Safety Assessment of Acrylamide/Acrylate Copolymers as Used in Cosmetics

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All interested persons are provided 60 days from the above release date (i.e., February 11, 2022) to comment on this safety assessment, and to identify additional published data that should be included or provide unpublished data which can be made public and included. Information may be submitted without identifying the source or the trade name of the cosmetic product containing the ingredient. All unpublished data submitted to the Cosmetic Ingredient Review (CIR) will be discussed in open meetings, will be available for review by any interested party, and may be cited in a peer-reviewed scientific journal. Please submit data, comments, or requests to the CIR Executive Director, Dr. Bart Heldreth

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ABBREVIATIONS

AMP	adenosine monophosphate
CAS	Chemical Abstracts Service
CIR	Cosmetic Ingredient Review
Council	Personal Care Products Council
Da	Daltons
DART	developmental and reproductive toxicity
DMSO	dimethyl sulfoxide
Dictionary	*International Cosmetic Ingredient Dictionary and Handbook*
EU	European Union
FDA	Food and Drug Administration
GD	gestation days
GRAS	generally recognized as safe
HCE	human corneal epithelium
HET-CAM	hen's egg test-chorioallantoic membrane
HRIPT	human repeat insult patch test
LC_{50}	lethal concentration 50
LD_{50}	median lethal dose
NOAEL	no-observable-adverse-effect-level
NR	not reported
OECD	Organisation for Economic Cooperation and Development
Panel	Expert Panel for Cosmetic Ingredient Safety
ppm	parts per million
TG	test guidelines
US	United States
VCRP	Voluntary Cosmetic Registration Program

ABSTRACT

The Expert Panel for Cosmetic Ingredient Safety (Panel) assessed the safety of 16 acrylamide/acrylate copolymers, most of which are reported to function in cosmetics as binders, film formers, and hair fixatives. The Panel reviewed the available data to determine the safety of these ingredients. The Panel stated that industry should continue to use good manufacturing practices to ensure that the concentration of acrylamide monomer in cosmetic formulations does not exceed 5 ppm, and concluded that the acrylamide/acrylate copolymers are safe in cosmetics in the present practices of use and concentration described in this safety assessment.

INTRODUCTION

This assessment reviews the safety of the following 16 acrylamide/acrylate copolymer ingredients as used in cosmetic formulations:

- Acrylamide/Ammonium Acrylate Copolymer
- Acrylamide/Sodium Acrylate Copolymer
- Acrylates/Acrylamide Copolymer
- Acrylates/*t*-Butylacrylamide Copolymer
- Acrylates/Methacrylamide Copolymer
- Acrylates/Octylacrylamide Copolymer
- AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide Copolymer
- AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide/Hydroxyethylacrylate Copolymer
- *t*-Butylacrylamide/Dimethylacrylamide/PEG-14 Diacrylate Crosspolymer
- Butyl Acrylate/Isopropylacrylamide/PEG-18 Dimethacrylate Crosspolymer
- Corn Starch/Acrylamide/Sodium Acrylate Copolymer
- Dimethyl Acrylamide/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer
- Dimethylacrylamide/Lauryl Methacrylate Copolymer
- Potassium Acrylates/Acrylamide Copolymer
- Sodium Acrylate/Hydroxyethyl Acrylamide Copolymer
- Starch/Acrylates/Acrylamide Copolymer

According to the web-based *International Cosmetic Ingredient Dictionary and Handbook (*wINCI *Dictionary)*, the majority of these ingredients are reported to function in cosmetics as binders, film formers, and hair fixatives (Table 1).[1] Other reported functions for ingredients in this group include viscosity-increasing agent, hair-waving/straightening agent, emulsion stabilizer, skin-conditioning agent – miscellaneous, dispersing agent – non-surfactant, antistatic agent, and hair conditioning agent.

These ingredients are being reviewed together as they share structural similarities. Specifically, each of these ingredients comprise a copolymer, polymerized from at least 1 acrylamide monomer and 1 acrylate monomer. The Expert Panel for Cosmetic Ingredient Safety (Panel) has previously reviewed the safety of several other polyacrylamides (Polyacrylate 2, Polyacrylamide, and Acrylamide/Sodium Acryloyldimethyltaurate Copolymer). Polyacrylate 2 and Acrylamide/Sodium Acryloyldimethyltaurate Copolymer were considered safe as used in the present practices of use and concentration (as described in that safety assessment).[2,3] Polyacrylamide was considered safe as used in the present practices of use and concentration (as described in that safety assessment), if the level of acrylamide monomer in formulation is not greater than 5 ppm.[4] In addition, aminomethyl propanol, an ingredient used in the neutralization process in the manufacturing of two of the acrylamide/acrylate copolymers, has previously been reviewed, and was considered safe as used in the present practices of use and concentration (as described in that safety assessment).[5] The full reports on these ingredients can be accessed on the Cosmetic Ingredient Review (CIR) website (https://www.cir-safety.org/ingredients).

This safety assessment includes relevant published and unpublished data that are available for each endpoint that is evaluated. Published data are identified by conducting an exhaustive search of the world's literature. A listing of the search engines and websites that are used and the sources that are typically explored, as well as the endpoints that the Panel typically evaluates, is provided on the CIR website (https://www.cir-safety.org/supplementaldoc/ preliminary-search-engines-and-websites; https://www.cir-safety.org/supplementaldoc/cir-report-format-outline). Unpublished data are provided by the cosmetics industry, as well as by other interested parties.

CHEMISTRY

Definition and Structure

All ingredients reviewed in this report comprise a copolymer, polymerized from at least 1 acrylamide monomer and 1 acrylate monomer. Acrylate monomers may comprise acrylic acid, methacrylic acid, or one of their esters.[1] For example, Acrylates/Methacrylamide Copolymer is a copolymer comprising methacrylamide and acrylate monomers, as demonstrated in idealized Figure 1. Two ingredients in this report, *t*-Butylacrylamide/Dimethylacrylamide/PEG-14 Diacrylate Crosspolymer and Butyl Acrylate/Isopropylacrylamide/PEG-18 Dimethacrylate Crosspolymer, are crosspolymers formed by crosslinking copolymer chains. The definitions and structures of all the ingredients are provided in Table 1.

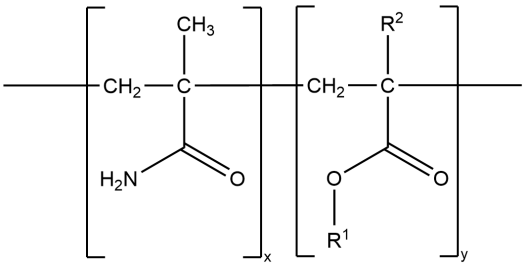


Figure 1. Acrylates/Methacrylamide Copolymer, wherein R^1 may be hydrogen, methyl, ethyl, propyl, or butyl; R^2 may be hydrogen or methyl; and, x and y are undefined.

According to a couple of suppliers, the acrylate/acrylamide copolymers reviewed in this report have large molecular weights ranging from 5000 to 250,000 g/mol.[6,7] Approximate molecular weights for AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide Copolymer, AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide/Hydroxyethylacrylate Copolymer, *t*-Butylacrylamide/Dimethylacrylamide/PEG-14 Diacrylate Crosspolymer, and Dimethyl Acrylamide/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer can be found in Table 2. Mean molecular weights, related weight distributions, and degrees of polymerization were neither found in the available literature nor submitted as unpublished data, for many of these ingredients.

Method of Manufacture

According to unpublished summary manufacturing data, the starting monomers of several of these ingredients (AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide Copolymer, AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide/Hydroxyethylacrylate Copolymer, Dimethyl Acrylamide/ Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer, and *t*-Butylacrylamide/ Dimethylacrylamide/PEG-14 Diacrylate Crosspolymer) are polymerized in ethanol, and then refined.[6-9] AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide Copolymer and AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide/Hydroxyethylacrylate Copolymer solutions are reported to be neutralized with 2-amino-2-methyl-1-propanol (aka aminomethyl propanol).

Composition and Impurities

Acrylamide/Ammonium Acrylate Copolymer

For Acrylamide/Ammonium Acrylate Copolymer, less than 2% of oligomers are < 500 Da.[10] In addition, this ingredient is not expected to contain 1,4-dioxane, ethylene oxide, solvent residues (e.g., benzene), free amines, or nitrosamines. Residual acrylamide amounts may be present at levels of 2 ppm.

AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide Copolymer

According to a manufacturer, less than 2000 ppm residual monomers were present in AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide Copolymer.[9] Acrylamide was not detected as an impurity.

AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide/Hydroxyethylacrylate Copolymer

Residual monomers were present in amounts of less than 3000 ppm in AMP-Acrylate/C1-18 Alkyl Acrylate/C1-8 Acrylamide/Hydroxyethylacrylate Copolymer.[8] Acrylamide was not detected as an impurity.

Dimethyl Acrylamide/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer

Dimethyl Acrylamide/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer contains less than 200 ppm residual monomers.[6] Acrylamide was not detected as an impurity.

USE

Cosmetic

The safety of the cosmetic ingredients addressed in this assessment is evaluated based on data received from the US Food and Drug Administration (FDA) and the cosmetics industry on the expected use of these ingredients in cosmetics. Use frequencies of individual ingredients in cosmetics are collected from manufacturers and reported by cosmetic product category in the FDA Voluntary Cosmetic Registration Program (VCRP) database. Use concentration data are submitted by the cosmetic industry in response to a survey, conducted by the Personal Care Products Council (Council), of maximum reported use concentrations by product category.

According to 2021 VCRP survey data, the ingredient with the highest number of uses, Acrylates/Octylacrylamide Copolymer, is reported to be used in 160 formulations; all other in-use ingredients are reported to be used in 14 formulations or less (Table 3).[11] The results of the concentration of use survey conducted by the Council in 2020 indicate that Acrylates/

t-Butylacrylamide Copolymer, Acrylates/Octylacrylamide Copolymer, and Dimethyl Acrylamide/Hydroxyethyl Acrylate/ Methoxyethyl Acrylate Copolymer are each used at up to 7% in leave-on formulations (i.e., aerosol hair sprays, mascaras, and tonics, dressings, and other hair grooming aids, respectively).[12] Use concentration data were reported for Dimethylacrylamide/Lauryl Methacrylate Copolymer, but no uses were received in the VCRP; it should be presumed that there is at least one use in every category for which a concentration is reported. The 6 ingredients not in use, according to the VCRP data and industry survey, are listed in Table 4.

Two ingredients are used in products that can potentially be ingested (Acrylamide/Sodium Acrylate Copolymer, used in lipstick (concentration not reported), and Acrylates/Octylacrylamide Copolymer, used in dentifrices (toothpaste) at up to 19.4%). Acrylates/Octylacrylamide Copolymer is also used in products used near the eye (i.e., eyeliners up to 4.6%, eye shadows up to 0.001%, and mascaras at up to 7%). In addition, mucous membrane exposure to these ingredients may occur (Acrylates/Acrylamide Copolymer is used in bath soaps and detergents (concentration not reported), and Corn Starch/ Acrylamide/Sodium Acrylate Copolymer is used in bath oils, tablets, and salts at up to 2%). Furthermore, some of these ingredients are used in cosmetic sprays and could possibly be inhaled; for example, Acrylates/ *t*-Butylacrylamide Copolymer is reported to be used at 7% in aerosol hair sprays and Acrylates/Octylacrylamide Copolymer is reportedly used in face powders (concentration not reported).

All of the acrylate/acrylamide copolymers named in this report are listed in the European Union inventory of cosmetic ingredients.[13] According to the European Commission, several of these ingredients (Acrylamide/Ammonium Acrylate Copolymer, Acrylamide/Sodium Acrylate Copolymer, Acrylates/Acrylamide Copolymer, AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide Copolymer, Corn Starch/Acrylamide/Sodium Acrylate Copolymer, Dimethyl Acrylamide/ Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer, Potassium Acrylates/Acrylamide Copolymer and Starch/ Acrylates/Acrylamide Copolymer) are linked to the entry for polyacrylamide, which states that the maximum residual acrylamide content in final formulations must not exceed 0.1 mg/kg in body care leave-on products and 0.5 mg/kg in other cosmetic products.[14] AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide/Hydroxyethylacrylate Copolymer and Dimethyl Acrylamide/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer are linked to the entry of monoalkylamines, monoalkanolamines, and their salts, which states that these substances should not be used with nitrosating systems, must have a minimum purity of 99%, must not exceed a nitrosamine content of 50 µg/kg, and must be kept in nitrite-free containers. In addition, finished products containing these ingredients should not exceed a secondary amine content of 0.5%.

Non-Cosmetic

Acrylate/Acrylamide Copolymer and Acrylamide/Sodium Acrylate Copolymer

Acrylate/Acrylamide Copolymer and Acrylamide/Sodium Acrylate Copolymer are used as indirect, direct, and secondary food additives. CFR citation details regarding these uses and relevant limitations can be found in Table 5.

TOXICOKINETIC STUDIES

Toxicokinetics studies were not found in the published literature, and unpublished data were not submitted.

TOXICOLOGICAL STUDIES

Acute Toxicity Studies

The acute dermal, oral, and inhalation studies summarized below can be found in Table 6.

The acute dermal LD_{50} was reported to be greater than 2000 mg/kg in rabbits dosed with Acrylates/Octylacrylamide Copolymer.[15] Acute oral toxicity assays were performed in rats using several test substances (Acrylates/Octylacrylamide Copolymer (15% solids), a 40% ethanolic solution of AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide Copolymer, a 40% ethanolic solution of AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide/Hydroxyethylacrylate Copolymer, and a 70% ethanol solution of Dimethyl Acrylamide/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer).[6,8,9,15] Oral D_{50}s reported for these assays were greater than 2000 mg/kg, excluding Acrylates/Octylacrylamide Copolymer, in which the reported LD_{50} was greater than 2300 mg solids/kg bw. An LC_{50} of greater than 3.4 mg/l was reported in an acute inhalation toxicity assay performed in rats exposed to Acrylates/Octylacrylamide Copolymer.[15]

Short-Term Toxicity Studies

Dermal

AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide/Hydroxyethylacrylate Copolymer

A 28-d dermal toxicity assay was performed in Wistar Han rats (5/sex/group).[16] The test substance (38% AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide/Hydroxyethylacrylate Copolymer in water; 2 ml/kg) was applied to the skin at doses of 0, 100, 300, and 1000 mg/kg bw/d, under semi-occlusive conditions, for 6 h/d. Clinical, hematological, urinary, and histopathological parameters were evaluated. Very slight erythema was observed between days 26 and 29 in two females dosed with 1000 mg/kg of the test substance. No other skin reactions were observed. No relevant adverse test item-related effects were observed throughout the study. The no-observed-adverse-effect level (NOAEL) was determined to be 1000 mg/kg bw/d.

Subchronic Toxicity Studies

Inhalation

Acrylates/Octylacrylamide Copolymer

Sprague-Dawley rats (10/sex/group) were exposed to 0, 199, 491, or 828 µg/m^3 Acrylates/Octylacrylamide Copolymer in ethanol (mean particle aerodynamic diameter of 1.9 µ), via a full body chamber, for 4 h/d, 7 d/wk, for 13 wk.[15] Clinical, hematological, and histopathological parameters were observed. The test substance did not produce any adverse effects.

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY STUDIES

AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide/Hydroxyethylacrylate Copolymer

A dermal prenatal development toxicity assay was performed in pregnant female Wistar rats (24/group).[17] The test substance (38% AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide/Hydroxyethylacrylate Copolymer in water; 2 ml/kg) was applied to the skin, in doses of 0, 100, 300, and 1000 mg/kg bw/d, under semi-occlusive conditions, on gestation days 5 to 19. Each application lasted for a duration of 6 h. Maternal skin reactions, body weight, clinical parameters, and gross pathological effects were observed. In addition, litter parameters and external, visceral, and skeletal observations of fetuses were performed. No adverse effects were observed for any of the evaluated parameters. The NOAEL for maternal and fetal toxicity was determined to be greater than 1000 mg/kg bw/d.

GENOTOXICITY

In Vitro

Acrylamide/Ammonium Acrylate Copolymer

The potential genotoxicity of Acrylamide/Ammonium Acrylate Copolymer (up to 5000 µg/plate) was evaluated via an Ames test *(Salmonella typhimurium* (strains not specified) and *Escherichia coli* WP2 (uvrA-)).[10] No other details regarding this study were provided. The test substance was considered to be non-genotoxic.

AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide Copolymer

A 40% ethanolic solution of AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide Copolymer was used in an Ames assay to determine potential genotoxicity.[9] No other details regarding this study were provided. The test substance was considered to be non-genotoxic.

AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide/Hydroxyethylacrylate Copolymer

An Ames assay was performed with and without metabolic activation using a mixture containing 38% AMP-Acrylates/C1-18 Alkyl Acrylate/C1-18 Alkyl Acrylamide/Hydroxyethylacrylate Copolymer (5, 15.81, 50, 158.1, 500, 1581, and 5000 µg/plate; dissolved in dimethyl sulfoxide (DMSO)) in *S. typhimurium* strains TA98, TA100, TA1535, TA1537, and TA102.[18] Negative (DMSO) and positive controls (2-nitrofluorene, sodium azide, 9-aminoacridine, mitomycin c, benzo[a]pyrene, 2-aminoanthracene) were used, and yielded expected results. The test substance was not considered to be mutagenic.

The same test substance (up to 300 µg/ml; dissolved in DMSO) was evaluated in an in vitro mammalian cell micronucleus assay using human peripheral blood lymphocytes, with and without metabolic activation.[19] Negative (DMSO) and positive controls (mitomycin C, cyclophosphamide, vinblastine) were used, and yielded expected results. The test substance did not induce micronuclei in cultured human peripheral blood lymphocytes.

Dimethyl Acrylamide/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer

The genotoxic potential of a 70% ethanolic solution of Dimethyl Acrylamide/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer was evaluated via an Ames assay.[6] No details regarding this assay were provided. The test material was considered to be non-genotoxic.

CARCINOGENICITY STUDIES

Carcinogenicity studies were not found in the published literature, and unpublished data were not submitted.

DERMAL IRRITATION AND SENSITIZATION

Details regarding the irritation and sensitization studies summarized below can be found in Table 7.

Reconstructed human epidermis cytotoxicity assays were performed using a mixture containing 32% Acrylamide/Ammonium Acrylate Copolymer and undiluted *t*-Butylacrylamide Copolymer.[20] Both test substances were considered to be non-irritating. In an animal assay, a neutralized, aqueous solution of Acrylates/Octylacrylamide Copolymer (15% solids) was applied to intact and abraded skin sites on New Zealand White rabbits, under occlusive conditions.[15] The test substance was considered to be mildly irritating. A primary skin irritation assay performed in rabbits using AMP-Acrylates/C1-18 Alkyl

Acrylate/C1-8 Alkyl Acrylamide Copolymer yielded negative results.[9] Mild irritation was noted in a primary skin assay performed in rabbits using a 10% aqueous solution of Dimethyl Acrylamide/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer; however the same test substance was non-irritating in a cumulative irritation assay performed in guinea pigs.[6] Mild irritation was also noted in a primary irritation assay performed in rabbits using a 40% ethanolic solution of AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide/Hydroxyethylacrylate Copolymer.[8] No irritation was noted in a human dermal irritation assay using a 5% aqueous solution of Acrylamide/Ammonium Acrylate Copolymer.[10] A human dermal irritation assay performed using a 50% aqueous solution of Dimethyl Acrylamide/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer yielded negative results.[6]

In vitro EpiSkin® dermal sensitization assays were performed on AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide Copolymer and a 50% aqueous solution of Dimethyl Acrylamide/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer.[6,9] Both test substances were considered to be non-sensitizing. The skin sensitization potential of a mixture containing 32% Acrylamide/Ammonium Acrylate Copolymer was evaluated in guinea pigs (tested undiluted under occlusive conditions).[21] No signs of sensitization were observed. Guinea pig maximization assays were performed to evaluate the potential sensitization of Acrylates/Octylacrylamide Copolymer (5 - 100%), a 40% ethanolic solution of AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide Copolymer, and a 70% ethanolic solution Dimethyl Acrylamide/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer.[6,9,15] All test substances were considered to be non-sensitizing. Similarly, no signs of sensitization were observed in a local lymph node assay performed in mice using a mixture containing 38% AMP-Acrylates/C1-18 Alkyl Acrylate/C1-18 Alkyl Acrylamide/Hydroxyethylacrylate Copolymer (5, 10, 25, and 50% in dimethylformamide).[22] Several test substances (mixture containing 0.66% Acrylamide/Ammonium Acrylate Copolymer, aqueous solution of neutralized Acrylates/Octylacrylamide Copolymer (15% solids), and a formula containing 13.34% Acrylates/*t*-Butylacrylamide Copolymer) were evaluated for potential sensitization via human repeat insult patch tests (HRIPTs).[10,15,23] All test substances evaluated were considered to be non-irritating and non-sensitizing.

OCULAR IRRITATION STUDIES

The ocular irritation studies summarized below can be found in Table 8.

In vitro ocular irritation assays performed using a 3% solution of Acrylamide/Ammonium Acrylate Copolymer, AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide Copolymer, and a 50% aqueous solution of Dimethyl Acrylamide/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer yielded negative results.[6,9,10] Mild irritation was noted in an in in vitro ocular irritation assay performed using a 40% ethanolic solution of AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide Copolymer.[6] No ocular irritation was noted in an ocular irritation assay performed on New Zealand White rabbits using Acrylates/Octylacrylamide Copolymer (tested at 100%).[15] However, mild ocular irritation was observed in an ocular irritation assay performed in New Zealand white rabbits using a neutralized, aqueous solution of Acrylates/Octylacrylamide Copolymer (15% solids). Slight irritation was observed in an ocular irritation assay performed on rabbits using a 40% ethanolic solution of AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide/Hydroxyethylacrylate Copolymer.[8] No irritation was noted in an ocular irritation assay performed in rabbits using a 10% aqueous solution of Dimethyl Acrylamide/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer.[6]

SUMMARY

The majority of the acrylamide/acrylate copolymers reviewed in this report are reported to function as binders, film formers, and hair fixatives. According to manufacturers, Acrylamide/Ammonium Acrylate Copolymer, AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide Copolymer, AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide/Hydroxyethylacrylate Copolymer, and Dimethyl Acrylamide/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer are reported to contain less than 3000 ppm residual monomers.

Based on 2021 FDA VCRP and data, Acrylates/Octylacrylamide Copolymer is reported to be used in 160 formulations. All other in-use formulations are reported to be used in 14 formulations or less. The results of the concentration of use survey conducted by the Council indicate that Acrylates/*t*-Butylacrylamide Copolymer, Acrylates/Octylacrylamide Copolymer, and Dimethyl Acrylamide/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer are used at up to 7% in leave-on formulations (i.e., aerosol hair sprays, mascaras, and tonics, dressings, and other hair grooming aids, respectively). According to the European Commission, several of the ingredients reviewed in this report are linked to entries for substances that may be used in cosmetics under certain restrictions. In addition, Acrylate/Acrylamide Copolymer and Acrylamide/Sodium Acrylate Copolymer are used as indirect, direct, and secondary food additives.

The acute dermal LD_{50} was reported to be greater than 2000 mg/kg in rabbits dosed with Acrylates/Octylacrylamide Copolymer. Acute oral toxicity assays were performed in rats using several test substances (Acrylates/Octylacrylamide Copolymer (15% solids), a 40% ethanolic solution of AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide Copolymer, a 40% ethanolic solution of AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide/Hydroxyethylacrylate Copolymer, and a 70% Dimethyl Acrylamide/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer). LD_{50}s reported for these assays were greater than 2000 mg/kg, excluding Acrylates/Octylacrylamide Copolymer, in which the reported LD_{50}

was greater than 2300 mg solids/kg bw. An LC_{50} of greater than 3.4 mg/l was reported in an acute inhalation toxicity assay performed in rats exposed to Acrylates/Octylacrylamide Copolymer.

In a 28-d dermal toxicity assay, Wistar rats were given 38% AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide/Hydroxyethylacrylate Copolymer in water in doses of up to 1000 mg/kg bw/d. The NOAEL was determined to be 1000 mg/kg bw/d. The potential subchronic inhalation toxicity of Acrylates/Octylacrylamide Copolymer in ethanol (up to 828 $\mu g/m^3$) was evaluated in Sprague-Dawley rats, for 13 wks. No adverse effects were observed.

Potential dermal developmental toxicity of 38% AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide/ Hydroxyethylacrylate Copolymer in water (up to 1000 mg/kg bw/d; semi-occlusive conditions; gestation days 5 - 19) was evaluated in pregnant female Wistar rats. The NOAEL for maternal and fetal toxicity was determined to be greater than 1000 mg/kg bw/d.

