aquatic toxicity when acute aquatic toxicity values are greater than 100 mg/L (CPA 2017c). Confidence in this classification is high because it is based on well-conducted studies.

- **Authoritative and Screening Lists**
  - **Authoritative**: Not listed on any authoritative lists for this endpoint.
  - **Screening**: Not listed on any authoritative lists for this endpoint.

- **Methyl Acetate (CAS #79-20-9)**
  - **ECB 2003**
    - 48-hour LC50 (*Leuciscus idus*, ide) = 225 mg/L
    - 96-hour LC50 (*Pimephales promelas*, fathead minnow) = 320 mg/L
  - **ECB 2003, ECHA 2017b**
    - 48-hour mobility EC50 (*Daphnia magna*) = 1,027 mg/L (GLP-compliant, OECD Guideline 202/EU Method C.2/ISO 6341 15/DIN 38412 Part 11)
    - 72-hour growth EC50 (*Scenedesmus subspicatus*, green algae) = greater than 120 mg/L (GLP-compliant, OECD Guideline 201/EU Method C.3)
  - **ECHA 2017b**
    - 96-hour LC50 (*Danio rerio*, zebrafish) = 250-350 mg/L (GLP-compliant, OECD Guideline 203/EU Method C.1)

**Chronic Aquatic Toxicity (CA) Score (vH, H, M, or L): L**

Methyl acetate was assigned a score of Low for chronic aquatic toxicity based on the measured chronic value of 72.1 mg/L in fish supported by modeled data in daphnia and algae. GreenScreen® criteria classify chemicals as a Low hazard for chronic aquatic toxicity when the chronic aquatic toxicity values are greater than 10 mg/L (CPA 2017c). Confidence in this score is high because it is based on a measured value in fish.

- **Authoritative and Screening Lists**
  - **Authoritative**: Not listed on any authoritative lists for this endpoint.
  - **Screening**: Not listed on any authoritative lists for this endpoint.

- **Methyl Acetate (CAS #79-20-9)**
  - **ECB 2003, ECHA 2017b**
    - 72-hour growth NOEC (*S. subspicatus*, green algae) = 120 mg/L (GLP-compliant, OECD Guideline 201/EU Method C.3)
  - **U.S. EPA 2012a**
    - Methyl acetate has a measured chronic aquatic toxicity value of 72.1 mg/L in fish.
    - Methyl acetate is designated to the esters ECOSAR chemical class. The most conservative predicted chronic values are 12.16 mg/L in fish, 333.68 mg/L in daphnia, and 23.308 mg/L in green algae. See Appendix D for modeling results.
Environmental Fate (Fate)

Persistence (P) Score (vH, H, M, L, or vL): vL
Methyl acetate was assigned a score of Very Low for persistence because it was readily biodegradable in an OECD Guideline 301D test and because it is predicted to mainly partition to water and soil. GreenScreen® criteria classify chemicals as a Very Low hazard for persistence when they primarily partition to soil and water and are readily biodegradable (CPA 2017c). Confidence in this classification is high because it is based on a well-conducted study.

- Authoritative and Screening Lists
  - Authoritative: Not listed on any authoritative lists for this endpoint.
  - Screening:
    - EC - CEPA DSL – Persistent
    - Based on measured degradation rates in the air
- Methyl Acetate (CAS #79-20-9)
  - ECB 2003, ECHA 2017b
    - A GLP-compliant ready biodegradability test conducted according to OECD Guideline 301 D (Closed Bottle Test)/EU Method C.4-E/ISO DIS 10707 was performed with non-adapted activated domestic sludge exposed to methyl acetate (99.9% purity) at 3.6 mg/L (5.44 mg/L COD) for 28 days. The level of degradation was 74% after 14 days, 75% after 19 days, and 70% after 28 days. The 10-day window was met and the study authors concluded that methyl acetate was readily biodegradable in this test.
  - ECHA 2017b
    - A ready biodegradability test conducted according to OECD Guideline 301 C (Modified MITI Test) was performed with
  - U.S. EPA 2012b
    - The BIOWIN modeling Ready Biodegradable Predictor indicates that methyl acetate is expected to be readily biodegradable. Fugacity modeling predicts 41.2% will partition to water with a half-life of 15 days, 40.2% will partition to soil with a half-life of 30 days, and 18.5% will partition to air with a half-life of 31 days. See Appendix E for modeling results.

