Derived No-Effect Levels (DNELs) of TCDDA

CAS 42594-17-2

Exposure pattern	DNEL	
	Workers	**General population**
Acute - inhalation, systemic effects	No hazard identified	
Acute - dermal, local effects	No hazard identified	
Acute - inhalation, local effects	No hazard identified	
Long-term - dermal, systemic effects	Not relevant	Not relevant
Long-term - dermal, local effects	No hazard identified	No hazard identified
Long-term - inhalation, systemic effects	4.94 mg/m^3	Not relevant
Long-term - inhalation, local effects	No hazard identified	No hazard identified
Long-term - oral, systemic effects	Not relevant	0.50 mg/kg bw/day

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1. Toxicological profile

The toxicological profile of Triclyclodecane dimethanol diacrylate (TCDDA) has been described in detail in the disseminated ECHA dossier[i]. TCDDA has no harmonized classification according to Regulation (EC) No. 1272/2008 and is self-classified as Repr 1B, Skin Sens. 1B and Aquatic Chronic 1.

1.1. Toxicokinetics

Specific toxicokinetic or dermal absorption studies are not available for TCDDA. Despite its low water solubility (9.78 mg/L) and high log Kow (4.64), QSAR models predict high oral absorption. Dermal uptake however is expected to be low (≤10%) based on IH SkinPerm (QSAR). This result is consistent with its solubility, acrylate reactivity, and an acute dermal toxicity study in rats (2000 mg/kg) showing no systemic toxicity. In addition, a GPMT sensitization study indicates limited but sufficient uptake to elicit sensitization. However, a molecular weight below 500 g/mol is considered conducive to dermal absorption.
Inhalation absorption is considered minimal due to its very low vapor pressure (0.0274 Pa). Distribution is predicted to be moderate, with a low unbound plasma fraction (13.9%) and limited blood–brain barrier penetration. No metabolic data are available. Elimination is expected to be low, mainly via feces, consistent with its low solubility and low predicted total clearance.

1.2. Acute toxicity

Acute studies are available by oral (OECD 423) and dermal route (OECD 402) and showed no death at the maximal dose of 2000 mg/kg. No data is available by inhalation.

1.3. Corrosion / Irritation

Two in vitro tests are available to evaluate the irritancy potential of Tricyclododecane dimethanol diacrylate. The Episkin irritation test (OECD 439) showed no skin irritation with 109% of viability cells. And the Bovine Corneal Opacity and Permeability (BCOP) test (OECD 437) showed no eye irritation with an In Vitro Irritancy Score (IVIS) of -1. Therefore, Tricyclododecane dimethanol diacrylate is considered to be not skin or eye irritating.

1.4. Sensitization

A Freund's Complete Adjuvant test (OECD 406) is available on Tricyclododecane dimethanol diacrylate. Based on the results of this test, Tricyclododecane dimethanol diacrylate is recognized as a skin sensitizer in guinea pigs.

1.5. Repeated dose toxicity

Oral administration of Tricyclodecane dimethanol diacrylate to Sprague Dawley rats at doses of 100, 300 or 1000 mg/kg/day for 13 weeks was well-tolerated with only a mild effect on bodyweight gain at 1000 mg/kg/day and minimal changes in clinical pathology parameters which were considered non-

adverse. There were no changes in organ weights or any macroscopic or microscopic changes at any dose level.

Under the experimental conditions of the OECD 407 study, following daily administration of Tricyclodecane dimethanol diacrylate for 4 weeks by oral route to male and female Sprague-Dawley rats at dose levels of 100, 300 or 1000 mg/kg/day in corn oil, the No Observed Adverse Effect Level (NOAEL) was considered to be at 1000 mg/kg/day in absence of adverse effects at this dose.

1.6. Genetic toxicity

Three in vitro tests were performed on Tricyclododecane dimethanol showing negative results. Based on these results, TCDDA is not classified for genetic toxicity according to the Regulation EC no. 1272/2008.

