Memorandum

To: CIR Expert Panel Members and Liaisons
From: Priya Cherian, Scientific Analyst/Writer
Date: November 15, 2019
Subject: Draft Report on Polysilicone-11

Enclosed is the Draft Report on the Safety Assessment of Polysilicone-11 as Used in Cosmetics (polisy122019rep). This ingredient is a crosslinked dimethylsiloxane, formed by the reaction of bis-vinyl(dimethicone and hydrogen dimethicone, that is reported to function as a film former in cosmetics. Following an intensive search of information in the published scientific literature, online databases, and other sources on this ingredient, there was insufficient information found to justify preparation of a formal Scientific Literature Review (SLR). Therefore, in July 2019, CIR issued a SLR Notice to Proceed (NTP) for Polysilicone-11 to alert interested parties that a safety assessment is being prepared and to request information in multiple areas, including:

- Chemistry information, including composition and structure, method of manufacture, and impurity data
- Toxicokinetics data relevant to routes of exposure expected with cosmetic use
- General toxicity data
- Developmental and reproductive toxicity data
- Genotoxicity data
- Carcinogenicity data
- Dermal irritation and sensitization data
- Inhalation toxicity data
- Any other relevant safety information that may be available

Since the issuing of the NTP, the following unpublished data have been received and included in this packet:

- Summary information regarding 2 HRIPTs on a leave-on product containing 9.675% Polysilicone-11 and a rinse-off product containing 19.830% Polysilicone-11 (polisy122019data1)
- An in vitro tissue equivalent assay to evaluate the ocular irritation potential of a face cream containing 1.6% Polysilicone-11 (polisy122019data2)
- A human cumulative irritation patch test on a face cream containing 1.6% Polysilicone-11 (polisy122019data2)
- Acute oral toxicity, skin irritation, eye irritation, sensitization, and genotoxicity summary information on different mixtures containing Polysilicone-11 (polisy122019data3)
- General method of manufacturing information (polisy122019data4)
- A 48-hour patch test performed using a lipstick containing 1.8% Polysilicone-11 (polisy122019data5)
- A MatTek EpiOcular™ methylthiazole tetrazolium (MTT) viability assay on a test substance containing 98.5% Polysilicone-11 (polisy122019data6)
- A human dermal maximization assay performed to evaluate the contact-sensitization potential of a liquid blend containing 24.625% Polysilicone-11 (polisy122019data6)
- An HRIPT on a product containing 1.45% Polysilicone-11 (polisy122019data7)
Also included in this package for your review are the CIR report history\textit{(polysil122019hist)}, flow chart\textit{(polysil122019flow)}, literature search strategy\textit{(polysil122019strat)}, ingredient data profile\textit{(polysil122019prof)}, 2018 use concentration data\textit{(polysil122019data8)}, and 2019 FDA VCRP data\textit{(polysil122019fda)}.

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

INGREDIENT/FAMILY  Polysilicone-11  
MEETING  December 2019

Public Comment  CIR  Expert Panel  Report Status

Priority List INGREDIENT  

Notice to Proceed without an SLR July 2, 2019  

Draft Report  

DRAFT REPORT  Dec 2019  

IDA Notice  Draft TR  Tentative Report  Draft FR  Final Report

DRAFT TENTATIVE REPORT  

DRAFT FINAL REPORT  

Issue TR  Different Conclusion  Issue FR

PUBLISH

60 day public comment period

60 day Public comment period

Table  IDA  TR  Table  IDA  TR  Table  IDA  TR  Table  IDA  TR
Polysilicone-11 History

July 2019

-A notice to proceed (NTP) was issued and the following data was requested:
  - Chemistry information, including composition and structure, method of manufacture, and impurity data
  - Toxicokinetics data relevant to routes of exposure expected with cosmetic use
  - General toxicity data
  - Developmental and reproductive toxicity data
  - Genotoxicity data
  - Carcinogenicity data
  - Dermal irritation and sensitization data
  - Inhalation toxicity data
  - Any other relevant safety information that may be available

-The following unpublished data was received:
  - HRIPTs on a leave-on product containing 9.675% Polysilicone-11 and a rinse-off product containing 19.830% Polysilicone-11 was received
  - Summary toxicity information received on various mixtures containing Polysilicone-11
  - An in vitro tissue equivalent assay to evaluate the ocular irritation potential of a face cream containing 1.6% Polysilicone-11
  - A human cumulative irritation patch test on a face cream containing 1.6% Polysilicone-11

August 2019

-The following unpublished data was received:
  - General method of manufacturing information
  - A 48-hour patch test performed using a lipstick containing 1.8% Polysilicone-11
  - A MatTek EpiOcular™ methyl thiazole tetrazolium (MTT) Viability Assay on a test substance containing 98.5% Polysilicone-11
  - A human dermal maximization assay performed to evaluate the contact-sensitization potential of a liquid blend containing 24.625% Polysilicone-11
  - An HRIPT on a product containing 1.45% Polysilicone-11

December 2019

-Panel reviews the draft report
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<thead>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Polysilicone-11</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

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

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

#### Typical Search Terms

- INCI name
- CAS numbers
- chemical/technical names

#### Key Words: dermal, irritation, sensitization, inhalation, metabolism, toxicity
Typical Search Terms

- INCI names
- CAS numbers
- chemical/technical names
- additional terms will be used as appropriate

Search Engines

- Toxnet (https://toxnet.nlm.nih.gov/)(includes Toxline; HSDB; ChemIDPlus; DART; IRIS; CCRIS; CPDB; GENE-TOX)
- Scifinder (https://scifinder.cas.org/scifinder)

appropriate qualifiers are used as necessary
search results are reviewed to identify relevant documents