Bioaccumulation (B) Score (vH, H, M, L, or vL): vL
Methyl acetate was assigned a score of Very Low for bioaccumulation based on its predicted BCF of 0.9433 and measured log K_{ow} of 0.18. GreenScreen® criteria classify chemicals as a Very Low hazard for bioaccumulation when the BCF is less than 100 and the log K_{ow} is less than 4 (CPA 2017c). Confidence in this classification is high because it is based on a measured log K_{ow}.

- Authoritative and Screening Lists
  - Authoritative: Not listed on any authoritative lists for this endpoint.
  - Screening: Not listed on any authoritative lists for this endpoint.
- Methyl Acetate (CAS #79-20-9)
  - ECHA 2017b
    - Methyl acetate has an experimental partition coefficient (log K_{ow}) of 0.18.
  - U.S. EPA 2012b
    - BCFBAF predicts BCF of 0.9433 based on a log K_{ow} of 0.18. See Appendix E for modeling results.
Physical Hazards (Physical)

Reactivity (Rx) Score (vH, H, M, or L): L
Methyl acetate was assigned a score of Low for reactivity because it is not explosive or oxidizing. GreenScreen® criteria classify chemicals as a Low hazard for reactivity when they are explosive or oxidizing (CPA 2017c). Confidence in this score is high because it is based on the conclusions drawn by an authoritative body.

- Authoritative and Screening Lists
  - Authoritative: Not listed on any authoritative lists for this endpoint.
  - Screening: Not listed on any authoritative lists for this endpoint.
- Methyl Acetate (CAS #79-20-9)
  - ECB 2003
    - Methyl acetate is not explosive or oxidizing.

Flammability (F) Score (vH, H, M, or L): H
Methyl acetate was assigned a score of High for flammability because it is associated with the authoritative H225 list and classified as a GHS Category 2 flammable liquid. GreenScreen® criteria classify chemicals as a High hazard for flammability when they are associated with H225 and when they are classified as GHS Category 2 flammable liquids (CPA 2017c). Confidence in this score is high because it is based on an authoritative list and measured data.

- Authoritative and Screening Lists
  - Authoritative:
    - EU - GHS (H-Statements) - H225 - Highly flammable liquid and vapor
    - EU - R-phrases - R11 - Highly flammable (LIQUID)
  - Screening:
    - New Zealand - GHS - 3.1B - Flammable Liquids: high hazard
      - Based on a flash point of -10°C in a closed cup test and a boiling point of 56.8°C (CCID 2017)
    - Japan - GHS - Flammable liquids - Category 2
    - Malaysia - GHS - H225 - Highly flammable liquid and vapor
    - Australia - GHS - H225 - Highly flammable liquid and vapor
- Methyl Acetate (CAS #79-20-9)
  - ECB 2003
    - Flash point = -10°C, boiling point = 57°C
  - ECHA 2017b
    - Methyl acetate has a flash point of -13°C at 1,013 hPa in a close cup test.
    - Methyl acetate has a self-ignition temperature of 454°C at 1,013 hPa.
- Based on the weight of evidence, ToxServices classified methyl acetate as a Category 2 flammable liquid under GHS criteria (UN 2015) because it has a flash point < 23°C and a boiling point > 35°C.
References


European Comission (EC). 2008. Draft Assessment Report (DAR). Initial risk assessment provided by the rapporteur Member State Germany for the existing active substance acetic acid of the fourth stage of GreenScreen® Version 1.3 Assessment Template – February 2017. GS-896 Limited license provided to University of Massachusetts Lowell for public distribution through the University of Massachusetts Lowell website, publications, presentations and for no other purpose whatsoever. Further copying, resale, and distribution are expressly prohibited.


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APPENDIX A: Hazard Benchmark Acronyms
(in alphabetical order)

(AA) Acute Aquatic Toxicity
(AT) Acute Mammalian Toxicity
(B) Bioaccumulation
(C) Carcinogenicity
(CA) Chronic Aquatic Toxicity
(D) Developmental Toxicity
(E) Endocrine Activity
(F) Flammability
(IrE) Eye Irritation/Corrosivity
(IrS) Skin Irritation/Corrosivity
(M) Mutagenicity and Genotoxicity
(N) Neurotoxicity
(P) Persistence
(R) Reproductive Toxicity
(Rx) Reactivity
(SnS) Sensitization- Skin
(SnR) Sensitization- Respiratory
(ST) Systemic/Organ Toxicity
## APPENDIX B: Results of Automated GreenScreen® Score Calculation for Methyl Acetate (CAS #79-20-9)

