Hydroxypropyl acrylate (all isomers)

(CAS No: 25584-83-2)

Health-based Reassessment of Administrative Occupational Exposure Limits

Committee on Updating of Occupational Exposure Limits,
a committee of the Health Council of the Netherlands

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1 Introduction

The present document contains the assessment of the health hazard of hydroxypropyl acrylates by the Committee on Updating of Occupational Exposure Limits, a committee of the Health Council of the Netherlands. The first draft of this document, which initially concerned 2-hydroxy-1-propyl acrylate only, was prepared by AAE Wibowo, Ph.D. (Coronel Institute, Academic Medical Centre, Amsterdam, the Netherlands).

In October 1997, literature was searched in the on-line databases Medline, Toxline, Chemical Abstracts, Embase (starting from 1966, 1967, 1970, and 1988, respectively), and HSELINE, NIOSHTIC, CISDOC, and MHIDAS (backwards from 1997), databases available from CD-ROM, using the following key words: 2-hydroxypropyl acrylate and 999-61-1. The final search was carried out in October 1997.

In December 1998, the President of the Health Council released a draft document on 2-hydroxy-1-propyl acrylate for public review. Comments were received from the following individuals and organisations: A Aalto (Ministry of Social Affairs and Health, Tampere, Finland).

Thereafter, when finalising the document for publication, the committee came across an evaluation of hydroxypropyl acrylate completed in March 1998 by the Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area of the Deutsche Forschungsgemeinschaft (DFG) - further referred to as German MAK-Kommission (DFG01). This evaluation addresses all hydroxypropyl acrylate isomers and their mixtures, amongst others presenting and discussing data from unpublished studies. The committee considered this information very useful. Therefore, the committee decided to evaluate the health hazards of all isomers and to extend the document with this information, mainly by citing from the German report unless indicated otherwise in the text. In addition, in October 2004, literature was searched in Medline and Toxline, starting from 1997, and using the following key words: hydroxypropyl acrylate, 25584-83-2, 999-61-1, 2918-23-2, and 2761-08-2.

In December 2004, the President of the Health Council released a revised draft of the document for public review. No comments were received.

2 Identity

name	hydroxypropyl acrylate (all isomers)	2-hydroxy-1-propyl acrylate	1-hydroxy-2-propyl acrylate	1-hydroxy-3-propyl acrylate
synonyms	acrylic acid, hydroxypropyl ester; 2-propenoic acid, hydroxypropyl ester; propylene glycol monoacrylate; acrylic acid, monoester with propanediol	1,2-propanediol-1-acrylate; 2-propenoic acid, 2-hydroxypropyl ester; ß-hydroxypropyl acrylate; propylene glycol monoacrylate; acrylic acid, 2-hydroxypropyl ester; 2-propanoic acid, monoester with 1,2-propanediol	1,2-propanediol-2-acrylate; 2-propenoic acid, 2-hydroxy-1-methylethyl ester	1,3-propanediol-1-acrylate; 2-propenoic acid, 3-hydroxypropyl ester
molecular formula	$C_6H_{10}O_3$	$C_6H_{10}O_3$	$C_6H_{10}O_3$	$C_6H_{10}O_3$
structural formula		$R\text{-}CH_2\text{-}CH(OH)CH_3$	$R\text{-}CH(CH_3)\text{-}CH_2OH$	$R\text{-}CH_2\text{-}CH_2\text{-}CH_2OH$
CAS number	25584-83-2	999-61-1	2918-23-2	2761-08-2

R: $H_2C{=}CH\text{-}CO\text{-}O\text{-}$

3 Physical and chemical properties

	hydroxypropyl acrylate (all isomers) (CAS No: 25584-83-2)	2-hydroxy-1-propyl acrylate (CAS No: 999-6-1)
molecular weight	130.14	130.14
boiling point	83ºC	225ºC
melting point	<-50ºC	-30ºC
flash point	not available	100ºC (open cup); 97ºC (closed cup); 65ºC
vapour pressure	10^{-4} Pa	at 20ºC: 5 Pa
solubility in water	not available	miscible
log $P_{octanol/water}$	not available	0.35 (experimental); 0.17 (estimated)
conversion factors	not applicable	at 20ºC, 101.3 kPa: 1 mg/m³ = 0.18 ppm 1 ppm = 5.42 mg/m³

Data from ACG02, DFG01, IPCS01, NLM04, http://www.syrres.com/esc/est_kowdemo.htm.