Table 1: Summary of Mutagenicity studies

Study	Type	OECD Guideline	Result
In vitro	Bacterial Reverse Mutation Assay	OECD TG 471	Negative
	In Vitro Mammalian Cell Gene Mutation Test	OECD TG 476	Negative
	In vitro Mammalian Cell Micronucleus Test	OECD TG 487	Negative

1.7. Toxicity to reproduction

A developmental study on rat according to OECD TG 414 is available on the substance. Pregnant Sprague-Dawley rats were dosed by oral gavage from implantation, throughout organogenesis and throughout the gestation period at 0, 100, 300, or 1000 mg/kg/day, assessing maternal toxicity, embryo-fetal survival, growth, and developmental abnormalities. All animals survived to scheduled necropsy with no treatment-related clinical signs, and no effects on maternal body weight, weight gain, food consumption, gravid uterine weight, macroscopic findings, thyroid/parathyroid weights, or thyroid hormone levels. Reproductive and litter parameters—including implantations, resorptions, pre- and post-implantation loss, live fetuses, sex ratio, and anogenital distance were unaffected at all dose levels. However, at 1000 mg/kg/day, ten fetuses from two litters exhibited limb and rib malformations at incidences exceeding historical control data, and although limited to these litters, a treatment relationship could not be excluded. Additionally, supernumerary 14th ribs were increased at 300 and 1000 mg/kg/day, considered non-adverse but potentially treatment-related. Based on these findings, the maternal NOAEL and the NOAEL for embryo-fetal survival and growth were 1000 mg/kg/day, while the NOAEL for embryo-fetal development was 300 mg/kg/day due to the malformations observed at the high dose.

In the screening study on reproduction (OECD 421), Tricyclodecane dimethanol diacrylate was administered daily by oral gavage to male and female Sprague Dawley rats, for 2 weeks before pairing, during pairing, gestation and until Day 4 post-partum, at dose-levels of 100, 300 or 1000 mg/kg/day.

The study showed no unscheduled deaths or treatment-related systemic toxicity in parental animals, with ptyalism being the only clinical sign observed at 300 and 1000 mg/kg/day, considered of minimal toxicological relevance; body weight, food consumption, organ weights, and macro- and microscopic examinations revealed no adverse effects. Reproductive performance was unaffected, with normal mating and fertility outcomes, gestation length, numbers of corpora lutea and implantations, and pre-implantation loss; although a slight increase in post-implantation loss was noted at 1000 mg/kg/day (14.6% vs. 6.9% in controls), this was driven by two females and deemed non-adverse due to unchanged litter size. No toxicologically relevant effects were observed in pups regarding viability, body weight, sex ratio, or macroscopic findings, and clinical signs in one litter were considered unlikely to be treatment-related. Overall, the NOAEL for parental systemic toxicity, reproductive performance, and offspring development was established at 1000 mg/kg/day.

2. DNELs (Derived No-Effect Levels)

Adverse effects on embryo-fetal development (increased incidence of forepaw, forelimb, hindlimb and rib malformations) were observed at the high dose group, and therefore, the NOAEL (OECD 414) of 300 mg/kg/day was chosen as the most relevant dose descriptor.

For workers, inhalation exposure is considered the primary route, since aerosols, dust, or mist may be generated during certain processes such as spraying, mixing, or UV curing, even though the vapour pressure is low (calculated 0.027Pa at 25°C). Dermal exposure is not considered relevant, as dermal absorption is very low and appropriate protective measures are mandatory in occupational settings.

For consumers, oral exposure is regarded as the most relevant route, primarily due to potential migration from materials in contact with food, combined with the high predicted oral bioavailability. Although dermal contact with residual unreacted substance in articles or products may occur, dermal absorption is negligible and therefore not considered relevant for DNEL derivation.

