

Annex I to the CLH report

Proposal for Harmonised Classification and Labelling

**Based on Regulation (EC) No 1272/2008 (CLP Regulation),
Annex VI, Part 2**

**International Chemical Identification:
methacrylic acid, monoester with propane-1,2-diol (HPMA)**

EC Number: 248-666-3
CAS Number: 27813-02-1
Index Number: NA

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CONTENTS

1	TOXICOKINETICS (ABSORPTION, METABOLISM, DISTRIBUTION AND ELIMINATION)	4
1.1.1	[OASIS TIMES]	4
1.1.2	[Munksgaard, 1990]	7
1.1.3	[Anonymous, 2017]	7
2	HEALTH HAZARDS	8
2.1	SERIOUS EYE DAMAGE/EYE IRRITATION	8
2.1.1	Animal data	8
2.1.1.1	[Anonymous, 1978]	8
2.2	RESPIRATORY SENSITISATION	11
2.2.1	Human data	12
2.2.1.1	[Lindstrom, 2002]	12
2.2.1.2	[Sauni et al. 2008]	12
2.2.1.3	[Vaccaro, 2014]	14
2.2.2	Other data	14
2.2.2.1	[QSAR Toolbox]	15
2.3	SKIN SENSITISATION	16
2.3.1	Animal data	16
2.3.1.1	[Scholes, 1992]	16
2.3.1.2	[Clemmensen, 1984]	19
2.3.1.3	[Rao, 1981]	20
2.3.1.4	[Basketter, 1992]	21
2.3.1.5	[Björkner, 1984]	23
2.3.2	Human data	24
2.3.2.1	[Björkner, 1984]	24
2.3.2.2	[Kanerva, 1989]	24
2.3.2.3	[Lovell, 1985]	25
2.3.2.4	[Kanerva, 1993]	26
2.3.2.5	[Kanerva, 1988]	27
2.3.2.6	[Jordan, 1975]	28
2.3.2.7	[Marren, 1991]	29
2.3.2.8	[Romaguera, 1989]	30
2.3.2.9	[Uter, 2015]	30
2.3.2.10	[Ramos, 2014]	32
2.3.2.11	[Heratizadeh, 2018]	33
2.3.2.12	[Alcantara-Nicolas, 2016]	35
2.3.2.13	[Raposo, 2017]	36
2.3.2.14	[Stingeni, 2015]	37
2.3.2.15	[Aalto-Korte, 2008]	38
2.3.2.16	[Aalto-Korte, 2007]	39
2.3.2.17	[Aalto-Korte, 2010]	40
2.3.2.18	[Christoffers, 2012]	41
2.3.2.19	[Gatica-Ortega, 2017]	42
2.3.2.20	[Gatica-Ortega, 2018]	43
2.3.2.21	[Spencer, 2016]	43
2.3.2.22	[Kanerva, 1997]	45
2.3.2.23	[Lazarov, 2007]	45
2.3.2.24	[Kanerva, 1995a]	46
2.3.2.25	[Kanerva, 1995b]	47
2.3.2.26	[Teik-Jin Goon, 2007]	48
2.3.2.27	[Goncalo, 2018]	49
2.3.2.28	[Pestana, 2016]	51
2.3.2.29	[Muttardi, 2016]	52
2.3.2.30	[Aalto-Korte, 2021]	53
2.3.2.31	[Rustemeyer, 1996]	54
2.3.2.32	[Tucker, 1999]	56
2.3.2.33	[Eslander, 1996]	56
2.3.2.34	[Hemmer, 1996]	57
2.3.2.35	[Cravo, 2008]	58
2.3.2.36	[Vaccaro, 2014]	58

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL
(HPMA)

2.3.2.37	[Le, 2015]	60
2.3.2.38	[Romita, 2020]	61
2.3.2.39	[Alves, 2020]	62
2.3.2.40	[Fisch, 2019]	62
2.3.2.41	[Rodenas-Herranz, 2020]	63
2.3.2.42	[Kanerva, 1992]	64
2.3.2.43	[Weber-Muller, 2004]	64
2.3.2.44	[Llamas, 2010]	65
2.3.2.45	[Goulding, 2011]	66
2.3.2.46	[Maio, 2012]	66
2.3.2.47	[Kiec-Swierczynska, 2013]	67
2.3.2.48	[DeKoven, 2017]	67
2.3.2.49	[Conde-Salazar, 2017]	69
2.3.2.50	[Kanerva, 1991]	70
2.3.2.51	[Eslander, 1990]	71
2.3.2.52	[Linstrom, 2002]	74

1 TOXICOKINETICS (ABSORPTION, METABOLISM, DISTRIBUTION AND ELIMINATION)

1.1.1 [OASIS TIMES]

Metabolic map_HPMA_in vitro rat S9_Phase I, as predicted by OASIS TIMES.

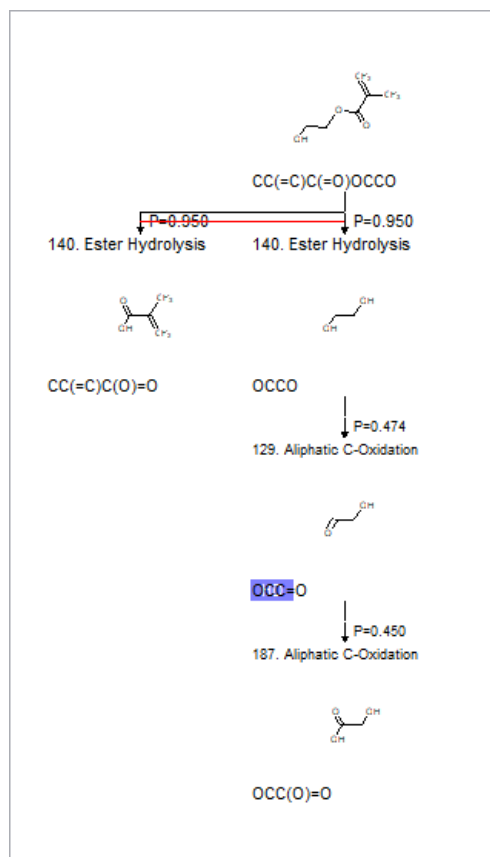
- **P (Prob., intrinsic)** is the probability of the current transformation from transformation table.
- **Quantity of metabolite** depends on both – probability to be obtained and probability to metabolize:

$$Q = \langle \text{probability to obtain} \rangle \times (1 - \langle \text{probability to metabolize} \rangle)$$

Quantity of parent is calculated under the assumption that the probability to obtain is equal to 1:
 $\langle \text{probability to obtain} \rangle = 1$

$$Q(\text{parent}) = 1 - \langle \text{probability to metabolize} \rangle$$

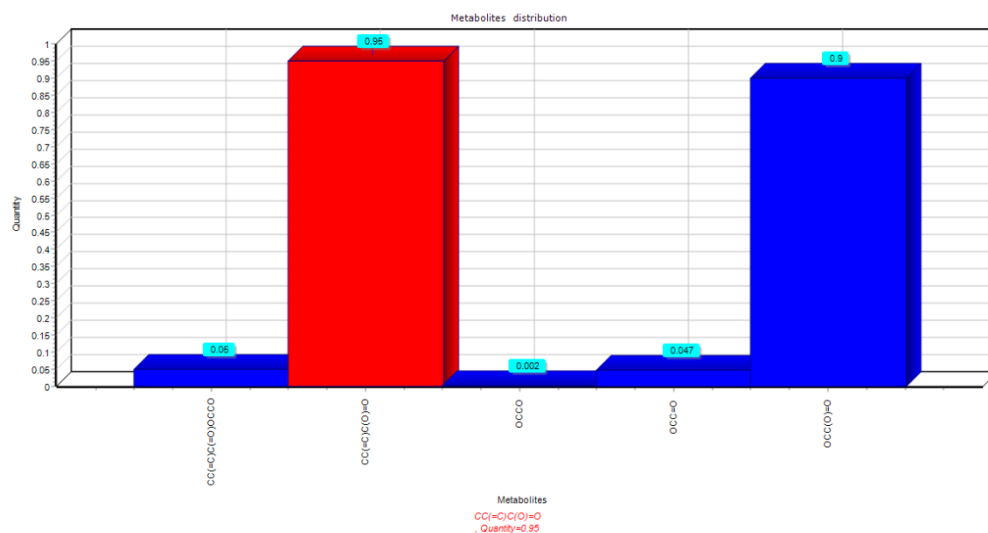
Hydrolysis is indicated with red horizontal line.



CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)



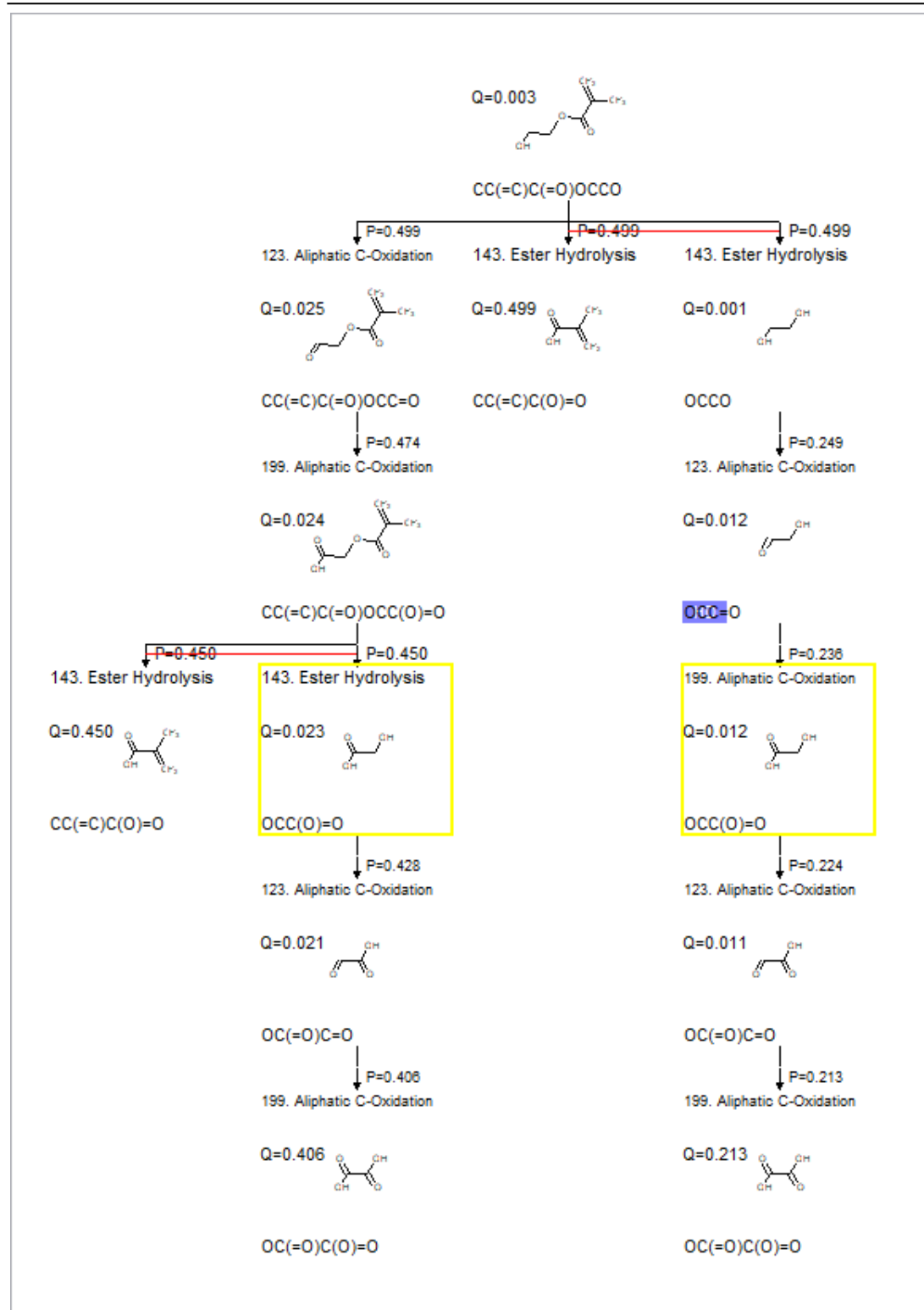
Graph Report



The parent (the first structure, in the first bar) is predicted almost completely metabolised.

HEMA_rat in vivo (Phase I reactions only) as predicted by OASIS Times

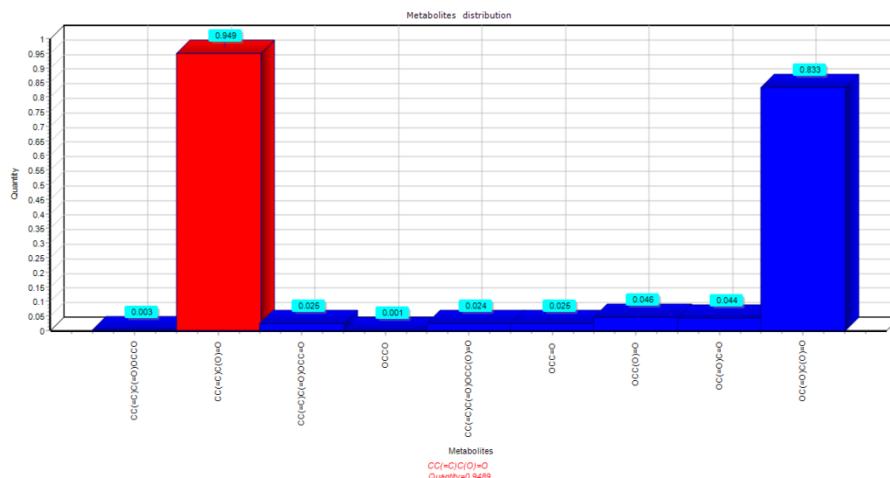
Hydrolysis is marked with horizontal read line in the graph. Yellow squares indicate metabolites, that were experimentally observed.



CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)



Graph Report



The parent is first structure (in the first bar).

1.1.2 [Munksgaard, 1990]

Study reference:

Munksgaard E.C., Freund M. Enzymatic hydrolysis of (di)methacrylates and their polymers (publication), Scand. J. Dent. Res. 1990;98: 261-267.

Detailed study summary and results:

Test type

Details on test system: Porcine liver esterase obtained from Sigma Chemical Company, St. Louis, USA

20.0 mg polymer powder was suspended in 10.0 mL 0.01 M phosphate, pH 6.5 and 10 U esterase/mL was added. The suspension was slowly stirred at 37 deg C, and aliquots taken after various periods of time were filtered to separate the polymer from the solution.

Identification and measurement of monomers and methacrylic acid were performed by high pressure liquid chromatography.

Results

Hydroxypropyl methacrylate is hydrolyzed to methacrylic acid and 1,2-propanediol at pH 6.5 and 37 deg. C catalysed by an unspecific esterase (Porcine liver esterase). Methacrylic acid and alcohol formation were determined by HPLC analysis. The substance is absorbable through the skin and is hydrolysed in the body.

1.1.3 [Anonymous, 2017]

Study reference:

Anonymous. 2017

Detailed study summary and results:

Test type

This non-GLP pharmacokinetic study of HPMA in rats via intravenous (IV) administration was conducted to evaluate the potential quick hydrolysis of HPMA *in vivo*.

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

Appropriate amounts of HPMA were added to sterile saline to obtain the appropriate dose of 5 mg/kg bw using aseptic techniques. The amount of dose solution administered was targeted at ~2.5 mL/kg bw and injected over a minimum of 45 seconds which corresponded to injection rates ranging from 0.7 to 0.8 mL/minute based on the averaged body weight of 0.2 kg.

Two male rats (Fischer 344/DuCrj) were intravenously administered HPMA individually at 5.0 mg/kg dose level with saline as the dose vehicle. After dose administration, blood samples (200 µL) were collected at 5, 10, 30, 60, and 180 minutes into individual glass vials containing ethyl acetate (600 µL) acidified with 1% formic acid. After vortexing, the levels of HPMA in the blood samples were quantitatively analyzed by GC/MS-MS.

Results

The results showed that levels of HPMA dropped rapidly after administration and were not quantifiable by 60 minutes with limit of quantitation (LOQ) of 48.8 ng/mL (HPMA). The estimated half-lives for HPMA were less than or near 1 minute (mean T_{1/2} around 1 min (0.69 and 0.95 min for each animal, respectively)), indicating that the current study results support the assumption that HPMA were quickly hydrolyzed after intravenous administration in rats.

2 HEALTH HAZARDS

2.1 Serious eye damage/eye irritation

2.1.1 Animal data

2.1.1.1 [Anonymous, 1978]

Study reference:

Study report. Anonymous. 1978

Detailed study summary and results:

Test type

Guideline: Appraisal of the safety of Chemicals in foods, drugs and cosmetics by staff of the Division of Pharmacology, FDA acc. to Draize

GLP: no

Test substance

- Methacrylic acid, monoester with propane-1,2-diol
- EC number: 248-666-3
- Is the substance skin corrosive or skin irritant? No

Test animals

- Rabbits, New Zealand White
- 6 animals
- Weight at study initiation: 2.4 to 2.6 kg

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

- Housing: individual cages
- Diet : standard diet (Höing 222)- Water ad libitum

Administration/exposure

- 0.1 ml of tested substance
- Vehicle: no (unchanged)
- Time points at which grading/scoring took place, (24, 48, 72 hours, 4, 5, 7 days)
- Removal of test substance (e.g. water or solvent): no washing
- SCORING SYSTEM: Scoring system for the evaluation of ear lesions Scores

1. Cornea

A. Opacity - Grade of opacity (the most opac area will be used for evaluation)

No opacity: 0

Mottled or diffuse opacity (details if iris good visible): 1

Slightly differentiated opac areas, details of iris slightly ambiguous: 2

Opac areas, no details of iris are visible, size of pupil hardly visible: 3

Opacity, iris invisible: 4

B. Size of involved total area or less but not zero: 1

More than $\frac{1}{4}$, but less than $\frac{1}{2}$: 2

Larger than $\frac{1}{2}$ but less than $\frac{3}{4}$: 3

Larger than $\frac{3}{4}$ up to total area: 4

A x B x 5 total maximum number = 80

2. Iris

A. Evaluation Normal: 0

Increasing wrinkle formation (washy trabecules) Blood overfilling, swelling, vascular dilatation at the edge of cornea (when one or more symptoms occur) iris shows still light reaction (delayed reaction is deemed to be positive): 1

No reaction against light, bleeding, changes in iris structure (one or more symptoms): 2

A x 5 total maximum number =10

3. Conjunctiva

A. Redness

Vascular normal: 0

Vascular definitely more than normal injected: 1

More diffuse crimson colour, single vascular difficult to identify: 2

Diffuse flesh colour: 3

B. Chemosis

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

No swelling: 0

More than normal swelling (including nictitating membrane): 1

Definite swelling with lifting the lids: 2

Swelling with semi-closed lids: 3

Swelling that lids are more than semi-closed or totally closed: 4

C. Secretion

No secretion: 0

Every increased secretion (not included the physiological secretion at the inner canthus): 1

Secretion with moistening the lids and the neighboring hairs: 2

Secretion with wettening the lids and the neighboring hairs largely beyond the eye: 3

Total number (A+B+C) x 2 total maximum number = 20

The total number for the eye is the summation of the scores for cornea, iris and conjunctiva

Results and discussion

		Day						
Animal No. 1		1	2	3	4	5	6	7
1. Cornea	A	1	1	1	0	0	0	0
	B	2	2	2	0	0	0	0
2. Iris	A	0	0	0	0	0	0	0
3. Conjunctiva	A	2	1	1	0	0	0	0
	B	0	0	0	0	0	0	0
	C	1	1	1	0	0	0	0

		Day						
Animal No. 2		1	2	3	4	5	6	7
1. Cornea	A	1	1	1	0	0	0	0
	B	2	2	2	0	0	0	0
2. Iris	A	0	0	0	0	0	0	0
3. Conjunctiva	A	2	2	2	0	0	0	0
	B	0	0	0	0	0	0	0
	C	1	1	1	0	0	0	0

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

		Day						
Animal No. 3		1	2	3	4	5	6	7
1. Cornea	A	1	1	1	0	0	0	0
	B	2	2	2	0	0	0	0
2. Iris	A	0	0	0	0	0	0	0
3. Conjunctiva	A	2	1	0	0	0	0	0
	B	0	0	0	0	0	0	0
	C	1	1	0	0	0	0	0

		Day						
Animal No. 4		1	2	3	4	5	6	7
1. Cornea	A	1	1	1	0	0	0	0
	B	2	2	2	0	0	0	0
2. Iris	A	0	0	0	0	0	0	0
3. Conjunctiva	A	2	1	0	0	0	0	0
	B	1	0	0	0	0	0	0
	C	1	1	0	0	0	0	0

		Day						
Animal No. 5		1	2	3	4	5	6	7
1. Cornea	A	0	0	0	0	0	0	0
	B	0	0	0	0	0	0	0
2. Iris	A	0	0	0	0	0	0	0
3. Conjunctiva	A	1	0	0	0	0	0	0
	B	0	0	0	0	0	0	0
	C	2	0	0	0	0	0	0

		Day						
Animal No. 6		1	2	3	4	5	6	7
1. Cornea	A	1	1	1	0	0	0	0
	B	2	2	2	0	0	0	0
2. Iris	A	0	0	0	0	0	0	0
3. Conjunctiva	A	2	1	0	0	0	0	0
	B	1	0	0	0	0	0	0
	C	3	1	0	0	0	0	0

Summary of the eye observations							
	Day						
Animal No.	1	2	3	4	5	6	7
1	16	14	14	0	0	0	0
2	16	16	16	0	0	0	0
3	16	14	10	0	0	0	0
4	18	14	10	0	0	0	0
5	6	0	0	0	0	0	0
6	22	14	10	0	0	0	0
Mean	15.67	12	10	0	0	0	0

2.2 Respiratory sensitisation

2.2.1 Human data

2.2.1.1 [Lindstrom. 2002]

See summary below in skin sensitisation endpoint

2.2.1.2 [Sauni et al. 2008]

Study reference:

Sauni R, Kauppi P, Alanko K, Henriks-Eckerman ML, Tuppurainen M, Hannu T. Occupational asthma caused by sculptured nails containing methacrylates. Am J Ind Med. 2008 Dec;51(12):968-74.

Detailed study summary and results:

Test type

Case report.

One of the patients (Patient 1) was referred to Finnish Institute of Occupational Health (FIOH) for specialist examinations from a local central hospital and the other (Patient 2) from a local occupational health service unit.

Spirometry was performed with a rolling-seal spirometer (Mijnhardt, Vicatest 3, Bunnik, Netherlands) connected to a microcomputer (Medicro MR-3, Kuopio, Finland), and Viljanen's [1982] reference values were used. The histamine challenge test was performed according to the method of Sovijärvi et al. [1993], following the forced expiratory volume in 1 s (FEV1) values with a Vitalograph S bellow spirometer (Vitalograph, Buckingham, UK). Measurements of exhaled nitric oxide (NO) were carried out using a chemiluminescence gas analyzer (NIOX, Aerocrine AB, Solna, Sweden) according to ATS FENO guidelines; values of >30 ppb were considered to be over normal values [Piipari et al., 2002; ATS/ERS, 2005]. Peak expiratory flow (PEF) measurements were performed at home and at the workplace according to the method of Burge [1982].

Bronchial provocation tests were performed in an 8-m³ challenge chamber according to international guidelines [Allergy Practice Forum, 1992; Piirilä et al., 1998]. As a reference challenge test, Coca solution and lactose powder were used in Patients 1 and 2, respectively. In the active challenge test, the patients simulated their work in the challenge chamber using their own products including Mas (methacrylates), i.e., they attached the plastic nail with a glue, and then iled and sculptured the nails. During the active challenge test, which took 30 min, three sculptured nails were produced. The patients were monitored for 24 hr after each challenge test. A portable, pocketsize spirometer (One Flow, STI MEDICAL, Saint-Romans, France) recorded the lung function measurements (FEV1, PEF); a drop of 20% in PEF or FEV1 was regarded as significant. An asthmatic reaction was defined as follows: an immediate reaction causing a decrease of 20% in the FEV1 or PEF during the first post-challenge hour; a delayed reaction causing a similar decrease in FEV1 or PEF after the first post-challenge hour; and a dual reaction as a combination of the aforementioned. Clinical symptoms and lung auscultation were recorded as well.

Acetone-soluble acrylates and methacrylates in gel nail materials and in gel nails were identified by gas chromatography-mass spectrometry (GC-MS) and quantified by liquid chromatography with ultraviolet (UV) detection at 210 nm. These were determinated in the case of Patient 2; in the case of Patient 1, the products were not available for analysis.

