Compound	2,2-Dimethylpropane-1,3-diol (neopentyl glycol)		*Data collection sheet (1/1)*
N°CAS 126-30-7	**EU- Classification:** **CLP:** Self-classification by industry: Eye dam. 1 (H318); Skin irrit. 2 (H315); STOT SE 3 (H335)		
Organisation name	**REACH registrants**	**REACH registrants**	**AgBB NIK-AG**
Risk value name	DNEL (general population)	DNEL (worker)	NIK
Risk value	8.7 mg/m³	35 mg/m³	1 mg/m³
Reference period	Chronic	Chronic (worker)	Chronic
Year	Not reported (2013 or later)	Not reported (2013 or later)	2012
Key study	BASF SE (2013)	BASF SE (2013)	Biosafety Research Center, Japan (1993)
Study type	Repeated dose toxicity study (OECD 408)	Repeated dose toxicity study (OECD 408)	Combined repeated dose tox. study with reproduce-tive/developmental tox. screening test (OECD 422)
Species	Rat	Rat	Rat
Duration of exposure in key study	90 d	90 d	45 d (males); ca. 60 d (females)
Critical effect	No treatment-related adverse findings	No treatment-related adverse findings	Males: increased liver and kidney weights; moderate tubular nephropathy
Critical dose value	NOAEL (oral): 1000 mg/kg bw x d	NOAEL (oral): 1000 mg/kg bw x d	NOAEL (oral): 300 mg/kg bw x d
Adjusted critical dose	434.8 mg/m³	881.6 mg/m³	130.4 mg/m³
Single assessment factors	2 (study length) x 2.5 (interspecies) x 10 (intraspecies) = 50	2 (study length) x 2.5 (interspecies) x 5 (intraspecies) = 25	6 (study length) x 2 (interspecies) x 10 (intraspecies) = 120
Other effects			

Compound	**Neopentyl glycol C5H12O2**		***Factsheet***
Parameter	**Note**	**Comments**	**Value / descriptor**
EU-LCI value and status			
EU-LCI value	1	Mass/volume [µg/m^3]	8700
EU-LCI status	2	Draft/Final	Final
EU-LCI year of issue	3	Year when the EU-LCI value has been issued	2020
General information			
CLP-INDEX No	4	INDEX	-
EC No	5	EINECS – ELINCS - NLP	204-781-0
CAS No	6	Chemical Abstracts Service number	126-30-7
Harmonised CLP classification	7	Human health risk related classification	Not available
Molar mass and conversion factor	8	[g/mol] and [ppm – mg/m^3]	104.15 1 ppm = 4.29 mg
Key data / database			
Key study, author(s), year	9	Critical study with lowest relevant effect level	BASF, 2013 (cited in ECHA, 2020)
Read across compound	10	Where applicable	-
Species	11	Rat, human etc.	Rat
Route/type of study	12	Inhalation, oral feed etc.	Oral
Study length	13	Days, subchronic, chronic	Subchronic (90 d)
Exposure duration	14	Hrs/day, days/week	Continuous
Critical endpoint	15	Effect(s), site of	No treatment-related adverse findings
Point of departure (POD)	16	LOAEC*L, NOAEC*L, NOEC*L, Benchmark dose, etc.	Adjusted NOAEL
POD value	17	[mg/m^3] or [ppm] or [mg/kg$_{BW}$×d]	500 mg/kg$_{BW}$ x d
Assessment factors (AF)	**18**		
Adjustment for exposure duration	19	Study exposure hrs/day, days/week	1
Study length	20	sa→ sc→ c *(R8-5)*	2
Route-to-route extrapolation factor	21		1.15 m^3/kg$_{BW}$ x d
Dose-response	22 a	Reliability of dose-response, LOAEL → NOAEL	1
	22 b	Severity of effect *(R 8-6d)*	1
Interspecies differences	23 a	Allometric Metabolic rate *(R8-3)*	1[1]
	23 b	Kinetic + dynamic	2.5
Intraspecies differences	24	Kinetic + dynamic Worker - general population	10
AF (sensitive population)	25	Children or other sensitive groups	1

[1] Allometric scaling issues are included in the route-to-route extrapolation factor (line 21).

Other adjustment factors Quality of whole database	26	Completeness and consistency Reliability of alternative data *(R8-6 d,e)*	1
Result			
Summary of assessment factors	27	Total Assessment Factor (TAF)	57.5
POD/TAF	28	Calculated value (µg/m³ and ppb)	8696 µg/m³ (2027 ppb)
Molar adjustment factor	29	Used in read-across	-
Rounded value	30	[µg/m³]	8700
Additional comments	31		
Rationale section	32		

Data compilation and evaluation for neopentyl glycol is based on a project funded by the German Environment Agency (UBA) (Werschkun, 2020).