Ames assays were performed on several test substances (Acrylamide/Ammonium Acrylate Copolymer, a 40% ethanolic solution of AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide Copolymer, a mixture containing 38% AMP-Acrylates/C1-18 Alkyl Acrylate/C1-18 Alkyl Acrylamide/Hydroxyethylacrylate Copolymer, and a 70% ethanolic solution of Dimethyl Acrylamide/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer). All test substances were considered to be non-genotoxic. In addition, negative results were obtained in an in vitro mammalian cell micronucleus assay performed in human peripheral blood lymphocytes using a mixture containing 38% AMP-Acrylates/C1-18 Alkyl Acrylate/C1-18 Alkyl Acrylamide/Hydroxyethylacrylate Copolymer.

Reconstructed human epidermis cytotoxicity assays were performed using a mixture containing 32% Acrylamide/ Ammonium Acrylate Copolymer and undiluted *t*-Butylacrylamide Copolymer. Both test substances were considered to be non-irritating. In an animal assay, a neutralized, aqueous solution of Acrylates/Octylacrylamide Copolymer (15% solids) was applied to intact and abraded skin sites on New Zealand White rabbits, under occlusive conditions. The test substance was considered to be mildly irritating. A primary skin irritation assay performed in rabbits using AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide Copolymer yielded negative results. Mild irritation was noted in a primary skin assay performed in rabbits using a 10% aqueous solution of Dimethyl Acrylamide/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer; however, the same test substance was non-irritating in a cumulative irritation assay performed in guinea pigs. Mild irritation was also noted in a primary irritation assay performed in rabbits using a 40% ethanolic solution of AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide/Hydroxyethylacrylate Copolymer. No irritation was noted in a human dermal irritation assay using a 5% aqueous solution of Acrylamide/Ammonium Acrylate Copolymer.[10] A human dermal irritation assay performed using a 50% aqueous solution of Dimethyl Acrylamide/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer yielded negative results.

In vitro EpiSkin® dermal sensitization assays were performed on AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide Copolymer and a 50% aqueous solution of Dimethyl Acrylamide/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer. Both test substances were considered to be non-sensitizing. The skin sensitization potential of a mixture containing 32% Acrylamide/Ammonium Acrylate Copolymer was evaluated in guinea pigs (tested undiluted under occlusive conditions). No signs of sensitization were observed. Guinea pig maximization assays were performed to evaluate the potential sensitization of Acrylates/Octylacrylamide Copolymer (5 - 100%), a 40% ethanolic solution of AMP-Acrylates/ C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide Copolymer, and a 70% ethanolic solution Dimethyl Acrylamide/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer. All test substances were considered to be non-sensitizing. Similarly, no signs of sensitization were observed in a local lymph node assay performed in mice using a mixture containing 38% AMP-Acrylates/C1-18 Alkyl Acrylate/C1-18 Alkyl Acrylamide/Hydroxyethylacrylate Copolymer (up to 50% in dimethyl-formamide). Several test substances (mixture containing 0.66% Acrylamide/Ammonium Acrylate Copolymer, aqueous solution of neutralized Acrylates/Octylacrylamide Copolymer (15% solids), and a formula containing 13.34% Acrylates/ *t*-Butylacrylamide Copolymer) were evaluated for potential sensitization via HRIPTs. All test substances evaluated were considered to be non-irritating and non-sensitizing.

In vitro ocular irritation assays performed using a 3% solution of Acrylamide/Ammonium Acrylate Copolymer, AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide Copolymer, and a 50% aqueous solution of Dimethyl Acrylamide/ Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer yielded negative results. Mild irritation was noted in an in in vitro ocular irritation assay performed using a 40% ethanolic solution of AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide Copolymer. No ocular irritation was noted in an ocular irritation assay performed on New Zealand White rabbits using Acrylates/Octylacrylamide Copolymer. However, mild ocular irritation was observed in an ocular irritation assay performed in New Zealand white rabbits using a neutralized, aqueous solution of Acrylates/Octylacrylamide Copolymer (15% solids). Slight irritation was observed in an ocular irritation assay performed on rabbits using a 40% ethanolic solution of AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide/Hydroxyethylacrylate Copolymer. No irritation was noted in an ocular irritation assay performed in rabbits using a 10% aqueous solution of Dimethyl Acrylamide/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer.

DISCUSSION

This assessment reviews the safety of 16 acrylamide/acrylate copolymers as used in cosmetic formulations. The Panel reviewed the available data and concluded that these ingredients are safe in the present practices of use and concentration as described in the safety assessment. Formulators of these ingredients should ensure that the concentration of acrylamide monomer in cosmetic formulations does not exceed 5 ppm.

The Panel determined that the available chemistry, method of manufacturing, composition and impurities, systemic toxicity, and dermal irritation/sensitization data were sufficient to support the safety of these ingredients. Safety was further supported by the large molecular weights of these ingredients, which precludes dermal absorption, and the use of these ingredients as food and water additives. The possibility of the presence of residual monomers in these ingredients was noted, and the Panel stated that formulators should minimize the presences of residual monomer, and ensure that the concentration of acrylamide monomer in cosmetic formulations does not exceed 5 ppm. In addition, it should be noted that these ingredients are insoluble and are unlikely to form nitrosamines or nitrosamides.

The Panel discussed the fact that some of these ingredients are used in formulations that could result in incidental inhalation (e.g., Acrylates/ *t*-Butylacrylamide Copolymer is used at up to 7% in aerosol and pump hair sprays). The limited toxicity data that were available did not report adverse effects. Additionally, the Panel noted that in aerosol products, 95% – 99% of droplets/particles would not be respirable to any appreciable amount. Furthermore, droplets/particles deposited in the nasopharyngeal or bronchial regions of the respiratory tract present no toxicological concerns based on the chemical and biological properties of these ingredients. Coupled with the small actual exposure in the breathing zone, the concentrations at which the ingredients are used, the large, irrespirable molecule sizes, and a lack of systemic toxicity, the available information indicates that incidental inhalation would not be a significant route of exposure that might lead to local respiratory or systemic effects. A detailed discussion and summary of the Panel's approach to evaluating incidental inhalation exposures to ingredients in cosmetic products is available at https://www.cir-safety.org/cir-findings.

CONCLUSION

The Expert Panel for Cosmetic Ingredient Safety concluded that the following 16 acrylamide/acrylate copolymers are safe in cosmetics in the present practices of use and concentration as described in this safety assessment.

Acrylamide/Ammonium Acrylate Copolymer
Acrylamide/Sodium Acrylate Copolymer
Acrylates/Acrylamide Copolymer
Acrylates/*t*-Butylacrylamide Copolymer
Acrylates/Methacrylamide Copolymer
Acrylates/Octylacrylamide Copolymer
AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide Copolymer
AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide/Hydroxyethylacrylate Copolymer*
t-Butylacrylamide/Dimethylacrylamide/PEG-14 Diacrylate Crosspolymer*
Butyl Acrylate/Isopropylacrylamide/PEG-18 Dimethacrylate Crosspolymer*
Corn Starch/Acrylamide/Sodium Acrylate Copolymer
Dimethyl Acrylamide/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer
Dimethylacrylamide/Lauryl Methacrylate Copolymer
Potassium Acrylates/Acrylamide Copolymer*
Sodium Acrylate/Hydroxyethyl Acrylamide Copolymer*
Starch/Acrylates/Acrylamide Copolymer*

**Not reported to be in current use. Were ingredients in this group 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.*

TABLES

Table 1. INCI names, definitions, and reported functions of the Acrylamide/Acrylate Copolymer ingredients in this safety assessment[1, CIR Staff]