Apart from estimated log $P_{octanol/water}$ coefficients of 0.17 and 0.25 for 1-hydroxy-2-propyl and 1-hydroxy-3-propyl acrylate, respectively (http://esc.syrres.com), the committee did not find data on the physical and chemical properties of these 2 isomers.

2-Hydroxy-1-propyl acrylate is a clear to light yellow liquid with a sweetish, solvent odour (ACG02).

4 Uses

Hydroxypropyl acrylates, usually as isomer mixtures, are used in the industrial production of acrylate polymers for lacquers and artificial resins (DFG01), and as a co-monomer in adhesives, elastomers, inks, and oil additives and as a viscosity reducer (NLM04). Commercially available mixtures may consist of 75% 2-hydroxy-1-propyl acrylate and 25% 1-hydroxy-2-propyl acrylate or of 66% 2-hydroxy-1-propyl acrylate, 33% 1-hydroxy-2-propyl acrylate, and 1% free acrylic acid (DFG01). 2-Hydroxy-1-propyl acrylate is a monomer used in the manufacture of thermosetting resins for surface coatings (ACG02).

5 Biotransformation and kinetics

The committee did not find data on the biotransformation and kinetics of hydroxypropyl acrylate isomers.

6 Effects and mechanism of action

Human data

Data on effects of exposure to hydroxypropyl acrylates are limited to cases of allergenic effects and are summarised in Table 1.

Animal data

Irritation and sensitisation

When instilled into the eyes of rabbits, 2-hydroxy-1-propyl acrylate scored an injury grade of 7 on a scale of 1 to 10, which was defined as producing an injury grade of up to 5.0 points (out of a maximum of 20) 18 to 24 hours after instillation of an ‘excess’ of a 15% solution of the test substance (instillation of 0.5 µL undiluted material and a 40% solution give over 5.0 points (Smy69; see also Car46).

Citing unpublished information, the German MAK-Kommission reported that hydroxypropyl acrylate mixtures (75% 2-hydroxy-1-propyl acrylate and 25% 1-hydroxy-2-propylacrylate or 66% 2-hydroxy-1-propyl acrylate, 33% 1-hydroxy-2-propylacrylate, and 1% free acrylic acid) or 1-hydroxy-3-propyl acrylate were highly irritating or corrosive to the eyes of rabbits (DFG01).

Table 1 Summary of positive patch test results with hydroxypropyl acrylates on patients with suspected acrylate allergy (adapted from Gre01).

number of persons tested	concentration (vehicle)	results	remarks	reference
1 patient with conjunctivitis	not specified	(2+)	hearing aid laboratory worker who used also UV-cured lacquers	Est96
5 patients	5% (olive oil)	2/5 (both 2+)	sensitisation from adhesive tape acrylate components; hydroxypropyl acrylate produced moderate irritation in 'most' control persons	Jor75
5 patients (4 dental assistants, 1 dentist)	0.17% (petrolatum)	2/5 (2+ and 3+)	patients with suspected occupational sensitisation from acrylates in dental composite resins	Kan89
1 dentist	0.1% (petrolatum)	(3+)	patient with pharyngitis, no skin symptoms / reactions to 16 acrylates and methacrylates	Kan92
124 patients	0.1-0.5% (not specified)	12/124 (no other details)	summary of patch test results during 1985-1990 of patients with a history of exposure to (meth)acrylates; testing on the back with an occlusion time of 1 day (September 1985-1988) or 2 days (1989-1990)	Kan95[a]
8 patients	0.1 % (not specified)	2/8 (no other details)	summary of patch test results during 1991-1995 of patients with a history of exposure to (meth)acrylates; testing on the back with an occlusion time of 2 days	Kan97[a]
23 patients	0.1 % (petrolatum)	1/23 (2+; readings on 2nd and 3nd days)	summary of patch test results during 1990-1994 of patients with a history of exposure to acrylates; testing on the back for 2 days	Kie96
13 patients	0.5% (petrolatum)	6/13 (no other details)	reactions in 5/10 patients with artificial finger nails / also irritative reaction possible	Kop95
1 patient	1 % (petrolatum)	(2+; read after 2 and 4 days)	marked irritation 6-12 hours after occupational contact with hydroxypropyl acrylate; renewed skin reactions on returning to work after 6 months; in 6 control persons no reactions	Lov85
	0.1 % (petrolatum)	(2+, read after 48 and 96 hours)	acrylate lacquer of a leg prosthesis / reactions to 14 acrylates and methacrylates	Rom90
210 patients	0.5%	19/210 (no details)	retrospective appraisal of all patch test records from between January 1983 and March 1998 of patients with history of exposure to (meth)acrylates.	Tuc99