Therefore, the following DNELs have been established for TCDDA, reflecting the likely route(s), duration and frequency of exposure:

2.1. Workers - Hazard via inhalation route

2.1.1. Systemic effects

Relevant dose descriptor: NOAEL (OECD 414) = 300 mg/kg bw/d

Conversion of an oral rat NOAEL into a corrected inhalatory NOAEC to assess human inhalatory exposure:

$$\text{Corrected NOAEC} = \text{Oral NOAEL} * \frac{50\%\ \text{oral absorption}}{100\%\ \text{inh absorption}} * \frac{1}{0.38 \frac{m^3}{kg}} * \frac{6.7\ m^3(8\text{h})}{10\ m^3(8\text{h})} * \frac{7\text{d}}{5d}$$

$$= 370.26\ \text{mg/m}^3$$

When no route-specific absorption data are available for the initial route, a default factor of 2 is recommended for oral-to-inhalation extrapolation. This means the absorption for the initial (oral) route is considered to be half that of the final (inhalation) route. The oral dose for the rat is converted

to the corresponding air concentration using a standard breathing volume for the rat (0.38 m^3/kg for 8 hours exposure of workers). Moreover, for workers the resulting air concentration needs to be additionally corrected for the difference between basal caloric demand and caloric demand under light activity. This correction factor derives from the respiratory volumes in 8 hours under the respective conditions (6.7 m^3 for base level, 10 m^3 for light activity). The oral NOAEL is further adjusted to reflect the different exposure frequency for workers, who are exposed 5 days per week rather than the 7 days per week used in the study.

Assessment factors (AF) based on ECHA Guidance document[ii]:

AF for		**Value**
interspecies differences	Differences in metabolic rate (rat)	not applicable[1]
	Remaining uncertainties[2]	2.5
intraspecies differences	Workers	5
duration of exposure transfer	Subacute to chronic	6
dose-response	NOAEL -> NOAEC	1
data base quality	Good quality	1
Other		1
Total		75

The DNEL is calculated using the values given above as

$$Workers - Inhalation - Systemic\ DNEL = \frac{\text{NOAEC}}{\text{Overall AF}} = \frac{\frac{370.26\text{mg}}{\text{m}^3}}{75} = 4.94\ \text{mg/m}^3$$

2.2. Consumers- Hazard via oral route

2.2.1. Systemic effects

Relevant dose descriptor: NOAEL (OECD 414) = 300 mg/kg bw/d

Assessment factors (AF) based on ECHA Guidance document:

[1] It is assumed to be already scaled according to the allometric principle, since ventilation rate and food intake directly depend on the basal metabolic rate.
[2] It is assumed that humans would be more sensitive than animals to effects on the respiratory tract.

AF for		Value
interspecies differences	Differences in metabolic rate (rat)	4
	Remaining uncertainties [2]	2.5
intraspecies differences	Consumers	10
duration of exposure transfer	OECD 414	6
dose-response	NOAEL -> NOAEL	1
data base quality	Good quality	1
Other		1
Total		600

The DNEL is calculated using the values given above as

$$Consumers - Oral - Systemic\ DNEL = \frac{\text{NOAEL}}{\text{Overall AF}} = \frac{300\ \frac{\text{mg}}{\text{kg}}\text{bw}}{600} = 0.50\ mg/kg\ bw/d$$

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References

[i] ECHA. (2025b). *ECHA CHEM CAS 42594-17-2*. Europa.eu. https://chem.echa.europa.eu/100.050.802/dossier-view/6fbb52a3-ef6f-428d-831f-1adbdc056e76/81e2e8b7-603a-4a62-8dd1-3b4b44f82787_81e2e8b7-603a-4a62-8dd1-3b4b44f82787?searchText=42594-17-2

[ii] ECHA. (2012). *Guidance on information requirements and chemical safety assessment Chapter R.8: Characterisation of dose [concentration]-response for human health*. https://echa.europa.eu/documents/10162/13632/information_requirements_r8_en.pdf/e153243a-03f0-44c5-8808-88af66223258