

## BENZOYL PEROXIDE

**CAS number:** 94-36-0

**Synonyms:** Dibenzoyl peroxide, benzoperoxide, benzoyl superoxide, diphenylglyoxal peroxide

**Chemical formula:** C<sub>14</sub>H<sub>10</sub>O<sub>4</sub>

### Workplace exposure standard (retained)

**TWA:** 5 mg/m<sup>3</sup>

**STEL:** —

**Peak limitation:** —

**Notations:** DSEN

**IDLH:** 1,500 mg/m<sup>3</sup>

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

### Recommendation and basis for workplace exposure standard

A TWA of 5 mg/m<sup>3</sup> is recommended to protect for irritation of the skin, mucous membranes and upper respiratory tract in exposed workers.

### Discussion and conclusions

Similar to other organic peroxides, benzoyl peroxide is used to generate reactive organic radicals for curing and finishing processes in the food, chemical and niche pharmaceutical industries. Due to this reactivity, benzoyl peroxide causes irritation on contact with skin, mucous membranes and the upper respiratory tract (ACGIH, 2018; DFG, 1990). It is considered a dermal sensitiser based on positive results in repeat dermal dose studies in humans (NICNAS, 2016). Intoxication from skin absorption and systemic distribution is unlikely due to its local metabolism at the point of contact (DFG, 1990).

Despite its demonstrated mutagenicity *in vitro* (DFG, 1990), benzoyl peroxide is not shown to be carcinogenic in animals or humans (ACGIH, 2018; HCOTN, 2012).

The TWA is derived from a NOAEL of 5.25 mg/m<sup>3</sup> measured by upper respiratory irritation in a case study of workers at a formulation plant.

### Recommendation for notations

Not classified as a carcinogen according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS).

Classified as a skin sensitiser and not a respiratory sensitiser according to the GHS.

A skin notation is not warranted as there is no evidence of systemic effects resulting from skin absorption in human studies.

## APPENDIX

### Primary sources with reports

Source	Year set	Standard
<b>SWA</b>	<b>Year</b>	<b>TWA: 5 mg/m<sup>3</sup></b>
<b>ACGIH</b>	<b>2001</b>	<b>TLV-TWA: 5 mg/m<sup>3</sup></b>
<p>TLV-TWA intended to minimise the potential for irritation of the skin, mucous membranes and upper respiratory tract.</p> <p>Not classifiable as a human carcinogen based on repeat skin application study in mice.</p> <p>Insufficient data available to recommend Skin or SEN notations or a TLV-STEL.</p> <p>Summary of data:</p> <p>Human data:</p> <ul style="list-style-type: none"> <li>• NOAEL: 5.25 mg/m<sup>3</sup> measured by upper respiratory tract irritation in case study of formulation plant workers (duration unspecified) <ul style="list-style-type: none"> <li>◦ LOAEL: 12.2 mg/m<sup>3</sup></li> </ul> </li> <li>• Unknown cumulative effects in humans; no cases of chronic exposure are reported</li> <li>• There were 32% positive responses, including sensitisation, to challenge patch following 10 repeat applications on the arm (5% benzoyl peroxide, solvent and concentration expression unspecified)</li> <li>• TLV-TWA may not protect individuals who are hypersusceptible to effects of benzoyl peroxide exposure.</li> </ul> <p>Animal data:</p> <ul style="list-style-type: none"> <li>• No inhalational toxicity data available for benzoyl peroxide <ul style="list-style-type: none"> <li>◦ LC<sub>50</sub> values for structurally related organic peroxides correlate well with their corresponding intraperitoneal and oral LD<sub>50</sub> values</li> </ul> </li> <li>• Exposure to structurally related organic peroxides: LD<sub>50</sub>: ≈90 mg/kg (mice, intraperitoneal); LC<sub>50</sub>: ≈220–500 ppm (mice, 4 h) <ul style="list-style-type: none"> <li>◦ the calculated LC<sub>50</sub> of benzoyl peroxide for mice is ≈700 ppm (calculated, 4 h)</li> </ul> </li> <li>• Repeat dose intraperitoneal injections of related organic peroxides at 20% of the LD<sub>50</sub> caused death (rats, 3 d/wk, 7 wk) <ul style="list-style-type: none"> <li>◦ benzoyl peroxide is speculated to have similar cumulative toxicity</li> </ul> </li> <li>• Repeat skin application did not cause cancer in mice (concentration and duration unspecified)</li> <li>• Tumour promoter in mice and hamsters; no reports of complete carcinogenic or tumour initiating activity</li> <li>• NOAEL: &gt;2,800 mg/kg measured by tumour incidence in repeat feeding study (mice, rats, 80 wk).</li> </ul>		
<b>DFG</b>	<b>1969</b>	<b>MAK: 5 mg/m<sup>3</sup></b>
<p>Summary of additional data:</p> <ul style="list-style-type: none"> <li>• Assessment grouped with other organic peroxides and hydrogen peroxide</li> <li>• Allergic contact dermatitis due to exposure has been reported</li> <li>• Phototoxic effects reported but not confirmed</li> </ul>		

