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## CAS Registry Numbers: 520-45-6, 16807-48-0, 4418-26-2

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## Preface

This assessment was carried out by staff of the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) using the Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework.

The IMAP framework addresses the human health and environmental impacts of previously unassessed industrial chemicals listed on the Australian Inventory of Chemical Substances (the Inventory).

The framework was developed with significant input from stakeholders and provides a more rapid, flexible and transparent approach for the assessment of chemicals listed on the Inventory.

Stage One of the implementation of this framework, which lasted 4 years from 1 July 2012, examined 3000 chemicals meeting characteristics identified by stakeholders as needing priority assessment. This included chemicals for which NICNAS already held exposure information, chemicals identified as a concern or for which regulatory action had been taken overseas, and chemicals detected in international studies analysing chemicals present in babies' umbilical cord blood.

Stage Two of IMAP began in July 2016. We are continuing to assess chemicals on the Inventory, including chemicals identified as a concern for which action has been taken overseas and chemicals that can be rapidly identified and assessed by using Stage One information. We are also continuing to publish information for chemicals on the Inventory that pose a low risk to



human health or the environment or both. This work provides efficiencies and enables us to identify higher risk chemicals requiring assessment.

The IMAP framework is a science and risk-based model designed to align the assessment effort with the human health and environmental impacts of chemicals. It has 3 tiers of assessment, with the assessment effort increasing with each tier. The Tier I assessment is a high throughput approach using tabulated electronic data. The Tier II assessment is an evaluation of risk on a substance-by-substance or chemical category-by-category basis. Tier III assessments are conducted to address specific concerns that could not be resolved during the Tier II assessment.

These assessments are carried out by staff employed by the Australian Government Department of Health and the Australian Government Department of the Environment and Energy. The human health and environment risk assessments are conducted and published separately, using information available at the time, and may be undertaken at different tiers.

This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

For more detail on this program please visit: www.nicnas.gov.au.

## Disclaimer

NICNAS has made every effort to assure the quality of information available in this report. However, before relying on it for a specific purpose, users should obtain advice relevant to their particular circumstances. This report has been prepared by NICNAS using a range of sources, including information from databases maintained by third parties, which include data supplied by industry. NICNAS has not verified and cannot guarantee the correctness of all information obtained from those databases. Reproduction or further distribution of this information may be subject to copyright protection. Use of this information without obtaining the permission from the owner(s) of the respective information might violate the rights of the owner. NICNAS does not take any responsibility whatsoever for any copyright or other infringements that may be caused by using this information.

Acronyms & Abbreviations

## **Grouping Rationale**

This Tier II assessment considers the environmental risks associated with the industrial uses of dehydroacetic acid (DHA) and its sodium salt, sodium dehydroacetate. DHA has fungicidal and bactericidal properties. It is widely used as a preservative in consumer products including personal care products and cosmetics.

The use of DHA in personal care products and cosmetics will lead to release of the chemical into sewers, which may result in emissions to the aquatic environment in the treated effluents produced by sewage treatment plants (STP). This is of potential environmental concern because chemicals with preservative and biocidal properties are often very toxic to aquatic life. This assessment will evaluate the potential for emissions of DHA to the environment in Australia and whether risk reduction measures are required for industrial uses of the chemicals in this group.

The sodium cation, which is the counter ion to the dehydroacetate mono-anion in sodium dehydroacetate, is a ubiquitous, naturally occurring inorganic species that is essential for many biological functions. This inorganic cation is not further considered in this assessment.

# **Chemical Identity**

DHA is a mixture of readily interconvertible isomers, or tautomers. This acid has a β-diketone sub-structure (keto tautomer) and tautomerism in solution involves rapid interconversion between one keto and three enol tautomers (Chalaça and Figueroa-Villar, 2000). The keto tautomer (CAS RN 520-45-6) and an enol tautomer (CAS RN 16807-48-0) of DHA are both listed on the Inventory. According to a study on the tautomerism of DHA (Chalaça and Figueroa-Villar, 2000), the predominant tautomer in polar and non-polar solvents is the enol, 2*H*-pyran-2-one, 3-acetyl-4-hydroxy-6-methyl- (CAS RN 771-03-9). This tautomer is not listed on the Inventory.