Neopentyl glycol was included in the OECD assessment programme for high production volume chemicals in the 1990s. A screening information data set (SIDS) summarising available toxicity data was published (OECD, 2002), but no risk assessment was conducted. A more recent assessment was conducted by BASF as part of the REACH registration dossier, which is published on the ECHA dissemination site (ECHA, 2020). Targeted searches were conducted in HSDB, TOXLINE and PubMed to identify additional relevant information.

Neopentyl glycol is a water-soluble solid that is primarily excreted in urine as glucuronic acid conjugate (Gessner et al., 1960). Its odour is described as 'sweetish', but no information on an odour threshold could be found. It is a slight skin irritant and can cause serious eye damage. Its acute systemic toxicity is low for all exposure routes. Relevant information on repeated dose toxicity is only available for oral exposure. A combined repeated dose toxicity study with a reproductive/developmental toxicity screening test (OECD test guideline 422) performed in Japan was reported in the OECD SIDS (2002). A subchronic toxicity study (OECD test guideline 408) was conducted by BASF and is included in the REACH registration dossier (ECHA, 2020).

In the OECD 408 study, Wistar rats were dosed with 50, 250 and 1000 mg/kg$_{BW}$ x d neopentyl glycol in drinking water for a period of 90 days. The performed examinations included clinical signs, body weight, food and water consumption, ophthalmoscopic examination, haematology, clinical chemistry, urinalysis, neurobehavioural examination, oestrous cycle determination, sperm parameters, gross pathology, and histopathology of all organs. No treatment-related adverse effects were observed in any dose group. Observed changes such as increases in haematocrit and urine volume in high dose females as well as an increase in cholesterol and a decrease in urine pH in high dose males were judged as possibly treatment-related but not adverse. Increases in relative kidney weights in males of the two highest dose groups and in relative liver weights in high dose males were regarded as adaptive rather than adverse, because there were no concurrent histopathological changes. Therefore, the NOAEL derived from this study is ≥ 1000 mg/kg$_{BW}$ x d.

In the OECD 422 study, Sprague-Dawley rats received 100, 300, or 1000 mg/kg$_{BW}$ x d neopentyl glycol per gavage over 45 days (males) or from 14 d premating until day 4 of lactation (females), respectively. No treatment-related effects were observed in maternal animals and in offspring. In male animals of the parent generation, elevated levels of total protein, albumin and bilirubin were measured in the two higher dose groups. At these doses, absolute and relative liver weights were also increased. However, as histopathological examination revealed no lesions of the liver, the observed changes are considered an adaptive reaction rather than an adverse effect. Male animals dosed with 1000 mg/kg$_{BW}$ x d also had increased absolute and relative kidney weights and histopathological changes in the kidneys such as basophilic alteration of the renal tubular epithelium and increased incidences in hyaline droplets and protein casts. These changes are considered treatment-related adverse effects. However, the reported findings indicate that the observed nephrotoxicity is likely to be caused by α_{2u}-globin *via* a mode of action (MoA) that is specific for male rats. Typical signs of this MoA include the absence of nephrotoxicity in females, the formation of hyaline droplets and an increased number of granular casts, as they are reported

here. Since humans, like female rats, do not produce a protein like α_{2u}-globulin, such effects are not considered relevant for human health risk assessment (Hard et al., 1993; Swenberg, 1993).

In conclusion, the NOAEL value of 1000 mg/kg$_{BW}$ x d (BASF, 2013, cited in ECHA, 2020) is considered most relevant for the derivation of an EU-LCI value for neopentyl glycol. This value is adjusted by a default factor of 2 to account for potential differences in absorption between the oral and inhalation routes, respectively, to give a POD value of 500 mg/kg$_{BW}$ x d.

Assessment factors are chosen as follows:

- Study length: 2 for subchronic to chronic extrapolation
- Route-to-route extrapolation: 1.15
- Interspecies differences: 2.5 (default value for kinetic and dynamic differences)
- Intraspecies difference: 10 (default value for the general population)

With a total assessment factor of 57.5 and a POD of 500 mg/kg$_{BW}$ x d, the LCI value is calculated as 8696 µg/m^3 (2027 ppb) and rounded to 8700 µg/m^3.

References:

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