Safety Assessment of Acryloyloxyethyl Phosphorylcholine Polymers as Used in Cosmetics

Status:	Draft Report for Panel Review
Release Date:	February 16, 2021
Panel Meeting Date:	March 11-12, 2021

The Expert Panel for Cosmetic Ingredient Safety members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; David E. Cohen, M.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; Lisa, A. Peterson, Ph.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The Cosmetic Ingredient Review (CIR) Executive Director is Bart Heldreth, Ph.D. This report was prepared by Wilbur Johnson, Jr., M.S., Senior Scientific Analyst/Writer.

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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons

From: Wilbur Johnson, Jr.
Senior Scientific Analyst/Writer, CIR

Date: February 16, 2021

Subject: Safety Assessment of Acryloyloxyethyl Phosphorylcholine Polymers as Used in Cosmetics

Enclosed is the Draft Report of the Safety Assessment of Acryloyloxyethyl Phosphorylcholine Polymers (*acrylo032021rep*) as Used in Cosmetics. It should be noted that a Scientific Literature Review (SLR) Notice to Proceed (NTP) was announced on May 19, 2020. This announcement was made because an intensive search of the published information on Acryloyloxyethyl Phosphorylcholine Polymers resulted in insufficient information to justify preparation of a formal SLR. Use concentration data (*acrylo032021data1,* received prior to NTP announcement) and in vitro skin and ocular irritation data (*acrylo032021data2*) were received from the Council. These data are enclosed and summarized in the draft report, along with the limited safety test data that have been identified in the published literature. Additionally, data (toxicity and other relevant data) on poly(2-methacryloyloxyethyl phosphorylcholine-co-n-butyl methacrylate), which is very similar structurally to Polyquaternium-51 (which is poly(2-methacryloyloxyethyl phosphorylcholine-co-n-propyl methacrylate)) are included in this safety assessment. The Panel will need to determine the relevance of these data.

Also included in this package for your review are the report history (*acrylo032021hist*), flow chart (*acrylo032021flow*), literature search strategy (*acrylo032021strat*), ingredient data profile (*acrylo032021prof*), and 2021 FDA VCRP data (*acrylo032021FDA*).

After reviewing these documents, if the available data are deemed sufficient to make a determination of safety, the Panel should issue a Tentative Report with a safe as used, safe with qualifications, or unsafe conclusion, and Discussion items should be identified. If the available data are insufficient, the Panel should issue an Insufficient Data Announcement (IDA), specifying the data needs therein.

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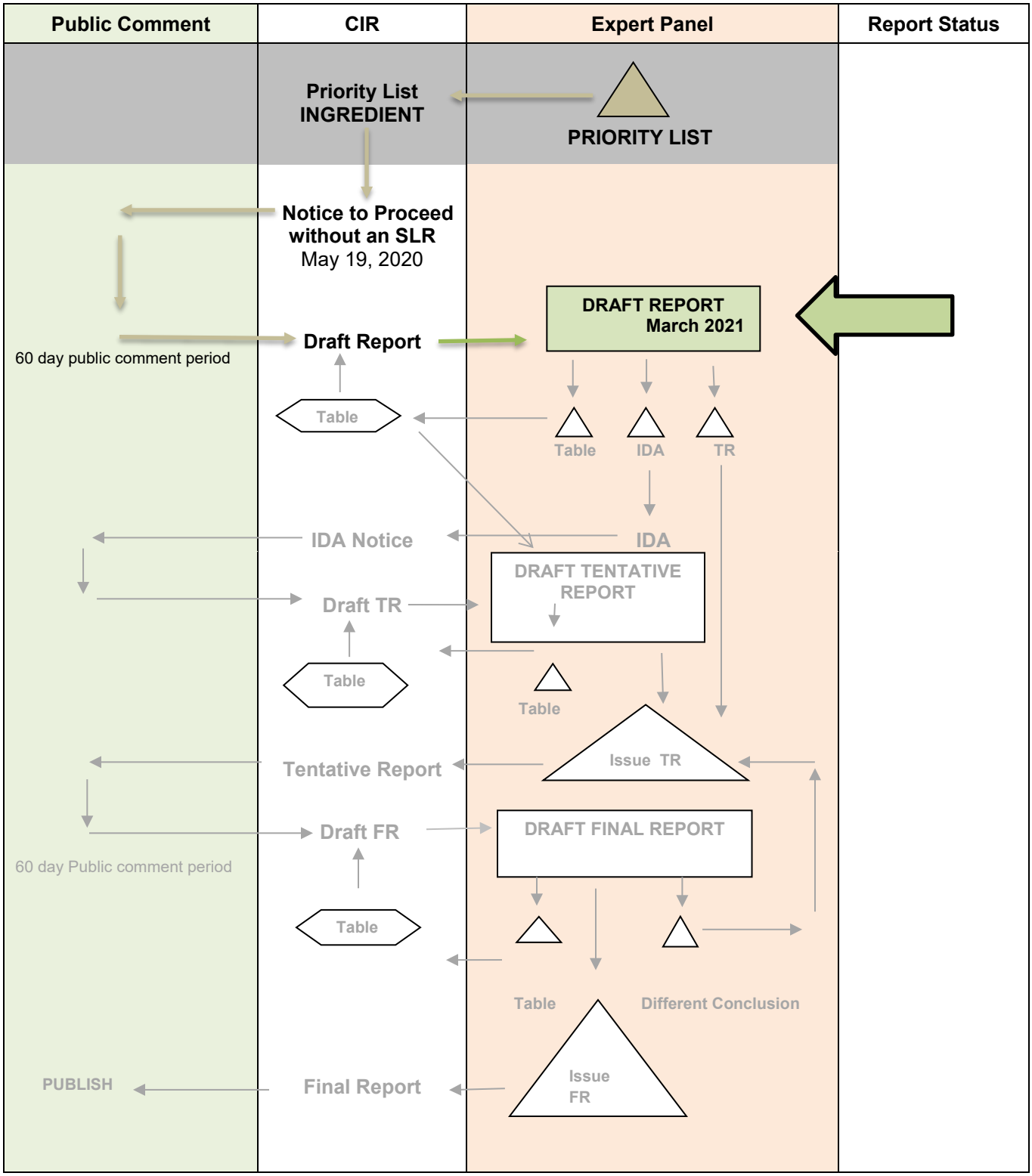
SAFETY ASSESSMENT FLOW CHART

INGREDIENT/FAMILY Acryloyloxyethyl Phosphorylcholine Polymers

MEETING March 2021



CIR History of:

Acryloyloxyethyl Phosphorylcholine Polymers

A Scientific Literature Review (SLR) Notice to Proceed (NTP) on Polyquaternium-6 was issued on May 19, 2020.

Draft Report, Teams/Panel: March 11-12, 2021

The draft report also contains 2020 use concentration data and in vitro skin and ocular irritation data that were received from the Council.

Acryloyloxyethyl Phosphorylcholine Polymers Data Profile* – March 11-12, 2021 – Wilbur Johnson, Jr.																														
						Toxico-kinetics		Acute Tox			Repeated Dose Tox			DART		Genotox		Carci		Dermal Irritation			Dermal Sensitization				Ocular Irritation		Clinical Studies	
	Reported Use	GRAS	Method of Mfg	Constituents	Impurities	Dermal Penetration	ADME	Dermal	Oral	Inhalation	Dermal	Oral	Inhalation	Dermal	Oral	In Vitro	In Vivo	Dermal	Oral	In Vitro	Animal	Human	In Vitro	Animal	Human	Phototoxicity	In Vitro	Animal	Retrospective/ Multicenter	Case Reports
Acrylic Acid/Phosphorylcholine Glycol Acrylate Crosspolymer			X																											
C4-18 Alkyl Methacrylate/Methacryloyloxyethyl Phosphorylcholine Copolymer			X																											
Hydroxyethylcellulose/Phosphorylcholine Glycol Acrylate Copolymer			X																											
Phosphorylcholine Glycol Methacrylate/PEG-10 Dimethacrylate Crosspolymer			X																											
Polyphosphorylcholine Glycol Acrylate	12		X																											
Polyquaternium-10/Phosphorylcholine Glycol Acrylate Copolymer			X																											
Polyquaternium-51	275		X	X	X															X							X			
Polyquaternium-61	2		X						X							X				X		X						X		

* “X” indicates that data were available in a category for the ingredient

[Acryloyloxyethyl Phosphorylcholine Polymers – 4-3-2020; 1-11-2021]