Results

The patient 1 was a 30-year-old female who had worked for 6 years as a manicurist and a nail technician. Her main job was to apply sculptured nails and artificial tips to nails.

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

About 4 years prior to the examinations at the FIOH, she experienced rhinitis, wheezing, and dyspnea during exercise. In pulmonary examinations at a local central hospital, spirometry was normal but the bronchodilatation test was positive. In the histamine challenge test, there was moderate bronchial hyperresponsiveness (PD15 0.226 mg), and the patient had typical asthmatic symptoms (dyspnea and wheezing). Asthma was diagnosed, and regular inhaled fluticasone medication with salbutamol on demand was started. Because she had respiratory symptoms when applying artificial nails, her asthma was also suspected to have an occupational origin. The patient was referred to FIOH for further respiratory investigations. At FIOH, the patient had no respiratory symptoms, and lung auscultation was normal. SPTs to common environmental allergens, formaldehyde, and methacrylates were negative. X-Rays of the thorax and nasal sinuses were normal. Spirometry showed mild peripheral obstruction without a bronchodilatation effect. The exhaled NO was normal (17.1 ppb). In the histamine challenge test, mild bronchial hyperresponsiveness (PD15 0.649 mg) occurred. A significant variation was noted in the PEF measurements at home and at the workplace: the PEF values varying from 360 to 580 L/min with a maximal diurnal variation of 26% and frequent bronchodilating effects up to 43%. The reference bronchial challenge test was negative. In the active bronchial challenge test, a dual asthmatic reaction was noted: an immediate significant decrease of 25% in the FEV1, and 4 hr after the start, a delayed significant decrease of 37% in the FEV1. After the delayed significant decrease, the patient received short-acting bronchodilating medication, after which the FEV1 returned to normal. On the basis on the work-related respiratory symptoms and findings in the workplace PEF follow-up, as well as the positive work simulation test, occupational asthma due to exposure to sculptured nails containing methacrylates was diagnosed. Minimizing the exposure to methacrylates was recommended, and asthma medication was continued with a combination of inhaled fluticasone and salmeterol. At the 6-month follow-up examination at FIOH, which is a normal procedure among patients in whom occupational disease is diagnosed at FIOH, the patient complained of nasal symptoms after long working days, but she had been able to continue her work as a nail technician.

The **patient 2** was a 27-year-old woman who had worked for 5 years both as a hairdresser and as a nail technician preparing artificial gel nails. The process of preparing gel nails and the used products were similar to that described in Patient 1.

About 5 years prior to examinations at FIOH, she had developed rhinitis, loss of voice, and recurrent sinusitis. The symptoms began during the first year after she started to apply gel nails. In pulmonary examinations at a local central hospital, the spirometry was normal, but there was significant diurnal variation in the PEF measurements and recurrent bronchodilating effects. In the histamine challenge test, there was mild bronchial hyperresponsiveness (PD15 0.154 mg). On the basis of these examinations, bronchial asthma was diagnosed and asthma medication was started with inhaled corticosteroids. In spite of the asthma medication, she experienced dry cough, wheezing, and shortness of breath, especially when preparing gel nails. The patient was referred to FIOH for further examinations due to the clinical suspicion of occupational asthma. This patient had no skin symptoms. At FIOH, the patient had no respiratory symptoms, and her lung auscultation was normal. Spirometry showed mild peripheral obstruction. Moderate bronchial hyperresponsiveness (PD15 0.29 mg) was noted in the histamine challenge test, and the exhaled NO value was increased (64.9 ppb). In the workplace PEF follow-up, there were no significant diurnal variations, but the patient did not prepare nails during the follow-up. SPTs to common environmental allergens showed allergy to animal epithelia (dog, cat) and to common pollens (alder, hay, mugwort) but no allergy to persulfates; methacrylates were not tested. The reference bronchial challenge test was negative. In the active bronchial challenge test, a dual asthmatic reaction occurred. An immediate significant decrease of 20% in the PEF (and a drop of 16% in FEV1) occurred 35 min after the start. After 8 hr, a delayed significant drop of 27% in the PEF (19% in FEV1) could be seen. The delayed drop fluctuated and was sustained until the patient received shortacting bronchodilating medication, after which the PEF and FEV1 returned to normal. On the basis of the work-related respiratory symptoms and findings in the pulmonary investigations, including a positive bronchial provocation test, occupational asthma due to exposure to sculptured nails containing methacrylates was diagnosed. Minimizing the exposure to methacrylates by using respiratory protective equipment was recommended, and asthma medication was continued with inhaled budesonide. At the 6-month followup at FIOH, the patient had been unable to continue her work as a nail technician because of respiratory symptoms.

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

The concentrations of methacrylates in the gel nail materials and in the gel nails themselves were determined after the active challenge test of Patient 2. The main methacrylate was HEMA (8%) in the bonding agent and bis-GMA(42%) in the sculpture resin. The sculpture resin also contained 7% of volatile hydroxypropyl methacrylate (HPMA). The identification of the main methacrylates in the sealing resin could not be confirmed. Hardened gel nails contained no detectable amounts of HEMA or aliphatic dimethacrylates.

TABLE I. Concentrations of Methacrylates Identified in Gel Nail Materials and in Gel Nails

Product	Identified methacrylates	Concentration (% w/w)	Identification
Bonding agent	HEMA	7.5	GC-MS/LC
	EGDMA	0.8	GC-MS/LC
	TREGDMA	0.2	GC-MS/LC
	Ethyleneglycol acrylate methacrylate	1	GC-MS
	Ethyleneglycol-based dimethacrylates ^a	2	GC-MS
	Ethyleneglycol monomethacrylate	0.5	GC-MS
Sealing resin	MMA	<0.05	GC-MS/LC
	HEMA	<0.01	GC-MS/LC
	MMA	<0.01	GC-MS/LC
	EGDMA	0.1	GC-MS/LC
Sculpture resin	Ethyleneglycol-based dimethacrylates ^a	20	GC-MS
	HEMA	0.03	GC-MS/LC
	MMA	<0.01	GC-MS/LC
	HPMA	6.7	GC-MS/LC
	TREGDMA	≤0.1	GC-MS
	BUDMA	≤0.1	GC-MS
	Ethyleneglycol-based dimethacrylates ^a	12	GC-MS
	Bis-GMA	42	GC-MS/LC
Gel nails	HEMA	<0.01	GC-MS
	Aliphatic dimethacrylates	<0.01	GC-MS

HEMA, hydroxyethyl methacrylate; EGDMA, ethyleneglycol dimethacrylate; TREGDMA, triethyleneglycol dimethacrylate; MMA, methylene methacrylate; HPMA, hydroxypropyl methacrylate; BUDMA, butandiol methacrylate; Bis-GMA, 2,2-bis-(4-(2-hydroxy-3-methacryloxypropoxy)phenyl)-propane; GC-MS, gas chromatography with mass selective detection; LC, liquid chromatography.

^aTentatively identified according to the presence of the ions 69 and 113 in the mass spectrum.

The authors concluded that the mechanism of occupational asthma (OA) induced by MAs is unclear. Both of the patients displayed a dual type of asthmatic reaction. In association with specific bronchial challenge tests, mainly late or dual asthmatic reactions has been reported to occur in dental personnel exposed to MAs [Piirilä et al., 1998] or in other occupations exposed to other acrylates (e.g., cyanoacrylates) [Savonius et al., 1993]. These modes of asthmatic reactions refer usually, but not necessarily, to reactions other than hypersensitivity type I. Taken together, although the results do not rule out a possible IgE-mediated mechanism, the pathophysiology of OA in relation to MA exposure probably involves other immunological mechanisms.

2.2.1.3 [Vaccaro. 2014]

See summary below in skin sensitisation endpoint

2.2.2 Other data

2.2.2.1 [QSAR Toolbox]

Profiling method : respiratory sensitisation

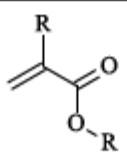
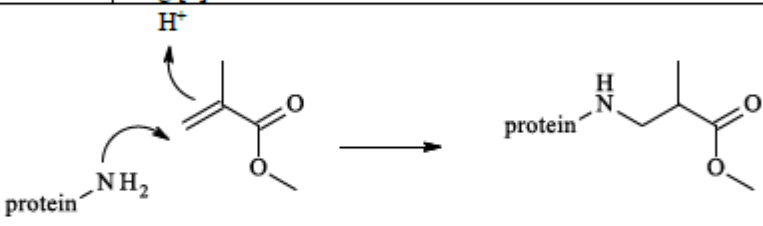
Short description

This profiler is intended to be used for the assessment of respiratory sensitisation potential of low molecular weight chemicals. The profiler has been developed from mechanistic knowledge of the elicitation phase of respiratory sensitisation, thus identifies chemicals able to covalently bind to proteins in the lung. This mechanistic hypothesis makes the profiler suitable for identifying chemicals capable of inducing respiratory sensitisation via both the skin and lung (as the chemistry (for a given structural alert) must be the same in both the induction and elicitation phases of sensitisation).

This profiler should be used with caution due to the limited data available for the development of structural alerts. This is due to the lack of a standardised assay (in vivo or in vitro) suitable for identifying potential respiratory sensitisers. The available data are drawn from clinical reports of occupational asthma in humans, which in a number of cases results structural alerts which have been defined from a low number of chemicals. However, all structural alerts have a clear mechanistic rationale associated with them (in terms of covalent protein binding).

The structural boundaries used to define the chemical classes (e.g. “Alcohol” – chemical class from “Organic functional group” profiler) or alerting groups responsible for the binding with biological macromolecules (e.g. “Aldehydes” – structural alert for protein binding), represent structural functionalities in the molecule which could be used for building chemical categories for subsequent data gap filling. They are not recommended to be used directly for prediction purposes (as SARs).

Result

Individual profile/alert/boundaries/other info applicable for defining categories within a profiler		
Name	Methacrylates	
Type of profile/alert	Structural alert	
Description/applicability domain	 <p>R = any carbon</p> <p>Organic chemicals with a molecular weight less than 1000g/mol</p>	
Mechanism	<p>A Michael addition mechanism has been suggested to be responsible for the ability of these types of chemicals to react with proteins in the lung [1].</p> 	
Set of chemicals used for profile development (local training set)	<p>The dataset from which the profiler was developed contained a single chemical containing this alert, which has been reported as being a respiratory sensitiser in humans.</p> <p>[hyperlink to Excel file containing the data: Methacrylates]</p>	
Data/Knowledge used for profile development	<p>There has been numerous peer-reviewed report of this chemical causing respiratory sensitisation in humans in the work place [2-5].</p>	
Profile/alert analysis	Profile/alert	Number chemicals analysed (Total/Sensitisers)
	Methacrylates	1/1
References	<p>[1] Enoch SJ et al (2012) <i>Development of mechanism-based structural alerts for respiratory hazard identification</i>. Chemical Research in Toxicology, 25, p2490-2498.</p> <p>[2] Borak J et al (2011) <i>Methyl methacrylate and respiratory sensitization: A Critical review</i>. Critical Reviews in Toxicology, 41, p230-268.</p> <p>[3] Henriks-Eckerman ML et al (2012) <i>Exposure to Airborne Methacrylates in Nail Salons</i>. Journal of Occupational and Environmental Hygiene, 9, pD146-D150.</p> <p>[4] Jaakkola MS et al (2007) <i>Respiratory effects of exposure to methacrylates among dental assistants</i>. Allergy, 62, p648-654.</p> <p>[5] Kauppi P et al (2007) <i>Occupational asthma due to occupational exposure to Methacrylates in a nail technician</i>. Allergologie, 2007. 30, p440-440.</p>	

2.3 Skin sensitisation

2.3.1 Animal data

2.3.1.1 [Scholes, 1992]

Study reference:

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

Scholes EW, Basketter DA, Sarll AE, Kimber I, Evans CD, Miller K, Robbins MC, Harrison PT, Waite SJ. The local lymph node assay: results of a final inter-laboratory validation under field conditions. J Appl Toxicol. 1992 Jun;12(3):217-22.

Information below related to LLNA assay

Detailed study summary and results:

Test type

Similar to OECD TG 429 (LLNA)

Interlaboratory study / validation study

GLP: not specified

Test substance

- 2-Hydroxypropyl methacrylate, Purity unknown
- From BDH Laboratory Supplies

Test animals

- Mouse CBA/Ca females
- 4/group
- Source: Harlan Olac Ltd., Bicester, Oxon or Barriered Animal Breeding Unit, Alderley Park
- Age at study initiation: young adult, 8-12 weeks

Administration/exposure

- Vehicle: acetone olive oil (AAO) or dimethylformamide (DMF)
- Choice of vehicle and test concentrations based primarily upon the physicochemical properties of the test chemical (e.g. solubility and viscosity) and potential toxicity.
- Concentration tested substance: 5.0, 10.0, 25.0, 50.0%
- 25 µL of one of the three concentrations of the test chemical on the dorsum of both ears daily for 3 consecutive days; termination after 5 days. Control mice received an equal volume of the relevant vehicle alone. Five days after the initiation of exposure, all mice were injected intravenously via the tail vein with 250 µL of PBS containing 20 µCi of [3H]methyl thymidine. Five hours later, the mice were sacrificed and the draining (auricular) lymph nodes were excised and pooled for each experimental group. Single-cell suspensions of lymph node cells (LNC) were prepared by gentle mechanical disaggregation through stainless steel gauze (200 mesh size). The pooled LNC were pelleted by centrifugation at 190 g for 10 min, washed twice with 10ml of PBS and resuspended in 3 ml of 5% trichloroacetic acid (TCA). Following overnight incubation at 4°C, the precipitates were recovered by centrifugation, resuspended in 1 ml of TCA and transferred to 10 ml of scintillation fluid (Optiphase MP; LKB). 3HTdR incorporation was measured by β scintillation counting. The proliferative activity of LNC was expressed as the number of radioactive disintegrations per minute (dpm) per lymph node for each experimental group. The ratio of 3HTdR incorporation by LNC of test lymph nodes relative to that recorded for control lymph nodes test/control (T/C) ratio was calculated for each test group.
- Positive control: not specified (validation study for LLNA)

Information below related to Maximisation assay

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

Detailed study summary and results:

Test type

According to Magnusson and Kligman method

GLP: not specified

Test substance

- 2-Hydroxypropyl methacrylate (among 9 different chemical tested), Purity unknown
- From BDH Laboratory Supplies

Test animals

- Dunkin Hartley strain guinea pigs
- N = 10 for treated groups and N = 4 for the negative control
- 300-350g
- Source: Harlan Porcellus, Heathfield, Sussex, UK

Administration/exposure

- Preliminary skin irritation studies were conducted to determine suitable concentrations of test chemical for induction and elicitation of sensitization. Test guinea pigs (n = 10) were sensitized by a series of intradermal injections of a slightly irritant concentration of test chemical in combination with Freund's complete adjuvant (FCA) in the shoulder region. Six to eight days later a mildly irritant concentration of test chemical was applied over the injection site using a 48-h occluded patch. Control guinea pigs (n = 4) were treated similarly, but with vehicle alone. After 12-14 days all animals were challenged with the maximum non-irritant concentration of test chemical on one clipped and razored flank using a 24-h occluded patch. The potential of a test chemical to cause skin sensitization was determined by visual assessment of erythema at the challenge sites, 24 and 48 h after removal of challenge patches. The sensitization potential was expressed as the percentage of test guinea pigs exhibiting a reaction significantly greater than in control guinea pigs.
- Positive control: not specified

Results and discussion

- Not sensitizing

LLNA						Guinea pig maximisation test (GPMT)			
Chemical	Conc (%)	LLNA result (T/C ratio)				GPMT protocol			GPMT result (% +ve)
		Lab. A (veh.)	Lab. B (veh.)	Lab. C (veh.)	Lab. D (veh.)	intradermal conc. (%)	Topical induction conc. (%)	Challenge conc. (%)	
HPMA	5.0	1.1 (AOO)	- (AOO)	- (AOO)	- (DMF)	1.0	100.0	10.0	0
	10.0	1.2	0.8	1.0	1.4	0	0	10.0	0
	25.0	1.3	1.0	1.9	0.7				
	50.0	-	0.9	0.8	0.9				

2.3.1.2 [Clemmensen, 1984]

Study reference:

Clemmensen S. Cross-reaction patterns in guinea pigs sensitized to acrylic monomers. Drug Chem Toxicol. 1984;7(6):527-40.

Detailed study summary and results:

Test type

According to Magnusson and Kligman method

GLP: no specified

Test substance

- 2-Hydroxypropyl methacrylate (HPMA) (among other acrylates/methacrylates), Purity unknown

Test animals

- Outbred Guinea pig, SSc:AL
- Females
- Approximately 1 month old; weight: 300-350g
- Source: Statens Seruminstitut, Copenhagen, Denmark
- 4/cage; 12 animals/group

Administration/exposure

- Irritation threshold: naïve guinea pigs were injected in the nape of the neck with 2x 50µL FCA-emulsion 14 days before determination of the minimally irritating and maximally non-irritating concentration. For the pre-test 25 µl aliquots of several concentrations were either injected into the flank skin or applied for 24 hours in aluminium chambers (Finn Chambers). The test sites were examined 24 and 48 hours later. Concentrations giving a definite irritative reaction, pale pink edema with a diameter of 10 mm on intradermal or confluent erythema on topical application were selected for induction. Only concentrations giving no reactions were used for challenge.
- Induction day 0: hair was removed from an area of 4x6 cm in the shoulder region with a small animal clipper. Three pairs of injections were then made just within the boundaries of the 2x4 cm patch to be applied one week later
 - 2x50 µL of a suspension of FCA in sterile water (1:1)
 - 2x50 µL of test substance in the chosen vehicle (1:1)
 - 2x50 µL of test substance emulsified in FCA and water (1/1)
 - Controls received the same treatment with test substance omitted.
- Induction Day 7 and 8: the same area on the neck was clipped on day 7 and approximately 250 mg 10% SDS in petroleum gently massaged into the test area and left uncovered for 24 hours. On day 8, 400 µL of the liquid test solution or an equivalent amount of petroleum was applied on a 2x4 cm piece of Whatman 3 MM filter paper. The patch was covered by impermeable tape and secured with an elastic bandage. The dressing was left in place for 48 hours. Controls received the same treatment, but with the test substance omitted.
- Challenge: hair was removed from the left flank on day 21 by clipping and shaving. Up to six patches were applied three hours later. A small disk of Whatmann 3 MM filter paper was inserted in the bottom of the chamber when the preparation was liquid. An elastic bandage kept the patches in

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

position for 24 hours. Readings were made 48 and 72 hours (days 23 and 24) after application. Control and test animals received identical treatment. The procedure was repeated on virgin skin on the opposite flank from day 35 on, if required.

- Vehicle: water
- 1st application: Induction 10 % other: intradermal injection
- 2nd application: Induction 100 % occlusive epicutaneous
- 3rd application: Challenge 25 % occlusive epicutaneous

Results and discussion

The hydroxyalkylesters sensitised between 25 and 100% of the treated animals and exhibited extensive cross-reactions.

3 of 12 animals reacted positively with a challenge concentration of 25% HPMA in water.

Cross-reactions were found with other acrylates.

Sensitization to Hydroxyalkyl-substituted Monomers in the GPM test.

INDUCTION	3% MMA	25% HEMA	25% HPMA	0.3% HEA	0.3% HPA
HEMA 25% id, 100% top,	0/15	7/15	5/15	2/15	2/15
HPMA 10% id, 100% top,	1/12	2/12	3/12	nt	nt
HEA 0.5% id, 25% top,	nt	7/12	8/12	12/12	12/12
HPA 05% id, 25% top,	nt	2/12	2/12	12/12	12/12

No positive reactions in controls. nt = not tested.

2.3.1.3 [Rao, 1981]

Study reference:

Rao KS, Betso JE, Olson KJ. A collection of guinea pig sensitization test results--grouped by chemical class. Drug Chem Toxicol. 1981;4(4):331-51.

Detailed study summary and results:

Test type

Maguire method derived from the Split adjuvant technique

GLP: not specified

Test substance

- hydroxypropylmethacrylate (among different chemicals), Purity unknown

Test animals

- Guinea pigs
- Males
- 7 animals per group
- Approximately 300 g

Administration/exposure

- Prior to conducting the sensitization test, the test material was applied as received to the clipped flanks of guinea pigs to determine if primary irritation would occur. If significant irritation was observed, dilutions of the test material were made in a suitable solvent. The highest concentration which did not cause primary irritation was used for the guinea pig sensitisation test.
- A typical test procedure consisted of topical application of a 0.1 ml aliquot of the test material to the clipped and depilated backs of guinea pigs 4 times in 10 days. At the time of the third application, 0.2 ml of Freund's adjuvant was injected intradermally at one point adjacent to the insult site. After a 2-week rest period, the guinea pigs were challenged on the clipped flanks with the test material on one flank and a solvent (if used) on the other flank. The challenge site was evaluated for erythema and/or oedema at 24 and 48 hours.
- Along with each test series, 10 guinea pigs were routinely subjected to the same dosing regimen with the diglycidyl ether of 2,2-di-(p,p'-hydroxyphenyl)propane as known sensitizer to serve as a positive control.

Results and discussion

- 0 out of 7 animals were sensitized.
- Positive control sensitizes at least 70% of the guinea pigs each time.

2.3.1.4 [Basketter, 1992]

Study reference:

Basketter DA, Scholes EW. Comparison of the local lymph node assay with the guinea-pig maximization test for the detection of a range of contact allergens. Food and Chemical Toxicology. 1992. Volume 30, Issue 1, Pages 65-69

Information below related to LLNA assay

Detailed study summary and results:

Test type

LLNA

GLP: not specified

Test substance

- 2-Hydroxypropyl methacrylate (among 40 different chemicals)
- The vast majority of the tested chemical were more than 98% pure; however, specific details have not been given

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

- Supplier: BDH Chemicals Ltd. (Poole, Dorset, UK)

Test animals

- CBA/Ca mice
- 4/group
- Animals of both sexes were used but single experiments were limited to one sex (females).
- 8-12 weeks

Administration/exposure

- Vehicle: AAO
- Concentrations: 10, 25, 50%
- Animals were treated by a daily topical application of 25 µL of each concentration on the dorsal surface of each ear for 3 consecutive days. Control mice were treated with vehicle alone. 4-5 days after the first topical application, all mice were injected intravenously through the tail vein with 250 µL PBS containing [3H]methyl thymidine. After 5 hour the mice were killed by carbon dioxide asphyxiation, and the draining auricular lymph nodes were excised and pooled for each experimental group. A single-cell suspension of lymph node cells (LNC) was prepared by gentle mechanical disaggregation through a stainless-steel gauze (200-mesh size), using the plunger of a syringe. Pooled LNC were pelleted at 190g for 10 min, washed twice with 10 ml PBS and resuspended in 3 ml trichloroacetic acid (TCA; 5%) for the precipitation of macromolecules. After an overnight incubation with TCA at 4°C, the precipitate was recovered by centrifugation, resuspended in 1 ml TCA and transferred to 10ml scintillation fluid. 3HTdR incorporation was measured by β-scintillation counting. The proliferative response of LNC was expressed as radioactive disintegrations per min per lymph node (dpm/node), and as the ratio of 3HTdR incorporation into LNC of test nodes relative to that recorded for control.

Results and discussion

- Not sensitizer: T/C ratio: 1.1; 1.2; 1.3

Information below related to Maximisation assay

Detailed study summary and results:

Test type

According to Magnusson and Kligman method

GLP: not specified

Test substance

- 2-Hydroxypropyl methacrylate (among 40 different chemicals)
- The vast majority of the tested chemical were more than 98% pure; however, specific details have not been given
- Supplier: BDH Chemicals Ltd. (Poole, Dorset, UK)

Test animals

- Albino Dunkin-Hartley Guinea pig; sex not given
- 10 animals/dose
- Approximately 350 g at the start of the study

Administration/exposure

- Preliminary irritation tests were carried out to determine the concentrations suitable for induction and challenge phases
- Tested concentration: 1% intradermal; 100% topical induction and challenge
- Series of 6 intradermal injections in the shoulder region to induce sensitization. After 6-8 days, sensitization was boosted by a 48h occluded patch placed over the injection site. 12-14 days later, the animals were challenged on one flank by a 24 hour occluded patch at the maximum non irritant concentration. Challenge sites were scored for erythema (scale 0-3) and oedema 24 and 48 hours after removal of the patches.
- Vehicle: none for topical application

Results and discussion

- None of the test animals (0 out of 10) was judged to be positive at 24 and/or 48 hours.

2.3.1.5 [Björkner, 1984]

Study reference:

Björkner B. Contact allergy to 2-hydroxypropyl methacrylate (2-HPMA) in an ultraviolet curable ink. Acta Derm Venereol. 1984;64(3):264-7.

