



TRIGLYCIDYLISOCYANURATE (TGIC)

CAS number: 2451-62-9

Synonyms: PT-810, 1,3,5-triazine-2,4,6-(1H,3H,5H)-trione, TEPIC, TGIC, tris (2,3-epoxypropyl) isocyanurate, 1,3,5-tris (oxiranylmethyl)-1,3,5-triazin-2,4,6(1H,3H,5H)trion

Chemical formula: $C_{12}H_{15}N_3O_6$

Structural formula: —

Workplace exposure standard (interim)

TWA: 0.05 mg/m³

STEL: —

Peak limitation: —

Notations: Sk., 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 0.05 mg/m³ is recommended to minimise potential for dermal sensitisation and adverse haematological and fertility effects 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

Triglycidylisocyanurate (TGIC) is used as a powder coating resin.

The critical effects of exposure are dermal sensitisation and adverse haematological and fertility effects.

Human data are limited to case reports of dermal sensitisation and intravenous injection studies.

Dermal sensitisation reported in exposed workers and affirmed with positive sensitisation results in animal studies (ACGIH, 2018; DFG, 2014). The available data suggest potential respiratory sensitisation in exposed workers; an immunological mechanism of action is not identified (DFG, 2014; NICNAS, 2001). A LOAEL of 2.3 mg/kg (lowest dose used; intravenous dose) for adverse haematological effects are reported in phase I clinical trials for cancer therapeutics (ACGIH, 2018). No chronic inhalation studies are available (ACGIH, 2018; ECHA, 2020). However, a NOAEC for fertility endpoints at 2.5 to 7.8 mg/m³ reported in repeat (five days) reproductive, inhalation studies in mice depending on experimental conditions (ACGIH, 2018).

In the absence of suitable chronic inhalation data, ACGIH (2018) recommend a TWA of 0.05 mg/m³, which is substantially lower than the lowest NOAEC of 2.5 mg/m³ for adverse fertility effects in mice;

and thereby is also expected to be protective of adverse haematological changes and dermal sensitisation. DFG (2014) does not recommend a numerical TWA equivalent based on evidence for dermal and potential respiratory sensitisation in humans. In view of the uncertainty in the available database, the TWA of 0.05 mg/m³ by ACGIH (2018) is recommended to be adopted in the interim.

Further assessment of additional sources is recommended during subsequent reviews of the WES because of the unresolved potential for respiratory sensitisation.

Recommendation for notations

Not classified as a carcinogen according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS). No entry for the substance was identified in the HCIS database.

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

A skin notation is warranted as evidence indicates contact dermatitis in humans.

APPENDIX

Primary sources with reports

| Source | Year set | Standard |
|--|-------------|---------------------------------------|
| SWA | 1994 | TWA: 0.08 mg/m³ |
| ACGIH | 2001 | TLV-TWA: 0.05 mg/m³ |
| <p>TLV-TWA intended to protect for sensitisation, adverse haematopoietic, spermatogonial and fertility effects.</p> <p>Summary of information:</p> <p>TLV-TWA based on NOAEC of 2.5 mg/m³ for sperm cell toxicity in mice; UF of 50 applied to account for uncertainty in the database regarding chronic inhalation exposure and unresolved, but indicative, evidence for sensitisation potential. Agency notes occupational exposure typically involves the polymeric form, which is expected to be less toxic based on a NOAEC of 100 mg/m³ for sperm cell toxicity in mice.</p> <p>Human data:</p> <ul style="list-style-type: none"> • Plasma $t_{1/2}$: 0.7–1.4 min • Haematological changes including leukopenia, thrombocytopenia, platelet suppression and myelosuppression commonly observed at 2.3–50 mg/kg IV doses in phase I clinical trials of substance as cancer therapeutic • Allergic contact dermatitis associated with occupational exposure to powder coating: <ul style="list-style-type: none"> ○ pure substance elicited stronger response than powder coating product. <p>Animal data:</p> <ul style="list-style-type: none"> • LC₅₀ of 2,000 mg/m³ (mice, 4 h); no microscopic lesions or mortality at 2,480–11,640 mg/m³ of polymeric powder coating • Equivocal results for dermal sensitisation in several studies in guinea pigs (no further details) • NOAEL of 27 mg/kg/d for diarrhoea, lethargy, moderate to severe adverse haematopoietic changes, reduced kidney, heart and liver weights and necrosis of gastric mucosae in repeat IV injection study (mice, 5 d); LOAEL of 53 mg/kg/d: <ul style="list-style-type: none"> ○ similar effects at lower endpoints in parallel study with dogs. NOAEL of 0.8 mg/kg/d and a LOAEL 8 mg/kg/d • No chronic bioassays available for carcinogenicity • A tumour promotion study considered inadequate: <ul style="list-style-type: none"> ○ no skin tumour promoting effect when co-administered with dimethylbenzanthracene in dermal application study (mice, 26 wk) • Pure substance was mutagenic <i>in vitro</i> in bacteria with or without metabolic activation; powder coating product was not • NOAEC of 2.5 mg/m³ for toxicity to dividing spermatogonial cells and chromosomal aberrations <i>in vivo</i> in repeat whole-body inhalation study (mice, 6 h/d, 5 d); observations at 10 and 50 mg/m³ confounded by cytotoxicity: <ul style="list-style-type: none"> ○ NOAEC of 7.8 mg/m³ in separate nose-only inhalation study (mice, 6 h/d, 5 d) ○ chromosomal aberrations also evidenced in repeat gavage study at 43 or 128 mg/kg/d (mice, 5 d) • Reduced fertility and no sex-linked recessive lethal mutations at 10 mg/m³ and 50 mg/m³ (mice, 6 h/d, 5 d); NOAEC of 2.5 mg/m³. | | |

