



## DIQUAT

**CAS number:** 85-00-7

**Synonyms:** 1,1'-Ethylene-2,2'-bipyridylium ion, diquat dibromide (ISO)

**Chemical formula:**  $C_{12}H_{12}Br_2N_2$

**Structural formula:** —

### Workplace exposure standard (amended)

**TWA:** 0.5 mg/m<sup>3</sup> (inhalable);  
0.1 mg/m<sup>3</sup> (respirable)

**STEL:** —

**Peak limitation:** —

**Notations:** DSEN

**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 0.5 mg/m<sup>3</sup> (inhalable fraction) and 0.1 mg/m<sup>3</sup> (respirable fraction) are recommended to protect for potential lung irritation and chronic cataract formation in exposed workers.

### Discussion and conclusions

Diquat is primarily used as a herbicide.

Animal studies report critical effects of exposure are lung irritation and cataract formation on chronic exposure; these effects have not been confirmed in occupational studies of workers applying or manufacturing the substance (ACGIH, 2018). Only one primary source was available.

The current TWA of 0.5 mg/m<sup>3</sup> for inhalable fractions (with mass median aerodynamic diameters (MMAD) greater than 5 µm) which was adopted from ACGIH (2018) by analogy to paraquat is recommended to be retained. This approach is supported by low absorption rates reported in humans (ACGIH, 2018). An additional TWA of 0.1 mg/m<sup>3</sup> derived by ACGIH for respirable fractions is recommended based on a NOAEC of 0.097 mg/m<sup>3</sup> (1.5 µm MMAD), for lung irritation reported in sub-chronically exposed rats (ACGIH, 2018). The combination of TWA for inhalable and respirable fractions of diquat is considered protective for the critical end points.

### 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. However, inconsistencies in the notation for sensitising potential were found during the evaluation. No

experimental evidence for skin or respiratory sensitisation is presented in the available data, which is inconsistent with the notations currently assigned in the HCIS database. The current skin sensitisation is retained in accordance with GHS. An examination of the available data for these notations is recommended for subsequent reviews.

There are insufficient data to recommend a skin notation. However, inconsistencies in the notation for dermal toxicity were found during the evaluation. Evidence for dermal toxicity is equivocal. Urinary concentrations following dermal exposure in volunteers were very low, and limited evidence for systemic toxicity in animals (ACGIH, 2018); although a skin notation was assigned by this agency.

DRAFT

## APPENDIX

### Primary sources with reports

Source	Year set	Standard
<b>SWA</b>	<b>1991</b>	<b>TWA: 0.5 mg/m<sup>3</sup></b>
<b>ACGIH</b>	<b>2001</b>	<b>TLV-TWA (Inhalable): 0.5 mg/m<sup>3</sup>; (Respirable): 0.1mg/m<sup>3</sup></b>
<p>TLV-TWA intended to minimise lung irritation and formation of cataracts from chronic exposure.</p> <p>Summary of data:</p> <p>TLV-TWA (respirable) is derived from NOAEL of 0.097 mg/m<sup>3</sup> for reversible lung irritation in rats in sub-chronic inhalation studies exposed to aerosols of MMAD 1.5–1.9 µm; the TLV-TWA of 0.5 mg/m<sup>3</sup> (inhalable) is recommended for aerosols greater than 5 µm MMAD (no further details provided).</p> <p>Human data:</p> <ul style="list-style-type: none"> <li>61% of IV dose recovered in urine of volunteers (10 h), but only 0.3% in dermal dose</li> <li>No detectable inhalational exposure in workers applying substance as herbicide <ul style="list-style-type: none"> <li>negligible inhalational exposure to workers during aerial application as herbicide (no further details provided)</li> </ul> </li> <li>Occupational hygiene studies found no signs of upper respiratory tract irritation in workers exposed at average air concentrations of 0.002 mg/m<sup>3</sup>.</li> </ul> <p>Animal data:</p> <ul style="list-style-type: none"> <li>Oral LD<sub>50</sub>: 62–200 mg/kg depending on species and sex (rats, mice, rabbits, dogs, no exposure data provided) <ul style="list-style-type: none"> <li>at lethal doses, symptoms appear after 24 h and include lethargy, respiratory difficulty, weight loss and weakness, and cause death after 2–14 d</li> </ul> </li> <li>Low oral absorption reported in metabolic studies (rats, 4–6%; 10–20% dogs)</li> <li>LD<sub>50</sub>: &gt;400 mg/kg (rabbits, 24 h, dermal); no effects observed at this concentration</li> <li>Sub-chronic inhalation exposure study with exposure groups of 0, 0.49, 1.1 and 3.8 mg/m<sup>3</sup> as aerosol (rats, 6 h/d, 5 d/wk, 3 wk): <ul style="list-style-type: none"> <li>LOAEC of 0.49 mg/m<sup>3</sup> for histopathological changes/lesions in lungs</li> <li>3.8 mg/m<sup>3</sup> group showed bw loss and abnormal respiratory sounds</li> <li>all adverse effects were reversible (observation period not specified)</li> <li>follow-up study found NOAEC of 0.097 mg/m<sup>3</sup> under the same conditions with slightly smaller aerosol particle size</li> </ul> </li> <li>Dose-dependent cataract formation reported in a chronic feeding study, treatment range: 0, 0.5, 25, and 50 mg/kg/d (rats, 2 yr); no other pathological effects in blood, urine, growth, or carcinogenicity noted: <ul style="list-style-type: none"> <li>NOAEL of 0.5 mg/kg/d for cataract formation</li> <li>complete opacities appeared within 6 mo in 25% of rats at 50 mg/kg/d</li> <li>second study of same duration and lower treatment range reported NOAEL &gt;0.22 mg/kg/d and &lt;0.66 mg/kg/d</li> <li>similar dose-response relationship in 4 yr study in dogs, and a NOAEL of 1.7 mg/kg/d for cataract formation</li> </ul> </li> <li>No evidence for carcinogenicity in chronic feeding study at 0, 30, 150, or 500 ppm in diet (mice, 80 wk); 500 ppm were reduced to 400 then 300 ppm after 3 and 5 wk, respectively</li> <li>No evidence for reproductive toxicity in 3 generation study at 0, 250 and 500 ppm in diet of rats</li> </ul>		



