Committee for Risk Assessment

RAC

Opinion

proposing harmonised classification and labelling
at EU level of

7,7,9(or 7,9,9)-trimethyl-4,13-dioxo-3,14-dioxa-5,12-diazahexadecane-1,16-diyl bismethacrylate

EC Number: 276-957-5
CAS Number: 72869-86-4

CLH-O-0000007057-74-01/F

Adopted

26 November 2021

26 November 2021

CLH-O-0000007057-74-01/F

OPINION OF THE COMMITTEE FOR RISK ASSESSMENT ON A DOSSIER PROPOSING HARMONISED CLASSIFICATION AND LABELLING AT EU LEVEL

In accordance with Article 37 (4) of Regulation (EC) No 1272/2008, the Classification, Labelling and Packaging (CLP) Regulation, the Committee for Risk Assessment (RAC) has adopted an opinion on the proposal for harmonised classification and labelling (CLH) of:

Chemical name: **7,7,9(or 7,9,9)-trimethyl-4,13-dioxo-3,14-dioxa-5,12-diazahexadecane-1,16-diyl bismethacrylate**

EC Number: **276-957-5**

CAS Number: **72869-86-4**

The proposal was submitted by **Finland** and received by RAC on **9 October 2020.**

In this opinion, all classification and labelling elements are given in accordance with the CLP Regulation.

PROCESS FOR ADOPTION OF THE OPINION

Finland has submitted a CLH dossier containing a proposal together with the justification and background information documented in a CLH report. The CLH report was made publicly available in accordance with the requirements of the CLP Regulation at ***http://echa.europa.eu/harmonised-classification-and-labelling-consultation/*** on **9 November 2020**. Concerned parties and Member State Competent Authorities (MSCA) were invited to submit comments and contributions by **22 January 2021**.

ADOPTION OF THE OPINION OF RAC

Rapporteur, appointed by RAC: **Beata Pęczkowska**

The opinion takes into account the comments provided by MSCAs and concerned parties in accordance with Article 37(4) of the CLP Regulation and the comments received are compiled in Annex 2.

The RAC opinion on the proposed harmonised classification and labelling was adopted on **26 November 2021** by **consensus**.

Classification and labelling in accordance with the CLP Regulation (Regulation (EC) 1272/2008)

	Index No	Chemical name	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors and ATE	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entry	No current Annex VI entry										
Dossier submitters proposal	TBD	7,7,9(or 7,9,9)-trimethyl-4,13-dioxo-3,14-dioxa-5,12-diazahexadecane-1,16-diyl bismethacrylate	276-957-5	72869-86-4	Skin Sens. 1B	H317	GHS07 Wng	H317			
RAC opinion	TBD	7,7,9(or 7,9,9)-trimethyl-4,13-dioxo-3,14-dioxa-5,12-diazahexadecane-1,16-diyl bismethacrylate	276-957-5	72869-86-4	Skin Sens. 1B	H317	GHS07 Wng	H317			
Resulting Annex VI entry if agreed by COM	TBD	7,7,9(or 7,9,9)-trimethyl-4,13-dioxo-3,14-dioxa-5,12-diazahexadecane-1,16-diyl bismethacrylate	276-957-5	72869-86-4	Skin Sens. 1B	H317	GHS07 Wng	H317			

GROUNDS FOR ADOPTION OF THE OPINION

RAC general comment

7,7,9(or 7,9,9)-trimethyl-4,13-dioxo-3,14-dioxa-5,12-diazahexadecane-1,16-diyl bismethacrylate (UDMA) has no current entry in Annex VI to the CLP regulation.

The CLH report has been created based on data submitted by the lead registrant in the REACH registration dossier for UDMA. The unpublished full study reports were made available to the DS by the lead registrant. In addition, open literature publications and patient exposure data from the Finnish Institute of Occupational Health were used.

HUMAN HEALTH HAZARD EVALUATION

RAC evaluation of skin sensitisation

Summary of the Dossier Submitter's proposal

The Dossier Submitter (DS) evaluated skin sensitising potential of UDMA based on results of one animal study, the local lymph node assay (LLNA), and human data.

Animal data

The LLNA was conducted in accordance with OECD TG 429 (2002) and GLP (Anonymous 2009f) and is considered reliable. A pre-test was performed in two animals with concentrations of 25 and 50% to determine the highest non-irritant test concentration on three consecutive days. At these concentrations, the animals did not show any signs of irritation or systemic toxicity.

