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Safety Assessment of Cross-Linked Alkyl Acrylates as Used in Cosmetics

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Abstract

The Cosmetic Ingredient Review (CIR) Expert Panel assessed the safety of cross-linked alkyl acrylates as used in cosmetics. The 23 cross-linked alkyl acrylates included in this safety assessment are reported to function as absorbents, film formers, emulsion stabilizers, viscosity increasing agents, suspending agents, binders, and/or skin-conditioning agents. The Panel reviewed available animal and clinical data, as well as information from previous CIR reports on monomer components. Because data were not available for the individual ingredients, and because residual monomer may be present, the Panel extrapolated from previous reports to support safety. The Panel concluded that cross-linked alkyl acrylates are safe in the present practices of use and concentration, provided that they are not polymerized in benzene. For those ingredients polymerized in benzene, the data available were insufficient to make a determination of safety. A risk assessment for the amount of benzene present would be needed.

Keywords

cross-linked alkyl amides, safety, cosmetics

Introduction

This draft final report includes information relevant to the safety of 23 cross-linked alkyl acrylates as used in cosmetic formulations. These cross-linked polymers consist of comonomers of at least 1 of the following: acrylic acid, sodium acrylate, methacrylic acid, or alkyl acrylate that share chemical properties, including a general lack of chemical reactivity. The ingredients included in this group are:

Acrylates/C10-30 alkyl acrylate cross polymer
Acrylates/C12-13 alkyl methacrylates/methoxyethyl acrylate cross polymer
Acrylates cross polymer
Acrylates/ethylhexyl acrylate cross polymer
Acrylates/ethylhexyl acrylate/glycidyl methacrylate cross polymer
Acrylates/PEG-4 dimethacrylate cross polymer
Acrylates/Steareth-20 methacrylate cross polymer
Acrylates/vinyl isodecanoate cross polymer
Acrylates/vinyl neodecanoate cross polymer
Allyl methacrylate/glycol dimethacrylate cross polymer
Allyl methacrylates cross polymer
Butyl acrylate/glycol dimethacrylate cross polymer
C8-22 alkyl acrylates/methacrylic acid cross polymer
Glycol dimethacrylate/vinyl alcohol cross polymer
Lauryl methacrylate/glycol dimethacrylate cross polymerr
Lauryl methacrylate/sodium methacrylate cross polymer
Methacrylic acid/PEG-6 methacrylate/PEG-6 dimethacrylate cross polymer
PEG/PPG-5/2 methacrylate/methacrylic acid cross polymer
Potassium acrylates/C10-30 alkyl acrylate cross polymer
Sodium acrylates cross polymer 2
Sodium acrylates/C10-30 alkyl acrylate cross polymer
Sodium acrylates/vinyl isodecanoate cross polymer
Stearyl/lauryl methacrylate cross polymer

These ingredients are reported to function in cosmetics as absorbents, film formers, emulsion stabilizers, viscosity increasing agents, suspending agents, binders, or skin-conditioning agents.

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In 2002, the Cosmetic Ingredient Review (CIR) published the Final Report on the Safety Assessment of Acrylates Copolymer and 33 Related Cosmetic Ingredients.[1] The Panel concluded that those ingredients were safe for use in cosmetics when formulated to avoid skin irritation. While copolymers are polymers synthesized from 2 or more different monomers, cross polymers are polymers that are cross-linked (ie, individual polymer chains are connected by bridging molecules [cross-linking agents]). Cross-linked polymers are generally less chemically reactive and less soluble (if not totally insoluble) than their respective non-cross-linked counterparts.

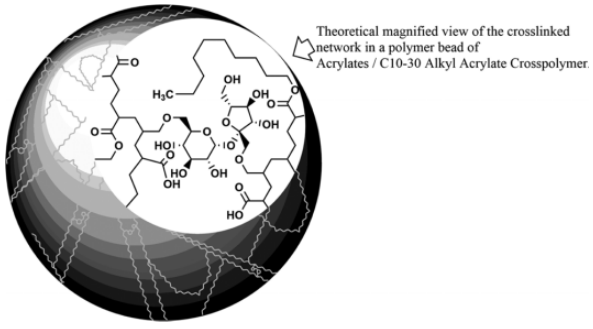
A CIR report on another family of polymers is also available. In 1982, the CIR published the Final Report on the Safety Assessment of Carbomers-934, -910, -934P, 940, -941, and -962, in which it was concluded that carbomers are safe as used.[2] That conclusion was reaffirmed in 2003.[3] A carbomer is a homopolymer of acrylic acid cross-linked with an allyl ether of pentaerythritol, an allyl ether of sucrose, or an allyl ether of propylene.[4]

Due to the paucity of published safety and toxicity data on these ingredients, this report includes summary information included in technical data sheets, ingredient specification sheets, and material safety data sheets (MSDSs); this information is identified as such.

Chemistry

Definition and Structure

Cross-linked alkyl acrylates are cross-linked polymers in which the comonomers consist of at least 1 of the following: acrylic acid, sodium acrylate, methacrylic acid, or alkyl acrylate. Whereas polymers consisting purely of acrylic acid are often referred to as "carbomers," copolymers comprised of mixtures of acrylic acid and alkyl acrylate monomers may sometimes be referred to as "alkyl carbomers." In that vein, most of the ingredients in this report could be classified as *cross-linked* alkyl carbomers. For example, dodecyl (C12 alkyl) acrylate, acrylic acid, and methacrylic acid could be copolymerized and cross-linked with diallyl sucrose to form an acrylates/C10-30 alkyl acrylate cross polymer with the internal structure.



Accordingly, although all of the monomers and cross-linking agents may be the same, 2 polymers with very different physical properties may share the same name under INCI conventions. The definitions and structures of the ingredients included in this review are provided in Table 1.

Physical and Chemical Properties

The available physical and chemical property information is provided in Table 2. The properties of a single ingredient, such as the above cross polymer, can vary from a highly swellable, soft material to an unswellable, very hard material because of the multitude of possible reaction conditions and the methods involved in the manufacture of these polymers. The nature of these ingredients is highly dependent on the identity of the alcohol radicals of these acrylate esters (eg, the stearyl and lauryl groups of stearyl/lauryl methacrylate cross polymer).[5] Acrylate cross polymers that correspond to 1 INCI name often have many trade names, and production processes may vary for different trade name products bearing the same INCI name. Since the products may have different properties, the trade name is included in parenthesis when available.

The polymers in this group share a general lack of chemical reactivity that renders them nearly impervious to degradation. These ingredients are essentially insensitive to solar ultraviolet light (UV) degradation, as the primary UV absorption of acrylics is at a lower wavelength.

Method of Manufacture

Cross-linked alkyl acrylates are typically produced via free radical, head-to-tail chain-propagation polymerization.[5] The most common method is the emulsion method, but bulk and solution methods are also used. The marked variability in the identity of monomers and cross-linking agents, the ratio of comonomers, the order of addition of comonomers, the level of cross-linking, and other reaction conditions in the polymerization process can significantly alter the polymeric structure and properties of the product.[6] Additionally, postsynthesis, mechanical processing of these products can also significantly affect the consistency of these ingredients. These variables will likely differ from vendor to vendor, and possibly even from batch to batch.

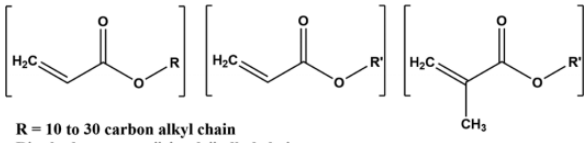
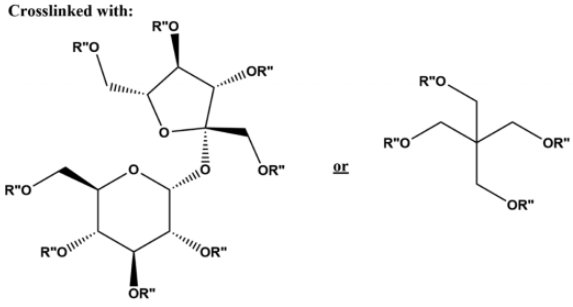
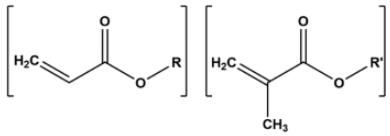
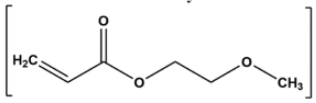
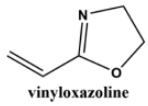
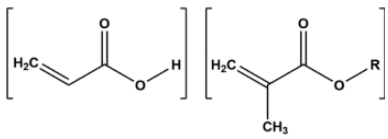
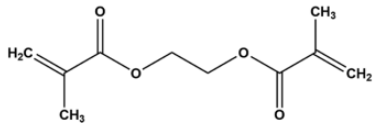
Table 3a lists the monomers used to create these cross polymers (based on INCI definition), and Table 3b names the cross-linking compounds and initiators used.[4]

Acrylates/C10-30 alkyl acrylate cross polymer. According to a trade product technical data sheet, acrylates/C10-30 alkyl acrylate cross polymer (as Pemulen) is polymerized in an ethyl acetate–cyclohexane mixture.[7] Another source reports that acrylates/C10-30 alkyl acrylate cross polymer may be polymerized in benzene.[8] A third supplier reports that acrylates/C10-30 alkyl acrylate cross polymer is polymerized in n-hexane.[9]

Acrylates/steareth-20 methacrylate cross polymer. Acrylates/steareth-20 methacrylate cross polymer (as Aculyn 88 polymer) is manufactured by an emulsion polymerization process.[10]

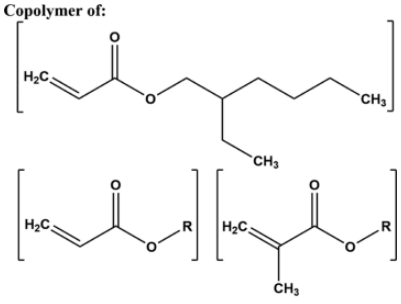
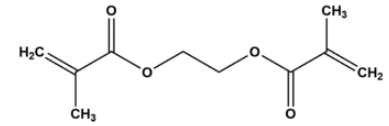
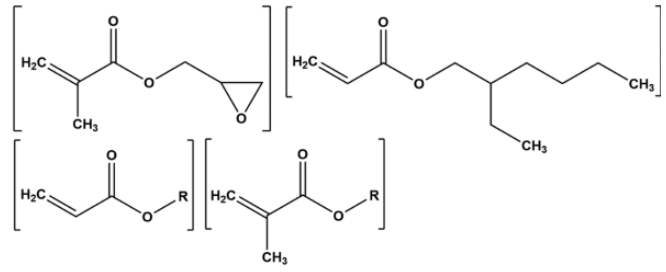
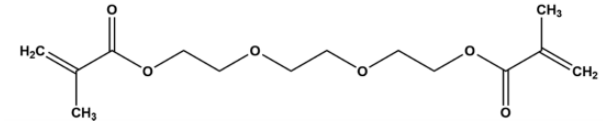
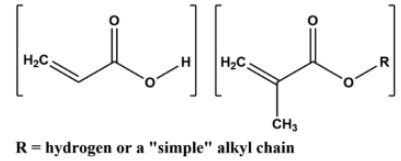
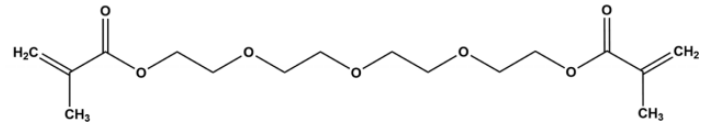
Acrylates/vinyl isodecanoate cross polymer. Acrylates/vinyl isodecanoate cross polymer (as Stabylen 30) is produced synthetically by a free radical polymerization.[11]

Table 1. Definitions, Functions, and Structures.[a]

Ingredient/CAS Number	Definition/Structure	Reported Function(s)
Acrylates/C10-30 alkyl acrylate cross polymer	A copolymer of C10-30 alkyl acrylate and 1 or more monomers of acrylic acid, methacrylic acid or 1 of their simple[b] esters cross-linked with an allyl (2-propenyl) ether of sucrose or an allyl ether of pentaerythritol **Copolymer of:**  **R = 10 to 30 carbon alkyl chain** **R' = hydrogen or a "simple" alkyl chain** **Crosslinked with:**  **R" = hydrogen or 2-propenyl, wherein at least two R" groups are 2-propenyl**	Emulsion stabilizer; viscosity increasing agent—aq; viscosity increasing agent—nonaq
Acrylates/C12-13 alkyl methacrylates/ methoxyethyl acrylate cross polymer	A copolymer of C12-13 alkyl methacrylates, methoxyethyl acrylate, and 1 or more monomers of acrylic acid, methacrylic acid, or 1 of their simple esters, cross-linked with vinyloxazoline **Copolymer of:**  **R = hydrogen or a "simple" alkyl chain** **R' = a 12 or 13 carbon alkyl chain**  **Crosslinked with:**  **vinyloxazoline**	Hair fixative
Acrylates cross polymer 26794-61-6 (when R is butyl) 74464-10-1 (when R is isobutyl)	A copolymer of acrylic acid, methacrylic acid, or 1 of its simple esters, cross-linked with glycol dimethacrylate **Copolymer of:**  **R = hydrogen or a "simple" alkyl chain** **Crosslinked with:** 	Absorbent