CAS RN	520-45-6
Chemical Name	2 <i>H-</i> Pyran-2,4(3 <i>H</i> )-dione, 3-acetyl-6-methyl-
Synonyms	dehydroacetic acid (DHA) methylacetopyronone (keto tautomer)
Structural Formula	H <sub>3</sub> C
Molecular Formula	C <sub>8</sub> H <sub>8</sub> O <sub>4</sub>
Molecular Weight (g/mol)	168.15
SMILES	C(C)(=O)C1C(=O)C=C(C)OC1=O
CAS RN	16807-48-0
Chemical Name	4 <i>H</i> -Pyran-4-one, 3-acetyl-2-hydroxy-6-methyl-
Synonyms	dehydroacetic acid (DHA) methylacetopyronone (enol tautomer)
Structural Formula	

	H <sub>3</sub> C
Molecular Formula	C <sub>8</sub> H <sub>8</sub> O <sub>4</sub>
Molecular Weight (g/mol)	168.15
SMILES	C(C)(=O)C1C(=O)C=C(C)OC=1O
CAS RN	4418-26-2
Chemical Name	2 <i>H</i> -Pyran-2,4(3 <i>H</i> )-dione, 3-acetyl-6-methyl-, ion(1-), sodium
Synonyms	sodium dehydroacetate
Structural Formula	$ \begin{array}{c}                                     $
Molecular Formula	C <sub>8</sub> H <sub>7</sub> NaO <sub>4</sub>
Molecular Weight (g/mol)	190.13
SMILES	[Na+].CC(=O)[C-]1C(=O)C=C(C)OC1=O

## **Physical and Chemical Properties**

Experimental physical and chemical property data for DHA were retrieved from the peer-reviewed records for the chemical as listed on the Hazardous Substances Data Bank (HSDB) of the United States (US) National Library of Medicine (HSDB, 2003). DHA is identified with CAS RN 520-45-6 on the HSDB. The octanol-water partition coefficients (log K<sub>ow</sub>) for the neutral DHA tautomers were calculated (US EPA, 2011). Information on the properties of sodium dehydroacetate presented below is from the dossier for this substance submitted under the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) legislation in the European Union (REACH, 2019a):

Chemical	dehydroacetic acid	sodium dehydroacetate
Physical Form	solid	solid
Melting Point	109°C (exp.), sublimes	>280°C (exp.), decomposes
Boiling Point	270°C (exp.)	-
Vapour Pressure	0.147 Pa (exp.) at 25°C	-
Water Solubility	690 mg/L at 25°C (exp.)	231 000 mg/L at 20°C (exp.)
Ionisable in the Environment?	yes	yes
log K <sub>ow</sub>	-1.31 to 0.78 (calc.)	-

The octanol-water partition coefficients of the various DHA tautomers are low, indicating DHA is hydrophilic. DHA is moderately soluble in water. It is a weak acid with a measured acid dissociation constant ( $pK_a$ ) in water of 5.26 (Tan, et al., 1983). Dissociation of DHA forms the dehydroacetate mono-anion which is an enolate ion (Alousi, et al., 2008). Based on the acid-base chemistry of DHA, the chemical will be fully ionised in water, except under acid conditions. Sodium dehydroacetate is readily soluble in water and is expected to dissociate into its constituent dehydroacetate mono-anions and sodium cations in solution.

# Import, Manufacture and Use

## Australia

No specific Australian use, import or manufacturing information has been identified for the chemicals in this group.

DHA is used as a microbial preservative in topical medicines for dermal applications, such as sunscreens and an antiseptic lotion, as listed in the Australia Register of Therapeutic Goods (TGA, 2019) and (TGA, 2007). These non-industrial uses of DHA

are beyond the scope of this assessment.

## International

DHA is manufactured on an industrial scale by dimerization of diketene (CAS RN 674-82-8) (Penta, 2017). DHA and its sodium salt are used as preservatives in cosmetics and personal care products (Danish Environmental Protection Agency, 2015). They are also used as plasticisers in synthetic resins (Jilalat, et al., 2017). DHA is also used as an intermediate in the synthesis of pharmaceuticals (Penta, 2017).

DHA (CAS RN 520-45-6) is currently registered for use in the European Union (EU) at 100 to 1000 tonnes per annum (REACH, 2019b), and sodium dehydroacetate (CAS RN 4418-26-2) is registered for use at 1000 to 10 000 tonnes per annum (REACH, 2019a).

DHA has non-industrial uses as a fungicide for processed fruits and vegetables, and as a preservative in pharmaceuticals (Jilalat, et al., 2017). The chemical is a food preservative that is permitted for direct addition to food for human consumption (HSDB, 2003). The sodium salt may also be used as a wood preservative (NCBI, 2019). These non-industrial uses are beyond the scope of this assessment.

