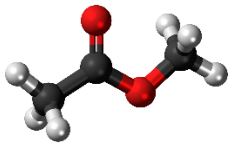
CAS Number: 79-20-9

QCAT Evaluation: Methyl acetate
Author: Lynn Coleman
Title: Environmental engineer
Organization: State of Washington
Date: November 29, 2016

Peer review:
Reviewer: Alex Stone
Title: Safer Chemical Alternative Chemist
Organization: WA Dept. of Ecology
Date: 15 February 2017

QCAT Chemical Assessment

Chemical Name:	Methyl acetate
CAS #:	79-20-9
Also Called:	Acetic acid, methyl ester, methyl ethanoate
Identify Applications/Functional Uses:	Solvent for: glues, paints, nail polish removers
Molecular Formula:	$C_3H_6O_2$ CH3COOCH3
Molecular Weight:	74.1
Chemical Structure:	
Optional Physicochemical Properties:	Flash point = -10°C (closed cup) Boiling point = 57°C GHS flammable liquid = Category 2 Not considered a HAP, TAP or VOC under the Washington Clean Air Act

Hazard Summary Table:

Human Health Group 1 (HH1)					Human Health Group 2 (HH2)							Ecological			Fate		Physical	
C	M	R	D	E	AT	ST	N	SnS	SnR	IrS	IrE	AA	CA	E_o	P	B	Ex	F
DG	L	L	M	DG	L							L			M	vL		

Grades		
Initial	**Data Gap**	**Final**
B	**C**	**C_{dg}**

The Pharos database was accessed on October 20, 2016 and used to research all Step 1 sources.

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Summary

An initial QCAT score of B is assigned to methyl acetate due to moderate scores for developmental toxicity and persistence. The final score is C_{dg} because there are data gaps for carcinogenicity and endocrine disruption. Other endpoint scores are low or very low.

Mutagenicity/genotoxicity data in Step II sources indicate negative results. A QCAT low level of concern is assigned. Reproductive toxicity data in Step II sources include inhalation No Observable Adverse Effects Concentrations (NOAECs). The assessor elected to use the available NOAEC data as a conservative indicator of LOAEC because NOAEC data are available in QCAT sources and LOAEC data are not. The NOAEC for this chemical meets QCAT technical criteria for a low level of concern. Therefore, the LOAEC for the chemical would also meet the technical criteria for a low level of concern as typically NOAEC values are lower than the LOAEC equivalent. A low level of concern for reproductive toxicity is assigned. Step I and II sources contain information on developmental toxicity. The Step II source provides information on an inhalation NOAEC. Information in both sources equates to a QCAT level of concern of medium for developmental toxicity.

For Acute Mammalian Toxicity, a single Step I source and three Step II sources have data. Step II sources include both oral and inhalation exposure. All equate to a low QCAT level of concern. Step II sources exist for Acute Aquatic Toxicity and all three equate to a level of concern of low.

Environment and Health Canada lists the chemical as persistent which equates to very high level of concern. Other sources include low to very high assessments for the persistence endpoint. The assessor elected a medium ranking based on the mid-point of the range and modeling which indicates the majority of partitioned chemical degrades in timeframes equating to low to medium concern. Modeled results for bioaccumulation all equate to a hazard level of concern of very low.

There are no data in the QCAT sources for carcinogenicity and endocrine disruption. These data gaps change the ranking from an initial B to a C_{dg}.

Human Health Effects – Group I

Carcinogenicity (C) Hazard Level (H, M, L or DG): DG

- Research Summary: There are no Step I sources with information on carcinogenicity of methyl acetate. A single Step II ource, SIDS, stated "No data are known which give relevant concern on cancerogenicity sic)….". The assessor elected to assign a ranking of data gap.

- References:

  - SIDS - No data are known which give relevant concern on cancerogenicity following methyl acetate exposure, although in methanol studies on rats and mice an increased incidence of lung adenoma/adenomatosis was seen in high dose male rats only.

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Mutagenicity and Genotoxicity (M) Hazard Level (H, M, L or DG): L

- Research Summary: There are no Step I sources containing information on the mutagenicity and genotoxicity of methyl acetate. Two Step II sources cite bacterial mutation tests and a rat bone marrow test. The EU risk assessment for methyl acetate states the chemical should not be classified as a mutagen. The HSBD cites studies with negative results. These both equate to a QCAT ranking of low which is selected as the ranking for the endpoint.

