baua:
Bundesanstalt für Arbeitsschutz
und Arbeitsmedizin
Federal Institute for Occupational
Safety and Health

Federal Office for Chemicals

Contact: Nirtharsan Paransothy
chemg@baua.bund.de
RN: 5.0-721 65/03.00953-C

ECHA Classification
Hazard I Unit

Dortmund, 05. January 2021

Comment on the proposed harmonised Classification and Labelling for tetramethylene dimethacrylate (EC: 218-218-1; CAS-no: 2082-81-7) submitted by Finland

Skin sensitization:

The dossier submitter states that "animal data is sufficient for sub-categorization" (see CLH report p. 22). Concretely, in the view of the dossier submitter the outcome of an LLNA indicates that tetramethylene dimethylacrylate should be classified as skin sensitiser in sub-category 1B.

Regarding this LLNA, we would appreciate if the dossier submitter could assess in more detail the clinical findings that have been observed during the study:

Clinical findings observed in the LLNA (Anonymous 2014)	Treated group		
	25%	50%	100%
Trying to burrow oneself in the bedding	one hour after the third application		
Ruffled fur	day 3	days 3+4	days 3+4
Hunched posture	day 3	day 3	day 3 day 4
Reduced spontaneous activity	day 3	day 3	day 3 day 4 (2/5 animals)
Eyelid closure	-	day 3	day 3
Abnormal walk	-	day 3	day 3

We think such assessment is advisable because OECD testing guideline 429 specifies with respect to dose selection "that the highest concentration maximises exposure while avoiding systemic toxicity" (see OECD TG 429, par. 18).

Notably, it is mentioned in the CLH report that "according to the authors, it cannot be confirmed whether these symptoms were signs of systemic toxicity or mere reactions to the irritant nature of the test

Sitz Dortmund
Friedrich-Henkel-Weg 1-25
44149 Dortmund
Telefon (02 31) 90 71-0
Telefax (02 31) 90 71-2454

Standort Berlin
Nöldnerstr. 40/42
10317 Berlin
Telefon (0 30) 5 15 48-0
Telefax (0 30) 5 15 48-4170

Standort Dresden
Fabricestr. 8
01099 Dresden
Telefon (03 51) 563 9-5
Telefax (03 51) 56 39-5210

Außenstelle Chemnitz
Jagdschänkenstr. 33
09117 Chemnitz
Telefon (03 71) 3 35 18-0
Telefax (03 71) 3 35 18-6222

Bankverbindung - Bundeskasse Trier
Deutsche Bundesbank - Filiale Saarbrücken
BLZ: 590 000 00 - Konto- Nr.: 590 010 20
BIC : MARKDEF1590 (für Auslandszahlungen)
IBAN: DE81590000000059001020

substance" (see CLH report, p. 13). What is the dossier submitter's opinion on this issue? Do you have access to more detailed information (e.g. regarding grade, onset (immediately or delayed after test substance application?) and duration (hours/minutes?) of effects? Is a dermal acute toxicity study available that might provide information on possible systemic toxicity caused by tetramethylene dimethylacrylate?

For now, we have doubts to consider the observed symptoms as pure reactions to the skin irritating potential of the test substance due to the low grade of the observed erythema:

Group treated with 25% concentration: score 1 (days 3+4)
Group treated with 50% concentration: score 1 (days 3-5)
Group treated with 100% concentration: score 1 (days 2+6), score 2 (days 3-5)

According to OECD TG 429, score 1 characterizes "very slight erythema (barely perceptible)" and score 2 "well-defined erythema" (see OECD TG 429, table 1).

We think it is crucial to discuss the above-mentioned clinical findings in more detail because they may have an influence on the acceptability of the LLNA to be used as basis for sub-categorisation.

In principle, however, we agree with the dossier submitter's proposal to classify tetramethylene dimethylacrylate as skin sensitiser since human evidence is also available.