Pertinent Websites

- wINCI - http://webdictionary.personalcarecouncil.org
- FDA databases http://www.ecfr.gov/cgi-bin/ECFR?page=browse
- FDA search databases: http://www.fda.gov/ForIndustry/FDABasicsforIndustry/ucm234631.htm;
- GRAS listing: http://www.fda.gov/food/ingredientspackaginglabeling/gras/default.htm
- SCOQS database: http://www.fda.gov/food/ingredientspackaginglabeling/gras/scogs/ucm2006852.htm
- Indirect Food Additives: http://www.accessdata.fda.gov/scripts/fdcc/?set=IndirectAdditives
- Drug Approvals and Database: http://www.fda.gov/Drugs/InformationOnDrugs/default.htm
- FDA Orange Book: https://www.fda.gov/Drugs/InformationOnDrugs/ucm129662.htm
- (inactive ingredients approved for drugs: http://www.accessdata.fda.gov/scripts/cder/iig/
- HPVIS (EPA High-Production Volume Info Systems) - https://ofmext.epa.gov/hpvis/HPVISlogon
- NIOSH (National Institute for Occupational Safety and Health) - http://www.cdc.gov/niosh/
- NTIS (National Technical Information Service) - http://www.ntis.gov/
- NTP (National Toxicology Program ) - http://ntp.niehs.nih.gov/
- Office of Dietary Supplements https://ods.od.nih.gov/
- FEMA (Flavor & Extract Manufacturers Association) - http://www.femaflavor.org/search/apachesolr_search/
- EU CosIng database: http://ec.europa.eu/growth/tools-databases/cosing/
ECETOC (European Centre for Ecotoxicology and Toxicology of Chemicals) - http://www.ecetoc.org

International Programme on Chemical Safety http://www.inchem.org/

www.google.com - a general Google search should be performed for additional background information, to identify references that are available, and for other general information

Botanical Websites, if applicable
- National Agricultural Library NAL Catalog (AGRICOLA) https://agricola.nal.usda.gov/
- The Seasoning and Spice Association List of Culinary Herbs and Spices
  http://www.seasoningandspice.org.uk/ssa/background_culinary_herbs-spices.aspx

Fragrance Websites, if applicable
- IFRA (International Fragrance Association) – http://www.ifraorg.org/
- Research Institute for Fragrance Materials (RIFM)
Safety Assessment of Polysilicone-11
as Used in Cosmetics

Status: Draft Report for Panel Review
Release Date: November 15, 2019
Panel Meeting Date: December 9 – 10, 2019

The 2019 Cosmetic Ingredient Review Expert Panel members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; James G. Marks, Jr., M.D.; Lisa A. Peterson, Ph.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The CIR Executive Director is Bart Heldreth, Ph.D. This safety assessment was prepared by Priya Cherian, Scientific Analyst/Writer.
INTRODUCTION

This is a safety assessment of Polysilicone-11 as used in cosmetic formulations. According to the web-based International Cosmetic Ingredient Dictionary and Handbook (wINCI; Dictionary), Polysilicone-11 functions as a film former in cosmetics. Polysilicone-11 is the product of a reaction between bis-vinyldimethicone and hydrogen methicone; the Panel has previously evaluated the safety of both bis-vinyldimethicone and hydrogen methicone, and concluded that these ingredients are safe in the present practices of use and concentration in cosmetics. The full reports on these ingredients can be accessed on the CIR website (https://www.cir-safety.org/ingredients); therefore, data on these previously reviewed ingredients will not be included in this report.

This safety assessment includes relevant unpublished data that are available for each endpoint that is evaluated. An exhaustive search of the world’s literature was performed, and very little published data were found regarding this ingredient. A listing of the search engines and websites that are used and the sources that are typically explored, as well as the endpoints that CIR typically evaluates, is provided on the CIR website (https://www.cir-safety.org/supplementaldoc/preliminary-search-engines-and-websites; https://www.cir-safety.org/supplementaldoc/cir-report-format-outline). Unpublished data were provided by the cosmetics industry, as well as by other interested parties.

CHEMISTRY

Definition and Structure

According to the Dictionary, Polysilicone-11 (CAS No: 63394-02-5, 156065-02-0) is a crosslinked dimethylsiloxane formed by the reaction of bis-vinyldimethicone and hydrogen dimethicone.¹

For use in cosmetics, copolymers, such as Polysilicone-11, are typically supplied to finishing houses as swollen gels (i.e. trade name mixtures) that contain 1 or more solvents (e.g., cyclopentasiloxane).² The addition of the comonomer (i.e. the vinyl-substituted dimethicone) affects both the chemical and the rheological properties of the resultant ingredient. Furthermore, the degree of crosslinking could also significantly affect these properties. Accordingly, this 1 copolymer ingredient theoretically represents a wide variety of materials ranging from liquids to elastomeric solids.

Physical and Chemical Properties

While no material properties were found or submitted for this ingredient alone, specifications for tradename mixtures comprising, in part, Polysilicone-11 were found.³⁻⁵ For 3 different tradename mixtures, Polysilicone-11 was stated to comprise 10 – 20% of the mixture composition. The composition remainder of these mixtures (i.e. the other 80 – 90%) was reported to be isododecane, cyclopentasiloxane, or, dimethicone. Each of these tradename mixtures is a clear liquid, with a viscosity ranging from 300 to 500 pascal second (Pa·s).

Method of Manufacture

According to a supplier, Polysilicone-11 is manufactured in cosmetic grade cyclopentasiloxane (D5) solvent, preferable from low cyclotetrasiloxane (D4) feedstock using a hydrosilation catalyst.⁶

Impurities

According to a manufacturer, Polysilicone-11 generally contains less than 20 ppm platinum catalyst from hydrosilation.⁶

USE

Cosmetic

The safety of the cosmetic ingredient addressed in this assessment is evaluated based on data received from the US Food and Drug Administration (FDA) and the cosmetics industry on the expected use of these ingredients in cosmetics. Use frequencies of individual ingredients in cosmetics are collected from manufacturers and reported by cosmetic product category in the FDA Voluntary Cosmetic Registration Program (VCRP) database. Use concentration data are submitted by the cosmetic industry in response to a survey, conducted by the Personal Care Products Council (Council), of maximum reported use concentrations by product category.
According to the 2019 VCRP survey data, Polysilicone-11 is reported to be used in 420 total formulations (412 of which are leave-on formulations; Table 1). The majority of these uses are in face and neck (excluding shave) products, moisturizing products, eye lotions, and foundations. The results of the 2018 concentration of use survey conducted by the Council indicate Polysilicone-11 is used at up to 35% in products that have dermal exposure (i.e., face and neck products; not spray). This ingredient may result in incidental ingestion as it is reported to be used in 8 lipstick formulations at up to 8.8%. In addition, Polysilicone-11 may also be used near the eyes, as it is reported to be used in eyeliner (1 formulation; concentration of use not reported), eye shadows (28 formulations; up to 9.4%), eye lotions (43 formulations; up to 12.2%), mascaras (3 formulations; up to 0.59%), and other eye makeup preparations (19 formulations; up to 0.24%).