In the main study, three treated groups of four CBA/CaOlaHsd female mice were topically treated to the dorsal surface of ears with test concentrations of 10, 25 and 50% (w/v) in dimethylformamide. The control group of four mice received vehicle only. Five days after the topical application, all mice were given 250 µl of 79.9 µCi/ml 3H-methyl thymidine (corresponds to 20.0 µCi 3H-methyl thymidine) by intravenous injection via the tail vein. The proliferative capacity of lymph node cells was determined by the incorporation of 3H-methyl thymidine measured on a β-scintillation counter.

No mortality or clinical signs were observed during the study period, and the body weight of the animals remained within the normal range. In this study, Stimulation Indices (SIs) of 1.58, 1.70 and 4.44 were determined at concentrations of 10, 25 and 50%, respectively. The EC3 value was 36.9% (w/w). A dose-related increase in the SI values was observed and the threshold positive value of 3 was exceeded at 50% concentration.

Human data

The most relevant clinical studies for UDMA, 27 in total, are presented in table below. The studies comprise a total of 169 patients who tested positive to the substance. In all studies, the diagnostic method was patch testing. Data on skin exposure to UDMA is scarce.

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
CASE REPORTS				
Case report	UDMA (concentration and vehicle not defined)	47-year-old woman had used acrylic nails for 10 years. She presented with periungual dermatitis of all the fingernails. Symptoms had begun 6 months earlier.	She tested positive to 11 acrylic compounds including UDMA. UDMA reaction was + at 96 hours.	Paley *et al.* (2006)
PATIENT SERIES				
Patient series	UDMA	Report of 22 patch-tested hearing-aid users with severe dermatitis in the ear canal	Positive reaction to UDMA in 2 (9.1%) of the patients	Meding & Ringdahl (1992)
Patient series	UDMA (0.6% and 0.2% in pet.) purity 97%	Report on 5 cases with severe skin symptoms in the fingers from photo-bonded acrylic nails at the Dermatologic and Pediatric Allergy Clinic in Wilhelminen Hospital, Vienna, Austria	Positive reaction to UDMA in 2 (40%) of the patients.	Hemmer *et al.* (1996)
Patch test	UDMA (2% in pet.), purity 95%	126 dental technicians were tested with (meth)acrylates in 1995-1999	3 of 126 (2.4%) patients reacted ambiguously to UDMA; no clearly positive reactions. UDMA was a common constituent of products and authors considered that the technicians had daily contact with UDMA. They considered that sensitisation was low.	Peiler *et al.* (2000)
Patients series	UDMA (1% in pet.)	A retrospective study of 13 833 patients tested for contact allergy at the Department of Dermatology, Catholic University (Leuven, BE) in 1978-1999	Positive reaction to UDMA in 1 of 72 (1.4%) patients who were positive to some (meth)acrylate It is unclear how many patients were tested with (meth)acrylates.	Geukens & Goossens (2001)

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
Patient series	UDMA (2% in pet.)	The incidence of allergic contact dermatitis was studied in 79 dentists and 46 dental nurses who were referred to the Institute of Occupational Medicine (Lodz, PL) in 1990-2000. All were tested with the European standard set, dental screening test and additional allergens.	In dentists sensitised to acrylic resins, 6 of 20 patients (30%) reacted positively to UDMA. There were no positive reactions to the test substance in dental nurses.	Kiec-Swierczynska & Krecisz (2002)
Patient series	UDMA (2% in pet.)	27 patients in contact with artificial nails (16 nail technicians, 11 customers) tested with acrylic compounds and apparently positive to some acrylic compound at the Departments of Dermatology in Universities of Ghent and Leuven, BE)	Positive reaction to UDMA in 2 (10%) of 20 patients tested with UDMA	Constandt *et al.* (2005)
Patient series	UDMA (2% in pet.)	473 patients were tested with a (meth)acrylate series at Finnish Institute of Occupational Health (Helsinki, FI) in 1994-2006. 32 patients with allergic reaction to some (meth) acrylate and working in dental professions (dentist, dental nurse, dental technician) were identified.	Positive reactions to UDMA in 3 cases: 1 dentist (+ reaction), 2 dental nurses (++ reaction and + reaction). UDMA was not mentioned in the safety data sheets of the products used by these 3 patients.	Aalto-Korte *et al.* (2007)
Patient series	UDMA (2% in pet.)	8 patients with severe skin reactions after use of a UDMA-containing UV-curing nail polish were patch tested with the components	Positive reactions to UDMA in 7 patients (87.5%) All 8 patients had known exposure to UDMA.	Dahlin *et al.* (2016)

