GREEN

Polyquaternium-22

CIR EXPERT PANEL MEETING

DECEMBER 12-13, 2011

Cosmetic Ingredient Review
Commitment . . . Credibility
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November 21, 2011

Memorandum

To: CIR Expert Panel

From: Wilbur Johnson, Jr.
Manager/Lead Specialist

Subject: Draft Report on Polyquaternium-22 and Polyquaternium-39

A Scientific Literature Review (SLR) Notice on these ingredients was announced on August 11, 2011. Unpublished data received during the 60-day comment period are summarized in the draft report.

A copy of the draft report on Polyquaternium-22 and Polyquaternium-39 is included along with the CIR report history, Literature search strategy, Ingredient Data profile, Revised SLR Notice on Polyquaternium-22 and Polyquaternium-39 (notice, pdf file), CIR final report on Polyquaternium-10 (final1, pdf file), CIR final report on Polyquaternium-11(final2, pdf file), CIR final report on Polyquaternium-7 (final3, pdf file), and the CIR Re-review summary on Polyquaternium-7 (re-rev, Word file). The unpublished data included with this report are:

1. Summary information on studies of an oxidative hair dye containing 0.16% Polyquaternium-22 submitted on 10-21-2011 (data 1 pdf file);
2. Use concentration data on Polyquaternium-22 and Polyquaternium-39 from Council survey submitted on 10-25-2011 (data 2, pdf file)

CIR published safety assessments on Polyquaternium-10, Polyquaternium-11, and Polyquaternium-7 are included for the Panel's use in determining whether data from these reports should be considered when assessing the safety of Polyquaternium-22 and Polyquaternium-39 in cosmetics. If the Panel determines that any of those data are relevant, they will be added.

The Panel needs to determine whether the available data on these 2 ingredients, together with any of the data from prior Polyquaternium safety assessments, are sufficient for arriving at a conclusion on the safety of Polyquaternium-22 and Polyquaternium-39 in cosmetic products.

If additional data are needed, an insufficient data announcement should be issued with a list of those data needs.

If the available data are sufficient to support the safety of these ingredients, then a tentative conclusion should be developed with a rationale to be included in the discussion section, and a tentative report issued for public comment.

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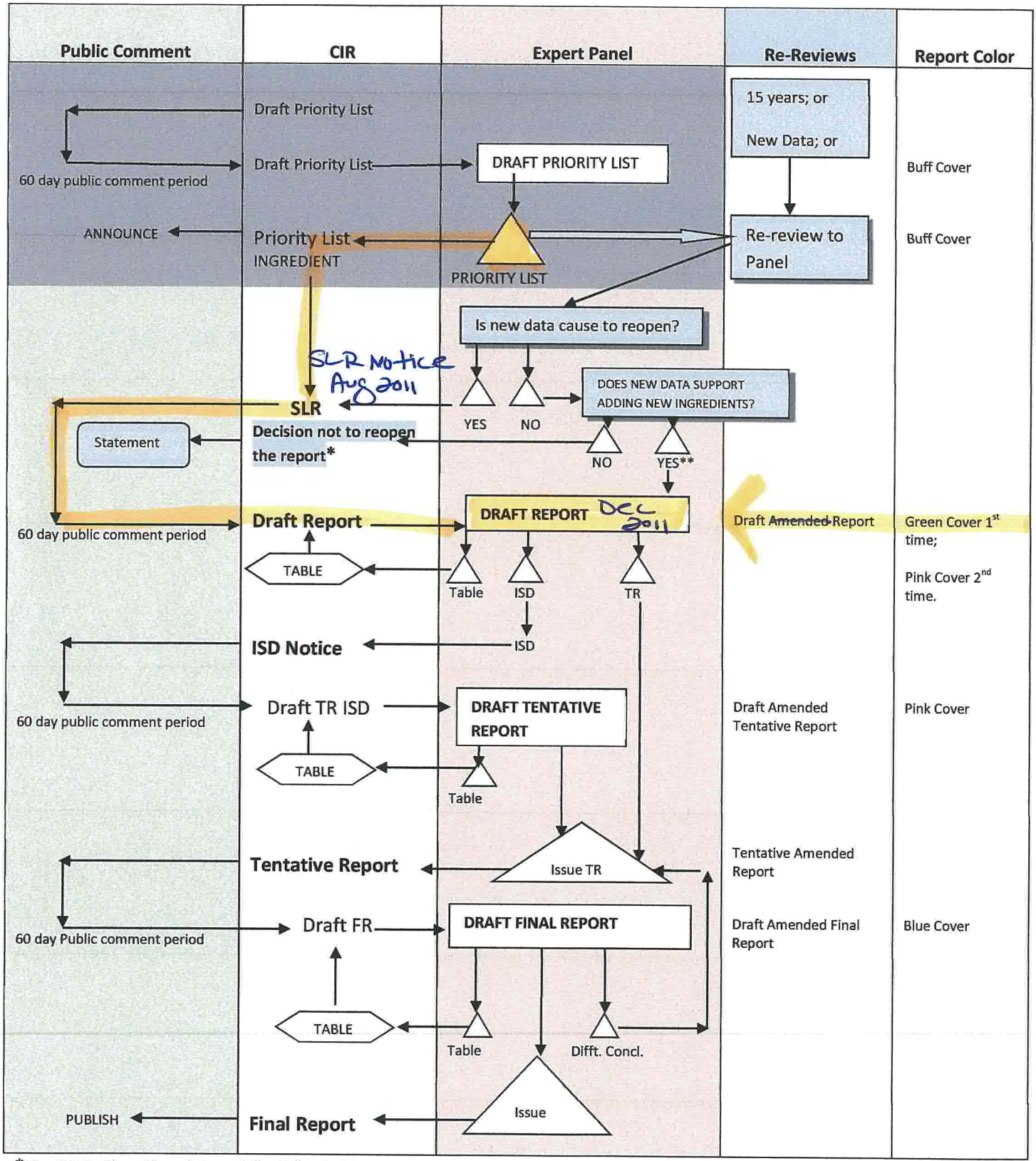
Phone 202.331.0651 FAX 202.331.0088 http://www.cir-safety.org

Polyquaternium-22

SAFETY ASSESSMENT FLOW CHART



*The CIR Staff notifies of the public of the decision not to re-open the report and prepares a draft statement for review by the Panel. After Panel review, the statement is issued to the Public.

**If Draft Amended Report (DAR) is available, the Panel may choose to review; if not, CIR staff prepares DAR for Panel Review.

Expert Panel Decision

Document for Panel Review

Option for Re-review

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Revised Scientific Literature Review Notice – August 11, 2011

Polyquaternium-22 and Polyquaternium-39

Cosmetic Ingredient Review (CIR) procedures call for the development of a review of the available scientific literature for each cosmetic ingredient (and wherever appropriate, closely related ingredients), on the basis of the annual priority list. The Scientific Literature Review (SLR) shall consist of a bibliography of relevant scientific literature, study reports that have been submitted by interested parties, and a description of each literature reference or submitted study report.

For Polyquaternium-22 and Polyquaternium-39, an intensive search of the published information on these ingredients has found insufficient information to justify preparation of a formal SLR. CIR, therefore, is issuing this SLR Notice to alert interested parties that a safety assessment is being prepared. The only information found in the published literature was in the form of numerous patents, most of which were on hair care products. All interested persons are provided 60 days from the above date to submit comments and/or additional published or unpublished data.[1]

Both ingredients are quaternary ammonium salts. Polyquaternium-22 is the copolymer of dimethyl diallyl ammonium chloride and acrylic acid. Polyquaternium-39 is the copolymer of dimethyl diallyl ammonium chloride, acrylic acid, and acrylamide.

A draft report will be reviewed at the **December 12-13, 2011** meeting of the CIR Expert Panel. CIR will include relevant data from its existing safety assessment of Polyquaternium-7 (J. Am. Coll. Toxicol. 14(6):476-84, 1995), which is a copolymer of dimethyl diallyl ammonium chloride and acrylamide, and information on acrylamide monomer toxicity from its existing safety assessment of Polyacrylamide (Int. J. of Toxicol. 24(S2):21-50, 2005). If additional data are provided in response to this notice, those data will be incorporated into the draft report and reviewed by the Panel.

Given that this notice is issued because of a general absence of information, CIR is seeking information in a wide range of areas, including:

- Chemistry information, including composition and structure, method of manufacture, and impurity data;
- Toxicokinetics data, specifically dermal absorption; if these ingredients were to have appreciable dermal absorption, oral animal toxicity data, including reproductive/developmental toxicity and carcinogenicity data, are needed, as are genotoxicity data; these data may not be crucial if these ingredients have no appreciable dermal penetration, however if they were available, they would improve the resulting safety assessment;
- Dermal toxicity data;
- Dermal irritation and sensitization data; and
- Any other relevant safety information that may be available.

Please forward comments and data to Wilbur Johnson, Jr., Manager/Lead Specialist, CIR.

[1] Because all unpublished data submitted to CIR will be evaluated in public meetings and may be included in the CIR final published safety assessment, CIR may not accept any confidential or proprietary data or information that cannot be made public. Information may be submitted without identifying the source or the trade name of the cosmetic product containing the ingredient.

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CIR History of:

Polyquaternium-22
Polyquaternium-39

A Scientific Literature Review (SLR) Notice was announced on August 11, 2011, and unpublished data from the Personal Care Products Council (Council) were received during the 60-day comment period.

Draft Report, Belsito and Marks Teams/Panel: December 12-13, 2011

The SLR (now a draft report) was revised to include the following unpublished data received from the Council:

1. Summary information on studies of an oxidative hair dye containing 0.16% Polyquaternium-22 submitted on 10-21-2011;
2. Use concentration data on Polyquaternium-22 and Polyquaternium-39 from Council survey submitted on 10-25-2011

Polyquaternium-22 and Polyquaternium-39 Check List for December, 2011. Writer – Wilbur Johnson																					
			Acute toxicity					Repeated dose toxicity				Irritation			Sensitization						
	Skin Penetration	Penetration Enhancement	ADME	Oral	Parenteral	Dermal	Inhale	Oral	Parenteral	Dermal	Inhale	Ocular Irritation	Dermal Irr. Animal	Dermal Irr Human	Sensitization Animal	Sensitization Human	Repro/Devel toxicity	Genotoxicity	Carcinogenicity	Phototoxicity
Polyquaternium-22												**X**		**X**						
Polyquaternium-39																				

Literature Searches on Polyquaternium-22 and Polyquaternium-39*

Ingre-dients	Toxline &PubMed	ChemIDplus	Multidatabase (See legend*)	DART	SciFinder	RTECS
P-22	0		0	0	141	0
P-39	0		0	0	146	0

*Data in Table: Publications found; Multidatabase = HSDB, CCRIS, ITER, IRIS, Gene-Tox, and LacMed

Searches Performed on7/28/2011
Search updated on 11/7/2011 using PubMed, Toxline, and SciFinder

INGREDIENTS

Polyquaternium-22 (P-22)
Acrylic Acid-Diallyldimethylammonium Chloride Polymer
53694-17-0

Polyquaternium-39 (P-39)
Acrylic Acid, Polymer with Acrylamide and Diallyldimethylammonium Chloride
2-Propen-1-aminium, N,N-Dimethyl-N-2-Propenyl-. Chloride, Polymer with 2-Propenamide and 2-Propenoic Acid
25136-75-8

Search Strings (NLM databases)

Polyquaternium-22 OR "Acrylic Acid-Diallyldimethylammonium Chloride Polymer" OR 53694-17-0

Polyquaternium-39 OR "Acrylic Acid, Polymer with Acrylamide and Diallyldimethylammonium Chloride" OR 25136-75-8

SciFinder Search Terms

Polyquaternium-22
Polyquaternium-39

Report

Draft Safety Assessment

Polyquaternium-22 as Used in Cosmetics

December 13, 2011

All interested persons are provided 60 days from the above date to comment on this Draft 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 CIR will be discussed in open meetings, will be available at the CIR office 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 Director, Dr. F. Alan Andersen.

The 2011 Cosmetic Ingredient Review Expert Panel members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Ronald A Hill, Ph.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; James G. Marks, Jr., M.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The CIR Director is F. Alan Andersen, Ph.D. This report was prepared by Wilbur Johnson, Jr., M.S., Manager/Lead Specialist.

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TABLE OF CONTENTS

INTRODUCTION

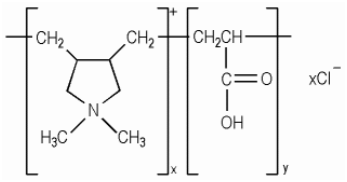
Available data relevant to the safety of polyquaternium-22 and polyquaternium-39 as used in cosmetics are reviewed in this draft report. Both ingredients function as antistatic agents, film formers, and hair fixatives in cosmetic products. Because a search of the published literature did not identify toxicity/other data that could be used to evaluate the safety of these ingredients, an SLR Notice specifying the types of studies that generally would be needed by CIR to assess safety was announced on August 11, 2011. Data summaries received from the Personal Care Products Council in response to this notice are included in this report.

The Expert Panel previously issued final reports on the safety assessment of Polyquaternium-7[1], Polyquaternium-10[2] and Polyquaternium-11[3], having concluded that these cosmetic ingredients are safe in the present practices of use and concentration. This conclusion on Polyquaternium-7 was confirmed by the Panel during a re-review of the safety of this ingredient in cosmetics in 2010.[4] The Panel also determined that the amount of residual acrylamide in Polyquaternium-7 is not of concern. The Panel's conclusions on Polyquaternium-10 and Polyquaternium-11 were also confirmed.[5,6]

CHEMISTRY

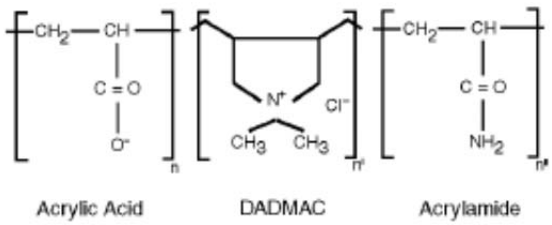
Definition and Structure

Polyquaternium-22 is defined as a copolymer of dimethyldiallyl ammonium chloride and acrylic acid that conforms to the following structural formula: [7]



Another name for this copolymer is acrylic acid-diallyldimethylammonium chloride polymer.