Additionally, Polysilicone-11 is used in cosmetic sprays and could possibly be inhaled; for example, it is reported to be used in suntan pump sprays at up to 0.04%. The number of uses in this product category was not reported. In practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters > 10 µm, with propellant sprays yielding a greater fraction of droplets/particles < 10 µm compared with pump sprays. Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and thoracic regions of the respiratory tract and would not be respirable (i.e. they would not enter the lungs) to any appreciable amount. Polysilicone-11 was reportedly used in face powders at concentrations up to 3.5% and could possibly be inhaled. Conservative estimates of inhalation exposures to respirable particles during the use of loose powder cosmetic products are 400-fold to 1000-fold less than protective regulatory and guidance limits for inert airborne respirable particles in the air.

Polysilicone-11 is listed in the European Union inventory of cosmetic ingredients with no restrictions.

**TOXICOKINETIC STUDIES**

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

**TOXICOLOGICAL STUDIES**

**Acute Toxicity Studies**

An acute oral toxicity study was performed on Sprague Dawley rats (5/sex) using a test substance consisting of 6% Polysilicone-11 and 94% cyclotetrasiloxane. The test substance was administered undiluted. The LD<sub>50</sub> was reported to be > 5 g/kg. No other details regarding this study were provided.

**Short-Term, Subchronic, and Chronic Toxicity**

Short-term, subchronic, and chronic toxicity studies on Polysilicone-11 were neither found in the published literature, nor were these data submitted.

**GENOTOXICITY**

The genotoxic potential of a mixture consisting of 14% Polysilicone-11, 47% dimethicone, and 39% cyclopentasiloxane, was evaluated in an Ames assay. Bacterial cell lines (Salmonella typhimurium strains TA98 and TA100) were tested with and without metabolic activation. The test substance was tested at concentrations of 50, 100, 500, 1000, and 5000 µg/plate, and was considered to be non-mutagenic.

**CARCINOGENICITY STUDIES**

Data on the carcinogenicity of Polysilicone-11 were neither found in the published literature, nor were these data submitted.

**DERMAL IRRITATION AND SENSITIZATION**

Details of the dermal irritation and sensitization studies summarized below are provided in Table 2.

**Irritation**

A skin irritation study was performed on 6 New Zealand white albino rabbits. The test substance (6% Polysilicone-11 and 94% cyclotetrasiloxane) was applied in an amount of 0.5 g, undiluted, under a patch, on intact and abraded skin. The test substance was not considered to be a primary irritant. A 48-h patch test was performed on 50 subjects using a lipstick containing 1.8% Polysilicone-11 (0.2 mL) under semi-occlusive conditions. No dermal irritation was observed. Similarly, a 7-day dermal irritation study was performed on 38 subjects using a face cream containing 1.6% Polysilicone-11 (0.2 g) under semi-occlusive conditions. The subjects showed no evidence of irritation to the test substance.

**Sensitization**

No sensitization was observed in a human repeated insult patch test (HRIPT) performed on 51 subjects using a facial product containing 9.68% Polysilicone-11. The test substance was applied neat, under semi-occlusive conditions. Another HRIPT was performed, according to the same procedure, on 110 subjects using a facial product containing 19.83%
Polysilicone-11. Applications were made using a 10% dilution of the test substance under a semi-occlusive patch. No sensitization was observed. The amount of test substance used was not stated in either study. An HRIPT was performed on 50 subjects using a test substance consisting of 11% Polysilicone-11 and 89% cyclopentasiloxane. All applications were performed neat. No other details regarding this study were provided. The test substance was considered to be non-irritating and non-sensitizing. An HRIPT was also performed to evaluate the sensitization potential of a product containing 1.45% Polysilicone-11. The test article (0.1 g – 0.15 g) was placed on the skin of 54 subjects, under an occlusive patch. No evidence of irritation or sensitization was observed. A maximization assay was performed on 17 subjects to evaluate the sensitization potential of a test substance containing 24.625% Polysilicone-11 (0.05 mL; applied undiluted). No instances of contact allergy were recorded at either 48 or 72 h after the application of the challenge patch. The test substance was not considered to possess a detectable contact-sensitizing potential.

**OCULAR IRRITATION STUDIES**

**In Vitro**

A tissue equivalent assay was performed with EpiOcular™ cultures to evaluate the ocular irritation potential of a face cream containing 1.6% Polysilicone-11. The chemical was tested neat, the test samples were treated in duplicate, and the exposure periods were 8, 16, 20, and 24 h. The amount of test substance used was not specified. Appropriate negative and positive controls were used. The ET<sub>50</sub> (i.e., the time at which the tissue viability was reduced 50% compared to negative control tissues) for Polysilicone-11 and the positive control were 18.2 h and 30.3 minutes, respectively.

A MatTek EpiOcular™ methyl thiazole tetrazolium (MTT) viability assay was also performed to evaluate the ocular irritation potential of a test substance containing 98.5% Polysilicone-11. The chemical was tested neat (100 µL), the test samples were treated in duplicate, and the exposure periods were 64, 256, and 1200 min. Appropriate negative and positive controls were used. The ET<sub>50</sub> (i.e., the time at which the EpiOcular™ tissue viability was reduced 50% compared to control tissues) was 725.9 min, and the ocular irritancy classification for this test substance was “non-irritating, minimal.”

**Animal**

An acute eye irritation study was performed on 6 New Zealand albino rabbits using a test substance consisting of 6% Polysilicone-11 and 94% cyclotetrasiloxane. Approximately 0.1 mL of the test substance was applied to the eye, undiluted. No other details regarding this study were provided. The test substance was reported to be minimally irritating.

**SUMMARY**

This is a safety assessment of Polysilicone-11 as used in cosmetics. According to the Dictionary, Polysilicone-11 is a crosslinked dimethyl siloxane formed by the reaction of bis-vinyl(dimethicone and hydrogen peroxide, and is reported to function as a film former in cosmetics.

According to 2019 VCRP data, Polysilicone-11 is reported to be used in 420 formulations, 412 of which are leave-on formulations. The majority of these uses are in face and neck (excluding shave) products, moisturizing products, eye lotions, and foundations. The result of the 2018 concentration of use survey conducted by the Council indicate Polysilicone-11 is used at a maximum concentration of up to 50% in face and neck products (not spray).