# **Environmental Regulatory Status**

## Australia

The use of the chemicals in this group is not subject to any specific national environmental regulations.

## **United Nations**

No chemicals in the group are currently identified as a Persistent Organic Pollutant (UNEP, 2001), ozone depleting substance (UNEP, 1985), or hazardous substance for the purpose of international trade (UNEP & FAO, 1998).

## OECD

No chemicals in the group have been sponsored for assessment under the Cooperative Chemicals Assessment Programme (CoCAP) (OECD, 2013).

## Canada

The chemicals in this group are on the Domestic Substances List (DSL) (Environment and Climate Change Canada, 2019). All chemicals in this group (as well as CAS RN 771-03-9) were categorised as not Persistent (not P), not Bioaccumulative (not B), and not Inherently Toxic to the Environment (not  $iT_E$ ) during the Categorization of the DSL (Environment and Climate Change Canada, 2019).

# **European Union**

The keto-tautomer of DHA (CAS RN 520-45-6) and sodium dehydroacetate are both registered under the REACH legislation (REACH, 2019c). The enol tautomer with CAS RN 771-03-9 is pre-registered under REACH (REACH, 2019d).

All of the chemicals in this group (as well as CAS RN 771-03-9) are listed in the Cosmetic ingredient database (CosIng) as preservatives allowed in cosmetic products with a maximum concentration in ready for use preparations of 0.6% (Danish

Environmental Protection Agency, 2015). The chemicals in this group are not on the list of approved substances under the EU Biocidal Products Regulation (REACH, 2019e).

## **United States of America**

The keto tautomer of DHA (CAS RN 520-45-6) and sodium dehydroacetate are both listed on the United States Environmental Protection Agency (US EPA) Chemical Substance Inventory, established under the Toxic Substances Control Act 1976. Both chemicals are registered as 'active' on the Chemical Substance Inventory, which indicates that they have recently been manufactured, imported or processed by industry in the USA (US EPA, 2019a).

DHA (CAS RN 520-45-6) is listed on the US EPA Safer Chemical Ingredients List under the preservatives and antioxidants functional use category (US EPA, 2019b). This list identifies chemicals deemed to be safer alternatives to other chemicals employed for the same functional use. The criteria for adding chemicals to the list cover a broad range of human health and environmental toxicological effects.

## **Environmental Exposure**

DHA can be released to the environment as a result of both industrial and non-industrial uses. Emissions of DHA to the environment from industrial uses are expected to occur mainly from use of the chemical or its sodium salt as a preservative in personal care products and cosmetics.

Chemicals used in personal care products and cosmetics are typically released to sewers in wastewater as a normal part of their use pattern. Depending on degradation and partitioning processes of chemicals in sewage treatment plants, some fraction of the quantity of chemicals in wastewater entering STPs can be emitted to the air compartment, to rivers or oceans in treated effluent, or to soil through application of biosolids to agricultural land (Struijs, 1996). Based on a recent international study of preservatives in rinse-off and leave-on cosmetic products, 10% of rinse-off products evaluated contained DHA as one of the preservatives (Danish Environmental Protection Agency, 2015). The formulation of such products on the Australian market is assumed to not differ significantly from those found internationally. Therefore, DHA has the potential to be emitted to the environment in Australia from its use in personal care products and cosmetics depending on the removal efficiency for this chemical in STPs.

Another industrial use of the chemicals in this group is as plasticisers in synthetic resins. Chemicals that are not irreversibly bound to the polymer matrix of resins can be emitted to the environment indirectly as a result of their migration to the surface of plastic articles, including imported articles, as well as through abrasion and wear of these articles during their normal use (OECD, 2011). Use of articles containing DHA and its sodium salt in indoor applications could potentially lead to the occurrence of these chemicals in household dust as a result of this emission pathway. Chemicals in household dust can be released to wastewater through cleaning and washing of surfaces and fabrics, which provides another potential source of DHA emissions to the environment from industrial uses. However, it is noted that the majority of the quantity of these chemicals used as plasticisers in articles would be expected to remain associated with the article throughout its service life before disposal in landfill.

Non-industrial uses of DHA and sodium dehydroacetic acid in pharmaceuticals and food also have the potential to release these chemicals into the wastewater system. The quantities of DHA emitted to wastewater from these non-industrial uses is currently unknown, and it is not clear what proportion of releases is from non-industrial use.