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
		and ingredients of the nail polish at 5 dermatology departments in Sweden.		
Patient series	UDMA (2% in pet.)	A retrospective study on patients diagnosed with allergic contact dermatitis caused by (meth)acrylates in long-lasting nail polish at dermatology departments of 4 Spanish hospitals in 2013-2016	A total of 2353 patients were patch tested during the study period. 43 (1.82%) were diagnosed with ACD due to (meth)acrylates in long lasting nail polish. In this group, positive reaction to UDMA in 6 of 36 (16.7%) patients tested with UDMA	Gatica-Ortega *et al.* (2017)
Patients series	UDMA (Chemotechnique's or Trolab's test substance i.e. 2% in pet.)	A retrospective study of the European Environmental Contact Dermatitis Research Group (EECDRG) on allergic contact dermatitis from (meth)acrylates due to artificial nails diagnosed in 11 clinics in 9 European countries in 2013-15	A total of 202 patients were positive to some acrylic compound and 10 (2.0%) were positive to UDMA. It is not clear how many patients were tested with UDMA.	Gonçalo *et al.* (2018)
Patient series	UDMA (2% in pet.)	A retrospective study on patients suspected of nail manicure-related sensitisation to (meth)acrylates at dermatology departments of 3 Spanish hospitals in 2008-2017	208 patients tested with (meth)acrylates. 66 patients reacted positively to at least one (meth)acrylate and the sensitisation was due to nail products. In this group, positive reactions to UDMA in 6 of 26 (23.1%) patients tested with the substance.	Marrero-Alemán *et al.* (2019)
Patient series	UDMA (2%; AllergEAZE's test substance, i.e. in pet.)	A retrospective study on 156 patch-tested patients with a profession associated with -cosmetic nail procedures or use of	37 (23.7%) patients were positive to UDMA 116 patients had positive reactions to some (meth)acrylate. The UDMA-positive	Gregoriou *et al.* (2020)

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
		such services at the Department of Dermatology and Venereology, Athens, GR in 2014-2018	cases constituted 31.9% of these.	
CROSS-SECTIONAL STUDIES				
Cross-sectional study	UDMA (2% in pet.)	A questionnaire was sent to 1132 dental technicians and 173 answered. 55 cases were patch tested.	UDMA was positive in 1 (2%) case with hand dermatitis	Rustemeyer & Frosch (1996)
Cross-sectional study	UDMA (2%, Chemotechnique's test substances i.e. in pet.)	A questionnaire was sent to 3500 Swedish dentists and 1287 answered. 191 with hand eczema were invited to patch tests and 147 attended.	UDMA was positive in 2 (1.4%) patients	Wallenhammar *et al.* (2000)
Cross-sectional study	UDMA (Chemotechnique's test substance i.e. 2% in pet.)	49 out of 1038 dental technicians voluntarily participated a study on patch testing at the Department of Dermatology in the Catholic University of Korea, Soeul, Korea.	Positive reaction to UDMA in 1 case, 2.1% of those tested. 7 patients were positive to some acrylic substance. The UDMA positive case constituted 14% of this group.	Lee *et al.* (2001)
CLINICAL PATCH TEST DATA ON SELECTED PATIENTS (AIMED TESTING WITH ACRYLIC COMPOUNDS); Frequency of positive reactions among tested individuals given				
Patch test data, selected patients	UDMA (2%, Chemotechnique's test substance i.e. in pet.)	A retrospective study on patients tested with (meth)acrylate patch test series at the Section of Dermatology in the Finnish Institute of Occupational Heath in 1985-1995	Positive reaction to UDMA in 1 (0.4%) of 273 patients tested with UDMA. 48 patients reacted positively to some (meth)acrylate. The UDMA-positive case constituted 2% of these.	Kanerva *et al.* (1997)
Patch test data, selected patients	UDMA (2%, Chemotechnique's test substance i.e. in pet.)	A retrospective study of patch test records at the Section of Dermatology, University of Manchester (Salford, UK) in 1983-1998 440 patients with a	Positive reaction to UDMA in 2 of 268 (0.7%) patients tested with UDMA	Tucker & Beck (1999)