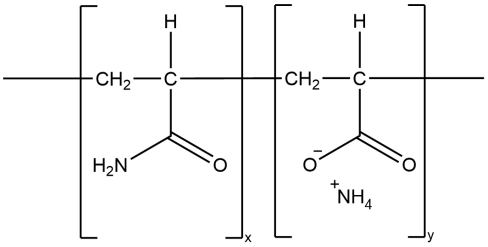
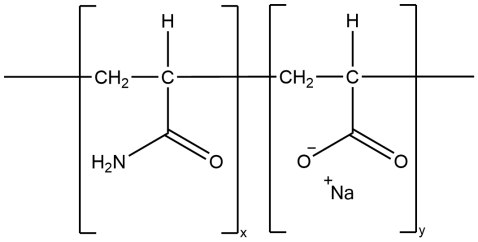
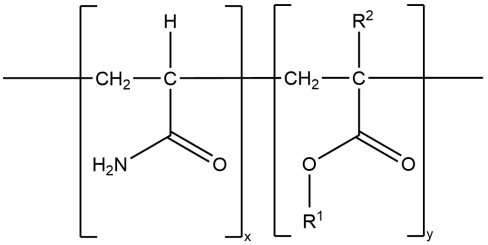
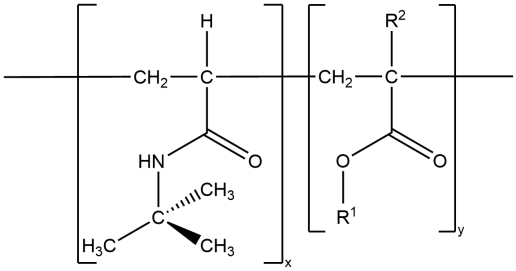
Ingredient (CAS No.)	Definition	Function
Acrylamide/Ammonium Acrylate Copolymer [26100-47-0]	Acrylamide/Ammonium Acrylate Copolymer is a copolymer of Acrylamide and Ammonium Acrylate monomers. 	Binders; Film Formers; Hair Fixatives
Acrylamide/Sodium Acrylate Copolymer [25085-02-3; 25987-30-8]	Acrylamide/Sodium Acrylate Copolymer is a copolymer of Acrylamide and sodium acrylate monomers. 	Binders; Film Formers; Viscosity Increasing Agents - Aqueous
Acrylates/Acrylamide Copolymer [9003-06-9]	Acrylates/Acrylamide Copolymer is a copolymer of Acrylamide and one or more monomers of Acrylic Acid, Methacrylic Acid or one of their simple esters. 	Binders; Film Formers; Hair Fixatives
Acrylates/*t*-Butylacrylamide Copolymer	Acrylates/t-Butylacrylamide Copolymer is a copolymer of t-Butylacrylamide and one or more monomers of Acrylic Acid, Methacrylic Acid, or one of their simple esters.  **wherein R^1 may be hydrogen, methyl, ethyl, propyl, or butyl; and R^2 may be hydrogen or methyl**	Binders; Film Formers; Hair Fixatives

Table 1. INCI names, definitions, and reported functions of the Acrylamide/Acrylate Copolymer ingredients in this safety assessment[1, CIR Staff]

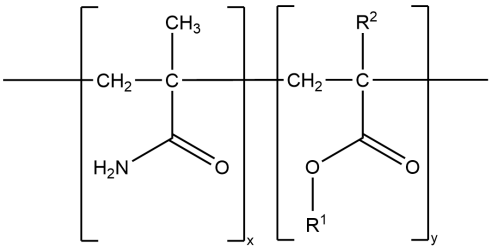
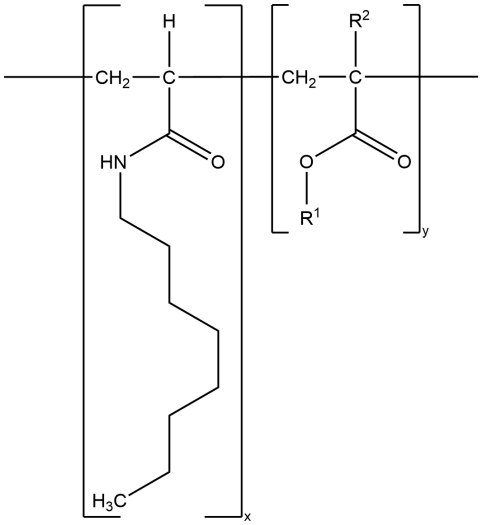
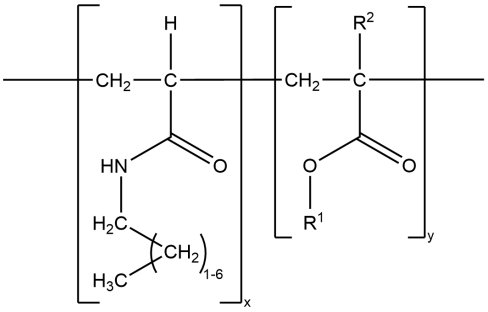
Ingredient (CAS No.)	Definition	Function
Acrylates/Methacrylamide Copolymer	Acrylates/Methacrylamide Copolymer is a copolymer of Methacrylamide and one or more monomers of Acrylic Acid, Methacrylic Acid or one of their simple esters.  **wherein R^1 may be hydrogen, methyl, ethyl, propyl, or butyl; and R^2 may be hydrogen or methyl**	Film Formers; Hair Fixatives
Acrylates/Octylacrylamide Copolymer [129702-02-9]	Acrylates/Octylacrylamide Copolymer is a copolymer of octylacrylamide and one or more monomers consisting of Acrylic Acid, Methacrylic Acid or one of their simple esters. 	Film Formers; Hair Fixatives
AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide Copolymer	AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide Copolymer is a polymer of C1-18 Alkyl Acrylate, C1-8 Alkyl Acrylamide and the aminomethylpropanol salt of a monomer consisting of Acrylic Acid, Methacrylic Acid or one of their simple esters.  **wherein R^1 may be hydrogen, C1-18-alkyl, or a salt of 3-aminopropanol; and R^2 may be hydrogen or methyl**	Film Formers; Hair Fixatives

Table 1. INCI names, definitions, and reported functions of the Acrylamide/Acrylate Copolymer ingredients in this safety assessment[1, CIR Staff]

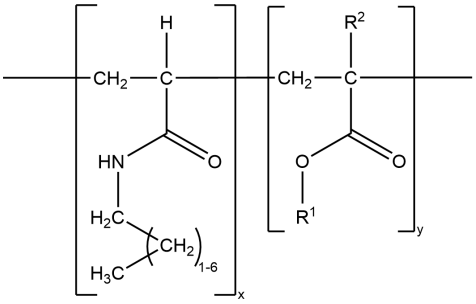
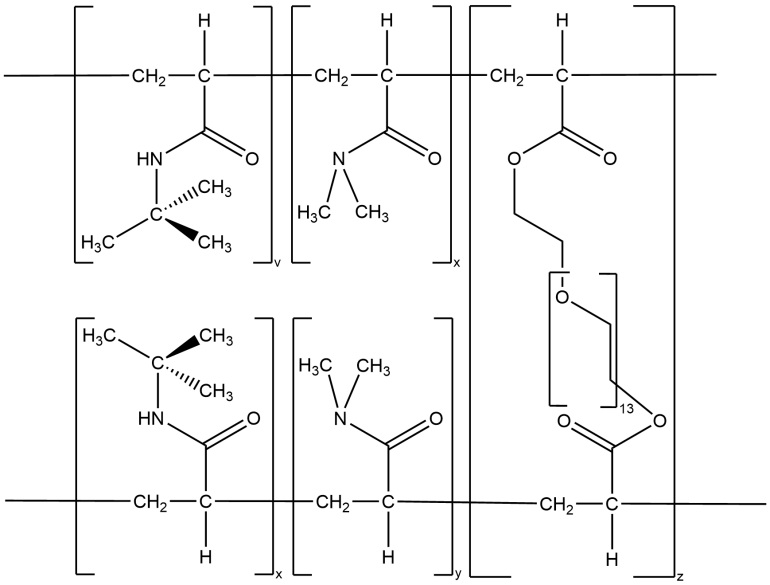
Ingredient (CAS No.)	Definition	Function
AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide/Hydroxyethylacrylate Copolymer	AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide/Hydroxyethylacrylate Copolymer is a polymer of C1-18 Alkyl Acrylate or C1-18 alkyl methacrylate, C1-8 Alkyl Acrylamide, 2-Hydroxyethyl Acrylate, and the aminomethylpropanol salt of a monomer consisting of Acrylic Acid, Methacrylic Acid or one of their simple esters.  **wherein R^1 may be hydrogen, C1-18-alkyl, 2-hydroxyethyl, or a salt of 3-aminopropanol; and R^2 may be hydrogen or methyl**	Hair-Waving/Straightening Agents
t-Butylacrylamide/Dimethylacrylamide/PEG-14 Diacrylate Crosspolymer	t-Butylacrylamide/Dimethylacrylamide/PEG-14 Diacrylate Crosspolymer is a copolymer of t-Butylacrylamide and Dimethylacrylamide, cross-linked with PEG-14 diacrylate. 	Hair Fixatives

Table 1. INCI names, definitions, and reported functions of the Acrylamide/Acrylate Copolymer ingredients in this safety assessment[1, CIR Staff]