[a] This summary may include case reports that are reported by this group and listed in this table (Est96, Kan89, Kan92).

Following uncovered application of 0.01 mL of undiluted material to the clipped skin (abdomen) of albino rabbits (n=5), 2-hydroxy-1-propyl acrylate scored an injury grade of 5 on a scale from 1 to 10, which was defined as giving rise to strong erythema, oedema, or slight necrosis (Smy69; see also Smy49).

Unoccluded application of the aforementioned 75:25% isomer mixture to the intact skin of rabbits caused moderate irritation, while severe, deep-seated necrosis occurred within 8 days following occlusive application of the 66:33:1% mixture and of 1-hydroxy-3-propyl acrylate for 15 minutes and 4 hours, respectively. In a dermal LD_{50} test (value: 0.11 mL/kg bw or 118 mg/kg bw; see section 'Acute toxicity'), occluded application of a 75:25% mixture caused severe skin irritation leading to ecchymosis and oedema, and to necrosis at doses of 0.2 mL/kg bw (211 mg/kg bw) (DFG01).

In a Magnusson-Kligman guinea pig maximisation test, 12/12 female guinea pigs (SSc:Al) reacted positive when challenged on day 21 to 25 µL of a 3% solution of 2-hydroxypropyl acrylate in petrolatum (readings made 48 and 72 hours after challenge). In the induction phase, animals were, amongst others, treated with an intradermal injection of a 5% aqueous 2-hydroxy-1-propyl acrylate solution and a 48-hour occlusive application of 0.4 mL of a 25% 2-hydroxy-1-propyl acrylate solution. When similar inductions with 2-hydroxy-1-propyl acrylate were followed by challenges with 25 µL of solutions of 2-hydroxyethyl acrylate (3%), 2-hydroxyethyl methacrylate (25%), or 2-hydroxypropyl methacrylate (25%) in petrolatum, 12/12, 2/12, and 2/12 animals, respectively, reacted positive (Cle84). In another guinea pig maximisation test, no cross-sensitisation was observed in any of 10 guinea pigs when challenged with 2-hydroxy-1-propyl acrylate (2% in petrolatum) following intradermal and topical induction with 2-hydroxylpropyl methacrylate (5% in olive oil/acetone and 25% in petrolatum, respectively (Bjö84). In a summary on split adjuvant guinea pig sensitisation tests, Rao et al. reported that hydroxylpropyl acrylate (not further specified) induced no sensitising effects in any of 9 male guinea pigs (Hartley) following a challenge application of hydroxypropyl acrylate (not further specified) after a 2-week rest period following 4 topical applications to the clipped depilated skin in 10 days. Simultaneously to the third application, Freund's adjuvant was injected intradermally adjacent to the insult site. Actual concentrations applied were not presented but they were stated to be the highest not irritating concentration (Rao81).

Acute toxicity

No mortality was found in rats (n=6; strain and sex not indicated) following an 8-hour exposure to 'concentrated vapour'* of 2-hydroxy-1-propyl acrylate

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* Theoretically, the concentration in saturated air can amount to 50 ppm or ca. 270 mg/m^3 (calculated from: (vapour pressure in Pa x 10^6 ppm)/10^5 Pa)).

(concentration not reported; observation time: 14 days) (Smy69; see also Smy62).