## **Environmental Fate**

## **Dissolution, Speciation and Partitioning**

DHA is expected to be ionised in environmental waters and may react with naturally occurring inorganic cations to form metal complexes.

DHA and sodium dehydroacetate will both dissociate in water to release the enolate anion. The enolate anion is readily soluble in water. In environmental waters, the enolate may form stable complexes with naturally occurring inorganic cations, especially

copper(2+) cations (Alousi, et al., 2008).

### Degradation

DHA is expected to be rapidly biodegraded in the environment.

DHA (CAS RN 520-45-6) was rapidly biodegraded (84% of the theoretical biological oxygen demand (BOD) for mineralisation) over 14 days in a ready biodegradability study conducted in accordance with OECD Test Guideline (TG) 301C (NITE, 2014) and (HSDB, 2003). The study was conducted using an activated sludge inoculant with an initial DHA concentration of 100 mg/L. The high level of biodegradation achieved at this test concentration suggests that DHA is not harmful to activated sewage sludge microorganisms.

In another biodegradation study conducted according to OECD TG 301F with 38 mg/L sodium dehydroacetate, 70% degradation was reached after 28 days, meeting the 10 day window test for ready biodegradability. No inhibitory effect of this chemical on the inoculum was seen in the toxicity control (REACH, 2019a).

### **Bioaccumulation**

DHA is expected to have a low potential to bioaccumulate.

There are no measured bioaccumulation data for DHA. The calculated log  $K_{ow}$  values for the tautomers of DHA are in the range from -1.31 to 0.78, which indicates that this acid will have a very low tendency to partition from water into biological membranes. The more water soluble enolate ion is expected to have an even lower tendency to partition into biological membranes. Based on these considerations, DHA is expected to have a low potential for bioaccumulation.

## Transport

DHA is expected to be rapidly degraded and/or transformed into other chemical species in the environment and is, therefore, unlikely to undergo long range transport.

## Predicted Environmental Concentration (PEC)

No environmental monitoring data were identified for these chemicals. The concentration of DHA in treated effluents from STPs in Australia is estimated to be 22 micrograms per litre ( $\mu$ g/L).

No Australian or international environmental monitoring data were identified for DHA. In the absence of monitoring data, standard exposure modelling for the release of chemicals to surface waters in STP effluents (Struijs, 1996) was used to estimate concentrations of DHA in the aquatic environment. These calculations are based on an assumed annual introduction volume of 100 tonnes per annum for each of the three chemicals in this group (NICNAS, 2013). It is assumed that 100% of the introduced quantity of chemicals is released to STPs nationwide as the main industrial uses of these chemicals in Australia are expected to be in personal care products and cosmetics. Based on this scenario, 87% of the quantity of the chemical in wastewater entering an STP is predicted to be removed as a result of biodegradation, with a calculated concentration of DHA in treated effluents of 22  $\mu$ g/L. It is noted that this calculation does not include contributions from quantities of DHA that may be released into wastewater from non-industrial uses.

## **Environmental Effects**

DHA has low acute and chronic aquatic toxicity to algae and aquatic invertebrates. There is currently no information on the effects of DHA on fish exposed to the chemical through water.

Sodium dehydroacetate was used as the test substance in all of the studies outlined below. The active substance in solution is assumed to be the enolate anion, and therefore these toxicity studies are relevant for both DHA and sodium dehydroacetate.

## Effects on Aquatic Life

## Acute toxicity

The following measured median effective concentration (EC50) values for the effects of sodium dehydroacetate on model organisms across two trophic levels were reported in the REACH Registration Dossier for this chemical (REACH, 2019a):

Taxon	Endpoint	Method
Invertebrates	48 h EC50 ≥ 100 mg/L	Experimental <i>Daphnia magna</i> (water flea) OECD TG 202 Static
Algae	72 h E <sub>r</sub> C50 = 32.1 mg/L	Experimental <i>Pseudokirchneriella subcapitata</i> (green algae) OECD TG 201 Static

Although a dietary exposure fish study is available (REACH, 2019b) there is an absence of aquatic exposure tests for fish on DHA or its sodium salt. The non-guideline dietary study involved force feeding *Cyprinus carpio* (carp) up to 415 mg/kg body weight of DHA in gelatin capsules. The fish were observed for up to 70 hours. No effects were observed. The dietary fish test was conducted prior to the drafting of the OECD test guidelines.