Polyquaternium-39 is defined as a polymeric quaternary ammonium salt of acrylic acid, dimethyl ammonium chloride (DADMAC) and acrylamide.[7] The structural formula of this chemical is:[8]



Other names for this polymeric quaternium ammonium salt include acrylic acid, polymer with acrylamide and diallyl-dimethyl ammonium chloride and 2-propen-1-aminium, N,N-dimethyl-N-2-propenyl-, chloride, polymer with 2-promenamide and 2-propenoic acid.[7]

Chemical and Physical Properties

Specifications for Polyquaternium-22 and Polyquaternium-39 are as follows:

Polyquaternium-22[9]

- Appearance (viscose water clear liquid)
- Solid (40 ± 1%)
- pH (2 to 5, for 1% aqueous solution)
- Viscosity (3,000 to 7,500 cps, @ 25°C)

Polyquaternium-39[10]

- Appearance (clear viscose liquid)
- Solid (9 to 11%)
- pH (5.5 to 7.2)
- Viscosity (2,000 to 20,000 cps, @ 25°C)

USE

Cosmetic

The 2 ingredients reviewed in this safety assessment function as antistatic agents, film formers, and hair fixatives in cosmetic products.[7] According to information supplied to the Food and Drug Administration (FDA) by industry as part of the Voluntary Cosmetic Registration Program (VCRP) in 2011, both Polyquaternium-22 and Polyquaternium-39 were being used in cosmetic products.[11] These data are summarized in Table 1. Results from a survey of ingredient use concentrations provided by the Personal Care Products Council (also included in Table 1) in 2011 indicate that these 2 ingredients were being used at concentrations up to 2% (Polyquaternium-22, in a rinse-off product) and up to3 % (Polyquaternium-39, in a rinse-off product).[12]

Cosmetic products containing the ingredients reported as being used may be applied to the skin and hair, or, incidentally, may come in contact with the eyes and mucous membranes. Products containing these ingredients may be applied as frequently as several times per day and may come in contact with the skin or hair for variable periods following application. Daily or occasional use may extend over many years.

Noncosmetic

Polyquaternium-39 is included among the substances that may be safely used as components of paper and paperboard in contact with aqueous and fatty foods.[13]

TOXICOKINETICS

Data on the absorption, distribution, metabolism, and excretion of Polyquaternium-22 or Polyquaternium-39 were not found in the published literature.

TOXICOLOGY

Acute/repeated dose toxicity studies on Polyquaternium-22 or Polyquaternium-39 were not found in the published literature.

Ocular Irritation

The ocular irritation potential of a 0.16% Polyquaternium-22 (pH = 9.5 to 10) oxidation dye was evaluated *in vitro* using the the hen's egg test on the chorioallantoic membrane (HET-CAM test).[14] The dye was tested at a concentration of 10% (0.016% active Polyquaternium-22), and was classified as a slight irritant (irritation scores of 2.38, 4.51, or 4.60). The positive controls, sodium hydroxide (0.1 M) and sodium dodecyl sulfate (SDS, 1%), yielded scores of 19.98 and 10.21, respectively. The negative control (0.9% sodium chloride) yielded a score of 0.

Skin Irritation

The skin irritation potential of a 0.16% Polyquaternium-22 (pH = 9.5 to 10) oxidation dye was evaluated using 30 subjects (ages not stated).[14] In a single, occlusive patch test, a 10% concentration of the dye (0.016% active Polyquaternium-22) was applied for 24 h. Reactions were scored at 24 h, 48 h, and 72 h post-application, and the dye was not predicted to be a skin irritant (OIS [not defined] = 0.07). The negative control (water) yielded a score of 0, and the positive control (1% SDS) yielded a score of 0.92. The same test concentration of the dye was also applied to 30 subjects (ages not stated) in a multiple patch test.[14] Three 24 h applications of the dye were made to each subject and reactions were scored according to the same schedule. The dye was not predicted to be a skin irritant (OIS = 0.07). Water (negative control) yielded a score of 0 and 0.3% SDS (positive control) yielded a score of 0.50.

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

Reproductive/developmental toxicity data on Polyquaternium-22 or Polyquaternium-39 were not found in the published literature.

GENOTOXICITY

Studies evaluating the genotoxicity of Polyquaternium-22 or Polyquaternium-39 were not found in the published literature.

CARCINOGENICITY

Carcinogenicity data on Polyquaternium-22 or Polyquaternium-39 were not found in the published literature.

SUMMARY

Polyquaternium-22 and Polyquaternium-39 function as antistatic agents, film formers, and hair fixatives in cosmetic products. According to information supplied to the Food and Drug Administration (FDA) by industry as part of the Voluntary Cosmetic Registration Program (VCRP) in 2011, both ingredients were being used in cosmetic products. Results from a survey of ingredient use concentrations provided by the Personal Care Products Council in 2011 indicate that these 2 ingredients were being used at concentrations up to 2% (Polyquaternium-22, in a rinse-off product) and up to3 % (Polyquaternium-39, in a rinse-off product).

A 0.16% Polyquaternium-22 oxidation dye, tested at a concentration of 10% (0.016% active Polyquaternium-22) in an *in vitro* HET-CAM test, was classified as a slight ocular irritant. In single and multiple application occlusive patch tests, the same test concentration of the dye was not predicted to be a skin irritant in human subjects. The following types of data were not found in the published literature: toxicokinetics, acute and repeated dose toxicity, reproductive and developmental toxicity, genotoxicity, and carcinogenicity.

Table 1. Current Frequency of Use According to Duration and Type of Exposure Provided in 2011[11,12]

	Polyquaternium-22		**Polyquaternium-39**	
	# of Uses	Conc. (%)	# of Uses	Conc. (%)
Exposure Type				
Eye Area	NR	NR	1	1
Incidental Ingestion	NR	NR	NR	NR
Incidental Inhalation-sprays	NR	NR	NR	NR
Incidental Inhalation-powders	NR	NR	NR	NR
Dermal Contact	9	0.2	40	0.1 to 3
Deodorant (underarm)	NR	NR	NR	NR
Hair - Non-Coloring	47	0.3 to 1	37	0.01 to 3
Hair-Coloring	425	0.03 to 2	NR	0.3
Nail	NR	NR	NR	NR
Mucous Membrane	NR	0.2	19	0.1 to 1
Baby Products	NR	NR	2	NR
Duration of Use				
Leave-On	14	0.4 to 0.5	22	0.01 to 3
Rinse off	467	0.03 to 2	47	0.1 to 3
Diluted for (bath) use	NR	NR	8	NR
Totals/Conc. Range	481	0.03 to 2	77	0.01 to 3

NR = Not Reported; NS = Not Surveyed; Totals = Rinse-off + Leave-on Product Uses.
Note: Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure type uses may not equal the sum total uses.

References

1. Andersen, F. A. Final report on the safety assessment of Polyquaternium-7. *J.Am.Coll.Toxicol.* 1995;14(6):476-484.

2. Elder, R. L. Final report on the safety assessment of polyquaternium-10. *J Am Coll Toxicol*. 1988;7(3):335-352.

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13. Food and Drug Administration (FDA). Components of paper and paperboard in contact with aqueous and fatty foods. Polyquaternium-39. 21 CFR 176.170. 2010.

14. Personal Care Products Council. 2010. Summary information on studies of an oxidative hair dye containing 0.16% polyquaternium-22. Unpublished data submitted by the Personal Care Products Council on 10-21-2011.

Data

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: F. Alan Andersen, Ph.D.
Director - COSMETIC INGREDIENT REVIEW (CIR)

FROM: Halyna Breslawec, Ph.D.
Industry Liaison to the CIR Expert Panel

DATE: October 21, 2011

SUBJECT: Summary Information on Studies of an Oxidative Hair Dye Containing 0.16% Polyquaternium-22

1101 17th Street, N.W., Suite 300 | Washington, D.C. 20036-4702 | 202.331.1770 | 202.331.1969 (fax) | www.personalcarecouncil.org

HUMAN IRRITATION

Test Material	Test Material Concentration	pH of test material	Active Polyquaternium-22 Amount	Test Pop.	Procedure	Study Dates	Results	Testing Facility
Polyquaternium -22 (0.16%) in oxidative hair dye	10%	9.5 - 10	0.016%	30 Subjects	Human Single Patch Test, 24 hour application under occlusion, test concentration 10%, reading times 24h, 48h and 72h. Negative control (water). Positive control (1% SDS)	January 19 to January 22, 2010	Not predicted to be a skin irritant (OIS 0.07). Negative control (0.00), Positive control (0.92)	proDerm, Institut für Angewandte Dermatologische Forschung GmbH, Schenefeld, Germany
Polyquaternium -22 (0.16%) in oxidative hair dye	10%	9.5 - 10	0.016%	30 Subjects	Human Multiple Patch Test, 3x24 hour application under occlusion, test concentration 10%, reading times 24h, 48h and 72h. Negative control (water). Positive control (0.3% SDS).	July, 2010	Not predicted to be a skin irritant (OIS 0.07). Negative control (0.00), Positive control (0.50)	GTLF Therapy and Performance Research Institute, Weismain, Germany

In Vitro Ocular Irritation

Test Material	Test Material Concentration	Active Polyquaternium-22 Amount	pH of test material	Test	Study Dates	Results	Testing Facility
Polyquaternium -22 (0.16%) in oxidative hair dye	10%	0.016%	9.5 - 10	HET-CAM	September 21, 2010	Slight irritant with an Irritation Score of 2.38, 4.51, or 4.60. Positive controls NaOH, (0.1M) 19.98, SDS (1%) 10.21. Negative control NaCl (0.9%) 0.00.	Harlan CCR, Rossdorf, Germany

Personal Care Products Council
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Memorandum

TO: F. Alan Andersen, Ph.D.
Director - COSMETIC INGREDIENT REVIEW (CIR)

FROM: Halyna Breslawec, Ph.D.
Industry Liaison to the CIR Expert Panel

DATE: October 25, 2011

SUBJECT: Concentration of Use by FDA Product Category: Polyquaternium-22 and Polyquaternium-39

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Concentration of Use by FDA Product Category
Polyquaternium-22 and Polyquaternium-39

Ingredient	Product Category	Maximum Concentrations of Use
Polyquaternium-22	Hair conditioners	0.5-1%
Polyquaternium-22	Shampoos (noncoloring)	0.3-0.8%
Polyquaternium-22	Tonics, dressings and other hair grooming aids	0.4-0.5%
Polyquaternium-22	Hair dyes and colors (all types requiring caution statement and patch test)	0.03-2%
Polyquaternium-22	Other hair coloring preparations	1%
Polyquaternium-22	Other personal cleanliness products	0.2%
Polyquaternium-39	Eye makeup remover	1%
Polyquaternium-39	Hair conditioners	0.1-0.4%
Polyquaternium-39	Shampoos (noncoloring)	0.3-3%
Polyquaternium-39	Tonics, dressings and other hair grooming aids	0.01-3%
Polyquaternium-39	Hair dyes and colors (all types requiring caution statement and patch test)	0.3%
Polyquaternium-39	Bath soaps and detergents	0.1%
Polyquaternium-39	Other personal cleanliness products Liquid hand soap	1%
Polyquaternium-39	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.1-0.2%
Polyquaternium-39	Depilatories	0.5%
Polyquaternium-39	Face and neck creams, lotions and powders	0.8-3%
Polyquaternium-39	Body and hand creams, lotions and powders	2%

Information collected in 2011
Table prepared October 25, 2011

JOURNAL OF THE AMERICAN COLLEGE OF TOXICOLOGY
Volume 7, Number 3, 1988
Mary Ann Liebert, Inc., Publishers

3

Final Report on the Safety Assessment of Polyquaternium-10

Polyquaternium-10 is a polymeric quaternary ammonium derivative of hydroxyethyl cellulose that is used in cosmetics as a conditioner, thickener, and emollient at concentrations of ≤0.1%–5%. Polyquaternium-10 has, at most, only a low potential to penetrate the stratum corneum but is adsorbed by keratinous surfaces. The oral LD_{50} of Polyquaternium-10 was not obtained at 16 g/kg in rats. Inhalation, dermal, and ocular animal test data indicated, at most, only a low degree of toxicity at test concentrations of Polyquaternium-10 greater than that used in cosmetic products. Polyquaternium-10 with and without metabolic activation was not a mutagen in three separate assay systems. Polyquaternium-10 was neither an irritant nor a human sensitizer when tested at 2.0%. Cosmetic products containing up to 1% Polyquaternium-10 were not human irritants, sensitizers, or photosensitizers. On the basis of the information presented, it is concluded that Polyquaternium-10 is safe as a cosmetic ingredient in the present practices of use.

INTRODUCTION

Polyquaternium-10 is a cationic form of hydroxyethyl cellulose that adsorbs and sorbs well to proteinaceous surfaces. It is used in cosmetics as a conditioner, thickener, and emollient in hair care products, lotions, and makeup.

CHEMISTRY

Definition

Polyquaternium-10, also known as Quaternium-19, is a polymeric quaternary ammonium salt of hydroxyethyl cellulose reacted with a trimethyl ammonium substituted epoxide. There are various grades of Polyquaternium-10 with different average molecular weights generally ranging from 250,000 to 600,000. Polyquaternium-10 has three CAS numbers: 53568-66-4, 54351-50-7, and 55353-19-0.[1-3]

Chemical and Physical Properties

Polyquaternium-10 is a white granular powder with a characteristic amine odor. It is soluble in water and insoluble in alcohol and nonpolar organic sol-

vents. Polyquaternium-10 used in cosmetics has 0.5% maximum water insolubles, 1.7 to 2.2% nitrogen-containing components, 2% maximum ash (NaCl), and 6% maximum volatile material. The particle size specifications are 95% minimum through a 20 mesh filter and 85% minimum through a 40 mesh filter. The viscosity of a 2% aqueous solution (25°C) is between 60 and 150 centipoises.[4]

Polyquaternium-10 alters the surface tension of aqueous solutions of anionic surfactants. Addition of 1% and 2% Polyquaternium-10 lowered the surface tension of aqueous solutions of sodium lauryl sulfate, sodium tridecylbenzenesulfonate, and potassium laurate.[5]

Reactivity

Polyquaternium-10 is a cationic, surface-active polymer that is adsorbed by keratinous surfaces, such as hair and skin (stratum corneum). The adsorption of the polymer was not readily affected by pH in the range of 4 to 10. It undergoes slow hydrolytic cleavage outside this pH range. Sorption of Polyquaternium-10 to keratinous surfaces was decreased by the addition of electrolytes (salts), such as aluminum, iron, calcium, or sodium. Polyquaternium-10 is biologically degradable. The presence of ethyl alcohol or propylene glycol adds to the stability of Polyquaternium-10.[6-9]

Analytical Methods

The most common analytical method for quaternary ammonium compounds is colorimetric testing following separation by acid extraction.[10]

Method of Manufacture

Polyquaternium-10 is generally produced by reacting hydroxyethylcellulose with epichlorhydrin, followed by quaternization using trimethylamine. It is stable within a pH rane of 4 to 8.