Ingredient	CAS #	InfoBase	SciFinder	PubMed	TOXNET	FDA	EU	ECHA	IUCLID	SIDS	HPVIS	NICNAS	NTIS	NTP	WHO	FAO	ECE-TOC	Web
Polyquaternium-51	125275-25-4	Yes		41/11		No	No	No	No	No	No	No	No	No	No	No	No	Yes
Polyquaternium-61		Yes		0/		No	No	No	No	No	No	No	No	No	No	No	No	Yes
Polyphosphorylcholine Glycol Acrylate	67881-99-6	Yes		0/		No	No	No	No	No	No	No	No	No	No	No	No	Yes
Acrylic Acid/Phosphorylcholine Glycol Acrylate Crosspolymer		Yes		0/		No	No	No	No	No	No	No	No	No	No	No	No	Yes
C4-18 Alkyl Methacrylate/Methacryloyloxyethyl Phosphorylcholine Copolymer		Yes		0/		No	No	No	No	No	No	No	No	No	No	No	No	Yes
Hydroxyethylcellulose/Phosphorylcho-line Glycol Acrylate Copolymer		Yes		0/		No	No	No	No	No	No	No	No	No	No	No	No	Yes
Phosphorylcholine Glycol Methacrylate/PEG-10 Dimethacrylate Crosspolymer		Yes		0/		No	No	No	No	No	No	No	No	No	No	No	No	Yes
Polyquaternium-10/Phosphorylcholine Glycol Acrylate Copolymer		Yes		0/		No	No	No	No	No	No	No	No	No	No	No	No	Yes

Note: CIR has reviewed the safety of Polyquaternium-22 and Polyquaternium-39; has also reviewed safety of Trimoniums, which includes some polyquaternium compounds; need to search for other Polyquaterniums that have been reviewed by CIR

Search Strategy

[*document search strategy used for SciFinder, PubMed, and Toxnet*]

[*identify total # of hits /# hits that were useful or examined for usefulness*]

LINKS

InfoBase (self-reminder that this info has been accessed; not a public website) - http://www.personalcarecouncil.org/science-safety/line-infobase
ScfFinder (usually a combined search for all ingredients in report; list # of this/# useful) - https://scifinder.cas.org/scifinder
PubMed (usually a combined search for all ingredients in report; list # of this/# useful) - http://www.ncbi.nlm.nih.gov/pubmed
Toxnet databases (usually a combined search for all ingredients in report; list # of this/# useful) – https://toxnet.nlm.nih.gov/ (includes Toxline; HSDB; ChemIDPlus; DAR; IRIS; CCRIS; CPDB; GENE-TOX)

FDA databases – http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm (CFR); then,
list of all databases: http://www.fda.gov/ForIndustry/FDABasicsforIndustry/ucm234631.htm; then,
http://www.accessdata.fda.gov/scripts/fcn/fcnnavigation.cfm?rpt=eafuslisting&displayall=true (EAFUS);
http://www.fda.gov/food/ingredientspackaginglabeling/gras/default.htm (GRAS, SCOGS database);
http://www.accessdata.fda.gov/scripts/fdcc/?set=IndirectAdditives (indirect food additives list);
http://www.fda.gov/Drugs/InformationOnDrugs/default.htm (drug approvals and database);
https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm (drugs@FDA)
http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/UCM135688.pdf (OTC ingredient list);
http://www.accessdata.fda.gov/scripts/cder/iig/ (inactive ingredients approved for drugs)

EU (European Union); check CosIng (cosmetic ingredient database) for restrictions and SCCS (Scientific Committee for Consumer Safety) opinions - http://ec.europa.eu/growth/tools-databases/cosing/
ECHA (European Chemicals Agency – REACH dossiers) – http://echa.europa.eu/information-on-chemicals;jsessionid=A978100B4E4CC39C78C93A851EB3E3C7.live1
IUCLID (International Uniform Chemical Information Database) - https://iuclid6.echa.europa.eu/search
OECD SIDS documents (Organisation for Economic Co-operation and Development Screening Info Data Sets)- http://webnet.oecd.org/hpv/ui/Search.aspx
HPVIS (EPA High-Production Volume Info Systems) - https://ofmext.epa.gov/hpvis/HPVISlogon
NICNAS (Australian National Industrial Chemical Notification and Assessment Scheme)- https://www.nicnas.gov.au/
NTIS (National Technical Information Service) - http://www.ntis.gov/
NTP (National Toxicology Program) - http://ntp.niehs.nih.gov/
WHO (World Health Organization) technical reports - http://www.who.int/biologicals/technical_report_series/en/
FAO (Food and Agriculture Organization of the United Nations) - http://www.fao.org/food/food-safety-quality/scientific-advice/jecfa/jecfa-additives/en/ (FAO);
FEMA (Flavor & Extract Manufacturers Association) - http://www.femaflavor.org/search/apachesolr_search/
Web – perform general search; may find technical data sheets, published reports, etc
ECETOC (European Center for Ecotoxicology and Toxicology Database) - http://www.ecetoc.org/

Botanical Websites, if applicable
Dr. Duke's https://phytochem.nal.usda.gov/phytochem/search
Taxonomy database - http://www.ncbi.nlm.nih.gov/taxonomy
GRIN (U.S. National Plant Germplasm System) - https://npgsweb.ars-grin.gov/gringlobal/taxon/taxonomysimple.aspx
Sigma Aldrich plant profiler http://www.sigmaaldrich.com/life-science/nutrition-research/learning-center/plant-profiler.html

Fragrance Websites, if applicable
IFRA (International Fragrance Association) – http://www.ifraorg.org/

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INTRODUCTION

The safety of the following 8 acryloyloxyethyl phosphorylcholine polymers as used in cosmetics is reviewed in this safety assessment.

Acrylic Acid/Phosphorylcholine Glycol Acrylate Crosspolymer
C4-18 Alkyl Methacrylate/Methacryloyloxyethyl Phosphorylcholine Copolymer
Hydroxyethylcellulose/Phosphorylcholine Glycol Acrylate Copolymer
Phosphorylcholine Glycol Methacrylate/PEG-10 Dimethacrylate Crosspolymer
Polyphosphorylcholine Glycol Acrylate
Polyquaternium-10/Phosphorylcholine Glycol Acrylate Copolymer
Polyquaternium-51
Polyquaternium-61

According to the web-based *International Cosmetic Ingredient Dictionary and Handbook* (wINCI; *Dictionary*), most acryloyloxyethyl phosphorylcholine polymers are reported to function as film formers and hair/skin conditioning agents in cosmetic products (See Table 1).[1] Two other functions associated with ingredients in this group include humectant and viscosity increasing agent. These ingredients are all vinyl-type polymers and share in common certain phosphorylcholine acrylate monomers.

This safety assessment includes relevant published and unpublished data that are available for each endpoint that is evaluated. The published data in this document were identified by conducting an exhaustive search of the world's literature. A list of the search engines and websites that are used, and the sources that are typically explored, as well as the endpoints that the Expert Panel for Cosmetic Ingredient Safety (Panel) typically evaluates, is available on the Cosmetic Ingredient Review (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 may be provided by the cosmetics industry, as well as by other interested parties. These searches yielded limited toxicity data relating to the 8 acryloyloxyethyl phosphorylcholine polymer ingredients listed above. Of these ingredients, only safety test data on Polyquaternium-61 were identified. Additionally, data (toxicity and other relevant data) on poly(2-methacryloyloxyethyl phosphorylcholine-co-n-butyl methacrylate), which is very similar structurally to Polyquaternium-51 (which is poly(2-methacryloyloxyethyl phosphorylcholine-co-n-***propyl*** methacrylate)) are included in this safety assessment.

CHEMISTRY

Definition

Acryloyloxyethyl phosphorylcholine polymers have been defined as amphiphilic block copolymers comprising, at least in part, 2-acryloyloxyethyl phosphorylcholine monomers.[2] The ingredients are constructed as vinyl-type polymers and share in common these phosphorylcholine substituted acrylate monomers. For example, Polyquaternium-61 (no CAS No.) comprises the two monomers shown in Figure 1. The definitions, idealized structures, and CAS Nos. of the acryloyloxyethyl phosphorylcholine polymers included in this safety assessment are presented in Table 1.[1] The only ingredients with reported CAS Nos. in this safety assessment are Polyphosphorylcholine Glycol Acrylate (CAS No. 67881-99-6) and Polyquaternium-51 (125275-25-4).