## **Chronic toxicity**

The no-observed-effect concentration (NOE<sub>r</sub>C) value for the effect of sodium dehydroacetate on the growth rate of algae was reported in the REACH Registration Dossier for this chemical (REACH, 2019a):

Taxon	Endpoint	Method
Algae	72 h NOE <sub>r</sub> C = 10.0 mg/L	Experimental <i>Pseudokirchneriella subcapitata</i> (green algae) OECD TG 201 Static

## Predicted No-Effect Concentration (PNEC)

The PNEC for DHA is calculated to be 100 µg/L.

Based on the availability of a range of acute and chronic toxicity data across two trophic levels, an assessment factor of 100 was used for DHA (EPHC, 2009). The chronic algal toxicity endpoint was used to derive the most conservative PNEC of 100  $\mu$ g/L.

## **Categorisation of Environmental Hazard**

The categorisation of the environmental hazards of the chemicals in this group according to domestic environmental hazard thresholds is presented below (EPHC, 2009) and (NICNAS, 2013):

## Persistence

Not Persistent (Not P). Based on the measured rates of biodegradation of DHA and sodium dehydroacetate, the chemicals in this group are categorised as Not Persistent.

## **Bioaccumulation**

Not Bioaccumulative (Not B). Based on the hydrophilic properties of DHA and its conjugate base mono-anion the chemicals in this group are categorised as Not Bioaccumulative.

# Toxicity

Not Toxic (Not T). Based on measured acute toxicity endpoints greater than 1 mg/L and a chronic toxicity endpoint greater than 0.1 mg/L, the chemicals in this group are categorised as Not Toxic.

## Summary

2*H*-Pyran-2,4(3*H*)-dione, 3-acetyl-6-methyl; 4*H*-pyran-4-one, 3-acetyl-2-hydroxy-6-methyl; and 2*H*-pyran-2,4(3*H*)-dione, 3-acetyl-6-methyl-, ion(1-), sodium are categorised as:

- Not P
- Not B
- Not T

## **Risk Characterisation**

The below risk quotient (RQ = PEC ÷ PNEC) for the riverine compartment has been calculated based on the PEC and PNEC values determined for DHA:

PEC (µg/L)	PNEC (µg/L)	RQ
22	100	0.22

The RQ value for DHA is less than 1. This indicates that the environmental concentrations of DHA are unlikely to exceed levels which cause toxic effects in exposed organisms. Therefore, the chemicals in this group are considered to be of low environmental concern.

DHA has a number of potential non-industrial uses, such as pharmaceutical preservatives, which may contribute to the environmental concentrations of this substance. The environmental risks resulting from these additional sources of emissions of DHA are beyond the scope of this assessment.

## **Key Findings**

Dehydroacetic acid (DHA) and its sodium salt are widely used preservatives. Industrially, they are used mainly as preservatives in personal care products and cosmetics. They are also used as plasticisers in synthetic resins.

DHA is rapidly degraded in the environment, has low potential to bioaccumulate and has low aquatic toxicity to algae and aquatic invertebrates. There are currently no aquatic toxicity data available for fish, which is considered to be a gap in the available environmental hazard information for these chemicals.

The risks to the aquatic environment associated with emissions of these chemicals in treated effluent from STPs is not considered to be of concern based on the available information.

The chemicals in this group are not PBT substances according to domestic environmental hazard criteria.

## Recommendations

No further assessment is currently required under the IMAP Framework.

## **Environmental Hazard Classification**

In addition to the categorisation of environmental hazards according to domestic environmental thresholds presented above, the classification of the environmental hazards of 2*H*-pyran-2,4(3*H*)-dione, 3-acetyl-6-methyl; 4*H*-pyran-4-one, 3-acetyl-2-hydroxy-6-methyl; and 2*H*-pyran-2,4(3*H*)-dione, 3-acetyl-6-methyl-, ion(1-), sodium according to the third edition of the United Nations' Globally Harmonised System of Classification and Labelling of Chemicals (GHS) is presented below (UNECE, 2009):

Hazard	GHS Classification (Code)	Hazard Statement
Acute Aquatic	Category 3 (H402)	Harmful to aquatic life
Chronic Aquatic	Not classified	-

The classification of the aquatic hazards of the chemicals in this group was based on the ecotoxicity data for sodium dehydroacetate presented in this assessment. The chronic toxicity is not classified taking into account the low acute toxicity of DHA and its rapid biodegradability and low potential to bioaccumulate in aquatic life.

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