Impurities

Inorganic impurities of Polyquaternium-10 used in cosmetics include water (up to 0.5%), nitrogen (1.7 to 2.2%), and ash (NaCl up to 2%). Information was not available on organic impurities of Polyquaternium-10.[4] Epichlorhydrin was not detected in any of six different Polyquaternium polymers analyzed with an average detection limit of about 0.5 ppm.[11] A maximum of 10.8 ppm Trimethylamine was detected in lots of Polyquaternium-10 that were produced and sold during 1985.[12]

USE

Purpose in Cosmetics

Polyquaternium-10 is used as a conditioner, emollient and viscosity controlling agent in cosmetics.[3,13,14]

Scope and Extent of Use in Cosmetics

Polyquaternium-10 is used primarily in hair care products, skin cleansers, and skin moisturizers in concentrations of ≤0.1%–5%. One hundred thirty-nine (139) of the voluntarily filed cosmetic product formulations were reported to the Food and Drug Administration to contain Polyquaternium-10.[15] The cosmetic product formulation data that are made available by the FDA are compiled through voluntary filing of such data in accordance with Title 21 part 720.4 of the Code of Federal Regulations.[16] Ingredients are listed in prescribed concentration ranges under specific product type categories. Since certain cosmetic ingredients are supplied by the manufacturer at less than 100% concentration, the value reported by the cosmetic formulator may not necessarily reflect the actual concentration found in the finished product; the actual concentration would be a fraction of that reported to the FDA. Data submitted within the framework of preset concentration ranges provide the opportunity for overestimation of the actual concentration of an ingredient in a particular product. An entry at the lowest end of a concentration range is considered the same as one entered at the highest end of that range, thus introducing the possibility of a 2- to 10-fold error in the assumed ingredient concentration (Table 1).

Polyquaternium-10 has been generally or individually approved for use in cosmetic formulations marketed in Japan.[17]

Surfaces, Frequency, and Duration of Application

The hair care products containing Polyquaternium-10 are, for the most part, applied for a few minutes, then rinsed off. However, Polyquaternium-10 is incorporated in these products for its "substantivity" (sorption) and would be expected to remain in contact with the hair between treatments. Skin cleansers and moisturizers have the potential to remain in continuous contact with the skin and nails for extended periods of time.

BIOLOGY

Penetration, Sorption, and Permeation Through Stratum Corneum

Approximately 1 ml of a 5% (w/v) water solution of ^{14}C-Polyquaternium-10 (uniformly labeled on the pendant side chain) was applied to the backs of 12 Fischer 344 rats. The total dose of 4.0 ml/kg was occluded for the test period 1, 3, and 24 h. Six rats were placed in Roth-type glass metabolism cages designed for the separate collection of urine, feces, and expired air for the entire 24-h exposure period. The remaining 6 exposed animals were killed, 3 at 1 h and 3 at 6-h postexposure. Blood measured at 1 h and 3 h for the interim sacrifices and for the 6 material balance rats killed at 24 h had no radioactivity above background. There was no radioactivity above background in any of 9 tissues examined in the 6 animals that were killed at 24 h. Less than 0.02% of the administered dose was found in the urine and less than 0.1% in the feces; no radioactivity was recovered in CO_2. Of the 83.7% of the total dose that was recovered from the male rats, 75.2% was from the occlusive materials and 7.1% was found

TABLE 1. Product Formulation Data for Polyquaternium-10[15]

Product category	*Total no. of formulations in category*	*Total no. containing ingredient*	*No. of product formulations within each concentration range (%)*			
			Unreported concentration	*>1–5*	*>0.1–1*	*≤0.1*
Bubble baths	475	1	–	–	1	–
Mascara	397	5	–	–	–	5
Hair conditioners	478	16	–	6	9	1
Hair sprays (aerosol fixatives)	265	1	–	–	1	–
Permanent waves	474	6	–	1	5	–
Hair shampoos (noncoloring)	909	62	–	9	46	7
Tonics, dressings, and other hair grooming aids	290	4	–	–	3	1
Wave sets	180	6	–	2	3	1
Other hair preparations (noncoloring)	177	1	–	–	1	–
Hair shampoos (coloring)	16	3	–	–	3	–
Makeup bases	831	2	–	–	–	2
Bath soaps and detergents	148	1	–	–	1	–
Skin cleansing preparations (cold creams, lotions, liquids, and pads)	680	6	2	–	1	3
Face, body, and hand skin care preparations (excluding shaving preparations)	832	8		–	3	5
Moisturizing skin care preparations	747	12	1	–	3	8
Night skin care preparations	219	1	–	–	–	1
Paste masks (mud packs)	171	1	–	–	–	1
Skin fresheners	260	1	–	–	–	1
Wrinkle smoothers (removers)	38	1	–	–	–	1
Other skin care preparations	349	1	–	–	1	–
1981 TOTALS		139	3	18	81	37

in or around the skin at the dose site. The fraction of the applied material that did penetrate the skin amounted to less than 1.5% of the administered radioactivity. The investigators noted the low total recovery of the applied radioactivity; however, if the data were normalized to 100%, less than 1.75% of the applied dose would have penetrated the skin. The authors concluded that Polyquaternium-10 is unlikely to penetrate the human skin in toxicologically significant amounts.[18,19]

The anti-irritant effect of hydroxyl and quaternary ammonium compounds, including Polyquaternium-10, has been investigated in recent years. It has been hypothesized that the sorption properties of Polyquaternium-10 enable the polymer to block keratin reactive sites, thus reducing the topical and eye irritant effects of surfactants in shampoo and cleanser formulations.[20,21]

Several studies have investigated the passage of Polyquaternium-10 and surfactants, such as sodium lauryl sulfate, into and through isolated stratum corneum from the skin of fetal pigs, neonatal rats, and adult humans. The fetal pigskin was frozen, and on warming, the stratum corneum was gently separated from the underlying epidermis. Neonatal rat skin was removed following death by CO_2 inhalation. The skin was placed in a desiccator jar and exposed to ammonia vapor for 1–3 h, then put in water to remove the epidermis from the dermis. After 1 h the epidermis was recovered on a paper towel, and the malpighian layer was scraped off, leaving the stratum corneum to dry. The various preparations were exposed to ^{14}C-Polyquaternium-10 and/or surfactant (in aqueous solution) in vials or permeability cells[22] to quantify sorption and permeability and to evaluate the effects of the polymer on the preparations. The results indicated that Polyquaternium-10 slowly diffused into the outer layer of the stratum corneum (all three species) rather than forming multilayers on the surface. Although ionic surfactants did reduce polymer sorption, pretreatment of the stratum corneum with 1% Polyquaternium-10 greatly reduced the amount of surfactant that passed through the preparation. This reduction in permeation of surfactant supported the hypothesis that Polyquaternium-10 is an anti-irritant in the presence of ionic (i.e., irritant) surfactants. The kinetics of polymer/surfactant sorption and permeation indicated that the polymer did not act primarily as a barrier to penetration, but rather it helped to maintain the physical integrity of the stratum corneum preparation.

Pretreatment of the stratum corneum of neonatal rats with Polyquaternium-10 slightly increased the hydration of the membrane and reduced swelling after surfactant exposure.[2,9,23,24]

ANIMAL TOXICOLOGY

Oral Toxicity

Three lots of Polyquaternium-10 were tested for acute oral toxicity by intubation in rats. Three studies at maximum doses of 16 g/kg, 13.1 g/kg, 16 g/kg did not achieve the LD_{50}.[25–27]

The acute oral toxicity of 1.0% Polyquaternium-10 in a shampoo and a conditioner was tested by gavage. The LD_{50} of the two formulations was not reached at 5 g/kg.[28,29] Results are summarized in Table 2.

TABLE 2. Acute Oral Toxicity

Compound	*No. of rats*	*Vehicle*	*LD_{50}*	*Comments*	*Reference*
Polyquaternium-10 (Lot 1)	10	Corn oil	>16 g/kg	3/10 died; sluggish, wet fur and diarrhea on one day; low order of toxicity	25
Polyquaternium-10 (Lot 1)	3	Water	Not reached	None died; sluggish at 4 g/kg	25
Polyquaternium-10 (Lot 2)	10	Corn oil	13.1 g/kg	7/10 died; sluggish, wet fur, nose covered with blood on 1 day	26
Polyquaternium-10 (Lot 2)	10	Corn oil	Not reached	None died at 8 g/kg; appeared normal	26
Polyquaternium-10 (Lot 2)	5	Water	Not reached	None died at 2 g/kg; appeared normal	26
Polyquaternium-10 (Lot 3)	5	Corn oil	>16.0 g/kg	None died at 16.0 g/kg; wet fur and diarrhea at 1 day	27
Polyquaternium-10 (Lot 3)	3	Water	Not reached	None died at 4 g/kg; animals sluggish	27
Polyquaternium-10 1% in shampoo	10	Formulation	>5 g/kg	None died; nontoxic	28
Polyquaternium-10 1% in conditioner	10	Formulation	>5 g/kg	None died; nontoxic	29

Inhalation Toxicity

Inhalation tests of three lots of Polyquaternium-10 were conducted using individual groups of 6 rats and an exposure period of 8 h. The rats were exposed to a substantial aerosol concentration that was prepared by placing 50 g of test material on a 200 cm^2 tray for 16 h before testing in a sealed chamber and during the 8-h exposure period. A fan was operated intermittently to agitate the internal chamber atmosphere. No signs of toxicity were observed during the exposure period.[25]

Dermal Toxicity and Irritation

Three lot samples of Polyquaternium-10 were tested individually using three groups of 5 rabbits each. No deaths occurred when 4.0 g/kg was applied directly to the skin and the application site covered. Erytheme developed, but no other remarkable gross lesions were observed. The three lot samples were considered, at most, slightly toxic.[25-27]

Three lots of Polyquaternium-10 were tested on the clipped uncovered intact skin of the abdomen of 5 rabbits at individual lot concentrations of 2%, 5%,

and 10% (in water). At 2% concentration, no irritation was observed in 4 rabbits, and moderate erythema was seen in 1 rabbit. At 5.0% concentration, no irritation was observed in 3 rabbits, and moderate erythema was seen in 2 rabbits. At 10% concentration, no irritation was observed in 2 rabbits, and moderate erythema was observed in 3 rabbits. The investigator termed the observed irritation a trace reaction.[25-27]

A shampoo containing 0.5% Polyquaternium-10 had a primary irritation index (PII) of 5.37 (max. 8) in a study performed according to CFR Title 16: 1500.3(c)(4) and 1500.41.[30] The test used 12 rabbits, dosed at 0.5 ml of the shampoo, with 6 having intact skin and 6 having abraded skin. The shampoo was a severe skin irritant.[28,31]

The dermal toxicity of a shampoo containing 0.5% Polyquaternium-10 was evaluated according to the procedures in the CFR Title 16:1500.3(c)(1)(ii)(c) and 1500.40.[30] The product was tested on the clipped skin of 5 rabbits and 5 that were both clipped and abraded. The dermal LD_{50} of the formulation was greater than 2 g/kg.[28,31]

A 21-day subchronic dermal toxicity study was conducted with a conditioner containing 1% Polyquaternium-10. Five male and five female rabbits were given 0.5 ml undiluted product once a day for 21 consecutive days. The test material was applied to the clipped dorsal trunk of the rabbits, and the skin of 5 of 10 animals was abraded before application of the test material. The test material remained in contact with the skin 6 h daily, and sites were uncovered. A control group of 5 male and 5 female rabbits had tap water applied to intact and abraded skin. No rabbits died during the test period, both groups had normal weight gains, and no lesions were observed at necropsy. Initial and terminal hematological and urinalysis values were within normal range. The product was not a cumulative dermal toxin.[32]

Six New Zealand rabbits were used to evaluate the primary skin irritation of a conditioner containing 1% Polyquaternium-10. One-half (0.5) milliliter of the test material was administered to 1 intact and 1 abraded test site per animal. The clipped test sites were covered by occlusive patches for 24 h, and test sites were scored for irritation immediately after patch removal and 48 h later. The group PII was 0.0 (max. 8). The product was not a primary skin irritant[29] (Table 3).

Ocular Toxicity

Three lots of Polyquaternium-10 were tested for ocular toxicity, both as a dry powder and as an aqueous solution using groups of 5 animals. No irritation was produced by the powder form of any lot. When applied as the aqueous solution, no irritation was produced by lot 1 at a 20% concentration or by lot 2 at a 5% concentration. A trace of irritation was produced by lot 3 at a 10% concentration.[25-27]

A shampoo containing 0.5% Polyquaternium-10 was tested for ocular irritation in two groups of 12 rabbits according to the procedures given in the CFR Title 16:1500.3(c)(4) and 1500.42.[30] One group received full-strength instillations of the shampoo; a second received instillation of a 5% dilution. The eyes of half of the rabbits of each group were rinsed after product instillation. No irri-

TABLE 3. Dermal Toxicity and Irritation

Compound	*No. of rabbits*	*Vehicle*	*Concentration*	*Method*	*Results*	*Reference*
Polyquaternium-10 (Lot 1)	5	None	4 g/kg	Applied directly to clipped intact skin, occluded for 24 h	No deaths; erythema at 24 h; no remarkable gross pathological results	25
Polyquaternium-10 (Lot 2)	5	None	4 g/kg	Applied directly to clipped intact skin, occluded for 24 h	No deaths; erythema at 24 h; no remarkable gross pathological results	26
Polyquaternium-10 (Lot 3)	5	None	4 g/kg	Applied directly to clipped intact skin, occluded for 24 h	No deaths; erythema at 24 h; no remarkable gross pathological results	27
Polyquaternium-10 (Lot 1)	5	Water	2%	0.01 ml applied to clipped intact bellies for 24 h	No irritation in 4; moderate capillary injection in 1 rabbit	25
Polyquaternium-10 (Lot 2)	5	Water	5%	0.01 ml applied to clipped intact bellies for 24 h	No irritation in 3; moderate capillary injection in 2 rabbits	26
Polyquaternium-10 (Lot 3)	5	Water	10% (suspension)	0.01 ml applied to clipped intact bellies for 24 h	No irritation in 2; moderate capillary injection in 3 rabbits	27
Shampoo containing 1.0% Polyquaternium-10	12	Direct	1.0%	CFR 16:1500.3(C)(4), 1500.41; 6 with intact and 6 with abraded skin	PII 5.37 (max. 8); shampoo was classified as severe irritant	28, 31
Conditioner containing 1.0% Polyquaternium-10	6	Direct	1.0%	0.5 ml applied to each intact and abraded area; occluded for 24 h	PII 0.0 (max. 8); conditioner was not skin irritant	29

tation was observed in the eyes of any animal. The full-strength shampoo was not an eye irritant.[31,33]

The ocular irritation or a conditioner containing 1% Polyquaternium-10 was evaluated in 9 New Zealand rabbits. One-tenth (0.1) milliliter of the test material was instilled into one eye of each rabbit, and the other eye served as an untreated control. The eyes of 3 rabbits were rinsed 15 sec after application of the test solution. No irritation was observed in rinsed or unrinsed eyes 1, 2, 3, 4, and 7 days after application of the product. The conditioner was not an eye irritant.[29] A summary of ocular test data is given in Table 4.