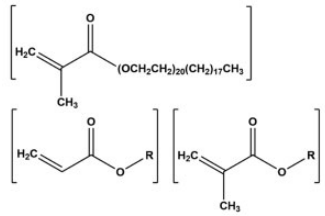
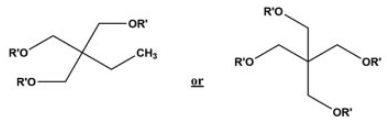
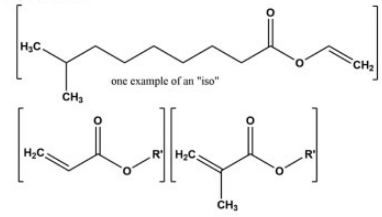
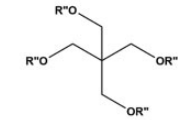
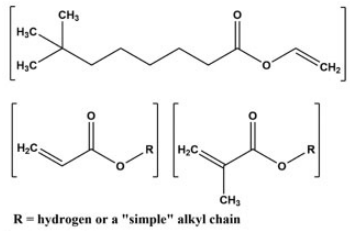
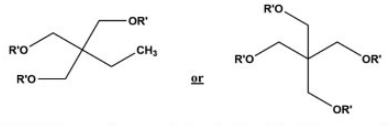
(continued)

Table 1. (continued)

Ingredient/CAS Number	Definition/Structure	Reported Function(s)
Acrylates/ethylhexyl acrylate cross polymer	A copolymer of 2 ethylhexylacrylate and 1 or more monomers of acrylic acid, methacrylic acid, or 1 of their simple esters, cross-linked with ethylene glycol dimethacrylate **Copolymer of:**  **R = hydrogen or a "simple" alkyl chain** **Crosslinked with:** 	Binder
Acrylates/ethylhexyl acrylate/glycidyl methacrylate cross polymer	A copolymer of 2-ethylhexyl acrylate, glycidyl methacrylate, and 1 or more monomers consisting of acrylic acid, methacrylic acid, or 1 of their simple esters, cross-linked with triethylene glycol dimethacrylate **Copolymer of:**  **R = hydrogen or a "simple" alkyl chain** **Crosslinked with:** 	Film former
Acrylates/PEG-4 dimethacrylate cross polymer 50657-38-0	A copolymer of 1 or more monomers of acrylic acid, methacrylic acid, or 1 of their simple esters cross-linked by PEG-4 dimethacrylate **Copolymer of:**  **R = hydrogen or a "simple" alkyl chain** **Crosslinked with:** 	Film former

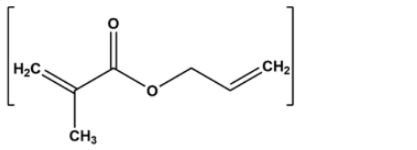
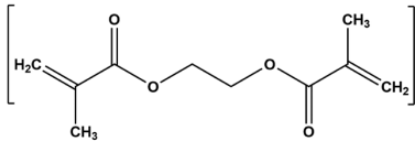
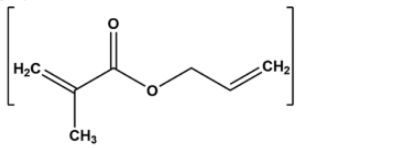
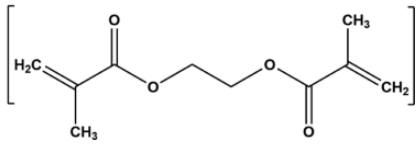
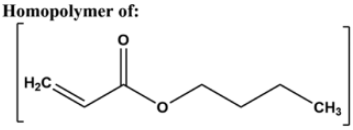
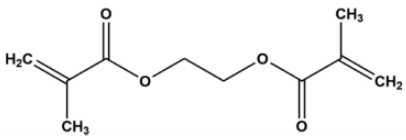
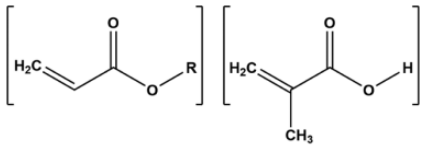
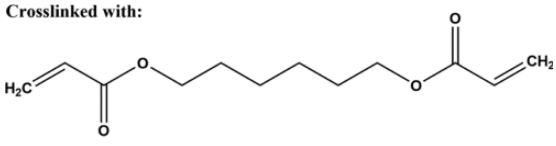
(continued)

Table 1. (continued)

Ingredient/CAS Number	Definition/Structure	Reported Function(s)
Acrylates/Steareth-20 methacrylate cross polymer	A copolymer of steareth-20 methacrylate and 1 or more monomers consisting of acrylic acid, methacrylic acid, or 1 of their simple esters, cross-linked with an allyl ether of pentaerythritol or an allyl ether of trimethylolpropane **Copolymer of:**  **R = hydrogen or a "simple" alkyl chain** **Crosslinked with:**  **R' = hydrogen or 2-propenyl, wherein at least two R' groups are 2-propenyl**	Film former; suspending agent—nonsurfactant
Acrylates/vinyl isodecanoate cross polymer	A copolymer of the ester of vinyl isodecanoate and 1 or more monomers of acrylic acid, methacrylic acid, or 1 of their simple esters cross-linked with polyalkenyl polyether **Copolymer of:**  **R = isododecyl (branched, 12 carbon chain)** **R' = hydrogen or a "simple" alkyl chain** **Crosslinked with a "polyalkenyl polyether." One example of such could be:**  **R" = hydrogen or 2-propenyl, wherein at least two R" groups are 2-propenyl**	Emulsion stabilizer; suspending agent—nonsurfactant; viscosity increasing agent—aq
Acrylates/vinyl neodecanoate cross polymer	A copolymer of vinyl neodecanoate and 1 or more monomers of acrylic acid, methacrylic acid, or 1 of their simple esters cross-linked with an allyl ether of trimethylolpropane or pentaerythritol **Copolymer of:**  **R = hydrogen or a "simple" alkyl chain** **Crosslinked with:**  **R' = hydrogen or 2-propenyl, wherein at least two R' groups are 2-propenyl**	Emulsion stabilizer; film former; viscosity increasing agent—aq

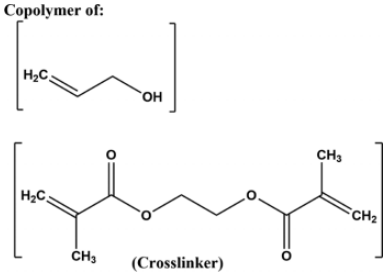
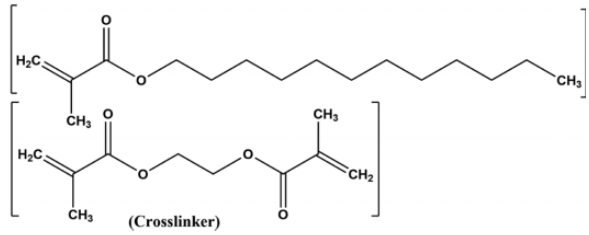
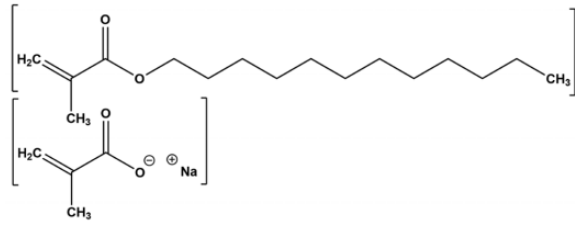
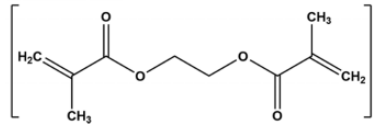
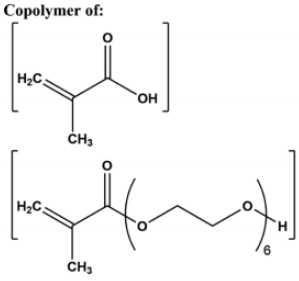
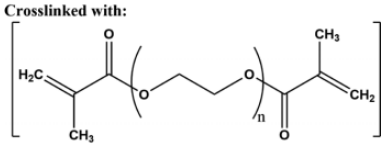
(continued)

Table 1. (continued)

Ingredient/CAS Number	Definition/Structure	Reported Function(s)
Allyl methacrylate/glycol dimethacrylate cross polymer 779327-42-3	A highly cross-linked polymer of allyl methacrylate and ethylene glycol dimethacrylate (diisopropyl peroxydicarbonate initiated) **Copolymer of:**   **Both of which can function as crosslinking agents**	Oral care agent; skin protectant; skin-conditioning agent—emollient; skin-conditioning agent—misc
Allyl methacrylates cross polymer 182212-41-5	A copolymer of allyl methacrylate cross-linked with ethylene glycol dimethacrylate **Copolymer of:**   **Both of which can function as crosslinking agents**	Emulsion stabilizer; opacifying agents; viscosity increasing agent—nonaq
Butyl acrylate/glycol dimethacrylate cross polymer	A homopolymer of butyl acrylate cross-linked with ethylene glycol dimethacrylate **Homopolymer of:**  **Crosslinked with:** 	Absorbent; film former
C8-22 alkyl acrylates/ methacrylic acid cross polymer	A copolymer of C8-22 alkyl acrylate and methacrylic acid cross-linked with hexanediol diacrylate **Copolymer of:**  **R = C8-22 alkyl chain** **Crosslinked with:** 	Film former; hair fixative; hair waving/ straightening agent

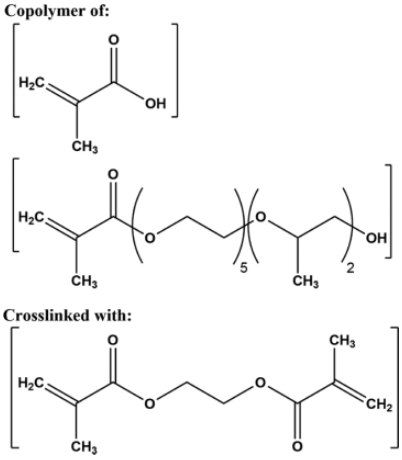
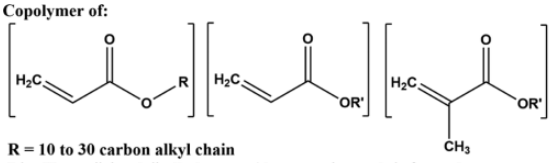
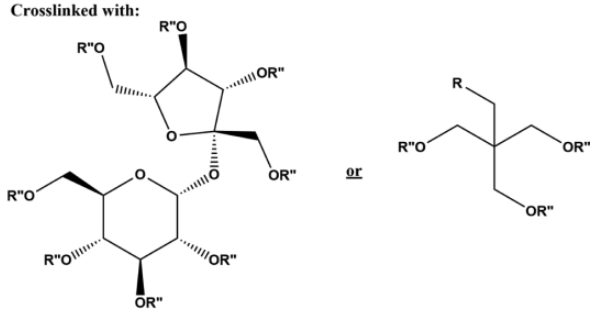
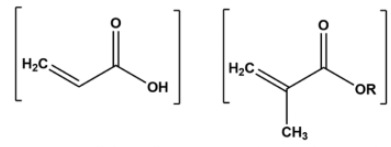
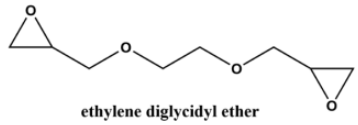
(continued)

Table 1. (continued)

Ingredient/CAS Number	Definition/Structure	Reported Function(s)
Glycol dimethacrylate/vinyl alcohol cross polymer	Vinyl alcohol and ethylene glycol dimethacrylate **Copolymer of:**  **(Crosslinker)**	Film former
Lauryl methacrylate/glycol dimethacrylate cross polymer	A cross-linked copolymer of lauryl methacrylate and ethylene glycol dimethacrylate monomers **Copolymer of:**  **(Crosslinker)**	Film former; hair fixative
Lauryl methacrylate/sodium methacrylate cross polymer	A copolymer of lauryl methacrylate and sodium methacrylate cross-linked with ethylene glycol dimethacrylate. **Copolymer of:**  **Crosslinked with:** 	Slip modifier; surface modifier
Methacrylic acid/PEG-6 methacrylate/PEG-6 dimethacrylate cross polymer	a copolymer of methacrylic acid and PEG-6 methacrylate cross-linked with polyethylene glycol dimethacrylate **Copolymer of:**  **Crosslinked with:**  wherein "n" is variable	Film former