Detailed study summary and results:

Test type

According to Magnusson and Kligman method

GLP: no

Test substance

- Methacrylic acid, monoester with propane-1,2-diol
- Purity: > 95 %
- Manufactured by BDH Chemicals Ltd, England

Test animals

- Guinea pig; sex not given
- 10 animals/dose for treated and control groups

Administration/exposure

Five percent of HPMA solved in a mixture of olive oil and acetone (10:1) was used for intradermal induction. To achieve a uniform dispersion of HPMA in petrolatum, only 25% w/w was used for topical induction. Pretreatment with 10% w/w sodium lauryl sulphate (SLS) in water was performed, as 25% w/w concentration did not give any irritation. Challenge was performed with HPMA (2% w/w in pet).

The sensitisation procedure was repeated once with other guinea pigs that used in the first experiment.

Results and discussion

- 1 animal out of 10 reacted to HPMA. All control animals were negative.
- The repeated sensitisation procedure gave the same results.

2.3.2 Human data

2.3.2.1 [Bjorkner, 1984]

Study reference: Björkner B. Contact allergy to 2-hydroxypropyl methacrylate (2-HPMA) in an ultraviolet curable ink. *Acta Derm Venereol.* 1984;64(3):264-7.

Detailed study summary and results:

Test type

Case report

A 52 year old patient who has been employed for 10 years in an ink laboratory, formulating inks and varnishes for UV cure, developed a dermatitis on his hands.

The ink consisted of a polyesteracrylate as a polymer and 2-HPMA as a monomer. He was tested with UV-B and UV-A and photo patch tested with the standard test series and also with the ink he has been working with in a concentration from 1% w/w diluted down to 0.01% w/w in methyl ethyl ketone. He was patch tested with polyesteracrylate (Ebecryl 810) and 2-HPMA (BDH Chemicals Ltd, England) in a concentration of 2% w/w in petrolatum. He was also patch tested with other acrylates.

The photopatch test was negative for the standard test series but positive for the ink used both at the irradiated and covered test sites with a test concentration of 1% and 0.1% in MEK but negative for 0.01%. Photo tests were normal for UV-A and UV-B. The standard epicutaneous patch test was negative. Tests using the different acrylates showed positive reaction only for 2-HPMA.

2.3.2.2 [Kanerva, 1989]

Study reference:

Kanerva L, Estlander T, Jolanki R: Allergic contact dermatitis from dental composite resins due to aromatic epoxy acrylates and aliphatic acrylates; *Contact Dermatitis.* 1989; 20: 201-211

Detailed study summary and results:

Test type

Case report

Altogether 7 patients (6 dental nurses and one dentist; all females) with allergic contact dermatitis due to DCR (dental composite resin) products have been detected. Patient nos. 1-6 were dental nurses and patient no. 7 a dentist. 3 were atopies and 2 others had atopy in their family. All had hand eczema, particularly on their fingers, and 3 also had intermittent dermatitis on the face. In all, a predisposing or concomitant occupational contact dermatitis had been or was detected.

Exposure has in all cases been occupational. Prick tests with common environmental allergens and patch tests are performed on every patient with contact dermatitis in the clinic.

Patch testing was done on the back using Finn Chambers, with an occlusion time of 24 hours and at least 3 readings by a dermatologist. Patch tests have been scored according to the recommendations of the Finnish Contact Dermatitis Group: - = negative; + = erythema; ++ = erythema and oedema; +++ = erythema, oedema and vesicles; ++++ = bullous or ulcerative reaction. In addition to the European standard series, the patients were tested with some specific series (dental, acrylates, antimicrobials, rubber) and also in most cases with substances brought in by the patients themselves (DCR, other acrylate products, glove materials, and disinfectants).

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

Since September 1985, authors have used the (meth)acrylate series of Chemotechnique Diagnostics AB (Malmo, Sweden), containing 28 substances, including 4 epoxy acrylates.

All patients were allergic to their DCR.

Extracted from table 1 of the publication:

Table 1. Patch test results of (meth)acrylate series and epoxy resin										
Compound		Purity* % (w/w)	Concentration % (w/w) pet.	Patient no. 1	Patient no. 2	Patient no. 3	Patient no. 4	Patient no. 5	Patient no. 6	Patient no. 7
2-hydroxypropyl methacrylate	(2-HPMA)	—	2	ND	ND	—	2+	—	2+	3+

ND: not done

2.3.2.3 [Lovell, 1985]

Study reference:

Lovell CR, Rycroft RJG, Williams DMJ, Hamlin JW: Contact dermatitis from the irritancy (immediate and delayed) and allergenicity of hydroxypropyl acrylate; Contact Dermatitis. 1985; 12: 117-118.

Detailed study summary and results:

Test type

Case report

Case report in a company involved in the manufacture of HPMA for 2 years and hydroxyethyl methacrylate for 3 months before beginning the manufacture of hydroxypropyl acrylate (HPA). Typical purity of hydroxyl ethyl and propylmethacrylate > 90%.

A 39-year-old man had worked as a maintenance fitter since the introduction of the acrylate process. The normal protective clothing then worn by the maintenance fitter when engaged on work involving HPA included conventional leather safety boots, 16 inch nitrile rubber gauntlet gloves, cotton overalls and safety goggles. 6 h after removing some HPA polymer fouling from a basket strainer, he noticed a small abrasion resembling a chemical burn, on his right foot. Some 12 h later, the right foot had become swollen and a number of blisters had developed. 6 months later, he developed an erythematous papular eruption on the forearms, thighs and groins after he had spent 1 day working on the HPA unit. The eruption cleared within a few days. On the day after returning to work, the eruption reappeared. He had not been working on the plant and would not have been in contact with contaminated equipment. However, he had worn boots which might have been previously contaminated with HPA. After 6 h, the eruption spread to his hands, forearms, abdomen, thighs and genitalia. This again cleared within a few days. Since then he has not worked on the process and has had no further relapse.

Patch Tests

	2 days	4 days
hydroxypropyl acrylate 1% pet.	++	++
hydroxypropyl methacrylate 2% pet.	+	+
hydroxyethyl methacrylate 2% pet.	+	+
methacrylic acid 0.1% MEK	—	—
acrylic acid 0.1% pet.	—	—
monomethyl ether of hydroquinone 1% pet.	—	—
methyl methacrylate 2% pet.	—	—
ICDRG standard series	—	—

Patch tests to the acrylates in 6 control subjects were negative.

No skin problems were noted before the introduction of HPA. 150 other workers are employed in the same plant, none of whom have developed allergic contact dermatitis from acrylates. However, 3 other maintenance fitters and 8 process operatives developed irritation immediately after contact with HPA monomer. In 2 workers, blistering occurred at the sites of contact 5-6 h after exposure, in the absence of an immediate sensation of irritation.

It appears that the patient was sensitized by hydroxypropyl acrylate and developed cross-sensitivity with the methacrylates to which he was previously exposed. The mechanism of delayed irritation in other workers remains unclear.

2.3.2.4 [Kanerva, 1993]

Study reference:

Kanerva L, Estlander T, Jolanki R, Tarvainen K: Occupational allergic contact dermatitis caused by exposure to acrylates during work with dental prostheses; Contact Dermatitis. 1993; 28: 268-275

Detailed study summary and results:

Test type

Case report

4 patients with occupational allergic contact dermatitis caused by working with dental prostheses and diagnosed in the authors' Institute between 1 January 1974 and 31 July 1992 underwent patch testing on the upper back with the Finn Chamber method. Each patient was patch tested with the European standard series and additional series that were selected on the basis of the patient's exposure history.

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

Table 1. Data of 4 patients who developed allergic contact dermatitis from working with prostheses

Patient no.	1	2	3	4
age (years)	32	23	24	25
occupation	dentist	dental technician apprentice	dental technician	dental worker
exposure before sensitization (years)	2	1.5	3	2
year of diagnosis	1982	1982	1983	1992
localization of dermatitis	fingertips	fingertips, hands, face	fingertips	fingertips
patch test sessions	1	2	3	2
patch tests				(see Table 2)
acrylics				
butyl acrylate (BA)	1% pet.	2+	3+	
tert. butyl acrylate (t-BA)	1% pet.	—	—	
ethyl acrylate (EA)	1% pet.	3+	1+	
2-ethylhexyl methacrylate (2-EHMA)	1% pet.	2+	3+	
2-hydroxypropyl methacrylate (2-HPMA)	1% pet.	—	—	
N-tert. butylacryl amide (N-t-BAA)	1% pet.	2+	3+	
methyl methacrylate (MMA)	1–10% pet.	—	—	
own methacrylates				
polymethacrylate powder	100%	NT	2+	—
liquid acrylate monomer	1% pet.	3+	2+	2+ (2% pet.)
other positive acrylates	—	EGDMA 2+	Palavit G® 1%, 3+ Opaquer® 1%, 3+	De Trey Dentsply, 2%, 2+ Special Tray Liq, 2%, 2+
other positive patch tests	—	rubber glove 2+	EGDMA 2+ TREGDMA 2+ formaldehyde 2+ glutaraldehyde 2+ p.tert-butylphenol- formaldehyde resin 3+ dequalon 3+ neomycin 3+ bacitracin 3+	several (Table 2) own rubber glove 2+ hexamethylenetetramine 2+ 1–3-diphenylguanidine 1+

2.3.2.5 [Kanerva, 1988]

Study reference:

Kanerva L, Estlander T, Jolanki R: Sensitization to patch test acrylates; Contact Dermatitis. 1988; 18: 10-15

Detailed study summary and results:

Test type

Clinical study

Data on allergic contact dermatitis from acrylates and 4 patients sensitized during routine patch testing are reported. During 1982-1985, authors used 7 different acrylates for tests. Since September 1985, they have used a commercial (meth)acrylate series containing 28 substances.

Nowadays, practically every patient with contact dermatitis was tested. In all cases, authors used at least the European standard series. Depending on exposure, authors used further commercial series, and test with substances brought in by patients ("own substances"). The Finn-chamber method with an occlusion time of 24 hours was used. The tests were applied on the back with a non-occlusive porous tape (Scanpor® Surgical Tape, Norgeplaster A/S, Norway); or when the back was full of patch tests, authors used the thighs. The tests were read on removal and 24 h, 48 h, and 96-120 h after removal (at least 3 readings). All readings were made by a dermatologist. Here, authors reported the patch test observations with (meth)acrylates, and the case reports of the patients that they sensitized during 1982-1986.

Series of seven acrylic compounds used for patch tests in 1982-1985 included hydroxypropyl methacrylate (2-HPMA) at 1% in pet. The commercial (meth)acrylate series (Chemothechnique, 2) was used for patch testing since September 1985 and included 2-hydroxypropyl methacrylate at 2% in pet.

Observation during 1982-1985:

Acrylate series were tested in cases where contact allergy to acrylates was suspected.

12 of 22 (=54.5%) patients tested showed no reaction to the acrylates. 10 patients showed slight to moderate irritation at 24h, this was often still visible at 48h and sometimes at 72-96h. One of these patients was sensitized (see below). Of the 10 patients that showed irritation, 1 had irritation to 2-HPMA.

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

Patient sensitized to acrylates (iatrogenic sensitization to a chemical induced by application of a patch test) : One patient was sensitized (patient 4 of the table below)

Allergic contact dermatitis from acrylates: 4/22 patients tested had an allergic occupational contact dermatitis from acrylates. Case no. 1 was a 32-year-old female dentist who showed a positive reaction to her own substances that contained MMA, in the test series, she was allergic to different acrylates including HPMA. Case no. 2 was a 23-year-old dental technician student, who was positive to the same substances. Case no. 3 was a 24-year-old dental technician, who was positive to different acrylates including HPMA. Case no. 4 was a 34-year-old man, who had been working in a paint stock for 18 years where he was exposed to different types of paint. He was negative to acrylate series, but showed a strong positive reaction to his own acrylate paint. 10 control persons were negative. Details of the acrylates in the paints were not obtained.

Observations during 1985-1986

12 of 24 patients showed no reactions to the (meth)acrylate series.

Patients sensitized to acrylates: 3 patients (12.5%) were actively sensitized (patients 1-3 of the table below).

Allergic contact dermatitis from acrylates: 3 patients had a relevant allergic patch test. Case no. 1 was a dentist who was test positive to the different acrylates including HPMA. Some of the reactions were obviously cross reactions. Case no. 2 was a dental assistant allergic to BIS-GMA. In the (meth)acrylate series, she also reacted to epoxy acrylate and in the standard series to epoxy resin. She showed slight irritation to 2-HEA at the 24- and 48-h reading. Case no. 3 was a car furnisher who became allergic to the anaerobic Loctite glue-sealants. In addition to these substances, she reacted to 2-HEMA, 2-HPMA, TREGDA and TREGDMA.

*Table 4. Characteristics of patients sensitized to (meth)acrylates**

Characteristics	Patient no.			
	1	2	3	4
sex	F	M	F	F
age	36	27	23	38
occupation	dental assistant	laboratory technician	car painter's apprentice	dentist
irritant reactions at initial patch testing with (meth)acrylates	EA 2-HEA HPA	EA 2-HEA HPA	EA 2-HEA HPA	EA BA
patch test sites actively sensitized	EA 2-HEA HPA	EA 2-HEA HPA	EA 2-HEA HPA	EA BA
interval (days) between application of patch test and signs of active sensitization	18	19	19	21
atopy (criteria of Hanifin & Rajka, 8)	+	+	-	+
positive (meth)- acrylates when retested	EA 2-HEA HPA	ND	EA BA 2-HEA HPA 2-HEMA 2-HPMA	EA BA

ND = not done.

2.3.2.6 [Jordan, 1975]

Study reference:

Jordan WP: Cross-sensitization patterns in acrylate allergies; Contact Dermatitis. 1975; 1: 13-15

Detailed study summary and results:

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

Test type

Case report.

Five subjects developed allergic contact dermatitis to one or more acrylate components used in a commercial adhesive tape. Patch testing to acrylic monomers was performed to examine their cross-reaction patterns.

Subjects were initially reacting to 2 EHA (2-ethylhexyl-acrylate) (subjects 1-3) and 2 EHA plus NTBM (N-tert-butyl maleamic acid) (subjects 4 and 5). Subjects 4 and 5 were further tested to HPMA among other (meth)acrylates. HPMA was tested at 5% in olive oil.

Subjects	1	2	3	4	5
Initial Positive Acrylates	$\text{CH}_2=\text{C}(\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3)\text{C}(=\text{O})\text{CH}_2\text{CH}_3$ <p>2 ethyl hexyl acrylate (2 EHA)</p>			$\text{HO}-\text{C}(=\text{O})-\text{CH}=\text{CH}-\text{C}(=\text{O})-\text{NH}-\text{C}(\text{CH}_3)_2$ <p>and 2 EHA (N-tert butyl maleamic acid)</p>	
Methacrylates tested					
$\text{CH}_2=\text{C}(\text{CH}_3)\text{C}(=\text{O})\text{O}-$	R				
1. Methyl	-CH ₃	-	-	-	-
2. hydroxy propyl	-CH(OH)-CH ₂ -CH ₃	NT	NT	NT	++
3. 2 ethyl hexyl	-CH ₂ -CH(CH ₂ CH ₃)-CH ₂ -CH ₂ -CH ₂ -CH ₃	-	-	-	-
Acrylonitrile	(CH ₂ =CH-CN)	-	-	-	-
N-tert butyl acrylamide	$\text{CH}_2=\text{CH}-\text{C}(=\text{O})\text{NH}-\text{C}(\text{CH}_3)_2$	-	-	-	-

2.3.2.7 [Marren, 1991]

Study reference:

Marren P, De Berker D, Powell S: Methacrylate sensitivity and transcutaneous electrical nerve stimulation (TENS); Contact Dermatitis. 1991; 25: 190 - 191

Detailed study summary and results:

Test type

Case report

A 35-year-old nurse had had chronic low back pain for many years, with 2 unsuccessful laminectomies. TENS (transcutaneous electrical nerve stimulation) applied for 16 h a day had provided effective analgesia for 18 months and, unlike oral analgesics, had been free of gastrointestinal side-effects. However, 9 months after starting treatment with this device, she developed a florid eczema immediately beneath the electrode pads, which recurred at new sites of electrode application. Her skin improved when she discontinued the use of the system and applied topical betamethasone valerate, but recurred when she resumed its use. She was

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

patch tested with the European standard series (Chemotechnique Diagnostics AB), a (meth)- acrylate series (Chemotechnique Diagnostics AB) and the following TENS accessories: Tac conductivity gel (as is), carbon rubber electrode shavings, hydropad conductive pad (inner and outer surfaces), Mictopore adhesive tape and glycerol.

	D2	D4
hydropad (inner surface)*	?+	?+
2-hydroxyethyl methacrylate 2% pet.	+++	+
2-hydroxypropyl methacrylate 2% pet.	++	+
ethylene glycol dimethacrylate 2% pet.	++	+

2.3.2.8 [Romaguera, 1989]

Study reference:

Romaguera C, Vilaplana J, Grimalt F., Ferrando J.: Contact Sensitivity to Met(Acrylates) in a Limb Prosthesis; American Journal of Contact Dermatitis. 1989; 1(3): 183-185

Detailed study summary and results:

Test type

Case report

A 51-year-old male took advantage of a readjustment of his lower-leg prosthesis to have it revarnished on the exterior and the upper part of the interior. Use of the newly-varnished prosthesis coincided with the appearance of pruriginous papulo-erythematous lesions in the area of the amputation stump and thigh with, in some places, hyperkeratotic lesions. Itchy lesions spread to the hands, upper limbs, left lower limb and trunk, sparing the face and scalp. After ceasing use of the prosthesis, the patient improved greatly. He was patch tested with the GEIDC standard series, the authors' prosthesis series, a plastics and glues series (Chemotechnique), and a meth(arylate) series (Chemotechnique), with positive (++) reactions at 48 and 96 hours to: methyl methacrylate (2%), ethyl methacrylate (2%), hydroxyethyl methacrylate (2%), hydroxypropyl methacrylate (2%), methacrylic acid (0.1 %), acrylonitrile (0.1 %), butyl methacrylate (2%), butyl acrylate (0.1%), ethylhexyl acrylate (0.1%), hydroxypropyl acrylate (0.1%), ethyleneglycol dimethacrylate (2%), triethyleneglycol dimethacrylate (2%), butanediol dimethacrylate (2%), urethane dime_thacrylate (2%), and triethyleneglycol diacrylate (0.1 %), all pet.

2.3.2.9 [Uter, 2015]

Study reference:

Uter W, Geier J: Contact allergy to acrylates and methacrylates in consumers and nail artists - data of the Information Network of Departments of Dermatology, 2004-2013 Contact Dermatitis. 2015 Apr;72(4):224-8.

Detailed study summary and results:

Test type

Retrospective study

A retrospective analysis of patch test results with (meth)acrylates, along with clinical and demographic data, was performed. Patients were subdivided according to (i) a potentially exposed occupation and (ii) nail cosmetics as the suspected cause of contact dermatitis.

For the present analysis, data of all patients patch tested between 2004 and 2013 in the IVDK (Information Network of Departments of Dermatology), in the course of 114 440 consultations were considered. In cases of multiple consultations by one patient, only the first consultation was chosen. According to the documented

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

(i) occupation and (ii) ‘contactants’ (product categories presumably causing or worsening dermatitis), patients were subdivided into four groups:

- Patients in whom nail care/sculpturing material was considered to be causative (n=89) and who worked either as nail artists (n=31) or as cosmetologists (n=58)
- Patients who worked as nail artists (n=31) or cosmetologists (n=307), but in whom nail materials were not explicitly mentioned as culprit products [n(total)=338]
- Patients who worked neither as nail artists nor as cosmetologists, but in whom nail cosmetics/materials were documented as culprit product (n=325)
- Finally, all remaining patients (n=110 289)

The prevalence of positive patch test reactions to each one of the (meth)acrylate allergens, and the concomitant reactivity between different substances, were analysed following pertinent guidelines. Age-adjusted time trends were analysed with log-binomial regression analyses. The demographic and clinical profile of patients in the four above-mentioned subgroups was described according to the MOAHLFA index. For data management and analysis, R statistical software, version 3.1.1, was used.

Table 1. Distribution of MOAHLFA factors in the four subgroups defined by (i) occupation with potential exposure to acrylic nails (Occ+) and (ii) nail materials having caused dermatitis (Cont+), patch tested in the Information Network of Departments of Dermatology 2004–2013

	Occ–, Cont–	Occ–, Cont+	Occ+, Cont–	Occ+, Cont+
Number	110 289	325	338	89
Male	37.1	4.3	1.2	2.2
Occupational	15.5	18.2	42.6	75.3
Atopic eczema	20.1	25.2	29	19.1
Site: hand	27.3	43.4	51.8	70.8
Site: leg	11.1	1.2	2.1	0
Site: face	15.9	32.3	16.3	15.7
Age ≥ 40years	71.8	57.5	44.4	42.7

Results

Among the 114 440 patients patch tested, 72 244 were female and were considered further. Eighty-nine patients both worked as nail artists/cosmetologists and suspected nail cosmetics as the cause of dermatitis. Among these, 47.1% reacted to at least one (meth)acrylate, most often to 2-hydroxyethyl methacrylate (n=27), 2-hydroxypropyl methacrylate, and hydroxyethyl acrylate (n=26 each), with marked coupled reactivity.

As patients in the three subgroups of interest were almost exclusively female, the following analyses, focusing on the pattern of sensitization, are restricted to female patients.

In the 10-year period, the proportion of female patients tested with the special series containing (meth)acrylates increased by some percentage points ($p < 0.0001$, Cochran–Armitage trend test): whereas 10.5% had initially been patch test with at least one of the acrylates considered, this share was 13.7% in 2013. Concerning patch testing with at least one of the methacrylates, the proportions were 14.9% and 17.6%, respectively. Although the number of patients reacting to acrylates or methacrylates also increased significantly in a univariate analysis ($p = 0.025$, Cochran–Armitage trend test), a log-binomial regression showed no indication of a significant increase in the proportion of positive reactions.

The frequencies of positive reactions to the set of (meth)acrylates considered and the epoxy resin (bisphenol A diglycidyl ether) tested in the baseline series are shown in Table 2.

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

Table 2. Frequency of positive reactions to potentially important (meth)acrylate allergens and epoxy resin [bisphenol A diglycidyl ether (BADGE)] from the baseline series in the four subgroups (female patients only)

Allergen	%	Occ–, Cont– Positive/tested % positive (95% CI)	Occ–, Cont+ Positive/tested % positive (95% CI)	Occ+, Cont– Positive/tested % positive (95% CI)	Occ+, Cont+ Positive/tested % positive (95% CI)
2-Hydroxyethyl methacrylate	1	227/9770 2.3 (2–2.6)	39/172 22.7 (16.6–29.7)	16/73 21.9 (13.1–33.1)	27/74 36.5 (25.6–48.5)
2-Hydroxypropyl methacrylate	2	218/8112 2.7 (2.3–3.1)	36/166 21.7 (15.7–28.7)	16/70 22.9 (13.7–34.4)	26/75 34.7 (24–46.5)

Finally, the pattern of cross-reactivity between different compounds was assessed in the subset of female patients in whom nail care/sculpturing material was considered to be causative ('Occ–, Cont+' and 'Occ+, Cont+') and who were patch tested with all of the substances of interest.

Table 3. Cross-reactivity between six (meth)acrylates, examined in 193 female patients from subgroups 'Occ–, Cont+' and 'Occ+, Cont+' in whom all six allergens had been patch tested

Allergen n (positive)	2-HEMA 51	2-HPMA 52	EDGMA 43	TEGDMA 26	MMA 14	HEA 56
2-HEMA	–	42	41	16	11	42
2-HPMA	–	–	39	19	11	43
EDGMA	–	–	–	17	10	39
TEGDMA	–	–	–	–	9	21
MMA	–	–	–	–	–	11

EDGMA, ethyleneglycol dimethacrylate; HEA, hydroxyethyl acrylate; MMA, methyl methacrylate; TEGDMA, triethyleneglycol dimethacrylate; 2-HEMA, 2-hydroxyethyl methacrylate; 2-HPMA, 2-hydroxypropyl methacrylate.

2.3.2.10 [Ramos, 2014]

Study reference:

Ramos L, Cabral R, Gonçalo M. Allergic contact dermatitis caused by acrylates and methacrylates--a 7-year study. *Contact Dermatitis*. 2014 Aug;71(2):102-7.

Detailed study summary and results:

Test type

Retrospective study

An observational and retrospective study (January 2006–April 2013) was performed, evaluating and correlating epidemiological and clinical parameters and positive patch test results with (meth)acrylates.

