# 3,3'-Dichlorobenzidine

| CAS number: | 91-94-2 |
| --- | --- |
| Synonyms: | DCB, o,o'-Dichlorobenzidine |
| Chemical formula: | C12H10Cl2N2 |

Workplace exposure standard (amended)

| TWA: | **0.1 ppb (1.2 µg/m3)** |
| --- | --- |
| STEL: | **—** |
| Peak limitation: | **—** |
| Notations: | **Carc. 1B, Sk.** |
| IDLH: | **—** |
| **Sampling and analysis**: The recommended value is likely to be below the current limit of detection for standard sampling and analysis techniques. | |

## Recommendation and basis for workplace exposure standard

A TWA of 0.1 ppb (1.2 µg/m3) is recommended to reduce the risk of cancer in exposed workers.

## Discussion and conclusions

3,3’‑Dichlorobenzidine (DCB) is used in the manufacture of azo dyes, as an intermediate for Benzidine Yellow pigments, and possesses similar physical and chemical properties to benzidine.

Evidence derived from animal studies suggest carcinogenic potential for humans. In combination with the positive mutagenicity results and DCB’s similarity to benzidine (a confirmed human carcinogen), the mode of action for carcinogenicity is considered genotoxic. DCB is characterised as a non-threshold genotoxic carcinogen as there is insufficient evidence to establish a threshold exposure concentration at which zero risk of cancer exists (ACGIH, 2018; DFG, 1993; NICNAS, 2014; US EPA, 2006).

The recommended TWA is derived at a minimal cancer risk level using a cancer slope factor based on studies reporting statistically significantly increased tumour incidences in rats, mice and dogs (US EPA, 2006).

## 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.

A skin notation is recommended based on evidence suggesting potential dermal absorption and adverse systemic effects in animals.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA 1991 NA | |
| Probable human carcinogen, not currently possible to assign an appropriate exposure standard.  Absorption through the skin may be a significant source of exposure. |
| ACGIH 2001 NA |
| No numerical TLV assigned.  Summary of data:  DCB possesses similar physical and chemical properties to benzidine.  Benzidine is an acknowledged human bladder carcinogen.  Human data:   * Considered an eye and upper respiratory tract irritant * Reported upper respiratory infection and sore throat by workers handling DCB hydrochloride * One author concluded no evidence of cancer developing among the exposed workers * Insufficient evidence regarding carcinogenicity in humans.   Animal data:   * Limited acute data; 1 h exposure of undisclosed concentration of DCB dust caused some irritation and moderate pulmonary congestion * 4/5 rabbits died following application of 1 g/kg to skin for 24 h * Oral LD50 in rats 7 g/kg for base and 3.82 g/kg for hydrochloride salt; GIT congestion and haemorrhaging * 9/14 rats survived 288 d following ingestion of 700 mg/kg 5 d/wk; liver damage and 1 tumour identified * Rats fed DCB demonstrated tumours of the skin, sebaceous (zymbal gland) and mammary glands and papillomas of the bladder; carcinogenic in mice, dogs, rats and hamsters by oral administration. |
| DFG 1993 NA |
| No MAK recommended due to potential carcinogenic properties.  Summary of additional data:   * Positive genotoxicity in *Salmonella typhimurium* strains * Various tumours developed after oral or subcutaneous administration of DCB to mice, rats, hamsters and dogs. |
| SCOEL NA NA |
| No report. |
| OARS/AIHA NA NA |
| No report. |
| HCOTN NA NA |
| No report. |

### Secondary source reports relied upon

| Source |  | Year | Additional information |
| --- | --- | --- | --- |
| NICNAS |  | 2014 | * Epidemiological studies are inadequate to evaluate the relationship between human cancer and exposure * Ability to form DNA adducts and the metabolic pathways in animals, for the chemicals, are similar to benzidine which is a known human carcinogen. |
| US EPA |  | 2006 | * Mutagenic in *salmonella typhimurium* both in the presence and absence of metabolic activation by S-9 liver preparations * Sufficient data exists in animals as to carcinogenicity; several studies presented * Liver carcinoma and bladder papillary transitional cell carcinomas in female beagles orally dosed over 7 yr. |

### 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? | Yes |
| Cancer slope factor (1/(mg/kg/day)) | 4.5 x 10-1 |
| Calculated TWA value (µg/m3) | 1.2 |

## Notations

| Source | Notations |
| --- | --- |
| SWA | Carc. 2 |
| HCIS | Carcinogenicity – category 1B |
| NICNAS | Carc. Cat. 2 |
| EU Annex | Carcinogenicity – category 1B |
| ECHA | Carcinogenicity – category 1B |
| ACGIH | Carcinogenicity – A3, Skin |
| DFG | H (skin) |
| SCOEL | NA |
| HCOTN | NA |
| IARC | Carcinogenicity – Group 2B |
| 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: |  |  |  |  | | Dermal LD50 ≤1000 mg/kg: | yes | 3.00 |  |  | | Dermal repeat-dose NOAEL ≤200 mg/kg: |  |  |  |  | | Dermal LD50/Inhalation LD50 <10: |  |  |  |  | | *In vivo* dermal absorption rate >10%: |  |  |  |  | | Estimated dermal exposure at WES >10%: |  |  |  |  | |  |  | 3 | **consider assigning a skin notation** | | |

### IDLH

| Is there a suitable IDLH value available? | No |
| --- | --- |

## Additional information

| Molecular weight: | 253.13 |
| --- | --- |
| Conversion factors at 25°C and 101.3 kPa: | 1 ppm = Number mg/m3; 1 mg/m3 = 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 7th Edition Documentation, CD-ROM, Single User Version. Copyright 2018. Reprinted with permission. See the [*TLVs® and BEIs® Guidelines section*](http://www.acgih.org/tlv-bei-guidelines/policies-procedures-presentations) on the ACGIH website.

European Chemicals Agency (ECHA) (2019) 3,3'-Dichlorobenzidine – REACH assessment.

Deutsche Forschungsgemeinschaft (DFG) (1993) 33′‐Dimethoxybenzidine – MAK value documentation.

International Agency for Research on Cancer (IARC) (1987) 3,3'-Dichlorobenzidine. IARC Monographs on the evaluation of the carcinogenic risk to humans. 29, Sup 7.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2014) [1,1'-Biphenyl]-4,4'-diamine, 3,3'-dichloro-: 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 Environmental Protection Authority (US EPA) (2006) Integrated Risk Information System (IRIS) Chemical Assessment Summary – 3,3'-Dichlorobenzidine.