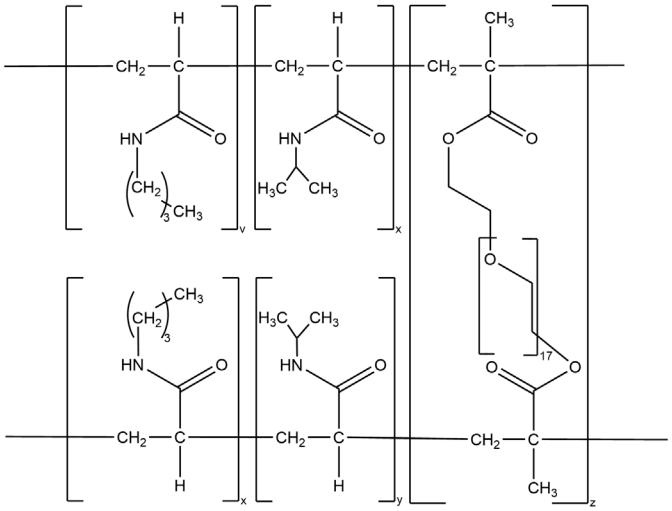
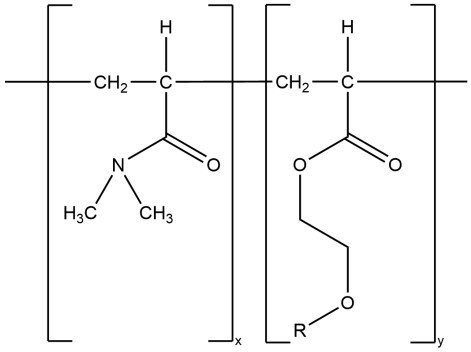
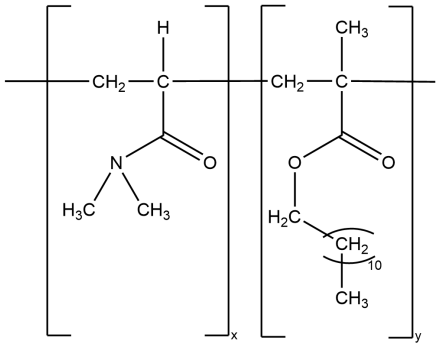
Ingredient (CAS No.)	Definition	Function
Butyl Acrylate/Isopropylacrylamide/PEG-18 Dimethacrylate Crosspolymer	Butyl Acrylate/Isopropylacrylamide/PEG-18 Dimethacrylate Crosspolymer is a crosslinked copolymer of Butyl Acrylate, Isopropylacrylamide and PEG-18 dimethacrylate monomers.	Emulsion Stabilizers; Film Formers; Skin-Conditioning Agents - Miscellaneous
		
Corn Starch/Acrylamide/Sodium Acrylate Copolymer	Corn Starch/Acrylamide/Sodium Acrylate Copolymer is a polymer of Zea Mays (Corn) Starch, Acrylamide and sodium acrylate monomers.	Dispersing Agents - Nonsurfactant; Emulsion Stabilizers; Film Formers; Hair Fixatives
Dimethyl Acrylamide/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer	Dimethyl Acrylamide/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer is a copolymer of Dimethylacrylamide, 2-Hydroxyethyl Acrylate and Methoxyethyl Acrylate monomers.  wherein R may be hydrogen or methyl	Hair Fixatives
Dimethylacrylamide/Lauryl Methacrylate Copolymer [103479-14-7]	Dimethylacrylamide/Lauryl Methacrylate Copolymer is a copolymer of Dimethylacrylamide and Lauryl Methacrylate. 	Binders; Film Formers; Hair Fixatives

Table 1. INCI names, definitions, and reported functions of the Acrylamide/Acrylate Copolymer ingredients in this safety assessment[1, CIR Staff]

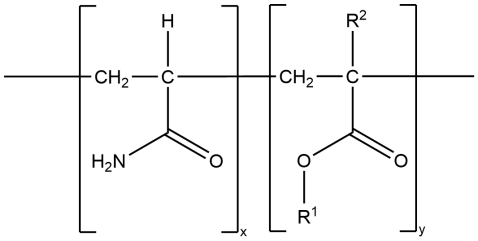
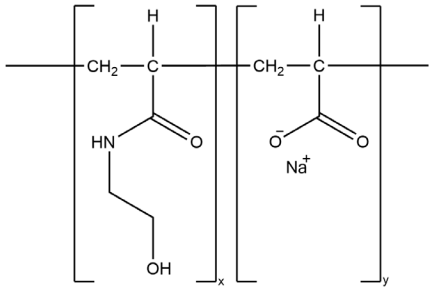
Ingredient (CAS No.)	Definition	Function
Potassium Acrylates/Acrylamide Copolymer	Potassium Acrylates/Acrylamide Copolymer is the potassium salt of Acrylates/Acrylamide Copolymer.  **wherein R^1 may be hydrogen, methyl, ethyl, propyl, or butyl; and R^2 may be hydrogen or methyl**	Film Formers
Sodium Acrylate/Hydroxyethyl Acrylamide Copolymer	Sodium Acrylate/Hydroxyethyl Acrylamide Copolymer is a copolymer of sodium acrylate and Hydroxyethyl Acrylamide that conforms generally to the formula: 	Antistatic Agents; Film Formers; Hair Conditioning Agents; Hair Fixatives
Starch/Acrylates/Acrylamide Copolymer	Starch/Acrylates/Acrylamide Copolymer is a polymer of starch, Acrylamide and a monomer consisting of Acrylic Acid, Methacrylic Acid or one of their simple ester.	Film Formers; Viscosity Increasing Agents - Aqueous

Table 2. Molecular weights of the acrylamide/acrylate copolymers

Ingredient	Approximate Molecular Weight (g/mol)	Reference
AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide Copolymer	24,000 (percent molecular weight less than 500 Da: 0.0001%)	[9]
AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide/Hydroxyethylacrylate Copolymer	250,000 (percent molecular weight less than 500 Da: 0%)	[8]
t-Butylacrylamide/Dimethylacrylamide/PEG-14 Diacrylate Crosspolymer	5000 (percent molecular weight less than 500 Da: < 0.0005%)	[7]
Dimethyl Acrylamide/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer	10,000 (percent molecular weight less than 500 Da: 0.0124%)	[6]

Da = Daltons

Table 3. Frequency (2021) and concentration (2020) of use according to duration and exposure[11,12]

	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)
	Acrylamide/Ammonium Acrylate Copolymer		**Acrylamide/Sodium Acrylate Copolymer**		**Acrylates/Acrylamide Copolymer**	
Totals*	**1**	**NR**	**14**	**0.5 – 2.8**	**7**	**0.41**
Duration of Use						
Leave-On	*1*	*NR*	*13*	*NR*	*4*	*0.41*
Rinse-Off	*NR*	*NR*	*1*	*NR*	*3*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type						
Eye Area	NR	NR	NR	NR	NR	NR
Incidental Ingestion	NR	NR	2	NR	NR	NR
Incidental Inhalation-Spray	1[a]	NR	6[a]; 5[b]	2.8[a]	2[b]	NR
Incidental Inhalation-Powder	NR	NR	5[b]	0.5[c]	2[b]	NR
Dermal Contact	1	NR	10	0.5 – 2.8	7	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	2	2.8	NR	0.41
Hair-Coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	2	NR	3	NR
Baby Products	NR	NR	NR	NR	NR	NR
	Acrylates/*t*-Butylacrylamide Copolymer		**Acrylates/Methacrylamide Copolymer**		**Acrylates/Octylacrylamide Copolymer**	
Totals*	**4**	**0.06 – 7**	**2**	**NR**	**160**	**0.00097 – 19.4**
Duration of Use						
Leave-On	*4*	*0.06 – 7*	*NR*	*NR*	*160*	*0.00097 – 7*
Rinse Off	*NR*	*NR*	*2*	*NR*	*NR*	*4.9 – 19.4*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type						
Eye Area	NR	NR	NR	NR	17	0.00097 – 7
Incidental Ingestion	NR	NR	NR	NR	NR	19.4
Incidental Inhalation-Spray	1	0.06 – 7; 5[a]	NR	NR	123; 6[a]	0.5 – 3.2
Incidental Inhalation-Powder	NR	NR	NR	NR	3	NR
Dermal Contact	NR	NR	NR	NR	136	0.00097 – 4.9
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	4	0.06 – 7	2	NR	15	0.5 – 3.2
Hair-Coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	2	NR
Mucous Membrane	NR	NR	NR	NR	NR	19.4
Baby Products	NR	NR	NR	NR	NR	NR
	AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide Copolymer		**Corn Starch/Acrylamide/Sodium Acrylate Copolymer**		**Dimethyl Acrylamide/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer**	
Totals*	**4**	**0.032 – 5**	**5**	**0.002 – 2**	**7**	**0.26 – 7**
Duration of Use						
Leave-On	*4*	*0.032 – 5*	1	*0.002*	7	*0.26 – 7*
Rinse Off	*NR*	*NR*	NR	*NR*	NR	*NR*
Diluted for (Bath) Use	*NR*	*NR*	4	*2*	NR	*NR*
Exposure Type						
Eye Area	NR	NR	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	2	1.3 – 3.9; 0.032 – 5[a]	1[b]	NR	2	0.26; 7[a]
Incidental Inhalation-Powder	NR	NR	1[b]	0.002[c]	NR	NR
Dermal Contact	2	0.032 – 0.05	5	0.002 – 2	NR	NR
Deodorant (underarm)	NR	0.05	NR	NR	NR	NR
Hair - Non-Coloring	2	0.3 – 5	NR	NR	5	0.26 – 7
Hair-Coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	2	NR
Mucous Membrane	NR	NR	4	2	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR

Table 3. Frequency (2021) and concentration (2020) of use according to duration and exposure[11,12]

	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)
	Dimethylacrylamide/Lauryl Methacrylate Copolymer					
Totals*	**NR**	**0.5**				
Duration of Use						
Leave-On	*NR*	*NR*				
Rinse Off	*NR*	*0.5*				
Diluted for (Bath) Use	*NR*	*NR*				
Exposure Type						
Eye Area	NR	NR				
Incidental Ingestion	NR	NR				
Incidental Inhalation-Spray	NR	NR				
Incidental Inhalation-Powder	NR	NR				
Dermal Contact	NR	0.5				
Deodorant (underarm)	NR	NR				
Hair - Non-Coloring	NR	NR				
Hair-Coloring	NR	NR				
Nail	NR	NR				
Mucous Membrane	NR	0.5				
Baby Products	NR	NR				

*Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.
[a] It is possible these products are sprays, but it is not specified whether the reported uses are sprays.
[b] Not specified whether a spray or a powder, but it is possible the use can be as a spray or a powder, therefore the information is captured in both categories
[c] It is possible these products are powders, but it is not specified whether the reported uses are powders
NR – not reported

Table 4. Acrylate/Acrylamide Copolymers with no reported uses, according to the VCRP and Council survey

AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide/Hydroxyethylacrylate Copolymer
t-Butylacrylamide/Dimethylacrylamide/PEG-14 Diacrylate Crosspolymer
Butyl Acrylate/Isopropylacrylamide/PEG-18 Dimethacrylate Crosspolymer
Potassium Acrylates/Acrylamide Copolymer
Sodium Acrylates/Hydroxyethyl Acrylamide Copolymer
Starch/Acrylates/Acrylamide Copolymer

Table 5. CFR Citations for Acrylate/Acrylamide Copolymer and Acrylamide/Sodium Acrylate Copolymer

CFR Citation	Limitations
	Acrylate/Acrylamide Copolymer
21CFR176.110 Indirect food additives: paper and paperboard components	Acrylamide-acrylic acid resins may be safely used as components of articles in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food under the following limitations: -acrylamide-acrylic acid resins are produced by the polymerization of acrylamide with partial hydrolysis or by the copolymerization of acrylamide and acrylic acid -the acrylamide-acrylic acid resins contain less than 0.2% residual monomer -the resins are used as adjuvants in the manufacture of paper and paperboard in amounts not to exceed that necessary to accomplish the technical effect and not to exceed 2% by weight of the paper or paperboard
21CFR573.120 Food additives permitted in feed and drinking water of animals	Acrylamide-acrylic acid resin may be used safely under the following limitations: -the additive is produced by polymerization of acrylamide with partial hydrolysis, or by copolymerization of acrylamide and acrylic acid with the greater part of the polymer being composed of acrylamide units -the additive meets the following specifications: a) a minimum molecular weight of 3 million b) viscosity range: 3000 to 6000 centipoises at 77° F in a 1% aqueous solution as determined by LVF Brookfield Viscometer or equivalent using a number 6 spindle at 20 rpm c) residual acrylamide: not more than 0.05% -it is used as a thickener and suspending agent in non-medicated aqueous suspensions intended for addition to animal feeds
21CFR173.357 Secondary direct food additives permitted in food for human consumption	May be used as a fixing material in the immobilization of glucose isomerase enzyme preparations for use in the manufacture of high fructose corn syrup in accordance with CFR 184.1372
	Acrylamide/Sodium Acrylate Copolymer
21CFR172.710 Food additives permitted for direct addition to food for human consumption	Sodium acrylate and acrylamide copolymer with a minimum average molecular weight of 10,000,000 in which 30% of the polymer is comprised of acrylate units and acrylamide units, for use as a drift control agent in herbicide formulations applied to crops at a level not to exceed 0.5 oz of the additive per acre

Table 5. CFR Citations for Acrylate/Acrylamide Copolymer and Acrylamide/Sodium Acrylate Copolymer

CFR Citation	Limitations
21CFR173.310 Secondary direct food additives permitted in food for human consumption	Boiler water additives may be safely used in the preparation of steam that will contact food under the following conditions: -the amount of additive is not in excess of that required for its functional purposed, and the amount of steam in contact with food does not exceed that required to produce the intended effect in or on food -acrylamide-sodium acrylate resin may not contain more that 0.05% by weight of acrylamide monomer
40CFR180.960 Polymers; exemptions from the requirement of a tolerance	Exempted from the requirement of a tolerance under FFDCA section 408
Acrylate/Acrylamide Copolymer and Acrylamide/Sodium Acrylate Copolymer	
21CFR173.5 Secondary direct food additives permitted in food for human consumption	Acrylate-acrylamide resins may be safely used in food under the following conditions: 1. the additive consists of one of the following: a. acrylamide-acrylic resin (hydrolyzed polyacrylamide) is produced by the polymerization of acrylamide with partial hydrolysis, or by copolymerization of acrylamide and acrylic acid, with the greater part of the polymer being composed of acrylamide units b. sodium polyacrylate-acrylamide resin is produced by the polymerization and subsequent hydrolysis of acrylonitrile in a sodium silicate-sodium hydroxide aqueous solution, with the greater part of the polymer being composed of acrylate units 2. the additive contains not more than 0.05% of residual monomer calculated as acrylamide 3. the additive is used or intended for use as follows: a. the additive is used as a flocculent in the clarification of beet sugar juice and liquor of cane sugar juice and liquor or corn starch hydrolysate in an amount not to exceed 5 ppm by weight of the juice or 10 ppm by weight of liquor or the corn starch hydrolysate b. the additive is used to control organic and mineral scale in beet sugar juice and liquor or cane sugar juice and liquor in an amount not to exceed 2.5 ppm by the weight of the juice or liquor

Table 6. Acute toxicity studies

Test Substance	Animals	No./Group	Concentration/Dose/Protocol	LD_{50}/LC_{50}/Results	Reference
DERMAL					
Acrylates/Octylacrylamide Copolymer	albino rabbits (strain not reported)	10	2000 mg/kg; occlusion not reported; animals observed for 14 d	greater than 2000 mg/kg	[15]
ORAL					
Acrylates/Octylacrylamide Copolymer (aqueous solution ; 15% solids)	Charles River albino rats	2/sex/group	1000, 1500, 2300 mg solids/kg bw; method of oral administration not reported	greater than 2300 mg/kg	[15]
AMP-Acrylates/C1-18 Alkyl Acrylate/ C1-8 Alkyl Acrylamide Copolymer (40% ethanol solution)	rats (strain not reported)	NR	2000 mg/kg	greater than 2000 mg/kg	[9]
AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide/ Hydroxyethylacrylate Copolymer (40% ethanol solution)	rats (strain not reported)	NR	2000 mg/kg	greater than 2000 mg/kg	[8]
Dimethyl Acrylamide/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer (70% ethanol solution)	rats (strain not reported)	NR	2000 mg/kg	greater than 2000 mg/kg	[6]
INHALATION					
Acrylates/Octylacrylamide Copolymer (aqueous solution; 10% solids)	Sprague-Dawley rats	5/sex	whole body chamber (exposure concentration of 3.4 mg polymer/l; particle size 5.5 µm; 84% of the aerosol was less than 10 µ in size); animals observed for 14 d	greater than 3.4 mg/l	[15]

