Ethyl laurate

Toxicity monograph

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Prepared by:

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INTRODUCTION

(b) (4) was asked to produce a toxicity monograph of ethyl laurate (CAS RN[1] 106-33-2), focussing on the inhalation route of exposure. Data on the inhalation of tobacco smoke containing the ingredient (if available) have not been included in this monograph.

EXPERTISE

(b) was founded[2] 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 the 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

As instructed by the client, searches for toxicity data were restricted to the (b) (4) databank (see the Appendix for details) and the TOXNET system of databases and databanks (which includes Toxline (the toxicity subset of Medline), HSDB, GENETOX, DART, CCRIS, IRIS, ITER and CPDB). Since these searches could not necessarily be relied upon specifically to identify cardiopulmonary data, additional searches were conducted in PubMed tailored to identify such information.

All searches were conducted in September 2016 using the CAS RN and (in PubMed only) names identified below, as appropriate.

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

IDENTIFICATION, REACH STATUS AND EU CLASSIFICATION

Identifier / status	
Name	Ethyl laurate
Synonym(s)	Ethyl dodecanoate

[1] Chemical Abstracts Service Registry Number.

[2] as the (b) (4)

CAS RN	106-33-2
REACH registration number	Not REACH registered
Classification, according to EU CLP (EC 1272/2008)	Harmonised classification: None available

TOXICOLOGY

LOCAL EFFECTS

Respiratory tract irritation

No substance-specific data were identified.

Skin irritation

Human

Covered contact for 48 hours with ethyl laurate at 12% in petrolatum was not irritating to skin of 25 subjects (Kligman, 1973). [See also Skin sensitisation section.]

Non-human

Neat ethyl laurate applied to the intact or abraded skin of rabbits under an occluded patch for 24 hours was not irritating (Moreno, 1973).

Eye irritation

No substance-specific data were identified.

Other local effects

No substance-specific data were identified.

SENSITISATION AND INTOLERANCE

Respiratory tract sensitisation

No substance-specific data were identified.

Skin sensitisation

Human

No evidence of sensitisation was seen in a maximisation test[3] on 25 subjects using 12% ethyl laurate in petrolatum (Kligman, 1973). [See also Skin irritation section.]

Non-human

No substance-specific data were identified.

Oral allergy/intolerance

No substance-specific data were identified.

[3] The test procedure typically involves an initial induction phase of five 48-hour covered patch tests, followed 10-14 days later by a 48-hour covered challenge patch.

INHALATION TOXICITY STUDIES

No substance-specific data were identified.

TOXICITY STUDIES – OTHER EXPOSURE ROUTES

Single dose toxicity

Human

No substance-specific data were identified.

Non-human

Oral and dermal LD_{50} values[4] of >5000 mg/kg bw have been reported for rats and rabbits, respectively (Moreno, 1973).

Groups of 3 young male or 3 young female albino rats were given an oral gavage dose of 0.9 or 2 "mM per sq. dm. body surface", respectively [equivalent to approximately 3289 or 8109 mg/kg bw, respectively[5]]. No increase in acetone bodies was reported, suggesting a lack of ketogenic activity of ethyl laurate (MacKay *et al.*, 1940).

Repeated dose toxicity

Human

No substance-specific data were identified.

Non-human

"No adverse effects" were reported in a 12-week dietary study in which groups of 15 rats/sex were fed "mixed esters" [presumably of ethyl laurate[6]] at a dose of 3.7 mg/kg bw/day [no further details in the citing source] (Oser, 1967).

Ethyl laurate was added to the diet of young rats at 25% or 35-40% [providing doses of approximately 26,000 mg/kg bw/day or 36,000-41,000 mg/kg bw/day[7]] for an unspecified period. No deaths occurred at the low dose but diffuse interstitial myocarditis and death due to heart failure occurred within 3-6 days at the high dose [no further details in the citing source] (Kesten *et al.*, 1945). [See also Cardiopulmonary effects section.]

GENOTOXICITY

No substance-specific data were identified.

CARCINOGENICITY

No substance-specific data were identified.

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[4] Lethal Dose 50, i.e. the dose that is lethal to 50% of the exposed group.

[5] The doses are given in "mM per sq. dm. body surface". It is possible that "mM" indicates mmol. The dose conversions were based on the average reported body weights of 187.5 g and 169 g for males and females, respectively, an estimated surface area of 300 cm^2/rat, and an assumption of 0.9 or 2 mmol/100 cm^2 surface area.

[6] The meaning of the phrase "mixed esters" in unclear as the information is given for ethyl laurate.

[7] Dose conversion (for these young animals) based on a body weight of 175 g and food consumption of 18 g/day.

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

No substance-specific data were identified.

CARDIOPULMONARY EFFECTS[8]

Diffuse interstitial myocarditis and death due to heart failure occurred within 3-6 days after rats were fed diets containing 35-40% ethyl laurate [providing a dose of approximately 36,000-41,000 mg/kg bw/day[9]] [no further details in the citing source] (Kesten *et al.*, 1945). [See also Repeated dose toxicity section.]

REFERENCES

JECFA (1967). Toxicological evaluation of some flavouring substances and non-nutritive sweetening agents. 11th Report of the Joint FAO/WHO Expert Committee on Food Additives. FAO Nutrition Meetings Report Series No. 44. World Health Organization, Geneva. http://www.inchem.org/documents/jecfa/jecmono/v44aje14.htm

Kesten HD, Salcedo J Jr and Stetten DeW Jr (1945). Fatal myocarditis in choline deficient rats fed ethyl laurate. Journal of Nutrition 29, 171-177 [cited in von Oettingen, 1960].

Kligman AM (1973). Report to RIFM, 12 August [cited in Opdyke, 1975].

MacKay EM, Wick AN and Barnum CP (1940). Ketogenic action of short chain, even numbered carbon fatty acids in carbohydrate-fed animals. Journal of Biological Chemistry 135, 183-187.

Moreno OM (1973). Report to RIFM, 18 May [cited in Opdyke, 1975].

Opdyke DLJ (1975). Monographs on Fragrance Raw Materials: Ethyl laurate. Food and Cosmetics Toxicology 13, 93-94.

Oser BL (1967). Unpublished report [cited in JECFA, 1967].

von Oettingen WF (1960). The aliphatic acids and their esters: Toxicity and potential dangers. The saturated monobasic acids and their esters: aliphatic acids with three to eighteen carbons and their esters. AMA Archives of Industrial Health 21, 100-113.

[8] Potential effects on the heart, blood vessels and/or respiratory tract.

[9] Dose conversion (for these young animals) based on a body weight of 175 g and food consumption of 18 g/day.

APPENDIX: (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, OEHHA 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)) Toxicity Profiles