Authors reviewed the files of patients with suspected ACD (allergic contact dermatitis) caused by (meth)acrylates who were patch tested between January 2006 and April 2013 in their department. Patient data (sex and age, occupational activity, and atopy), clinical characteristics of the dermatitis, patch test results, agreement between reactivity to HEMA and reactivity to 2-hydroxypropyl methacrylate (HPMA) and the capacity of HEMA as a screening allergen were assessed. Statistical analysis was performed with spssTM18. All patients were tested with the Portuguese and European baseline series, an extended series of 15–17 (meth)acrylates (Chemotechnique Diagnosis, Vellinge, Sweden), and other patch test series, according to the clinical information. According to recommendations, a 5–7-mm ribbon of the patch test preparation (equivalent to 20 mg) was placed in 8-mm Finn Chambers on Scanpor tape (Epitest Ltd Oy, Tuusula, Finland), immediately applied on the upper back to prevent evaporation, and left under occlusion for 48 hr. Readings were performed at D2 and D3 or D4, and scored according to the guidelines of the International Contact Dermatitis Research Group as weak (+), strong (++), and extreme (+++). Only + or stronger reactions were considered.

Results

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

Among 2263 patch tested patients, 122 (112 females and 10 males) underwent aimed testing with an extended (meth)acrylate series mainly because of: oral lesions related to dental prostheses (n=54), problems associated with orthopaedic prostheses (n=8), exposure to acrylic gel in nail beauty technicians or users (n=35), and occupational contact with dentistry products in dentists and dental prosthetics technicians (n=7).

37 (30.3%) showed positive and relevant reactions. Of the 37 patients, only 6 (16.2%) reacted to a single (meth)acrylate, whereas 31 (83.8%) reacted to multiple (meth)acrylates. The main positive patch test reactions were to : HEMA 2% pet. (30, 81.1%), HPMA 2% pet. (29, 78.4%), 2-hydroxyethyl acrylate 0.1% pet. (20, 54.1%), triethyleneglycol diacrylate (TREGDA) 0.1% pet. (16, 43.3%), ethyl acrylate 0.1% pet. (14, 37.8%), ethyleneglycol dimethacrylate (EGDMA) 2% pet. (12, 32.4%), and tetraethyleneglycol dimethacrylate 2% pet. (12, 32.4%)

Table 1. Reactivity to the different (meth)acrylates among the 122 patients tested

Contact allergen*	Concentration and vehicle	Number and % positive test reactions
2-Hydroxyethyl methacrylate	2% pet.	30 (81.1)
2-Hydroxypropyl methacrylate	2% pet.	29 (78.4)

Twenty five cases (67.6%) were occupational. Hand eczema with pulpitis was observed in 32 patients. Twenty-eight cases were related to artificial nails, 3 were related to dental materials, and 2 were industrial workers. Oral lesions associated with dental prostheses were observed in 4 patients. In our sample, beauty technicians working with artificial nails were the most affected group (80% of occupational cases).

In order to assess cross-reactivity between HEMA and HPMA, the results concerning these two allergens were also analysed. Thirty-four patients had concordant results, with the kappa coefficient (0.749) reflecting good agreement between these two allergens.

Table 4. Agreement between 2-hydroxyethyl methacrylate (HEMA) and 2-hydroxypropyl methacrylate (HPMA) reactivity on patch testing

	HPMA-negative	HPMA-positive	Total
HEMA-negative	6	1	7
HEMA-positive	2	28	30

2.3.2.11 [Heratizadeh, 2018]

Study reference:

Heratizadeh A, Werfel T, Schubert S, Geier J, IVDK. Contact sensitization in dental technicians with occupational contact dermatitis. Data of the Information Network of Departments of Dermatology (IVDK) 2001-2015. Contact Dermatitis. 2018 Apr;78(4):266-273.

Detailed study summary and results:

Test type

Retrospective study

A retrospective analysis of Information Network of Departments of Dermatology patch test data from the years 2001–2015 concerning DTs (dental technicians, current profession at the time of patch testing) with OCD (occupational contact dermatitis) was performed.

Altogether, 163 261 patients were patch tested in the IVDK (Information Network of Departments of Dermatology) in these years, and, of these, 399 were DTs. According to the final assessments, 226 DTs

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

suffered from OCD, and 124 did not. For 49 patients, no decision was made in this respect or no information on work-relatedness was given. The 226 DTs with OCD formed the study group for the present analysis. For the comparison of reactions to ubiquitous allergens, the 124 DTs without OCD served as a control group.

All IVDK members are also members of the DKG (German Contact Dermatitis Research Group). Patch tests are performed and read according to DKG and ESCD guidelines. For this data analysis, patch test reactions on day (D) 3 were selected. In only a few exceptional cases, when a reading was performed on D4 instead of D3, the D4 reading was chosen. Readings coded as +, ++, or +++, that is, positive reactions with erythema, infiltration, papules, and/or (coalescing) vesicles, according to scoring, were rated as positive in dichotomized analyses.

The patch test exposure times were 2 days in 81% of the patients, and 1 day in 19% of the patients. With a few (temporary) exceptions, Finn Chambers® on Scanpor® tape (8mm inner diameter) were used as test chambers.

In order to allow a meaningful comparison of sensitization frequencies between the study and the control group, reaction prevalences were standardized for age and sex by the use of previously published methods. The statistical significance ($p < 0.05$) of differences in sensitization frequencies was determined by the use of non-overlapping 95% confidence intervals (CIs) of reaction prevalences. Differences in proportions of population characteristics between the study group and the control group were tested for statistical significance with the chi²-test. Data management and analysis were performed with the statistical analysis software SAS®, version 9.4 (SAS Institute, Cary, NC, USA).

The DKG baseline series was patch tested in 203 patients (90%) of the study group and in 112 patients (90%) of the control group. Two other DKG test series include allergens that are occupationally relevant for DTs, namely the ‘dental technicians’ and ‘dental metals’ series. The first was patch tested in 172 DTs with OCD, and the latter in 129.

Results

Table 1. MOAHLEA indices of 226 dental technicians (DTs) with occupational contact dermatitis (OCD) (study group) and 124 DTs without OCD (control group)

	Study group (n = 226)		Control group (n = 124)		Chi ² -test
	No.	%	No.	%	p-value
Male	105	46.5	39	31.5	0.006
Occupational dermatitis	226	100.0	0 ^a	0.0	NT
Atopic dermatitis (past or present)	67	29.6	40	32.3	0.61
Hand dermatitis	200	88.5	42	33.9	<0.0001
Leg dermatitis	0	0.0	3	2.4	0.044 ^b
Face dermatitis	12	5.3	28	22.6	<0.0001
Age ≥ 40 years	117	51.8	65	52.4	0.91

NT, not tested because the difference is attributable to group definition.

^aNo observation, because of group definition.

^bBecause of a small expected single cell content, Fisher's exact test was used instead of the chi²-test.

Sixty-seven patients reacted to methacrylates and/or acrylates. Of these, 63 patients reacted to at least one methacrylate, and 24 patients to one or both of the acrylates tested. Concomitant reactions were frequent.

Table 3. Patch test results with allergens from the German Contact Dermatitis Research Group test series 'dental technicians' and 'dental metals' in the study group. Except for copper sulfate, which was tested in aq., the vehicle was pet. throughout

Allergen	Test concentration	No. tested	Negative	?+	+	++	+++	Irritant	% positive
Dental technicians series									
Acrylates									
Ethyl acrylate	0.1	175	151	5	17	2	0	0	10.9
Pentaerythritol triacrylate	0.1	174	164	3	6	1	0	0	4.0
Methacrylates									
2-Hydroxyethyl methacrylate	1	188	138	10	25	15	0	0	21.3
2-Hydroxypropyl methacrylate	2	188	137	11	24	16	0	0	21.3
Methyl methacrylate	2	194	145	7	25	16	0	1	21.1
Ethyl methacrylate	2	174	133	8	27	6	0	0	19.0
Ethylene glycol dimethacrylate	2	189	145	11	22	11	0	0	17.5
Triethylene glycol dimethacrylate	2	193	164	9	14	4	0	2	9.3
Tetrahydrofurfuryl methacrylate	2	174	151	7	14	2	0	0	9.2
1,4-Butanediol dimethacrylate	2	187	166	5	14	2	0	0	8.6
Diurethane dimethacrylate	2	147	144	3	0	0	0	0	0.0

2.3.2.12 [Alcantara-Nicolas, 2016]

Study reference:

Alcantara-Nicolás FA, Pastor-Nieto MA, Sánchez-Herreros C, Pérez-Mesonero R, Melgar-Molero V, Ballano A, De-Eusebio E. Allergic contact dermatitis from acrylic nails in a flamenco guitarist Occup Med (Lond). 2016 Dec;66(9):751-753.

Detailed study summary and results:

Test type

Case report

A 40-year-old non-atopic male, working as a flamenco guitarist and formerly as a construction worker, consulted with a 1-year history of changes affecting the first four nails of his right hand. The lesions were confined to the fingers where acrylic materials were used in order to strengthen his nails for guitar playing and consisted of dystrophy, onycholysis and paronychia. He had been intermittently applying a liquid monomer containing ethyl methacrylate (EMA), triethyleneglycol-dimethacrylate (TEGDMA) and N,Ndimethyl-p-toluidine and a powder composed of polyethyl methacrylate, polymethyl methacrylate, benzoyl peroxide and silica for >10 years that he bought from sellers over the internet. He noticed improvement whenever he stopped using these materials and intense itching and worsening once he began reusing them. Microbiological culture was positive for *Candida albicans*; however, antifungal therapy was undertaken without improvement.

Patch tests with allergens were performed and positive results obtained with 2-hydroxyethyl methacrylate (2-HEMA), 2-hydroxyethyl acrylate (2-HEA), ethyleneglycol-dimethacrylate (EGDMA) and 2-hydroxypropyl methacrylate (2-HPMA). Based on the clinical findings and despite the results of the patch tests (that yielded positive results with acrylic compounds different from those included in the labels of his own nail materials), the patient was diagnosed with occupational allergic contact dermatitis likely caused by acrylic nails.

Table 1. Patch tests results

Series and allergens ^a	Readings	
	Day 2	Day 4
Standard (GEIDAC) ^b	–	–
2-HEMA	++	++
2-HEA	++	++
EGDMA	++	++
2-HPMA	++	++
Butyl acrylate	–	–
Ethyl methacrylate	–	–
Tetrahydrofurfuryl methacrylate	–	–
Ethyl acrylate	–	–
Bisphenol A glycidylmethacrylate (BIS-GMA)	–	–
Bisphenol A	–	–
Dimethyl-p-toluidine	–	–
Methyl methacrylate	–	–
TEGDMA	–	–
N,N-Dimethyl-4-toluidine	–	–
Benzoyl peroxide	–	–
Eugenol	–	–
Hydroquinone	–	–
Resorcinol	–	–

^aAll performed allergens by True test and AllergEaze, SmartPractice, Canada.

^bGEIDAC: Spanish Contact Dermatitis Research Group Series.

2.3.2.13 [Raposo, 2017]

Study reference:

Raposo I, Lobo I, Amaro C, de Lurdes Lobo M, Melo H, Parente J, Pereira T, Rocha J, Cunha AP, Baptista A, Serrano P, Correia T, Travassos AR, Dias M, Pereira F, Gonçalo M. Allergic contact dermatitis caused by (meth)acrylates in nail cosmetic products in users and nail technicians - a 5-year study. *Contact Dermatitis*. 2017 Dec;77(6):356-359.

Detailed study summary and results:

Test type

Retrospective study

Authors reviewed files of patients with ACD caused by (meth)acrylates related to nail cosmetic products, who were patch tested between January 2011 and December 2015 in 13 departments of dermatology in Portugal.

All patients were patch tested with the Portuguese and European baseline series and an extended series of 15–17 (meth)acrylates (Chemotechnique Diagnostics, Vellinge, Sweden). The indication for patch testing was based on the presence of eczema in users or technicians exposed to nail cosmetic products. The allergens were placed in Finn Chambers® on Scanpor® tape (20 mg in 8-mm chambers), and immediately applied to the patient's upper back. Allergens were left in place for 2 days, and readings were performed on day (D) 3 for all patients. Patients were instructed to return on D7 if later additional reactions were observed, which is a common practice to reduce false-negative readings in our Portuguese network. Scoring of positive reactions comprised weak (+), strong (++) and extreme (+++) positive reaction grades according to ICDRG and ESCD criteria. Demographic and clinical profiles of all patients were collected according to the MOAHLFA index (Male, Occupational, Atopy, Hand, Leg, Face, Age ≥40 years).

Results

During the study period, among a total of 11 639 patients patch tested in the 13 departments. Two-hundred and thirty cases (1.97%) of ACD caused by (meth)acrylates (55 technicians, 56 consumers, and 119 with mixed exposure) had been documented, mostly as chronic hand eczema (93%).

Regarding the source of exposure, 23.9% (n=55) were occupationally exposed, 24.4% (n=56) were consumers, and 51.7% (n=119) were exposed both as consumers and occupationally. The mean age of the patients was 36.9 years (age range 20–65 years), and all patients were females.

The most common sensitizers were: 2-hydroxyethyl methacrylate (HEMA), which was positive in 90% of the tested patients, 2-hydroxypropyl methacrylate (HPMA), which was positive in 64.1% (120/187 tested patients), and ethyleneglycol dimethacrylate, which was positive in 54.5%.

Of the 22 patients who did not react to HEMA, 7 reacted to HPMA. The combination of these two allergens (HEMA+HPMA) identified a total of 93.4% of our patients, and the addition of EGDMA (i.e., HEMA+HPMA+EGDMA) identified 96.8%.

2.3.2.14 [Stingeni, 2015]

Study reference:

Stingeni L, Cerulli E, Spalletti A, Mazzoli A, Rigano L, Bianchi L, Hansel K. The role of acrylic acid impurity as a sensitizing component in electrocardiogram electrodes Contact Dermatitis. 2015 Jul;73(1):44-8.

Detailed study summary and results:

Test type

Case report

A 64-year-old non-atopic man was referred to the authors with multiple, itchy, eczematous patches on the anterior aspect of his chest, corresponding to the sites of contact with disposable pre-gelled F2060® electrodes (Fiab SpA, Vicchio, Florence, Italy) used for Holter ECG monitoring. The device was applied 24 hour before the patient presented to the authors. The eruption consisted of vesicles, with intense erythema and swelling, which resolved in 2 weeks with the use of systemic and topical corticosteroids. The patient's past medical history included chronic ischaemic heart disease since 2010; after that, he had undergone Holter ECG monitoring every 3 months. He had not had any dental or orthopaedic implants. One month after the resolution of skin lesions, patch tests were performed with the Società Italiana di Dermatologia Allergologica, Professionale e Ambientale (SIDAPA) baseline series and the individual components of F2060® ECG electrodes: the central metal part, the central hydrogel part, and the outer annular adhesive and non-adhesive sides of the foam. The allergens (FIRMA Diagent, Florence, Italy) were tested on the upper back with Haye's Test Chambers (Haye's Service B.V., Alphen aan den Rijn, The Netherlands) on Soffix™ tape (Artsana, Grandate, Italy), and removed after 2 days. The readings (20 min, D2, D4, and D7) were performed according to ICDRG criteria. Patch testing showed a positive reaction to nickel sulfate (+) and strong positive reactions to the hydrogel part of the electrode (+++) and adhesive foam (++). There were no other additional positive reactions at D7. To exclude the presence of nickel sulfate impurity in the hydrogel part, this was patch tested in 20 nickel-positive subjects, with negative results.

The technical data sheet from the manufacturer of the F2060® electrodes was requested. The manufacturer informed that the metal part contained nickel-free stainless steel, and that the non-adhesive and adhesive sides of the foam were, respectively, made of a polyethylene plastic holder and of poly-acrylate derivatives. The hydrogel part was made of water, glycerol, potassium chloride, and poly-acrylic acid (poly 2-propenoic acid). Poly-acrylic acid (0.1%, 1% and 2% pet.), glycerol and potassium chloride were subsequently patch tested, with negative results. In addition, the acrylate and the dental series were tested.

Results

The patient was contact-allergic to electrode hydrogel but not to its separate constituents. Positive reactions were observed to 2-hydroxyethylmethacrylate (2-HEMA), 2-hydroxypropyl methacrylate (2-HPMA) and

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

ethyleneglycol dimethacrylate (EGDMA). Subsequent analysis showed that the electrode hydrogel contained acrylic acid as an impurity. The latter was subsequently patch tested, with a positive result.

Table 2. Patch test results for (meth)acrylates of the dental and acrylate series

Patch test	D2	D4
Ethyleneglycol dimethacrylate (2%)*	++	++
2-Hydroxyethyl methacrylate (5%)*	+++	+++
2-Hydroxypropyl methacrylate (2%)*	+++	+++
2,2-Bis[4-(2-hydroxy-3-methacryloxypropoxy)phenyl]propane (2%)*	–	–
<i>N,N</i> -dimethylaminoethyl methacrylate (0.2%)*	–	–
1,6-Hexanediol diacrylate (0.1%)*	–	–
Methyl methacrylate (5%)*	–	–
Tetraethyleneglycol dimethacrylate (2%)*	–	–
Tetrahydrofurfuryl methacrylate (2%)*	–	–
Triethyleneglycol dimethacrylate (2%)*	–	–
Urethane dimethacrylate (2%)*	–	–
Acrylic acid (2.0%)†	+++	+++
Acrylic acid (1.0%)†	+++	+++
Acrylic acid (0.1%)†	+++	+++
Acrylic acid (0.01%)†	++	++
Acrylic acid (0.001%)†	–	–

*All in pet.

†All in saline solution.

2.3.2.15 [Aalto-Korte, 2008]

Study reference:

Aalto-Korte K, Alanko K, Kuuliala O, Jolanki R. Occupational methacrylate and acrylate allergy from glues. *Contact Dermatitis*. 2008 Jun;58(6):340-6.

Detailed study summary and results:

Test type

Retrospective study

This study aimed to analyse patterns of allergic patch test reactions to acrylic monomers in relation to exposure in patients sensitized from glues. Authors screened the patch test files at the Finnish Institute of Occupational Health from 1994 to 2006 for allergic reactions in the ‘Methacrylate series’ and analysed the clinical records of sensitized patients. Only patients who had handled acrylic glues at work were included.

The patch tests were performed using the Finn Chambers (Epitest, Tuusula, Finland) according to the recommendations of the International Contact Dermatitis Research Group. Authors read the tests 2 or 3 times on D2–(D3)–D4/5/6 depending on the day of their application. The series is based on the allergens provided by Chemotechnique (Vellinge, Sweden), but several preparations of Trolab (Hermal, Reinbek, Germany) and in-house test substances have also been used. The vehicle is petrolatum (pet.) in all the test substances. The composition of the series varied during the study period, and different test substances were tested on a different number of patients. The clinical records of patients with allergic reaction (+/++/+++) to at least one acrylic monomer in the Methacrylate series were reviewed. Authors analysed their clinical records for

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

occupation, symptoms, safety data sheets (SDSs), the results of the chemical analyses of the actual products used by the patients, patch test reactions to patients' own acrylate products, and the diagnosis.

During the study period (between September 1994 and August 2006), a total of 473 patients were tested with the Methacrylate series. 61 patients had allergic reaction to at least one allergen. Of these, 32 patients working in dental professions have been reported recently. The files of 10 patients showed present occupational exposure to acrylic glues.

Results

Table 1. Allergens of the Methacrylate series, their concentrations in petrolatum, providers, and abbreviations, and patch test results of the 10 patients sensitized from acrylic glues

Test substance	Concentration (%), provider	Abbreviation	Patch tests		
			+ / + + / + + +	? +	Total
2-Hydroxypropyl methacrylate	2, C	2-HPMA	9	0	10

C, Chemotechnique, Vellinge, Sweden

2.3.2.16 [Aalto-Korte, 2007]

Study reference:

Aalto-Korte K, Alanko K, Kuuliala O, Jolanki R. Methacrylate and acrylate allergy in dental personnel Contact Dermatitis. 2007 Nov;57(5):324-30.

Detailed study summary and results:

Test type

Retrospective study

The study aimed to analyse patch test reactivity to 36 acrylic monomers in dental personnel in relation to exposure. Authors reviewed the test files at the Finnish Institute of Occupational Health from 1994 to 2006 for allergic reactions to acrylic monomers in dental personnel and analysed the clinical records of the sensitized patients.

The patch tests were performed using the Finn Chambers (Epitest, Tuusula, Finland) according to the recommendations of the International Contact Dermatitis Research Group. Authors read the tests twice or 3 times [on D2-(D3)-D4/5/6] depending on the day of their application. Our series is based on the allergens provided by Chemotechnique (Vellinge, Sweden), but several Trolab's (Hermal, Reinbek, Germany) preparations and in-house test substances have also been used. The composition of the series varied during the study period, and different test substances were tested on a different number of patients.

In the present study, authors included only dentists, dental nurses, and dental technicians with allergic reaction (+ / + + / + + +) to at least 1 acrylic monomer in the Methacrylate Series and analysed their clinical records for symptoms, exposure [safety data sheets (SDSs) /the results of the chemical analyses of their own products], patch test reactions to their own acrylic products, and diagnosis.

During the study period (between September 1994 and August 2006), a total of 473 patients were tested with the Methacrylate Series. This included 55 dentists (12%), 192 dental nurses (41%) and 11 dental technicians (2%).

Results

The most commonly positive allergens were 2-hydroxyethyl methacrylate (2-HEMA) and ethyleneglycol dimethacrylate (EGDMA) both in 24 cases (75%), and 2-hydroxypropyl dimethacrylate (2-HPMA) in 23 cases (72%).

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

Table 1. The reactions and exposure to various acrylic monomers in 9 dentists, and the abbreviations, concentrations in petrolatum (pet.) and providers of the test substances which gave allergic reactions in at least 1 of the patients in the whole study group. The test substances, which gave no allergic reactions in dental personnel are listed in the footnote.

Patient number		1	2	3	4	5	6	7	8	9
Year of investigation		1995	1995	1997	2000	2000	2001	2002	2004	2004
Test substance	Concentration provider (%)									
2-Hydroxypropyl methacrylate	2, C	+++	++	++	++	++	++	+	–	++

C, Chemotechnique, Vellinge, Sweden.

Table 2. The reactions and exposure to the same acrylic monomers in 15 dental nurses (Patients no. 10–24)

Patient number	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
Year of investigation	1995	1995	1996	1996	1997	1997	1998	1998	1998	1998	1998	99	2001	2002	2002
Test substance															
2-HPMA	++	++	++	++	++	?+	+	++	–	++	++	+	++	–	–

Table 3. The reactions and exposure to the same acrylic monomers in 8 dental technicians (Patients no. 25–32)

Patient number	25	26	27	28	29	30	31	32
Year of investigation	1995	1998	1999	1999	2000	2002	2002	2002
Test substance								
2-HPMA	–	++	–	?+	++	+	?+	+

2-HPMA was positive in 23 (72%) patients, but all of these patients also reacted to 2-HEMA (22 allergic reactions and 1 doubtful ?+ reaction). In animal studies, 2-HEMA has induced strong cross-reactions to 2-HPMA. In the present study, 2-HPMA was not mentioned in the SDSs of our patients or detected in the analyses of their products. In a previous study by FIOH, HPMA was present as an impurity (0.3%) in 2 dental products, 1 bonding material, and 1 glass ionomer. Considering the large number of 2-HPMA reactions, we assume that most of them probably derive from cross-allergy to 2-HEMA.

2.3.2.17 [Aalto-Korte, 2010]

Study reference:

Aalto-Korte K, Henriks-Eckerman ML, Kuuliala O, Jolanki R. Occupational methacrylate and acrylate allergy--cross-reactions and possible screening allergens. *Contact Dermatitis*. 2010 Dec;63(6):301-12.

Detailed study summary and results:

Test type

Retrospective study

Authors reviewed the patch test files for the years 1994–2009 at the Finnish Institute of Occupational Health for allergic reactions to acrylic monomers, and analysed the clinical records of sensitized patients.

This was a retrospective study based on clinical investigations of patients suspected of having occupational contact dermatitis. Authors used Finn Chambers (Epitest, Tuusula, Finland), and read the tests two or three times, depending on the day of application (D2, D3 and D4; D2, D3 and D6; or D2 and D5). The patch test methods at the FIOH have previously been described more thoroughly. The composition of the (meth)acrylate series has varied over the years.