MUTAGENICITY AND GENOTOXICITY

Polyquaternium-10 was tested in triplicate and at five concentrations for mutagenic activity in the *Salmonella typhimurium* assay (Ames test) on TA-98, TA-100, TA-1535, TA-1537, and TA-1538 tester strains without and with metabolic activation. The metabolic activation was induced with S9 liver homogenate from male Sprague-Dawley rats pretreated with Aroclor 1254. In this setting, Polyquaternium-10 was not mutagenic in any of the five bacterial strains tested with and without metabolic activation.[34]

Chinese hamster ovary (CHO) cells were exposed for 5 h to five concentrations of Polyquaternium-10 (0.12–0.285% in DMSO) without and with addition of S9 liver homogenate for metabolic activation (as in the Ames assay). Although some degree of mutagenicity was observed in both of the duplicate assays in the absence as well as in the presence of S9 homogenate, the response was not dose dependent. Polyquaternium-10 was thus considered to be nonmutagenic in the CHO test. In sister chromatid exchange (SCE) assays, Polyquaternium-10 in CHO cells both with and without enzyme induction by S9 liver homogenate did not increase the frequency of SCE over the range of concentrations tested (0.14–0.23%).[34]

Polyquaternium-10 was evaluated also for its genotoxic effect in the rat hepatocyte primary culture/DNA repair test in six concentrations between 0.0009 and 0.23%. The results from duplicate samples indicate significant genotoxicity of this cosmetic ingredient at three of six doses. However, the measured activity, which was not dose dependent, was determined with hepatocytes from a single preparation and quantitated by liquid scintillation counting rather than by the more reproducible quantitative autoradiography.[34] The results of this study do not allow a valid conclusion about the activity of Polyquaternium-10 in hepatocyte DNA repair test.

Polyquaternium-10 was tested for its in vivo clastogenic activity in female Swiss mice by injecting single doses of 0.125, 0.25, and 0.4 g/kg, respectively, into the peritoneal cavity of 5 males and 5 females. Blood samples were collected 24, 48, and 72 h after the injection. Blood smears were prepared and stained for evaluating the possible presence of micronuclei. No statistically significant increases in micronucleated polychromatophilic erythrocytes were reported.[34]

TABLE 4. Ocular Toxicity

Compound	*No. of rabbits*	*Vehicle*	*Concentration*	*Method*	*Results*	*Reference*
Polyquaternium-10 (Lot 1)	5	Powder	Direct	Single instillation into conjunctival sac	No irritation	25
Polyquaternium-10 (Lot 1)	5	Water	2%	0.5 ml single instillation into conjunctival sac	No irritation	25
Polyquaternium-10 (Lot 2)	5	Powder	Direct	0.5 ml single instillation into conjunctival sac	No irritation	26
Polyquaternium-10 (Lot 2)	5	Water	5%	0.5 ml single instillation into conjunctival sac	No irritation	26
Polyquaternium-10 (Lot 3)	5	Powder	Direct	0.5 ml single instillation into conjunctival sac	No irritation	27
Polyquaternium-10 (Lot 3)	5	Water	10% (suspension)	0.5 ml single instillation into conjunctival sac	Trace irritation in 1 eye, none in 4	27
Shampoo containing 0.5% Polyquaternium-10	12	Direct and 5% dilution	1.0 and 0.05%	CFR 16:1500.3(C)(4) and 1500.42; half of test eyes were rinsed	No irritation at either concentration, rinsed or unrinsed	28, 31
Conditioner containing 1.0% Polyquaternium-10	9	Direct	0.1 ml of conditioner	Direct application, 3 eyes rinsed	No irritation, not an eye irritant	29

CLINICAL ASSESSMENT OF SAFETY

Primary Skin Irritation, Sensitization, and Photosensitization

A lot of Polyquaternium-10 was tested for primary skin irritation on 106 subjects. A 5% w/v solution in water was applied to the skin under occlusive patches for 48 h. No skin irritation was observed at 48 and 72 h after application.[35] No irritation was observed when a 5% Polyquaternium-10 solution was applied daily under occlusive conditions for 21 days to 27 subjects.[36]

Three separate lots of Polyquaternium-10 were tested by a repeated insult patch test (RIPT) protocol using 50 subjects. A 2% w/v solution in water was applied to the skin on lintine disks under occlusive patches for 24 h. The treatment reaction sites were scored at 24 h. Following a 24-h nontreatment period, the sites were again exposed to the test samples. A 2-week nontreatment period followed the 15th application. The test sites were evaluated and then treated in a similar manner and scored at 24 and 48 h. No evidence of either irritation or sensitization was observed in any subject when exposed to the three lot samples of Polyquaternium-10.[37-39]

There was no irritation or sensitization when a 5% w/v solution of Polyquaternium-10 was used in an RIPT on 203 subjects.[40]

A shampoo containing 0.5% Polyquaternium-10 was evaluated for primary irritation and sensitization by a prophetic patch test[41] and an RIPT.[42] One hundred subjects participated in the prophetic patch test, and no reactions were observed to either of the two closed patches applied. Fifty-three subjects completed the RIPT, and no reactions were observed during induction or at challenge. Photosensitization also was evaluated in these two studies by exposure of the sites to UV light during the induction phase of the RIPT study and during the challenge phase of the prophetic patch test. The undiluted shampoo was not a primary skin irritant, sensitizer, or photosensitizer.[31,43]

The primary irritation, sensitization, and photosensitization of an undiluted shampoo containing 0.5% Polyquaternium-10 was evaluated in an RIPT according to the procedures of Shelanski and Shelanski[42] using a 25-member panel. The UV light was applied during the induction phase of the study. The shampoo was tested at full strength. The product was nonirritating, nonsensitizing, and nonphotosensitizing.[44]

Forty-six panelists participated in an RIPT of a conditioning product containing 1% Polyquaternium-10. Patches containing 0.2 ml undiluted conditioner were applied to the inner arm or back of each subject on Mondays, Wednesdays, and Fridays for a total of 10 induction patches. After a 10–20 day nontreatment period, two challenge patches were applied simultaneously, one to the original test site and the other to an untreated site. One panelist had minimal erythema (score of ± on a 0–4 scale) to induction patch 9, and another panelist had a ± reaction to induction patch 10. Two panelists reacted at challenge; 1 had ± reactions at the 24-h reading of both challenge patches, and another had scores of 1 and 2, and 2 and 2 at the 24-h and 48-h readings of the original site patch and untreated site patch, respectively. After rechallenge, the same panelist had no reactions. The conditioner was not an irritant or sensitizer.[45]

A controlled use study following CTFA guidelines[46] was performed using a shampoo containing 0.5% Polyquaternium-10. Eighty-three subjects participated

in the 4-week study, which required daily product use. The scalp, neck, face, and hair of each subject were examined for irritation. The shampoo was nonirritating under the conditions of this test.[31,47] Results are summarized in Table 5.

Moderation of Skin Irritants

An extensive study was undertaken to determine the capacity of Polyquaternium-10 to moderate reactions to skin irritants. The first phase of the study ex-

TABLE 5. Clinical Assessment of Safety

Test type[a]	*No. of subjects*	*Product type*	*Polyquaternium-10 concentration (%)*	*Comments*	*Reference*
RIPT	50	Polyquaternium-10 (Lot 1)	2	No reactions; not an irritant or sensitizer	37
RIPT	50	Polyquaternium-10 (Lot 2)	2	No reactions; not an irritant or sensitizer	38
RIPT	50	Polyquaternium-10 (Lot 3)	2	No reactions; not an irritant or sensitizer	39
Prophetic patch test	100	Shampoo	0.5	No reactions; not an irritant, sensitizer, or photosensitizer	43
RIPT	53	Shampoo	0.5	No reactions; not an irritant, sensitizer, or photosensitizer	43
RIPT	25	Shampoo	0.5	No reactions; not an irritant, sensitizer, or photosensitizer	44
RIPT	46	Conditioner	1	Two minimal reactions during induction, one minimal and one moderate reaction at challenge; rechallenge to moderate reactor was negative; not an irritant or sensitizer	45
Controlled use	83	Shampoo	0.5	No reactions; not an irritant	31, 47

[a]See text for details of experimental procedure.

amined the cutaneous toxicity and effects on wound healing of Polyquaternium-10. The Polyquaternium-10 used in this study had a molecular weight of approximately 400,000. Six subjects were given single 0.1 ml intradermal injections of 0.25% and 1.0% aqueous Polyquaternium-10 into the back. The injection sites were observed daily for 1 week, and no reactions were observed at the 0.25% Polyquaternium-10 sites. The 1.0% injections produced small (5 mm) inflamed nodules within 24 h. The nodules disappeared without residue within a few days.

The effect of Polyquaternium-10 on wound healing was studied by applying 1% or 2% Polyquaternium-10 to raw blisters produced by 15% ammonia solutions. A single application or five daily applications enhanced wound healing if the 2% Polyquaternium-10 was allowed to dry before the site was bandaged. If the test site was bandaged before the polymer dried, healing was slower than untreated control sites. These studies suggest that Polyquaternium-10 protected the wound surface and promoted reepithelialization.

The second phase of this study evaluated moderation by Polyquaternium-10 of inflammatory reactions to sodium lauryl sulfoacetate, shampoos, a depilatory cream, *Rhus* (poison ivy) dermatitis, and soap. In all cases, pretreatment and/or concurrent treatment of the test site with Polyquaternium-10 resulted in less severe reactions to the irritants[48] (Table 6).

SUMMARY

Polyquaternium-10, a white granular powder, is a polymeric quaternary ammonium derivative of hydroxyethyl cellulose with cationic surface-active properties. The product for cosmetic use varies in molecular weight from 250,000 to 600,000. Polyquaternium-10 is soluble in water and insoluble in alcohol and nonpolar organic solvents. Results of studies in rats indicated that Polyquaternium-10 has, at most, only a low potential to penetrate the stratum corneum. it is adsorbed by keratinous surfaces. The ingredient is used in cosmetics as a conditioner, thickener, and emollient in hair care products, lotions, and makeup products at reported ranges of concentration of $\leq$0.1%–5%.

Polyquaternium-10 with and without metabolic activation was assayed for mutagenicity in 5 *S. typhimurium* tester strains, in Chinese hamster ovarian cells, for in vitro sister chromatid exchange in CHO cells, and for clastogenic activity in female Swiss mice. Polyquaternium-10 was negative for mutagenicity in these four short-term tests. In the rat hepatocyte primary culture/DNA repair test, genotoxicity was present but was not dose related.

Polyquaternium-10 permeates and adsorbs into isolated stratum corneum obtained from fetal pigs, neonatal rats, and humans. LD_{50}s for lots of Polyquaternium-10 in corn oil were not obtained at 16 g/kg in two lots or 13.1 g/kg in a third lot. Signs of toxicity were not observed when rats were exposed for 8 h to a vapor containing Polyquaternium-10. Acute dermal exposure of rats to undiluted Polyquaternium-10 produced erythema only. In other skin irritation studies using rabbits, 2%, 5%, and 10% concentrations of Polyquaternium-10 produced only slight irritation. Polyquaternium-10 was not an irritant when tested for ocular irritation in powder form and aqueous solutions at concentrations up to 10%.

TABLE 6. Moderation of Irritant Reactions by Polyquaternium-10[48]

Irritant[a]	*No. of subjects*	*Group average without Polyquaternium-10 (0–4 scale)*	*Group average with 2% Polyquaternium-10 (0–4 scale)*
5% sodium lauryl sulfate (pre-treated with polymer)	10	3.6	1.1
5% sodium lauryl sulfate	10	3.6	1.4
Shampoo	5	2.6[b]	1.4[b]
Shampoo	5	3.0[b]	1.6[b]
Depilatory cream	6	2.0	0.8
Rhus (poison ivy) (pretreated with polymer)	5	3.6	1.4
Rhus	5	3.8	1.2[c]
Soap	5	3.4	1.8[d]

[a]Concurrent treatment with polymer unless otherwise noted.
[b]1–3 scale.
[c]1% Polyquaternium-10.
[d]2.5% Polyquaternium-10.

Products containing up to 1% Polyquaternium-10 were practically nontoxic to rats when given by acute oral and dermal routes. These products were not skin or eye irritants, except for one shampoo that was a primary skin irritant in rabbits. Polyquaternium-10 was neither an irritant nor a sensitizer for humans when it was tested using a 50-member panel and at 2.0% in a repeat insult patch test.

Products containing up to 1% Polyquaternium-10 were nontoxic in clinical studies. Conditioners and shampoos containing Polyquaternium-10 were not irritants, sensitizers or photosensitizers in a prophetic patch test, repeat insult patch tests, and a controlled use study. Polyquaternium-10 at 1% concentration was minimally irritating when administered as a single intradermal injection. The polymer enhanced wound healing of minor skin lesions. Pretreatment and concurrent treatment with 1–2% Polyquaternium-10 reduced inflammatory and/or dermatitic reactions to known irritants, such as sodium lauryl sulfate and *Rhus* (poison ivy).

DISCUSSION

Acute toxicity studies indicate that Polyquaternium-10 has a low order of toxicity. Subchronic studies were not available; however, skin penetration studies indicate that Polyquaternium-10 adsorbs on keratin tissue and is poorly absorbed.