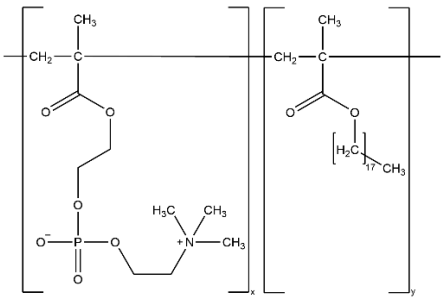


Figure 1. Polyquaternium-61

Chemical Properties

Chemical properties data for these ingredients were neither found in the available literature nor submitted as unpublished data.

Method of Manufacture

No ingredient-specific methods of manufacture were found in the literature or submitted as unpublished data. However, some general methodologies were found in the literature, and a sample is provided below.

Amphiphilic block polymers composed of poly(butylacrylate) and poly(2-acryloyloxyethyl phosphorylcholine) have been produced using reversible addition fragmentation transfer (RAFT) polymerization.[2] According to another source, amphiphilic block copolymers based on poly(2-acryloyloxyethyl phosphorycholine) were prepared via RAFT polymerization. Specifically, the block copolymers are prepared by dissolving 1 g (1.11 x 10^{-4} mol) macroRAFT agent (M_n = 9000 Da) and 2 mg (1.21 x 10^{-5} mol) 2,2′- azoisobutyronitril (AIBN) in 15 ml *N*-methylpyrrolidone (NMP). 2-Acryloyloxyethyl phosphorylcholine (APC, 7.3 g [0.026 mol]) was dissolved in 25 ml methanol and added to the solution of RAFT agent and initiator in NMP. The sample was sealed and degassed by purging nitrogen through the solution. The sample was heated in an oil bath (60 °C) with vigorous stirring. Samples were taken with a gastight syringe at preset reaction times. The conversion was determined using nuclear magnetic resonance spectroscopy (solvent: deuterated methanol/chloroform 2:1). The polymers were purified by dissolving the final product in methanol and dialyzing for several days against water using cellulose tubular membranes (molecular weight cut-off: 10 kDa).

The synthesis of the polymer, poly(methyl methacrylate-co-methyl acrylate-co-2-acryloyloxyethyl phosphorylcholine) has also been described.[3] Radical copolymerization of methyl methacrylate (146 mg, 1.46 mmol), methyl acrylate (300 mg, 3.75 mmol), and 2-acryloyloxyethyl phosphorylcholine, initiated with α,α'-azoisobutyronitril (8 mg, 1.5 wt %) was performed in methanol (15 ml) at a concentration of 3.5 x 10^{-2} g/ml. The stirred solution was degassed with argon, the tubes were sealed, and the temperature of the solution was increased and maintained at 55 ºC. Next, the reaction was stopped by cooling at room temperature, and the tubes were stored at -18 ºC to allow precipitation of more of the polymer. The polymer was rinsed in methanol, centrifuged, and dried over phosphorus pentoxide.

Impurities

Polyquaternium-51

According to one source, the purity of Polyquaternium-51 is ≥ 94%.[4] In addition, the same source indicates that the heavy metals content of Polyquaternium-51 is ≤ 10 ppm, and the arsenic content is ≤ 2 ppm.

USE

Cosmetic

The safety of acryloyloxyethyl phosphorylcholine polymers 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 FDA's Voluntary Cosmetic Registration Program (VCRP) database. Use concentration data are submitted by the cosmetics industry in response to surveys, conducted by the Personal Care Products Council (Council), of maximum reported use concentrations by product category.

According to 2021 VCRP data, Polyquaternium-51 is reported to be used in 275 cosmetic products (245 leave-on products and 30 rinse-off products; Table 2).[5] Of the acryloyloxyethyl phosphorylcholine polymers that are being reviewed in this safety assessment, this is the greatest reported use frequency. The results of a concentration of use survey completed in 2019 - 2020 and provided by the Council in 2020 indicate that Polyquaternium-51 is being used at maximum use concentrations up to 0.14% in leave-on products (face and neck products (not spray); Table 2).[6] This is the highest maximum cosmetic use concentration that is being reported for the acryloyloxyethyl phosphorylcholine polymers that are being reviewed in this safety assessment. Polyquaternium-61 is being used at the highest concentration in rinse-off products, at maximum use concentrations up to 0.01% in (hair conditioners).

According to VCRP and Council survey data, 4 of the 8 acryloyloxyethyl phosphorylcholine polymers reviewed in this safety assessment are not currently in use in cosmetic products.[5,6] These ingredients are presented in Table 3.

Cosmetic products containing acryloyloxyethyl phosphorylcholine polymers may be applied to the skin/hair or, incidentally, may come in contact with the eyes at concentrations up to 0.05% (Polyquaternium-51 in eye makeup preparations).[6] Acryloyloxyethyl phosphorylcholine polymers are being used in cosmetic products that come in contact with mucous membranes (e.g., Polyquaternium-51 in bath soaps and detergents and personal cleanliness products [concentrations not available]). Products containing acryloyloxyethyl phosphorylcholine polymers may be applied as frequently as several times per day and may come in contact with the skin for variable periods following application. Daily or occasional use may extend over many years.

Polyquaternium-61 is reported to be used in aerosol hair sprays at maximum use concentrations up to 0.000006%.[6] In practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters > 10 µm, with propellant sprays yielding a greater fraction of droplets/particles below 10 µm, compared with pump sprays.[7-10] Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and bronchial regions and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.[7,8] Polyquaternium-61 is reported to be used in face powders at maximum use concentrations up to 0.0069%. Conservative estimates of inhalation exposures to respirable particles during the use of loose powder cosmetic products are 400-fold to 1000-fold less than protective regulatory and guidance limits for inert airborne respirable particles in the workplace.

The acryloyloxyethyl phosphorylcholine polymers are not restricted from use in any way under the rules governing cosmetic products in the European Union.[11]

Non-Cosmetic

No non-cosmetic uses were found.

TOXICOKINETIC STUDIES

Dermal Penetration

Polyquaternium-51

Excised abdominal skin from male hairless rats (WBM/ILA-Ht strain) was positioned in a Franz-type diffusion cell (effective diffusion area = 3.14 cm^2).[12] A 5% fluorescent isothiocyanate-labeled poly(2-methacryloyloxyethyl phosphorylcholine-*co*-*n*-butyl methacrylate) (as a read across source for Polyquaternium-51) solution (2 ml) or free fluorescent isothiocyanate was applied on the stratum corneum. Phosphate buffered saline (~ 17 ml, receptor fluid) was on the dermal side. The skin surface was washed with distilled water at the end of the 6-h permeation experiment, and fluorescence (from the skin surface to 0 μm thickness) was observed using confocal laser scanning microscopy. At 6 h after application of 5% fluorescent isothiocyanate-labeled poly(2-methacryloyloxyethyl phosphorylcholine-*co*-*n*-butyl methacrylate) solution, the fluorescent dye was found evenly on the skin surface. However, when free fluorescent isothiocyanate was applied, it was distributed mainly to the corneocytes (confocal laser scanning microscopy image not available).

TOXICOLOGICAL STUDIES

Acute Toxicity Studies

Data on the acute toxicity of acryloyloxyethyl phosphorylcholine polymers reviewed in this safety assessment were neither found in the published literature, nor were these data submitted.

Short-Term Toxicity Studies

Intraperitoneal

Polyquaternium-51

Information relating to the toxicity of poly(2-methacryloyloxyethyl phosphorylcholine-*co*-*n*-butyl methacrylate) (as a read across source for Polyquaternium-51) is included in a short-term study on the antitumor activity of this polymer.[13] The study involved groups of 4 female BALB/cA nude mice. Two MX-1 tumor (human breast tumor, 3 mm x 3 mm x 3 mm) tissue fragments were inoculated into the subcutaneous tissue of the bilateral dorsum of each animal. Treatment with the test substance was initiated when the tumor weight reached 200 to 300 mg. The test substance was administered intraperitoneally (i.p., in weekly cycles) at doses of 50 mg/kg and 200 mg/kg) over a 2-wk period. Toxicity was not observed in mice dosed with 50 mg/kg or 200 mg/kg poly(2-methacryloyloxyethyl phosphorylcholine-co-n-butyl methacrylate). Results relating to antitumor activity are included in the Cytotoxicity section of this safety assessment.