NR = not reported

Table 7. Dermal irritation and sensitization

Test Article	Dose/Concentration	Test Population	Procedure	Results	Reference
IRRITATION					
In Vitro					
Acrylamide/Ammonium Acrylate Copolymer (mixture containing 32%)	10 µl; administered neat	reconstructed human epidermis	reconstructed human epidermis cytotoxicity assay; application time 15 min; incubation time 42 h	non-irritating	[20]
Acrylates/t-Butylacrylamide Copolymer	10 mg; 100%	reconstructed human epidermis	reconstructed human epidermis cytotoxicity assay; application time 15 min; incubation time 42 h	non-irritating	[20]
Animal					
Acrylates/Octylacrylamide Copolymer (neutralized, aqueous solution ; 15% solids)	0.5 ml; applied neat	6 New Zealand White rabbits (sex not reported)	test substance applied to intact and abraded skin sites; occlusive conditions; duration of application was not reported.	erythema observed 24 and 72 h after application, in both intact and abraded sites; test substance considered to be mildly irritating; primarily irritation score of 2.9	[15]
AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide Copolymer	NR	rabbits (strain and number of animals not reported)	primary skin irritation assay; Draize method; details not provided	non-irritating	[9]
AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide/Hydroxyethylacrylate Copolymer (40% ethanol solution)	NR	rabbits (strain and number of animals not reported)	primary skin irritation assay; Draize method; details not provided	mildly irritating; PII = 0	[8]
Dimethyl Acrylamide/Hydroxyethyl Acrylate/ Methoxyethyl Acrylate Copolymer (10% aqueous solution)	applied neat	rabbits (strain and number of animals not reported)	primary skin irritation assay; Draize method; details not provided	mildly irritating; PII = 0	[6]
Dimethyl Acrylamide/Hydroxyethyl Acrylate/ Methoxyethyl Acrylate Copolymer (10% aqueous solution)	applied neat	guinea pigs (strain and number of animals not reported)	cumulative skin irritation assay; details not provided	non-irritating	[6]
Human					
Acrylamide/Ammonium Acrylate Copolymer (5% aqueous solution)	applied neat	20 subjects	test substance applied to skin, under occlusive conditions, for 48 h	non-irritating	[10]
Dimethyl Acrylamide/Hydroxyethyl Acrylate/ Methoxyethyl Acrylate Copolymer (50% aqueous solution)	applied neat	40 subjects	patch test; no other details reported	non-irritating	[6]
SENSITIZATION					
In Vitro					
AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide Copolymer	NR	reconstructed human epidermis	EpiSkin® method	non-sensitizing	[9]
Dimethyl Acrylamide/Hydroxyethyl Acrylate/ Methoxyethyl Acrylate Copolymer (50% aqueous solution)	applied neat	reconstructed human epidermis	EpiSkin® method	non-sensitizing	[6]
Animal					
Acrylamide/Ammonium Acrylate Copolymer (mixture containing 32%)	applied neat; 0.5 ml (dermal induction); 0.25 ml (dermal challenge)	22 female Dunkin-Hartley guinea pigs	For the intradermal induction, animals were treated with an injection of Freund's Complete Adjuvant and 0.9 % saline. Animals then received a dermal induction application of the test substance, under occlusive conditions for 48 h. A challenge patch was performed 29 d later, using the undiluted test material, under occlusive conditions, for 48 h	non-sensitizing	[21]

Table 7. Dermal irritation and sensitization

Test Article	Dose/Concentration	Test Population	Procedure	Results	Reference
Acrylates/Octylacrylamide Copolymer (aqueous solution and powder form)	intradermal induction: 5% aqueous solution; dermal induction: powder applied neat ; dermal challenge: aqueous solution (100% solids and 50% solids)	20 female guinea pigs/group (strain not reported)	guinea pig maximization assay; animals were exposed to a two-part induction phase: -part 1: injection with of solution containing Acrylates/Octylacrylamide Copolymer (5%) with and without Freund's Complete Adjuvant) -part 2: dermal induction with Acrylates/Octylacrylamide Copolymer powder (8 cm^2 patch; moistened) for 48 h; use of occlusion not reported Animals were then exposed to a challenge phase: -1 saturated, occlusive patch (4 cm^2) of an aqueous solution of Acrylates/Octylacrylamide Copolymer (100% solids) and 1 saturated, occlusive patch (4 cm^2) of an aqueous solution of Acrylates/Octylacrylamide Copolymer (50% solids); both patches were left on for 24 h	non-irritating and non-sensitizing	[15]
AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide Copolymer (40% ethanol solution)	applied neat	guinea pigs (strain not reported)	guinea pig maximization assay; no other details provided	non-sensitizing	[9]
AMP-Acrylates/C1-18 Alkyl Acrylate/C1-18 Alkyl Acrylamide/ Hydroxyethylacrylate Copolymer in dimethylformamide (mixture containing 38%)	25 µl; 5, 10, 25, 50, and 75%	female CBA/J mice (4/group)	LLNA in accordance with OECD TG 429; positive control: α-hexylcinnamaldehyde in acetone/olive oil; negative control: *N,N*-dimethylformamide; 3-d applications	non-sensitizing; stimulation index: 0.8 – 1.5% (comparable to negative control); no local ear skin irritation; EC3 value was not calculable	[22]
Dimethyl Acrylamide/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer (70% ethanolic solution)	applied neat	guinea pig (strain not reported)	guinea pig maximization assay; no other details provided	non-sensitizing	[7]
Human					
Acrylamide/Ammonium Acrylate Copolymer (mixture containing 0.66%)	applied neat	109 subjects	HRIPT; induction phase consisted of 3 applications of the test substance, under occlusive conditions, each wk, for 3 wk; after a 2-wk rest period, challenge patch was applied to an untreated skin site, under occlusive conditions; all patches were applied for 48 h	Mild patch test responses occasionally accompanied by mild papular responses were observed in 28 subjects during the induction and/or challenge phase. The test substance was considered to be non-irritating and non-sensitizing.	[24]
Acrylamide/Ammonium Acrylate Copolymer (5% aqueous solution)	applied neat	50 subjects	HRIPT; details not provided	non-irritating and non-sensitizing	[10]
Acrylates/Octylacrylamide Copolymer (neutralized, aqueous solution; 15% solids)	applied neat	25 subjects/sex	HRIPT; use of occlusion not reported; 24-h patch application	Thirty subjects responded to the application of the test material with very slight to mild erythema. The test substance as considered to be non-irritating and non-sensitizing.	[15]
Acrylates/ *t*-Butylacrylamide Copolymer (formula containing 13.34%)	applied neat; 0.2 ml	96 subjects	HRIPT; semi-occlusive conditions; 2 cm x 2 cm patch	non-irritating and non-sensitizing	[23]

HRIPT: human repeat insult patch test; LLNA: local lymph node assay; NR = not reported; OECD TG: Organisation for Economic Co-operation and Development Test Guidelines

Table 8. Ocular irritation studies

Test Article	Concentration	Test Population	Procedure	Results	Reference
			IN VITRO		
Acrylamide/Ammonium Acrylate Copolymer (3% in water and 0.5% sodium chloride)	applied neat	NR	HET-CAM assay	non-irritating	[10]
AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide Copolymer	100%	NR	SkinEthic™ HCE (human corneal epithelium) assay	non-irritating	[9]
Dimethyl Acrylamide/ Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer (50% aqueous solution)	applied neat	NR	SkinEthic™ HCE (human corneal epithelium) assay	non-irritating	[6]
			ANIMAL		
Acrylates/Octylacrylamide Copolymer	100%	6 New Zealand White rabbits	ocular irritation assay; irritation of cornea, iris, and conjunctiva observed on days 1, 2, and 3 post-instillation	Non-irritating	[15]
Acrylates/Octylacrylamide Copolymer (neutralized, aqueous solution ; 15% solids)	applied neat	6 New Zealand White rabbits	ocular irritation assay	Iritis and mild conjunctival irritation were noted in 3/6 and 6/6 animals, respectively. Effects were fully reversible within 24 h. The test substance was considered to be mildly irritating.	[15]
AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide Copolymer (40% ethanolic solution)	applied neat	NR	ocular irritation assay performed according to the Draize method	slightly irritating	[9]
AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide/ Hydroxyethylacrylate Copolymer (40% ethanol solution)	applied neat	rabbits (strain and number of animals not reported)	ocular irritation assay performed according to the Draize method	Slightly irritating	[8]
Dimethyl Acrylamide/ Hydroxyethyl Acrylate/ Methoxyethyl Acrylate Copolymer (10% aqueous solution)	applied neat	rabbits (strain and number of animals not specified)	ocular irritation assay performed according to the Draize method	Non-irritating	[6]

HET-CAM = hen's egg test chorioallantoic membrane; NR = not reported

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