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
		history of exposure to (meth)acrylates were identified and patch tested with (meth)acrylates		
Patch test data, selected patients	UDMA (concentration or vehicle not stated)	A retrospective study on patients patch tested with dental screening series in 7 dermatology clinics in Finland in 1994-1998	9 (0.4%) allergic reactions to UDMA in 2408 patients tested. The frequency of allergic reactions varied between 0.0% and 1.5% in different clinics.	Kanerva *et al.* (2001)
Patch test data, selected patients	UDMA (2% in pet.)	109 patients (all dental personnel) were tested with a dental screening series at the Department of Occupational and Environmental Dermatology (Stockholm, SE) in 1995-1998	Positive reaction to UDMA in 2 (1.8%) of 109 patients tested with (meth)acrylates 24 patients had allergic reactions to some (meth)acrylate. The 2 UDMA-positive cases constituted 8.3% of these	Wrangsjö *et al.* (2001)
Patch test data, selected patients	UDMA (2% in pet.)	A retrospective study of patch test records of 1632 patients tested with dental patient and/or dental personnel series at the Department of Occupational and Environmental Dermatology in Malmö University Central Hospital (SE) in 1995-2004	Positive reaction to UDMA in 1 (0.06%) of 1632 patients tested 48 patients reacted positively to at least one (meth)acrylate. The UDMA-positive case constituted 2.1% of these.	Goon *et al.* (2006)
Patch test data, selected patients	UDMA (2% in pet.)	A retrospective study on 451 patients suspected of having occupational contact dermatitis and tested with a (meth)acrylate series at Finnish Institute of Occupational Health (Helsinki, FI) in 1994-2009	Positive reactions to UDMA in 5 (1.1%) of the patients tested. 66 patients reacted positively to at least one (meth)acrylate. Positive reaction to UDMA in 5 (7.6%) of these 66 patients	Aalto-Korte *et al.* (2010) Includes the patients in Aalto-Korte *et al.* (2007)

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
Patch test data, selected patients	UDMA (2%; Chemotechnique's test substance i.e. in pet.)	A retrospective study on patients tested with a (meth)acrylate series at the Department of Dermatology, University Medical Centre in Groningen (NL) in 1993-2012	Positive reactions in 4 of 151 (2.6%) patients tested with UDMA. 24 patients reacted positively to some (meth)acrylate. The positive reactions to UDMA constituted 16.7% of these.	Christoffers *et al.* (2013)
Patch test data, selected patients	UDMA (2% in pet.)	122 patients were tested with an extended series of (meth)acrylates at the Department of Dermatology (Coimbra, PT) in 2006-2013	Positive reaction to UDMA in **7** patients, 5.7% of 122 tested. 37 patients reacted positively to (meth)acrylates. The UDMA-positive cases constituted 18.9% of these.	Ramos *et al.* (2014)
Patch test data, selected patients	UDMA (vehicle and concentration not stated)	6775 patients were tested with a series intended for dental technicians with occupational dermatitis. UDMA was included in this series. The patch tests were performed in dermatology clinics of the IVDK network in German-speaking countries in 2008−2015.	47 patients tested positive to UDMA (0.7% of 6775 patients tested). UDMA was the least frequent allergen among the (meth)acrylates in this series.	Geier & Schnuch (2016)
Patch test data, selected patients	UDMA (2% in pet.)	475 patients were tested with a series of (meth)acrylates at the Cutaneous Allergy Unit (Birmingham, UK) in 2002-2015	Positive reactions to UDMA in 6 (1.3%) patients tested with UDMA. 52 patients reacted positively to (meth)acrylates. The positive reactions to UDMA constituted 11.5% of these.	Spencer *et al.* (2016)
Patch test data, selected patients	UDMA 2% (vehicle not stated; FIRMA Diagent allergen)	A prospective study on screening contact allergy to acrylic acid on consecutively patch-tested patients in 3 Italian patch test clinics in	The study comprises a total of 436 consecutive patients. 30 patients were tested with (meth)acrylates	Hansel *et al.* (2020)

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
		January-March 2018. Additional patch tests with a (meth)acrylate series were performed in patients positive to acrylic acid or 2-hydroxyethyl methacrylate or with a history of (meth)acrylate allergy	including UDMA. Positive reaction in 1 patient (3.3% of those tested)	

Diagnostic patch testing is conducted in order to diagnose contact allergy to a substance. Selected patients are patients with dermatitis suspected of having contact with acrylic compounds or special occupational groups (aimed testing). Consecutive or unselected patients are groups of patients for whom allergic contact dermatitis is generally suspected.

There are no studies on diagnostic patch tests with UDMA in general population or unselected dermatitis patients.