An LD<sub>50</sub> of > 5 g/kg was established in an acute oral toxicity study performed on Sprague-Dawley rats given a test substance consisting of 6% Polysilicone-11 and 94% cyclotetrasiloxane.

No mutagenicity was reported in an Ames assay performed using a mixture consisting of 14% Polysilicone-11, 47% dimethicone, and 39% cyclopentasiloxane. The test substance was tested on S. typhimurium (TA98 and TA100) at concentrations of up to 5000 µg/plate.

No irritation was observed in a skin irritation study performed on New Zealand white albino rabbits using a test substance consisting of 6% Polysilicone-11 and 94% cyclotetrasiloxane. A 48-hour patch test performed was performed on 50 subjects using a lipstick containing 1.8% Polysilicone-11. No irritation was observed. In addition, no dermal irritation was observed in a 7-day dermal irritation study performed on 38 subjects using a face cream containing 1.6% Polysilicone-11.

No sensitization was observed in multiple HRIPTs using the following test materials: a facial product containing 9.68% Polysilicone-11, a 10% dilution of a facial product containing 19.83% Polysilicone-11, a mixture of 11% Polysilicone-11 and 89% cyclopentasiloxane, or a product containing 1.45% Polysilicone-11. In a sensitization study performed on 27 subjects using a pre-treatment with SLS, the test substance (24% Polysilicone-11) was considered to be non-sensitizing.

An in vitro tissue equivalent assay was performed in order to evaluate the ocular irritation potential of a face cream containing 1.6% Polysilicone-11. The t<sub>50</sub> for Polysilicone-11 and the positive control were 18.2 h and 30.3 minutes, respectively. A MatTek EpiOcular™ MTT viability assay was also performed to evaluate the ocular irritation potential of a test substance containing 98.5% Polysilicone-11. The ET<sub>50</sub> was 725.9 min, and the ocular irritancy classification for this test substance was “non-irritating, minimal.” In an ocular irritation study in New Zealand white rabbits, a test substance consisting of 6% Polysilicone-11 and 94% cyclotetrasiloxane applied to the eyes was considered to be minimally irritating.
DISCUSSION

To be developed.

CONCLUSION

To be determined.
<table>
<thead>
<tr>
<th>Exposure Type</th>
<th>Total Use</th>
<th>Max Conc. of Use (%)</th>
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</thead>
<tbody>
<tr>
<td><strong>Duration of Use</strong></td>
<td></td>
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<tr>
<td>Leave-On</td>
<td>412</td>
<td>0.025 – 35</td>
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<tr>
<td>Rinse-Off</td>
<td>8</td>
<td>0.061 – 5.8</td>
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<tr>
<td>Diluted for (Bath) use</td>
<td>NR</td>
<td>NR</td>
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<tr>
<td><strong>Exposure Type</strong></td>
<td></td>
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<tr>
<td>Eye Area</td>
<td>94</td>
<td>0.24 – 12.2</td>
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<tr>
<td>Incidental Ingestion</td>
<td>8</td>
<td>7.2 – 8.8</td>
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<tr>
<td>Incidental Inhalation-Spray</td>
<td>100, 90</td>
<td>0.04; 0.47 – 0.48</td>
</tr>
<tr>
<td>Incidental Inhalation-Powder</td>
<td>8, 100</td>
<td>0.025 – 3.5; 0.08 – 35</td>
</tr>
<tr>
<td>Dermal Contact</td>
<td>407</td>
<td>0.025 – 35</td>
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<tr>
<td>Deodorant (underarm)</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Hair - Non-Coloring</td>
<td>1</td>
<td>0.48</td>
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<tr>
<td>Hair-Coloring</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Nail</td>
<td>1</td>
<td>NR</td>
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<tr>
<td>Mucous Membrane</td>
<td>8</td>
<td>7.2 – 8.8</td>
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<tr>
<td>Baby Products</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>

*Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.*

*Not specified whether a spray or a powder, but it is possible the use can be as a spray or a powder, therefore the information is captured in both categories.*

*b It is possible these products are sprays, but it is not specified whether the reported uses are sprays.*

*c It is possible these products are powders, but it is not specified whether the reported uses are powders.*