The safety of poly(2-methacryloyloxyethyl phosphorylcholine-*co*-*n*-butyl methacrylate) of different formula weights (FW; 30,000 and 100,000 Da) was evaluated using groups (3 per group) of specific pathogen-free male Wistar rats.[14] Each copolymer was administered orally as a 10% solution in distilled water (dose volume = 10 ml/kg/d), once daily for 14 successive days. The control group was dosed with distilled water. The animals were killed 24 h after the last dose, and the following organs were removed and examined microscopically: kidneys, liver, small intestine, and large intestine. There was no evidence of lesions in these organs. Furthermore, there were no statistically significant differences in the following biomarkers of toxicity between test and control groups: serum creatinine, blood urea nitrogen, aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase.

Subchronic Toxicity Studies

Data on the subchronic toxicity of acryloyloxyethyl phosphorylcholine polymers reviewed in this safety assessment were neither found in the published literature, nor were these data submitted.

Chronic Toxicity Studies

Data on the chronic toxicity of acryloyloxyethyl phosphorylcholine polymers reviewed in this safety assessment were neither found in the published literature, nor were these data submitted.

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY STUDIES

Data on the developmental and reproductive toxicity of acryloyloxyethyl phosphorylcholine polymers reviewed in this safety assessment were neither found in the published literature, nor were these data submitted.

GENOTOXICITY STUDIES

Data on the genotoxicity of acryloyloxyethyl phosphorylcholine polymers reviewed in this safety assessment were neither found in the published literature, nor were these data submitted.

CARCINOGENICITY STUDIES

Data on the carcinogenicity of acryloyloxyethyl phosphorylcholine polymers reviewed in this safety assessment were neither found in the published literature, nor were these data submitted.

ANTI-CARCINOGENICITY STUDIES

Polyquaternium-51

The antitumor activity of poly(2-methacryloyloxyethyl phosphorylcholine-co-n-butyl methacrylate) (as a read across source for Polyquaternium-51) was evaluated using groups of 4 female BALB/cA nude mice.[13] Two MX-1 Tumor (MX-1, human breast tumor, 3 mm x 3 mm x 3 mm) tissue fragments were inoculated into the subcutaneous tissue of the bilateral dorsum of each animal. Treatment with the test substance was initiated when the tumor weight reached 200 to 300 mg. The test substance was administered i.p. (in weekly cycles) at doses of 50 mg/kg and 200 mg/kg) over a 2-wk period. Relative mean tumor weight (T) of the treated group and the relative mean tumor weight of the control group (C) at any given time were determined. Antitumor efficacy was evaluated based on the lowest T/C value (%) during the experiment. Antitumor activity was not observed at either dose of poly(2-methacryloyloxyethyl phosphorylcholine-co-n-butyl methacrylate).

OTHER RELEVANT STUDIES

Cytotoxicity

The cytotoxicity studies below maybe useful in terms of evaluating a potentially anti-carcinogenic effect of Polyquaternium-51 using in vitro methodology.

Polyquaternium-51

The cytotoxicity of poly(2-methacryloyloxyethyl phosphorylcholine-co-n-butyl methacrylate) (as a read across source for Polyquaternium-51) was evaluated in the in vitro lactase dehydrogenase (LDH) assay using the MBT-2 cell line (mouse bladder cancer cell line).[15] This assay is used to examine damage to the cell membrane, and is based on the leakage of LDH from cytosol. Cytotoxicity was not observed at test substance concentrations up to 5%.

In another cytotoxicity evaluation of poly(2-methacryloyloxyethyl phosphorylcholine-co-n-butyl methacrylate), the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay was used.[13] Testing involved the following cell types (breast cancer cells): MCF-7, SK-BR-3, and MX-1 cells. The test substance (concentration not stated) did not cause growth inhibition in any of the cell types.

Hemolytic Activity

The in vitro experiment relating to hemolytic activity is included below because the red blood cell hemolytic assay has been found to be a useful and rapid test for use as a screening method to assess the irritation potential of cosmetic products.[16]

Polyquaternium-51

A hydrogel containing a 2-methacryloyloxyethyl phosphorylcholine moiety was formed from aqueous solution with a water-soluble 2-methacryloyloxyethyl phosphorylcholine polymer with carboxylic acid and alkyl groups because of hydrogen bonding formation.[17] The alkyl 2-methacryloyloxyethyl phosphorylcholine polymer was poly(2-methacryloyloxyethyl phosphorylcholine-*co*-*n*-butyl methacrylate) (as a read across source for Polyquaternium-51). The biocompatibility of the spontaneously formed 2-methacryloyloxyethyl phosphorylcholine polymer hydrogel was investigated using a hemolysis test involving human whole blood. Absorbance at 405 nm of the supernatant (of the erythrocyte suspension) was measured after addition of the polymer at final concentrations of 0.1, 0.5, and 2 wt %. The absorbance corresponded to the number of hemolyzed erythrocytes.

Results for the polymer were compared to those for the erythrocyte suspension in Hank's balanced salt solution (HBSS). The relative absorbance was as low as HBSS, even at the highest concentration of 2 wt %, indicating low hemolytic activity.

Inhibition of Skin Penetration

Polyquaternium-51

The inhibitory effect of poly(2-methacryloyloxyethyl phosphorylcholine-*co*-*n*-butyl methacrylate) (as a read across source for Polyquaternium-51) on the in vitro skin permeation of methylparaben and *n*-butylparaben was evaluated.[12] Excised abdominal skin from male hairless rats (WBM/ILA-Ht strain) was positioned in a Franz-type diffusion cell (effective diffusion area = 3.14 cm^2). Methylparaben (10 mM) and *n*-butylparaben (1 mM) aqueous solution with or without 5%

poly(2-methacryloyloxyethyl phosphorylcholine-*co*-*n*-butyl methacrylate) were used as the donor solution. Phosphate buffered saline (receptor fluid, ~17 ml) was on the dermis side. The addition of 5% poly(2-methacryloyloxyethyl phosphorylcholine-*co*-*n*-butyl methacrylate) decreased the skin penetration of methylparaben and *n*-butylparaben. Using the cumulative amount permeated over 8 h, the skin permeation of methylparaben and *n*-butylparaben was decreased by 54.8% and 85.6%, respectively, by the addition of 5% poly(2-methacryloyloxyethyl phosphorylcholine-*co*-*n*-butyl methacrylate). These results suggest that the inhibitory effect of 5% poly(2-methacryloyloxyethyl phosphorylcholine-*co*-*n*-butyl methacrylate) on the skin penetration of parabens was more marked for a more lipophilic compound.

Tissue Regeneration

The toxicogenomics field aims to understand and predict toxicity using omics data (high throughput biochemical assays) in order to study systems-level responses to compound treatments. Thus, the following study, indicating an effect on gene expression by a read-across source chemical for Polyquaternium,-51, may be of some relevance in a safety evaluation.

Polyquaternium-51

A study was performed to promote the understanding of initial host body reactions toward successful tissue regeneration.[18] Three-dimensional porous polyethylene scaffolds with collagen (bioactive) and poly(2-methacryloyloxyethyl phosphorylcholine-*co*-*n*-butyl methacrylate) (as a read across source for Polyquaternium-51) were used, and the genetic level of host body reactions was analyzed. Scaffolds were implanted subcutaneously (s.c.) into male Wistar rats and male C57BL/6 mice. One mouse was used for comprehensive genetic analysis and 3 rats were used for immunohistochemistry. The scaffolds were resected with surrounding tissue at 7 d after operation, and, after immunostaining of tissues for CD68 on macrophages, the early foreign body reaction to the scaffolds was assessed. Host body reactions at scaffolds were studied using a DNA microarray assay. Local ribonucleic acids (RNAs) in infiltrating cells into the porous scaffolds were extracted using a laser microdissection technique. The relationships between the expression levels of important genes for tissue regeneration on the collagen and poly(2-methacryloyloxyethyl phosphorylcholine) surface scaffold were discussed in combination with histological results. A significant number of monocytes/macrophages surrounded the scaffold. The DNA microarray assay showed that a number of genes may be involved in actively neglecting the poly(2-methacryloyloxyethyl phosphorylcholine-*co*-*n*-butyl methacrylate)-coated scaffold. The authors noted that these results suggest that macrophages may also play a significant role in host body suppressing reactions. The poly(2-methacryloyloxyethyl phosphorylcholine-*co*-*n*-butyl methacrylate)-coated scaffold slightly up-regulated genes that are related to suppression of inflammation and wound healing.