UDMA is usually tested as part of (meth)acrylate patch test series. Its established test concentration is 2% in petrolatum. A total of 11 studies on diagnostic patch testing in selected patients could be identified for UDMA. The frequency of positive reactions varied between 0.06% and 5.7% (median 1.1%). The lowest frequencies were seen in earlier reports from clinics investigating general dermatology patients.

No strict workplace studies could be identified for UDMA. However, three cross-sectional studies on risk occupations share a similar design. The risk occupations for contact allergy to acrylic compounds were dentists in one study and dental technicians in two studies (Rustemeyer & Frosch 1996, Wallenhammar *et al.* 2000, Lee *et al.* 2001). Workers with skin symptoms suggesting possible contact allergy (hand dermatitis, for instance) were patch tested. Frequency of positive patch test reactions to UDMA varied between 1.4% and 2.1% in tested individuals.

The rest of the identified studies were either case reports (one report of a single case) or reports describing patient series without clearly stating the frequency of reaction to UDMA in all patients tested with the substance during the same time period. The number of patients in these ten reports were between 5 and 202, and the groups comprised for instance of patients sensitised to some acrylate or methacrylate. The frequency of positive reactions to UDMA within these patient groups varied between 0% and 88% of patients. The highest frequency was in a report of eight cases who had developed severe skin symptoms while using a UDMA-containing UV-cured nail polish (Dahlin *et al.* 2016). On patch testing, seven of the patients had allergic reactions to UDMA. The remaining one patient developed no contact allergy. In contrast to this finding, Peiler *et al.* (2000) patch tested 126 dental technicians with daily contact with UDMA-containing products and found no clearly positive reactions to UDMA. The authors considered that sensitisation was low. Dental technicians' skin exposure to UDMA may vary within countries. For instance in Finland, only one dental technician out of eight had used UDMA-based products (Aalto-Korte *et al.* 2007).

The DS has proposed classification and labelling sub-category 1B for skin sensitisation with the corresponding hazard statement H317: May cause an allergic skin reaction. There is no adequate and reliable scientific information available to set a specific concentration limit for the substance.

Comments received during consultation

Three MSCA commented the proposed classification for skin sensitisation hazard and two of them supported the DS proposal for classification as Skin Sens. 1B, H317.

One MSCA noted that based on results of the LLNA, criteria for Skin Sens. 1B are fulfilled. According to CLP guidance document the available studies on selected patients show a high frequency of occurrence of skin sensitisation (>1%) and the high number of published cases (>100). Assessment of exposure data is lacking from the CLH report. Considering the high frequency of occurrence of skin sensitisation based on human data, if no adequate exposure data are available, a sub-categorisation as Skin Sens. 1A cannot be excluded. In this context, sub-categorisation may be not possible. MSCA suggested discussion at the RAC level if classification as Skin Sens. 1 instead of 1B as proposed is more appropriate.

In response the DS pointed out that the assessment of human exposure is not included in the CLH report as there is no adequate data available. Proposed sub-categorization as 1B is based on reliable LLNA. In this case, the DS is of the opinion that insufficient human exposure data would not overtake animal data. However, the DS agree that it is for the RAC to consider the most appropriate classification.

Assessment and comparison with the classification criteria

Animal data

There are positive results from one animal study available. In this key LLNA (in compliance with OECD TG 429 and GLP), UDMA showed an EC3 value of 36.9% (w/w), thus criterion of CLP regulation (Annex I Table 3.4.4) for classification in subcategory 1B (EC3>2%) was met, indicating a low to moderate skin sensitisation potency according to the current Guidance on the Application of the CLP Criteria (Table 3.6). Since LLNA study results shown linear dose-response relationship (SI values of 1.58, 1.7 and 4.4 at concentrations of 10, 25 and 50%, correlation coefficient r=0.9472), extrapolation of results to lower concentrations is appropriate. Classification in sub-category 1A can be excluded even though concentrations lower than 2% have not been tested.

Human data

According to the classification criteria of Regulation (EC) 1272/2008 (Annex I section 3.4.2.2.2) human evidence for sub-categories 1A and 1B, respectively, can include the following type of data:

	Human data
Sub-category 1A	(a) positive responses at ≤ 500 µg/cm2 (HRIPT, HMT – induction threshold); (b) diagnostic patch test data where there is a relatively high and substantial incidence of reactions in a defined population in relation to relatively low exposure; (c) other epidemiological evidence where there is a relatively high and substantial incidence of allergic contact dermatitis in relation to relatively low exposure.
Sub-category 1B	(a) positive responses at > 500 µg/cm2 (HRIPT, HMT – induction threshold); (b) diagnostic patch test data where there is a relatively low but substantial incidence of reactions in a defined population in relation to relatively high exposure; (c) other epidemiological evidence where there is a relatively low but substantial incidence of allergic contact dermatitis in relation to relatively high exposure.

