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# Ethyl-2,4-dioxohexanoate

Toxicity monograph (with existing HCVs)

May 2018

Prepared by:

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## Ethyl-2,4-dioxohexanoate

### Toxicity monograph (with existing HCVs)

#### INTRODUCTION

(b) (4) was asked to produce a toxicity monograph of ethyl-2,4-dioxohexanoate (CAS RN<sup>1</sup> 13246-52-1), focussing on the inhalation route of exposure, with inclusion of existing Health Criteria Values (HCVs) where available. Data on the inhalation of tobacco smoke containing the substance (if available) have not been included in this monograph.

#### EXPERTISE

(b) (4) was founded<sup>2</sup> in 1961 to provide independent, high-quality research, information and advice on chemical toxicology to industry and governmental departments. Its risk assessors have been working together for many years (more than 40 years in some instances) and have a record of objectivity and scientific excellence. All senior and principal scientists in the current team are accredited and listed in the European (Eurotox) and UK Royal Society of Biology/British Toxicology Society Registers of Toxicologists and are thus bound by their specific codes of conduct.

#### TOXICITY DATA SEARCH CRITERIA<sup>3</sup>

(b) (4) access to a wide range of data sources, including the unique (b) (4) databank (see the [Appendix](#) for details), PubMed, the TOXNET system of databases and databanks (which includes Toxline (the toxicity subset of Medline), HSDB, GENETOX, DART, CCRIS, IRIS, ITER and CPDB), and eChemPortal.

All searches were conducted in May 2018 using the CAS RN and (in PubMed only) name and/or synonyms identified below, as appropriate.

The data summarised in this report refers to the unheated form unless otherwise stated.

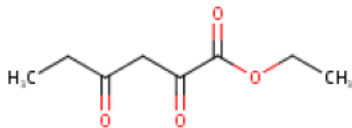
#### IDENTIFICATION, REACH STATUS AND EU CLASSIFICATION

Identifier	
Name	Ethyl-2,4-dioxohexanoate
Synonyms(s)	Ethyl 2,4-diketocaproate Ethyl <i>beta</i> -propionylpyruvate Hexanoic acid, 2,4-dioxo-, ethyl ester

<sup>1</sup> Chemical Abstracts Service Registry Number.

<sup>2</sup> as (b) (4)

<sup>3</sup> Disclaimer: searches are valid and complete as of the date of searching (b) (4) accepts no responsibility for the accuracy, completeness or sufficiency of any databases or searching platforms employed.

CAS RN	13246-52-1
REACH registration number <sup>4</sup>	Not REACH registered
Molecular formula	C <sub>8</sub> H <sub>12</sub> O <sub>4</sub>
Molecular weight	172.18
Structure	
Classification, according to EU CLP (EC 1272/2008)	Harmonised classification: Not available
	REACH joint registrants: Not available

## ADME<sup>5</sup>

No relevant data were identified on the ADME of inhaled ethyl-2,4-dioxohexanoate.

In an evaluation of a group of 47 aliphatic primary alcohols, aldehydes, carboxylic acids, acetals, and esters containing additional oxygenated functional groups (including ethyl-2,4-dioxohexanoate), the Joint FAO/WHO Expert Committee on Food Additives (JECFA) concluded that these substances “are readily hydrolysed [to their corresponding alcohol and acid components] and absorbed and are completely metabolized. Many of these substances or their metabolites are endogenous in humans” (JECFA, 2000).

## TOXICOLOGY

### LOCAL EFFECTS

#### Respiratory tract irritation

No substance-specific data were identified.

#### Skin irritation

No substance-specific data were identified.

#### Eye irritation

No substance-specific data were identified.

#### Other local effects

No substance-specific data were identified.

<sup>4</sup> REACH registration numbers are substance and company specific. Therefore, the substance-specific part of the registration number is included here, from data disseminated on the ECHA ‘registered substance’ website.

<sup>5</sup> Absorption, Distribution, Metabolism and Excretion.

## **SENSITISATION AND INTOLERANCE**

### **Respiratory tract sensitisation**

No substance-specific data were identified.

### **Skin sensitisation**

No substance-specific data were identified.

### **Oral allergy/intolerance**

No substance-specific data were identified.

## **INHALATION TOXICITY STUDIES – SYSTEMIC EFFECTS**

### **Single dose toxicity**

No substance-specific data were identified.

### **Repeated dose toxicity**

No substance-specific data were identified.

## **TOXICITY STUDIES – OTHER EXPOSURE ROUTES**

### **Single dose toxicity**

#### Expert-group opinion

No substance-specific data were identified.

#### Human

No substance-specific data were identified.