NR – no reported use
### Table 2. Dermal irritation and sensitization

<table>
<thead>
<tr>
<th>Test Article</th>
<th>Concentration/Dose</th>
<th>Test Population</th>
<th>Procedure</th>
<th>Results</th>
<th>Reference</th>
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<tbody>
<tr>
<td><strong>ANIMAL</strong></td>
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<tr>
<td>6% Polysilicone-11 and 94% cyclotetrasiloxane</td>
<td>100%; 0.5 g</td>
<td>6 New Zealand White Rabbits</td>
<td>The test substance was applied under a 2.5 cm² patch on intact and abraded skin</td>
<td>Non-irritating</td>
<td>17</td>
</tr>
<tr>
<td>Lipstick containing 1.8% Polysilicone-11</td>
<td>Concentration not reported; 0.2 mL</td>
<td>50</td>
<td>The test material was applied to a 1” x 1” absorbent pad portion of a clear adhesive dressing, and placed on the back. This dressing formed a semi-occlusive patch. The material remained on the skin for 2 days.</td>
<td>Non-irritating</td>
<td>18</td>
</tr>
<tr>
<td>Face cream containing 1.6% Polysilicone-11</td>
<td>100%; 0.2 g</td>
<td>38</td>
<td>On day 1, the undiluted test substance (0.2 g) was applied to the back, under semi-occlusive conditions. After approximately 24 h, patches were removed. Twenty to 40 minutes after patch removal, sites were evaluated, and identical patches were applied to the same site. This process was repeated daily for a total of 7 days. Distilled water and 0.75% sodium lauryl sulfate (SLS) served as the negative and positive controls, respectively.</td>
<td>Non-irritating</td>
<td>19</td>
</tr>
<tr>
<td>Facial product containing 9.68% Polysilicone-11</td>
<td>100%; amount of test substance not reported</td>
<td>51</td>
<td>HRIPT; The test substance was applied neat, under a semi-occlusive patch, 3 times per week during the induction period. The amount of test substance used was not reported. Patches were removed 24 h after each application. After a 2-week rest period, a challenge patch was applied to a previously untreated test site. Patches were removed and the site was scored 24 and 72 h post-application.</td>
<td>Non-sensitizing</td>
<td>20</td>
</tr>
<tr>
<td>Facial product containing 19.83% Polysilicone-11</td>
<td>10%; amount of test substance not reported</td>
<td>110</td>
<td>HRIPT</td>
<td>Non-sensitizing</td>
<td>20</td>
</tr>
<tr>
<td>11% Polysilicone-11 and 89% cyclopentasiloxane</td>
<td>100%; amount of test substance not reported</td>
<td>50</td>
<td>HRIPT</td>
<td>Non-irritating; Non-sensitizing</td>
<td>20</td>
</tr>
<tr>
<td>Product containing 1.45% Polysilicone-11</td>
<td>Concentration not reported; 0.1 – 0.15 g</td>
<td>54</td>
<td>HRIPT</td>
<td>Non-irritating; Non-sensitizing</td>
<td>21</td>
</tr>
<tr>
<td>Liquid blend containing 24.625% Polysilicone-11</td>
<td>100%; 0.05 mL</td>
<td></td>
<td>Maximization assay. Approximately 0.05 mL of aqueous SLS was applied to the skin of each subject under occlusive conditions for 24 h. After 24 h, patches were removed and 0.05 mL of the test material was applied to the same site, and covered with occlusive tape. This induction patch was left in place for 48 or 72 h. After removal of the induction patches, if no irritation was present, a 0.25% SLS aqueous patch was again reapplied to the same site for 24 h, followed by reapplication of a fresh induction patch with the test material. This sequence of SLS pre-treatment followed by 48 h of test material application as continued for a total of 5 induction exposures. The induction phase was followed by a 10-day rest period. After the rest period, subjects were challenged with a single, 48-hour application of the test material to a previously untreated site. Pre-treatment with SLS was performed prior to challenge. Evaluations were performed 48 and 72 hours after application of challenge patch.</td>
<td>Non-sensitizing</td>
<td>22</td>
</tr>
</tbody>
</table>

**HRIPT** = Human repeated insult patch test; **SLS** = Sodium lauryl sulfate
REFERENCES


19. TKL Research I. 2013. Human cumulative irritation patch test (face cream with 1.6% Polysilicone-11). (Unpublished
data submitted by Personal Care Products Council on July 22, 2019.)

Personal Care Products Council on July 22, 2019.)

(Unpublished data submitted by Personal Care Products on August 26, 2019.)

22. KGL Inc. 2009. An evaluation of the contact-sensitization potential of a topical coded product in human skin by means
of the maximization assay (liquid blend containing 24.625% Polysilicone-11). (Unpublished data submitted by
Personal Care Products Council on August 19, 2019.)

23. Institute for In Vitro Sciences I. 2013. Tissue equivalent assay with Epiocular™ cultures (face cream containing 1.6%
Polysilicone-11).

data submitted by Personal Care Products Council on August 19, 2019.)
FDA VCRP Frequency of Use Data: Polysilicone-11

Total Uses: 420

03B - Eyeliner 1
03C - Eye Shadow 28
03D - Eye Lotion 43
03F - Mascara 3
03G - Other Eye Makeup Preparations 19
04C - Powders (dusting and talcum, excluding aftershave talc) 2
05G - Tonics, Dressings, and Other Hair Grooming Aids 1
07A - Blushers (all types) 3
07B - Face Powders 6
07C - Foundations 42
07D - Leg and Body Paints 75
07E - Lipstick 8
07F - Makeup Bases 13
07G - Rouges 2
07I - Other Makeup Preparations 16
08G - Other Manicuring Preparations 1
11A - Aftershave Lotion 1
12A - Cleansing 4
12C - Face and Neck (exc shave) 75
12D - Body and Hand (exc shave) 24
12E - Foot Powders and Sprays 1
12F - Moisturizing 61
12G - Night 21
12H - Paste Masks (mud packs) 4
12I - Skin Fresheners 1
12J - Other Skin Care Preps 33
13B - Indoor Tanning Preparations 6
Memorandum

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

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

DATE: July 22, 2019

SUBJECT: Polysilicone-11

### Summaries of HRIPTs of Products Containing Polysilicone-11

<table>
<thead>
<tr>
<th>Product Type</th>
<th>Polysilicone-11 Concentration</th>
<th>Study Type</th>
<th>Subjects No.</th>
<th>Study Conditions</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leave-on Facial</td>
<td>9.675%</td>
<td>HRIPT</td>
<td>51</td>
<td>Neat/Semi-occlusive</td>
<td>The test material did not induce irritation nor any evidence of induced sensitization in human subjects.</td>
</tr>
<tr>
<td>Rinse-off Facial</td>
<td>19.830%</td>
<td>HRIPT</td>
<td>110</td>
<td>10% dilution/Semi-occlusive</td>
<td>The test material did not induce irritation nor any evidence of induced sensitization in human subjects.</td>
</tr>
</tbody>
</table>

The HRIPT is summarized as follows: 1) During the induction phase, patches were applied 3 times per week (Monday, Wednesday, and Friday) for a total of nine applications. Patch was removed after 24 hours application, the evaluation was made just prior to re-application, rest periods consisted of 24 hours following each Tuesday and Thursday removal, and 48 hours following each Saturday removal. 2) Approximately 2 weeks after the final induction patch application, a challenge patch was applied to a virgin test site adjacent to the original induction patch site. The patch was removed and the site was scored at 24 and 72 hours post-application.
Memorandum

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

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

DATE: July 22, 2019

SUBJECT: Polysilicone-11

Institute for In Vitro Sciences, Inc. 2013. Tissue equivalent assay with Epiocular™ cultures (face cream containing 1.6% Polysilicone-11).

TKL Research, Inc. 2013. Human cumulative irritation patch test (face cream with 1.6% Polysilicone-11).
FINAL REPORT

Study Title

TISSUE EQUIVALENT ASSAY WITH EPIOCULAR™ CULTURES

Test Articles

Face cream containing 1.6% polysilicone-11

Authors

Greg Mun, B.A.
Lindsay Krawiec, B.S.