Source	Year set	Standard
<ul style="list-style-type: none"> <li>Further study required to determine potential direct or indirect carcinogenesis from radical metabolites</li> <li>Systemic toxic effects following dermal application are unlikely due to complete metabolism of the peroxide to benzoic acid in the epidermis and relatively slow skin absorption rate (5.1 µg/cm<sup>2</sup>/d).</li> </ul> <p>Animal data:</p> <ul style="list-style-type: none"> <li>Separate studies report LD<sub>50</sub> of &gt;950 and &gt;5000 mg/kg (rats, oral)</li> <li>LC<sub>50</sub>: &gt;24.3 g/m<sup>3</sup> (rats, 4 h)</li> <li>No skin irritation in rabbits, eye irritation &gt; 24 h of application (concentration unspecified)</li> <li>Moderate erythema on guinea pig skin (10% solution in propylene glycol)</li> <li>Single and repeat dermal studies without co-application of tumour initiators suggest no primary carcinogenic activity, tumour promotion demonstrated in combination with tumour initiators: <ul style="list-style-type: none"> <li>no tumours at 120 mg (rats, 20% starch suspension, concentration expression not specified)</li> <li>no tumours at 2.9 mg (rats, 0.2 ml tricaprylin, twice/wk, 12 wk)</li> <li>melanomas at 80–160 mg after tumour initiation 1 wk prior with 10 mg/kg DMBA (hamsters, peroxide in 1 ml acetone, 3 times/wk, 16 mo)</li> </ul> </li> <li>Bacterial <i>in vitro</i> studies indicate no mutagenicity; DNA strand breaks reported in mouse cell assay</li> <li><i>In vitro</i> mutagenicity studies are inconclusive for benzoyl peroxide, but other related organic peroxides are evidently mutagenic.</li> </ul>		
<b>SCOEL</b>	<b>NA</b>	<b>NA</b>
No report.		
<b>OARS/AIHA</b>	<b>NA</b>	<b>NA</b>
No report.		
<b>HCOTN</b>	<b>2012</b>	<b>Not Assigned</b>
<p>Summary of additional data:</p> <p>Human data:</p> <ul style="list-style-type: none"> <li>No increased risk of malignant melanomas reported in case control study (159 cases, 213 controls) of acne patients.</li> </ul> <p>Animal data:</p> <ul style="list-style-type: none"> <li>NOAEL: 28 mg/kg measured by bw in repeat feeding study (cited by ACGIH, 2001)</li> <li>Evidence of tumour promoting activity in combination with common initiating agents: DMBA, methylnitrosoguanidine and benzo(a)pyrene, but not ultraviolet light.</li> </ul>		

## Secondary source reports relied upon

Source	Year	Additional information
NICNAS	✓ 2016	<ul style="list-style-type: none"> <li>Considered to have low acute toxicity following dermal exposure, no acute or chronic dermal exposure data available</li> <li>LC<sub>50</sub>: &gt;24.3 mg/L (rats, 4 h)</li> </ul>



Source	Year	Additional information
		<ul style="list-style-type: none"> <li>○ at these concentrations salivation, squinting, breathing difficulty, lacrimation, erythema, changed respiratory rates, motor activity and ocular irritation were noted</li> <li>• Patch tests using 1%, 0.5% or 0.25% (concentration expression not specified) resulted in 16/30 positive responses.</li> <li>• Human maximisation test (n=50) using 5 and 10% gels (composition unspecified) gave 38/50 positive results for skin sensitisation.</li> </ul>
US NIOSH	✓ 1994	<ul style="list-style-type: none"> <li>• IDLH: 1,500 mg/m<sup>3</sup> from acute inhalation toxicity data in animals.</li> </ul>

### Carcinogenicity — non-threshold based genotoxic carcinogens

Is the chemical mutagenic? Insufficient data

Is the chemical carcinogenic with a mutagenic mechanism of action? No

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

### Notations

Source	Notations
SWA	Sen
HCIS	Skin sensitisation – category 1
NICNAS	Skin sensitisation – category 1
EU Annex	Skin sensitisation – category 1
ECHA	NA
ACGIH	Carcinogenicity – A4
DFG	—
SCOEL	NA
HCOTN	—
IARC	Carcinogenicity – Group 3
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: no

Dermal LD<sub>50</sub> ≤ 1000 mg/kg:

Dermal repeat-dose NOAEL ≤ 200 mg/kg:

Dermal LD<sub>50</sub>/Inhalation LD<sub>50</sub> < 10:

*In vivo* dermal absorption rate > 10%:

Estimated dermal exposure at WES > 10%:

**a skin notation is not warranted**

## IDLH

Is there a suitable IDLH value available? Yes

## Additional information

Molecular weight: 242.22 g/mol

Conversion factors at 25°C and 101.3 kPa: 1 ppm = Number mg/m<sup>3</sup>; 1 mg/m<sup>3</sup> = Number ppm

This chemical is used as a pesticide: ☐

This chemical is a biological product: ☐

This chemical is a by-product of a process: ☐

A biological exposure index has been recommended by these agencies: ☐ ACGIH ☐ DFG ☐ SCOEL

## Workplace exposure standard history

Year	Standard
Click here to enter year	

## References

American Conference of Industrial Hygienists (ACGIH®) (2018) TLVs® and BEIs® with 7<sup>th</sup> 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) (1990) Organic peroxides – MAK value documentation.

Health Council of the Netherlands (HCOTN) (2012) (Di)benzoyl peroxide. Health-based calculated occupational cancer risk values. The Hague: Health Council of the Netherlands; publication no. 2012/24.

International Agency for Research on Cancer (IARC) (1987) Benzoyl peroxide. IARC Monographs on the evaluation of the carcinogenic risk to humans volume 71.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2016) Peroxide, dibenzoyl: Human health tier II assessment – IMAP report.

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).

US National Institute for Occupational Safety and Health (NIOSH) (1994) Immediately dangerous to life or health concentrations – Benzoyl peroxide.

DRAFT