### Table 1: Hazard Table

<table>
<thead>
<tr>
<th>Chemical</th>
<th>CAS#</th>
<th>Group I Human</th>
<th>Group II and III Human</th>
<th>Ecotox</th>
<th>Fate</th>
<th>Physical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methyl Acetate</td>
<td>79-20-9</td>
<td>L L L M M L M M M L L L H L L vL vL L H</td>
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<td></td>
<td></td>
<td></td>
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### Table 2: Chemical Details

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<th>Chemical Name</th>
<th>CAS#</th>
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<th>M</th>
<th>R</th>
<th>D</th>
<th>E</th>
<th>AT</th>
<th>STE</th>
<th>STTr</th>
<th>Ns</th>
<th>Nr</th>
<th>SNS*</th>
<th>SNR*</th>
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<th>CA</th>
<th>P</th>
<th>B</th>
<th>Rs</th>
<th>F</th>
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<td>79-20-9</td>
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<td>L</td>
<td>L</td>
<td>L</td>
<td>H</td>
<td>L</td>
<td>L</td>
<td>vL</td>
<td>vL</td>
<td>L</td>
<td>H</td>
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### Table 3: Hazard Summary Table

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<th>Benchmark</th>
<th>Chemical Name</th>
<th>Preliminary GreenScreen® Benchmark Score</th>
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</thead>
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<td>1</td>
<td>Methyl Acetate</td>
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<tr>
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</tr>
<tr>
<td>3</td>
<td>STOP</td>
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</tr>
<tr>
<td>4</td>
<td>STOP</td>
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</tr>
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</table>

### Table 4: Chemical Name

<table>
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<th>Chemical Name</th>
<th>Preliminary GreenScreen® Benchmark Score</th>
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<tr>
<td>Methyl Acetate</td>
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### Table 5: Data Gap Assessment Table

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<th>Chemical Name</th>
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<td></td>
</tr>
<tr>
<td>3</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>4</td>
<td>Yes</td>
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</tr>
</tbody>
</table>

### Table 6: Chemical Name

<table>
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<th>Chemical Name</th>
<th>Final GreenScreen® Benchmark Score</th>
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</thead>
<tbody>
<tr>
<td>Methyl Acetate</td>
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</tr>
</tbody>
</table>

Note: Chemical has not undergone a data gap assessment. Not a Final GreenScreen™ Score.

After Data gap Assessment

Note: No Data gap Assessment Done if Preliminary GS Benchmark Score is 1.

---

GreenScreen® Version 1.3 Assessment Template – February 2017

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### APPENDIX C: Pharos Output for Methyl Acetate (CAS #79-20-9)

#### [79-20-9] METHYL ACETATE

<table>
<thead>
<tr>
<th>Direct Hazards:</th>
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<tbody>
<tr>
<td><strong>DEVELOPMENTAL</strong></td>
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<tr>
<td>MAK - Pregnancy Risk Group C</td>
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<tr>
<td><strong>ORGAN TOXICANT</strong></td>
</tr>
<tr>
<td>Japan - GHS - Specific target organs/systemic toxicity following repeated exposure - Category 1</td>
</tr>
<tr>
<td>Japan - GHS - Specific target organs/systemic toxicity following single exposure - Category 1</td>
</tr>
<tr>
<td>Japan - GHS - Specific target organs/systemic toxicity following single exposure - Category 1-2</td>
</tr>
<tr>
<td><strong>FLAMMABLE</strong></td>
</tr>
<tr>
<td>EU - GHS (H-Statements) - H225 - Highly flammable liquid and vapour</td>
</tr>
<tr>
<td>Québec CSST - WHMIS 1988 - Class B2 - Flammable liquids</td>
</tr>
<tr>
<td>New Zealand - GHS - 3.1B - Flammable Liquids: high hazard</td>
</tr>
<tr>
<td>Japan - GHS - Flammable liquids - Category 2</td>
</tr>
<tr>
<td>EU - R-phrases - R11 - Highly flammable (LIQUID)</td>
</tr>
<tr>
<td>Malaysia - GHS - H225 - Highly flammable liquid and vapour</td>
</tr>
<tr>
<td>Australia - GHS - H225 - Highly flammable liquid and vapour</td>
</tr>
<tr>
<td><strong>NEUROTOXICITY</strong></td>
</tr>
<tr>
<td>EU - GHS (H-Statements) - H336 - May cause drowsiness or dizziness</td>
</tr>
<tr>
<td>Boyes - Neurotoxicants - Neurotoxic</td>
</tr>
<tr>
<td>EU - R-phrases - R67 - Vapors may cause drowsiness and dizziness</td>
</tr>
<tr>
<td>Malaysia - GHS - H336 - May cause drowsiness or dizziness</td>
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<tr>
<td>Australia - GHS - H336 - May cause drowsiness or dizziness</td>
</tr>
<tr>
<td>Category</td>
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</tr>
<tr>
<td>MAMMALIAN</td>
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</tr>
<tr>
<td>EYE IRRITATION</td>
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<td>SKIN IRRITATION</td>
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<td>MULTIPLE</td>
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<tr>
<td>PERSISTENT</td>
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<tr>
<td>EXEMPT</td>
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</tbody>
</table>
APPENDIX D: ECOSAR Modeling Results for Methyl Acetate (CAS #79-20-9)