| Source | Year set | Standard |
|--|-------------|---------------------|
| Insufficient data to recommend a TLV-STEL or notations for carcinogenicity, skin absorption, sensitisation. | | |
| DFG | 2014 | Not assigned |
| <p>Summary of additional information:</p> <p>No MAK established due to weight of evidence for dermal sensitisation in well-documented clinical studies of occupational contact dermatitis, supported by positive sensitisation results in several studies with guinea pigs. Respiratory sensitisation suggested in some human studies; agency considered immunological mechanism of action probable but unaffirmed. Therefore, dermal and respiratory sensitizer notations recommended.</p> <p>Human data:</p> <ul style="list-style-type: none"> Positive dermal sensitisation reactions reported in several patch test studies: <ul style="list-style-type: none"> 2-fold positive reaction to 0.1, 0.5, 1 and 2% solutions of pure substance in petrolatum (petroleum jelly) in production worker. No reaction in control subjects 2-fold positive reaction in 4/5 polyester resin workers to 1% solution pre-orbital eczema/swelling in 3 workers, who reacted positively to 1% solution. No reaction in 10 controls 6/182 positive reactions in patients suspected of allergic contact dermatitis to epoxy resins. Several cases of respiratory sensitisation reported in support of a respiratory sensitizer notation: <ul style="list-style-type: none"> asthma developed in powder coating workers (n=6), 4/6 had non-specific bronchial hyperactivity; decreased forced expiratory second volume (FEV₁) in 2 of these 4 patients at bronchial challenges with 0.3 and 2 g of heated substance (7, 11, 16 or 60 min) compared with 3 controls immediate 25–30% decrease in FEV₁ in 2 /4 workers with occupationally-derived respiratory symptoms; 1 of these 2 patients had non-specific bronchial hyperactivity no specific immunological reaction in powder coating worker who developed asthma symptoms 4 mo after beginning employment no evidence for respiratory sensitisation in worker with confirmed dermal sensitisation. <p>Animal data:</p> <ul style="list-style-type: none"> Several dermal sensitisation studies with guinea pigs presented in support of sensitisation evidence in humans; DFG notes these studies do not comply with current guidelines: <ul style="list-style-type: none"> positive reaction in 4/20 animals compared to controls in occlusive patch test 1 wk after induction with 40 mg and challenge with 120 mg positive reactions in 12/20 and 18/20 animals compared to controls with 0.05% technical-grade product as induction and challenge with 50% solution reported in 2 separate studies. | | |
| 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 | ✓ 2001 | <ul style="list-style-type: none"> Classified as a skin sensitiser and category 2 mutagen Several case reports of allergic dermatitis and occupational asthma in workers: <ul style="list-style-type: none"> positive patch tests confirmed skin sensitisation of these workers Respiratory hypersensitivity reported in 2 case studies (also reported in DFG, 2014): <ul style="list-style-type: none"> no immunological mechanism reported Weak direct-acting mutagen based on mutagenicity assays <i>in vitro</i> with bacteria Powder coating product mutagenic in forward mutation assay with mouse lymphoma cells with or without metabolic activation Low DNA covalent binding potential in rat and human livers <i>in vivo</i> reported in 1 study Equivocal evidence for dominant lethal mutations in mice Insufficient data to classify carcinogenic potential. |
| Nordic Council | ✓ 2001 | <ul style="list-style-type: none"> Contact dermatitis evidenced in workers Genotoxic potential demonstrated <i>in vitro</i> and <i>in vivo</i>, reduced number of spermatozoa (rats) and fertility (mice) Not possible to identify threshold exposure for adverse effects from currently available data. |
| ECHA | ✓ 2020 | <ul style="list-style-type: none"> No long-term dermal or long-term inhalation studies available Long-term worker DNEL adopted from ACGIH (2018) TLV-TWA recommendation. |

Carcinogenicity — non-threshold based genotoxic carcinogens

Is the chemical mutagenic? Yes

Is the chemical carcinogenic with a mutagenic mechanism of action? Insufficient data

Insufficient data are available to determine if the chemical is a non-threshold based genotoxic carcinogen.

Notations

| Source | Notations |
|----------|---------------------------------|
| SWA | Sen |
| HCIS | NA |
| NICNAS | — |
| EU Annex | Skin sensitisation – category 1 |
| ECHA | Skin Sens. 1 |



| Source | Notations |
|----------|---|
| ACGIH | — |
| DFG | Sa (respiratory sensitiser), Sh (dermal sensitiser) |
| 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:
 Dermal LD₅₀ ≤ 1000 mg/kg:
 Dermal repeat-dose NOAEL ≤ 200 mg/kg:
 Dermal LD₅₀/Inhalation LD₅₀ < 10:
In vivo dermal absorption rate > 10%:
 Estimated dermal exposure at WES > 10%:

yes

no

a skin notation is warranted

IDLH

Is there a suitable IDLH value available?

No

Additional information

| | |
|---|--|
| Molecular weight: | 297.3 |
| Conversion factors at 25°C and 101.3 kPa: | 1 ppm = 12.15 mg/m ³ ; 1 mg/m ³ = 0.082 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

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) (2014) Triglycidylisocyanurat – MAK value documentation, German language edition.

European Chemicals Agency (ECHA) (2020) 1,3,5-tris(oxiranylmethyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione – REACH assessment.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2001) Triglycidylisocyanurate (TGIC): Priority Existing Chemical Secondary Notification Assessment Report No. 1S.

Nordic Expert Group for Criteria Documentation of Health Risks of Chemicals (2001) 128. Triglycidyl isocyanurate. NR 2001:18.

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).