The patch test records from September 1994 to March 2009 were reviewed for allergic reactions to all acrylic monomers, including those not included in our (meth)acrylate series. Authors included all patients who were

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

tested with the (meth)acrylate series and had at least one allergic reaction (+/++/+++ to some acrylic monomer. Authors analysed their clinical records for occupation, symptoms, material safety data sheets, results of the chemical analyses of patients' own products, patch test reactions to their own acrylate products, and their diagnosis. When acrylic monomer was not tested in the (meth)acrylate series at the FIOH, because of a previously diagnosed allergy, authors included the patch test results from local hospitals in the analyses. For chemical analyses, the product samples were dissolved in acetone, and monomethacrylates and dimethacrylates were analysed by gas chromatography with a mass selective detector at the FIOH (Turku), as previously described. Unknown compounds were identified as acrylates if the main ions in their mass spectra had masses of 55, 99 and/or 113, all of which typical of diacrylates and triacrylates.

The present study group consists of 66 patients with contact allergy to some acrylic monomer, and they represent 2.1% of all patients investigated during the study period. Of the 66 patients, 57 were occupational cases, in which the source of sensitization was considered to be highly probably at work. Of the remaining 9 cases, 1 resulted from using artificial nails, 1 was a dental patient, and 7 had an unknown source of sensitization. Forty-eight of the occupational cases were mainly exposed to methacrylates. They were: 34 dental workers (9 dentists, 15 dental nurses and 10 dental technicians), 12 glue-derived cases and 2 artificial nail-derived cases.

Results

The most commonly found positive acrylic monomers in this group of 66 patients were EGDMA, 2-HEMA and 2-HPMA, which elicited allergic reactions in almost equal proportions (64–65%) of the patients.

Table 1. The number of allergic reactions (+/++/+++ in a group of 66 patients with contact allergy to acrylic monomers and tested with the (meth)acrylate series

Acrylic monomer	Abbreviation	No. of patients reacting positively, N (%)	No. of tested patients in the group
2-Hydroxypropyl methacrylate 2%	2-HPMA	42 (64)	66

Table 4. The numbers of allergic reactions in various subgroups of the 13 most important acrylic monomers

Acrylic monomer	Patients mainly exposed to methacrylates (dental workers, a dental patient, cases related to glue and artificial nails) N = 50	Patients mainly exposed to acrylates (see Table 3) N = 9	Patients with uncertain exposure to acrylic monomers N = 7	All N = 66
2-HPMA	40	1	1	42

Table 7. Number of (cross)-reactions to 2-hydroxyethyl methacrylate and 2-hydroxypropyl methacrylate in the 66 (meth)acrylate-allergic patients of the study group

		2-Hydroxyethyl methacrylate		
		+ / + + + / + + + +	? +	Negative
2-Hydroxypropyl methacrylate	+ / + + + / + + + +	38	3	2
	? +	1	2	0
	Negative	2	0	18

2.3.2.18 [Christoffers, 2012]

Study reference:

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

Christoffers WA, Coenraads PJ, Schuttelaar MLA. Two decades of occupational (meth)acrylate patch test results and focus on isobornyl acrylate Contact Dermatitis. 2013 Aug;69(2):86-92.

Detailed study summary and results:

Test type

Retrospective study

Patch test database was screened for positive reactions to (meth)acrylates between 1993 and 2012. Readings were performed on D2, D3, and D7.

Results

One hundred and fifty-one patients were tested with the (meth)acrylate series; 24 had positive reaction to at least one acrylate. Most positive reactions were to 2-hydroxypropyl acrylate, 2-hydroxyethyl acrylate, 2-hydroxypropyl methacrylate (2% pet.), and diethyleneglycol diacrylate.

Table 1. Patch test results between January 1993 and July 2012 according to the International Contact Dermatitis Research Group (ICDRG) guidelines

Acrylate	Patient number																							
	1 ^a	2 ^b	3 ^a	4 ^a	5 ^b	6 ^b	7 ^b	8 ^a	9 ^a	10 ^b	11 ^b	12 ^a	13 ^a	14 ^b	15 ^c	16 ^a	17 ^b	18 ^a	19 ^a	20 ^a	21 ^a	22 ^b	23 ^a	24 ^a
2-Hydroxypropyl methacrylate 2%	++	+	-	+	-	-	-	+	-	+	-	++	+	+	+	-	-	-	-	+	-	-	-	+
	Total																							11/151
	Rank																							4

2.3.2.19 [Gatica-Ortega, 2017]

Study reference:

Gatica-Ortega ME, Pastor-Nieto MA, Mercader-García P, Silvestre-Salvador JF. Allergic contact dermatitis caused by (meth)acrylates in long-lasting nail polish - are we facing a new epidemic in the beauty industry? Contact Dermatitis. 2017 Dec;77(6):360-366.

Detailed study summary and results:

Test type

Observational and retrospective study.

The files of patients with ACD caused by (meth)acrylates in long-lasting nail polish diagnosed between January 2013 and June 2016 in four dermatology departments in Spain were reviewed. Patients were followed up by telephone interview.

The (meth)acrylate allergens were supplied by AllergEaze® (Calgary, Canada) in three departments, and by Chemotechnique (Vellinge, Sweden) in one department. These were filled into Curatest® chambers (Lohmann & Rauscher, Neuwied, Germany), and immediately applied on the back and fixed with an adhesive tape, for example Omnifix E® (Hartmann, Heidenheim, Germany). The exposure time was 2 days, readings were performed on day (D) 2 and D4, and results were scored according to the international guidelines

Results

Overall, 2353 patients were patch tested. Forty-three (1.82%) were diagnosed with ACD caused by (meth)acrylates in long-lasting nail polish during that period; all were female, and all had hand dermatitis. Patients were mostly less than 40 years old (72.1%), non-atopic (95.4%) and had an occupational cause of their dermatitis (93%), which developed ~10.1 months after they had started to use this technique. The most frequent positive allergens were: 2-hydroxypropyl methacrylate, 2-hydroxyethyl methacrylate, and tetrahydrofurfuryl methacrylate.

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

Table 3. Positive results of patch tests with (meth)acrylic allergens (number and percentage)

Allergen	Abbreviation	Test concentration (in pet.) (%)	N positive (%)
2-Hydroxypropyl methacrylate	HPMA	2	41/43 (95.3)

2.3.2.20 [Gatica-Ortega, 2018]

Study reference:

Gatica-Ortega ME, Pastor-Nieto MA, Gil-Redondo R, Martínez-Lorenzo ER, Schöendorff-Ortega C. Non-occupational allergic contact dermatitis caused by long-lasting nail polish kits for home use: ‘the tip of the iceberg’. *Contact Dermatitis*. 2018; 78, 261–265

Detailed study summary and results:

Test type

Case report

Cases of consumers sensitised to these nail products (inexpensive kits for home use have been available for purchase in many stores or through the Internet). Patch test results and evaluation of ingredient labelling of products brought in by the patients.

All 4 patients were females, with a mean age of 50 years (range: 35–65 years): 3 had non-specific dry fingertip dermatitis involving the hyponychium of all fingers and paraesthesia, and 1 had hand dermatitis without involvement of the fingertips. The mean duration of symptoms was 6.7 months (range: 1–12 months). None of the patients had ever used acrylic or gel nails. All patients were patch tested with the Spanish Contact Dermatitis Research Group (GEIDAC) baseline series, with TRUE Test® and supplementary allergens supplied by AllergEaze (Calgary, Canada), and with an acrylates series (Chemotechnique Diagnostics, Vellinge, Sweden). Pet. was used as the vehicle in all preparations. The allergens were prepared on Curatest® chambers (Lohmann&Rauscher, Neuwied, Germany), applied on the patient’s back, and fixed with adhesive tape (Omnifix E®; Hartmann, Heidenheim, Germany). Exposure time was 2 days, and readings were performed on day (D) 2 and D4, and scored according to ESCD guidelines

Results

Four new cases are presented. Three of the patients reacted to 2-hydroxypropyl methacrylate, 2-hydroxyethyl methacrylate and ethyleneglycol dimethacrylate (EGDMA), and all 4 to 2-hydroxy ethylacrylate.

Table 1. Patch test results with the (meth)acrylic allergen series based on day 4 readings

Allergens	Abbreviations	Concentration (%)	No. 1	No. 2	No. 3	No. 4
2-Hydroxypropyl methacrylate	HPMA	2	+++	+	–	++

2.3.2.21 [Spencer, 2016]

Study reference:

Spencer A, Gazzani P, Thompson DA. Acrylate and methacrylate contact allergy and allergic contact disease: a 13-year review. *Contact Dermatitis*. 2016 Sep;75(3):157-64.

Detailed study summary and results:

Test type

Retrospective study

Authors conducted a retrospective review of results from a subset of patients with suspected contact allergy and allergic contact disease to (meth)acrylates who were patch tested at one Cutaneous Allergy Unit over a

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

thirteen-year period (July 2002 to September 2015). The subset of individuals was identified from a patch test database of 6502 patients held at this unit, with 475 (7.3%) patients tested to an extended series of 28 (meth)acrylates (Chemotechnique Diagnostics®, Vellinge, Sweden), following suspected potential exposure from their clinical history. No additional (meth)acrylates or cyanoacrylates were tested during this period, although patients were tested to other series and to their own products as clinically indicated; these included diluted glues and other adhesives, as well as fragments of wound dressings. The case records of patients with positive results were reviewed and data collected on sex, age, occupation, clinical presentation, presence of atopy, source of (meth)acrylate allergy and patch test results. Manufacturers of products provided by patients which yielded positive patch test reactions were requested to provide information on individual product ingredients, and samples of these for further patch testing. IQ Ultra™ Test chambers (64mm²; capacity 32µl) (Chemotechnique Diagnostic®, Vellinge, Sweden) were filled with (meth)acrylate preparation and transferred immediately to the skin on the patient's back or other most appropriate site. These remained under occlusion until the first reading on day (D) 2, with a subsequent reading performed on D4. Reactions were scored as irritant (IR), negative (-), doubtful (?), weak (+), strong (++), and extreme (+++), according to the guidelines of the International Contact Dermatitis Research Group. Only +, ++ or +++ reactions were considered positive.

Results

A series of 28 (meth)acrylates was applied to 475 patients. Results were positive in 52 cases (at least 1 positive reaction), with occupational sources identified in 24. Industrial exposures and acrylic nails were responsible for 13 and 10 cases respectively, with wound dressings implicated in 7.

The ages of patients with (meth)acrylate contact allergy and allergic contact disease ranged between 15 and 82 years, with a mean of 43.3 years and mode of 42 years. Thirty-two of 47 patients (68.1%) were female. Seventeen of 47 patients (36.2%) had a past history of atopy. Interestingly atopy was reported in only 1 of 21 patients patch tested before 2008, and 16 of 26 patients after this time.

12 cases were seen in consumers of nail products who did not have relevant occupations. These patients were younger (mean age 36.8 years), and all were female.

Authors found that 4 individual (meth)acrylates (2-hydroxyethyl acrylate, 2-hydroxypropyl methacrylate, bisphenol A glycerolate dimethacrylate and ethyl acrylate), if used as a screening tool, could have identified 47 (90.4%) of our positive cases.

Table 1: Reactivity to all 28 of the (meth)acrylates in our series, with concentrations (in pet.) used for patch testing

	Concentration (pet.)	Number (and %) positive reactions (52 patients tested)
2-hydroxypropyl methacrylate (2-HPMA)	2.00%	29 (55.8%)

Table 3: Cross-reactivity between the six most commonly positive (meth)acrylates

The kappa coefficient, which measures concordance between variables, is shown in brackets.

	2-hydroxyethyl acrylate (n=32)	2-HPMA (n=29)	2-HEMA (n=29)	EGDMA (n=28)	Ethyl acrylate (n=25)	Hydroxypropyl acrylate (n=24)
2-hydroxyethyl acrylate	-	22 (0.328)	23 (0.407)	22 (0.373)	19 (0.276)	23 (0.622)
2-HPMA	-	-	26 (0.766)	26 (0.806)	22 (0.617)	21 (0.581)

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

Table 4: Sensitivity as screening allergens of the most commonly positive (meth)acrylates, overall and amongst specific exposure groups

	Sensitivity as a screening allergen:				
	Overall	Nail workers/consumers	Industry (manufacture)	Dressings	Dental prostheses
2-HPMA	29/52 (55.8%)	13/22 (59.1%)	8/13 (61.5%)	2/7	1/3

2.3.2.22 [Kanerva, 1997]

Study reference:

Kanerva L, Jolanki R, Estlander T. 10 years of patch testing with the (meth)acrylate series. Contact Dermatitis. 1997 Dec;37(6):255-8.

Detailed study summary and results:

Test type

Retrospective study

Statistics on 10 years of patch testing with 30 (meth)acrylates were compiled.

Altogether 275 patients were patch tested during 1985-1995 with a history of exposure to (meth)acrylates.

Patch test with the (meth)acrylate series of Chemotechnique Diagnostics (Malmo, Sweden) containing about 30 (meth)acrylates. Patch testing and scoring were performed on the back with an occlusion time of 1 day (September 1985-1988) or 2 days (1989-1995). All patients were not uniformly tested to all acrylates.

Results

48 patients (17.5%) had an allergic reaction to at least 1 (meth)acrylate.

The (meth)acrylates most often provoking an allergic patch test reaction were 2-hydroxyethyl acrylate (2-HEA; 12.1%), 2-hydroxypropyl methacrylate (2-HPMA; 12.0%) and 2-hydroxyethyl methacrylate (2-HEMA; 11.4%).

Table 1. Allergic (meth)acrylate reactions in (a) 1985–1995, (b) 1985–1990 and (c) 1991–1995; 48 patients showed at least one allergic patch test reaction; the results have been compared to the sensitizing capacity of (meth)acrylates, based on animal studies, according to Björkner (2); Sensitizing capacity: NG, not given; I, weak; II mild; III, moderate; IV, strong; V, extreme

(Meth)acrylate series	Abbreviation	Patch test conc. (%) (w/w)	1985–1995			1985–1990			1991–1995			sensitizing capacity
			allergic/ tested	allergic (%)	rank order	allergic/ tested	allergic (%)	"top ten"	allergic/ tested	allergic (%)	"top ten"	
2-hydroxypropyl methacrylate	2-HPMA	2	29/242	12.0	2	15/124	12.1	1	14/118	11.9	4	1

2.3.2.23 [Lazarov, 2007]

Study reference:

Lazarov A. Sensitization to acrylates is a common adverse reaction to artificial fingernails. J Eur Acad Dermatol Venereol. 2007 Feb;21(2):169-74.

Detailed study summary and results:

Test type

Retrospective study

A 4-year retrospective study of patients with suspected ACD from artificial nails (ANs) was conducted (2001-2004). The patients were evaluated clinically and were patch tested with the European standard series, the methacrylate artificial nail (MAAN) series and additional allergens in personal cosmetics, including nail lacquer and ethyl cyanoacrylate, where appropriate.

Patients tested with the MAAN series were evaluated clinically and patch test results were analysed.

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

Patch testing was performed using the IQ Chambers. The methodology of the procedure was in accordance with the International Contact Dermatitis Research Group (ICDRG) guidelines, with an application time of 2 days and readings performed on the second and third day after application. The clinical relevance of the positive reactions was evaluated. A positive reaction was considered to have current clinical relevance if the patient had cutaneous exposure to a product known to contain the allergen to which the patient reacted. The exposure assessment was based on information from packages and safety data sheets when available. Data were recorded on a standardized computer entry form and analysed statistically.

Results

The study was conducted on 55 female patients aged 20–68 years (mean age 44.5 years). Sixteen of these patients suffered from seasonal rhinitis and/or asthma. All patients had been in contact with different types of ANs.

ACD to components of ANs may be a frequent cause of hand eczema, as observed in more than one-third of our patients (21 patients, 38.2%). About half of the patients were beauticians specializing in nail sculpturing who developed occupationally related ACD.

The most frequent allergens triggering ACD were 2-hydroxyethyl methacrylate (2-HEMA) and 2-hydroxypropyl methacrylate (2-HPMA).

Authors found that one-third of the beauticians with OACD (occupational allergic contact dermatitis) had exacerbation of pre-existing asthma during exposure to acrylates.

Table 2 Patch test results with allergens from the MAAN series

Allergen in petrolatum	Abbreviation	Positive reactions	Percentage
2-Hydroxypropyl methacrylate 2.0%	2-HPMA	17	17.5

Table 3 Comparison of patch test results with allergens from the MAAN series in occupational and non-occupational induced ACD

Allergen*	No. of positive reactions in the occupational cases	No. of positive reactions in the non-occupational cases
2-HPMA	9	8

2.3.2.24 [Kanerva, 1995a]

Study reference:

Kanerva L, Jolanki R, Leino T, Estlander T. Occupational allergic contact dermatitis from 2-hydroxyethyl methacrylate and ethylene glycol dimethacrylate in a modified acrylic structural adhesive. *Contact Dermatitis*. 1995 Aug;33(2):84-9.

Detailed study summary and results:

Test type

Case report

A 38-year-old non atopic woman patient sensitized to acrylic glue, and developing hand dermatitis that spread to the lower arms, chest, neck and face, is presented.

For the last 6 years, she had been working in the production of car rear-view mirrors. Her job was to glue the mirrors to the windscreen. In this task, she used a component adhesive based on isophorone diisocyanate

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

(IPDI) and 4,4'-diphenylmethane diisocyanate (MDI), and a component adhesive based on acrylate compounds.

Results

Her glue was analyzed by gas chromatography/mass spectrometry (GC/MS) and contained 24.6% 2-hydroxyethyl methacrylate (2-HEMA) and 0.4% ethylene glycol dimethacrylate (EGDMA).

A modified European standard series revealed allergic patch test reactions to fragrance mix (++), balsam of Peru (++) and neomycin (+). In the series of fragrances, isoeugenol induced a + allergic reaction. A series of plastics and glues (50 chemicals) was negative except for some acrylate reactions. The epoxy resin series was negative but the (meth)acrylate series gave a large number of allergic patch test reactions

2-HEMA and EGDMA, as well as her glue, provoked an allergic patch test reaction. Also many other acrylate compounds, including HPMA, gave an allergic reaction indicating cross-allergy. The patient could not continue in her previous workplace because of severely relapsing skin symptoms.

Table 2. Composition (%) of acrylate and other compounds from one batch of the patient's Penloc GZH glue according to gas chromatography/mass spectrometry (GC/MS) analysis, and 2 material safety data sheets (MSDS)

	GC/MS (%)	MSDS1	MSDS2
2-hydroxyethyl methacrylate	24.6	30–60	40–50
ethylene glycol dimethacrylate	0.4	ND	ND
isobornyl acrylate	61.9	ND	ND
oligomethacrylate based on ethylene glycol	10.0	ND	ND
unidentified	0.4	ND	ND
polyurethane resin	NA	20–40	ND
acrylic acid	–	0.5–4	4–5
maleic acid	NA	NA	2–3

ND: not declared.

NA: not analyzed.

MSDS1: material safety data sheet from the patient's work place, dated 1984.

MSDS2: material safety data sheet from the Finnish distributor, dated 1989.

Table 4. Patch test results of (meth)acrylate series (day 2, 3 and 6 readings)

Compound		Concentration % (w/w)	D 2	D 3	D 4
10. 2-hydroxypropyl methacrylate	(2-HPMA)	2	+++	+++	+++

2.3.2.25 [Kanerva, 1995b]

Study reference:

Kanerva L, Estlander T, Jolanki R, Tarvainen K. Statistics on Allergic Patch Test Reactions Caused by Acrylate Compounds, Including Data on Ethyl Methacrylate. *American Journal of Contact Dermatitis*. 1995; Vol 6, No 2 (June); pp 75-77

Detailed study summary and results:

Test type

Clinical study

During a period of 52 months, authors patch tested 124 patients with the large (meth)acrylate series of Chemotechnique Diagnostics (Maim6, Sweden). All patients had anamnestic data on acrylate exposure. Patch testing was performed on the back with 24- or 48-hour occlusion.

Results

Twenty-three patients showed at least one positive patch test reaction, and 6 had an allergic patch test reaction with EMA. The three acrylate compounds most often positive were 2-hydroxypropyl methacrylate (15 positive), 2-hydroxyethyl acrylate (14 positive), and 2-hydroxyethyl methacrylate (13 positive).

Table 1. Results of Patch Testing 124 Patients With the (Meth)acrylate Series

(Meth)acrylate Series	% (wt/wt)	Allergic/ Tested	Sensitizing Capacity
2-Hydroxypropyl methacrylate	2	15/124	I

I: weak

2.3.2.26 [Teik-Jin Goon, 2007]

Study reference:

Teik-Jin Goon A, Bruze M, Zimerson E, Goh CL, Isaksson M. Contact allergy to acrylates/methacrylates in the acrylate and nail acrylics series in southern Sweden: simultaneous positive patch test reaction patterns and possible screening allergens Contact Dermatitis. 2007 Jul;57(1):21-7.

Detailed study summary and results:

Test type

Retrospective study

This is a 10 year retrospective study of patients patch tested to the acrylate series and nail acrylics series in the Department of Occupational and Environmental Dermatology, Malmo University Hospital, Sweden, from 1 January 1995 to 31 December 2004.

Authors studied 90 patients tested to the acrylate and nail acrylics series over a 10 year period to see whether screening allergens could be found. Patch testing with an acrylate and nail acrylics series was performed.

The allergens were applied onto small (Ø8 mm) Finn Chambers (Epitest Ltd Oy, Tuusula, Finland) on Scanpor (Norgesplaster A/S, Vennesla, Norway). The tests were applied to the upper part of the back and left for 48 h. Tests were read on day 3 (D3) or D4 and D7 by a dermatologist, and the reactions were scored according to ICDRG criteria.

There were 52 women (mean age 39.8 years, range 19–63) and 38 men (mean age 43.8 years, range 22–64). There were patients with dermatitis suspected to be caused by acrylates/methacrylates, who had been tested to the acrylate and/or the nail acrylics series during the study period. Authors excluded patients who had been seen for suspected allergies to dental acrylates who had been tested to either of their dental series, as well as patients involved in screening studies in various acrylate/methacrylate-using industries, where the populations included subjects with no clinical evidence of dermatitis.

Results

There were 24 patients (mean age 42.3 years, range 20–64) with positive patch tests to acrylate/methacrylate allergens.

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

Table 2. Patients with positive reactions to acrylates/methacrylates in the acrylate and nail acrylates series* in Malmö from 1 January 1995 to 31 December 2004, with abbreviations as in Table 1. All patch test readings are shown as first reading (D3/D4)/second reading (D7)

Patient no.	Group	Sex	Age	2-EA	BA	2-HEA	2-HPA	MMA	EMA	2-HEMA	2-HPMA	EGDMA	TREGDMA	BUDMA	DEGDA	TPGDA	TMPTA	PETA	OTA480	EpoxyA	al-UDA	ar-UDA	TREGDA	BUDA	HDDA	THFMA
1	A	F	20	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-
2	A	F	35	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-
3	A	M	28	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-
4	A	M	42	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-
5	A	M	46	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-
6	A	M	47	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-
7	A	M	48	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-
8	A	M	53	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-
9	A	M	56	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-
10	A	M	64	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-
11	N	F	26	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-
12	N	F	28	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-
13	N	F	31	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-
14	N	F	33	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-
15	N	F	36	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-
16	N	F	39	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-
17	N	F	41	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-
18	N	F	42	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-
19	N	F	44	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-
20	N	F	44	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-
21	N	F	50	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-
22	N	F	51	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-
23	N	F	54	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-
24	N	F	56	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-	-/-

A, occupational acrylate allergy group; F, female; M, male; N, nail acrylic allergy group; nr, not read; NT, not tested. There were no positive reactions to 2-EHA, BMA, UEDMA, bis-EMA, MbAcryl, bis-MA, bis-GMA, ECA, MA, and PMA.

2.3.2.27 [Goncalo, 2018]

Study reference:

Gonçalo M, Pinho A, Agner T, Andersen KE, Bruze M, Diepgen T, Foti C, Giménez-Arnau A, Goossens A, Johanssen JD, Paulsen E, Svedman C, Wilkinson M, Aalto-Korte K. Allergic contact dermatitis caused by nail acrylates in Europe. An EECDRG study. Contact Dermatitis. 2018 Apr;78(4):254-260.

Detailed study summary and results:

Test type

Retrospective study

Review of all cases of ACD caused by acrylates related to cosmetic nail procedures (artificial gel nails, glued nails, dipping nails, and acrylate nail varnish) diagnosed during a period of 3 years (2013–2015) in 11 European Environmental Contact Dermatitis Research Group (EECDRG) clinics from nine European countries – Bari (Italy), Barcelona (Spain), Coimbra (Portugal), Copenhagen and Odense (Denmark), Heidelberg (Germany), Helsinki (Finland), Leeds (United Kingdom), Leuven (Belgium), and Malmö (Sweden).