DERMAL IRRITATION AND SENSITZATION STUDIES

Irritation

In Vitro

Polyquaternium-51

The skin irritation potential of a trade name mixture containing 1.4% Polyquaternium-51 was evaluated in the Irrectection® assay.[19] This in vitro system involves use of a proprietary solution comprised of both proteins and macromolecules in a well that is covered by a membrane. The mixture (doses of 25, 50, 75, 100, and 125 µl) was applied to the membrane and diffused into the well. According to the protocol for this assay, proteins and macromolecules undergo conformational changes based on the irritancy of the diffused material. The conformational changes cause the solution to become turbid, and there is a direct correlation between the irritancy level of the material and the solution's turbidity. Irritancy is measured quantitatively using a spectrophotometer. The samples were left at room temperature for a period of 24 h prior to spectrophotometry. The mixture was classified as a non-irritant over the range of doses tested.

Sensitization

Data on the sensitization potential of acryloyloxyethyl phosphorylcholine polymers reviewed in this safety assessment were neither found in the published literature, nor were these data submitted.

OCULAR IRRITATON STUDIES

In Vitro

Polyquaternium-51

The ocular irritation potential of a trade name mixture containing 1.4% Polyquaternium-51 was evaluated in the Irrectection® assay.[19] The mixture was evaluated at doses of 25, 50, 75, 100, and 125 µl. Details relating to the protocol for this assay are included in the preceding section on Skin Irritation (In Vitro). The mixture was classified as a slight ocular irritant over the range of doses tested.

SUMMARY

The safety of 8 acryloyloxyethyl phosphorylcholine polymers as used in cosmetics is reviewed in this safety assessment. Most polymers are reported to function as film formers and hair/skin conditioning agents in cosmetic products. These ingredients are all vinyl-type polymers and share in common certain phosphorylcholine acrylate monomers.

According to one source, the purity of Polyquaternium-51 is ≥ 94%. The heavy metals content of Polyquaternium-51 is ≤ 10 ppm, and the arsenic content is ≤ 2 ppm.

According to 2021 VCRP data, Polyquaternium-51 is reported to be used in 275 cosmetic products (245 leave-on products and 30 rinse-off products). Of the acryloyloxyethyl phosphorylcholine polymers that are being reviewed in this safety assessment, this is the greatest reported use frequency. The results of a concentration of use survey completed in 2019 - 2020, and provided by the Council in 2020, indicate that Polyquaternium-51 is being used at maximum use concentrations up to 0.14% in leave-on products (face and neck products [not spray]). Additionally, according to both VCRP and Council survey data, the following 4 acryloyloxyethyl phosphorylcholine polymers are not being used in cosmetic products: C4-18 Alkyl Methacrylate/Methacryloyloxyethyl Phosphorylcholine Copolymer, Hydroxyethylcellulose/ Phosphorylcholine Glycol Acrylate Copolymer, Phosphorylcholine Glycol Methacrylate/PEG-10 Dimethacrylate Crosspolymer, and Polyquaternium-10/Phosphorylcholine Glycol Acrylate Copolymer.

A skin penetration experiment was performed using excised abdominal skin from male hairless rats (WBM/ILA-Ht strain). The test substance was a 5% fluorescent isothiocyanate-labeled poly(2-methacryloyloxyethyl phosphorylcholine-*co*-*n*-butyl methacrylate) (as a read across source for Polyquaternium-51) solution. At 6 h post-application, the fluorescent dye was found evenly on the skin surface. However, when free fluorescent isothiocyanate was applied, it was distributed mainly to the corneocytes.

In a study involving groups of 4 female BALB/cA nude mice previously injected with human breast tumor, poly(2-methacryloyloxyethyl phosphorylcholine-*co*-*n*-butyl methacrylate) (as a read across source for Polyquaternium-51) was administered i.p. at doses of 50 mg/kg and 200 mg/kg) over a 2-wk period. Toxicity was not observed in either of the 2 dose groups. The safety of poly(2-methacryloyloxyethyl phosphorylcholine-*co*-*n*-butyl methacrylate) of different FW (30,000 and 100,000 Da) was evaluated using groups (3 per group) of specific pathogen-free male Wistar rats. Each polymer was administered orally as a 10% solution in distilled water (dose volume = 10 ml/kg/d), once daily for 14 successive days. There was no evidence of organ lesions at microscopic examination. Additionally, there were no statistically significant differences in the following toxicity biomarkers between test and control groups: serum creatinine, blood urea nitrogen, aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase. The antitumor activity of poly(2-methacryloyloxyethyl phosphorylcholine-co-n-butyl methacrylate) was evaluated using groups of 4 female BALB/cA nude mice. Tumor (MX-1, human breast tumor, 3 mm x 3 mm x 3 mm) tissue fragments were injected subcutaneously, and the test substance was administered i.p. (in weekly cycles) at doses of 50 mg/kg and 200 mg/kg) over a 2-wk period. Antitumor activity was not observed at either dose of poly(2-methacryloyloxyethyl phosphorylcholine-co-n-butyl methacrylate).

The cytotoxicity of poly(2-methacryloyloxyethyl phosphorylcholine-co-n-butyl methacrylate) was evaluated in the in vitro LDH assay using the MBT-2 cell line (mouse bladder cancer cell line). Cytotoxicity as not observed at test substance concentrations up to 5%. Another assay, MTT assay, was used to evaluate the cytotoxicity of poly(2-methacryloyloxyethyl phosphorylcholine-co-n-butyl methacrylate) (as a read across source for Polyquaternium-51; concentration not stated) in the following breast cancer cells: MCF-7, SK-BR-3, and MX-1 cells. There was no evidence of growth inhibition.

The inhibitory effect of poly(2-methacryloyloxyethyl phosphorylcholine-co-n-butyl methacrylate) (as a read across source for Polyquaternium-51) on the in vitro skin permeation of methylparaben (10 mM aqueous solution) and n-butylparaben (1 mM aqueous solution) was evaluated using excised abdominal skin (male hairless rats) in a Franz-type diffusion cell. The addition of 5% poly(2-methacryloyloxyethyl phosphorylcholine-co-n-butyl methacrylate) decreased the skin penetration of methylparaben (by 54.8%) and n-butylparaben (by 85.6%).

A study was performed to promote the understanding of initial host body reactions toward successful tissue regeneration. Three-dimensional porous polyethylene scaffolds with collagen (bioactive) and poly(2-methacryloyloxyethyl phosphorylcholine-co-n-butyl methacrylate) (as a read across source for Polyquaternium-51) were implanted s.c. into male 3 Wistar rats and 1 male C57BL/6 mouse. Host body reactions at scaffolds were studied using a DNA microarray assay. This assay showed that a number of genes may be involved in actively neglecting the poly(2-methacryloyloxyethyl phosphorylcholine-co-n-butyl methacrylate)-coated scaffold. The poly(2-methacryloyloxyethyl phosphorylcholine-co-n-butyl methacrylate)-coated scaffold slightly up-regulated genes that are related to suppression of inflammation and wound healing.

The skin irritation potential of a trade name mixture containing 1.4% Polyquaternium-51 was evaluated in the in vitro Irrectection® assay. The mixture was classified as a non-irritant over the range of doses tested (25, 50, 75, 100, and 125 µl).

The ocular irritation potential of a trade name mixture containing 1.4% Polyquaternium-51 was evaluated in the in vitro Irrectection® assay. The mixture was classified as a slight ocular irritant over the range of doses tested (25, 50, 75, 100, and 125 µl).