Source	Year set	Standard
<ul style="list-style-type: none"> <li>maternal and natal cataract formation observed at 500 ppm</li> <li>No teratogenic effects, but foetal mortality and resorption occurred at 15 mg/kg by IV on GD 7–21 (rats)</li> <li>Equivocal mutagenicity data: negative results for Ames tests with <i>E. coli</i> and dominant lethal test, but positive for DNA aberrations in <i>Saccharomyces cerevisiae</i> and human SV-40 cells.</li> </ul> <p>No evidence for carcinogenicity found in chronic exposure studies with mice, which supports an A4 classification. Limited dermal studies with rats and rabbits suggest a skin notation is required. Insufficient data to assign a STEL or sensitisation notation.</p>		
<b>DFG</b>	<b>NA</b>	<b>NA</b>
No report.		
<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>NA</b>	<b>NA</b>
No report.		

## Secondary source reports relied upon

Source	Year	Additional information
HSE	✓ 2002	<ul style="list-style-type: none"> <li>8 h TWA: 0.5 mg/m<sup>3</sup>; 15 min STEL: 1 mg/m<sup>3</sup>.</li> </ul>
NICNAS	✓ 2018	<ul style="list-style-type: none"> <li>Tier I assessment: agricultural and therapeutic uses are excluded from assessment.</li> </ul>
US EPA	✓ 1994	<ul style="list-style-type: none"> <li>Reference oral dose derived from same studies as reported in ACGIH (2018); additional teratology study reports (rabbits, no further experimental details provided):               <ul style="list-style-type: none"> <li>systemic NOEL of 1.25 mg/kg/day</li> <li>teratogenic NOEL of 5.0 mg/kg/day for maternal weight loss</li> </ul> </li> <li>Carcinogenicity not evaluated</li> <li>Sensitisation potential not discussed.</li> </ul>
ECHA	✓ 2019	<ul style="list-style-type: none"> <li>May cause an allergic skin reaction and respiratory irritation (no further information provided).</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	NA
EU Annex	NA
ECHA	Skin Sens. 1
ACGIH	Carcinogenicity – A4, Skin
DFG	NA
SCOEL	NA
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: no  
 Dermal LD<sub>50</sub> ≤ 1000 mg/kg: yes  
 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%:

**consider assigning a skin notation**

## IDLH

Is there a suitable IDLH value available? No

## Additional information

Molecular weight:	344.1
Conversion factors at 25°C and 101.3 kPa:	1 ppm = 14.07 mg/m <sup>3</sup> ; 1 mg/m <sup>3</sup> = 0.07 ppm
This chemical is used as a pesticide:	✓
This chemical is a biological product:	<input type="checkbox"/>
This chemical is a by-product of a process:	<input type="checkbox"/>



Molecular weight:	344.1
Conversion factors at 25°C and 101.3 kPa:	1 ppm = 14.07 mg/m <sup>3</sup> ; 1 mg/m <sup>3</sup> = 0.07 ppm
This chemical is used as a pesticide:	✓
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

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.

European Chemicals Agency (ECHA) (2019) Diquat dibromide – REACH assessment.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2018) Dipyrido[1,2-a:2',1'-c]pyrazinediium, 6,7-dihydro-, dibromide: Human health tier I assessment – IMAP report.

Tenth Adaptation to Technical Progress Commission Regulation (EU Annex) 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) (1994) Integrated Risk Information System (IRIS) Chemical Assessment Summary – Diquat.