- References:

  - EU Risk Assessment

    - Conclusion on mutagenicity. Methyl acetate is negative in a bacterial mutation test and a rat bone marrow micronucleus test. Furthermore, the hydrolysis products methanol and acetic acid do not reveal evidence for a mutagenic potential. There is no concern with respect to mutagenicity. Methyl acetate should not be classified as a mutagen. → **L**

  - HSDB

    - In an ... unpublished bacterial mutagenicity study, methyl acetate did not produce an increase in revertants in Salmonella typhimurium strains TA 98, TA 100, TA 1535, TA 1537 and TA 1538, and Escherichia coli WP2uvrA, in the absence or presence of Aroclor-induced rat liver S-9 mix. Methyl acetate was tested up to 5,000 ug/plate. → **L**

    - Negative results were ... obtained in a study using Salmonella typhimurium strains TA97, TA98, TA100, TA1535 and TA1538 in the absence of an metabolic activation system and in the presence of rat or hamster liver S-9 mix, when tested up to 10,000 ug/plate. This study employed a 20-minute preincubation period. → **L**

- **Reproductive Toxicity (R) Hazard Level (H, M, L or DG): L**

  - Research Summary: There are no Step I sources on reproductive toxicity for methyl acetate. Two Step II sources cite a single two generation inhalation rat study where the No Observed Adverse Effect Concentration (NOAEC) for fertility was estimated at 3.0 mg/l based on toxicity of intermediate metabolites, methanol and acetic acid. No LOAEC data are included in QCAT sources for this endpoint. The assessor elected to use the available NOAEC data as a conservative substitute for LOAEC as NOAEC values are typically lower than the LOAEC equivalent. The NOAEC for this chemical meets the QCAT technical criteria for a low level of concern. A low level of concern is assigned.. The assessor selected this ranking based on the quantitative EPA characterization criteria rather than a ranking of moderate which is the QCAT ranking when there is "Indication of reproductive toxicity". Additional research may change the ranking for this endpoint.

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- References:
  - UNEP SIDS - No data are available on the reproductive toxicity of methyl acetate itself. However, due to the rapid hydrolysis of the compound hazards with respect to reproduction can be assessed on the toxicological properties of the immediate metabolites. Methanol and acetic acid are the intermediate metabolites. A NOEC/fertility for methanol of 1000 ppm (1.3 mg/l) was derived from a 2-generation inhalation study with rats. Assuming an immediate degradation of methyl acetate to methanol at a molar ratio of 1, this value corresponds to a NOAEC/fertility of about 3.0 mg methyl acetate/l. → **L**
  - EU Risk Assessment. Conclusion on toxicity for reproduction. There are no data on reproductive toxicity of methyl acetate. However, due to the rapid hydrolysis of this compound it is justified to base hazard assessment with respect to reproduction on the toxicological properties of the immediate metabolites. Concerning the metabolites of methyl acetate, acetic acid appears to be of less significance, since there are no indications of a fetotoxic or teratogenic potential, whereas for methanol some embryo-/fetotoxic and teratogenic effects were demonstrated in rodents, however at relatively high concentrations, respectively maternal toxic concentrations only. A NOEC/fertility for methanol of 1,000 ppm (1,300 mg methanol/m3) was derived from a 2-generation inhalation study in rats (NEDO, 1987). With the assumption that methyl acetate is immediately degraded to methanol at a molar ratio of 1, this value can be converted to NOAEC/fertility of about 3,000 mg methyl acetate/m3. → **L**

Development Toxicity incl. Developmental Neurotoxicity (D) Hazard Level (H, M, L or DG): M

- Research Summary: A single Step I source, the German MAK, classifies methyl acetate as Pregnancy Risk Group C which equates to a QCAT ranking of moderateAdditional data may change this ranking in the future.
- References:
  - German MAK – Pregnancy Risk Group C → **M**

Endocrine Disruption (E) Hazard Level (H, M, L or DG): DG

- Research Summary: No sources of information on endocrine disruption were found for methyl acetate. A ranking of data gap is assigned.
- References:

  None

Human Health Effects – Group II

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Acute Mammalian Toxicity (AT) Hazard Level (vH, H, M, L or DG): L

- Research Summary: A single Step I source had information on acute mammalian toxicity for methyl acetate. The New Zealand GHS rates it as "Acutely toxic" which equates to a QCAT ranking of low. Other animal testing information comes from the EU risk assessment, RTECS, and HSDB. Oral rat, dermal rat, inhalation mouse, and inhalation cat data all equate to a QCAT ranking of low. The assessor assumes that inhalation data are based on exposure to vapor rather than gas. The technical criteria in QCAT distinguish between these.