All patients had been patch tested with the European baseline series, and, prompted by their history, also with the acrylate series used in the respective centres (Chemotechnique Diagnostics, Vellinge, Sweden; or Trolab Allergens, SmartPractice, Europe, Reinbeck, Germany). Allergens were applied on the back for 48 h with 8-mm Finn Chambers® on Scanpor® tape (Smartpractice, Europe), IQ or IQ-ultra™ patch test chambers (ChemotechniqueDiagnostics), or the Al Test® (Euromedical, Calolziocorte, Italy). Readings and relevance were assessed according to the ESCD guidelines for diagnostic patch testing (18). Only + or stronger patch test reactions were considered to be allergic reactions.

The following data were retrieved from the files of patients with positive reactions to acrylates with relevance for nail aesthetics: age and sex, history of atopy, anatomical site and characteristics of cutaneous and nail lesions, type of exposure to nail acrylates (occupational versus non-occupational), and haptens leading to positive reactions on patch testing. In occupational cases, the time spent at work before the development of cutaneous lesions and the subsequent outcome at work were documented. Data were statistically analysed with spss software (Version 21.0; IBM, Armonk, NY, USA). The t-test for independent samples was used to compare quantitative variables (e.g. age) between groups (e.g. occupational versus non-occupational exposure). Fisher's exact test and the chi2 test with the Yates correction, two-sided, were used to compare nominal variables between different groups. p-Values of < 0.05 were considered to be significant. The confidence intervals (CIs) for proportions were set at 95%.

Results

Among 18 228 studied patients, 136 had ACD caused by nail acrylates (0.75%; 95%CI: 0.60–0.90), representing 67.3% (95%CI: 60.4–73.7) of ACD cases caused by acrylates. There were 135 females and 1

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

male, with a mean age±standard deviation of 36.7±12.2 years; 59 (43.4%) were exposed as consumers, and 77 (56.6%) were occupationally exposed. Occupational cases were more frequent in southern Europe (83.7%), and were younger (mean age of 33.4±8.9 years); most developed ACD during the first year at work (65.0%), and at least 11.7% had to leave their jobs. Skin lesions involved the hands in 121 patients (88.9%) and the face in 50(36.8%), with the face being the only affected site in 14 (10.3%).

Most patients reacted on patch testing, mainly to 2-hydroxyethyl methacrylate (HEMA), 2-hydroxypropyl methacrylate, ethylene glycol dimethacrylate, and ethyl cyanoacrylate.

Table 4. Main allergens tested, with the number of patients tested, and number and percentage of positive reactions

Allergens	Patch tested patients (n)	Positive reactions	
		n	%
2-Hydroxyethyl methacrylate 2%	135	124	91.9
Hydroxypropyl methacrylate 2%	119	99	83.2
Ethylene glycol dimethacrylate 2%	117	81	69.2
Triethylene glycol dimethacrylate 2%	98	31	31.6
Methyl methacrylate 2%	114	30	26.3
Ethyl cyanoacrylate 10%	111	11*	9.9

All allergens in pet.

*Eight of the 11 cases reacting to ethyl cyanoacrylate were observed among UK consumers; isolated reactions were observed in 2 cases.

In the present study, 87.5% of the patients had two or more positive reactions to acrylates, mostly associated with HEMA and/or HPMA. These can be explained either by concomitant sensitization or by cross-sensitization.

Table 5. Main allergens tested, with the total number of patients tested with each allergen, and the numbers of positive, negative and concomitant reactions

Allergens		HEMA			HPMA			EGDMA			TEGDMA			MMA		
Total tested/reactivity		Positive	Negative	NT	Positive	Negative	NT	Positive	Negative	NT	Positive	Negative	NT	Positive	Negative	NT
HEMA total tested	135															
HEMA-positive	124	124	0													
HEMA-negative	11	0	11													
HEMA NT	1	0	0	1												
HPMA total tested	119															
HPMA-positive	99	97	2	0												
HPMA-negative	20	11	9	0												
HPMA NT	17	16	0	1												
EGDMA total tested	117															
EGDMA-positive	81	81	0	0	68	3	10									
EGDMA-negative	36	27	9	0	23	9	4									
EGDMA NT	19	16	2	1	8	8	3									
TEGDMA total tested	98															
TEGDMA-positive	31	30	1	0	26	1	4	23	5	3						
TEGDMA-negative	67	57	10	0	56	7	4	28	27	12						
TEGDMA NT	38	37	0	1	17	12	9	30	4	4						
MMA total tested	114															
MMA-positive	30	29	1	0	22	4	4	24	3	3	13	16	1			
MMA-negative	84	80	4	0	61	15	8	41	29	14	14	41	29			
MMA NT	22	15	6	1	16	4	5	16	4	2	4	10	8			
ECA total tested	111															
ECA-positive	11	9	2	0	8	3	0	9	1	1	3	7	1	5	4	2
ECA-negative	100	97	2	1	87	7	6	66	19	15	26	55	19	20	64	16
ECA NT	25	18	7	0	4	10	11	6	16	3	2	5	18	5	16	4

ECA, ethyl cyanoacrylate; EGDMA, ethylene glycol dimethacrylate; HEMA, 2-hydroxyethyl methacrylate; HPMA, 2-hydroxypropyl methacrylate; MMA, methyl methacrylate; NT, not tested; TEGDMA, triethylene glycol dimethacrylate.

2.3.2.28 [Pestana, 2016]

Study reference:

Pestana C, Gomes R, Pinheiro V, Gouveia M, Antunes I, Gonçalo M. Main Causes of Occupational Allergic Contact Dermatitis: A Three Year Study in the Center of Portugal. Acta Med Port. 2016 Aug;29(7-8):449-455

Detailed study summary and results:

Test type

Retrospective study

Authors performed a 3-year retrospective study at the allergology section in the Dermatology Clinic of the University Hospital of Coimbra to evaluate the main occupations diagnosed as occupational allergic contact dermatitis, most common allergens and the effect of the modification of the work station in the evolution of the disease.

The patients with positive patch testing to allergens present at the workplace and with a sufficiently significant exposure as to have contributed to trigger or to aggravate the dermatitis were included in the study. The following parameters were assessed: patient gender, age, personal history of atopy, affected areas of the body and an indication for a systemic treatment reflecting the clinical severity of the pathology, duration of the lesions, occupation and time at the job up to onset of dermatitis, tested allergen series, positive allergens and whether any workplace modification took place (complete cessation of occupation or only allergen avoidance or reduced exposure) and subsequent outcome.

Allergens were applied to the dorsal area using Finn Chambers® on Scanpor® Tape (Almirall Hermal GmbH, Germany) or using IQ-Ultra™ (Chemotechnique Diagnostics™, Vellinge, Sweden) chambers and were removed 48 hours later. The European and GPEDC (Grupo Português de Estudo das Dermatites de Contacto) Portuguese baseline series was applied to all the patients as well as supplemental series of allergens based on patient's exposure or other data (Trolab, Almirall Hermal GmbH, Germany or Chemotechnique Diagnostics™, Vellinge, Sweden). Patch or open testing were sometimes performed using products brought in by the patients and collected from patient's workplace or own environment. Tests were read on the second or third day (D2/D3) and on the fourth or seventh day (D4/D7), in accordance to the recommendations of the International Contact Dermatitis Research Group and the European Society of Contact Dermatitis (ESCD). Positive reactions were interpreted as showing current, past or unknown relevance or showing cross-reactivity.

Chi-square non-parametric test, using IBM SPSS Statistics for Windows, version 22.0 software, was used for the statistical analysis.

Results

During 2012 - 2014 among the 941 patch tested patients, 77 (8.2%) were diagnosed with occupational allergic contact dermatitis, with 169 positive patch tests related to occupational exposure, 55 detected within the baseline and 114 in complementary test series. In most cases allergic contact dermatitis involved the hands (88.3%), main professional activities were nail estheticians and hairdressers due to the manipulation of (meth)acrylates, the most common allergen in the study. After the diagnosis, 27.3% abandoned the work, 23.4% changed the work station, 49% avoided exposure to the responsible allergen. Contact dermatitis resolved in 39% of the patients, improved in 39% but had no change in the remaining 22%.

Overall, hydroxyethylmethacrylate (HEMA) (n = 30; 17.8%), hydroxypropylmethacrylate (HPMA) (n = 26; 15.4%), methylisothiazolinone (n = 12; 7.1%), thiuram mix (n = 9; 5.3%) and diallyl disulphide (n = 7; 4.1%) were the leading allergens found. An association with the use of (meth)acrylate (n = 32; 42%) used by nail beauticians (n = 27; 35%) and by dentistry assistants (n = 3) was found in most patients.

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

Table 3 - Positive reactions to allergens from supplemental series and to allergens brought in by the patient and their relation with the occupational ACD

Allergens	n	Cause
(Meth)acrylate series (n = 65)		
2-hydroxyethyl methacrylate (HEMA) 2% vas	30	Nail aesthetics, dental prosthesis
2-hydroxypropyl methacrylate (HPMA) 2% vas	26	Nail aesthetics, dental prosthesis
Triethylene-glycol-dimethacrylate (TEGDMA) 2% vas	4	Nail aesthetics
Ethylene-glycol-dimethacrylate (EGDMA) 2% vas	3	Nail aesthetics
Ethyl acrylate 0.1% vas	1	Nail aesthetics
2-Hydroxyethyl acrylate 0.1% vas	1	Nail aesthetics

2.3.2.29 [Muttardi, 2016]

Study reference:

Muttardi K, White IR, Banerjee P. The burden of allergic contact dermatitis caused by acrylates. Contact Dermatitis. 2016 Sep;75(3):180-4.

Detailed study summary and results:

Test type

Retrospective study

A retrospective observational study on 241 consecutive patients patch tested with meth(acrylates) and cyanoacrylates between January 2012 and February 2015 was conducted.

Demographic data and clinical information, including site of eczema and history of atopy, were obtained for each patient. Occupational history, including the use of gel nails, was assessed. In patients with no occupational exposure, the use of eyelash glues, acrylic nails and gel nails was considered. All patients were tested with an extended European baseline series [Allmiral (Trolab), Reinbek, Germany] and mini-acrylate or extended acrylate series (Chemotechnique Diagnostics, Vellinge, Sweden) by the use of Finn Chambers® on Scanpor® tape. The mini-acrylate series is the main screening tool. Readings were performed on day (D)2 and D4, and scored in accordance with European Society of Contact Dermatitis guidelines. Only readings of + and above on D4 were included. Patients with multiple acrylate allergies were analysed.

Table 1. Mini-acrylate series used to screen for meth(acrylate) and cyanoacrylate allergy (6)

Acrylate	Concentration in pet. (%)
Bisphenol A-glycidyl methacrylate	2
1,6-Hexanediol diacrylate	0.1
Ethyl cyanoacrylate	10
2-Hydroxypropyl acrylate	2
2-Hydroxyethyl methacrylate	2
Ethyleneglycol dimethacrylate	2

Results

Approximately 1500 patients are patch tested by the authors annually. Between January 2012 and February 2015, 241 patients were tested with the mini-acrylate or extended acrylate series. Sixteen patients with a positive patch test reaction to a (meth)acrylate or cyanoacrylate were identified. Their age ranged from 14 to 62 years (mean 36 years), and there was a female predominance (male/female ratio of 1:15). Nine (56%) patients had a history of atopy.

Overall, 2-hydroxyethyl methacrylate (2-HEMA) was the most common allergen; allergy to this was found in 12 patients. Ethyleneglycol methacrylate (EGMA) and 2-hydroxypropyl acrylate (2-HPA) were the second most common allergens. Eleven patients were allergic to more than one acrylate. Seven patients were allergic to 2-HEMA, EGMA and 2-HPA simultaneously; this was the most prevalent combination of acrylate

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

reactions. Most of the patients with multiple acrylate allergies had an occupational cause of their contact allergy.

Table 2. Table showing the breakdown patch test results of 16 patients with contact allergy to (meth)acrylates and ethyl cyanoacrylate in our centre

Patient number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Age (years) /sex	40/F	23/F	37/F	56/F	24/F	47/F	40/F	47/F	34/F	62/M	37/F	21/F	14/F	31/F	45/F	17/F
Atopy	Yes	Yes	Yes	Yes	Yes	No	No	No	No	No	Yes	Yes	No	Yes	Yes	No
Occupation	Housewife	Speech therapy	IT	Dental nurse	Public relations	Beautician	Nail technician	Beautician	Beautician	Electrician	Beautician	Dental nurse	Student	Carer	Courier	Nail technician
Presentation	Facial	Postoperative rash	Nail changes and hands	Eyelids	Hands	Fingertips	Fingertips	Hands	Nail changes and hands	Hands, arms, and face	Nail changes and hands	Fingertips	Face	Face	Face	Fingertips and perungual changes
Allergy to acrylate/methacrylate	ECA	2-HEMA	2-HEMA, EGDMA, 2-HPA	2-HEMA	ECA	EGDMA, HDDA, 2-HPA	2-HEMA, EGDMA, 2-HPA	ECA, 2-HEMA, 2-HPA, 2-HMA, 2-HPMA, diethylene glycol diacrylate, 1,6-hexanediol diacrylate	2-HEMA, EGDMA, 2-HPA	ECA, 2-HEMA, EGDMA, 2-HPA	2-HEMA, EGDMA, 2-HPA	2-HEMA, EGDMA, 2-HPA	2-HEMA, EGDMA	ECA	ECA, 2-HEMA	2-HEMA, EGDMA, 2-HPA
Exposure	False eyelashes	Adhesive drape	False nails	False nails	False nails	Gel nails	Gel nails	Gel nails	Gel nails	Superglue™ and Loctite™ sealant	Gel nails	Dental	Earlobe clamp	False eyelashes	Operative drape	Gel nails
Other allergies	–	Nickel	Potassium dichromate	Caine mix	Colophonium, 2-ethoxyethyl p-methoxy cinnamate	–	–	–	–	p-Phenylenediamine, fragrance mix L, perfume, Myroxylon pereirae	–	–	Nickel, thiuram mix	Nickel	Nickel, p-phenylenediamine	–

ECA, ethyl cyanoacrylate; EGDMA, ethyleneglycol dimethacrylate; F, female; HDDA, Hexanediol diacrylate; 2-HEMA, 2-hydroxyethyl methacrylate; 2-HMA, 2-hydroxy methacrylate; 2-HPA, 2-hydroxypropyl acrylate; 2-HPMA, 2-hydroxypropyl methacrylate; M, male.

Most patients were young female nail technicians/beauticians. The most common allergy was to 2-HEMA, being found in a total of 12 (75%) patients. Some cases had multiple acrylate allergies, as shown.

2.3.2.30 [Aalto-Korte, 2021]

Study reference:

Aalto-Korte K, Suuronen K. Ten years of contact allergy from acrylic compounds in an occupational dermatology clinic. Contact Dermatitis. 2021;84:240–246

Detailed study summary and results:

Test type

Retrospective study

Authors included patients who had been tested with acrylate patch test series and displayed allergic reactions to at least one acrylic compound.

They performed patch tests using Finn Chambers (Smart Practice, Phoenix, Arizona), in accordance with the European Society of Contact Dermatitis guidelines. Authors read the tests two to three times: on day (D)2-D3-D4, D2-D3-D6, or D2-D5, depending on the day of application (Monday, Tuesday, or Wednesday). After patch tests, exposure to positive allergens is assessed in cooperation with a dermatologist and a chemist.

Results

During the 10-year period from 2010 to 2019, a total of 426 patients were tested with at least one acrylate series; this corresponded to 37% of all patch-tested patients. “Acrylate series A” was tested in 395 patients, “Acrylate series B” in 230 patients, and “Acrylate series C” in 183 patients. A total of 31 patients were tested with the previous “(Meth)acrylate series.”

During the study period, a total of 55 patients tested positive to some acrylic compound.

2-Hydroxypropyl methacrylate (2-HPMA) was positive in 16 cases and 5 of these had shown exposure to 2-HPMA.

Acrylic test substances in routine test series at FIOH, number of allergic reactions, and number of allergic reactions with shown exposure to the same allergen

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

Test substance, concentration in petrolatum	Abbreviation	Allergic reactions (order of frequency)	Number of patients with contact allergy and shown present exposure	Patients tested among 55 patients with allergic reactions to acrylic compounds
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ACRYLATES SERIES A (SCREENING)

2-Hydroxypropyl methacrylate 2%	2-HPMA	16 (3.)	5	55
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Positive patch tests with HPMA including :

- 5 cases of occupational allergic contact dermatitis caused by anaerobic sealants
- 4 cases of dental occupations
- 2 cases caused by UV-cured windscreen glues and resins
- 2 cases related to nail products
- 1 case related to paints and lacquers

2.3.2.31 [Rustemeyer, 1996]

Study reference:

Rustemeyer T, Frosch P J. Occupational skin diseases in dental laboratory technicians. (I). Clinical picture and causative factors. Contact Dermatitis. 1996; 34: 125–133.

Detailed study summary and results:

Test type

Clinical occupational study (Germany)

Questionnaires were sent to 1132 dental technicians and 50 employers. Seven laboratories were inspected. Between February 1993 and June 1994, 55 dental technicians with suspected, and reported to the insurer, occupational dermatoses were examined. Patch testing: The patient's own working materials, suspected to be a cause of the dermatitis, were tested whenever possible. If their basic ingredients were in other dental series, such products were not additionally tested. Among the dental technician series, 2-HPMA was tested at 2% in pet.

Results

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

Table 6a. Results of patch testing in 55 dental technicians

Name of chemical	n	(%)	Name of chemical	n	(%)
methyl methacrylate (MMA)	9	16	cobalt chloride	1	2
2-hydroxyethyl methacrylate (2-HEMA)	18	33	benzoyl peroxide	2	4
ethyleneglycol dimethacrylate (EGDMA)	15	27	hydroquinone	1	2
triethyleneglycol dimethacrylate (TREGDMA)	2	4	melamine-formaldehyde resin	4	7
2-hydroxypropyl methacrylate (2-HPMA)	7	13	phenol-formaldehyde resin	1	2
ethyl methacrylate (EMA)	6	11	dimethyl-p-toluidine	1	2
ethyl acrylate (EA)	3	6	p-aminoazobenzene	3	6
butyl acrylate (BA)	1	2	p-phenylenediamine	3	6
1,4-butanediol dimethacrylate (BUDMA)	1	2	thiuram mix	1	2
bis-GMA	1	2	diethyldithiocarbamate	1	2
urethane dimethacrylate (UEDMA)	1	2	colophony	1	2
pentaerythritol triacrylate (PETA)	2	4	glutaraldehyde	1	2
tris (2-hydroxyethyl) isocyanurate acrylate	1	2	formaldehyde	1	2
acrylated polyurethane	2	4	thimerosal	3	6
epoxy acrylic oligomer	1	2	p-tert. butylcatechol	1	2
acrylated epoxy oligomer	3	6	mercury ammonium chloride	1	2
epoxy resin	1	2	balsam of Peru	1	2
nickel sulfate	10	18	fragrance mix	4	7
palladium chloride	3	6	Amerchol	1	2
potassium dichromate	2	4	Kathon CG	1	2

Listed are all allergens positive in at least 1 case. The other allergens of Table 1 were negative. 2-HPMA was tested in 27 patients only.

Table 6b. Important allergens positive in the group of patients (n=35) with allergic contact dermatitis of the hands

Name of chemical	n	(%)	Name of chemical	n	(%)
methyl methacrylate (MMA)	9	26	bis-GMA	1	3
2-hydroxyethyl methacrylate (2-HEMA)	18	51	epoxy resin	1	3
ethyleneglycol dimethacrylate (EGDMA)	15	43	acrylated polyurethane	2	6
triethyleneglycol dimethacrylate (TREGDMA)	2	6	epoxy acrylic oligomer	1	3
2-hydroxypropyl methacrylate (2-HPMA)	7	20	acrylated epoxy oligomer	3	9
ethyl methacrylate (EMA)	6	17	nickel sulfate	10	29
ethyl acrylate (EA)	3	9	palladium chloride	3	9
butyl acrylate (BA)	1	3	potassium dichromate	2	6
1,4-butanediol dimethacrylate (BUDMA)	1	3	cobalt chloride	1	3
urethane dimethacrylate (UEDMA)	1	3	melamine-formaldehyde resin	4	11
pentaerythritol triacrylate (PETA)	2	6	dimethyl-p-toluidine	1	3
tris (2-hydroxyethyl) isocyanurate acrylate	1	3			

Table 7. Pattern of sensitization to 5 major methacrylates on patch testing 55 dental technicians (2-HPMA 27 patients): methyl methacrylate (MMA), ethyleneglycol dimethacrylate (EGDMA), 2-hydroxyethyl methacrylate (2-HEMA), 2-hydroxypropyl methacrylate (2-HPMA) and ethyl methacrylate (EMA)

Positive reactions to	MMA	EGDMA	2-HEMA	2-HPMA	EMA
MMA (n=9)	—	6	8	2	4
EGDMA (n=15)	6	—	14	7	6
2-HEMA (n=18)	8	14	—	7	6
2-HPMA (n=7)	2	7	7	—	4
EMA (n=6)	4	6	6	4	—

2.3.2.32 [Tucker, 1999]

Study reference:

Tucker SC, and Beck MH. A 15-year study of patch testing to (meth)acrylates. Contact. Derm. 1999; 40:278–279

Detailed study summary and results:

Test type

Retrospective study: between January 1983 and March 1998 (approximately 14,000 records).

Patients with a history of exposure to (meth)acrylates had been patch tested with the Chemotechnique series available at the time, and where possible to their own suspected product as well. Patch testing and scoring

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

were performed on the back using Finn Chambers on Scanpor tape, with an occlusion time of 2 days. Reactions were assessed at 2 and 4 days.

Results

440 patients with a history of exposure to acrylates were identified: 67 (15.2%) showed at least 1 relevant reactions. Of the 67 patients, 47 were sensitised at work.

(Meth)acrylate	Abbreviation	Patch test conc. (%) (w/w)	Allergic/ tested	%	Rank
2-hydroxypropyl methacrylate	(2-HPMA)	2	26/330	7.9	7

Table 2. Occupational cases

Occupation	Number (%) allergic (total 47)
dentistry	8 (17)
dental surgeons	2
orthodontists	3
dental nurses	1
dental technicians	2
printers/lithographers	8 (17)
gas workers	4 (8.5)
gearbox fitters	4 (8.5)
beauty therapists	3 (6.4)
others	20

2.3.2.33 [Eslander, 1996]

Study reference:

Estlander T, Kanerva L, Kari O, Jolanki R, Mölsä K. Occupational conjunctivitis associated with type IV allergy to methacrylates Case Reports. Allergy. 1996 Jan;51(1):56-9.

Detailed study summary and results:

Test type

Three patients, two dental laboratory workers and one hearing aid laboratory worker, are presented. All three had allergic contact dermatitis from MA (methacrylates) which disappeared after avoidance of contact with uncured MA compounds. Two of the patients, the dental laboratory assistant and the hearing aid worker, had also developed symptoms of conjunctivitis. Both were exposed to chemically curable and light-curable MAs.

Epicutaneous tests were conducted using the Finn Chambers (Epitest Ltd Oy, Finland). They included the European standard series, a dental screening series, and a (meth)acrylate series, all from Chemotechnique Diagnostics AB, Sweden. Patch tests were also carried out with acrylate and other products used at the workplaces.

Results

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

Table 3. Patch test results of two conjunctivitis patients with (meth)acrylate serie

(Meth)acrylate	Dental laboratory assistant (patient 1)	Hearing aid worker (patient 3)
Methylmethacrylate (MMA)	3+	2+
Ethylmethacrylate	2+	1+
2-Hydroxyethylmethacrylate (2-HEMA)	3+	2+
2-Hydroxypropylmethacrylate (2-HPMA)	3+	2+
Ethylacrylate	NT	2+
2-Hydroxyethylacrylate	NT	2+
2-Hydroxypropylacrylate	NT	2+
Ethyleneglycol dimethacrylate	3+	2+
Triethyleneglycol dimethacrylate	3+	1+
Triethyleneglycol diacrylate	Neg	2+
Tetrahydrofurfuryl dimethacrylate	2+	NT
1,4-Butanediol dimethacrylate	2+	Neg
1,4-Butanediol diacrylate	Neg	2+
1,6-Hexanediol diacrylate	Neg	2+
Diethyleneglycol diacrylate	Neg	2+
Urethanediacrylate, aromatic	Neg	2+
Pentaerythritol triacrylate	Neg	2+

NT: not tested; Neg: negative.

2.3.2.34 [Hemmer, 1996]

Study reference:

Hemmer W, Focke M, Wantke F, Gotz M, and Jarisch R. Allergic contact dermatitis to artificial fingernails prepared from UV light-cured acrylates. J. Am. Acad. Dermatol. 1996;35:377–380

Detailed study summary and results:

Test type

Case report

Five women with photobonded acrylic nails presented with a pruritic and painful perionychial and subonychia dermatitis for several months. They were patch tested with an acrylate battery and "hypoallergenic" commercial products.