ECOSAR Version 1.11 Results Page

SMILES: O=C(OC)C
CHEM: Acetic acid, methyl ester
CAS Num: 000079-20-9
ChemID1:
MOL FOR: C3 H6 O2
MOL WT: 74.08
Log K\text{ow}: 0.373 (EPISuite K\text{ow} win v1.68 Estimate)
Log K\text{ow}: 0.180 (User Entered)
Log K\text{ow}: 0.18 (PhysProp DB exp value - for comparison only)
Melt Pt: -98.00 (deg C, User Entered for Wat Sol estimate)
Melt Pt: -98.00 (deg C, PhysProp DB exp value for Wat Sol est)
Wat Sol: 1.436E+005 (mg/L, EPISuite WSK\text{ow} win v1.43 Estimate)
Wat Sol: 243.5 (mg/L, User Entered)
Wat Sol: 2.43E+005 (mg/L, PhysProp DB exp value)

Values used to Generate ECOSAR Profile

Log K\text{ow}: 0.180 (User Entered)
Wat Sol: 243.5 (mg/L, User Entered)

Available Measured Data from ECOSAR Training Set

<table>
<thead>
<tr>
<th>Measured CAS No</th>
<th>Organism</th>
<th>Duration</th>
<th>End Pt mg/L (ppm)</th>
<th>Ecosar Class</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>000079-20-9</td>
<td>Fish</td>
<td>ChV</td>
<td>72.1</td>
<td>Esters</td>
<td>DUL</td>
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<tr>
<td>000079-20-9</td>
<td>Fish</td>
<td>96-hr.</td>
<td>LC50 320</td>
<td>Esters</td>
<td>DUL</td>
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<tr>
<td>000079-20-9</td>
<td>Fish</td>
<td>96-hr.</td>
<td>LC50 399</td>
<td>Esters</td>
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ECOSAR v1.1 Class-specific Estimations

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<tr>
<th>Predicted</th>
<th>ECOSAR Class</th>
<th>Organism</th>
<th>Duration</th>
<th>End Pt mg/L (ppm)</th>
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<tbody>
<tr>
<td></td>
<td>Esters</td>
<td>Fish</td>
<td>96-hr.</td>
<td>LC50 114.467</td>
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<tr>
<td></td>
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<td>Daphnid</td>
<td>48-hr.</td>
<td>LC50 289.142 *</td>
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<tr>
<td></td>
<td>Esters</td>
<td>Green Algae</td>
<td>96-hr.</td>
<td>EC50 164.183</td>
</tr>
</tbody>
</table>
Esters: Fish                          ChV       12.617
Esters: Daphnid                       ChV       333.680 *
Esters: Green Algae                   ChV       23.308
Esters: Fish (SW) 96-hr. LC50 194.668
Esters: Mysid 96-hr. LC50 469.433 *
Esters: Fish (SW) ChV 20.108
Esters: Mysid (SW) ChV 1.41e+006 *
Esters: Earthworm 14-day LC50 3729.663 *

===========================  ==================  ========  ========
Neutral Organic SAR : Fish 96-hr. LC50 2623.274 *
(Baseline Toxicity) : Daphnid 48-hr. LC50 1259.104 *
                          : Green Algae 96-hr. EC50 468.172 *
                          : Fish ChV 210.309
                          : Daphnid ChV 76.922
                          : Green Algae ChV 84.330

Note: * = asterisk designates: Chemical may not be soluble enough to measure this predicted effect. If the effect level exceeds the water solubility by 10X, typically no effects at saturation (NES) are reported.