All rats (n=5; strain and sex not indicated) survived a 7-hour exposure to an atmosphere of the aforementioned 75:25% mixture, saturated at room temperature (total concentration: ca. 650 ppm or 3523 mg/m^3). No lung, liver, or kidneys changes were observed upon macroscopic examination of one animal. Exposure to an atmosphere of the 75:25% mixture generated at 100ºC (concentration ca. 6450 ppm or ca. 35,000 mg/m^3) killed all rats (n=5) within 4.5 hours (Dow83). In another experiment, exposure of 6 rats for 8 hours to a similar atmosphere was reported to have caused transient coordination loss (DFG01). When 12 rats were exposed for 8 hours to an atmosphere of the aforementioned 66:33:1% mixture (see '*Irritation and sensitisation*') saturated at room temperature, dyspnoea and marked mucosal membrane irritation were observed (DFG01).

A dermal LD_{50} of 0.16 mL/kg bw (ca. 170 mg/kg bw) has been reported for 2-hydroxy-1-propyl acrylate in rabbits (24-hour covered application; observation time: 14 days) (Smy69; see also Smy62). For the 75:25% mixture applied under occlusion, a dermal LD_{50} of 0.11 mL/kg bw (i.e., 118 mg/kg bw) was reported for rabbits; for 1-hydroxy-3-propyl acrylate (24-hour occluded application), between 1000 and 1600 mg/kg bw in rats (DFG01).

Oral LD_{50}s of 8.1 mmol/kg bw (ca. 1060 mg/kg bw) in male mice (Tan82) and 1.23 mL/kg bw (ca. 1300 mg/kg bw) in male rats (Smy69; see also Smy62) were found for 2-hydroxy-1-propyl acrylate. Referring to unpublished information, the oral LD_{50} for 2-hydroxy-1-propyl acrylate in rats was reported to range from 250 to 500 mg/kg bw (ACG02, Bis94). For the 75:25% and 66:33:1% mixtures, oral LD_{50} values in rats amounted to 950-1130 mg/kg bw (DFG01).

The intraperitoneal LD_{50} in mice for the 66:33:1% mixture was 950 mg/kg bw (DFG01).

Repeated-dose toxicity

Apart from a 30-day inhalation toxicity study with a mixture in several species, the committee did not find repeated-dose toxicity studies.

In this inhalation study, male rats (Sprague-Dawley; n=10/group), mice (Swiss-Webster; n=20/group), rabbits (New-Zealand white; n=4/group), and dogs (Beagle; n=2/group) were exposed to vapour concentrations of a mixture of 74% 2-hydroxy-1-propyl acrylate, 25% 1-hydroxy-2-propyl acrylate, and 0.73%

free acrylic acid of 0, 5, and 10 ppm (ca. 0, 27, and 53 mg/m^3)*, 6 hours/day, 5 days/week, for a total of 20 (dogs, rabbits) or 21 (rats, mice) exposures. Animals were observed for signs of toxicity and irritation throughout the study. Effects on haematology, clinical chemistry, and urinalysis parameters and on body and organ weights were recorded and macroscopic and microscopic examinations were performed. There were no mixture-related changes in haematology, clinical chemistry, and urinalysis parameters or organ weights in any of the groups of any of the species. Signs of toxicity observed during the exposure period, effects on body weights, and macroscopic and microscopic findings are presented in Table 2. Besides the effects summarised in the table, there were macroscopic and microscopic changes in the testes and prostrate of one dog exposed to 10 ppm and of 2 dogs exposed to 5 ppm, and microscopic lesions in lymphatic and thymus tissue of one dog exposed to 10 ppm. Dow considered these effects not to be primary treatment-related but to be secondary to the stress associated with the respiratory tract effects and the sexual immaturity of the dogs (Dow83).

From this 30-day inhalation study, the committee concludes that conjunctivitis and inflammatory, degenerative, and/or hyperplastic changes in the (upper) respiratory tract are the key effects following exposure to a mixture of hydroxypropyl acrylate isomers. Based on incidence and severity of these effects, the committee considers the dog as the most sensitive species followed by the rabbit and the rat. Mice were the least sensitive, 27 mg/m^3 (5 ppm) being a NOAEL. For the other species, the committee could not set a NOAEL since exposure to 27 mg/m^3 (5 ppm), the lowest level tested, was still an adverse effect level.

Mutagenicity and genotoxicity

2-Hydroxypropyl acrylate (CAS No 25584-83-2) was found negative when tested with metabolic activation in *S. typhimurium* strains TA102 and TA2638 at concentrations of 156-5000 µg/plate. Tested with metabolic activation in *E. coli* strains WP2/pKM101 and WP2 *uvrA*/pKM101 at concentrations of 313-5000 µg/plate, positive results were obtained at concentrations of 1250 and 2500 and of 1250, 2500, and 5000 µg/plate, respectively. These results were from 3 trials in 2 laboratories (Wat96).