#### Non-human

An oral LD<sub>50</sub> value<sup>6</sup> of 6450 mg/kg bw was reported following gavage administration of ethyl-2,4-dioxohexanoate to rats ([Wolven and Levenstein, 1969](#)).

### **Repeated dose toxicity**

No substance-specific data were identified.

## **GENOTOXICITY**

No substance-specific data were identified.

## **CARCINOGENICITY**

No substance-specific data were identified.

## **REPRODUCTIVE AND DEVELOPMENTAL TOXICITY**

No substance-specific data were identified.

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<sup>6</sup> Lethal Dose 50, i.e. the dose that is lethal to 50% of the exposed group.

## CARDIOPULMONARY EFFECTS<sup>7</sup>

No substance-specific data were identified.

## OTHER TOXICITY CONSIDERATIONS

No substance-specific data were identified.

## EXISTING HEALTH CRITERIA VALUES (HCVs)

No substance-specific existing HCVs were identified.

JECFA and, more recently, the European Food Safety Authority (EFSA), have concluded that ethyl-2,4-dioxohexanoate is of “no safety concern” at (‘current’) estimated levels [not further specified]<sup>8</sup> of dietary intake as a food additive (EFSA, 2011; JECFA,2000).

## REFERENCES

EFSA (2011). European Food Safety Authority. EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF). Scientific Opinion on Flavouring Group Evaluation 10, Revision 2 (FGE.10Rev2): Aliphatic primary and secondary saturated and unsaturated alcohols, aldehydes, acetals, carboxylic acids and esters containing an additional oxygenated functional group and lactones from chemical groups 9, 13 and 30. EFSA Journal 9(7), 2164. <https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2011.2164>

JECFA (2000). Safety evaluation of certain food additives and contaminants. Prepared by the fifty-third meeting of the Joint FAO/WHO Expert Committee on Food Additives. WHO Food Additives Series 44. <http://www.inchem.org/documents/jecfa/jecmono/v44jec01.htm>

Munro IC and Kennepohl E (2001). Comparison of estimated daily per capita intakes of flavouring substances with no-observed-effect levels from animal studies. Food and Chemical Toxicology 39, 331-354.

Wolven AM and Levenstein I (1969). Acute oral toxicity reports on rats. Diethylmalonate. Leberco Laboratories. Assay no. 23460. July 31, 1962. Unpublished data submitted by EFA to [EU] SCF [cited in EFSA, 2011].

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<sup>7</sup> Potential effects on the heart, blood vessels and/or respiratory tract.

<sup>8</sup> The highest EU/US per capita intake was reported to be 0.333 ng/kg bw/day (Munro and Kennepohl, 2001).

## APPENDIX: The (b) (4) database and databank

(b) (4)

(b) (4) includes information from peer-reviewed toxicology and nutrition journals as well as secondary sources and websites. In addition to primary literature on the health effects of chemicals, (b) (4) covers official publications and evaluations issued by authoritative groups including:

- WHO/IPCS reports and evaluations (including CICADs and EHCs, and IARC, JECFA and JMPR monographs), and the WHO Air Quality and Drinking-Water Quality Guidelines
- OECD SIDS dossiers/SIARS
- IUCLID data sets
- EU Risk Assessment Reports
- EU expert committee opinions (including EU scientific committees, and EFSA scientific panels) and other reports from EU agencies and institutes etc (including ECHA, ECVAM, EMA and CPS&Q)
- ECETOC, HERA, Council of Europe and other pan-European programmes
- UK government agency (including Defra, EA, FSA, DoH, HSE, HPA, PSD and VMD) and advisory committee (e.g. COT, COM, COC, ACNFP, SACN, ACP, ACAF, VPC, VRC and ACRE) reports and evaluations
- Opinions from other UK organisations such as the Royal Society
- US agency reports and evaluations (EPA, ATSDR, FDA, NTP, OSHA, NCEA, CFSAN, CERHR, NIEHS, CDC, OEHHHA and ACGIH)
- Health Canada evaluations
- BUA, DFG, BG Chemie and BfR reports and monographs
- Gezondheidsraad opinions, including those from its various committees such as DECOS
- RIVM reports
- Danish EPA reviews
- Reports and other information provided by Swedish governmental organisations, including the National Food Administration and the Swedish Chemicals Agency
- Nordic Expert Group for Criteria Documentation of Health Risks from Chemicals
- Australian agency reviews including NICNAS Priority Existing Chemical Assessments, APMVA reports and (jointly with New Zealand) FSANZ assessments
- Japanese Chemical Industry Ecology-Toxicology & Information Center reports
- CIR, RIFM and other specialist industry groups

• (b) (4) Toxicity Profiles  
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