-------------------------------
Class Specific LogK_{ow} Cut-Offs
-------------------------------
If the log K_{ow} of the chemical is greater than the endpoint specific cut-offs, presented below, then no effects at saturation are expected for those endpoints.

Esters:
------
Maximum LogK_{ow}: 5.0 (Fish 96-hr LC50; Daphnid LC50, Mysid LC50)
Maximum LogK_{ow}: 6.0 (Earthworm LC50)
Maximum LogK_{ow}: 6.4 (Green Algae EC50)
Maximum LogK_{ow}: 8.0 (ChV)

Baseline Toxicity SAR Limitations:
-------------------------------
Maximum LogK_{ow}: 5.0 (Fish 96-hr LC50; Daphnid LC50)
Maximum LogK_{ow}: 6.4 (Green Algae EC50)
Maximum LogK_{ow}: 8.0 (ChV)
APPENDIX E: EPISuite Modeling Results for Methyl Acetate (CAS #79-20-9)

CAS Number: 79-20-9
SMILES: O=C(OCC)
CHEM: Acetic acid, methyl ester
MOL FOR: C3 H6 O2
MOL WT: 74.08

Physical Property Inputs:
  Log K<sub>ow</sub> (octanol-water): 0.18
  Boiling Point (deg C): 57.00
  Melting Point (deg C): -98.70
  Vapor Pressure (mm Hg): 162.75
  Water Solubility (mg/L): 295
  Henry LC (atm-m<sup>3</sup>/mole): -----

Log Octanol-Water Partition Coef (SRC):
  Log K<sub>ow</sub> (K<sub>ow</sub>WIN v1.68 estimate) = 0.37
  Log K<sub>ow</sub> (Exper. database match) = 0.18

Boiling Pt, Melting Pt, Vapor Pressure Estimations (MPBPVP v1.43):
  Boiling Pt (deg C): 52.62 (Adapted Stein & Brown method)
  Melting Pt (deg C): -95.10 (Mean or Weighted MP)
  VP (mm Hg, 25 deg C): 222 (Mean VP of Antoine & Grain methods)
  VP (Pa, 25 deg C): 2.96E+004 (Mean VP of Antoine & Grain methods)
  MP (exp database): -98 deg C
  BP (exp database): 92 deg C
  VP (exp database): 2.16E+02 mm Hg (2.88E+004 Pa) at 25 deg C

Water Solubility Estimate from Log K<sub>ow</sub> (WSK<sub>ow</sub> v1.42):
  Water Solubility at 25 deg C (mg/L): 1.436e+005
  log K<sub>ow</sub> used: 0.18 (user entered)
  melt pt used: -98.70 deg C
  Water Sol (Exper. database match) = 2.43e+005 mg/L (20 deg C)

Water Sol Estimate from Fragments:
  Wat Sol (v1.01 est) = 1.1275e+005 mg/L

ECOSAR Class Program (ECOSAR v1.11):
  Class(es) found:
    Esters

Henry's Law Constant (25 deg C) [HENRYWIN v3.20]:
  Bond Method: 1.75E-004 atm-m<sup>3</sup>/mole (1.78E+001 Pa-m<sup>3</sup>/mole)
  Group Method: 1.17E-004 atm-m<sup>3</sup>/mole (1.19E+001 Pa-m<sup>3</sup>/mole)
Exper Database: 1.15E-04 atm-m³/mole (1.17E+001 Pa-m³/mole)

For Henry LC Comparison Purposes:
User-Entered Henry LC: not entered
Henry LC [via VP/WSol estimate using User-Entered or Estimated values]:
  HLC: 5.378E-002 atm-m³/mole (5.449E+003 Pa-m³/mole)
  VP: 163 mm Hg (source: User-Entered)
  WS: 295 mg/L (source: User-Entered)

Log Octanol-Air Partition Coefficient (25 deg C) [\(K_{ow}\) WIN v1.10]:
  Log \(K_{ow}\) used: 0.18 (user entered)
  Log \(K_{ow}\) used: -2.328 (exp database)
    Log \(K_{ow}\) (\(K_{ow}\) WIN v1.10 estimate): 2.508
    Log \(K_{ow}\) (experimental database): 2.310