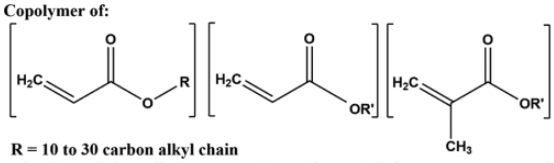
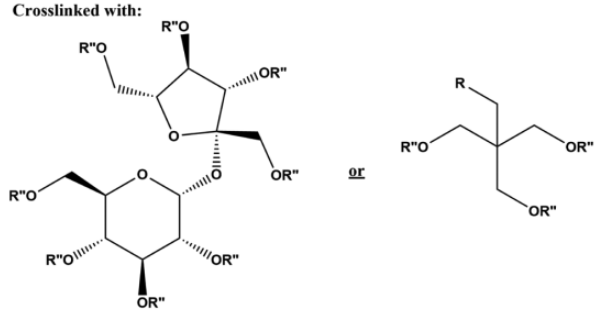
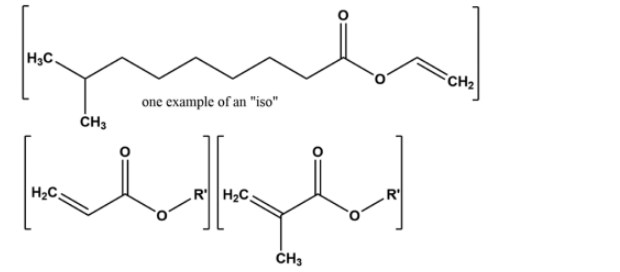
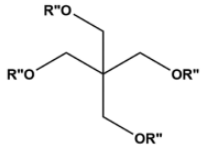
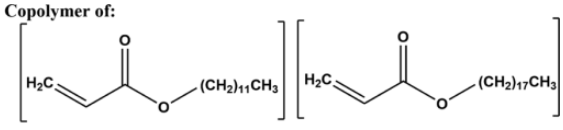
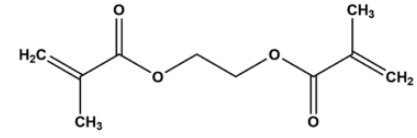
(continued)

Table 1. (continued)

Ingredient/CAS Number	Definition/Structure	Reported Function(s)
PEG/PPG-5/2 methacrylate/ methacrylic acid cross polymer	A copolymer of methacrylic acid and polyethylene glycol, polypropylene glycol methacrylate containing an average of 5 moles of ethylene oxide and 2 moles of propylene oxide, cross-linked with ethylene glycol dimethacrylate **Copolymer of:**  **Crosslinked with:** 	Film former
Potassium acrylates/C10-30 alkyl acrylate cross polymer	The potassium salt of acrylates/C10-30 alkyl acrylate cross polymer **Copolymer of:**  **R = 10 to 30 carbon alkyl chain** **R' = H or a "simple" alkyl group (the potassium salt is formed post-polymerization)** **Crosslinked with:**  **R" = hydrogen or 2-propenyl, wherein at least two R" groups are 2-propenyl**	Film former
Sodium acrylates cross polymer-2	The sodium salt of a copolymer of acrylic acid, methacrylic acid, or 1 or more of its simple esters, cross-linked with ethylene diglycidyl ether **Copolymer of:**  **R = H or a "simple" alkyl group (the sodium salt is formed post-polymerization)** **Crosslinked with:**  **ethylene diglycidyl ether**	Absorbent

(continued)

Table 1. (continued)

Ingredient/CAS Number	Definition/Structure	Reported Function(s)
Sodium acrylates/C10-30 alkyl acrylate cross polymer	The sodium salt of acrylates/C10-30 alkyl acrylate cross polymer **Copolymer of:**  **R = 10 to 30 carbon alkyl chain** **R' = H or a "simple" alkyl group (the sodium salt is formed post-polymerization)** **Crosslinked with:**  **R" = hydrogen or 2-propenyl, wherein at least two R" groups are 2-propenyl**	Film former
Sodium acrylates/vinyl isodecanoate cross polymer	The sodium salt of acrylates/vinyl isodecanoate cross polymer. **Copolymer of:**  **R = isododecyl (branched, 12 carbon chain)** **R' = H or a "simple" alkyl group (the sodium salt is formed post-polymerization)** **Crosslinked with a "polyalkenyl polyether." One example of such could be:**  **R" = hydrogen or 2-propenyl, wherein at least two R" groups are 2-propenyl**	Emulsion stabilizer; suspending agent—nonsurfactant; viscosity increasing agent—aq
Stearyl/lauryl methacrylate cross polymer	A copolymer of lauryl methacrylate and stearyl methacrylate cross-linked with ethylene glycol dimethacrylate **Copolymer of:**  **Crosslinked with:** 	Skin-conditioning agent—misc

Abbreviations: aq, aqueous; misc, miscellaneous.
[a]References.[4,8,48]
[b]According to the International Cosmetic Ingredient Dictionary and Handbook nomenclature conventions, "simple," as used herein, is "described as simple alkyls ranging from C1 to C4 (linear or branched)."

Table 2. Chemical and Physical Properties.

Property	Description	Reference
Acrylates/C10-30 alkyl acrylate cross polymer		
Appearance	White powder;	13-19
Odor	Slightly acetic	13-19
Activity, as supplied	Approximately 100% active	8
Molecular weight	>500 000 Da	8
Solubility	swells in water	39
pH	~2.5-3 at 1% in water[39]	
Heavy metals content	10 ppm (max), under all trade names	13-19
Specific gravity	1.4 (at 20°C)	39
Particle size (as tested by 1 source)	2-7 μm	23
Bulk density	<0.24 kg/L; <2 lb/gal	39
Acrylates cross polymer		
Particle size (as tested by 1 source)	18-22 μm	24
Heavy metal content	Lead, 10 ppm (max) arsenic, 2 ppm (max)	25
Acrylates/Steareth-20 methacrylate cross polymer		
Appearance (Aculyn 88 polymer)	Milk-white fluid	10
Solids content (Aculyn 88 polymer)	28.0%-30.0% by weight	10
Heavy metal content (Aculyn 88 polymer)	Iron, 1.028 ppm zinc, 0.082 ppm	
pH (Aculyn 88 polymer)	3.30-4.30	10
Acrylates/vinyl isodecanoate cross polymer		
Molecular weight	24 400 Da (average; <1% by weight is <1000 Da)	11
Acrylates/vinyl neodecanoate cross polymer		
Appearance (Aculyn 38 polymer)	Milk-white fluid	12
Solids content (Aculyn 38 polymer)	28.0%-30.0% by weight	12
Activity, as supplied	29% solids in 71% water	26
Heavy metal content (Aculyn 38 polymer)	Copper, 0.2 ppm iron, 0.5 ppm zinc, 1.2 ppm	12
pH (as Aculyn 38 polymer)	2.10-3.20	12
Allyl methacrylates cross polymer		
Appearance	Fine white powder	49,50
Solubility	Insoluble	49,50
Refractive index	1.517-1.519 1.511-1.513	49 50
Particle size (by laser diffraction)	5-15 μm 15-25 μm	49 50
Bulk density	0.03 g/cc	49,50
Water adsorption	Oleophilic (hydrophobic) dual: hydrophilic and oleophilic	50
Sodium acrylates cross polymer-2		
Appearance	White powder	28
Odor	Odorless	41
Solubility	Swells in water	41
pH	6-8	41
Particle size	Approx. 20 μm	28
Bulk density	0.75-0.95 g/ml	41
Stability	Stable at room temperature	41

Acrylates/vinyl neodecanoate cross polymer. Acrylates/vinyl neodecanoate cross polymer (as Aculyn 38 polymer) is manufactured by an emulsion polymerization process.[12]

Impurities and Residual Monomer or Solvent

Acrylates/C10-30 alkyl acrylate cross polymer. According to product specification sheets from 1 company, acrylates/C10-30 alkyl acrylate cross polymer can contain (total) residual solvent (ethyl acetate + cyclohexane) at a maximum of 0.45% (Carbopol 1382; Carbopol Ultrez 20; Carbopol Ultrez 21)[13-15] or 0.5% (Pemulen TR1; Pemulen TR2; Carbopol ETD 2020).[16-18] Another supplier, who uses n-hexane as a solvent, reported that the maximum residual solvent in the polymer is 0.2% n-hexane.[9]

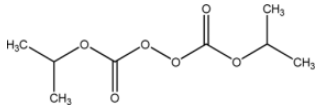
As Carbopol 1342, the product specifications state that acrylates/C10-30 alkyl acrylate cross polymer can contain 0.5%

Table 3a. Monomers Used to Create Cross-Linked Alkyl Acrylates.

Acrylic acid
Acrylic acid, simple esters (simple alkyls ranging from C1 to C4, linear or branched, ie, methyl, ethyl, propyl, and butyl esters, including branched versions: isopropyl, isobutyl, sec-butyl, and tert-butyl esters)
Butyl acrylate
C8-22 alkyl acrylate
2-Ethylhexyl acrylate
Glycidyl methacrylate
Lauryl methacrylate
Methacrylic acid
Methacrylic acid, simple esters (simple alkyls ranging from C1 to C4, linear or branched, ie, methyl, ethyl, propyl, and butyl esters, including branched versions: isopropyl, isobutyl, sec-butyl, and tert-butyl esters)
PEG-6 methacrylate
PEG/PPG-5/2
Sodium methacrylate
Steareth-20 methacrylate
Stearyl methacrylate
Vinyl alcohol
Vinyl isodecanoate, ester of
Vinyl neodecanoate

Table 3b. Cross-Linkers and Initiators Used in Manufacture of Acrylate cross polymers.

Allyl methacrylate
Ethylene diglycidyl ether
Glycol dimethacrylate
Hexanediol diacrylate
PEG-4 dimethacrylate
Pentaerythritol, allyl ether
Polyalkenyl polyether
Polyethylene glycol dimethacrylate
Sucrose, allyl ether
Triethylene glycol dimethacrylate
Trimethylolpropane, allyl ether
Diisopropyl peroxydicarbonate (initiator)



(max) residual benzene.[19] A supplier reported that analysis of 40 lots of Carbopol 1342 indicated that the average level of benzene was 0.25%, and the level ranged from 0.04% to 0.41% benzene.[20] (According to the European Commission Cosmetics Directive, benzene cannot be present as a constituent of other substances, or in mixtures, in concentrations equal to, or greater than 0.1% by weight.[21] As another point of reference, US Pharmacopeia limits for benzene for several carbomers manufactured with benzene range from 0.01% to 0.5%.[22])

One source stated that residual monomer content of acrylates/C10-30 alkyl acrylate cross polymer (trade name not provided) is typically less than 0.25% acrylic acid and less than 0.5% residual ester (C10-30 alkyl acrylate),[8] while another stated that acrylic acid monomer content is <0.1%.[23]

Acrylates cross polymer. One source reported that acrylates cross polymer contained <0.005% methyl methacrylate and <0.005% butyl acrylate,[24] and another reported 0.005% (max) of methyl methacrylate, ethylene methacrylate, and isobutyl methacrylate, and that acrylates cross polymer did not contain residual solvents or preservatives.[25]

Acrylates/steareth-20 methacrylate cross polymer. The composition of acrylates/steareth-20 methacrylate cross polymer (as Aculyn 88 polymer) is stated as 28.0% to 30.0% acrylates/steareth-20 methacrylate cross polymer, <0.01% residual monomer, 70.0% to 72.0% solvent (water), and 0.195% (max) sodium benzoate.[10] According to actual analytical specifications, the amount of residual ethyl acrylate present is ≤0.0001%.

Acrylates/vinyl isodecanoate cross polymer. The residual acrylic acid monomer content of acrylates/vinyl isodecanoate cross polymer (Stabylen 30) is reported to be <0.05% by weight.[11]

Acrylates/vinyl neodecanoate cross polymer. The composition of acrylates/vinyl neodecanoate cross polymer (as Aculyn 38 polymer) is stated as 28.0% to 30.0% acrylates/vinyl neodecanoate cross polymer, <0.1% residual monomer, and 70.0% to 72.0% solvent (water).[12] According to actual analytical specifications, the amount of residual ethyl acrylate present was ≤0.0001%.

Another source reported the residual monomer level of acrylates/vinyl neodecanoate cross polymer is <0.01%.[26]

Lauryl methacrylate/glycol dimethacrylate cross polymer. The residual monomer levels of lauryl methacrylate/glycol dimethacrylate cross polymer are <0.01% lauryl methacrylate and <0.01 ppm ethylene glycol dimethacrylate.[27] Lauryl methacrylate/glycol dimethacrylate cross polymer has a residual solvent level of ≤0.1% isopropanol. The ingredient can contain up to 2% adsorbed water.

Sodium acrylates cross polymer 2. The maximum amount of residual monomer content in sodium acrylates cross polymer 2 (Aqua Keep 10SH-NFC) is 0.02%.[28]

Use

Cosmetic

Cross-linked alkyl acrylates are reported to function as absorbents, film formers, emulsion stabilizers, viscosity increasing agents, suspending agents, binders, and/or skin-conditioning agents in cosmetic formulations.[4] Acrylates/C10-30 alkyl acrylate cross polymer functions as a primary emulsifier in oil-in-water emulsions.[7] Voluntary Cosmetic Registration Program data obtained in 2011,[29] and the concentration of use information received in response to a survey conducted by the Personal Care Products Council,[30] indicates that 11 of the 23 cross-linked alkyl acrylates named in this report currently are used

in cosmetic formulations. Acrylates/C10-30 alkyl acrylate cross polymer has the greatest number of uses, with 1,696 reported; 1,365 of those uses are in leave-on products. Acrylates cross polymer, acrylates/vinyl isodecanoate cross polymer, acrylates/vinyl neodecanoate cross polymer, allyl methacrylates cross polymer, lauryl methacrylate/glycol dimethacrylate cross polymer, lauryl methacrylate/sodium methacrylate cross polymer, and sodium acrylates/C10-30 alkyl acrylate cross polymer are all used in less than 75 formulations.