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* Mean analytical concentrations were 4.49±1.17 (range: 1.2-5.8 ppm) and 9.87±0.72 ppm (range: 8.5-10.9 ppm), respectively.

Table 2 Treatment-related effects in male rats, mice, rabbits, and dogs after inhalation exposure to a hydroxypropyl acrylate isomer mixture (74% 2-hydroxy-1-propyl acrylate, 25% 1-hydroxy-2-propyl acrylate, and 0.73% free acrylic acid), 6 hours/day, 5 days/week, for about 4 weeks (Dow83).

species (strain, number)	concentration (ppm)	findings
rat (Sprague-Dawley; n=20/group)	10	throughout study: in 5/10 slight corneal cloudiness; no effect on body weight post-mortem macroscopy: in 8/10 bilateral focal corneal clouding
	5	throughout study: no signs of toxicity; no effect on body weight post-mortem macroscopy: in 1/10 unilateral focal corneal clouding
	0	throughout study and post-mortem macroscopy: no effects
mouse (Swiss-Webster; n=20/group)	10	throughout study: in 3/20 eye irritation (no other details); weight loss during exposure (reversible during the exposure-free weekend) post-mortem macroscopy and histology (only 5 animals examined): no treatment-related effects
	5	throughout study and post-mortem macroscopy and histology (only 5 animals examined): no treatment-related findings
	0	no effects
rabbits (New Zealand White; n=4/group)	10	throughout study: in 4/4 slight rhinitis and moderate conjunctivitis; no effect on body weight post-mortem macroscopy: in 3/4 bilateral nasal discharge, in 1/4 bilateral conjunctivitis histology (4 animals examined): **upper respiratory passages:** in 4/4 mucopurulent rhinitis, squamous metaplasia and ulceration in the mucous membranes of the nasal concha; in 2/4 thickening of the mucous membranes of the nasal concha; in 1/4 subacute laryngitis **trachea:** in 3/4 subacute-chronic tracheitis; in 1/4 focal ulceration **lung:** in 2/4 subacute bronchiolitis, focal pneumonitis
	5	throughout study: in 2/4 slight rhinitis and eye irritation characterised by moderate conjunctivitis; no effect on body weight post-mortem macroscopy: in 4/4 nasal discharge histology (4 animals examined): **upper respiratory passages:** in 3/4 squamous metaplasia and ulceration in the mucous membranes of the nasal concha, mucopurulent rhinitis; in 1/4 subacute inflammation and focal mononuclear cells in the nasal mucosa; in 1/4 acute laryngitis **trachea:** in 3/4 subacute-chronic focal tracheitis **lung:** in 2/4 subacute focal pneumonitis; in 1/4 subacute bronchitis
	0	post-mortem macroscopy: in 1/4 minimal bilateral nasal discharge histology (4 animals examined): **upper respiratory passages:** in 4/4 focal mononuclear cells in nasal mucosa **trachea:** in 1/4 chronic focal tracheitis

dog (beagle; n=2/group)	10	throughout study: in 2/2 nasal discharge and bilateral corneal cloudiness, slight corneal oedema, bilateral suppurative conjunctivitis; weight loss during exposure, in some cases reversible during the exposure-free weekend post-mortem macroscopy: in 2/2 bronchopneumonia, in 1/2 nasal discharge and bilateral purulent conjunctivitis and keratitis histology (2 animals examined): **eye:** in 1/2 bilateral keratitis and conjunctivitis **upper respiratory passages:** in 2/2 continual purulent discharge from nose, marked inflammation, squamous metaplasia and hyperplasia and focal ulceration in the mucous membranes of the nasal concha **trachea:** in 2/2 tracheitis, changes in the mucous membranes as in upper respiratory passages **lung:** in 2/2 purulent bronchopneumonia
	5	throughout exposure: in1/2 slight rhinitis half-way study; no effect on body weight post-mortem macroscopy: no changes histology (2 animals examined): **eye**: in 1/2 chronic focal conjunctivitis **upper respiratory passages:** in 2/2 continual purulent discharge from nose, marked inflammation, squamous metaplasia and hyperplasia and focal ulceration in the mucous membranes of the nasal concha **lung:** in 1/2 focal interstitial pneumonia
	0	no effects