Animal studies using up to 5.0% Polyquaternium-10 indicate that this cosmetic ingredient is at most only mildly irritating to skin or eye. The severe skin irritation reported in one study, but not all studies, was most likely due to the shampoo ingredients and not the Polyquaternium-10. Studies of the ingredient at 2.0%, using human subjects, indicate that this ingredient was neither an irritant nor a sensitizer. Similar negative results were obtained from product formulations at 0.5%, including data that indicate the ingredient is not a photosensitizer.

CONCLUSION

On the basis of the information presented in this report, the CIR Expert Panel concludes that Polyquaternium-10 is safe as a cosmetic ingredient in the present practices of use.

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8

Final Report on the Safety Assessment of Polyquaternium-11

Polyquaternium-11 is a quaternized copolymer of vinylpyrrolidone and dimethylamine ethylmethacrylate, and is used at concentrations up to 50% in a variety of hair care preparations.

The acute oral LD50 in test animals of high molecular weight Polyquaternium-11 is estimated to be greater than 12.8 g/kg; the LD50 for the low molecular weight polymer is calculated to be 6.2 g/kg. At concentrations of up to 50% in water, the raw ingredient produced no signs of skin or eye irritation. There was no evidence of dermal toxicity in subchronic tests nor in a maximization test for sensitization. In clinical studies, 1 of 19 subjects showed slight skin irritation after a 24-hour single insult skin patch with 9.5% Polyquaternium-11 in water. Repeated insult patch tests at concentrations up to 50% produced no instances of skin sensitization and only isolated instances of transient skin irritation. Clinical photoreactivity studies on both low and high molecular weight polymers showed no evidence of phototoxicity or photoallergenicity.

From the available information, it is concluded that Polyquaternium-11 is safe as a cosmetic ingredient in the present practices of use.

INTRODUCTION

Whereas Polyquaternium-11 is the singular ingredient under review in this report, two distinct forms of the material are available in industry: a low molecular weight form dissolved in alcohol (50 ± 2%) and a high molecular weight form dissolved in water (19% minimum). The undiluted polymer per se is not available for incorporation into cosmetic products, although the potential exists for evaporation of the vehicle prior to formulation. An attempt is made here to distinguish between the pure Polyquaternium-11 polymer and the diluted products found in the industry by referring to the latter as "commercial Polyquaternium-11." Since all available safety data pertain to the material that is supplied by the manufacturer (commercial Polyquaternium-11), calculations of concentrations and doses back to the pure Polyquaternium-11 polymer are made where appropriate to aid in the assessment of safety.

CHEMISTRY

Structure

Polyquaternium-11 is a copolymer of vinylpyrrolidone and dimethylamine ethylmethacrylate, partially quaternized with diethyl sulfate. The general reaction sequence is as follows:[1,2]

Properties

Polyquaternium-11 is supplied by the manufacturer as either a low molecular weight polymer in alcohol (50 ± 2% solids) or a high molecular weight polymer in water (minimum 19% solids).[3] Chemical and physical properties of the two commercial forms of Polyquaternium-11 are listed in Table 1. These values are typical of the commercial products, but they are not specifications.

Reactivity

No information was available on the chemical reactivity of Polyquaternium-11.

Analytical Methods

Methods for the determinations of viscosity, residual vinylpyrrolidone content, and nonvolatile solids content have been described.[1] Infrared[3] and ultraviolet[4] spectra are available for both the low and high molecular weight products.

Impurities

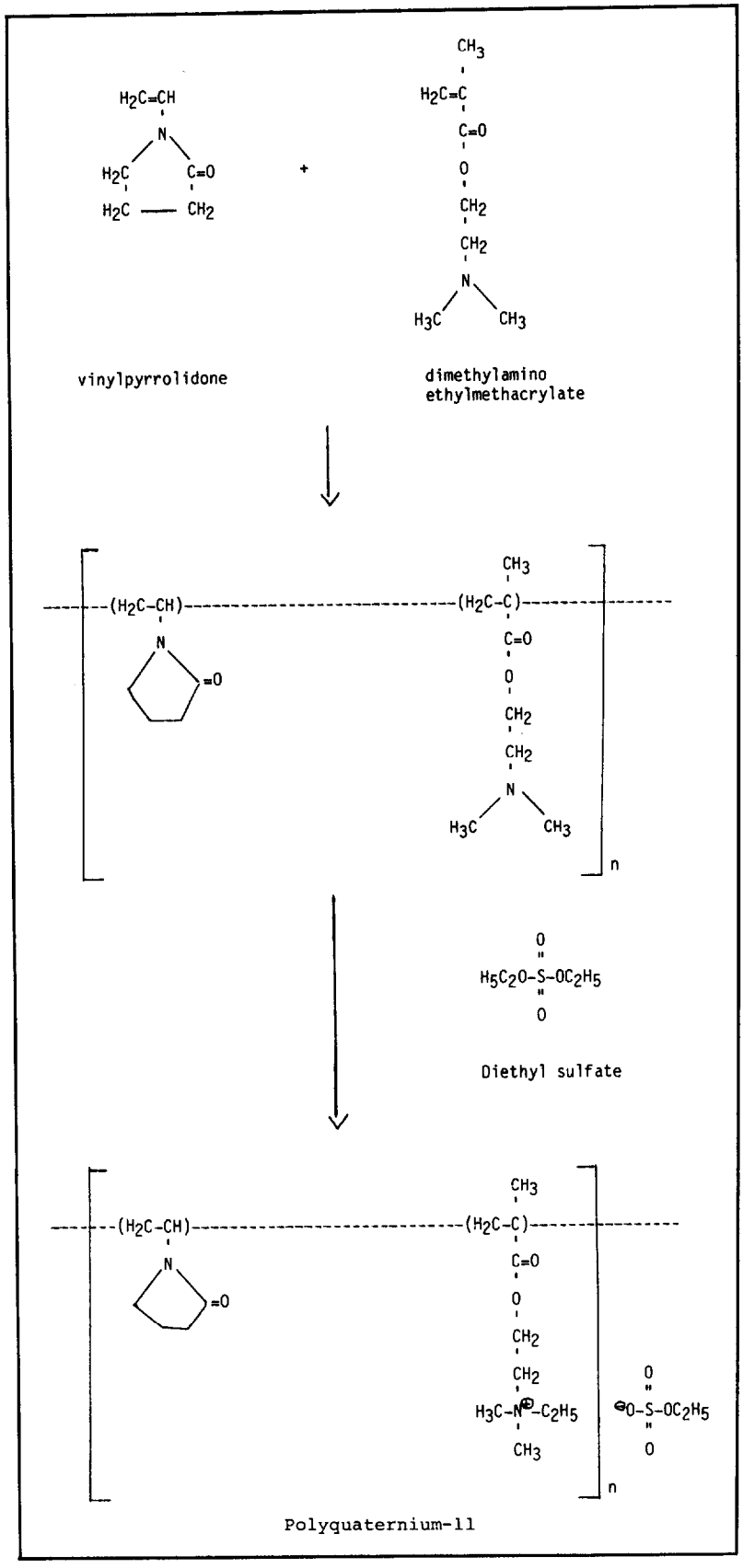
The low molecular weight and high molecular weight forms of Polyquaternium-11 are supplied in solution with ethanol (denatured with tertiary butyl alcohol and brucine, brucine sulfate, or quassin) and water, respectively. There are no known additives.[1,3] No information was available on the possible presence of nitrosamines.

Industry specifications for Polyquaternium-11 allow residual vinylpyrrolidone to a maximum concentration of 1.0%.[1,3] Free vinylpyrrolidone is a chemically

TABLE 1. Properties of Commercial Polyquaternium-11.[a]

	Low molecular weight polymer	*High molecular weight polymer*
Average molecular weight	<100,000	>1,000,000
Physical form (25°C)	Hazy, viscous liquid	Hazy, viscous liquid
Color	Light to dark straw	Light to dark straw
Vehicle	Alcohol	Water
Solids content	50 ± 2%	19% minimum
Relative viscosity (Ostwald-Fenske capillary viscometer)	2.5-3.5 (1% in anhydrous SD-40)	1.5-2.0 (0.1% in anhydrous SD-40)

[a]Data from Ref. 3.


vinylpyrrolidone
dimethylamino ethylmethacrylate
Diethyl sulfate
Polyquaternium-11

163

highly reactive species; however, the residual monomer is unlikely to be present at significant concentrations in product formulations.

Polyquaternium-11 does not contain as an impurity diethylsulfate, an alkylating agent and a direct-acting carcinogen in rats; diethylsulfate is hydrolyzed quickly in air.[5] Upon quaternization of the copolymer, the nonalkylating agent monoethylsulfate is formed.

USE

Purpose in Cosmetics

The principal use of Polyquaternium-11 in cosmetic products is in hair care preparations. It is a film-forming resin that is absorbed onto the hair shaft. The benefits claimed with application to the hair include improvements in holding and curl retention at high humidities, hair strength and weight, manageability, luster, smoothness, lubricity, and moisture retention.[3]

Scope and Extent of Use in Cosmetics

Table 2 lists the product types and the number of product formulations containing Polyquaternium-11 as reported by the Food and Drug Administration (FDA) in 1976. Although an analysis by type of product at each concentration level was not available for the more recent 1979 FDA data, the 1979 totals for all product categories are also listed in Table 2 for comparison to the 1976 total figures.

The cosmetic product formulation computer printout which is made available by the FDA is compiled through voluntary filing of such data in accordance with Title 21 Part 720.4 of the Code of Federal Regulations.[8] Ingredients are listed in prescribed concentration ranges under specific product type categories. Since certain cosmetic ingredients are supplied by the manufacturer at less than 100% concentration, the value reported by the cosmetic formulator may not necessarily reflect the true concentration found in the finished product; the actual concentration in such a case would be a fraction of that reported to the FDA. The fact that data are only submitted within the framework of preset concentration ranges also provides the opportunity for overestimation of the actual concentration of an ingredient in a particular product. An entry at the lowest end of a concentration range is considered the same as one entered at the highest end of that range, thus introducing the possibility of a two- to tenfold error in the assumed ingredient concentration.

In 1976, Polyquaternium-11 was listed in a variety of hair care preparations at concentrations up to 50%; it found only minimal use in other product categories. It is possible that some or all of the concentrations reported to the FDA by cosmetic formulators were those for the material that was supplied by the ingredient manufacturer. Since Polyquaternium-11 is supplied as a solute in an alcohol (50 ± 2% solids) or water (minimum 19% solids) vehicle, the concentrations of the polymer in cosmetic formulations may be from 19% to 50% of those shown in Table 2.

TABLE 2. Product Formulation Data.[a]

Product category[b]	Total no. containing ingredient	No. product formulations within each concentration range (%)[b]							
		Unreported concentration	>50	>25–50	>10–25	>5–10	>1–5	>0.1–1	≤0.1
Polyquaternium-11									
Hair conditioners	31	–	–		2	22	4	1	2
Hair sprays (aerosol fixatives)	2	–	–	–		–	2	–	–
Permanent waves	4	–	–	–		3	1	–	–
Hair rinses (noncoloring)	3	–	–	–		–	3	–	–
Hair shampoos (noncoloring)	5	–	–	–		–	–	5	–
Tonics, dressings, and other hair grooming aids	6	–	–	–		–	6	–	–
Wave sets	13	–	–	1	2	1	8	1	–
Other hair preparations (noncoloring)	9	–	–	–	2	–	5	1	1
Hair dyes and colors (all types requiring caution statement and patch test)	6	–	–	–	–	–	–	6	–
Hair rinses (coloring)	4	–	–	–	–	–	–	4	–
Hair bleaches	1	–	–	–	–	–	–	1	–
Shaving cream (aerosol, brushless, and lather)	4	–	–	–	–	–	–	4	–
Paste masks (mud packs)	1	–	–	–	1	–	–	–	–
1976 TOTALS	89	–	–	1	7	26	29	23	3
1979 TOTALS[c]	114	69	–	1	4	3	18	14	5

[a]Data from Ref. 6.

[b]Preset product categories and concentration ranges in accordance with federal filing regulations (21 CFR 720.4); see Scope and Extent of Use in Cosmetics.

[c]Data from Ref. 7.

Potential Interactions with Other Ingredients

Chemical interactions of Polyquaternium-11 with the other ingredients in cosmetic formulations have not been reported.

Vehicles Commonly Used

Denatured ethanol and water are the principal vehicles of low and high molecular weight Polyquaternium-11, respectively.[3]

Surfaces to Which Commonly Applied

Products containing Polyquaternium-11 are applied primarily to the hair. The ingredient finds limited use in products that are applied to the facial skin (Table 2).

Frequency and Duration of Application

The product formulation data[6] presented in Table 2 show that Polyquaternium-11 is contained in product formulations that are likely to be used no more than once a day. The resin films left by these products will remain in contact with the hair and scalp or facial skin for indefinite periods of time following each application. Daily or occasional use may extend over many years.

BIOLOGICAL PROPERTIES

General Effects

Antimicrobial[9,10] and antiheparin[11] activities have been attributed to quaternary ammonium polymers and their salts.

Although no information was available on the absorption, metabolism, storage, excretion, or any other general biological property of Polyquaternium-11, such polymers are generally considered to be biologically inert.

Animal Toxicology

Acute Studies

Oral Toxicity

Samples of low and high molecular weight Polyquaternium-11 in water, as well as six cosmetic formulations containing the ingredient, were evaluated for acute oral toxicity (Table 3). In each study, young adult albino rats or mice were fasted for 24 hours and administered a single dose of the test material by gastric intubation. They were then allowed free access to food and water for two weeks. The results and other details of these studies are summarized in Table 3. From these data, the acute oral LD50 of high molecular weight Polyquaternium-11 is greater than 12.8 g/kg; the LD50 for low molecular weight Polyquaternium-11 is calculated to be 6.2 g/kg.

Primary Skin Irritation

The potentials for primary skin irritation caused by samples of low and high molecular weight Polyquaternium-11 in water[20,21] and by five product formulations containing 0.19%–1.0% Polyquaternium-11 solids[22-26] were evaluated using the Draize rabbit skin patch test technique. In each study, the test material was applied and occluded for 24 hours, after which time the patch sites were graded for erythema and edema on the Draize scale. The results and other details of these studies are summarized in Table 4. The unformulated samples of Polyquaternium-11 in water, as well as the product formulations containing the ingredient, produced no signs of skin irritation.