Probability of Rapid Biodegradation (BIOWIN v4.10):
  Biowin1 (Linear Model): 0.8865
  Biowin2 (Non-Linear Model): 0.9976

Expert Survey Biodegradation Results:
  Biowin3 (Ultimate Survey Model): 3.1757 (weeks)
  Biowin4 (Primary Survey Model): 3.9698 (days)

MITI Biodegradation Probability:
  Biowin5 (MITI Linear Model): 0.8363
  Biowin6 (MITI Non-Linear Model): 0.9464

Anaerobic Biodegradation Probability:
  Biowin7 (Anaerobic Linear Model): 0.8488

Ready Biodegradability Prediction: YES

Hydrocarbon Biodegradation (BioHCwin v1.01):
  Structure incompatible with current estimation method!

Sorption to aerosols (25 Dec C)[AEROWIN v1.00]:
  Vapor pressure (liquid/subcooled): 2.17E+004 Pa (163 mm Hg)
  Log \(K_{oa}\) (Exp database): 2.310
  \(K_p\) (particle/gas partition coef. (m³/µg)):
    Mackay model: 1.38E-010
    Octanol/air (\(K_{oa}\)) model: 5.01E-011
  Fraction sorbed to airborne particulates (\(\phi\)):
    Junge-Pankow model: 4.99E-009
    Mackay model: 1.1E-008
    Octanol/air (\(K_{oa}\)) model: 4.01E-009

Atmospheric Oxidation (25 deg C) [AopWin v1.92]:
  Hydroxyl Radicals Reaction:
    OVERALL OH Rate Constant = 0.2598 E-12 cm³/molecule-sec
    Half-Life = 41.176 Days (12-hr day; 1.5E6 OH/cm³)
  Ozone Reaction:
    No Ozone Reaction Estimation
  Fraction sorbed to airborne particulates (\(\phi\)):
8.01E-009 (Junge-Pankow, Mackay avg)
4.01E-009 (K<sub>oa</sub> method)
Note: the sorbed fraction may be resistant to atmospheric oxidation

Soil Adsorption Coefficient (K<sub>oc</sub> WIN v2.00):
K<sub>oc</sub>: 3.064 L/kg (MCI method)
Log K<sub>oc</sub>: 0.486 (MCI method)
K<sub>oc</sub>: 9.101 L/kg (K<sub>ow</sub> method)
Log K<sub>oc</sub>: 0.959 (K<sub>ow</sub> method)

Aqueous Base/Acid-Catalyzed Hydrolysis (25 deg C) [HYDROWIN v2.00]:
Total Kb for pH > 8 at 25 deg C: 1.279E-001 L/mol-sec
Kb Half-Life at pH 8: 62.702 days
Kb Half-Life at pH 7: 1.717 years
(Total Kb applies only to esters, carboxmates, alkyl halides)

Bioaccumulation Estimates (BCFBAF v3.01):
Log BCF from regression-based method = 0.500 (BCF = 3.162 L/kg wet-wt)
Log Biotransformation Half-life (HL) = -1.9420 days (HL = 0.01143 days)
Log BCF Arnot-Gobas method (upper trophic) = -0.025 (BCF = 0.9433)
Log BAF Arnot-Gobas method (upper trophic) = -0.025 (BAF = 0.9433)
log K<sub>ow</sub> used: 0.18 (user entered)

Volatilization from Water:
Henry LC: 0.000115 atm·m<sup>3</sup>/mole (Henry experimental database)
Half-Life from Model River: 5.26 hours
Half-Life from Model Lake: 129.6 hours (5.398 days)

Removal in Wastewater Treatment:
Total removal: 7.29 percent
Total biodegradation: 0.09 percent
Total sludge adsorption: 1.68 percent
Total to Air: 5.52 percent
(using 10000 hr. Bio P,A,S)

Level III Fugacity Model:
<table>
<thead>
<tr>
<th>Mass Amount (percent)</th>
<th>Half-Life (hr.)</th>
<th>Emissions (kg/hr.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air</td>
<td>18.5</td>
<td>753</td>
</tr>
<tr>
<td>Water</td>
<td>41.2</td>
<td>360</td>
</tr>
<tr>
<td>Soil</td>
<td>40.2</td>
<td>720</td>
</tr>
<tr>
<td>Sediment</td>
<td>0.0808</td>
<td>3.24e+003</td>
</tr>
</tbody>
</table>
Persistence Time: 277 hr.
Licensed GreenScreen® Profilers

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