2-Hydroxypropyl acrylate was tested for chromosomal aberrations in Chinese hamster ovary cells (treatment time: 3 hours; sampling time: 20 hours) at doses of 15, 30, and 45 µg/mL in the absence or of 100, 140, and 160 µg/mL in the presence of an induced rat liver metabolic activating system. Higher concentrations were found to be cytotoxic (i.e., the number of viable cells was reduced by ca. 50% or more when compared to controls). A dose-dependent, statistically significant increase in the percentage of cells with chromosomal aberrations (without gaps) was observed at the 2 higher doses in the absence of metabolic activation. The aberrations consisted basically of chromatid deletions and exchanges and isolocus events. No statistically significant increases were seen when tested with a metabolic activating system (Cin02).

Reproduction toxicity

In a developmental toxicity study, pregnant rats (Sprague-Dawley; n=23-24/group) were exposed to concentrations of vaporised hydroxypropyl acrylate (purity: 97.5%; mixed isomers; composition not presented) of 0, 1, 5, and 10 ppm (ca. 0, 5.3, 27, and 53 mg/m^3), 6 hours/day, on gestational days 6 through 20, and sacrificed at gestational day 21. In the animals of the 10-ppm group, maternal weight gain during gestational days 6-13, absolute weight gain (defined as: body weight on day 21 minus gravid uterus weight minus body

weight on day 6), and food consumption were statistically significantly decreased when compared to controls, while in the animals exposed to 5 ppm a statistically significant decrease in absolute weight gain was observed. No statistically significant differences between treated and control groups were observed with respect to fetal weights, number of implantation sites and live fetuses, and the incidences of non-live implants, resorptions, and visceral and skeletal variations (Sai99). From this developmental toxicity study, the committee concludes that the NOAELs for maternal and developmental toxicity of a hydroxypropyl acrylate mixture in rats are 1 (5.3 mg/m^3) and ≥10 ppm (53 mg/m^3), respectively.

7 Existing guidelines

The current administrative occupational exposure limit (MAC) for 2-hydroxypropyl acrylate in the Netherlands is 3 mg/m^3, 8-hour TWA.

Existing occupational exposure limits for 2-hydroxypropyl acrylate in some European countries and in the USA are summarised in the annex.

8 Assessment of health hazard

The committee did not find data on the biotransformation and kinetics of hydroxypropyl acrylate isomers.

Data on the effects of exposure to hydroxypropyl acrylates in humans are limited to case and patch-test reports indicating that these acrylates are sensitising to the skin. The committee did not find data on effects on the respiratory tract.

In experimental animals, hydroxypropyl acrylates were highly irritating and corrosive to the eyes. Applied to the skin, they caused marked irritation and, occasionally, necrosis. In a guinea pig maximisation test with use of an adjuvant, hydroxypropyl acrylate was sensitising to the skin.

No mortality was observed in rats exposed to concentrated vapours of 2-hydroxy-1-propyl acrylate or to vapours of mixtures of isomers, saturated at room temperature, for 7-8 hours. Transient coordination loss or dyspnoea and marked mucosal membrane irritation were observed. Exposure to a vapour of an isomer mixture generated at 100°C was lethal to all 5 rats within 4.5 hours. Dermal LD_{50} values for 2-hydroxy-1-propyl acrylate and a mixture were ca. 170 and 118 mg/kg bw, respectively, in rabbits; for 1-hydroxy-3-propyl acrylate, they were between 1000 and 1600 mg/kg bw in rats. Oral LD_{50} values for 2-hydroxy-

1-propyl acrylate were ca. 1300 (males) or 250-500 mg/kg bw in rats and ca. 1060 mg/kg bw in (male) mice.