Eye Irritation

The Draize rabbit eye irritation procedure or a modification of the test was used to evaluate samples of low and high molecular weight Polyquaternium-11[27,28] and six product formulations containing 0.19%–2.0% Polyquaternium-11 solids.[14,29-33] In each study, a 0.1 ml sample of the test material was instilled into one eye of each rabbit with no subsequent washing; the untreated eye served as a control. Treated eyes were examined and graded on the Draize eye irritation scale at 1, 2, 3, 4, and 7 days. The results and other details of these studies are summarized in Table 5. The unformulated samples of Polyquaternium-11 in water produced no signs of ocular irritation; product formulations containing the ingredient produced no more than mild, transient, conjunctival irritation.

Subchronic Studies

Dermal Toxicity

A commercial sample of high molecular weight Polyquaternium-11 (approximately 19% in water) was tested for cutaneous toxicity in a 28-day study. The sample was administered as a 25% (w/v) solution in water for an effective concentration of 4.75% Polyquaternium-11 solids. Doses of 2.0 ml/kg of the solution or approximately 0.10 g/kg of polymer were applied to the shaved backs of ten albino rabbits, five days a week, for a total of 20 applications. The skin of four animals received epidermal abrasions prior to the first treatment. A group of ten untreated animals served as a control. None of the animals died, and there were no untoward behavioral or systemic reactions. Hematologic studies, clinical blood chemistries, and urinalyses revealed no significant adverse reactions. No significant pathologic alterations were noted on gross and microscopic observations other than in the skin at the site of contact. The test material was slightly to mildly irritating to the skin with gross skin changes characterized by barely perceptible to pale red erythema and slight edema. Microscopic changes were characterized by acanthosis, hyperkeratosis, and parakeratosis.[34]

Skin Sensitization

The Magnusson-Kligman[35] guinea pig maximization procedure was used to evaluate the potential for skin sensitization to a low molecular weight commercial sample of Polyquaternium-11 (50% in alcohol). During the induction phase

TABLE 3. Acute Oral Toxicity.

Material tested[a]	*Conc. of Polyquaternium-11 (%)*	*Dose*	*Dose of Polyquaternium-11 (adjusted for dilution)*	*Animals*	*LD50*	*Comments*	*Ref.*
Polyquaternium-11, low molecular weight polymer	25 in water	16.0–40.0 g/kg	1.0–2.5 g/kg	5 rats at each of 5 dose levels	6.2 g/kg	Alcohol vehicle evaporated and solids redissolved in water	12
Polyquaternium-11, high molecular weight polymer	19 in water	25.1–64.0 ml/kg	4.8–12.2 ml/kg	5 rats at each of 5 dose levels	>12.2 ml/kg (>12.8 g/kg)	No deaths	13
Setting lotion, 10% high molecular weight commercial Polyquaternium-11	2.0 in product formulation	15.0 g/kg	0.3 g/kg	5 rats		LD50 not reached with dose administered	14
Hair conditioner, 2.0% low molecular weight commercial Polyquaternium-11	1.0 in product formulation	1.0–16.0 g/kg	0.01–0.16 g/kg	5 rats at each of 5 dose levels		No deaths; no signs of toxicity	15

Hair conditioner, 2.0% high molecular weight commercial Polyquaternium-11	0.38 in product formulation	1.0–16.0 g/kg	0.0038–0.061 g/kg	5 rats at each of 5 dose levels	No deaths; no untoward signs at product dosage levels up to 8.0 g/kg; at 16.0 g/kg the animals were lethargic and had diarrhea	16
Hair conditioner, 1.5% high molecular weight commercial Polyquaternium-11	0.3 in product formulation	15 g/kg	0.045 g/kg	5 rats	No deaths; no signs of toxicity	17
Shampoo, 1.0% high molecular weight commercial Polyquaternium-11	0.19 in product formulation	15 ml/kg	0.028 ml/kg	10 mice	No deaths	18
Setting lotion, 0.6% low molecular weight commercial Polyquaternium-11	0.3 in product formulation	5.0 g/kg	0.015 g/kg	10 rats	No deaths; no signs of toxicity	19

[a]Low molecular weight polymer supplied as 50% solution in alcohol; high molecular weight polymer supplied as 19%–20% solution in water. Molecular weight of polymer tested inferred from the reported concentration and vehicle of the material supplied.

TABLE 4. Primary Skin Irritation.

Material tested[a]	*Conc. of Polyquaternium-11 (%)*	*No. of rabbits*	*Primary irritation index (max = 8.0)*	*Comments*	*Ref.*
Polyquaternium-11, low molecular weight polymer	50 in water	6	0.0	Alcohol vehicle evaporated and solids redissolved in water No signs of irritation	20
Polyquaternium-11, high molecular weight polymer	19 in water	6	0.0	No signs of irritation	21
Hair conditioner, 2.0% low molecular weight commercial Polyquaternium-11	1.0 in product formulation	6	0.0	No signs of irritation	22
Hair conditioner, 2.0% high molecular weight commercial Polyquaternium-11	0.38 in product formulation	6	0.0	No signs of irritation	23
Hair conditioner, 1.5% high molecular weight commercial Polyquaternium-11	0.3 in product formulation	9	0.0	No signs of irritation	25
Setting lotion, 0.6% low molecular weight commercial Polyquaternium-11	0.3 in product formulation	6	0.0	No signs of irritation	24
Shampoo, 1.0% high molecular weight commercial Polyquaternium-11	0.05 in diluted product formulation	3	0.0	No signs of irritation; product diluted 1:3 prior to patching	26

[a]Low molecular weight polymer supplied as 50% solution in alcohol; high molecular weight polymer supplied as 19%–20% solution in water. Molecular weight of polymer tested inferred from the reported concentration and vehicle of the material supplied.

of the test, ten female albino guinea pigs each received the following paired 0.05 ml intradermal injections in the shaven skin of the back: (1) 50% aqueous Freund's Adjuvant; (2) 5% commercial Polyquaternium-11 in 50% aqueous Freund's Adjuvant; and (3) 5% commercial Polyquaternium-11 in propylene glycol. One week after the induction injections, a topical "booster" was administered as a 48-hour occlusive patch over the initial injection site with 0.5 ml of 25% commercial Polyquaternium-11 in petrolatum. Two weeks after the topical

TABLE 5. Acute Eye Irritation.

Material tested[a]	*Conc. of Polyquaternium-11 (%)*	*No. of rabbits*	*Results*	*Ref.*
Polyquaternium-11, low molecular weight polymer	50 in water	6	Alcohol vehicle evaporated and solids redissolved in water No signs of irritation	27
Polyquaternium-11, high molecular weight polymer	19 in water	6	No signs of irritation	28
Setting lotion, 10% high molecular weight commercial Polyquaternium-11	2.0 in product formulation	3	Transient conjunctival irritation on day 1; all eyes normal by day 2	14
Hair conditioner, 2.0% low molecular weight commercial Polyquaternium-11	1.0 in product formulation	6	Transient conjunctival irritation in all animals at 1 hour; all eyes normal by 24 hours	29
Hair conditioner, 2.0% high molecular weight commercial Polyquaternium-11	0.38 in product formulation	6	Transient conjunctival irritation in all animals at 1 hour; mostly clear by 24 hours; all eyes normal by 48 hours	30
Hair conditioner, 1.5% high molecular weight commercial Polyquaternium-11	0.3 in product formulation	6	No signs of irritation	32
Setting lotion, 0.6% low molecular weight commercial Polyquaternium-11	0.3 in product formulation	6	No signs of irritation	31
Shampoo, 1.0% high molecular weight commercial Polyquaternium-11	0.05 in diluted product formulation	3	No signs of irritation; product diluted 1:3 prior to instillation	33

[a]Low molecular weight polymer supplied as 50% solution in alcohol; high molecular weight polymer supplied as 19%–20% solution in water. Molecular weight of polymer tested inferred from the reported concentration and vehicle of the material supplied.

booster, all animals were challenged at a previously untreated site with 0.5 ml of 5% commercial Polyquaternium-11 in petrolatum under an occlusive patch for 24 hours. The challenged sites were graded for erythema at 24 and 48 hours after patch removal. A similar test procedure was conducted with one vehicle-treated negative control group and one phenylacetaldehyde-treated positive control group. Phenylacetaldehyde produced an expected strong allergic reaction; Polyquaternium-11 and negative control groups showed no evidence of allergic skin sensitization.[36]

Polyquaternium-11 was evaluated for skin sensitization in another test on albino guinea pigs. A 0.5 ml dose of the high molecular weight polymer at 19% in water was applied under an occlusive patch and left in contact with the skin for six hours. The insult was repeated once a week for three weeks. Two weeks after the last induction exposure, the animals were challenged with an occlusive patch at a virgin site. The investigator concluded that the material was not a sensitizer in this test; experimental data were not available for review.[37]

Inhalation

A 13-week inhalation toxicity study was performed on an aerosol of a hair conditioner containing 1.5% commercial Polyquaternium-11 (approximately 20% high molecular weight polymer in water). Groups of 12 hamsters and 12 rats were exposed in a dynamic chamber 4 hours per day, 5 days per week, to a mean product concentration of 9.9 mg/m^3; the effective final concentration of Polyquaternium-11 solids was approximately 0.03 mg/m^3. There were neither deaths nor adverse local or systemic effects in either species. Gross and microscopic observations revealed nothing in the lungs or other tissues examined that distinguished exposed from control animals.[38]

Special Studies

Unreacted vinylpyrrolidone monomer, which is allowed by industry specifications as an impurity in Polyquaternium-11 at concentrations up to 1.0%, was found to be nonmutagenic in three different assays. In the mouse lymphoma forward mutation assay, concentrations up to 5.0 μl/ml did not induce a significant change in mutation frequency at the TK locus of L5178Y cells in the absence or presence of rat liver S-9 microsomal activation.[39] In the Balb/3T3 in vitro transformation assay, vinylpyrrolidone induced no significant increase in transformed foci over the applied concentration range of 0.5–0.1 μl/ml. This concentration range produced 52.3%–83% survival in the cytotoxicy test. The test material was considered to be mutagenically inactive.[40] In the primary rat hepatocyte unscheduled DNA synthesis assay, vinylpyrrolidone induced no detectable activity over an applied concentration range of 9.09–0.284 μl/ml. This concentration range produced a cell survival rate from 6.2% to 84.5% at 24 hours after treatment, whereas exposure to 18.2 μl/ml was completely lethal. The material was considered to be inactive as a genotoxic agent in this assay system.[41]

Data were not available on mutagenicity, carcinogenicity, or teratogenicity for the low or high molecular weight forms of Polyquaternium-11.

Clinical Assessment of Safety

Primary Skin Irritation

A 24-hour occlusive patch test procedure was used to evaluate the primary skin irritation caused by an aqueous solution of Polyquaternium-11[42] and by two product formulations containing Polyquaternium-11.[14,43] The results and other details of these studies are summarized in Table 6. Polyquaternium-11 at 9.5% in water produced only a slight degree of irritation in 1 of 19 subjects. A product formulation containing high molecular weight Polyquaternium-11 at

TABLE 6. Clinical Studies on Polyquaternium-11.

Test	*Material tested*[a]	*Conc. of Polyquaternium-11 (%)*	*Method*	*No. of subjects*	*Comments*	*Ref.*
Primary skin irritation	Polyquaternium-11, high molecular weight polymer	9.5 in 50% aqueous dilution of commercial raw ingredient	24-hour occlusive patch	19	One subject showed slight irritation (score = 1.0 out of 4.0 max.); all others exhibited no signs of irritation	42
	Setting lotion, 10% high molecular weight commercial Polyquaternium-11	2.0 in product formulation	24-hour occlusive patch	100	"Negative"	14
	Hair conditioner, 1.5% high molecular weight commercial Polyquaternium-11	0.3 in product formulation	24-hour occlusive patch	29	All subjects showed barely perceptible to mild irritation; PII = 0.52/4.0	43

TABLE 6. (Continued.)

Test	Material tested[a]	Conc. of Polyquaternium-11 (%)	Method	No. of subjects	Comments	Ref.
Skin sensitization	Polyquaternium-11, low molecular weight polymer	50 in alcohol	Draize–Shelanski Repeated Insult Patch Test; semiocclusive	150	Isolated, transient occurrences of skin irritation during induction phase (3 of 1421 patches); no skin sensitization	46
	Polyquaternium-11, high molecular weight polymer	19 in water	Draize–Shelanski Repeated Insult Patch Test; semiocclusive	150	Isolated, transient occurrences of skin irritation during induction phase (4 of 1421 patches); no skin sensitization	46
	Polyquaternium-11, high molecular weight polymer	9.5 in 50% aqueous dilution of commercial raw ingredient	Draize–Shelanski Repeated Insult Patch Test; occlusive	201	"Essentially nonirritating" during induction phase; no skin sensitization	47
	Hair conditioner, 5% high molecular weight commercial Polyquaternium-11	0.5 in 50% aqueous dilution of product formulation	Draize–Shelanski Repeated Insult Patch Test; occlusive	99	Mild primary irritation during induction phase; no evidence of skin sensitization at challenge with 25% aqueous dilution	48
Clinical use test	Hair condition, 5% high molecular weight commercial Polyquaternium-11	1.0 in product formulation	3 weeks normal use with additional 3-week use of control product	54	Skin and scalp effects comparable to those of control product; subjective irritation reported by 5 subjects; no empirical data available	49

[a]Low molecular weight polymer supplied as 50% in alcohol; high molecular polymer supplied as 19%–20% solution in water. Molecular weight of polymer tested inferred from the reported concentration and vehicle of the material supplied.

2.0% produced no irritation in 100 subjects; another formulation containing 0.3% high molecular weight Polyquaternium-11 produced up to mild skin irritation in 29 subjects.

Skin Sensitization

The Draize–Shelanski Repeated Insult Patch Test[44,45] or a modification of the test was used to evaluate Polyquaternium-11 at concentrations of 9.5% (201 subjects) and 19% (150 subjects) in water[46,47] and 50% (150 subjects) in alcohol.[46] The induction phase of the procedure consisted of a series of nine 24-hour occlusive or semiocclusive patch applications to the same site over a period of three consecutive weeks. A single challenge patch was applied to the original contact site and/or a virgin site after a 10- to 14-day rest period. The results and other details of these studies are summarized in Table 6. Polyquaternium-11 at concentrations of 9.5%–50% produced only minimal skin irritation during the induction phase of the procedure; there were no instances of skin sensitization.