DISCUSSION

To be developed…

CONCLUSION

To be determined…

TABLES

Table 1. Definitions, Functions, and Idealized Structures of the Ingredients in this Safety Assessment.[CIR Staff;1)]

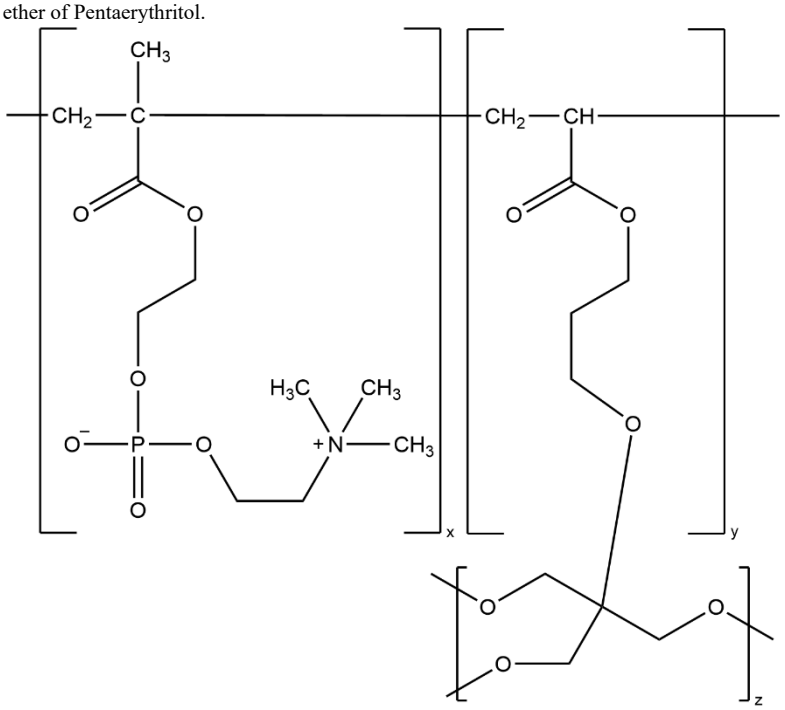
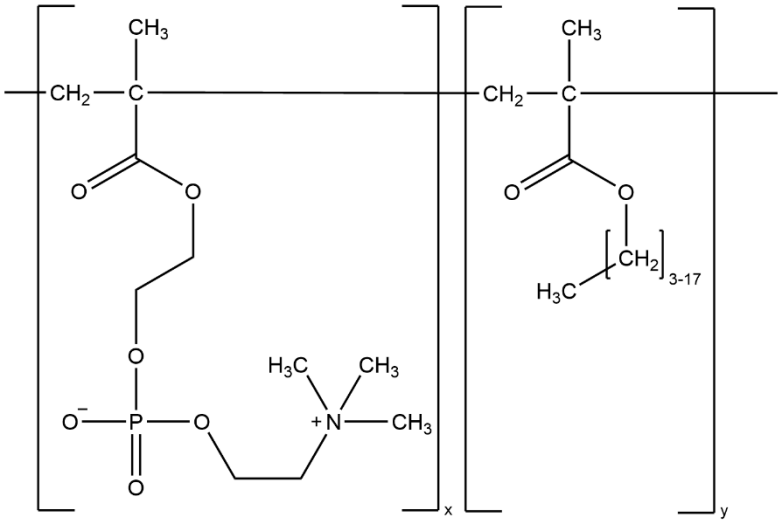
Ingredient/CAS No.	Definition & Structures	Function(s)
Acrylic Acid/Phosphorylcholine Glycol Acrylate Crosspolymer	Acrylic Acid/Phosphorylcholine Glycol Acrylate Crosspolymer is a copolymer formed from Acrylic Acid and phosphorylcholine glycol methacrylate, crosslinked with an allyl ether of Pentaerythritol. 	Viscosity Increasing Agents – Aqueous.[1]
C4-18 Alkyl Methacrylate/ Methacryloyloxyethyl Phosphorylcholine Copolymer	C4-18 Alkyl Methacrylate/Methacryloyloxyethyl Phosphorylcholine Copolymer is a copolymer of Methacryloyloxyethyl Phosphorylcholine and C4-18 alkyl methacrylate. 	Humectants
Hydroxyethylcellulose/ Phosphorylcholine Glycol Acrylate Copolymer	Hydroxyethylcellulose/Phosphorylcholine Glycol Acrylate Copolymer is the copolymer formed from Hydroxyethylcellulose and phosphorylcholine glycol methacrylate. *Not enough information available about connectivity to provide a structure.*	Film Formers; Hair Conditioning Agents; Humectants; Skin-Conditioning Agents - Miscellaneous

Table 1. Definitions, Functions, and Idealized Structures of the Ingredients in this Safety Assessment.[CIR Staff;1]

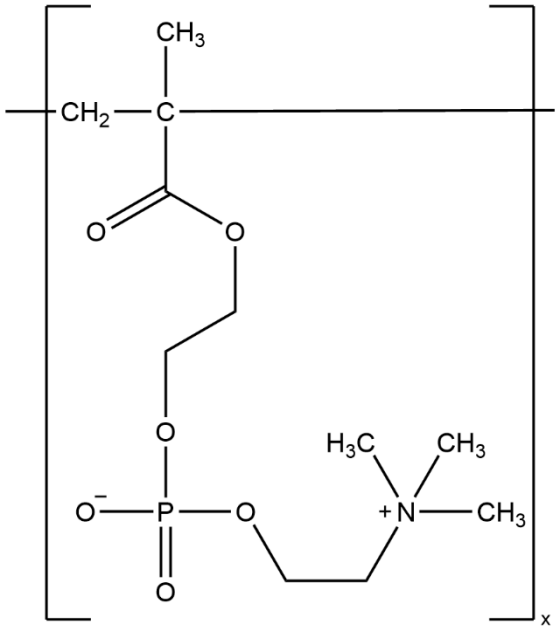
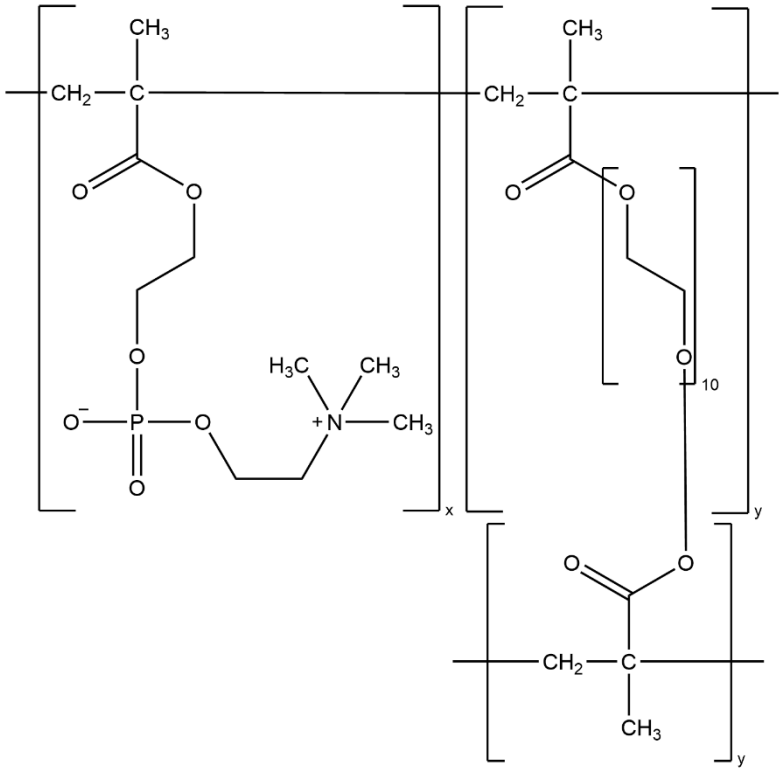
Ingredient/CAS No.	Definition & Structures	Function(s)
Polyphosphorylcholine Glycol Acrylate 67881-99-6	Polyphosphorylcholine Glycol Acrylate is the polymer that conforms generally to the formula: 	Film Formers; Skin-Conditioning Agents - Miscellaneous
Phosphorylcholine Glycol Methacrylate/PEG-10 Dimethacrylate Crosspolymer	Phosphorylcholine Glycol Methacrylate/PEG-10 Dimethacrylate Crosspolymer is the crosslinked polymer formed from phosphorylcholine glycol methacrylate and PEG-10 dimethacrylate monomers. 	Film Formers; Skin-Conditioning Agents - Humectant
Polyquaternium-10/ Phosphorylcholine Glycol Acrylate Copolymer	Polyquaternium-10/Phosphorylcholine Glycol Acrylate Copolymer is a copolymer of Polyquaternium-10 and phosphorylcholine glycol methacrylate. *Polyquaternium-10 is a polymeric quaternary ammonium salt of hydroxyethyl cellulose reacted with 2,3-epoxypropyltrimonium Chloride. Not enough information available about connectivity to provide a structure.*	Film Formers; Hair Conditioning Agents; Humectants; Skin-Conditioning Agents - Emollient