Male dogs, rabbits, rats, and mice were exposed to concentrations of vapours of a mixture of 74% 2-hydroxy-1-propyl acrylate, 25% 1-hydroxy-2-propyl acrylate, and 0.73% free acrylic acid of 0, 5, and 10 ppm (ca. 0, 27, and 53 mg/m^3)*, 6 hours/day, 5 days/week, for a total of 20 (dogs, rabbits) or 21 (rats, mice) exposures. Apart from weight losses in dogs and mice at 10 ppm, only effects indicative of (local) toxicity on the eyes and respiratory tract were found. Based on the incidence and severity of these effects, the committee considers the dog as the most sensitive, followed by the rabbit and the rat, and the mouse as the least sensitive species. For dogs, rabbits, and rats, the committee could not establish a NOAEL since the effects were still seen at 27 mg/m^3 (5 ppm), the lowest level tested. The committee did not find data on subchronic or chronic toxicity (including carcinogenicity) studies.

In vitro testing of 2-hydroxy-1-propyl acrylate with metabolic activation resulted in negative results in *S. typhimurium* but positive results in *E. coli*. The compound was positive when tested for chromosome aberrations in Chinese hamster cells in the absence, but negative in the presence of a metabolic activating system.

In a developmental toxicity study in which pregnant rats were exposed to concentrations of a vaporised mixture hydroxypropyl acrylate isomers (composition not presented) of 1, 5, and 10 ppm (ca. 5.3, 27, and 53 mg/m^3) on gestational days 6 through 20, the NOAELs for maternal and developmental toxicity were 1 (5.3 mg/m^3) and ≥10 ppm (53 mg/m^3), respectively, based on decreased maternal body weights at 10 ppm and absence of statistically significant differences between treated and control groups with respect to fetal weights, number of implantation sites and live fetuses, and the incidences of non-live implants, resorptions, and visceral and skeletal variations.

In the absence of a study with longer exposure duration, the committee takes the subacute inhalation studies, in which male dogs, rats, mice, and rabbits received 20-21 exposures to a mixture of hydroxypropyl acrylate isomers (Dow83), as a basis in deriving a health-based recommended occupational exposure limit (HBROEL). In these studies, conjunctivitis and upper and lower respiratory tract effects were the critical effects. The committee takes the LOAEL of 27 mg/m^3 (5 ppm) as the starting point for deriving an HBROEL. For the extrapolation to an HBROEL, the committee establishes an overall

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* Mean analytical concentrations were 4.49±1.17 (range: 1.2-5.8 ppm) and 9.87±0.72 ppm (range: 8.5-10.9 ppm), respectively.

assessment factor of 18. This factor covers the following aspects: the absence of a NOAEL, intraspecies variation, differences between experimental conditions and the exposure pattern of the worker, and the type of critical effect (i.e., local, but rather severe). The committee deems a factor for interspecies variation not necessary since four different species were tested in the key studies. Thus, applying this factor of 18 and the preferred-value approach, a health-based occupational exposure limit of 1 mg/m^3 (0.2 ppm) is recommended for hydroxypropyl acrylate isomers.

The committee recommends a health-based occupational exposure limit for hydroxypropyl acrylate (all isomers) of 1 mg/m^3 (0.2 ppm), as an 8-hour time-weighted average (TWA).

The committee notes that hydroxypropyl acrylates have skin-sensitising properties.

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Annex

Occupational exposure limits for 2-hydroxypropyl acrylate in various countries.

country - organisation	occupational exposure limit		time-weighted average	type of exposure limit	note[a]	reference[b]
	ppm	mg/m^3				
the Netherlands						
- Ministry of Social Affairs and Employment	0.5	3	8 h	administrative	S	SZW05
Germany						
- AGS	-	-				TRG04
- DFG MAK-Kommission	-	-[c, d]			sens	DFG05
Great-Britain						
- HSE	0.5	2.7	8 h	OES	S	HSE02
Sweden	-	-				Swe00
Denmark	0.5	3	8 h		S	Arb02
USA						
- ACGIH	0.5	-	8 h	TLV	S; sens	ACG05
- OSHA	-	-				ACG04
- NIOSH	0.5	3	10 h	REL	S	ACG04
European Union						
- SCOEL	-	-				EC05

[a] S = skin notation; which mean that skin absorption may contribute considerably to body burden; sens = substance can cause sensitisation.

[b] Reference to the most recent official publication of occupational exposure limits.

[c] Holds for all hydroxypropyl acrylate isomers (CAS number: 25584-83-2).

[d] Listed among compounds for which studies on effects in man or experimental animals have yielded insufficient information for the establishment of MAK values.