A 50% aqueous dilution of a hair conditioner containing 1.0% Polyquaternium-11 was also evaluated in a modified Draize-Shelanski Repeated Insult Patch Test on 99 subjects. The results and other details of this study are summarized in Table 6. The product produced mild primary skin irritation but no skin sensitization.[48]

Photoreactivity

The ultraviolet spectra of the different forms of Polyquaternium-11 are available.[4] The low and high molecular weight forms dissolved in methanol at concentrations of 74 mg/l and 181 mg/l, respectively, produced no indication of significant ultraviolet absorption. At 50% in methanol, the low molecular weight polymer showed no significant absorption, while the high molecular weight polymer showed a questionably significant peak at 284 nm. The FDA product formulation data include only one formulation in the >25%–50% concentration range (see Table 2).

Clinical photoreactivity studies on commercial samples of both low (50 ± 2% solids in alcohol) and high (19% solids in water) molecular weight Polyquaternium-11 have been conducted.[50,51] Each of the test materials was applied to the inner aspect of the forearms of 31 women ranging in age from 20 to 63. One forearm was designated as the irradiated site and the other as the control (nonirradiated) site. Approximately 0.2 ml of the test material was applied to a Webril occlusive patch; patches were applied to the contact sites and allowed to remain in place for 24 hours. Patches were removed, and test sites were exposed to 15 minutes of nonerythrogenic ultraviolet radiation for a total UV-A light dosage of 4400 $\mu W/cm^2$. The ultraviolet light source consisted of four GE F450 BL blacklight fluorescent tubes held at a distance of 10 cm; this light source had a wavelength of 320–400 nm. (There was no filter employed.) This procedure of patching followed by irradiation was repeated Monday, Wednesday, and Thursday until ten exposure were completed. After a 10- to 13-day rest period, patches and irradiation were again performed on virgin, adjacent sites. The results of these studies indicated that the low and high molecular weight forms of

Polyquaternium-11 were neither phototoxic nor photoallergenic in the assays employed.

Clinical Use

A hair conditioner containing 1.0% Polyquaternium-11 was used together with a test shampoo by a panel of 54 subjects for a three-week period. Dermatologic exams and subjective evaluations of irritation and gentleness were compared to those made during a three-week period of control shampoo and conditioner use. The results and other details of this study are summarized in Table 6. The test shampoo and conditioner effects did not differ from the control products in any significant way.[49]

SUMMARY

Polyquaternium-11 is a quaternized copolymer of vinylpyrrolidone and dimethylamine ethylmethacrylate. It is reported by the FDA to be used at concentrations up to 50% in a variety of hair care preparations; it finds very limited use in other product categories. Since Polyquaternium-11 is supplied solely in the form of a solution at concentrations up to 50% in alcohol (low molecular weight polymer) or 19% in water (high molecular weight polymer), the actual concentrations of the polymer in cosmetic formulations may be less than those reported by the FDA.

Three different assay systems showed the vinylpyrrolidone monomer to be nonmutagenic; there is some indication that unreacted vinylpyrrolidone may be present as an impurity, but the residual monomer is unlikely to be present at significant concentrations in product formulations. It is recognized that the vinylpyrrolidone monomer is a chemically reactive species, and the safety evaluation of Polyquaternium-11 is with the understanding that the monomer is present only in biologically insignificant amounts.

In rats, the acute oral LD50 of high molecular weight Polyquaternium-11 is estimated to be greater than 12.8 g/kg; the LD50 for the low molecular weight polymer is calculated to be 6.2 g/kg. At concentrations of up to 50% in water, the raw ingredient produced no signs of skin or eye irritation in Draize rabbit irritation tests. There was no evidence of dermal toxicity other than local skin changes in a 28-day subchronic study with rabbits. The Magnusson-Kligman guinea pig maximization test and another guinea pig sensitization procedure produced no evidence of allergic skin sensitization. A 13-week subchronic inhalation study showed no toxic effects for a product formulation containing a final aerosolized Polyquaternium-11 concentration of 0.03 mg/m^3.

In clinical studies, 1 of 19 subjects showed slight skin irritation after a 24-hour single insult skin patch with 9.5% Polyquaternium-11 in water. A product formulation containing the ingredient at 2.0% produced no irritation; another formulation containing 0.3% produced up to mild irritation. A number of Draize-Shelanski repeated insult patch tests were conducted on Polyquaternium-11 at concentrations of up to 50%; there were no instances of skin sensitization and only isolated instances of transient skin irritation with both low and high

molecular weight polymers in a total of 450 subjects. Clinical photoreactivity studies on both low and high molecular weight polymers showed no evidence of phototoxicity or photoallergenicity. The ultraviolet absorbance spectrum of high molecular weight Polyquaternium-11 at a high (50%) concentration indicated some absorption at 284 nm, which is of questionable clinical significance with regard to photoreactivity; the FDA product formulation data included only one formulation in the > 25%–50% concentration range. A clinical use test on a product formulation containing 1.0% Polyquaternium-11 showed the product to be comparable in dermatologic effects to a similar control product; both produced some subjective reports of scalp irritation.

CONCLUSION

From the available information, the Panel concludes that Polyquaternium-11 is safe as a cosmetic ingredient in the present practices of use.

ACKNOWLEDGMENT

Jeffrey Moore, Scientific Analyst and writer, prepared the technical analysis used by the Expert Panel in developing this report.

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Final Report on the Safety Assessment of Polyquaternium-7[1]

Abstract: The quaternary ammonium compound Polyquaternium-7 is used as an antistatic agent, film former, and hair fixative in a wide variety of cosmetics. This ingredient is formed by the polymerization of acrylamide with dimethyl dialylammonium chloride; residual acrylamide monomer can be found at levels as high as 10 ppm. An 8% aqueous solution of Polyquaternium-7 is typically supplied and this solution may be used in cosmetic formulations at a concentration as high as 5%. Most uses are at lower concentrations. Rats were fed up to 50,000 ppm of an 8% aqueous solution for 30 days; a decrease in organ weight was noted in the higher exposure groups. Dermal exposure of rats to 2.25 ml/kg per day for 14 weeks was nonirritating to both intact and abraded skin. Dermal exposure of rabbits to an 8% solution produced no irritation, and ocular exposure showed mild irritation that cleared after 24 h. Polyquaternium-7 was not mutagenic in an Ames test. Repeated insult patch test data suggest that 8% Polyquaternium-7 is at best a mild cumulative irritant, but not a sensitizer. Clinical tests with an 8% solution indicated that Polyquaternium-7 is not a photosensitizer. Given its structure, this material is considered not likely to be significantly absorbed in the skin and therefore is unlikely to produce general toxicity, developmental toxicity, or mutagenic/carcinogenic effects under use conditions. The presence of unreacted acrylamide monomer is considered sufficiently low so as to have no toxicologic significance. Based on the available data, it is concluded that Polyquaternium-7 is safe for use in cosmetic formulations. **Key Words:** Polyquaternium-7—Rat—Rabbit—Ocular irritation.

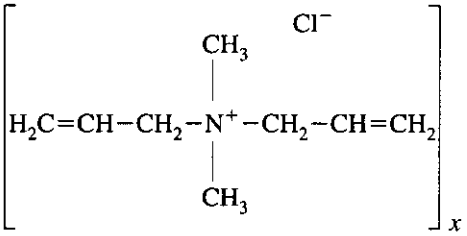
The following is a summary of data available to CIR concerning the chemistry, cosmetic use, and toxicity on Polyquaternium-7.

CHEMISTRY

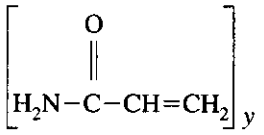
Definition

Polyquaternium-7 (CAS No. 26590-05-6) is a copolymer consisting of acrylamide and dimethyl diallyl ammonium chloride monomers (Wenninger and McEwen, 1993). The structure of the two monomers are as follows (STN International, 1994):

[1] Reviewed by the Cosmetic Ingredient Review Expert Panel.
Address correspondence and reprint requests to Dr. F. A. Andersen at Cosmetic Ingredient Review, 1101 17th Street, NW, Suite 310, Washington, DC 20036, U.S.A.



dimethyl diallyl ammonium chloride



acrylamide

It is difficult to assign a structure to the Polyquaternium-7 polymer as each functional group on the monomers can react in numerous ways with the others. By controlling the ratio of the two monomers and altering the catalyst system and experimental conditions different polymers can be created. For example, the two diallyl functional groups on the ammonium chloride monomer can cross-link with each other or they can react with acrylamide such that the ammonium chloride monomer becomes either a 5- or 6-membered ring. As a result, Polyquaternium-7 polymers produced by various manufacturers can differ from each other either in chain length, in the sequential arrangement of the two monomers, or in the types of bonds found between the monomers (Akerson, 1994).

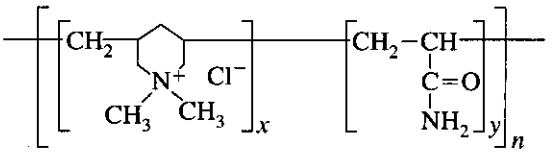
Polyquaternium-7 is also known as Quaternium-41; *N,N*-Dimethyl-*N*-2-Propenyl-2-Propen-1-ammonium Chloride, Polymer with 2-Propenamide; and 2-Propen-1-ammonium, *N,N*-Dimethyl-*N*-2-Propenyl-, Chloride, Polymer with 2-Propenamide (Wenninger and McEwen, 1993).

Chemical and Physical Properties

Polyquaternium-7 is supplied by one manufacturer as an 8% aqueous solution with 0.1% methylparaben and 0.02% propylparaben. The manufacturer reports a molecular weight for the solution of 1×10^6–10^7. This solution appears as a clear, colorless to pale yellow liquid with a molecular weight of approximately 1×10^6–10^7 and a pH of 6.5–7.5. The viscosity of the solution at 25°C is 7,500–15,000 cps. An ultraviolet absorption analysis of a 1.0% dilution of the 8% aqueous Polyquaternium-7 solution had absorbance peaks at 250–260 nm and 290–300 nm. The first peak was attributed to the paraben preservative system; the second peak to sodium salicylate impurities (Calgon, 1992*a*, 1992*b*).

Method of Manufacture

Calgon reports synthesizing Polyquaternium-7 by radical polymerization of equal amounts of acrylamide and dimethyl dialylammonium chloride (Calgon, 1992a). Under these conditions the following polymer is the predominant reaction product (Bozo Research Center, 1979):



As the majority of data presented in this review was supplied by this manufacturer, the structure of the Polyquaternium-7 polymer is consistent among the studies.

Impurities

Concentrations of reported impurities using the above-described method of manufacture are as follows: catalyst system, 0.6%; sodium salicylate, 0.04%; dimethyl diallylammonium chloride, 0.68–1.42%; and acrylamide, <5 ppm (Calgon, 1992*b*). A separate source cites that for "one company" the amount of acrylamide impurity is a maximum of 10 ppm (CTFA, 1992).

USE

Cosmetic

Polyquaternium-7 is a quaternary ammonium compound that is used as an antistatic agent, film former, and hair fixative (Wenninger and McEwen, 1992).

Table 1 reports the 1994 FDA voluntary submission data on formulations containing Polyquaternium-7 (FDA, 1994). Concentrations of use are no longer re-

TABLE 1. *Product formulation data for Polyquaternium-7*

Product category	Total no. of formulations in category	Total no. of formulations containing Polyquaternium-7
Baby shampoos	19	2
Other baby products	23	1
Bubble baths	214	2
Other bath preparations	132	4
Other fragrance preparations	136	2
Hair conditioners	614	16
Permanent waves	387	4
Rinses (non-coloring)	58	1
Shampoos (non-coloring)	852	37
Tonics, dressings and other grooming aids	563	19
Other hair preparations	376	3
Hair shampoos (coloring)	15	3
Bath soaps and detergents	343	26
Other personal cleanliness products	321	3
Aftershave lotion	229	1
Shaving cream	147	4
Cleansing	746	8
Other skin care preparations	790	1
Other suntan preparations	61	1
1994 Total		138

ported to FDA (Federal Register, 1992). However, in 1992 one cosmetic manufacturer reported the concentration of use of Polyquaternium-7 to be 0.04 to 0.17% (CTFA, 1992). Calgon (1992*b*) also reported typical concentration of use of their 8% aqueous solution in some formulation types: shampoo, 5.0%; creams/lotions, 2.0%; bar soap, 2.0% (active); liquid soap, 5.0%; sunscreens, 2.0%.

International

Polyquaternium-7 is approved by Japan for use in cosmetics (Rempe and Santucci, 1992).

ANIMAL TOXICOLOGY

Acute Toxicity

Oral

Polyquaternium-7, as supplied by one manufacturer in an 8% aqueous solution, has an oral LD_{50} of >39.8 g/kg (Calgon, 1992*b*). The details were not reported.

A dose of 25 ml/kg of the 8% aqueous solution of Polyquaternium-7 was orally administered by gastric intubation to five male and five female Charles River rats, CRCD strain. Feed had been withheld for 24 h prior to administration. No animals died during the 2-week observation period that followed and all had normal body weight gain (Merck, Sharp and Dohme Research Laboratories, 1978).

Dermal

The dermal LD_{50} of Polyquaternium-7 (8% aqueous) is >21.5 g/kg (Calgon, 1992*b*). The details were not reported.

An undiluted solution of 8% aqueous Polyquaternium-7 was applied as a 5 g/kg dose to the shaved back of four male and four female albino New Zealand rabbits (2.80–3.40 kg body weight). The skin of four animals (two of each sex) was abraded; the skin of the other four was left intact. Occlusive dressings were applied to maintain 24-h contact. When the dressings were removed 2 of 4 abraded sites showed very slight erythema and edema; the condition disappeared by the next day. No other irritation was noted during the 2-week observation period (Merck, Sharp and Dohme Research Laboratories, 1978).

Short-Term Toxicity

Oral

A 30-day feeding study of Polyquaternium-7 (8% aqueous) was performed using CD-CRJ (SD) rats, 10 male and 10 female per group (Bozo Research Center, 1979). Dose groups were 1,650; 5,000; 16,500, and 50,000 ppm. Body weight, feed consumption, and water consumption were measured every other day. Urine was collected. At the end of the dosing period, the animals were fasted 1 day, anesthetized, and bled. Hematology assays (red blood cell, leucocyte, hemoglobin, hematocrit, and leucocytes percent) and clinical chemistry assays (GOT, GPT,

AIP, total protein, A/G, total cholesterol, blood sugar, urea nitrogen, sodium, and potassium) were performed. All of the animals survived to the end of the study. The following organs were weighed and examined microscopically: brain, pituitary gland, thyroid gland, heart, lungs, liver, spleen, kidneys, adrenal glands, testes, and ovaries. In addition, the following organs were also grossly examined for anatomic changes: the salivary glands, thymus, pancreas, stomach, mesentery lymph nodes, and the small and large intestines.