Study Completion Date

12 June 2013

Performing Laboratory

Institute for In Vitro Sciences, Inc.
30 West Watkins Mill Road, Suite 100
Gaithersburg, MD 20878

Study Number

Laboratory Project Number

Page 1 of 14
# Tissue Equivalent Assay with Epiocular™ Cultures

## Summary

<table>
<thead>
<tr>
<th>IVS Test Article Number</th>
<th>Sponsor's Designation</th>
<th>Conc.</th>
<th>t₅₀ (hours) Preliminary (6 Feb 2013)</th>
<th>t₅₀ (hours) Trial 1 (27 Feb 2013)</th>
<th>pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Face cream with 1.6% polysilicone-11</td>
<td>Neat</td>
<td>&gt;16</td>
<td>18.2</td>
<td>5.0</td>
<td></td>
</tr>
<tr>
<td>Positive Control</td>
<td>0.3% Triton®-X-100</td>
<td>NA</td>
<td>30.0 minutes</td>
<td>30.3 minutes</td>
<td>NA</td>
</tr>
</tbody>
</table>

NA – Not Applicable
# TABLE OF CONTENTS

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QUALITY ASSURANCE STATEMENT .................................................................... 5  
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TEST ARTICLE RECEIPT ....................................................................................... 7  
TISSUE EQUIVALENT ASSAY WITH EPIOCULAR™ CULTURES  
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STATEMENT OF COMPLIANCE

The Tissue Equivalent Assay With EpiOcular™ Cultures of the test articles, polysilicone-11, was conducted in compliance with the U.S. FDA Good Laboratory Practice Regulations as published in 21 CFR 58 and the principles presented in the OECD series on Good Laboratory Practice in all material aspects with the following exceptions:

The identity, strength, purity and composition or other characteristics to define the test articles have not been determined by the testing facility. The certificates of analysis were not provided by the Sponsor.

The stability of the test articles under the storage conditions at the testing facility and under the actual test conditions has not been determined by the testing facility and is not included in the final report.

Greg Mun, B.A.
Study Director

12 June 2013
Date
QUALITY ASSURANCE STATEMENT

Study Title:  Tissue Equivalent Assay With EpiOcular™ Cultures

Study Number:  

Study Director:  Greg Mun, B.A.

This study was divided into a series of in-process phases. Using a random sampling approach, Quality Assurance monitored each of these phases over a series of studies. Procedures, documentation, equipment records, etc., were examined in order to assure that the study was performed in accordance with the U.S. FDA Good Laboratory Practice Regulations (21 CFR 58) and the OECD Principles of Good Laboratory Practice and to assure that the study was conducted according to the protocol and relevant Standard Operating Procedures.

The following are the inspection dates, phases inspected and report dates of QA inspections of this study:

<table>
<thead>
<tr>
<th>Phase Inspected</th>
<th>Audit Date(s)</th>
<th>Reported to Study Director</th>
<th>Reported to Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protocol and Initial Paperwork</td>
<td>05-Feb-13</td>
<td>05-Feb-13</td>
<td>05-Feb-13</td>
</tr>
<tr>
<td>Termination of Assay/Reading of Plates</td>
<td>07-Feb-13</td>
<td>07-Feb-13</td>
<td>08-Feb-13</td>
</tr>
<tr>
<td>Final Report</td>
<td>11-June-13</td>
<td>11-June-13</td>
<td>12-June-13</td>
</tr>
</tbody>
</table>

This report describes the methods and procedures used in the study and the reported results accurately reflect the raw data of the study.

Renee Forde, Ph.D.
Quality Assurance

12 June 2013
SIGNATURE PAGE

TISSUE EQUIVALENT ASSAY WITH EPIOCULAR™ CULTURES

Initiation Date: 4 February 2013

Completion Date: 12 June 2013

Sponsor:

Sponsor's Representative:

Testing Facility and Study Director
Address: Institute for In Vitro Sciences, Inc.
30 West Watkins Mill Road, Suite 100
Gaithersburg, MD 20878

Archive Location:

Study Director: Greg Mun, B.A. 12 June 2013

Laboratory Manager: Nathan R. Wilt, B.S.

Laboratory Supervisor: Allison Hilberer, M.S.
### TEST ARTICLE RECEIPT

<table>
<thead>
<tr>
<th>HVS Test Article Number</th>
<th>Sponsor's Designation</th>
<th>Physical Description</th>
<th>Receipt Date</th>
<th>Storage Conditions*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Face cream with 1.6% polysilicone-11</td>
<td>31 January 2013</td>
<td>room temperature</td>
</tr>
</tbody>
</table>

* - Protected from exposure to light
TISSUE EQUIVALENT ASSAY
WITH EPIOCULAR™ CULTURES
INTRODUCTION

The EpiOcular™ Human Cell Construct (MatTek Corporation) was used to assess the potential ocular irritancy of the test articles. The MTT (3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide) conversion assay, which measures the NAD(P)H-dependent microsomal enzyme reduction of MTT (and to a lesser extent, the succinate dehydrogenase reduction of MTT) to a blue formazan precipitate, was used to assess cellular metabolism after exposure to a test article for various exposure times\(^1\). The duration of exposure resulting in a 50% decrease in MTT conversion in test article-treated EpiOcular™ human cell constructs, relative to control cultures, was determined (\(t_{50}\)).

The purpose of this study was to evaluate the potential toxicity of the test articles, supplied by [Company Name], as measured by the conversion of MTT by EpiOcular™ human cell constructs after exposure to each test article for various exposure times. The laboratory phase of the study was conducted from 6 February 2013 to 28 February 2013 at the Institute for In Vitro Sciences, Inc. After a time range finding assay, the test articles were tested in a valid definitive assay to determine the time of exposure to each test article, which resulted in the \(t_{50}\) endpoint.

