

DIACETYL

CAS number: 431-03-8

Synonyms: Biacetyl, 2,3-butanedione, dimethylglyoxal, dimethyl diketone, 2,3-diketobutane

Chemical formula: C₄H₆O₂

Structural formula: —

Workplace exposure standard (new)

TWA: 0.01 ppm (0.04 mg/m³)

STEL: 0.02 ppm (0.07 mg/m³)

Peak limitation: —

Notations: Sk.

IDLH: —

Sampling and analysis: The recommended value is quantifiable through available sampling and analysis techniques.

Recommendation and basis for workplace exposure standard

A TWA of 0.01 ppm (0.04 mg/m³) and a STEL of 0.02 ppm (0.07 mg/m³) are recommended to protect for lung damage in exposed workers.

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

Discussion and conclusions

Diacetyl is a naturally occurring chemical found in butter, caramel and coffee. It is an aromatic component in tobacco smoke and occurs in fermented products including beer and wine. Commercially, it is used as a food additive where it is used for its buttery flavour.

The critical effects of exposure to diacetyl were subclinical changes in lung function, airway obstruction and irreversible bronchiolitis obliterans, which in some, led to death or lung transplant (DFG, 2014). Exposure to vapour in an occupational setting causes irritation of the eyes, skin, nose and throat. A NOAEC of 0.02 ppm was identified in popcorn workers for airway obstruction (DFG, 2014). This was extrapolated from a cumulative NOAELs of 0.65 ppm-years and 0.8 ppm-years over 40 years to concentrations of 0.016 ppm and 0.02 ppm, respectively (DFG, 2014). ACGIH (2018) recommended a TLV-TWA of 0.01 ppm in 2012 based on the same study later referenced by the DFG (2014). Based on the weight of evidence and applying caution due to the severity of potential outcome, a TWA of 0.01 ppm (0.04 mg/m³) is recommended.

Reports of short-term onset of respiratory symptoms highlight the importance of a STEL in protecting against the onset of symptoms. The ACGIH (2018) have recommended a STEL of 0.02 ppm with limited explanation. A STEL of 0.02 ppm is recommended as a precautionary measure with a review of the data recommended at the next scheduled review.

Recommendation for notations

Not classified as a 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.

A skin notation is recommended based on human cases of contact dermatitis following dermal exposures.

DRAFT

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	NA	NA
No report.		
ACGIH	2012	TLV-TWA: 0.01 ppm (0.04 mg/m³); TLV-STEL: 0.02 ppm (0.07 mg/m³)
<p>TLV recommended for the occupational exposure and the effects on the respiratory system.</p> <p>Summary of Data:</p> <p>Human data:</p> <ul style="list-style-type: none"> • LOAEL of 0.02 ppm for fixed airway obstruction; 6 popcorn production plant workers • Lung disease (bronchiolitis obliterans-like illness) identified in 8 former popcorn factory workers; airflow obstruction was irreversible • Study on 4/6 manufacturing plants from the study above concluded that a cumulative exposure of ≥ 0.8 ppm-yr was associated with airways obstruction (increased risk of decreased FEV₁); no reduction in mean FEV₁ from exposure at mean concentration of 0.01-0.07 ppm • Reports of bronchiolitis obliterans-like illness identified in other food manufacturing industries; no qualitative or exposure data • STEL based on potential for short-term peaks and genesis of disease; based on study that reported LOAEL of 0.02 ppm; no further details <p>Animal Data:</p> <ul style="list-style-type: none"> • LD₅₀: 250 mg/kg (oral, mice) • LD₅₀: >5,000 mg/kg (dermal, rabbits) • NOAEL: 90 mg/kg/d (rats, intraperitoneal) • NOAEL: 100 ppm (rats; acute inhalation); adverse effects to the upper respiratory tract • In a sub chronic study on mice showed evidence of peribronchial lymphocytic inflammation at 50 ppm (9/10 mice) and 25 ppm (5/10 mice), insufficient information to set a NOAEL. 		
DFG	2015	MAK: 0.02 ppm (0.07 mg/m³)
<p>MAK recommended to protect from irritative effects on the eyes, skin, nose and throat and subclinical changes in lung function and bronchiolitis obliterans in workers.</p> <p>Summary of additional data:</p> <p>In humans compared to rats it has been determined that concentrations in bronchiolar tissue was 5 times higher at rest when breathing through the nose, 7 times higher when breathing through the mouth and 40 times higher during low level activity whilst breathing through the mouth.</p> <p>Human data:</p> <p>Inhalation:</p> <ul style="list-style-type: none"> • A single worker exposure (non-smoker) to heated mixture for several hours caused reddened and sore eyes with sticky secretion which subsided with steroid and antihistamine treatment. After another exposure the same worker experienced respiratory distress and >9 mo worker had developed fixed airway obstruction of moderate severity (no further detail provided) • NOAEC of 0.65 ppm-yr cumulative exposure; 135 workers microwave popcorn production plant; excess rates of lung disease and lung function abnormalities 		