The 50,000 ppm–dosed group had decreased body weight gains; it was minor in the males and significant in the females. Males of the 50,000 ppm group had a small decrease in feed intake. The males of the 5,000 ppm group had incidental decrease and females of the 5,000 ppm group had incidental increase of water consumption. Otherwise, feed and water consumption in dosed animals were comparable with controls.

No differences in hematologic parameters were observed between test and control groups. There were no significant differences between test and control groups in any of the urine assays.

Changes in internal organ weights compared with controls were noted. In males, the thyroid gland weight was decreased in the 16,500 ppm group by an average of 20% and in the 50,000 ppm group by 26%; the heart weight was decreased by 13% in the 50,000 ppm group; the kidney weight (left) was increased in the 1,650 ppm group by 8%; and the weight of adrenal glands was decreased in the 5,000, 16,500, and 50,000 ppm groups by an average of 11%. In females, the liver weight was decreased in the 16,500 and 50,000 ppm groups by 11 and 9%, respectively; the spleen was decreased by 13% in the 50,000 ppm group. No other organ weight changes were noted in females.

Incidental bleeding of the thymus was observed in some animals and was the only anatomic abnormality noted.

Pathologic changes were noted in some of the animals; these changes were not significantly correlated with the dosing of Polyquaternium-7. Of note, a decrease of the follicle colloid of the thyroid gland was observed in some male animals. Circumscribed inflammatory cell infiltration in the heart was observed in one dosed (5,000 ppm) and one control male. Partial apneumatosis and partial pulmonary emphysema was seen in both dosed and control groups. Some animals had lymphocyte infiltration of Glisson's capsule of the liver. Chronic lipopexia was observed in some female animals. One male (50,000 ppm) had a granuloma in the liver. In the kidneys, lymphocyte infiltration was observed. An increase in cortex lipid of the adrenal glands was observed in some test and control animals.

Subchronic Toxicity

Dermal

A 14-week dermal toxicity study was performed using New Zealand albino rabbits. Groups of 4 animals of each sex received a dose of 0.25, 0.75, or 2.25 ml/kg per day of (8% aqueous) Polyquaternium-7 or physiologic saline. Four animals of each group—two male and two female—had treatment sites abraded during the first day of each week of the study. Doses were spread evenly every

day throughout the study (89 to 92 days). After 4–5 h of dermal contact, the excess material was removed. A control group of animals had saline applied to abraded and intact sites following the same schedule as described for the treated animals. Animals were examined daily for gross changes and weighed weekly. Ophthalmic examinations, hematologic and serum analyses, serum glutamic oxaloacetic transaminase (SGOT) tests, and alkaline phosphatase tests were performed at regular intervals. At the end of the study the animals were killed and necropsy and microscopic examinations were performed. All but one rabbit (a control) survived to the end of the study. Organs examined and weighed at necropsy included: heart, liver, kidneys, brain, adrenal glands, and testes.

In all treated groups except the 0.25 ml/kg per day on nonabraded skin there was a small but significant suppression of body weight gain as compared with saline controls; abrasion had no significant impact on this trend. The researchers attributed the loss of body weight to the stress caused by greater handling of treated animals, which was necessary to remove the hardened test substance off the skin between each daily exposure. No ophthalmic changes attributable to the test compound were observed. While there was a statistically significant decrease in serum alkaline phosphatase activity (in the 0.75 ml/kg, intact group) and an increase in SGOT activities (in drug weeks 7 and 11 in the 2.25 ml/kg groups), a treatment linked relationship could not be established. In fact, a decrease in serum alkaline phosphatase activity was observed in all groups including controls as compared with prestudy values and was a normal response to aging. Hematologic changes seen in two animals (slight anisocytosis in one animal, slight polychromasia in another) were deemed to be unrelated to the treatment. Nasal discharge was observed in some treated and control rabbits throughout the study.

Slight erythema but no edema was seen in animals with abraded skin after day 5. In 4 of 12 animals with abraded skin, there was a slight crust formation. Very slight to slight scabbing and redness were observed in control and treated groups with abraded skin. Of those treatment groups with abraded skin focal epidermal hyperplasia was noted in four animals; focal ulceration in one; and focal dermal cellular infiltration in three. Treatment with Polyquaternium-7 was considered essentially nonirritating to abraded skin and inert on intact epidermis (Merck, Sharp and Dohme Research Laboratories, 1978).

Dermal Irritation

A primary skin irritation study was conducted using six albino New Zealand rabbits (three of each sex) using 0.5 ml of a solution containing 8% Polyquaternium-7 in water. The test solution was applied to intact and abraded sites on shaved backs. The sites were covered to maintain contact for 24 h. Observations were made daily for 2 weeks following removal of the dressing and no evidence of irritation was found (Merck, Sharp & Dohme Research Laboratories, 1978).

Ocular Irritation

A dose of 0.1 ml of undiluted Polyquaternium-7 was instilled into the conjunctival sac of the left eye of three male and three female albino New Zealand rabbits.

The eyelids were held together for 1 min and then released. The eyes were not rinsed. The right eye of each animal served as a control. At 15 min and 2 h, a slight clear discharge was seen coming from all eyes that were treated and three of the treated eyes had a slight conjunctival injection. By 24 h all of the treated eyes appeared normal and no further irritation was noted during the 2-week observation period (Merck, Sharp & Dohme Research Laboratories, 1978).

MUTAGENICITY

Polyquaternium-7 in concentrations up to 0.1 ml/plate did not cause a significant increase in the number of revertants in *Salmonella typhimurium* strains TA92, TA98, TA100, and TA1537 regardless of S9 metabolic activation (Merck, Sharp & Dohme Research Laboratories, 1978).

CLINICAL ASSESSMENT

Irritation and Sensitization

A modified Shelanski repeated insult patch test (RIPT) was performed on two groups of volunteers (Product Investigations, Inc., June 1981). Induction occurred by applying 24-h occlusive patches containing 0.2 ml of Polyquaternium-7 (8% aq) to a specified area of the back 12 times over the course of 3 weeks. Panelists were checked for reactions at the time following removal of one patch and prior to application of a subsequent one. Induction was followed by a 2-week nontreatment period. Then, during the final week, four patches were administered to a new site. Reactions were graded after 24 h. There was no reaction in any of the 106 panelists to the initial application. During the induction period four panelists had irritation reactions to the treatment. In 3 of 4, the test material was determined to be a primary irritant of the cumulative type and in the remaining individual the response could not solely be attributed to the test material. During the challenge phase, five panelists had sensitization reactions to the treatment. Four of the five had reactions scored as 1; the fifth had a reaction scored as 3. This fifth responder was rechallenged with the test material and had reactions with a maximum score of 1 on three of four observation days following reapplication. The formulation, containing 8% Polyquaternium-7, was considered a very mild cumulative irritant.

A second RIPT was conducted, again by Product Investigations (January 1994). The protocol followed was identical to that used in the earlier RIPT except that there was only 1 week of nontreatment between induction and challenge. Of the 155 panelists who completed induction, two responded with faint erythema that disappeared within 24 h of detection. No adverse effects were observed in any of the 150 panelists who completed the study.

Photosensitization

A study to determine the photoallergic potential of Polyquaternium-7 was performed (Hill Top Research, Inc., December 1982). A pretest was conducted in which approximately 0.3 ml of an 8% aqueous solution of Polyquaternium-7 was

administered in a single-dose 24-h closed patch. Subsequently, eight patches were administered in a 3-week period. After each patch was removed the site was exposed to 30–40 min of sunlight between the hours of 11:00 a.m. and 4:00 p.m. A 2-week nontreatment period followed. The challenge phase consisted of two patches. After 24 h, one challenge site was exposed to sunlight as during induction. Responses were graded after 24 and 72 h. None of the 29 panelists who completed the study exhibited irritation, sensitization, or photosensitization to the treatment.

SUMMARY

Polyquaternium-7 is a copolymer of acrylamide and dimethyl diallyl ammonium chloride monomers. It is typically supplied as an 8% aqueous solution. It is used in cosmetic formulations as an antistatic agent, film former, and hair fixative at concentrations reported to be equal to or below 2%.

As supplied in an 8% solution, Polyquaternium-7 has an oral LD_{50} of >39.8 g/kg and a dermal LD_{50} of >21.5 g/kg. A single occlusive patch dose of 5 g/kg to the shaved backs of rabbits was nonirritating.

In a 30-day feed study using doses of Polyquaternium-7 (8%) up to 50,000 ppm, no significant differences between dosed and control rats were found in feed and water consumption and hematologic and urine parameters. Organ weights were decreased in males and females of the higher-dosed groups. No lesions were found in treated animals.

The results of a 14-week dermal study in rats using doses of 8% Polyquaternium-7 up to 2.25 ml/kg per day indicated that Polyquaternium-7 was essentially nonirritating to abraded skin and inert on intact skin. A single 24-h dermal exposure to 8% Polyquaternium-7 produced no irritation in rabbits.

Slight ocular irritation was noted in rabbits at 15 min and 2 h post-instillation of 0.1 ml of undiluted Polyquaternium-7; the irritation cleared by 24 h.

Polyquaternium-7 was nonmutagenic in an Ames assay.

Two RIPTs were performed. In one study the 8% Polyquaternium-7 solution was a mild cumulative irritant; in the other study, adverse reactions were not found in any panelist. Polyquaternium-7 as an 8% solution did not induce photosensitization in any of 29 panelists tested.

DISCUSSION

Although the results of only one mutagenicity assay are available in this review, the CIR Expert Panel decided that an additional mammalian genotoxicity assay was not necessary as the structure of Polyquaternium-7 suggests that it will not be significantly absorbed. Further, the results of the animal 14-week dermal study showed that whatever Polyquaternium-7 was absorbed had no effect. The Panel acknowledged the presence of acrylamide as an impurity but the reported maximum concentration of 10 ppm is sufficiently small so that is has no toxicologic significance. The Panel therefore issued a safe as used conclusion.

CONCLUSION

Based on available data, the CIR Expert Panel concludes Polyquaternium-7 to be safe as used in cosmetic formulations.

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Polyquaternium-7

CONCLUSION: In 1995, the Cosmetic Ingredient Review (CIR) Expert Panel stated that polyquaternium-7 was safe as used in cosmetic formulations.[1] The Expert Panel reviewed information available since that assessment,[2,3] along with updated frequency and concentration of use information. The Expert Panel determined to not initiate a rereview of the safety of polyquaternium-7 and confirmed the existing conclusion.

DISCUSSION: The use of polyquaternium-7 in cosmetic formulations has increased greatly, from 138 reported uses in 1994[1] to 975 uses in 2010.[4] Concentration of use was not reported to the Food and Drug Administration (FDA) in 1994, nor is it reported to FDA currently. In response to a survey conducted by the Personal Care Products Council, industry reported current use concentrations of 0.009-5% for polyquaternium-7[5] (Table 1).

The Panel noted that polyquaternium-7 is now used in aerosolized products, and noted the absence of inhalation toxicity data. However, in the absence of these data, the Panel determined that polyquaternium-7 can be used safely in hair sprays, because the product particle size is not respirable. The Panel reasoned that the particle size of aerosol hair sprays (around 38 μm) and pump hair sprays (>80 μm) is large compared to respirable particle sizes (≤10 μm). Polyquaternium-7 is now also used in leave-on type products and products that are applied to the eye. The Panel was satisfied that data in the report supported the safety of these uses.

In the original safety assessment, the Expert Panel acknowledged the presence of acrylamide as an impurity in polyquaternium-7. An extrapolation using the current use concentration and the greatest amount of acrylamide impurity given in the original report confirmed that the amount of residual acrylamide was not of concern. The Expert Panel confirmed that polyquaternium-7 is safe as used in cosmetic formulations.

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Table 1. **Current and historical uses of polyquaternium-7.**

Product	Frequency of Use 1994 (# in category)[1]	Frequency of Use 2010[4] (# in category-2009)[6]	Conc. Of Use 1994[1]	Conc. Of Use (%) 2010[5]
Baby Shampoos	2 (19)	7 (56)	NA	NR
Other Baby Products	1 (23)	8 (143)	NA	0.04
Bath Oils, Tablets, and Salts	NR	NR (313)	NR	0.009
Bubble Baths	2 (214)	15 (169)	NA	0.05-0.4
Other Bath Preparations	4 (132)	14 (234)	NA	NR
Eye Shadow	NR	2 (1215)	NR	NR
Mascara	NR	6 (499)	NR	NR
Other Fragrance Preparation	2 (136)	1 (566)	NA	NR
Hair Conditioner	16 (614)	31 (1226)	NA	0.01-0.3
Hair Spray (aerosol fixatives)	NR	10 (312)	NR	NR
Permanent Waves	4 (387)	1 (69)	NA	0.07-5
Rinses (non-coloring)	1 (58)	2 (33)	NA	0.2
Shampoos (non-coloring)	37 (852)	234 (1361)	NA	0.04-1
Tonics, Dressings, and Other Hair Grooming Aids	19 (563)	34 (1205)	NA	0.2-3
Other Hair Preparations	3 (376)	21 (807)	NA	0.2-3
Hair Dyes and Colors (req. caution stmts)	NR	16 (2393)	NR	0.04
Hair Shampoos (coloring)	3 (15)	1 (40)	NA	NR
Hair Color Sprays (aerosol)	NR	NR (7)	NR	0.02
Bath Soaps and Detergents	26 (343)	292 (1665)	NA	0.09-.3
Other Personal Cleanliness Products	3 (321)	198 (792)	NA	0.08-0.2
Aftershave Lotion	1 (229)	3 (367)	NA	0.2
Shaving Cream	4 (147)	2 (122)	NA	0.09
Shaving Soap	NR	1 (10)	NR	NR
Cleansing	8 (746)	51 (1446)	NA	0.02-1
Face and Neck (excl. shave)	NR	3 (1583)	NR	0.06-0.08
Body and Hand (excl. shave)	NR	9(1744)	NR	0.3
Moisturizing	NR	3 (2508)	NR	NR
Skin Fresheners	NR	1 (259)	NR	NR
Other Skin Care Preps	1 (790)	8 (1308)	NA	0.4
Other Suntan Preparations	1 (61)	1 (62)	NA	NR
TOTAL	**138**	**975**	**NA**	**0.009-5**

NR-not reported as used in that category
NA – concentration of use data not reported at that time