Some acrylates/C10-30 alkyl acrylate cross polymers are polymerized in benzene; the highest reported concentrations of use of this ingredient when polymerized in benzene are 0.4% and 1.1% for leave-on and rinse-off products, respectively.[31] The use concentrations for acrylates/C10-30 alkyl acrylate cross polymer not polymerized in benzene are up to 5% in leave-on and rinse-off products; 5% is the highest rinse-off concentration of use of the cross-linked alkyl acrylates. The highest concentration of use reported in leave-on cross-linked alkyl acrylates is 6% acrylates/ethylhexyl acrylate cross polymer.[30] Frequency and concentration of use data are provided in Table 4a. The ingredients not reported to be used are listed in Table 4b.

Products containing some cross-linked alkyl acrylates may be applied to baby skin, used near the eye area or mucous membranes, or could possibly be ingested or inhaled. In practice, 95% to 99% of the particles released from cosmetic sprays have aerodynamic equivalent diameters in the 10 to 110 μm range.[32,33] Therefore, most particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal region and would not be respirable to any appreciable level.[34,35] There is some evidence indicating that deodorant spray products can release substantially larger fractions of particulates having aerodynamic diameters in the range considered to be respirable.[35] However, the information is not sufficient to determine whether significantly greater lung exposures result from the use of deodorant sprays, compared to other cosmetic sprays.

All of the ingredients included in this review, with the exception of acrylates/C12-13 alkyl methacrylates methoxyethyl acrylate cross polymer and methacrylic acid/PEG-6 methacrylate/PEG-6 dimethacrylate cross polymer, are listed in the European Union inventory of cosmetic ingredients.[36] The 2 ingredients that are not included in the European Union inventory are in the process of being named and will be added once that process is complete.[37]

Noncosmetic

Acrylic ester polymers are used in coatings, textiles, adhesives, and paper manufacture.[5]

Toxicokinetics

Published toxicokinetics, absorption, distribution, metabolism, and excretion data were not found for the cross polymers. Large polymeric structures, however, such as cross-linked alkyl acrylates, generally are not absorbed through the skin. Toxicokinetics data on some of the monomers are provided in Table 5.

Effect on Skin Permeation

Acrylates/C10-30 alkyl acrylate cross polymer. A topical formulation vehicle that included acrylates/C10-30 alkyl acrylate cross polymer (Pemulen TR-2), in combination with PEG 400 and carbomer, reduced the permeation of *N*,*N*-diethyl-*m*-toluamide through skin.[38] Evaluations were made in vitro using excised rat skin and in vivo using Beagle dogs.

Toxicological Studies

To aid in the evaluation of the safety of these cross polymers, Table 5 provides a brief summary of relevant data on a number of monomer components. (This summary is not intended to be an all-encompassing review of these monomers.)

Single-Dose (Acute) Toxicity

Dermal

Acrylates/C10-30 alkyl acrylate *cross polymer.* According to an industry MSDS, the dermal LD_{50} of acrylates/C10-30 alkyl acrylate cross polymer (as Pemulen TR1) in rabbits is >2.0 g/kg.[39]

Acrylates/vinyl neodecanoate *cross polymer.* The dermal LD_{50} of acrylates/vinyl neodecanoate cross polymer (as Aculyn 38 polymer) in rabbits is >5.0 g/kg.[12]

Oral

Acrylates/C10-30 alkyl acrylate *cross polymer.* According to an industry MSDS, the oral LD_{50} of acrylates/C10-30 alkyl acrylate cross polymer (as Pemulen TR1) in rats is >10 g/kg.[39] Another source provided information from an MSDS, stating that the oral LD_{50} in rats is >2 g/kg.[23]

Acrylates/vinyl isodecanoate *cross polymer.* The oral LD_{50} acrylates/vinyl isodecanoate cross polymer (as Stabylen 30) in rats is >2 g/kg body weight.[40]

Acrylates/vinyl neodecanoate *cross polymer.* The oral LD_{50} of acrylates/vinyl neodecanoate cross polymer (as Aculyn 38 polymer) in rats is >5.0 g/kg.[12]

Sodium acrylates cross polymer 2. According to an industry MSDS, the oral LD_{50} of sodium acrylates cross polymer 2 (as Aqua Keep 10SH-NFC) in rats is >2 g/kg.[41]

Inhalation

Acrylates/vinyl neodecanoate *cross polymers.* The inhalation LC_{50} of acrylates/vinyl neodecanoate cross polymer (as Aculyn 38 polymer) in rats is >16.34 mg/L air (1 hour).[12]

Repeated Dose Toxicity

Inhalation

Acrylates/C10-30 alkyl acrylate *cross polymer.* In an industry MSDS for acrylates/C10-30 alkyl acrylate cross polymers (as Pemulen TR-1), a 2-year inhalation study in which rats were exposed to a respirable, water-absorbent sodium polyacrylate dust is described under toxicological information. Lung effects such as

Table 4a. Frequency and Concentration of Use According to Duration and Type of Exposure.

	# of Uses[29]	Concentration of Use (%)[30]		# of Uses[29]	Concentration of Use (%)[30]	# of Uses[29]	Concentration of Use (%)[30]
	Acrylates/C10-30 Alkyl Acrylate Cross Polymer			Acrylates Cross Polymer		Acrylates/Ethylhexyl Acrylate Cross Polymer	
Totals[a]	**1696**	**0.0002-5** (not Polymerized in Benzene[30])	**0.05-1.1** (Polymerized in Benzene[31])	**2**	**0.1-4**	**NR**	**4-6**
Duration of use							
Leave-on	*1365*	*0.0002-5*	*0.05-0.4*	*2*	*0.1-4*	*NR*	*4-6*
Rinse off	*313*	*0.002-5*	*0.2-1.1*	*NR*	*0.3-0.8*	*NR*	*NR*
Diluted for (bath) use	*18*	*1*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure type							
Eye area	132	0.003-2	NR	NR	0.8	NR	6
Incidental ingestion	3	0.5	NR	NR	4	NR	NR
Incidental inhalation—sprays	70[b,c]	0.03-2	NR	NR	NR	NR	NR
Incidental inhalation—powders	6	0.0002-0.1	NR	NR	2	NR	NR
Dermal contact	1591	0.0002-5	0.05-1.1	2	0.1-4	NR	4-6
Deodorant (underarm)	1	0.001	NR	NR	NR	NR	NR
Hair—non-coloring	77	0.1-2	0.2	NR	NR	NR	NR
Hair—coloring	11	0.4-5	NR	NR	NR	NR	NR
Nail	9	0.1-1	NR	NR	NR	NR	NR
Mucous membrane	111	0.002-3	NR	NR	4	NR	NR
Baby products	10	0.2	NR	NR	NR	NR	NR

	Acrylates/Steareth-20 Methacrylate Cross Polymer		Acrylates/Vinyl Isodecanoate Cross Polymer		Acrylates/Vinyl Neodecanoate Cross Polymer	
Totals[a]	**NR**	**0.1-2**	**33**	**0.2-0.5**	**10**	**2**
Duration of use						
Leave-on	*NR*	*0.1-2*	*25*	*0.3-0.5*	*4*	*NR*
Rinse off	*NR*	*1*	*8*	*0.2-0.5*	*4*	*2*
Diluted for (bath) use	*NR*	*NR*	*NR*	*NR*	*2*	*2*
Exposure type						
Eye area	NR	NR	NR	NR	NR	NR
Incidental ingestion	NR	NR	NR	NR	NR	NR
Incidental inhalation—sprays	NR	NR	NR	0.4	NR	NR
Incidental inhalation—powders	NR	NR	NR	NR	NR	NR
Dermal contact	NR	0.1-1	33	0.2-0.5	10	2
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair—non-coloring	NR	2	NR	NR	NR	NR
Hair—coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR
Mucous membrane	NR	1	NR	NR	6	2
Baby products	NR	NR	NR	NR	NR	NR

	Allyl Methacrylates Cross Polymer		Lauryl Methacrylate/Glycol Dimethacrylate Cross Polymer		Lauryl Methacrylate/Sodium Methacrylate Cross Polymer	
Totals[a]	**48**	**0.003-2**	**63**	**0.06-3**	**1**	**0.004-4**
Duration of use						
Leave-on	*44*	*0.003-2*	*56*	*0.06-3*	*1*	*0.1-4*
Rinse off	*4*	*0.1*	*7*	*0.2-3*	*NR*	*0.004-0.1*
Diluted for (bath) use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type						
Eye area	4	0.003-0.8	9	0.1-3	NR	NR
Incidental ingestion	16	0.04-0.2	8	0.06-2	NR	NR
Incidental inhalation—sprays	2[c]	NR	1[b]	0.3	NR	NR

(continued)

Table 4a. (continued)

	# of Uses[29]	Concentration of Use (%)[30]	# of Uses[29]	Concentration of Use (%)[30]	# of Uses[29]	Concentration of Use (%)[30]
	Allyl Methacrylates Cross Polymer		Lauryl Methacrylate/Glycol Dimethacrylate Cross Polymer		Lauryl Methacrylate/Sodium Methacrylate Cross Polymer	
Totals[a]	**48**	**0.003-2**	**63**	**0.06-3**	**1**	**0.004-4**
Incidental inhalation—powders	2	0.3-0.8	8	0.1-1	NR	NR
Dermal contact	31	0.003-2	53	0.06-3	1	0.004-4
Deodorant (underarm)	NR	NR	1	0.3	NR	NR
Hair—non-coloring	NR	NR	NR	NR	NR	NR
Hair—coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	1	NR	NR	NR
Mucous membrane	16	0.04-0.2	8	0.06-2	NR	NR
Baby products	NR	NR	NR	NR	NR	NR
	Sodium Acrylates/C10-30 Alkyl Acrylate Cross Polymer		Sodium Acrylates Cross Polymer-2			
Totals[a]	**6**	**NR**	**NR**	**0.8**		
Duration of use						
Leave-on	*6*	*NR*	*NR*	*0.8*		
Rinse off	*NR*	*NR*	*NR*	*NR*		
Diluted for (bath) use	*NR*	*NR*	*NR*	*NR*		
Exposure type						
Eye area	NR	NR	NR	NR		
Incidental ingestion	NR	NR	NR	NR		
Incidental inhalation—sprays	1	NR	NR	NR		
Incidental inhalation—powders	NR	NR	NR	NR		
Dermal contact	6	NR	NR	0.8		
Deodorant (underarm)	NR	NR	NR	NR		
Hair—non-coloring	NR	NR	NR	NR		
Hair—coloring	NR	NR	NR	NR		
Nail	NR	NR	NR	NR		
Mucous membrane	NR	NR	NR	NR		
Baby products	NR	NR	NR	NR		

Abbreviation: NR, no reported uses.
[a]Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types my not equal the sum of total uses.
[b]Includes deodorants, in that it is not known whether or not the product is a spray.
[c]Includes suntan products, in that it is not known whether or not the reported product is a spray.

inflammation, hyperplasia, and tumors were observed.[39] There were no observed adverse effects at exposures of 0.05 mg/m^3.

Reproductive and Developmental Toxicity

Published reproductive and developmental toxicity data were not found. Reproductive and developmental toxicity data on some of the monomers are provided in Table 5.

Genotoxicity

Genotoxicity data on some of the monomers are provided in Table 5.

Acrylates/C10-30 *alkyl acrylate cross polymer.* Acrylates/C10-30 alkyl acrylate cross polymer, tested at 156 to 500 μg/plate in dimethyl sulfoxide, was not mutagenic in an Ames assay with *Salmonella typhimurium* TA98 and TA100.[23] It is not stated directly, but it appears that the studies were performed with and without metabolic activation.

Acrylates/Steareth-20 *methacrylate cross polymer.* The acrylic copolymer of acrylates/steareth-20 methacrylate cross polymer (as Aculyn 88 polymer) was not mutagenic in an Ames test, with or without metabolic activation.[10] (Study performed using good laboratory practices [GLP]; details not provided.)

Acrylates/*vinyl neodecanoate cross polymer.* The acrylic copolymer of acrylates/vinyl neodecanoate cross polymer (as Aculyn 38 polymer) was not mutagenic in an Ames test, with or without metabolic activation.[12] (GLP study; details not provided).

Sodium *acrylates cross polymer 2.* According to an industry MSDS, sodium acrylates cross polymer 2 (as Aqua Keep 10SH-NFC) was negative in an Ames test using *S typhimurium* TA98, TA100, TA1535, and TA1537 and *Escherichia coli* WP2uvrA.[41]

Table 4b. Ingredients Not Reported to be Used.

Acrylates/C12-13 alkyl methacrylates/methoxyethyl acrylate cross polymer
Acrylates/ethylhexyl acrylate/glycidyl methacrylate cross polymer
Acrylates/PEG-4 dimethacrylate cross polymer
Allyl methacrylate/glycol dimethacrylate cross polymer
Butyl acrylate/glycol dimethacrylate cross polymer
C8-22 alkyl acrylates/methacrylic acid cross polymer
Glycol dimethacrylate/vinyl alcohol cross polymer
Methacrylic acid/PEG-6 methacrylate/PEG-6 dimethacrylate cross polymer
PEG/PPG-5/2 methacrylate/methacrylic acid cross polymer
Potassium acrylates/C10-30 alkyl acrylate cross polymer
Sodium acrylates/vinyl isodecanoate cross polymer
Stearyl/lauryl methacrylate cross polymer

Carcinogenicity

Published carcinogenicity studies were not found. Carcinogenicity data on some of the monomers are provided in Table 5.

Irritation and Sensitization

Irritation and sensitization data on some of the monomers are provided in Table 5.

Skin Irritation and Sensitization

Dermal irritation and sensitization studies, using alternative methods and nonhuman and human test populations, are presented in Table 6.