Table 1. Definitions, Functions, and Idealized Structures of the Ingredients in this Safety Assessment.[CIR Staff;1)]

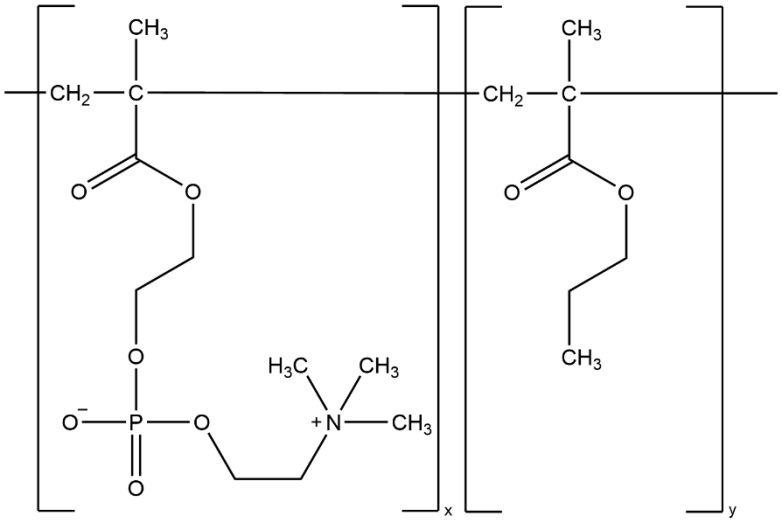
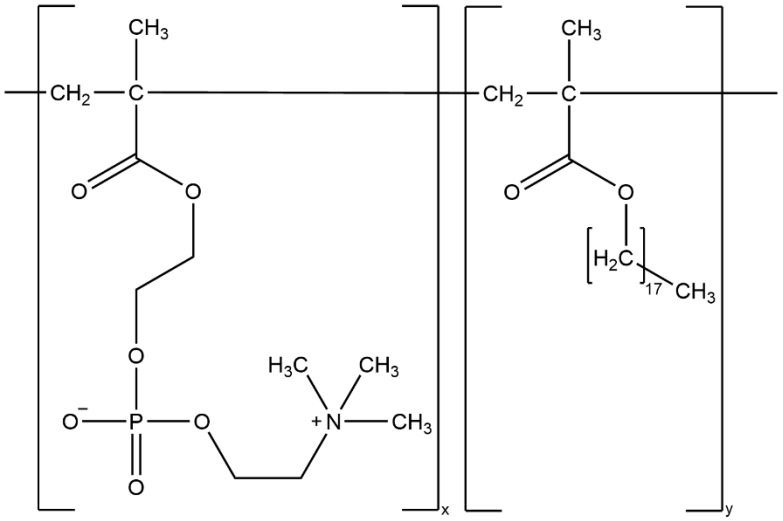
Ingredient/CAS No.	Definition & Structures	Function(s)
Polyquaternium-51 125275-25-4	Polyquaternium-51 is the polymeric quaternary ammonium salt that conforms generally to the formula: 	Film Formers; Skin-Conditioning Agents - Humectant
Polyquaternium-61	Polyquaternium-61 is the polymeric quaternary ammonium salt that conforms generally to the formula: 	Film Formers; Skin-Conditioning Agents - Humectant

Table 2. Frequency (2021) and Concentration of Use (2020) According to Duration and Type of Exposure.[5,6]

	Acrylic Acid/Phosphorylcholine Glycol Acrylate Crosspolymer		Phosphorylcholine Glycol Acrylate		Polyquaternium-51	
	# of Uses	Conc. (%)	# of Uses	Conc. (%)	# of Uses	Conc. (%)
Totals*	**NR**	**0.13**	**12**	**0.0005-0.075**	**275**	**0.000005-0.14**
Duration of Use						
Leave-On	*NR*	*0.13*	*11*	*0.0005-0.075*	*245*	*0.002-0.14*
Rinse off	*NR*	*NR*	*1*	*NR*	*30*	*0.000005-0.025*
Diluted for (bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type						
Eye Area	NR	NR	1	NR	23	0.021-0.05
Incidental Ingestion	NR	NR	NR	NR	NR	NR
Incidental Inhalation - Sprays	NR	NR	8[a];2[b]	0.0005[b]	79[a];88[b]	0.01[a]
Incidental Inhalation - Powders	NR	NR	2[b]	0.0005[b]	3;88[b]	0.008-0.14[c]
Dermal Contact	NR	0.13	6	0.0005-0.075	269	0.000005-0.14
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	6	NR	6	0.0005-0.025
Hair-Coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	0.1
Mucous Membrane	NR	NR	NR	NR	6	NR
Baby Products	NR	NR	NR	NR	NR	NR

	Polyquaternium-61	
	# of Uses	Conc. (%)
Totals/Conc. Range	**2**	**0.000006-0.01**
Duration of Use		
Leave-On	*2*	*0.000006-0.0069*
Rinse off	*NR*	*0.01*
Diluted for (bath) Use	*NR*	*NR*
Exposure Type		
Eye Area	NR	0.005
Incidental Ingestion	NR	NR
Incidental Inhalation - Sprays	1[a];1[b]	0.000006
Incidental Inhalation - Powders	1[b]	0.0069
Dermal Contact	2	0.001-0.0069
Deodorant (underarm)	NR	NR
Hair - Non-Coloring	NR	0.000006-0.01
Hair-Coloring	NR	NR
Nail	NR	NR
Mucous Membrane	NR	NR
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 that these products may be sprays, but it is not specified whether the reported uses are sprays
[b]Not specified that these products are sprays or powders, but it is possible the use can be as a spray or powder, therefore the information is captured in both categories
[c]It is possible that these products may be powders, but it is not specified whether the reported uses are powders

Table 3. Acryloyloxyethyl Phosphorylcholine Polymers With No Reported Uses.[5,6]

C4-18 Alkyl Methacrylate/Methacryloyloxyethyl Phosphorylcholine Copolymer
Hydroxyethylcellulose/Phosphorylcholine Glycol Acrylate Copolymer
Phosphorylcholine Glycol Methacrylate/PEG-10 Dimethacrylate Crosspolymer
Polyquaternium-10/Phosphorylcholine Glycol Acrylate Copolymer

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2021 FDA VCRP Data

Acrylic Acid/Phosphorylcholine Glycol Acrylate Crosspolymer

No FDA data

C4-18 Alkyl Methacrylate/Methacryloyloxyethyl Phosphorylcholine Copolymer

No FDA data

Hydroxyethylcellulose/Phosphorylcholine Glycol Acrylate Copolymer

No FDA data

Phosphorylcholine Glycol Methacrylate/PEG-10 Dimethacrylate Crosspolymer

No FDA data

Polyphosphorylcholine Glycol Acrylate

Eye Lotion	03D	1
Tonics, Dressings, and Other Hair Grooming Aids	05G	6
Cleansing	12A	1
Face and Neck (exc shave)	12C	2
Moisturizing	12F	1
Night	12G	1
Total		**12**

Polyquaternium-10/Phosphorylcholine Glycol Acrylate Copolymer

No FDA data

Polyquaternium-51

Eye Shadow	03C	6
Eye Lotion	03D	8
Eye Makeup Remover	03E	1
Other Eye Makeup Preparations	03G	8
Hair Conditioner	05A	1
Shampoos (non-coloring)	05F	4
Tonics, Dressings, and Other Hair Grooming Aids	05G	1
Face Powders	07B	3
Foundations	07C	40
Makeup Fixatives	07H	1
Other Makeup Preparations	07I	4
Bath Soaps and Detergents	10A	4
Other Personal Cleanliness Products	10E	2
Shaving Cream	11E	1
Cleansing	12A	15
Face and Neck (exc shave)	12C	66
Body and Hand (exc shave)	12D	22

Moisturizing	12F	66
Night	12G	8
Paste Masks (mud packs)	12H	2
Skin Fresheners	12I	4
Other Skin Care Preps	12J	8
Total		**275**

Polyquaternium-61

Face and Neck (exc shave)	12C	1
Night	12G	1
Total		**2**

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review

FROM: Carol Eisenmann, Ph.D.
Personal Care Products Council

DATE: February 27, 2020

SUBJECT: Concentration of Use Information by FDA Product Category: Acryloyloxyethyl Phosphoryl Choline Polymers

Concentration of Use by FDA Product Category – Acryloyloxyethyl Phosphoryl Choline Polymers*