HRIPT: Human Repeat Insult Patch Test; HMT: Human Maximisation Test

The Guidance on the Application of the CLP Criteria (Section 3.4.2.2.3.1., Table 3.2) further outlines how high or low frequency of occurrence of skin sensitisation shall be assessed):

Human diagnostic patch test data	**High frequency**	**Low/moderate frequency**	**UDMA**
General population studies	≥ 0.2 %	< 0.2 %	No studies
Dermatitis patients (unselected, consecutive)	≥ 1.0 %	< 1.0 %	No studies
Selected dermatitis patients (aimed testing, usually special test series)	≥ 2.0 %	< 2.0 %	11 studies 0.06% – 5.7% (median 1.1%)
Workplace studies: 1: all or randomly selected workers 2: selected workers with known exposure or dermatitis	≥ 0.4 % ≥ 1.0 %	< 0.4 % < 1.0 %	No studies (3 cross-sectional studies; 1.4% –2.1%)
Number of published cases	≥ 100 cases	< 100 cases	169 patch-test-positive cases

There are no studies on general population or on unselected consecutive dermatitis patients.

Frequencies of positive patch tests in 11 selected dermatitis patient materials (aimed testing) have varied around the limit of high frequency (0.06% – 5.7%; median 1.1%).

In three cross-sectional studies on risk occupations (mimicking workplace studies) the frequencies of positive patch tests were between 1.4% and 2.1%, i.e. above the cut-off value of 1.0%. Not all or randomly selected workers but those with skin symptoms were patch tested in these studies.

The number of published patch-test-positive cases, 169, exceeds the limit for high frequency.

Positive patch test reactions to UDMA are not extremely rare in patients sensitised to methacrylates, but specific exposure to the substance in sensitised patients or patients tested has rarely been described in the literature. Both the exposure and the lack of exposure to UDMA are typically difficult to assess in clinical work due to the unavailability of chemical analyses. Positive reactions may also arise from cross-reactivity to other methacrylates, yet true exposure to UDMA in clinical patients cannot be excluded. The only study confirming exposure to UDMA is by Dahlin *et al.* (2016) that describes a series of eight patients with severe skin symptoms due to use of a UV-cured nail polish containing 2-hydroxyethyl methacrylate (HEMA) and UDMA. Seven of these patients tested positive to UDMA (87.5%).

Based on analysis of human data RAC agrees with the DS that the frequency of positive reactions to UDMA in diagnostic patch tests can be considered high. However, there is no adequate information enabling the assessment of true exposure to the substance.

Application of The Guidance on the Application of the CLP Criteria (Section 3.4.2.2.3.1., Table 3.2) should permit sub-categorisation where the human data on exposure and sensitisation is clear.

According to section 3.4.2.2.4.2. of Annex I to Regulation (EC) 1272/2008: "*Evidence from animal studies is usually much more reliable than evidence from human exposure. However, in cases where evidence is available from both sources, and there is conflict between the results, the quality and reliability of the evidence from both sources must be assessed in order to resolve the question of classification on a case-by-case basis. Normally, human data are not generated in controlled experiments with volunteers for the purpose of hazard classification but rather as part of risk assessment to confirm lack of effects seen in animal tests. Consequently, positive human data on skin sensitisation are usually derived from case-control or other, less defined studies. Evaluation of human data must therefore be carried out with caution as the frequency of cases reflect, in addition to the inherent properties of the substances, factors such as the exposure situation, bioavailability, individual predisposition and preventive measures taken".*

In case of UDMA both human data and animal date were provided, but in line with above statement the reliable animal data are analysed for sub-categorisation purposes only.

Based on the available animal data, i.e. the key LLNA, RAC agrees with DS that sub-categorization is warranted. As sub-category 1A can be excluded, sub-category 1B can be applied instead of Category 1. Human data support the classification of UDMA as a skin sensitiser.

ANNEXES:

Annex 1 The Background Document (BD) gives the detailed scientific grounds for the opinion. The BD is based on the CLH report prepared by the Dossier Submitter; the evaluation performed by RAC is contained in 'RAC boxes'.

Annex 2 Comments received on the CLH report, response to comments provided by the Dossier Submitter and RAC (excluding confidential information).