In an alternative method study, acrylates/vinyl neodecanoate cross polymer was predicted to be a nonirritant. The nonhuman studies reported no to slight irritation with undiluted and weak sensitization with 2% aq, acrylates/C10-30 alkyl acrylate cross polymer, no irritation with acrylates cross polymer at 30% in olive oil, and no irritation or sensitization with sodium acrylates cross polymer 2 (concentration not specified). Mostly, human testing with undiluted acrylates/C10-30 alkyl acrylate cross polymer, acrylates cross polymer, and acrylates/ethylhexyl acrylate cross polymer, up to 2.5% aq acrylates/vinyl isodecanoate cross polymer, 1% aq dilutions of formulations containing 2% acrylates/vinyl neodecanoate cross polymer, and formulations containing up to 2.6% lauryl methacrylate/glycol dimethacrylate cross polymers do not indicate any dermal irritation or sensitization. The only exception was a weak irritant response noted during an intensified Shelanski human repeated insult patch test (HRIPT) with undiluted acrylates/C10-30 alkyl acrylate cross polymer.

Ocular Irritation

Alternative studies

Acrylates/vinyl isodecanoate *cross polymer.* The EYE-TEX alternative method was used to predict the in vivo ocular irritation classification of acrylates/vinyl isodecanoate cross polymer (as Stabylen 30).[40] The results obtained in a standard volume–response study using samples of $\leq$100 µl test material corresponded to a Draize ocular irritation classification of nonirritant.

Lauryl methacrylate/glycol dimethacrylate *cross polymer.* The EpiOcular Human Cell Construct (3-(4,5-Dimethylthiazol-2-yl)-2,5-Diphenyltetrazolium Bromide [MTT] assay), was used to assess the potential ocular irritation of a face powder containing 1% lauryl methacrylate/glycol dimethacrylate cross polymer.[42] The ET_{50} (duration of exposure resulting in a 50% decrease in MTT conversion) of the test material was >1,440 minutes, which was the maximum exposure time. (As a reference point, the ET_{50} of the positive control, 0.3% Triton X-100, was 16.3 minutes.)

Nonhuman

Acrylates/C10-30 alkyl acrylate *cross polymer.* The ocular irritation potential of acrylates/C10-30 alkyl acrylate cross polymer (as Carbopol ETD) was evaluated using groups of 3 albino rabbits.[43] The test material, undiluted and as a 1% neutralized solution (pH 6.9-7.0), was instilled into the conjunctival sac of 1 eye of each rabbit per group; the contralateral eyes served as a control. The eyes were not rinsed. The undiluted test material produced slight to moderate corneal and conjunctival irritation which cleared by day 7. Slight iridal and conjunctival irritation was observed with the 1% solution. All signs of irritation cleared within 72 hours.

In other studies using the same procedure, the ocular irritation potential of acrylates/C10-30 alkyl acrylate cross polymer (as Carbopol Ultrez 20 and Carbopol Ultrez 21) was evaluated using groups of 3 rabbits.[44,45] The test material was evaluated undiluted and as a 5% dilution in distilled water. The undiluted test material produced moderate corneal irritation and conjunctival irritation which cleared by day 21. (The maximum mean score [MMS] was 37.7/110.) Moderate conjunctival irritation (MMS 9.3/110) was observed with the 5% solution, which was classified as a minimal irritant.

The ocular irritation potential of acrylates/C10-30 alkyl acrylate cross polymer (as Pemulen) was evaluated by instilling 0.021 g of the test article into the conjunctival sac of 1 eye of 9 New Zealand White rabbits.[46] The contralateral eyes were untreated and served as the control. At 30 seconds postinstillation, both eyes of 3 rabbits were rinsed; the eyes of the other 6 rabbits were not rinsed. The eyes were examined for irritation for up to 72 hours following dosing. "Significant" ocular irritation was observed in 3 of the 6 unrinsed eyes. At 24 hours after instillation, corneal opacity was observed in 3 and iritis in 1 unrinsed eye; minimal conjunctivitis was seen in all 6 unrinsed eyes. These observations were resolved by 72 hours. "Less severe responses" were observed in the rinsed eyes. Iritis was observed in 1 and conjunctivitis in 3 of the rinsed eyes at 24 hours after dosing. At 48 hours after dosing, conjunctivitis was observed in 1 rinsed eye. Based on the observations made for

Table 5. Relevant Summary Information on Component Monomers.

Monomer Component	Parameter Evaluated	Outcome	Reference
Acrylic acid	Toxicokinetics	Dermal: radioactivity was recovered mostly in the skin trap, and then in expired CO_2	1
		Oral: in numerous studies using rats, the dose was primarily excreted in expired air in most cases; elimination was generally rapid; uptake and elimination appeared to be biphasic; absorption and excretion were also rapid in mice	
		Inhalation: rats were exposed to acrylic acid via inhalation; most of the radioactivity was found in the head and snout, with relatively large amounts also recovered in the upper respiratory tract	
	Toxicological studies	Single dose—dermal: LD_{50}—295-950 mg/kg in rabbits	1
		Oral: LD_{50}—2,100-3,200 mg/kg in rabbits and rats; produced gastric lesions	
		Inhalation: LC_{50}—3,600 mg/m^3 in rats	
		Repeated dose—dermal: 4% produced toxic effects in mice in a 13-week study	1
		Oral: toxic effects were observed in rats in a 90-day drinking water study with doses of $\leq$750 mg/kg and in a 90-day gavage study in rats doses with 150 or 375 mg/kg; stomach lesions were not observed with up to 500 ppm in a 12-month drinking study with rats	
		Inhalation: nasal irritation and/or lesions were observed in rats and/or mice exposed to 1500 ppm for 4-day up to 225 ppm for 2-week, 300 ppm for 20-day, and 75 ppm for 13-week	
	Reproductive and developmental toxicity	Oral: did not produce teratogenic effects in rats, NOAEL of 250 mg/kg; did affect body weights and some organ weights in the parental animals	1
		Inhalation: not teratogenic or embryotoxic in rats at concentrations up to 120 ppm; did produce maternal toxicity at concentrations of 120 ppm and greater	
	Genotoxicity	Genotoxic in mouse lymphoma assays, and in an in vitro cytogenetic assay; not genotoxic or mutagenic in Ames tests, unscheduled DNA synthesis (UDS) assay, micronucleus assay, in vivo transformation assay, Chinese hamster ovary (CHO)/HGPRT, in vivo cytogenetic assay, Drosophila test, or mouse dominant lethal assay	1
	Carcinogenicity	Dermal: in 1 study, 4% in acetone was a complete but weak carcinogen in mice; in another, 1% was not carcinogenic in mice	1, 68
		Oral: not carcinogenic in rats when given in drinking water at up to 1200 ppm	
		Parenteral: not carcinogenic when 1.4 mg was injected subcutaneously (sc) to mice	
		IARC evaluation: no epidemiological data relevant to carcinogenicity were available; no experimental data relevant to carcinogenicity were available; *not classifiable as to its carcinogenicity to humans (group 3)*	
	Irritation and sensitization	Skin: 4% was irritating to the skin of mice	1
		Mucosal: a 1% solution caused significant injury to the rabbit eye	
Methyl acrylate	Toxicokinetics	Dermal: in guinea pigs exposed dermally to methyl [2,3-^{14}C]acrylate, radioactivity was seen in the sc tissues and throughout the body	69
		Oral: the dose was primarily excreted in expired air; elimination was rapid (rats)	
	Toxicological studies	Single dose—oral: produced gastric lesions when given inhibited with 200 ppm hydroquinone monomethyl ether (HQMME)	1
		Repeated dose—oral: not toxic when given orally to rats (details not provided)	1
	Reproductive and developmental toxicity	Inhalation: up to 200 ppm did not produce teratogenic or reproductive effects in rats	1
	Genotoxicity	Genotoxic in mouse lymphoma and chromosomal aberration assays; positive in 1 and negative in 2 micronucleus tests; not mutagenic or genotoxic in an Ames, *Salmonella*/microsome, liquid incubation, monolayer, suspension, or AS52/XRPT assay	1
	Carcinogenicity	Inhalation: up to 135 ppm was not carcinogenic to rats	1
		IARC evaluation: no epidemiological data relevant to the carcinogenicity; *inadequate evidence* in experimental animals; *not classifiable as to its carcinogenicity to humans (group 3)*	69
Ethyl acrylate	Toxicokinetics	Oral: the dose was primarily excreted in expired air; elimination was rapid (rats)	1

(continued)

Table 5. (continued)

Monomer Component	Parameter Evaluated	Outcome	Reference
	Toxicological studies	Single dose—oral: produced gastric lesions when given inhibited with 15 to 20 ppm HQMME	1
		Repeated dose—oral: a 2-week study in rats with dosing via gavage or drinking water—gastric lesions were observed, primarily in the forestomach., at doses of 20 to 100 mg/kg given buy gavage and at concentrations1000 to 4000 ppm in drinking water; in a 13-week gavage study, doses of $\leq$200 mg/kg produced lesions in the forestomach of rats; stomach lesions were not observed at concentrations up to 2000 ppm in a 2-year drinking study with rats or up to 1000 ppm in a 2-year capsule study with dogs	1
		Inhalation: no nasal lesions were observed with up to 300 ppm in a 1-month study using rats and mice; nasal lesions were observed at concentrations of $\geq$242 ppm in rats in a 12-week study	
	Reproductive and developmental toxicity	Inhalation: up to 200 ppm was not embryotoxic or fetotoxic in rats; maternal toxicity observed with 150 ppm	1
	Genotoxicity	Genotoxic in a mouse lymphoma and chromosomal aberration assay; induced chromosomal malsegregation and mitotic recombination using *Salmonella cerevisiae*; positive in 1 and negative in 1 micronucleus assay; not mutagenic or genotoxic in an Ames, *Salmonella*/microsome, liquid incubation, monolayer, chromosomal, sister chromatid exchange (SCE), or Drosophila assay	1
	Carcinogenicity	Dermal: tested undiluted, not carcinogenic to mice	1
		Oral: in corn oil, carcinogenic in male and female rats and mice at 100 and 200 mg/kg	70
		Inhalation: up to 225 ppm was not carcinogenic in mice or rats	
		IARC evaluation: no epidemiological data relevant to the carcinogenicity; *sufficient evidence* in experimental animals; *possibly carcinogenic to humans (group 2B)*	
Butyl acrylate	Toxicokinetics	Oral: the dose was primarily excreted in expired air (rats)	1
	Toxicological studies	Single dose—oral: produced gastric lesions when given inhibited with 10 to 55 HQMME	1
		Repeated dose—oral: not toxic when given orally to rats (details not provided)	1
		Inhalation: toxicity was observed in rats and hamsters upon three 6-hour exposures to 820 and 817 ppm, respectively; nasal lesions were observed in rats exposed to concentrations $\geq$108 ppm in a 13-week study	
	Reproductive and developmental toxicity	Inhalation: no toxic effects were seen with 25 ppm; high concentrations had toxic effects on the fetuses and dams	1
	Genotoxicity	positive in 1 and negative in 1 chromosomal aberration assay; not mutagenic or genotoxic in an Ames, *Salmonella*/microsome, liquid incubation, UDS, micronucleus, or in vitro transformation assay	1
	Carcinogenicity	Dermal: 1% was not carcinogenic in mice	1
		Inhalation: up to 135 ppm was not carcinogenic to rats	71
		IARC evaluation: no epidemiological data relevant to the carcinogenicity; *inadequate evidence* in experimental animals; *not classifiable as to its carcinogenicity to humans (group 3)*	
2-Ethylhexyl acrylate	Toxicokinetics	Oral: the dose was primarily excreted in expired air; elimination was rapid (rats)	1
	Reproductive and developmental toxicity	Inhalation: up to 100 ppm did not produce teratogenic or reproductive effects in rats	1
	Genotoxicity	Genotoxic in a mouse lymphoma forward mutation assay with metabolic activation; equivocally genotoxic in mutation and aberrations assays; weakly mutagenic in SCE and UDS assays; not mutagenic or genotoxic in a microbial mutagen test, Ames test, mammalian cell transformation assay, micronucleus test, monolayer or suspension assay, CHO assay, or in vivo cytogenic assay	1
	Carcinogenicity	Dermal: carcinogenic at a dose of $\geq$21% when applied to mice—the carcinogenic response may have been associated with the severe skin irritation induced by the chemical	1 72

(continued)

Table 5. (continued)