All compounds were tested in white petrolatum on Finn Chambers. Readings were taken at 48 and 72 hours and scored according to the recommendations of the International Contact Dermatitis Research Group.

Results

Table I. Patch test results to (meth)acrylates in patients sensitized by acrylic nails made from light-cured premixed gels

Compound	Concentration* (%)	Patient No.				
		1	2	3	4	5

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

2-HPMA	0.6	+++	++	++	+	+
	0.2	++	+	+	+	+

2.3.2.35 [Cravo, 2008]

Study reference:

Cravo M, Cardoso J C, Gonçalo M, Figueiredo A. Allergic contact dermatitis from photobonded acrylic gel nails: a review of four cases. *Contact Dermatitis*. 2008; 59: 250–251.

Detailed study summary and results:

Test type

Case reports

Four female patients, aged 26–41 years old (mean 33.0 years), with allergic contact dermatitis from photobonded acrylic gel nails were observed. Two of these patients were both customers and professional nail beauticians.

The two customers developed periungual eczema 3 and 6 months after the first application of acrylic gel. One of the manicurists, in spite of having had acrylic gel nails for 2 years, only developed periungual and hand dermatitis after using acrylic nail gels professionally. The other nail beautician presented with eyelid dermatitis 5 months after starting work and had no hand/periungual lesions.

Patch tests with the Portuguese baseline series of contact allergens and an extended series of acrylates (Chemotechnique) applied using Finn Chambers on Scanpor tape (24-h occlusion and readings at D2 and D3/D4)

Results

Table 1. Positive patch tests

Patch tests	Patient 1 (♀, 41 years)	Patient 2 (♀, 26 years)	Patient 3 (♀, 38 years)	Patient 4 (♀, 27 years)
Baseline series	Parabens + Thiomersal +	Negative	Nickel ++ Thiomersal ++	Negative
Acrylate series	2-HEMA +++ 2-HPMA ++ EMA ++ 2-HEA ++ THFMA ++ TREGDMA ++ TEGDMA ++ TREGDA ++ HDDA ++	2-HEMA +++ 2-HPMA +++ EMA ++ 2-HEA ++ EA ++ EGDMA ++	2-HEMA ++ 2-HPMA ++	TREGDA ++

EA, ethyl acrylate; EMA, ethyl methacrylate; EGDMA, ethylene glycol dimethacrylate; HDDA, 1,6-hexanediol diacrylate; 2-HEA, 2-hydroxyethyl acrylate; 2-HEMA, 2-hydroxyethyl methacrylate; 2-HPMA, 2-hydroxypropyl methacrylate; TEGDMA, tetraethylene glycol dimethacrylate; THFMA, tetrahydrofurfuryl methacrylate; TREGDA, triethylene glycol diacrylate; TREGDMA, triethylene glycol dimethacrylate.

2.3.2.36 [Vaccaro, 2014]

Study reference:

Vaccaro M, Guarneri F, Barbuzza O, Cannavò S. Airborne contact dermatitis and asthma in a nail art operator. *Int J OccupMed Environ Health*. 2014; 27: 137–140.

Detailed study summary and results:

Test type

Case report

A 38-year-old woman, who was working as a nail art operator since she was 36, came to observation because of facial dermatitis and multiple episodes of asthma that occurred in the previous two months. She reported that all respiratory symptoms and worsening of dermatitis happened at her workplace, a rather small and not well ventilated room where she created nail decorations using acrylic resins. Remission of asthma and improvement of dermatitis were observed on the days when the subject did not work. In addition, the patient reported that self-measurement of PEF (Peak of Expiratory Flow) with a portable device, as suggested by her pneumologist, showed lower values at the workplace (65–70% of the predicted values) than at home (> 75% of the predicted values). Clinical history was negative for significant diseases, including allergy, and the use of medications, even occasional; routine laboratory test results were within normal ranges.

Results

Spirometry (with a Quark- SPIRO spirometer, COSMED, Roma, Italy) showed mild airflow obstruction: forced expiratory volume in 1 second (FEV₁), forced vital capacity (FVC), and FEV₁/FVC ratio equaled 73%, 89%, and 77% of the predicted values, respectively. The results were worse when spirometry was performed at the workplace: FEV₁, FVC and FEV₁/FVC were 64%, 78% and 69%, respectively. The bronchial provocation test performed according to the guidelines of ATS/ERS (American Thoracic Society/ European Respiratory Society) with a DeVilbiss 646 nebulizer (Sunrise Medical, Somerset, USA) driven by the KoKo Digidoser system (Pulmonary Data Service, Louis-ville, USA) revealed mild bronchial hyper-responsiveness: a 20% FEV₁ decrease from the baseline with a 2 mg/ml provocative concentration of methacholine. The reversibility test, performed according to the guidelines of ERS/ATS, showed a 14% increase of FEV₁ 15 min after administration of a short acting beta agonist (salbutamol).

Prick tests with commercial extracts of aeroallergens, food allergens and latex, performed according to the guidelines of SIAIC (Società Italiana di Allergologia ed Immu-nologia Clinica – Italian Society of Allergy and Clinical Immunology) were negative. The patch test was conducted according to the recommendations of ICDRG (International Contact Dermatitis Research Group) and SIDAPA (Società Italiana di Dermatologia Allergologica, Professionale e Ambientale – Italian Society of Allergo-logical, Occupational and Environmental Dermatology), with the use of baseline (standard) rubber, cosmetics and acrylate series (methylacrylate 1%, methyl methacrylate 5%, hydroxyethyl methacrylate 5%, hydroxypropyl methacrylate 2%, tetraethyleneglycol dimethacrylate 2%, triethyleneglycol dimethacrylate 2%, urethane dimeth-acrylate 2%, bis-GMA 2%, tetrahydrofurfuryl methacrylate 2%, hexanediol diacrylate 0.1%, N,N-dimethylamino-ethyl methacrylate 0.2% and ethyleneglycol dimethacrylate 2%, all in petrolatum), using haptens from FIRMA (Florence, Italy) in Hayes' chambers (Hayes Service BV, Alphen, the Netherlands). The results at D2 and D4 were positive for all acrylates except bis-GMA.

The manufacturer (Yiwu Qianshuo Nail Co., Ltd., Yiwu, Zhejiang, China) confirmed that some of the acrylates which the patient was allergic to were present in the products used (Lily Angel), but did not want to reveal the exact composition due to the fact that it was an industrial secret. Authors diagnosed airborne ACD (allergic contact dermatitis) and asthma caused by acrylates. The patient refused to be subjected to a bronchial challenge test with acrylates.

Table 1. Positive reactions to the patch test with acrylates observed at D4

Patch test	Reaction
Methyl acrylate 1% pet.	+++
Methyl methacrylate 5% pet.	+++
Hydroxyethyl methacrylate 5% pet.	+
Hydroxypropyl methacrylate 2% pet.	++
Tetraethyleneglycol dimethacrylate 2% pet.	++
Triethyleneglycol dimethacrylate 2% pet.	++
Urethane dimethacrylate 2% pet.	+
Tetrahydrofurfuryl methacrylate 2% pet.	++
Hexanediol diacrylate 0.1% pet.	++
N,N-dimethylaminoethyl methacrylate 0.2% pet.	+++
Ethyleneglycol dimethacrylate 2% pet.	++

pet. – petrolatum.

2.3.2.37 [Le, 2015]

Study reference:

Le Q, Cahill J, Palmer-Le A, Nixon R. The rising trend in allergic contact dermatitis to acrylic nail products. *Australas J Dermatol.* 2015; 56: 221–223.

Detailed study summary and results:

Test type

Case reports

Authors described four cases of allergic contact dermatitis (ACD) to acrylates found in Shellac nail products (type of long-wearing nail polish), involving three beauticians and one consumer who purchased the product over the internet.

They patch-tested to the Australian baseline series, the acrylate series, relevant cosmetic ingredients and many of their own appropriately diluted samples. Patch-testing was performed using Allerg-EAZE patch test chambers (SmartPractice, Phoenix, AZ, USA). Patch test results were read at 48 and 96 h.

Results

Patient 1: HPMA: ++

Patient 4: HPMA: +

For other patients, no reaction to HPMA was noted in the publication.

Over a 20-year period (1993–2013), 1320 of a total of 8334 patients were patch-tested at the Skin and Cancer Foundation Victoria to acrylates, and only 57 (4.3%) had positive reactions, of whom 14 were beauticians.

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

Table 1 Number of positive reactions in our 14 beauticians patch-tested to the acrylate series

Allergen	Abbreviations	Number of positive results to tested allergen (of 14 cases)
Hydroxyethyl methacrylate	HEMA	14
Ethylene glycol dimethacrylate	EGDMA	11
2-hydroxyethyl acrylate	2-HEA	10
2-hydroxypropyl methacrylate	2-HPMA	9
Triethylene glycol diacrylate	TREGDA	8
Triethylene glycol dimethacrylate	TREGDMA	8
Ethyl acrylate	EA	6
Tetrahydrofurfuryl methacrylate	THFMA	4
Ethyl methacrylate	EMA	4
Methyl methacrylate	MMA	3
1,6-hexanediol diacrylate	1,6-HDDA	2
Trimethylolpropane triacrylate	TMPTA	2
Butyl acrylate	BA	1

2.3.2.38 [Romita, 2020]

Study reference:

Romita P, Foti C, Barlusconi C, Hansel K, Tramontana M, Stingeni L. Contact allergy to (meth)acrylates in gel nail polish in a child: An emerging risk for children. Case Reports. Contact Dermatitis. 2020 Jul;83(1):39-40.

Detailed study summary and results:

Test type

Case report

A 10-year-old non-atopic girl presented with eczema on the dorsal aspect of the thumb and vesicular and bullous lesions on her fingertips, associated with itching and burning. The history revealed that the skin lesions appeared about 10 days after she applied her mother's gel nail polish for fun.

Patch tests with the SIDAPA (Società Italiana di Dermatologia Allergologica, Professionale e Ambientale) baseline series (FIRMADiagent, Florence, Italy) and the gel nail polish 1% pet. were performed. Patch testing was carried out with the Haye's Test Chambers (Haye's Service, Alphen aan den Rijn, The Netherlands) on Soffix tape (Artsana, Grandate, Italy) and readings were done on day (D)2, D4, and D7.

Results

At D4, strong (++) positive reactions to 2-hydroxyethyl methacrylate (2-HEMA) and to the gel nail polish were observed. Patch testing with the same gel nail polish in 20 healthy subjects was negative.

In a second round, methyl methacrylate (MMA) 2% pet., 2-hydroxypropyl methacrylate (HPMA) 2% pet., and ethylene glycol dimethacrylate (EGDMA) 2% pet. were patch tested, with strong (++) positive reactions to HPMA and EGDMA.

2.3.2.39 [Alves, 2020]

Study reference:

Alves F, Morgado F, Ramos L, Gonçalo M. Hand eczema from nail (meth)acrylates in an 11-year-old child Case Reports. Contact Dermatitis. 2020 May;82(5):315-316

Detailed study summary and results:

Test type

Case report

An 11-year-old girl with a personal history of asthma and rhinitis presented with persistent recalcitrant hand eczema, affecting predominantly the dorsal aspects of the fingers, despite topical corticosteroids. The child's mother was a nail aesthetician and the patient reported frequent manipulation and “playing” of the child with the mother's professional products, in particular those used for nail aesthetics.

Patch testing was performed with the Portuguese Contact Dermatitis Research Group baseline series, as well as with a few (meth)acrylates apart from 2-HEMA (hydroxyethyl methacrylate) present in the baseline series. Allergens were applied in IQ-ultra chambers (Chemotechnique Diagnostics, Vellinge Sweden) on the back for 48 hours and readings were performed on day (D) 3 and D7, according to ESCD guidelines.

Results

Strong (++) reactions to 2-HEMA, hydroxypropyl methacrylate (HPMA), hydroxyethyl acrylate (HEA), ethyleneglycol dimethacrylate (EGDMA), and urethane dimethacrylate (UDMA) were observed.

2.3.2.40 [Fisch, 2019]

Study reference:

Fisch A, Hamnerius N, Isaksson M. Dermatitis and occupational (meth)acrylate contact allergy in nail technicians-A 10-year study. Contact Dermatitis. 2019 Jul;81(1):58-60.

Detailed study summary and results:

Test type

Retrospective study

Data on all nail technicians in the department's test database between January 1, 2007 and December 31, 2016 were retrieved.

In addition to the Swedish baseline series, the patients were tested with an acrylate series, the composition of which varied during the study period. A number of patients were also tested with their own workplace materials. The commercial test haptens used were obtained from Chemotechnique Diagnostics (Vellinge, Sweden). Patch testing was performed with 8-mm Finn Chambers (Epitest, Tuusula, Finland or SmartPractice, Phoenix, Arizona) attached to Scanpor tape (Norgesplaster, Vennesla, Norway). Twenty milligrams of the pet. test preparations and 15 µL of liquid preparations, applied with a micropipette, were placed in the Finn Chambers, which were attached to the back of each patient. The occlusion time was 48 hours, and all test materials were removed by the patients themselves. Readings were performed on day (D) 3 or D4 and on D7 or D8, according to ICDRG and ESCD criteria. The statistical analyses were performed with SPSS Version 22 statistical software (IBM Corp., Armonk, New York). Comparisons were made between subjects with and without (meth)acrylate contact allergy by the use of a two-sided Fisher's exact test. P values of <0.05 were considered to be significant.

Results

Contact allergy to one or more (meth)acrylates was found in 57% (16/28) of patients; all allergies were classified as occupational and clinically relevant. All subjects were females and their age ranged from 21 to 52 years.

TABLE 1 Positive (meth)acrylate patch test reactions among 16 nail technicians^a

Hapten	Positive reactions, n (%)
2-Hydroxyethyl methacrylate 2%	10 (63)
Ethylene glycol dimethacrylate 2%	10 (63)
Hydroxypropyl methacrylate 2%	9 (56)
1,4-Butanediol diacrylate 0.1%	9 (56)
Triethylene glycol diacrylate 0.1%	8 (50)
Hydroxy propylacrylate 0.1%	6 (38)
Triethylene glycol dimethacrylate 2%	5 (31)
2-Hydroxyethyl acrylate 0.1%	5 (31)
Di(ethylene glycol) diacrylate 0.1%	4 (25)
Ethyl acrylate 0.1%	4 (25)
Tetrahydrofurfuryl methacrylate 2%	4 (25)
1,6-Hexanediol diacrylate 0.1%	4 (25)
Triethylene glycol diacrylate 0.1%	2 (13)
Tetraethylene glycol dimethacrylate 2%	2 (13)
2-(2-Ethoxyethoxy) ethyl acrylate 0.1%	2 (13)
1,4-Butanediol dimethacrylate 2%	2 (13)

All allergens in pet.

^aIn addition, single positive reactions were observed to glycerol dimethacrylate, methyl methacrylate, butyl acrylate, ethyl methacrylate, trimethylolpropane triacrylate, urethane dimethacrylate-aliphatic, tri(propylene glycol) diacrylate, pentaerythritol triacrylate, and oligotriacrylate (OTA 480), also tested in pet.

2.3.2.41 [Rodenas-Herranz, 2020]

Study reference:

Ródenas-Herranz T, Navarro-Triviño FJ, Linares-González L, Ruiz-Villaverde R, Brufau-Redondo C, Mercader-García P. Acrylate allergic contact dermatitis caused by hair prosthesis fixative. Case Reports. Contact Dermatitis. 2020 Jan;82(1):62-64.

Detailed study summary and results:

Test type

Case report

A 57-year-old male, with no personal or family history of interest, was followed up for scarring alopecia secondary to lichen planus. Four weeks after using a capillary prosthesis fixed by a liquid glue (Ghost Bond, Pro Hair Labs, Zephyrhills, Florida), the label of which specifies that it contains acrylates, he developed a pruritic rash on the scalp, with erythematous, squamous, and erosive lesions. There were also distant lesions on the face, armpits, and cervical region. Although the patient changed the fixation to double-side adhesive tapes (unknown brand), the lesions persisted.

The patient was patch tested with the baseline series of GEIDAC (allergEAZE, Phoenix, Arizona), a series of acrylates, a series of glues and plastics (both from allergEAZE), and the patient's own products "as is." The readings were done according International Contact Dermatitis Group (ICDRG) criteria.

Results

The reading on day (D) 2 and D4 was positive for hydroxypropyl methacrylate 2% pet. (++/+), hydroxyethyl acrylate 2% pet. (++/+), butyl acrylate (++/+), adhesive tape (++/+), and Ghost Bond glue (++/+). Moreover, patch tests were positive for formaldehyde 1% aq. (++/+), methylisothiazolinone (MI) 2000 ppm aq. (++/+), and methylchloroisothiazolinone (MCI)/MI 0.01% aq. (+++/+++).

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

The lesions in the neck and armpits were deemed related to the use of a gel and a shampoo containing MCI/MI, but those on the scalp were related to the acrylates present in the liquid glue and in the adhesives.

2.3.2.42 [Kanerva, 1992]

Study reference:

Kanerva L, Estlander T and Jolanki R. Active sensitization caused by 2-hydroxyethyl methacrylate, 2-hydroxypropyl methacrylate, ethyleneglycol dimethacrylate and N, N-dimethylaminoethyl methacrylate. Journal of the European Academy of Dermatology & Venereology, 1. 1992; 165-169

Detailed study summary and results:

Test type

Case report

A 45-year-old non-atopic orthodontist had suffered for six months from prolonged work-related cough that was suspected to be caused by acrylics. He had a history of daily acrylic exposure at work for more than 15 years. The patient's pulmonary function and provocation tests were normal. He had had no skin symptoms, but was patch tested because patch tests have been positive in patients with respiratory symptoms. Patch testing was performed and scored on the upper back with 48 h occlusion. The European standard series, the dental series and the methacrylate series (Chemotechnique Diagnostics, AB, Malmo, Sweden) were used.

Results

The 2, 3 and 4 day readings revealed no allergic patch test reactions, but on day 13 the patient experienced itching on the back and was re-examined on day 15. Four allergic patch test reactions were observed on the site where the (meth)acrylate series had been tested and one allergic reaction on the site of the dental series. The patient was retested 2.5 months later.

Results of second patch test session with (meth)acrylates

(Meth)acrylate series	% (w/w)	Day		
		2	3	4
10. 2-Hydroxypropyl methacrylate (2-HPMA)	2	2 +	2 +	3 +

2.3.2.43 [Weber-Muller, 2004]

Study reference:

Weber-Muller F, Reichert-Penetrat S, Schmutz JL, Barbaud A. Eczéma de contact aux polyacrylates du gel conducteur des électrodes de neurostimulation. Ann Dermatol Venereol 2004;131:478-80

Detailed study summary and results:

Test type

Case report

Results

A 50 year-old man suffered from post-traumatic lumbar pain. He developed eczematous lesions on the sites where the TENS electrodes were applied. Patch tests were positive with the TENS gel, with ethylene glycol dimethylacrylate (2 p. 100 petrolatum) and ethyl-acrylate (2 p. 100 petrolatum) on day 2 and 4 readings.

A 54 year-old man had a paralysis of the foot elevator following rupture of an aneurism. After 2 months, he had an eczema on the sites where the TENS electrodes were applied. Patch tests were negative with the

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

TENS electrodes but positive with 2-hydroxyethyl acrylate (0.1 p. 100 petrolatum), triethyleneglycol diacrylate (0.1 p. 100 petrolatum), 2-hydroxyethyl methacrylate (2 p. 100 petrolatum) and 2-hydroxypropyl methacrylate (2 p. 100 petrolatum) on day 2 (+/-) and 4 readings (+).

Tableau II. – Résultats des tests épicutanés (cas n° 2).

	48 heures	96 heures
Électrode Saint-Cloud, face interne avec gel	–	–
Électrode Saint-Cloud, face externe	–	–
Méthyl méthacrylate 2 % vaseline	–	–
Butyl acrylate 0,1 % vaseline	–	–
2 hydroxyéthyl acrylate 0,1 % vaseline	+	+
Triéthyléneglycol diacrylate 0,1 % vaseline	±	+
2 hydroxyéthyl méthacrylate 2 % vaseline	±	+
2 hydroxypropyl méthacrylate 2 % vaseline	±	+

2.3.2.44 [Llamas, 2010]

Study reference:

Llamas M, Santiago D, Navarro R, Sanchez-Perez J and Garcia-Diez A. Unusual allergic contact dermatitis produced by a transcutaneous electrical nerve stimulator. *Contact Dermatitis*. 2010; 62: 189–190

Detailed study summary and results:

Test type

Case report

For 5 months, a 42-year-old woman used TENS (transcutaneous electrical nerve stimulator) (Lifecare, Tiberias, Israel) for chronic lower back pain resistant to medical treatment. After 4 months of continuous usage of the TENS device she noted itchy erythematous papules and scaling where she applied the TENS electrodes. These lesions completely disappeared in 2 weeks when stopped using TENS and taken oral corticosteroids.

She was patch tested with Spanish baseline series and rubber series (Chemotechnique Diagnostics, Vellinge, Sweden) with positive results at D2 and at D4 to nickel (++) . An use test on her lower back with the TENS device ‘as is’ for few hours produced an eczematous reaction after 1 day. Some time later, she was patch tested with (meth)acrylates series (Chemotechnique Diagnostics, Vellinge, Sweden) and TENS components, supplied by Telic S.A. These supplementary series and substances were applied using Finn Chamber (Epitest Ltd Oy, Tuusula, Finland) fixed with Scanpor tape (Alpharma AS, Vennesla, Norway).

Results

Table 1. Our case and the other published ACD cases related with acrylates contained in TENS devices

Author	Sex/age (years)	Location	Period of use (months)	Continuous use period (hr)	Symptom latency (months)	Patch testing positivities (PPR)	D2	D4
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CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

Llamas	♀/42	Low back	5	10	4	TENS ^a (inner)	++	++
						TENS gel	++	++
						2-HEMA 2% pet.	++	++
						2-HPMA 2% pet.	++	++
						EGDMA 2% pet.	++	++
						Irgacure 1% pet.	++	++
						HDHA 0.1% pet	+	++

PPR, present positive relevance; 2-HEMA, 2-hydroxyethyl methacrylate; 2-HPMA, 2-hydroxypropyl methacrylate; 2-HEA, 2-hydroxyethyl acrylate; EGDMA, ethylene glycol dimethacrylate; TREGDMA, triethyleneglycol dimethacrylate; HDHA, 1,6-hexanediol diacrylate; pet., petrolatum; NR, non-reported; ACD, allergic contact dermatitis; TENS, transcutaneous electrical nerve stimulators.

^aSelf-adhesive electrodes of TENS.

2.3.2.45 [Goulding, 2011]

Study reference:

Goulding JMR and Finch TM. Acrylates tooth and nail: coexistent allergic contact dermatitis caused by acrylates present in desensitizing dental swabs and artificial fingernails. Case Reports. Contact Dermatitis. 2011 Jul;65(1):47-8.

Detailed study summary and results:

Test type

Case report

A 55-year-old woman presented after undertaking a series of home dental bleaching treatments. Tooth sensitivity led to the use of AcquaSeal desensitizing dental swabs. Marked symmetrical lip and gingival oedema and erythema were noted within days of the start of treatment, and a short course of oral prednisolone and antihistamines was prescribed by the local accident and emergency department. The patient had mild fingertip and neck dermatitis at the time of treatment, and was noted to be a wearer of artificial fingernails. Two days after she re-commenced use of the products, her lips flared again and treatment was discontinued.

Patch testing was performed with the British Society of Cutaneous Allergy baseline series and modified cosmetic, medicament, acrylate and dental series, in addition to the three dental products (allergens supplied by Chemotechnique Diagnostics, Vellinge, Sweden, and Trolab, Reinbek, Germany), using Finn Chambers. Patches were removed after 2 days, and final readings were taken on day 4. Results were graded according to the criteria of the International Contact Dermatitis Research Group.

Results

The following reactions were recorded at both day 2 and day 4: + reaction to 2-hydroxyethyl acrylate (0.1% pet.), 2+ reaction to 2-HEMA (2.0% pet.), 2+ reaction to 2-hydroxypropylmethacrylate (2.0%pet.), 2+ reaction to ethyleneglycol dimethacrylate (2.0% pet.), and 3+ reaction to AcquaSeal desensitizing dental swab solution ('as is' and 10.0% aq.). No reaction was detected to either the toothpaste or tooth-whitening gel, suggesting that the patient's earlier positive results were attributable to cross-contamination from the desensitizing dental swab solution.