Source	Year set	Standard
		<ul style="list-style-type: none"> derivation (0.65 ppm-yr÷40 yr [working life]) = 0.016 ppm NOAEC of 0.8 ppm-yr cumulative exposure; same as ACGIH (2018); no effects on the forced expiratory volume in one second and the vital capacity <ul style="list-style-type: none"> derivation (0.8 ppm-yr÷40 yr [working life]) = 0.02 ppm MAK based on above derivations; safety margin between MAK and critical effects of lung damage due to underestimation of the diacetyl concentrations and by extrapolation to 40 working years <p>Skin and mucous membrane:</p> <ul style="list-style-type: none"> Workers using butter flavouring with ambient air concentrations of 98 mL/m³ complained of eye, skin and nasal irritation Skin irritation reported at concentrations of 1.1 mL/m³ 24-h patch test using undiluted diacetyl cream on 8 subjects, reported work-related contact dermatitis from flavour handling, 1/8 patients produced a 2+ reaction and 6 patients a 3+ reaction. <p>Animal data:</p> <ul style="list-style-type: none"> NOAEC: 92.9 ppm (rats, acute inhalation); effects to the upper respiratory tract Necrotising rhinitis and lesions of the trachea observed in male rats after whole-body inhalation exposure to concentrations of 240 ppm for 6 h A NOAEC of 349 mg/m³ and a LOAEC of 697 mg/m³ were reported in male rats based on increased incidence of epithelial necrosis in the nose in an inhalation study. At the highest concentration (1,039 mg/m³ for 6 h), necrosis occurred in the trachea. No significant effects observed in the lungs Severe irritation of intact or shaved skin of rabbits exposed (undiluted) under occlusive conditions. Eye application caused severe damage to cornea and conjunctiva which did not subside for more than 21 d.
SCOEL	2014	TWA: 0.02 ppm (0.07 mg/m³); STEL: 0.10 ppm (0.36 mg/m³)
<p>Recommend OEL based on the primary critical health effect of subclinical to severe fixed airway obstruction.</p> <p>Summary of additional data:</p> <p>Human data:</p> <ul style="list-style-type: none"> NOAEC: 0.05 ppm derived from NOAEL of 0.65 ppm-yr cumulative exposure (DFG, 2014): <ul style="list-style-type: none"> (0.65 ppm-yr ÷ 40 yr [working life] × 3 for analytical bias) = 0.05 ppm 0.05/UF of 2 (sensitive groups) = 0.02 ppm (rounded). <p>Animal data:</p> <ul style="list-style-type: none"> LC₅₀: 2,250–5,200 ppm (rats, 4 h, inhalation) Sub chronic study on mice as summarised in ACGIH – no NOAEL determined due to evidence of peribronchial lymphocytic inflammation. SCOEL reviews concludes a LOAEL of 50 ppm and a NOAEL of 25 ppm. <p>Available data does not allow deriving a scientifically based STEL; STEL set by applying arbitrary assessment factor of 5 to TWA.</p>		
OARS/AIHA	NA	NA
No report.		

Source	Year set	Standard
HCOTN	NA	NA
No report.		

Secondary source reports relied upon

Source	Year	Additional information
US NIOSH	✓ 2016	<ul style="list-style-type: none"> Used same study as ACGIH and DFG data but determined 45-year working lifetime REL of 5 ppb (TWA) based on <1/1,000 excess risk of lung function falling below normal lower limits due to exposure. STEL: 0.025 ppm based on concern of greater toxicity in peak exposure than over longer time; 5 times the REL, based on past precautionary practices; limited evidence in animals to support; no further detail

Carcinogenicity — non-threshold based genotoxic carcinogens

Is the chemical mutagenic?

No

The chemical is not a non-threshold based genotoxic carcinogen.

Notations

Source	Notations
SWA	NA
HCIS	NA
NICNAS	NA
EU Annex	NA
ECHA	NA
ACGIH	Carcinogenicity – A4
DFG	H (skin), Sh (dermal sensitiser)
SCOEL	—
HCOTN	NA
IARC	NA
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

Adverse effects in human case study:	yes
Dermal LD ₅₀ ≤1000 mg/kg:	no
Dermal repeat-dose NOAEL ≤200 mg/kg:	
Dermal LD ₅₀ /Inhalation LD ₅₀ <10:	no
<i>In vivo</i> dermal absorption rate >10%:	
Estimated dermal exposure at WES >10%:	

a skin notation is warranted

IDLH

Is there a suitable IDLH value available? No

Additional information

Molecular weight:	86.09
Conversion factors at 25°C and 101.3 kPa:	1 ppm = 3.52 mg/m ³ ; 1 mg/m ³ = 0.284 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 checked="" 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
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References

American Conference of Industrial Hygienists (ACGIH®) (2018) TLVs® and BEIs® with 7th Edition Documentation, CD-ROM, Single User Version. Copyright 2018. Reprinted with permission. See the [TLVs® and BEIs® Guidelines section](#) on the ACGIH website.

Deutsche Forschungsgemeinschaft (DFG) (2015) Diacetyl – MAK value documentation.

EU Scientific Committee on Occupational Exposure Limits (SCOEL) (2014) Recommendation from the Scientific Committee on Occupational Exposure Limits for Diacetyl. SCOEL/SUM/149.

US National Institute for Occupational Safety and Health (NIOSH) (2016) Criteria for a recommended standard: occupational exposure to diacetyl and 2,3-pentanedione.