Monomer Component	Parameter Evaluated	Outcome	Reference
		Tested by skin application in 3 experiments in mice; it increased the incidence of squamous-cell carcinomas of the skin in 2 experiments and of malignant melanomas in 1 experiment; in the third experiment, in a different strain of mice, no increase skin tumor incidence was seen with or without subsequent application of 12-0-tetradecanoylphorbol 13-acetate	
		IARC evaluation: *inadequate evidence* in humans for carcinogenicity; *limited evidence* in experimental animals; *not classifiable as to its carcinogenicity to humans (group 3)*	
	Irritation and sensitization	Dermal—nonhuman: sensitization was observed when guinea pigs were treated with 2-ethylhexyl acrylate in Freund complete adjuvant	72 1
		Human: in a provocative test with 243 patients with a history of exposure to (meth)acrylates, none of the patients were sensitized with patches containing 0.1% to 0.5% 2-ethylhexyl acrylate	
Polyacrylic acid	Animal toxicology	Single dose—oral: LD_{50}—2500 mg/kg in rats	1
	CIR conclusion (2002)	*Safe as used when formulated to avoid skin irritation*	1
Sodium polyacrylate	Animal toxicology	Single dose—oral: LD_{50}—>40 g/kg in rats for a 15% solution	1
	Reproductive and developmental toxicity	Oral: up to 3000 mg/kg/d low-molecular weight and up to 1125 mg/kg/d high-molecular weight did not cause reproductive effects in rats	1
	Genotoxicity	Not genotoxic in an Ames assay, a plate test, a mouse lymphoma assay, chromosomal aberration assays, a UDS assay, or an in vivo mouse micronucleus assay	1
	Irritation and sensitization	Dermal—nonhuman: not an irritant to rabbit skin when applied undiluted	1
		Human: not an irritant or sensitizer (concentration not given)	
		Ocular: the greatest tolerated concentrations were 13% to 20% for unrinsed and 20% to 30% for rinsed rabbit eyes; in an irritant-threshold test, 2% was the greatest concentration that did not produce irritation in rabbit eyes	
	CIR conclusion (2002)	*Safe as used when formulated to avoid skin irritation*	1
Methacrylic acid	Toxicokinetics	Readily absorbed through the mucous membranes of the lungs and gastrointestinal tract of and the skin, and is readily distributed to all major tissues	73
	Animal toxicology	Single dose—dermal: reported LD_{50} values ranged from 500 to 1243 mg/kg for rabbits	73
		Oral: reported LD_{50} values ranged from 827 to 1600 mg/kg for mice, 277 to 2260 mg/kg for rats, and 280 to 1200 mg/kg for rabbits	
		Inhalation: reported LC_{50} values were 3657 ppm in mice, 1350 ppm/4 h in rats, and 2522 ppm/1 h in rabbits	
		Repeated dose—oral: no signs of toxicity in a short-term study	73
		Inhalation: nose and eye irritation and weight loss in rats with 5 exposures to 1300 ppm; only renal congestion in rats with 20 exposures to 300 ppm; in a 2-week study, repeated doses of $\geq$100 ppm caused reactions in rats, $\geq$500 ppm caused reactions in mice, and 1000 ppm killed all rats and mice; in a 90-day study, respiratory effects were seen in rats and mice exposed to 300 ppm—cytomegaly of renal tubular epithelium was observed in >50% of test male mice	
	Reproductive and developmental toxicity	Inhalation: no reproductive or developmental effects at concentrations up to 300 ppm	73
		In vitro: adverse effects were seen with exposure of rat embryos to $\geq$129 μg/ml	
	Genotoxicity	Positive in a DNA cell-binding assay; negative in an Ames test	73
	Carcinogenicity	It was reported that IARC reviewed methacrylic acid, but did not prepare a monograph because inadequate data were available	73
	Irritation and sensitization	Dermal—nonhuman: corrosive to rabbit and guinea pig skin; in a guinea pig maximization study, it was difficult to determine if observed reactions were hypersensitivity or irritation; guinea pigs were not sensitized in 3 other studies	73
		Mucosal: caused severe corneal, iridal, and conjunctival effects in rabbits in 1 study; in an inhalation study, 56 916 ppm was corrosive to rabbit eyes	
	Clinical use	Negative results were reported in a number of patch tests of patients allergic to methyl methacrylate and to workers exposed to acrylates	73

(continued)

Table 5. (continued)

Monomer Component	Parameter Evaluated	Outcome	Reference
	Discussion items	The Panel was concerned with the extreme corrosivity; a presentation demonstrated that a trained professional could apply the acid to the nail without exposure to the skin, but this could not be demonstrated for retail consumers; due to concerns that inhalation could affect the respiratory tract, and the nail technician could be subjected to increased exposure in a commercial setting, the NIOSH-recommended exposure limit of 20 ppm as a time-weighted average concentration should not be exceeded; the Consumer Product Safety Commission rule requires child-resistant packaging for liquid household products containing >5% methacrylic acid (wt to vol)	73
	CIR conclusion (2005)	*Safe as used as a nail primer by trained professionals; insufficient data for retail use by consumers*	73
Methyl methacrylate	Toxicokinetics	Can be absorbed through the skin of humans	74
	Animal toxicology	Repeated dose—oral: chronic exposure to $\leq$400 ppm did not cause tumors in hamsters or rats	75
	Genotoxicity	Genotoxic in a chromosomal aberration, SCE, and mouse lymphoma assay; not mutagenic in a *Salmonella*/microsome or liquid incubation assay	1
	Carcinogenicity	Oral: not carcinogenic in a drinking study using rats Inhalation: up to 400 ppm was not carcinogenic in mice or rats IARC evaluation: *inadequate evidence* in humans for carcinogenicity; *evidence suggesting lack of carcinogenicity* in experimental animals; *not classifiable as to its carcinogenicity in humans (group 3)*	74,75
	Irritation and sensitization	Dermal—nonhuman: sensitizing at 25% in guinea pigs; minimum induction concentration was 1 M; was a weak contact allergen in a local lymph node assay Human: the frequency of positive reactions among all patients to methyl methacrylate was 7/22; the frequency of positive reactions among patients with artificial nails was 1/10	76
Ethyl methacrylate	Genotoxicity	Not mutagenic in a *Salmonella*/microsome assay; genotoxicity in a mouse lymphoma cell assay was considered likely due to a clastogenic mechanism	1
	Irritation and sensitization	Dermal—human: the frequency of positive reactions among all patients tested was 14/22; the frequency of positive reactions among patients with artificial nails was 7/11 (64%),	76
	Discussion items	(This ingredient was reviewed for its use nail enhancement products.) The Panel was concerned with the strong sensitization and cross- or coreactivity potential of methacrylates; however, data were submitted that indicated there would be little monomer available for exposure to the skin; genotoxicity data indicated the some methacrylates could produce chromosome damage; the Panel restricted methacrylates to the nail, and they must not come in contact with skin; initial concern that exotherms created from the rapid polymerization of the monomers could damage the nail were alleviated	75
	CIR conclusion (2005)	*Safe as used in nail enhancement products when skin contact is avoided; products containing this ingredient should be accompanied with directions to avoid skin contact, because of the sensitizing potential of methacrylates*	75
Butyl methacrylate	Animal toxicology	Single dose—dermal: 10 cc/kg did not cause mortality in rabbits, but acute dermal irritation was reported; 1 LD_{50} value of >2000 mg/kg in rabbits was reported; the LD_{50} in guinea pigs was >20 ml/kg Oral: reported oral LD_{50} values in rats ranged from >2000 to >20 000 mg/kg Inhalation: reported LC_{50} value was 28 469 mg/m^3 rats	75
		Repeated dose—oral: in rats, the NOELS were 20 mg/kg/d in a 28-day study, 30 (males) and 300 (females) mg/kg/d in a 45-day study, and <30 (males) and 30 (females) mg/kg/d in a 50-day study Inhalation: caused upper airway irritation in a 28-day study in rats—the NOEL was 1801 mg/m^3	75
	Reproductive and developmental toxicity	Oral: a decrease in corpora lutea and implantations was reported in rats; the parental NOAELs were 1000 and 300 mg/kg/d for males and females, respectively Inhalation: threshold concentration for embryotoxic and teratogenic effects in rats was 0.1 mg/m^3; slight fetotoxicity was reported in rats exposed to $\leq$1200 ppm on days 6 to 20 of gestation	75

(continued)

Table 5. (continued)

Monomer Component	Parameter Evaluated	Outcome	Reference
	Genotoxicity	Not mutagenic in multiple Ames tests with or without metabolic activation; was mutagenic to *Salmonella typhimurium* TA1538 with metabolic activation in 1 study	75
	Irritation and sensitization	Dermal—nonhuman: a very strong sensitizer in 1 study using guinea pigs; considered a moderate sensitizer in another study using guinea pigs; in a few studies, a sensitization reaction was not produced Human: 1% caused 1 positive reaction in 12 patients in a Draize contact sensitization study; in provocative testing, 1% elicited positive reactions to patch tests Ocular: mildly irritating to rabbit eyes	75
	Discussion items	(This ingredient was reviewed for its use nail enhancement products.) The Panel was concerned with the strong sensitization and cross- or coreactivity potential of methacrylates; however, data were submitted that indicated there would be little monomer available for exposure to the skin; genotoxicity data indicated the some methacrylates could produce chromosome damage; the Panel restricted methacrylates to the nail, and they must not come in contact with skin; initial concern that exotherms created from the rapid polymerization of the monomers could damage the nail were alleviated.	75
	CIR conclusion (2005)	*Safe as used in nail enhancement products when skin contact is avoided; products containing this ingredient should be accompanied with directions to avoid skin contact, because of the sensitizing potential of methacrylates*	75
Isobutyl methacrylate	Animal toxicology	Single dose—dermal: the reported dermal LD_{50} was >20 ml/kg in guinea pigs Oral: reported LD_{50} values in rats ranged from >5,000 to 12,800 mg/kg Inhalation: 50% of mice died after exposure to 29.74 mg/L for 289 minutes; was considered a toxic (but not highly toxic) substance by inhalation exposure	75
	Genotoxicity	Not mutagenic in multiple Ames tests with or without metabolic activation	75
	Irritation and sensitization	Dermal—human: 1% caused no positive reaction in 11 patients in a contact sensitization study; in provocative testing, 1% elicited positive reactions to patch tests Ocular: mildly irritating to rabbit eyes	75
	Discussion Items	(This ingredient was reviewed for its use nail enhancement products.) The Panel was concerned with the strong sensitization and cross- or coreactivity potential of methacrylates; however, data were submitted that indicated there would be little monomer available for exposure to the skin; genotoxicity data indicated the some methacrylates could produce chromosome damage; the Panel restricted methacrylates to the nail, and they must not come in contact with skin; initial concern that exotherms created from the rapid polymerization of the monomers could damage the nail were alleviated.	75
	CIR conclusion (2005)	*Safe as used in nail enhancement products when skin contact is avoided; products containing this ingredient should be accompanied with directions to avoid skin contact, because of the sensitizing potential of methacrylates*	75
Lauryl methacrylate	Animal toxicology	Single dose—oral: no rats dosed with $\leq$21.5 ml/kg C12 to C18 methacrylate monomers died Inhalation: the RD_{50} was 3,900 mg/m^3 in mice Repeated dose—inhalation: not toxic to rats in a 20-day study	75 75
	Irritation and sensitization	Dermal—nonhuman: strong sensitizer in guinea pigs	75
	Discussion items	(This ingredient was reviewed for its use nail enhancement products.) The Panel was concerned with the strong sensitization and cross- or coreactivity potential of methacrylates; however, data were submitted that indicated there would be little monomer available for exposure to the skin; genotoxicity data indicated the some methacrylates could produce chromosome damage; the Panel restricted methacrylates to the nail, and they must not come in contact with skin; initial concern that exotherms created from the rapid polymerization of the monomers could damage the nail were alleviated.	75
	CIR conclusion (2005)	*Safe as used in nail enhancement products when skin contact is avoided; products containing this ingredient should be accompanied with directions to avoid skin contact, because of the sensitizing potential of methacrylates*	75

(continued)

Table 5. (continued)

Monomer Component	Parameter Evaluated	Outcome	Reference
PEG-4 dimethacrylate	Animal toxicology	Single dose—dermal: the LD_{50} was >3 g/kg in rats Oral: LD_{50} was >5,000 mg/kg in rats	75
	Genotoxicity	Not mutagenic in multiple Ames tests with or without metabolic activation; weakly positive in a mouse lymphoma cell assay with metabolic activation	75
	Carcinogenicity	Dermal: no increase in skin or visceral tumors in an 80-week study with 25 mg given twice weekly	75
	Irritation and sensitization	Dermal—nonhuman: moderate sensitizer in guinea pigs; not a sensitizer in 1 study Ocular: minimally irritating to rabbit eyes	75
	Discussion items	(This ingredient was reviewed for its use nail enhancement products.) The Panel was concerned with the strong sensitization and cross- or coreactivity potential of methacrylates; however, data were submitted that indicated there would be little monomer available for exposure to the skin; genotoxicity data indicated the some methacrylates could produce chromosome damage; the Panel restricted methacrylates to the nail, and they must not come in contact with skin; initial concern that exotherms created from the rapid polymerization of the monomers could damage the nail were alleviated.	75
	CIR conclusion (2005)	*Safe as used in nail enhancement products when skin contact is avoided; products containing this ingredient should be accompanied with directions to avoid skin contact, because of the sensitizing potential of methacrylates*	75

Abbreviations: CIR, Cosmetic Ingredient Review; IARC, International Agency for Research on Cancer; NIOSH, National Institute for Occupational Safety and Health.

the unrinsed eyes, the authors stated that this product was considered a borderline irritant.

Acrylates *cross polymer*. The ocular irritation potential of acrylates cross polymer was evaluated by instilling 0.1 ml of the test material, at a concentration of 50% in olive oil, into the conjunctival sac of 1 eye of 3 Japanese white rabbits.[24] The Draize score was 1.3. (Additional details were not provided.)

