

DIETHYL SULFATE

CAS number: 64-67-5

Synonyms: Diethyl sulphate, diethyl monosulphate, ethyl sulphate, ethyl sulfate, diethyl tetraoxosulfate

Chemical formula: C₄H₁₀O₄S

Structural formula: —

Workplace exposure standard (interim)

TWA: —

STEL: —

Peak limitation: —

Notations: Carc. 1B

IDLH: —

Sampling and analysis: N/A

Recommendation and basis for workplace exposure standard

A TWA is not recommended due to insufficient data to derive a concentration. Exposure should be minimised as far as possible to protect for potential carcinogenic effects.

Given the limited data available from the primary sources, it is recommended that a broader review of additional sources be conducted at the next scheduled review.

Discussion and conclusions

Diethyl sulfate is primarily used as an ethylating agent in the manufacture of dyes, pigments and textile chemicals, and as a finishing agent in textile production.

Diethyl sulfate is anticipated to be a human carcinogen. A nested case control study of 17 benign brain tumours in workers at a petrochemical plant found the risk of brain cancer to be associated with exposure to diethyl sulfate (NTP, 2016). It is reported to cause tumours both locally and systemically in rats at several different tissue sites and by several different routes of exposure. Positive results are reported in several *in vitro* tests for mutagenicity (DFG, 2003; HCOTN, 1999; SCOEL, 2009).

Evidence in animals and humans suggest that carcinogenicity may be due to a mutagenic mode of action. However, insufficient data exists to recommend a suitable TWA. Investigation of additional data sources is recommended at the next scheduled review.

Recommendation for notations

Classified as a category 1B carcinogen according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS).

Not classified as a skin sensitiser or respiratory sensitiser according to the GHS.

There are insufficient data to recommend a skin notation.

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	NA	NA
No report.		
ACGIH	NA	NA
No report.		
DFG	2003	Not assigned
<p>No MAK assigned due to clear carcinogenicity in animals.</p> <p>Summary of data:</p> <p>Human data:</p> <ul style="list-style-type: none"> No reports of effects of short-term or long-term exposure or of toxicity. <p>Animal data:</p> <ul style="list-style-type: none"> 250 ppm for 4 h for 14 d; 0/6 rat fatalities 500 ppm for 4 h for 14 d; 6/6 rat fatalities Reported as less acutely toxic than dimethyl sulfate No reports of effects on animals of long-term inhalation Causes malignant tumours in rats at the injection site after subcutaneous injection, in the stomach after administration by gavage, and neurinomas after transplacental exposure. <p>Positive results in several <i>in vitro</i> tests for mutagenicity including <i>E.coli</i>.</p>		
SCOEL	2009	Not assigned
<p>A health-based OEL cannot be derived.</p> <p>Summary of additional data:</p> <ul style="list-style-type: none"> Clearly directly mutagenic in virtually all test systems examined (<i>S. typhimurium</i>, plant cells, yeast, <i>Drosophila melanogaster</i>, cultured mammalian cells, rat hepatocytes, human lymphocytes and leucocytes, mice and rats) Reported as carcinogenic both systemically and locally Carcinogenicity data comparable with dimethyl sulfate; 0.5 ppm 6 h 2/wk carcinogenic in rats upon long-term inhalation exposure By analogy to dimethyl sulfate, a skin notation is applied. 		
OARS/AIHA	NA	NA
No report.		
HCOTN	1999	Not assigned
<p>Summary of additional data:</p> <ul style="list-style-type: none"> Insufficient evidence to undertake quantitative extrapolation to a health-based occupational lifetime cancer risk value for inhalation exposure. 		

Secondary source reports relied upon

Source	Year	Additional information
NTP	✓ 2016	<ul style="list-style-type: none"> Reasonably anticipated to be a human carcinogen A nested case control study of 17 benign brain tumours in workers at a petrochemical plant found brain cancer risk associated with estimated exposure to diethyl sulfate Data available from epidemiological studies are inadequate to evaluate the relationship between human cancer and exposure Caused tumours in rats at several different tissue sites and several routes of exposure.

Carcinogenicity — non-threshold based genotoxic carcinogens

Is the chemical mutagenic? Yes

Is the chemical carcinogenic with a mutagenic mechanism of action? Yes

The chemical is a non-threshold based genotoxic carcinogen.

Is a cancer slope factor or inhalation unit risk value available? No

Notations

Source	Notations
SWA	NA
HCIS	Carcinogenicity – category 1B
NICNAS	Carc. Cat. 2
EU Annex	Carcinogenicity – category 1B
ECHA	Carcinogenicity – category 1B
ACGIH	NA
DFG	Carcinogenicity – 2
SCOEL	Carcinogenicity – A, Skin
HCOTN	—
IARC	Carcinogenicity – Group 2A
US NIOSH	NA

NA = not applicable (a recommendation has not been made by this Agency); — = the Agency has assessed available data for this chemical but has not recommended any notations

Skin notation assessment

Calculation

Insufficient data to assign a skin notation.

IDLH

Is there a suitable IDLH value available? No

Additional information

Molecular weight:	154.2
Conversion factors at 25°C and 101.3 kPa:	1 ppm = Number mg/m ³ ; 1 mg/m ³ = Number ppm
This chemical is used as a pesticide:	<input type="checkbox"/>
This chemical is a biological product:	<input type="checkbox"/>
This chemical is a by-product of a process:	<input type="checkbox"/>
A biological exposure index has been recommended by these agencies:	<input type="checkbox"/> ACGIH <input type="checkbox"/> DFG <input type="checkbox"/> SCOEL

Workplace exposure standard history

Year	Standard
Click here to enter year	

References

Deutsche Forschungsgemeinschaft (DFG) (2003) Diethyl sulfate – MAK value documentation.

EU Scientific Committee on Occupational Exposure Limits (SCOEL) (2009) Recommendation from the Scientific Committee on Occupational Exposure Limits for diethyl sulphate. SCOEL/SUM/154.

European Chemicals Agency Regulation (ECHA) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH).

Health Council of the Netherlands (HCOTN) (1999) Diethylsulphate. Health-based calculated occupational cancer risk values. The Hague: Health Council of the Netherlands; publication no. 1999/08OSH.

International Agency for Research on Cancer (IARC) (1999) Volume 71 re-evaluation of some organic chemicals, hydrazine and hydrogen peroxide. IARC Monographs on the evaluation of the carcinogenic risk to humans.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2014) Sulfuric acid, diethyl ester: Human health tier II assessment – IMAF report.

National Toxicology Program (NTP) (2016) NTP-RoC: Diethyl Sulfate.

Tenth Adaptation to Technical Progress Commission Regulation (EU) No 2017/776 amending, for the purposes of its adaptation to technical and scientific progress, Regulation (EC) No 1272/2008 of the European Parliament and of the Council on classification, labelling and packaging of substances and mixtures (the CLP Regulation).