2.3.2.46 [Maio, 2012]

Study reference:

Maio P, Carvalho R, Amaro C, Santos R, Cardoso J. Allergic contact dermatitis from sculptured acrylic nails: special presentation with an airborne pattern. Dermatology Reports 2012; volume 4:e6

Detailed study summary and results:

Test type

Case report

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

Authors described 3 patients (women 35-50 year-old) with contact allergy to acrylates in artificial sculptured nails. Patch tests were performed with the Portuguese baseline series of contact allergens and an extended series of acrylates were applied. In particular, authors tested three female patients with allergic contact dermatitis from sculptured acrylic nails. Two of these patients were both customers and also technical nail beauticians. Two patients developed periungual eczema; one of them had clinically an airborne pattern. The third patient presented only with face and eyelid dermatitis had no other lesions.

Results

The tests showed positive reactions to 2-hydroxyethylmethacrylate (2-HEMA) and 2-hydroxypropylmethacrylate (2-HPMA) in three patients. Positive reactions to other acrylates were also found.

2.3.2.47 [Kiec-Swierczynska, 2013]

Study reference:

Kiec-Swierczynska M, Krecisz B and Chomiczewska-Skora D. Occupational contact dermatitis to acrylates in a Manicurist. Occupational Medicine. 2013;63:380–382

Detailed study summary and results:

Test type

Case report

32 year-old non atopic woman, who had been working as a manicurist for 3 months, developed redness and oozing skin lesions of the ears and external auditory canals, followed by hand eczema and bullous lesions on fingers. Skin symptoms were accompanied by nasal pruritus, rhinorrhoea and redness of the conjunctiva. Because of her skin disorder, she had to give up her job. After completing dermatological treatment, she started working as a dental nurse. Within 4 months, itching skin lesions of the ears and eczema of the fingers reappeared.

Authors performed patch tests with the European Baseline Series, (Meth) Acrylate Series (Nails-Artificial), Fragrance Series, glutaraldehyde, benzalkonium chloride, chlorhexidine digluconate (Chemotechnique®, Vellinge, Sweden) and disinfectant solutions prepared by our laboratory—0.5% chloramine and 2% glyoxal.

Results

Table 1. Positive patch test results at Days 2 and 4

Allergen	Day 2	Day 4
Nickel sulphate	+	++
Fragrance mix	++	++
Isoeugenol	+	++
2-HEMA	+++	+++
2-Hydroxypropyl methacrylate	+++	+++
EGDMA	+++	+++
TREGDMA	–	++
1,6-Hexandiol diacrylate	++	+++
2-Hydroxyethyl acrylate	+++	+++
Triethyleneglycol diacrylate	+++	+++

2.3.2.48 [DeKoven, 2017]

Study reference:

DeKoven S, DeKoven J, Holness DL. (Meth)Acrylate Occupational Contact Dermatitis in Nail Salon Workers: A Case Series. Journal of Cutaneous Medicine and Surgery. 2017;Vol. 21(4) 340–344

Detailed study summary and results:

Test type

Case report

Authors reported 6 cases of ACD (allergic contact Dermatitis) to acrylates and methacrylates, known collectively as (meth)acrylates, in nail technicians, representing a new trend in our clinic of nail technicians with occupational allergy.

All patients were seen at a major referral centre for suspected occupational ACD, within a 1-year period in 2015 and 2016. The patients were all women, ages 38 to 58, and none had personal or family histories of dermatoses aside from their presenting symptoms. The duration of symptoms ranged from 3 months to 5 years. Common symptoms included dermatitic eruptions of the dorsa of the hands (n = 5), palm (n = 2), and forearm (n = 3) and fissures on the fingertips (n = 4). Other less common symptoms included dermatitic eruptions of the face, including the periorbital region, eyelids, cheeks, and posterior ears. Some additional areas of involvement included the lateral and anterior neck, sacral area, gluteal cleft, lateral thighs, and dorsa of the feet.

Three patients were tested using a modified North American Standard series (Chemotechnique Diagnostics AB, Malmö, Sweden) using IQ Ultra Chambers (Chemotechnique) with Scanpor Tape (Norgesplaster Alpha A/S, Vennesla, Norway). For the North American tray, 2 substitutions were made: glutaraldehyde and glycerol thioglycolate were replaced with HEMA and decyl glucoside. The 3 other patients were tested with the North American Contact Dermatitis Group screening series (SmartPractice, Phoenix, Arizona) using Finn Chambers (Epitest Ltd Oy, Tuusula, Finland) and Scanpor Tape. Both series contained 3 (meth) acrylates: MMA, HEMA, and ethyl acrylate. All patients were additionally tested using the (Meth) Acrylate nail series (Chemotechnique). 2 patients were additionally tested using glove samples, and 2 patients were also tested using shellac.

Table 1. Nail Acrylate Tray: Haptens Tested.

2-hydroxyethyl methacrylate	Tetrahydrofurfuryl methacrylate
2-hydroxypropyl methacrylate	Butyl acrylate
Ethyleneglycol dimethacrylate	Triethyleneglycol dimethacrylate
2-hydroxyethyl acrylate	Ethyl methacrylate
Ethyl acrylate	Methyl methacrylate
Triethyleneglycol diacrylate	n-butyl methacrylate
1,6-hexanediol diacrylate	Trimethylolpropane triacrylate

Results

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

Table 2. Case Characteristics and Patch Test Results.

Patient	Age (y)	Location	Additional Testing	Positive Acrylate Reactions Screening Tray	Positive Additional Reactions: Nail Acrylate Tray
1 ^a	50	Fingertips, hand dorsum	Glove	HEMA, I+	Ethyl acrylate, I+ HPMA, I+ EGDMA, I+ HEA, I+ EGDMA, I+ TREGDMA, I+ HEA, I+ TREGDA, I+ Butyl acrylate, I+ HPMA, I+ EGDMA, I+ I,6-hexanediol diacrylate, I+ THFMA, I+ HEA, I+ TREGDA, I+ Butyl acrylate, I+ EMA, I+ HPMA, I+ THFMA, I Ethyl acrylate, ± HEA, I+ HPMA, I+ EGDMA, I+ I,6-hexanediol diacrylate, I+ I,6-Hexanediol diacrylate, I+ THFMA, I+ HEA, I+ TREGDA, 2+ Butyl acrylate, +/- HPMA, I+ EGDMA, I+ THFMA, I+ HEA, I+ TREGDA, I+ HPMA, I+ EGDMA, I+ I,6-hexanediol diacrylate, I+
2	48	Fingertips, hand dorsum, forearm	None	HEMA, I Ethyl acrylate, I	
3	38	Hand dorsum, face	Various gloves	HEMA, I+ Ethyl acrylate, I+ MMA, I+	
4	58	Fingertips, hand dorsum, palm, forearm, back, foot	None	HEMA, I+	
5	50	Fingertips, back, legs, feet	Shellac	HEMA, I+ Ethyl acrylate, I	
6	41	Fingertips, hand dorsum, forearm, face, neck	Shellac, nickel 5%	HEMA, I+	

Abbreviations: EGDMA, ethyleneglycol dimethacrylate; EMA, ethyl methacrylate; HEA, 2-hydroxyethyl acrylate; HEMA, hydroxyethyl methacrylate; HPMA, 2-hydroxypropyl methacrylate; MMA, methyl methacrylate; THFMA, tetrahydrofurfuryl methacrylate; TREGDA, triethyleneglycol dimethacrylate; TREGDMA, triethyleneglycol dimethacrylate.

^aPatient 1 also reacted to benzocaine, nickel sulfate hexahydrate, and fragrance mix I.

2.3.2.49 [Conde-Salazar, 2017]

Study reference:

Conde-Salazar L, Vargas I, Tevar E, Barchino L, Heras F. Sensitization to Acrylates in Varnishes. *Dermatitis*, Vol 18, No 1 (March), 2007: pp 45–48

Detailed study summary and results:

Test type

Case report

This article presents four cases of sensitization to acrylates among patients who work with varnishes.

Case 1: A 33-year-old woman with no prior skin disease presented with a history of erythematous itching exudative lesions followed by scaling, affecting the flexor surfaces of the forearms, abdomen, right thigh, and both cheeks. Ten days previously, she had begun working with new varnishes (Kupsaviol and Kupsirol, Industrias Quimicas Kupsa, Logrono, Spain) containing tripropylene glycol diacrylate, 203 acrylate, and glycerol propoxy triacrylate. Patch tests were performed with the standard battery of the Grupo Espanol de Investigacion de Dermatitis de Contacto (GEIDC) and with the acrylate series supplied by Chemotechnique

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

Diagnostics (Malmo, Sweden). Readings were performed at day 2 and day 4, according to the accepted criteria of the International Contact Dermatitis Research Group (ICDRG).

Case 2: A 41-year-old man with no prior skin disease presented with a history of eczema on the flexor surface of the right forearm, the front part of both thighs, and the right side of the trunk. Fifteen days previously, he had been working in a varnish plant, wearing rubber gloves. Patch testing was performed as with the patient in Case 1.

Case 3: A 40-year-old man with no prior skin disease presented with a history of eczema on the waist and on the right knee. The eczema had appeared a few days after casual contact with new varnishes (Kupsaviol and Kupsirol). He worked as a wood varnisher at the same workplace at which the patient of Case 1 worked, and he used rubber gloves for skin protection.

Case 4: 28-year-old man with no prior skin disease presented with a 15-day history of intensely itchy erythematous exudative lesions on his forearms, thighs, knees, and abdomen. He worked as a door varnisher and had used a new varnish (Valpol, Valresa, Spain) that contained dipropylene glycol diacrylate and tripropylene glycol diacrylate.

Results

Table 1. Results of Patch Tests with Acrylates at Day 4

Allergen	Reactions			
	Case 1	Case 2	Case 3	Case 4
2-Hydroxypropyl methacrylate 2%	—	—	++	+

2.3.2.50 [Kanerva, 1991]

Study reference:

Kanerva L, Turjanmaa K, Estlander T, Jolanki R. Occupational allergic contact dermatitis caused by 2-hydroxyethyl methacrylate (2-HEMA) in a new dentin adhesive. American Journal of Contact Dermatitis, 1991; vol2, No1 (march): pp 24-30

Detailed study summary and results:

Test type

Case report

Authors presented data concerning 6 patients: 3 dental nurses and 3 dentists who developed allergic contact dermatitis from a dentin adhesion promotor system.

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

Table 2. Characteristics of the Patients Sensitized to Components of the Dentin Adhesion Promoter

Patient	1	2	3	4	5	6
Occupation	Dental nurse	Dental nurse	Dental nurse	Dentist	Dentist	Dentist
Sex	Female	Female	Male	Female	Female	Female
Age (when diagnosis made)	49	36	40	48	45	47
Symptoms since	1987	1988	1989	1989	1990	1990
Years of diagnosis	1988	1989	1990	1990	1990	1990
Localization of dermatitis	Fingers, hands	Eyelids	Fingertips (left, 1-3)	Fingertips (left, 1-3; right, 1, 4)	—	Fingers (left, 2-3)
Own/family atopy	-/-	-/+	-/-	-/-	-/-	-/+
Use and type of protective gloves	PVC	PVC	PVC	PVC and rubber	Various, occasionally	No
Paresthesiae	No	No	Yes	Yes	No	Yes

Patch and prick skin tests were performed with an occlusion time of 48 hours. The patients were tested with the European standard series and a dental series and 2 of the patients were tested with the (meth)acrylate series.

Results

Table 3. Results of Patch Testing

(Meth) acrylates	% (wt/wt)	Patient					
		1	2	3	4	5	6
10. 2-Hydroxypropyl methacrylate (2-HPMA)	2	3+	3+	ND	ND	ND	ND

Abbreviation: ND, not done.

2.3.2.51 [Eslander, 1990]

Study reference:

Eslander T. Occupational skin disease in Finland. Observations made during 1974-1988 at the Institute of Occupational Health, Helsinki. *Acta Derm Venereol Suppl* (Stockh). 1990;155:1-85

Detailed study summary and results:

Test type

Clinical study

Altogether 3,376 patients suspected of having an occupational dermatosis were referred to the Section of Occupational Dermatology of the Institute during 1974-1988. Of these 1,622 were diagnosed as having an occupational skin disease. This study comprises 5 groups of patients examined during 1974-1988.

The Finn chamber method with an application time of 24h (48h since January 1988) has been used for patch testing. The test chambers were usually applied to the patient's back with porous non-occlusive colorless tape. The anterior aspects of the thighs have been used when necessary. The tests were read on removal and 24h and 48-120h (48-96h since January 1988) after removal. At least 3 readings were performed by a dermatologist. When necessary, the test results have been confirmed by retestings with a dilution series. Control tests have been performed with non-standardised and new allergens on 4-20 nonexposed patients. The test results have been scored according to the recommendations of the Finnish Contact Dermatitis Group. Reactions of 2+ or more were considered positive.

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

The first group is composed of all patients diagnosed as having an occupational skin disease during the first 10-year period 1974-1983. In this first group, a total of 1,082 cases of occupational skin diseases were detected.

The four other groups were selected of patients examined during the whole 15-year period:

- Allergy to gloves
- Allergy to dyes
- Allergy to formaldehyde
- Allergy to acrylates

Fourteen patients were diagnosed as having allergic eczema caused by various acrylates. Six of them were examined during 1974-1983.

Patch test were performed for every patients who used acrylic compounds or products at work, with other materials (gloves, disinfectants) and with a test series including one or more different acrylic compounds.

- Acrylate allergy in dental prosthetic work
 - o Patients from the study on dental technicians

A questionnaire was posted to 120 dental technicians registered with the local trade union in the greater Helsinki area. All who reported that they had hand dermatosis at the time of questionnaire then had a chance to undergo detailed dermatological examination. Twenty responded affirmatively to the question about present hand dermatosis, seven of whom came for dermatological examination.

- o Patients from the study on active sensitisation to acrylates

Twenty-two patients were examined during 1982-1985 because they were suspected of having occupational eczema due to acrylic compounds. Three of them were diagnosed as having allergic eczema developed in dental prosthetic work. Two of them were patients who had been examined during the first 10-year period.

- Acrylate allergy in dental restoration work

Altogether 7 patients were diagnosed between 1974 and 1987 as having allergic eczema caused by the acrylates to which they were exposed in dental restoration work. Two of these allergic eczema cases were detected during the 10-year period of 1974-1983.

- Acrylate allergy due to industrial exposures

4 patients diagnosed as having allergic eczema due to acrylic compounds developed in exposure other than dental work between 1974 and 1987 were included in this group. 2 of them were examined during the first 10-year period.

- Active sensitisation to acrylates

Patients who were actively sensitized to acrylates and the chemicals causing the sensitisation, were analysed in details. One of the 22 patients tested between 1982 and 1985 and 3/24 patients tested in 1985 and 1986 were actively sensitised to acrylates.

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

Seven acrylic compounds, used for patch tests in 1982-1985

Compound		Concentration (%) in pet
Butyl acrylate	(BA)	1 (F)
Tert-butyl acrylate	(t-BA)	1 (F)
Ethyl acrylate	(EA)	1 (F)
2-Ethylhexyl methacrylate		1 (F)
Hydroxypropyl methacrylate	(2-HPMA)	1 (F)
N-tert-butyl acrylamide		1 (F)
Methyl methacrylate	(MMA)	10 (H-S)

F Fluka Ab, Switzerland; H-S Hollister-Stier, USA

Patch test (meth)acrylate series used since September, 1985

Compound		Concentration (%) in pet
Ethyl acrylate	(EA)	0.5
Butyl acrylate	(BA)	0.5
2-Ethylhexyl acrylate		0.5
2-Hydroxyethyl acrylate	(2-HEA)	0.5
2-Hydroxypropyl acrylate	(2-HPA)	0.5
Methyl methacrylate	(MMA)	2.0
Ethyl methacrylate	(EMA)	2.0
n-Butyl methacrylate		2.0
2-Hydroxyethyl methacrylate	(2-HEMA)	2.0
2-Hydroxypropyl methacrylate	(2-HPMA)	2.0
Ethylene glycol dimethacrylate	(EGDMA)	2.0
Triethylene glycol dimethacrylate	(TREGDMA)	2.0
1,4-Butanediol dimethacrylate	(BUDMA)	2.0
Urethane dimethacrylate		2.0
2,2-bis[4-(2-methacryloxyethoxy)phenyl]propane		1.0
2,2-bis[4-(methacryloxy)phenyl]propane		2.0
2,2-bis[4-(2-hydroxy-3-methacryloxypropoxy)-phenyl]propane	(BIS-GMA)	2.0
1,4-Butanediol diacrylate		0.1
1,6-Hexanediol diacrylate		0.1
Diethylene glycol diacrylate		0.1
Tripropylene glycol diacrylate		0.1
Trimethylolpropane triacrylate		0.1
Pentaerythritol triacrylate		0.1
Oligotriacrylate 480		0.1
Epoxy diacrylate	(BIS-GA)	0.5
Urethane diacrylate (aliphatic)		0.1
Urethane diacrylate (aromatic)		0.1
Triethylene glycol diacrylate	(TREGDA)	0.1

Test substances from Chemotechnique Diagnostics Ab, Sweden

Results

Allergy to acrylates: the observations concerning 106 dental technicians participating in a study concerning occupational related hand dermatoses and allergies and concerning 14 patients who had allergic eczema caused by various acrylates or products containing acrylate were analysed. 6/14 patients sensitized to acrylic compounds were dental nurses, 2 were dentists, 2 were dental technicians. The others were a paint stock worker, a filer, a car furnisher and a pipe fitter.

Results related to HPMA:

- Patients from the study on active sensitisation to acrylates: 3/22 patients who were examined during 1982-1985 because they were suspected of having occupational dermatitis due to acrylates had allergic eczema developed in dental prosthetic work. 1 female dentist was patch test positive to 4 of the seven acrylic compounds tested, including HPMA. The 2 others were a female dental technician student and a female dental technician who were patch test positive to the same substances.
- Acrylate allergy in dental restoration work: 7 females patients had allergic eczema: 6 dental nurse and 1 dentist. The dentist and 2 dental nurses had allergic patch test reactions to many acrylates including HPMA.
- Acrylate allergy due to industrial exposures: 4 patients in this group; 2 with positive reactions to HPMA.

2.3.2.52 [Linstrom, 2002]

Study reference:

Lindström M, Alanko K, Keskinen H, Kanerva L. Dentist's occupational asthma, rhinoconjunctivitis, and allergic contact dermatitis from methacrylates. *Allergy*. 2002;57:543–5

Detailed study summary and results:

Test type

Case report

Occupational asthma and rhinoconjunctivitis were diagnosed in a dentist according to patient history, PEF monitoring, and a work-simulated bronchial provocation test. ACD (allergy contact dermatitis) was diagnosed by skin-patch testing with methacrylates with the occlusive Finn Chamber-technique.

Patient: A 47-year-old nonsmoking female dentist had been working in general dentistry for 22 years performing dental fillings, orthodontics, prosthetics and dental surgery. She had not had allergic symptoms as a child; however, her sister expressed an atopic constitution. When investigated at the authors' institute she had had symptoms of rhinoconjunctivitis and sneezing for 12 years, cough attacks for 10 years, and shortness of breath for 2 years. Furthermore, she had had hand and face dermatitis for 3 years. The symptoms were work-related and disappeared during weekends and holidays. The patient associated the eye and respiratory symptoms to making dental fillings with photo-bonded resins and to working with dental prostheses. The dermatitis also got worse from disinfectants and natural rubber latex gloves. The patient had occasionally used inhaled epinephrine or salbutamol for nearly 10 years. During the past few years, she needed bronchodilating medication almost every day at work. Asthma medication with inhaled steroids was begun more than 1 year ago. During this medication PEF-flow monitoring at work and at home (3 weeks) showed values between 540 and 500 l/min during days off, whereas the lowest values during working days were 420 l/min. The results pointed towards occupational asthma. The patient was remitted mainly because of the work-related respiratory symptoms but also because her hand dermatitis had worsened. When seen by the authors, a fissured, purulent pulpitis was observed on her left thumb, and milder dermatitis was present on the sides of the left thumb and the left forefinger. No asthmatic rales were heard from her lungs. She had been on sick leave for 2 weeks.

Spirometry was performed with a rolling-seal spirometer (Mijnhardt, Vicatest 3, Bunnik, The Netherlands) connected to a microcomputer (Medicro MR-3, Kuopio, Finland), and Viljanen's reference values were used. The histamine challenge test was performed according to Sovijarvi's method, following FEV1 (forced expiratory volume in one second) values with a Vitalograph S bellow spirometer (Vitalograph, Buckingham, UK). A 15% reduction in FEV1 was considered significant, and the provocative dose of histamine diphosphate causing a 15% reduction in FEV1 (PD15) was measured. The hyper-responsiveness was graded as strong (PD15<0.10 mg), moderate (0.11–0.40 mg) or slight (0.41–1.6 mg).

Routine skin prick tests (SPTs) to common environmental allergens were performed. Prick tests were also performed with natural rubber latex (Stallergenes S.A., Fresnes Cedex, France), chloramine T (1% and

CLH REPORT FOR METHACRYLIC ACID, MONOESTER WITH PROPANE-1,2-DIOL (HPMA)

human serum albumin (HSA) conjugate), and acrylates (Chemotechnique Diagnostics AB, Malmö, Sweden); 2-hydroxyethyl methacrylate (2-HEMA), methyl methacrylate, BIS-GMA, ethyleneglycol dimethacrylate, triethyleneglycol dimethacrylate (2%) and triethyleneglycol diacrylate (0.1%). 2-HEMA and BIS-GMA were also tested as HSA conjugates. Patch tests were performed according to the recommendations of the International Contact Dermatitis Research Group (ICDRG) with the occlusive Finn Chamber (Epitest, Tuusula, Finland) technique.

Inhalation challenge tests with a placebo (Coca solution) and dental liquid MAs were performed in a 6-m³ challenge chamber according to the international guidelines. The products used by the patient in her work were used in the work simulating challenge tests (ScotchbondH primer containing 40% of HEMA and adhesive containing 62% of BisGMA and HEMA 37%). No concentration measurements were carried out. The FEV1 and PEF values during the challenge test procedure were measured by a portable pocket-size spirometer (OneFlow tester ATS 94, Fuchs Medical, Saint Romans, France). The clinical symptoms and lung auscultation were recorded as well. The ocular reaction following the skin-patch tests to MAs was evaluated by an optometrist, as delayed conjunctivitis from MAs has earlier been reported.

Results

The patient's spirometry was normal and there was no significant response in the bronchodilation test (FVC 3.88 l, 108% of predicted, FEV1 3.12 l, 106% of predicted, and FEV1/FVC 80.55%, 98% of predicted). The histamine challenge test showed moderate bronchial hyper-reactivity with PD15 0.255 mg. The patient had been on sick leave for 2 weeks before the histamine challenge. There were no positive reactions in SPTs with common environmental allergens, natural rubber latex, chloramine-T, or acrylates. The total serum IgE was normal, 35 kU/l. The eosinophils in the peripheral blood were normal. The placebo challenge test was negative. In the first inhalation challenge test with metacrylates, the adhesive (20 drops altogether during 30 min) induced cough, rhinoconjunctivitis and a 10% decrease in FEV1 after 45 min. In the second test, with both the adhesive and the primer (40 drops during 30 min), an early late 23% FEV1 reduction was recorded, at a maximum at 3 h, as well as increased symptoms with dyspnea. Before the tests the inhaled steroids had been stopped for 8 days.

Patch testing with a MA series showed allergic reactions to several MAs, including 2-hydroxyethyl methacrylate (2-HEMA), present in Scotchbond (Table 1). In addition, patch testing induced itching, swelling and soreness of the eyelids, maximal during the 3-day patch test reading.

An optometrist's consultation indicated that the symptoms were in accordance to delayed allergic conjunctivitis.

She was ordered sick leave. On a control visit 10 months later, the patient did not have any symptoms of dermatitis or rhinoconjunctivitis. She still used inhaled steroids, and occasionally bronchodilators, e.g., when exposed to cigarette smoke. She did not use antihistamines, nasal steroids or eye drops. Two months before the control visit she had performed a work trial but developed strong respiratory reactions. It was concluded that she could not continue in her present work and needed retraining.

Table 1. The patient's positive patch test reactions with a (meth)acrylate series including 35 test substances

(Meth)acrylate	Source	Abbreviation	Patch test concentration (%) (w/w) (all allergens in petrolatum)	Patch test result
Glycidyl methacrylate	O	GMA	0.1	1+
Ethyl acrylate	C	EA	0.1	1+
Ethyl methacrylate	C	EMA	2	1+
2-Hydroxyethyl methacrylate	T	2-HEMA	1	2+
2-Hydroxypropyl methacrylate	C	2-HPMA	2	2+
Ethyleneglycol dimethacrylate	T	EGDMA	2	2+
Methyl methacrylate	C	MMA	2	1+

C = Chemotechnique (Malmö, Sweden); T = Trolab (Reinbek, Germany), O = prepared by ourselves.