MATERIALS AND METHODS

Receipt of the EpiOcular™ Human Cell Construct Model

Upon receipt of the EpiOcular™ Human Cell Construct Kit (MatTek Corporation), the solutions were stored as indicated by the manufacturer. The EpiOcular™ human cell constructs were stored at 2-8°C until used. On the day of dosing an appropriate volume of EpiOcular™ human cell construct assay medium was removed and warmed to approximately 37°C. Nine hundred µL of assay medium were aliquoted into the wells of 6-well plates. The six-well plates were labeled to indicate test article and exposure time. The samples were inspected for air bubbles between the agarose gel and cell culture insert prior to opening the sealed package. Cultures with air bubbles covering greater than 50% of the cell culture area were not used. The 24-well shipping containers were removed from the plastic bag and their surfaces were disinfected with 70% ethanol. The EpiOcular™ human cell constructs were transferred aseptically into the 6-well plates. The EpiOcular™ human cell constructs were then incubated at 37±1°C in a humidified atmosphere of 5±1% CO₂ in air for at least one hour. The medium was then aspirated and 0.9 mL of fresh medium was added to each assay well below the EpiOcular™ human cell construct. The plates were returned to the incubator until treatment was initiated. Upon opening the shipping bag, any remaining unused tissues were briefly gassed with an atmosphere of 5% CO₂/95% air and placed back at 2-8°C for later use.

Test Article Preparation

As instructed by the Sponsor, each test article was administered to the test system without dilution.

Assessment of Direct Test Article Reduction of MTT

Each test article was added to a 1.0 mg/mL MTT (Sigma) solution in warm Dulbecco’s Modified Eagle’s Medium (DMEM) supplemented with 2 mM L-glutamine (MTT Addition Medium) to assess its ability to directly reduce MTT. Approximately 100 µL of each test article were added to 1 mL of the MTT solution and the mixtures were incubated in the dark at 37°C for approximately one hour. If the MTT solution color turned blue/purple, the test article was presumed to have reduced the MTT.

The test articles were not observed to reduce MTT in the absence of viable cells.

pH Determination

The pH of each test article was measured using pH paper (EMD Chemicals Inc.). Initially, the test article was added to pH paper with 0-14 pH range in 1.0 pH unit increments to approximate a narrow pH range. Next, the test articles were added to pH paper with a narrower range of 0-6 or 5-10 pH units with 0.5 pH unit increments, to obtain a more accurate pH value. The pH values obtained from the narrower range pH paper are presented in Table 1.

Time Range Finding Assay

A time range finding assay was performed to establish an appropriate exposure time range to be used in the definitive assay for each test article. Four exposure times of 1, 4, 8, and 16 hours were tested in the time range finding assay. One culture was treated per exposure time
with 100 μL of the appropriate test article or control. The negative control, 100 μL of sterile, deionized water (Quality Biological), was exposed for 16 hours. The positive control, 100 μL of 0.3% Triton®-X-100 (Fisher), was exposed for 5, 15, and 45 minutes (one culture per exposure time). The exposed cultures were then incubated for the appropriate amount of time at 37±1°C in a humidified atmosphere of 5±1% CO₂ in air.

After the appropriate exposure time, the EpiOcular™ cultures were extensively rinsed with Calcium and Magnesium-Free Dulbecco's Phosphate Buffered Saline (Ca⁺⁺Mg⁺⁺-Free DPBS) and the wash medium was decanted. After rinsing, the tissue was transferred to 5 mL of Assay Medium for a 10 to 20 minute incubation at room temperature to remove any test article absorbed into the tissue. A 1.0 mg/mL solution of MTT in warm MTT Addition Medium was prepared no more than 2 hours before use. Three hundred μL of MTT solution were added to designated wells in a prelabeled 24-well plate. The EpiOcular™ constructs were transferred to the appropriate wells after rinsing with Ca⁺⁺Mg⁺⁺-Free DPBS. The trays were incubated at 37±1°C for approximately three hours in a humidified atmosphere of 5±1% CO₂ in air.

After the incubation period with MTT solution, the EpiOcular™ cultures were blotted on absorbent paper, cleared of excess liquid, and transferred to a prelabeled 24-well plate containing 2.0 mL of isopropanol in each designated well. The plates were sealed with parafilm and stored in the refrigerator (2-8°C) until the last exposure time was harvested. The plates were then shaken for at least two hours at room temperature.

At the end of the extraction period, the liquid within the cell culture inserts was decanted into the well from which the cell culture insert was taken. The extract solution was mixed and 200 μL were transferred to the appropriate wells of a 96-well plate. Two hundred μL of isopropanol were added to the two wells designated as the blanks. The absorbance at 550 nm (OD₅₅₀) of each well was measured with a Molecular Devices Vmax plate reader.

**Definitive Assay**

Based on the results of the time range finding assay, four exposure times were chosen for the definitive assay. The exposure times for the test article, 0.25, 4, 8, and 24 hours. The exposure times were chosen such that generally two exposure times were expected to result in survivals lower than 50% and two exposure times were expected to result in survivals greater than 50%. In general, the negative control exposure times were selected to fit the range of the test article or positive control exposure times. If all exposure times were less than one hour, a single negative control exposure time may have been used. The negative control (100 μL of sterile, deionized water) was exposed for 0.25, 4, 8, and 24 hours. The positive control (100 μL of 0.3% Triton®-X-100) was exposed for 5, 15 and 45 minutes. The procedures used to conduct the definitive assay were essentially the same as for the time range finding assay with the exception that at least duplicate cultures were dosed per exposure time.

**Presentation of Data**

The raw absorbance values were captured. The mean OD₅₅₀ value of the blank wells was calculated. The corrected mean OD₅₅₀ value of the negative controls was determined by subtracting the mean OD₅₅₀ value of the blank wells from their mean OD₅₅₀ values. The corrected OD₅₅₀ value of the individual test article exposure times and the positive control exposure times was determined by subtracting the mean OD₅₅₀ value of the blank control from
their OD₅₅₀ values. The individual % of Control values were averaged to get the mean % of Control value. All calculations were performed using an Excel spreadsheet. The following percent of control calculations were made:

\[
\% \text{ of Control} = \frac{\text{corrected OD}_{550} \text{ of Test Article or Positive Control Exposure Time}}{\text{appropriate corrected mean OD}_{550} \text{ of Negative Control}} \times 100
\]

Exposure time response curves were plotted with the % of Control on the ordinate and the test article or positive control exposure time on the abscissa. The t₅₀ value was interpolated from each plot. To determine the t₅₀, the two consecutive points were selected, where one exposure time resulted in a relative survival greater than 50%, and one exposure time resulted in less than 50% survival. Two select points were used to determine the slope and the y-intercept for the equation \( y = m(x) + b \). Finally, to determine the t₅₀, the equation was solved for \( y = 50 \). When all of the exposure times show less than 50% survival, the t₅₀ value was calculated based on 100% viability at zero exposure time and the shortest test article exposure time with less than 50% survival. When all of the exposure time points show greater than 50% survival, the t₅₀ value was presented as greater than the longest test article exposure time.