Polyquaternium-51
Polyquaternium-61
Polyquaternium-10/Phosphorylcholine Glycol Acrylate Copolymer
Polyphosphorylcholine Glycol Acrylate
Acrylic Acid/Phosphorylcholine Glycol Acrylate Crosspolymer
C4-18 Alkyl Methacrylate/Methacryloyloxyethyl Phosphorylcholine Copolmer
Hydroxyethylcellulose/Phosphorylcholine Glycol Acrylate Copolymer
Phosphorylcholine Glycol Methacrylate/PEG-10 Dimethacrylate Crosspolymer

Ingredient	Product Category	Maximum Concentration of Use
Polyquaternium-51	Other eye makeup preparations	0.021-0.05%
Polyquaternium-51	Hair conditioners	0.0005%
Polyquaternium-51	Shampoos (noncoloring)	0.0005-0.025%
Polyquaternium-51	Blushers	0.016%
Polyquaternium-51	Foundations	0.01-0.05%
Polyquaternium-51	Makeup bases	0.01%
Polyquaternium-51	Makeup fixatives	0.01%
Polyquaternium-51	Other makeup preparations	0.005-0.01%
Polyquaternium-51	Other manicuring preparations Leave-on	0.1%
Polyquaternium-51	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.000005-0.005%
Polyquaternium-51	Face and neck products Not spray	0.008-0.14%
Polyquaternium-51	Body and hand products Not spray	0.02%
Polyquaternium-51	Moisturizing products Not spray	0.002-0.09%
Polyquaternium-51	Night products Not spray	0.007%
Polyquaternium-51	Skin fresheners	0.01%
Polyquaternium-51	Other skin care preparation	0.03-0.05%
Polyquaternium-51	Suntan products Not spray	0.007%
Polyquaternium-61	Eye lotions	0.005%
Polyquaternium-61	Hair conditioners	0.01%
Polyquaternium-61	Hair sprays Aerosol	0.000006%
Polyquaternium-61	Face powders	0.0069%
Polyquaternium-61	Moisturizing products Not spray	0.001%
Polyphosphorylcholine Glycol Acrylate	Face and neck products Not spray	0.0005%

Polyphosphorylcholine Glycol Acrylate	Other skin care preparations	0.075%
Acrylic Acid/Phosphorylcholine Glycol Acrylate Crosspolymer	Foundations	0.18%
Acrylic Acid/Phosphorylcholine Glycol Acrylate Crosspolymer	Other skin care preparations	0.13%

*Ingredients included in the title of the table but not found in the table were included in the concentration of use survey, but no uses were reported.

Information collected in 2019-2020
Table prepared: February 26, 2020

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Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review

FROM: Carol Eisenmann, Ph.D.
Personal Care Products Council

DATE: June 16, 2020

SUBJECT: Polyquaternium-51

Active Concepts. 2009. AC Moisture-Plex Advanced (contains 1.4% Polyquaternium-51) Irritation Analysis.

AC Moisture-Plex Advanced Irritation Analysis

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AC Moisture-Plex Advanced contains 1.4% Polyquaternium-51

Abstract:

To confirm that **AC Moisture-Plex Advanced** is non-irritating, we used *in-vitro* dermal and ocular irritation assays.

The Irritection® assays purchased from InVitro International were used to determine the potential ocular and dermal irritancy of **AC Moisture-Plex Advanced**. The *in-vitro* system involves the use of a proprietary solution comprised of both proteins and macromolecules in a well that is covered by a membrane. Testing material is applied to the membrane and diffuses into the well. The proteins and macromolecules undergo conformational changes based on the irritancy of the diffused material, these changes are intended to mimic the biomolecular changes that occur when irritants are applied to both the eyes and skin. The conformational changes cause the solution to become turbid; there is a direct correlation between the irritancy level of the material and the solution's turbidity. Irritancy is quantitatively measured using a spectrophotometer.

Figure 1. The Ocular Irritection Model

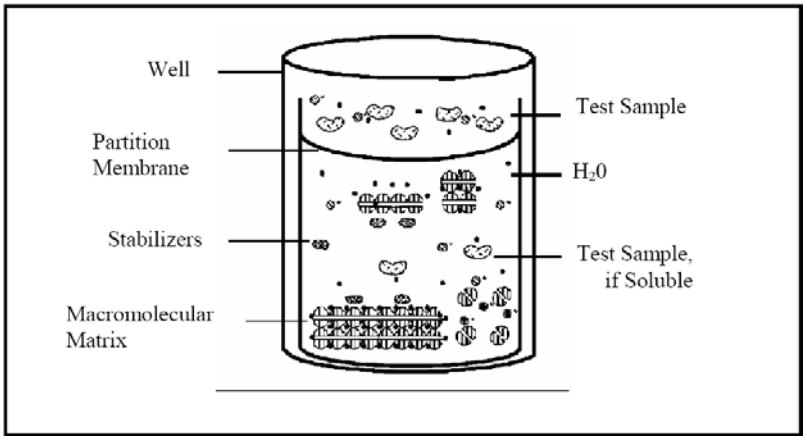
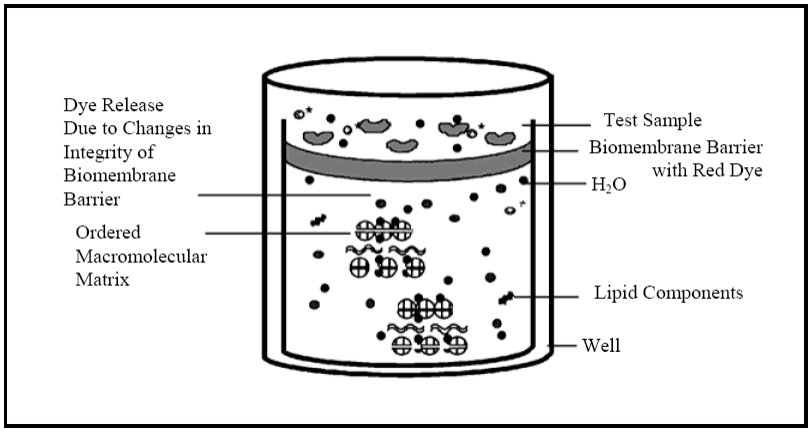


Figure 2. The Dermal Irritection Model



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AC Moisture-Plex Advanced Irritation Analysis

Materials and Methods:

For the ocular and dermal irritation assays, samples of **AC Moisture-Plex Advanced** were applied to Irritection® systems at concentrations of 25, 50, 75, 100 and 125 µl. The samples were left at room temperature for a period of 24 hours before they were analyzed with a spectrophotometer. The scales used to correlate the quantitative spectrophotometer value and potential irritancy for both ocular and dermal analysis follows.

Table 1. Ocular Irritancy Scale

Ocular Irritection Score	Ocular Irritancy Classification
0.0 – 12.5	Minimal Irritant
12.6 – 30.0	Mild Irritant
30.1 – 51.0	Moderate Irritant
51.1 – 80.0	Severe Irritant

Table 2. Dermal Irritancy Scale

Dermal Irritection Score	Dermal Irritancy Classification
0.0 – 0.90	Non-Irritant
0.91 – 1.20	Mild Irritant
1.21 – 5.00	Irritant

Results:

Ocular Assay:

Lot #	Sample	Dose (µl)	Irritection Score	Ocular Assay Classification
14195P	AC Moisture-Plex Advanced	25	2.9	Minimal Irritant
		50	3.2	Minimal Irritant
		75	3.4	Minimal Irritant
		100	3.7	Minimal Irritant
		125	3.9	Minimal Irritant

Dermal Assay:

Lot #	Sample	Dose (µl)	Irritection Score	Dermal Assay Classification
14195P	AC Moisture-Plex Advanced	25	0.26	Non-Irritant
		50	0.29	Non-Irritant
		75	0.32	Non-Irritant
		100	0.38	Non-Irritant
		125	0.39	Non-Irritant

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Discussion:

Irritation is defined by the American Heritage Dictionary as a condition of inflammation, soreness or irritability of a bodily organ or part. Physical irritation is usually characterized with hyperpigmentation, dry flakey skin and watery eyes. Both the dermal and ocular assays reveal that **AC Moisture-Plex Advanced** is non-irritating and should not cause any of the aforementioned conditions. Although the Irritection® scores vary per dose, all the scores fall within the non-irritant range for the dermal assay, and the minimal irritant range for the ocular assay.

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