- References:

  - New Zealand - GHS - 6.1E (oral) - Acutely toxic → **L**

  - EU Risk Assessment - Inhalation of methyl acetate causes severe headache and considerable somnolence in humans that need labelling with the EU risk phrase "R 67, Vapours may cause drowsiness and dizziness". For Classification, See Section 1.4, Acute toxicity data determined in tests with rats demonstrated an oral LD50 >5,000 mg/kg body weight and a dermal LD50 >2,000 mg/kg. Inhalation LC50 values of 24 mg/l/8 hours for mice and of >30 mg/l/10 hours for cats were detected. Basing on these data, a classification of the acute toxicity of methyl acetate as harmful is not appropriate. → **L**

  - RTECS
    - LD50 – Lethal dose, 50 percent kill, oral, rodent – rabbit = 3705 mg/kg → **L**

  - HSDB
    - LC50 – Lethal dose, 50 percent kill, inhalation, rat = > 49 mg/L 4hr → **L**

Environmental Health Effects

Acute Aquatic (AA) Toxicity Hazard Level: (vH, H, M, L or DG): L

- Research Summary: There were no Step I sources of information for methyl acetate for the acute aquatic endpoint. Three Step II sources provided information. Several species results are listed in the EU Risk Assessment, HSDB or Ecotox. Fathead minnow, water flea and green algae tests results all equated to a QCAT ranking of low.

- References:

  - EU Risk Assessment
    - Pimephales promelas LC50 (96 h) = 320 mg/l → **L**
    - Daphnia magna EC50 (48 h) = 1,027 mg/l → **L**
    - Scenedesmus subspicatus EC50 (72 h) = > 120 mg/l → **L**

  - HSDB
    - Pimephales promelas LC50 (96 h) = 399 mg/l → **L**

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- Ecotox
  - Pimephales promelas LC50 (96 h) = 320 to 422 mg/l → **L**

Environmental Fate

Persistence (P) Hazard Level: (vH, H, M, L, vL or DG): M

- Research Summary: A single Step I source had information on persistence for methyl acetate. Environment and Health Canada list the chemical as persistent which equates to a hazard level of concern of very high. Other sources included a range of assessments on persistence. The EU risk assessment lists it as readily biodegradable with a half-life in water less than 14 days which equates to a QCAT ranking of low. PBT Profiler lists methyl acetate half lives in media varying from 15 to 46 days. These equate to QCAT rankings of low for water (41% of methyl acetate is modeled as partitioning into this compartment); medium for soil (40% modeled as partitioning into this compartment), and very high for air (19% estimated to partition into this compartment). UNEP SIDS states methyl acetate is "readily biodegradable" and has an atmospheric half-life of 50.4 days. The air half-life value equates to a QCAT ranking of very high. The assessor elects to assign a ranking of moderate to bridge the very high persistence rankings in air with the lower persistence in water and soil. This also biases the use of the EU risk assessment and the larger percentage of methyl acetate that is estimated to partition into water and soil. More data on this endpoint might alter this ranking.

- References:

  - EC - CEPA DSL - Persistent → **vH**

  - EU Risk Assessment. The substance can be classified as "readily biodegradable" (aqueous medium) on the basis of an available study according to OECD-guideline 301 D (Hoechst AG, 1995b). This closed bottle test indicates 74% biodegradation after 14 days, 75% after 19 days and 70% after 28 day. → **L**

  - PBT Profiler half-lives and percent in each medium
    - Water, 15 days, 41% → **L**
    - Soil, 30 days, 40% → **M**
    - Air, 46 days, 19% → **vH**
    - Sediment, 46 days, 0% → **M**

  - UNEP SIDS - According to the physico-chemical properties the target compartment for this substance are the atmosphere (69.3 %) and the hydrosphere (30.7 %). Methylacetate is stable in neutral solution. The substance is classified as "readily biodegradable". An atmospheric half-life of 50.4 days was calculated for methylacetate. → **vH**

Bioaccumulation (B) Potential Hazard Level: (vH, H, M, L, vL or DG): vL

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- Research Summary: Methyl acetate is not ranked high on any authoritative lists for bioaccumulation. There are two Step II sources of information on bioaccumulation for this chemical, both based on physical chemical characteristics. PBT Profiler estimates the bioconcentration factor as 3.2 which equates to a QCAT ranking of very low. The UNEP SIDS lists the log Kow as 0.18 which also equates to a QCAT ranking of very low. .

- References:
  - PBT Profiler - BCF = 3.2 → **vL**
  - UNEP SIDS - Methylacetate has a water solubility of 250 -295 g/l, a vapor pressure of 217 hPa and a log Kow of 0.18. → **vL**