Sodium acrylates *cross* polymer 2. According to an industry MSDS, sodium acrylates cross polymer 2 (as Aqua Keep 10SH-NFC) is not an ocular irritant in rabbits.[41]

Clinical Assessment of Safety

Risk Assessment

Conservative risk assessments were submitted by the Personal Care Products Council's CIR Science and Support Committee (SSC) and by the CIR to address the carcinogenic endpoint for benzene, because it may be used as a solvent in the manufacture of acrylates/C10-30 alkyl acrylates cross polymer. Both assessments assumed the highest reported concentration of residual benzene in acrylates/C10-30 alkyl acrylates cross polymer used as a raw ingredient, the highest reported use concentration in a leave-on product of the raw ingredient polymerized in benzene, 10% evaporation of the residual benzene during manufacturing of the product, 10% benzene absorbed from the product through the skin, and the reported 50th and 95th percentiles of the amount of product used daily.

CIR SSC Risk Assessment[31]

The assumptions used to calculate CIR SSC's example exposure assessment were:

- 50th percentile use =7.63 g body lotion used/use day
- 95th percentile use =16.83 g body lotion used/use day
- 0.4% acrylates/C10-30 alkyl acrylate cross polymer in body lotion
- 0.41% benzene in acrylates/C10-30 alkyl acrylate cross polymer
- 10% benzene absorbed percutaneously

Estimated Exposure

0.41% benzene in raw material × 0.4% acrylates/C10-30 alkyl acrylates cross polymer in a body product
= 0.00164% benzene in the product

50th 7.63 g body product used/day × 0.00164%
= 0.000125 g/d
= 125 μg/d

absorb 10% × 125 μg/d
= 12.5 μg/d

95th 16.83 g body product used/d 0.00164%
= 0.000276 g/d
= 276 μg/d

absorb 10% × 276 μg/d
= 27.6 μg/d

The SSC Comparison to Risk Level

The Environmental Protection Agency (EPA) drinking water concentration associated with 10^6 cancer risk is 1 and 10 μg/L.[47] Assuming consumption of 2 L of water each day, this results in a value of 2 to 20 μg/d. The estimated exposure from the use of a leave-on body product at the 50th percentile, assuming the greatest concentration of acrylates/C10-30 alkyl acrylates cross polymer polymerized in benzene, is in within

Table 6. Dermal Irritation and Sensitization: Alternative, Nonhuman, and Human.

Test Article	Concentration/ Dose	Test Population	Procedure	Results	Reference
Alternative studies					
Acrylates/vinyl isodecanoate cross polymer					
As Stabylen 30 (tradename)			SKIN-TEX method; standard volume-response study using ≤100 ml samples	Nonirritant (predicted classification)	40
Nonhuman					
Acrylates/C10-30 alkyl acrylate cross polymer					
As Pemulen (trade name)	0.5 g undiluted	6 NZW rabbits	Semi-occlusive; abraded and nonabraded sites; 24 hours application	PII 0.42/8—negligible irritation potential very slight erythema was observed at 1 hour; no irritation observed at 72 hours	46
As Carbopol ETD (trade name)	0.5 g undiluted	3 rabbits	Semi-occlusive patch; nonabraded skin; 4 hours application	PII 0.0-1.5; non- to slight irritant very slight erythema and edema	43
	0.5 ml of a 1% neutralized solution			PII 0.0-0.1; non- to very slight irritant	
As Carbopol Ultrez-21 (trade name)	0.5 g, moistened with 0.5 ml water	3 rabbits	Semi-occlusive patch; nonabraded skin; 4 hours application	PII 0.3—produced slight irritation	44
As Carbopol Ultrez-20 (trade name)	0.5 g, moistened with 0.5 ml water	3 rabbits	Semi-occlusive patch; nonabraded skin; 4 hours application	PII 0.3—produced slight irritation	45
Acrylates/C10-30 alkyl acrylate cross polymer	2% aq	5 guinea pigs	Maximization (split adjuvant) test (details not provided)	Weak sensitizer	23
Acrylates cross polymer					
Acrylates cross polymer	30% in olive oil	3 rabbits	open application of 0.1 ml to a 2.5 cm × 2.5 cm site; 1 time daily for 4 days	No irritation	24
Sodium acrylates cross polymer 2					
As Aqua Keep 10SH-NFC (tradename)	Not stated	Rabbits Guinea pigs	Information provided in an industry MSDS	Not an irritant Not a sensitizer	41
Human					
Acrylates/C10-30 alkyl acrylate cross polymer					
Acrylates/C10-30 alkyl acrylate cross polymer	15 μl of 2% aq dilution	20 patients	Single 24-hour occlusive patch	24 hours: ± response in 3/20 patients 84 hours: ± response in 1/20 patients (results were based on Japanese criteria)	23
As Carbopol ETD (tradename)	Undiluted (>97.5%)[51]	100 patients	Material was applied to a 2 cm × 2 cm pad; patch was applied for 4 consecutive days during weeks 1 to 3; challenge was performed after 1 week and included 4 applications	Not an irritant or sensitizer	43
As Carbopol Ultrez 21 (tradename)	150 mg of a 10% dilution	111 patients	Test material was applied to a 2 cm × 2 cm pad; patch was applied for 4 consecutive days during weeks 1 to 3; challenge was performed after 1 week and included 4 applications	Not an irritant or sensitizer	44
As Carbopol Ultrez 20 (tradename)	150 mg of a 10% dilution	111 patients	Test material was applied to a 2 cm × 2 cm pad; patch was applied for 4 consecutive days during weeks 1 to 3;	Not an irritant or sensitizer	45

(continued)

Table 6. (continued)

Test Article	Concentration/ Dose	Test Population	Procedure	Results	Reference
			challenge was performed after 1 week and included 4 applications		
As Pemulen (tradename)	Undiluted (97.5%)[51]	54 patients	"Intensified" Shelanski HRIPT; test material was applied to a 1″ × 1″ patch	Weak irritant response; not a sensitizer During induction, faint or moderate erythema was observed once for 9 patients and twice for 2 patients; at challenge, faint erythema was observed once for 3 patients	46
Body lotion with 0.15% acrylates/C10-30 alkyl acrylate cross polymer	0.2 g	107 patients	Test material was applied to a 1″ × 1″ absorbent pad and allowed to volatize for several minutes; semi-occlusive patch; 24 hours applications made 3 times/wk for 3 weeks; challenge was applied after 2 weeks	not a dermal irritant or sensitizer	52
Crème with 0.60% acrylates/ C10-30 alkyl acrylate cross polymer	0.2 g	51 patients	Test material was applied to a 1″ × 1″ absorbent pad and allowed to volatize for several minutes; semi-occlusive patch; 24 hours semi-occlusive patches applied 3 times/ wk for 3 weeks; challenge was applied after 2 weeks	Not a dermal irritant or sensitizer	53
Acrylates cross polymer					
Acrylates cross polymer	15 μl; 30% in olive oil	20 patients	Single 24-hour occlusive patch	Not an irritant according to Japanese criteria	24
Eye lotion with 0.75% acrylates cross polymer	Undiluted	46 patients	HRIPT with occlusive patch	Not an irritant or sensitizer	54
Skin cleanser with 0.8% acrylates cross polymer	1% aq dilution	60 patients	HRIPT with occlusive patch	Not an irritant or sensitizer	54
Lipstick with 4% acrylates cross polymer	0.2 g	85 patients	HRIPT with occlusive patch	Not an irritant or sensitizer	55
Acrylates/ethylhexyl acrylate cross polymer					
Facial sunscreen with 6.8565% acrylates/ethylhexyl acrylate cross polymer	Undiluted	600 patients	Modified Draize RIPT with ten 48-hour induction patches using 0.5 in square occlusive patches; the first challenge was applied after a 2-week non-treatment period; an additional challenge application was made 1 week after the first challenge application	No evidence of primary irritation, skin fatigue, or sensitization	56
Acrylates/Steareth-20 methacrylate cross polymer					
The acrylic copolymer of Aculyn 88 Polymer (trade name)	Not stated	Not stated	21-day cumulative irritation study (GCP)	No irritation or sensitization	10
The acrylic copolymer of Aculyn 88 Polymer (trade name)	Not stated	Not stated	HRIPT (GCP)	No irritation or sensitization	10
Acrylates/vinyl isodecanoate cross polymer					
As Stabylen 30 (trade name)	0.5%-2.5% aq	25 patients	Kligman test (additional details were not provided)	Not an irritant or sensitizer	40
Acrylates/vinyl neodecanoate cross polymer					
The acrylic copolymer of Aculyn 38 Polymer (trade name)	Not stated	Not stated	21-day cumulative irritation study (GCP)	At most, a mild irritant with unformulated polymer and under worse-case conditions	12
The acrylic copolymer of Aculyn 38 Polymer (trade name)	Not stated	Not stated	HRIPT (GCP)	Not an irritant or sensitizer	12
	1% aq dilution	108 patients		Not an irritant or sensitizer	57

(continued)

Table 6. (continued)

Test Article	Concentration/ Dose	Test Population	Procedure	Results	Reference
Bath crème with 2% acrylates/ vinyl neodecanoate cross polymer			HRIPT; 24-hour occlusive patches applied 3 times/wk for 3 weeks; 24-hour challenge after a 2-week nontreatment period (size of patch was not provided)		
Bath crème with 2% acrylates/ vinyl neodecanoate cross polymer	1% aq dilution	109 patients	HRIPT; 24-hour occlusive patches applied 3 times/wk for 3 weeks; 24-hour challenge after a 2-week nontreatment period (size of patch was not provided)	Not an irritant or sensitizer	58
Bubble bath with 2% acrylates/ vinyl neodecanoate cross polymer	1% aq dilution	108 patients	HRIPT; 24-hour occlusive patches applied 3 times/wk for 3 weeks; 24-hour challenge after a 2-week nontreatment period (size of patch was not provided)	Not an irritant or sensitizer	59
Bath gel with 2% acrylates/vinyl neodecanoate cross polymer	1% aq dilution	108 patients	HRIPT; 24-hour occlusive patches applied 3 times/wk for 3 weeks; 24-hour challenge after a 2-week nontreatment period (size of patch was not provided)	Not an irritant or sensitizer	60
Bath product with 2% acrylates/ vinyl neodecanoate cross polymer	1% aq dilution	106 patients	HRIPT; 24-hour occlusive patches applied 3 times/week for 3 weeks; 24-hour challenge after a 2-week nontreatment period (size of patch was not provided)	Not an irritant or sensitizer	61
Bath foam with 2% acrylates/ vinyl neodecanoate cross polymer	1% aq dilution	106 patients	HRIPT; 24-hour occlusive patches applied 3 times/week for 3 weeks; 24-hour challenge after a 2-week nontreatment period (size of patch was not provided)	Not an irritant or sensitizer	62
Bath foam with 2% acrylates/ vinyl neodecanoate cross polymer	1% aq dilution	106 patients (same patients as above)	HRIPT; 24-hour occlusive patches applied 3 times/wk for 3 weeks; 24-hour challenge after a 2-week nontreatment period (size of patch was not provided)	Not an irritant or sensitizer	63
Bath foam with 2% acrylates/ vinyl neodecanoate cross polymer	1% aq dilution	106 patients (same patients as above)	HRIPT; 24-hour occlusive patches applied 3 times/wk for 3 weeks; 24-hour challenge after a 2-week nontreatment period (size of patch was not provided)	Not an irritant or sensitizer	64
Bubble bath with 2% acrylates/ vinyl neodecanoate cross polymer	1% aq dilution	107 patients	HRIPT; 24-hour occlusive patches applied 3 times/wk for 3 weeks; 24-hour challenge after a 2-week nontreatment period (size of patch was not provided)	Not an irritant or sensitizer	65
Lauryl methacrylate/glycol dimethacrylate cross polymer					
Face powder with 1% lauryl methacrylate/glycol dimethacrylate cross polymer	0.2 g	104 patients	HRIPT; 24-hour occlusive patches applied 3 times/wk for 3 weeks; 24-hour challenge after a 10- to 15-day nontreatment period (size of patch was not provided)	Not an irritant or sensitizer	66
exfoliator cream with 2.6% lauryl methacrylate/glycol dimethacrylate cross polymer	0.2 g	619 patients	HRIPT with ten 24 hours occlusive applications of a ¾″ × ¾″ patch; 24-hour challenge after a 2-week nontreatment period; rechallenge was performed on 2 patients using semi-occlusive and open repetitive application	Not an irritant or sensitizer After challenge, 1 patient had moderate (at 24 hours) and mild (at 72 hours) erythema and edema, and 1 patient had barely perceptible erythema at 72 hours; these results were not reproducible at rechallenge	67

Abbreviations: NZW, New Zealand White; HRIPT, human repeated insult patch test.

the range associated with a 10^6 cancer risk, while use at the 95th percentile is just above the range associated with a 10^6 risk. The SSC noted that significant volatilization of benzene would occur during the manufacture of the finished product because the temperatures reached during processing are at or near the boiling point of benzene (80.1°C). They indicated that assuming that only 10% of the residual benzene is volatilized during product manufacture, would yield an exposure within the range associated with a 10^{-6} risk for use of a body lotion at the 95th percentile.

CIR's Risk Assessment

The EPA presents the oral slope factor for benzene as a range, based on the assumption that benzene is 100% absorbed after oral exposure. Specifically, the slope factor ranges from 1.5×10^{-5} to 5.5×10^{-5} $(\mu g/kg/d)^{-1}$. The EPA drinking water concentration range (1-10 μg/L) representing a 10^{-6} lifetime cancer risk was calculated from the slope factor range, rounding down the lowest concentration of the range to 1 μg/L and rounding up the highest concentration to 10 μg/L.

General Equation

- [%] benzene in acrylates/C10-30 alkyl acrylates crosspolymer × [%] acrylates/C10-30 alkyl acrylates crosspolymer in body lotion × [g/d] body lotion × [%] benzene absorbed percutaneously × $[kg]^{-1}$ body weight × 10^6 [μg/g] conversion factor × slope factor $[\mu g/kg/d]^{-1}$ =Cancer Risk Estimate [unitless]

Using the EPA's highest cancer slope factor in the range (5.5×10^{-5} $[\mu g/kg/d]^{-1}$) in accordance with the EPA risk assessment guidelines yields an upper bound lifetime cancer risk estimate of 2.2×10^{-5}, assuming the 95th percentile product use and 70 kg body weight:

Upper Bound Risk for 95th Percentile Exposure

- $0.41\% \times 0.4\% \times 16.83\ g/d \times 10\% \times 1/70[kg]^{-1} \times 10^6\ \mu g/g \times 5.5 \times 10^{-5}[\mu g/kg/d]^{-1} = 2.17 \times 10^{-5}$

This estimate (2.2×10^{-5}) is 22 times higher than the upper bound risk estimate considered to be de minimis (10^{-6}).

Assuming that 10% of the benzene evaporates during the product manufacturing process reduces the upper bound estimate to 2×10^{-5} ($2.17 \times 10^{-5} \times 90\% = 1.95 \times 10^{-5}$), which is still about 20 times higher than 10^{-6}.

Using the EPA's lowest cancer slope factor in their range (1.5×10^{-5} $[\mu g/kg/d]^{-1}$), assuming 50th percentile product use, 10% percutaneous absorption, and 10% evaporation during the manufacturing process yields upper bound cancer risk estimates that still exceed 10^{-6} by 2- to 3-fold:

Upper Bound Risk for 50th Percentile Exposure

- $0.41\% \times 0.4\% \times 7.63\ g/d \times 10\% \times 1/70[kg]^{-1} \times 10^6\ \mu g/g \times 1.5 \times 10^{-5}\ [\mu g/kg/d]^{-1} \times 90\% = 2.41 \times 10^{-6}$

The SSC reported that the cancer risk would $<10^{-6}$, by comparing the estimated daily absorbed dose of benzene from the product to drinking water concentrations that EPA suggests represents a 10^{-6} lifetime risk. However, CIR calculated upper bound lifetime cancer risk estimates up to 20-fold greater than 10^{-6}, based on EPA's cancer slope factors for benzene.

Industrial Exposure Limits

According to an industry MSDS, no exposure limits have been established for acrylates/C10-30 alkyl acrylate cross polymer.[39] The industry-recommended permissible exposure limits for respirable polyacrylate dusts is 0.05 mg/m^3. Breathing of dust may cause coughing, mucous production, and shortness of breath. According to an industry MSDS, the exposure limit for respirable sodium acrylates cross polymer 2 dust (particle size <10 μm) is 0.05 mg/m^3.[41]

Summary

The cross-linked alkyl acrylates are cross-linked polymers and are very large molecules that consist of comonomers of acrylic acid, sodium acrylate, methacrylic acid, and/or alkyl acrylate, and they share chemical properties, including a general lack of chemical reactivity. Cross-linked alkyl acrylates are typically produced via free radical, head-to tail chain-propagation polymerization. Ethyl acetate + cyclohexane, water, n-hexane, and benzene are all named as solvents. Because of the manner in which these polymers are created and the mixture of monomers and cross-linking agents that can be used, 2 polymers that have the same INCI name can have very different physical consistencies. Small amounts of residual monomer and/or solvent may be present in the raw ingredients.

Cross-linked alkyl acrylates are reported to function in cosmetic formulations as absorbents, film formers, emulsion stabilizers, viscosity increasing agents, suspending agents, binders, and/or skin-conditioning agents. In 2011, it was reported that acrylates/C10-30 alkyl acrylate cross polymer was used in 1,696 cosmetic formulations; 1,365 of those uses are in leave-on products, and the reported concentration of use in these leave-on products is up to 5%. According to industry data, acrylates/ethylhexyl acrylate cross polymer had the highest concentration of use in a leave-on product at 6%; the highest concentration of use reported in rinse-off products was 5% acrylates/C10-30 alkyl acrylate cross polymer.

Toxicokinetic data were not found in the published literature. Little toxicity data were available; the acute dermal and oral toxicity data that were found indicated that these ingredients are not very toxic. The little genotoxicity data that were

available reported negative results in Ames tests. Carcinogenicity data were not found in the published literature for the polymers, but data were available for the monomers.

In an alternative method study, acrylates/vinyl neodecanoate cross polymer was predicted to be a nonirritant. The nonhuman studies reported no to slight irritation with undiluted and weak sensitization with 2% aq, acrylates/C10-30 alkyl acrylate cross polymer, no irritation with acrylates cross polymer at 30% in olive oil, and no irritation or sensitization with sodium acrylates cross polymer 2 (concentration not specified). Mostly, human testing with undiluted acrylates/C10-30 alkyl acrylate cross polymer, acrylates cross polymer, and acrylates/ethylhexyl acrylate cross polymer, up to 2.5% aq acrylates/vinyl isodecanoate cross polymer, 1% aq dilutions of formulations containing 2% acrylates/vinyl neodecanoate cross polymer, and formulations containing up to 2.6% lauryl methacrylate/glycol dimethacrylate cross polymers do not indicate any dermal irritation or sensitization. The only exception was a weak irritant response noted during an intensified Shelanski HRIPT with undiluted acrylates/C10-30 alkyl acrylate cross polymer.

Alternative test methods for ocular irritation indicated that acrylates/vinyl isodecanoate cross polymer and a formulation containing 1% lauryl methacrylate/glycol dimethacrylate cross polymer are not likely ocular irritants. In studies using rabbits, undiluted acrylates/C10-30 alkyl acrylate cross polymer produced minimal to moderate irritation, and it was considered a borderline irritant in unrinsed rabbit eyes. Acrylates cross polymer, at 50% in olive oil, and sodium acrylates cross polymer 2 did not appear to be ocular irritants in rabbit eyes.

Two different risk assessments evaluating the carcinogenic endpoint for benzene that may be present in acrylates/ C10-30 alkyl acrylates cross polymer resulted in different lifetime risk. One found that the risk was within the range associated with a 10^6 cancer risk, while the other reported a 20-fold greater risk.

Discussion

Few published data were available on the cross-linked alkyl acrylates. The CIR Expert Panel was provided with some summary information on the monomers for their use in evaluating these cross polymers.

The Panel noted that these cross-linked alkyl acrylates are macromolecules that are not expected to pass through the stratum corneum of the skin, so significant dermal absorption is not expected. Therefore, topically applied cosmetics are not expected to result in systemic or reproductive and developmental toxicity or to have genotoxic or carcinogenic effects upon use.

The Panel noted that cosmetic products containing these ingredients are reportedly used around the eyes, on the lips, and on other mucous membranes. Thus, cross-linked alkyl acrylates could be absorbed systemically through the relatively moist, thin stratum cornea of the conjunctiva, lips, and other mucous membranes, and through ingestion when applied to the lips. However, the Panel noted that any absorption through healthy intact mucous membranes is likely to be not significant, primarily because of the relatively large molecular sizes. Furthermore, the chemically inert nature of the polymers precludes degradation to smaller absorbable species. Absorption of the polymers and their residual monomers in cosmetic products also would be limited after application to the lips or eye area based on the relatively small fractions of the applied products that might be inadvertently ingested or make direct contact with the conjunctiva.

The Panel addressed the concern of residual monomer or solvent that might be present in the cross polymers. In most cases, taking into consideration the low amount of residual monomer in the cross polymers and the low use concentration of the polymers themselves, the Panel was not concerned that the presence of residual monomer would result in adverse effects. However, the use of benzene as a solvent is an exception and did cause concern. It cannot be predicted with certainty what quantity of benzene would be volatilized/leached from acrylates/C10-30 alkyl acrylates cross polymer during manufacture, formulation, or use. While some benzene is inevitably volatilized during manufacture, some benzene may be trapped in the polymer matrix and may leach out during formulation and use, but there is no way of knowing how much (or if *any*) benzene would leach out without appropriate data from a representative product formulation.

Conservative risk assessments were submitted by industry and by the CIR to address the carcinogenic endpoint for benzene, because it may be used as a solvent in the manufacture of acrylates/C10-30 alkyl acrylates cross polymer. Both assessments assumed the highest reported concentration of residual benzene in acrylates/C10-30 alkyl acrylates cross polymer used as a raw ingredient, the highest reported use concentration in a leave-on product of the raw ingredient polymerized in benzene, 10% evaporation of the residual benzene during manufacturing of the product, 10% benzene absorbed from the product through the skin, and the reported 95th percentile of the amount of product used daily. Industry reported that the cancer risk would $<10^{-6}$, by comparing the estimated daily absorbed dose of benzene from the product to drinking water concentrations that EPA suggests represents a 10^{-6} lifetime risk. However, CIR calculated upper bound lifetime cancer risk estimates up to 20-fold greater than 10^{-6}, based on EPA's cancer slope factors for benzene. Given the uncertainty of the assumptions used in the risk assessment, the Panel was not comfortable with using a risk assessment in evaluating the carcinogenic endpoint. Therefore, the Panel found the data insufficient to conclude that the residual benzene levels are safe.

Because these ingredients can be used in products that may be aerosolized, including sprays and powders, the Panel discussed the issue of potential inhalation toxicity. The limited data available from an acute exposure study suggested little potential for pulmonary overload or other respiratory effects at relevant doses. The Panel considered other data available to characterize the potential for cross-linked alkyl acrylates to cause systemic toxicity, irritation, sensitization, or other effects. They noted the lack of systemic toxicity at high doses

in several acute oral exposure studies, little or no irritation or sensitization in multiple tests of dermal and ocular exposure, and the absence of genotoxicity in Ames tests. In addition, these ingredients are macromolecules, insoluble in water, and chemically inert under physiological conditions or conditions of use, which supports the view that they are unlikely to be absorbed or cause local effects in the respiratory tract. Further, these ingredients are reportedly used at concentrations $\leq 4\%$ in cosmetic products that may be aerosolized. The Panel noted that 95% to 99% of particles produced in cosmetic aerosols would not be respirable to any appreciable extent. Coupled with the small actual exposure in the breathing zone and the concentrations at which the ingredients are used, this information indicates that inhalation would not be a significant route of exposure that might lead to local respiratory or systemic toxic effects.

Conclusion

The CIR Expert Panel concluded that the cross-linked alkyl acrylates listed below are safe in the present practices of use and concentration described in this safety assessment, except when they are polymerized in benzene. Acrylates/C10-30 alkyl acrylate cross polymer may be polymerized in benzene, and the available data are insufficient to make a determination of safety for this cross-linked alkyl acrylate when it is polymerized in benzene.

Acrylates/C10-30 alkyl acrylate cross polymer
Acrylates/C12-13 alkyl methacrylates/methoxyethyl acrylate cross polymer*
Acrylates cross polymer
Acrylates/ethylhexyl acrylate cross polymer
Acrylates/ethylhexyl acrylate/glycidyl methacrylate cross polymer*
Acrylates/PEG-4 dimethacrylate cross polymer*
Acrylates/Steareth-20 methacrylate cross polymer
Acrylates/vinyl isodecanoate cross polymer
Acrylates/vinyl neodecanoate cross polymer
Allyl methacrylate/glycol dimethacrylate cross polymer*
Allyl methacrylates cross polymer
Butyl acrylate/glycol dimethacrylate cross polymer*
C8-22 alkyl acrylates/methacrylic acid cross polymer*
Glycol dimethacrylate/vinyl alcohol cross polymer*
Lauryl methacrylate/glycol dimethacrylate cross polymer
Lauryl methacrylate/sodium methacrylate cross polymer
Methacrylic acid/PEG-6 methacrylate/PEG-6 dimethacrylate cross polymer*
PEG/PPG-5/2 methacrylate/methacrylic acid cross polymer*
Potassium acrylates/C10-30 alkyl acrylate cross polymer*
Sodium acrylates cross polymer 2
Sodium acrylates/C10-30 alkyl acrylate cross polymer
Sodium acrylates/vinyl isodecanoate cross polymer*
Stearyl/lauryl methacrylate cross polymer*

*Were the ingredients not in current use to be used in the future, the expectation is that they would be used in product categories and at concentrations comparable to others in this group.

Authors' Note

Unpublished sources cited in this report are available from the Director, Cosmetic Ingredient Review, 1620 L Street, NW, Suite 1200, Washington, DC 20036, USA.

Author Contributions

Fiume, M. contributed to conception and design, contributed to acquisition, analysis, and interpretation, and drafted manuscript; Heldreth, B. contributed to conception and design, contributed to acquisition, analysis, and interpretation, drafted manuscript, and critically revised manuscript; Boyer, I. contributed to conception and design, contributed to acquisition, analysis, and interpretation, drafted manuscript, and critically revised manuscript; Gill, L., Andersen, F. Alan, Bergfeld, W., Belsito, D. Hill, R., Klaassen, C., Liebler, D., Marks, J., Shank, R., Slaga, T., and Snyder, P. contributed to analysis and interpretation, contributed to conception and design, and critically revised the manuscript. All authors gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

Declaration of Conflicting Interests

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