**Criteria for a Valid Test**

The assay results were accepted if the tissues pass the quality control test at the MatTek Corporation. According to MatTek, the tissues will be considered acceptable if the positive control compound, 0.3% Triton®-X-100, causes a t₅₀ value within MatTek’s established acceptable range of 12.2 to 37.5 minutes.
RESULTS AND DISCUSSION

Time Range Finding Assay

A time range finding assay was performed, consisting of four exposure times of 1, 4, 8, and 16 hours for the test articles supplied by [redacted]. The exposure time response curves are included in Appendix B. Based upon the results of the time range finding assay, four exposure times were selected for each test article for the definitive assay (see Materials and Methods). The $t_{50}$ results for the time range finding assay are reported in Table 1, under “Preliminary”.

The test articles were not observed to reduce MTT in the absence of viable cells. Face cream w/ 1.6% polysilicone-11 could not be completely removed from the exposed tissues following the rinsing and soaking process after the 8 and 16 hour exposure times. The residual test article prolonged the exposure to the tissues, which may have influenced the toxic effect.

Definitive Assay

Face cream w/ 1.6% polysilicone-11

Four exposure times were treated in duplicate for each test article. [redacted]. The exposure times for the test article, [redacted], were 8, 16, 20, and 24 hours. The negative control was also exposed in duplicate for 0.25, 4, 8, and 24 hours. Table 1 summarizes the $t_{50}$ results of the definitive Tissue Equivalent Assay With EpiOcular™ Cultures for the test articles and the positive control, 0.3% Triton®-X-100, under “Trial 1”. The exposure time response curves are included in Appendix B. MatTek's ET30 for the positive control was 24.79 minutes. Since MatTek's positive control fell within the established acceptable range established at MatTek Corporation (12.2 – 37.5 minutes), the assay results were accepted.
Table 1

<table>
<thead>
<tr>
<th>IIVS Test Article Number</th>
<th>Sponsor's Designation</th>
<th>Conc.</th>
<th>t_50 (hours)</th>
<th>pH</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Preliminary (6 Feb 2013)</td>
<td></td>
</tr>
<tr>
<td>Face cream w/ 1.6% polysilicone-11</td>
<td>Neat</td>
<td>&gt; 16</td>
<td>18.2</td>
<td>5.0</td>
</tr>
<tr>
<td>Positive Control</td>
<td>0.3% Triton®-X-100</td>
<td>NA</td>
<td>30.0 minutes</td>
<td>30.3 minutes</td>
</tr>
</tbody>
</table>

NA – Not Applicable
**EPICULAR™ BIOASSAY**

**EXPERIMENT DATE:** 6-Feb-13  
**TEST MATERIAL:**  
**TEST ARTICLE:**  
**PRELIMINARY**  
**CONCENTRATION:** 100%

**Face cream w/ 1.6% polysilicone-11**  

$t_{50} = > 16$ Hour

<table>
<thead>
<tr>
<th>TIME EXPOSURE (Hours)</th>
<th>PERCENT VIABLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>107.4</td>
</tr>
<tr>
<td>4</td>
<td>121.8</td>
</tr>
<tr>
<td>8</td>
<td>94.1</td>
</tr>
<tr>
<td>16</td>
<td>58.7</td>
</tr>
</tbody>
</table>

\[ y = \text{Percent Viable} \]
\[ x = \text{Exposure Time} \]
\[ \text{slope} = \frac{\text{new} - \text{old}}{\text{new} - \text{old}} \]
\[ y_{\text{intercept}} = y_{\text{new}} - y_{\text{slope}} \]

<table>
<thead>
<tr>
<th>X</th>
<th>Y</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>16.0</td>
</tr>
<tr>
<td>2</td>
<td>16.0</td>
</tr>
<tr>
<td>3</td>
<td>#DIV/0!</td>
</tr>
</tbody>
</table>

**Face cream w/ 1.6% polysilicone-11**

**CONCENTRATION:** 100%  
**PRELIMINARY**

![Graph showing percent of control over exposure time](image)

B3
### EPIOCULAR™ BIOASSAY

**EXPERIMENT DATE:** 6-Feb-13  
**TEST MATERIAL:** 0.3% TRITON®-X-100  
\[ t_0 = 30.0 \text{ Minutes} \]

#### TIME EXPOSURE (Minutes) | PERCENT VIALBLE
---|---
5 | 99.7  
15 | 70.6  
45 | 29.6

\[
y = \text{Percent Viable} \\
x = \text{Exposure Time} \\
slope = \frac{\text{rise}}{\text{run}} = \frac{y_1 - y_2}{x_1 - x_2} \\
y \text{ intercept} = y - (\text{slope} \cdot x)
\]

<table>
<thead>
<tr>
<th>TIME</th>
<th>EXPOSURE (Minutes)</th>
<th>PERCENT VIALBLE</th>
<th>Y</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>15.0</td>
<td>1</td>
<td>70.5</td>
</tr>
<tr>
<td>2</td>
<td>45.0</td>
<td>2</td>
<td>28.5</td>
</tr>
<tr>
<td>3</td>
<td>30.0</td>
<td>3</td>
<td>50</td>
</tr>
</tbody>
</table>

\[
slope = -1.366687 \\
y \text{ intercept} = 91
\]

### 0.3% TRITON®-X-100

**6-Feb-13**  

**Graph:**  
- **X-axis:** Exposure Time (minutes)  
- **Y-axis:** Percent of Control  
- The graph shows a downward trend with decreasing percent viable as exposure time increases.
## EPIOCULAR™ BIOASSAY

**EXPERIMENT DATE:** 27-Feb-13

**TEST MATERIAL:** [Redacted]

**TEST ARTICLE:** Face cream w/ 1.6% polysilicone-11

**t_{50} = 18.2 Hours**

### TRIAL 1

**CONCENTRATION:** 100%

<table>
<thead>
<tr>
<th>TIME EXPOSURE (Hours)</th>
<th>PERCENT VIALBLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>95.2</td>
</tr>
<tr>
<td>16</td>
<td>57.2</td>
</tr>
<tr>
<td>20</td>
<td>44.0</td>
</tr>
<tr>
<td>24</td>
<td>28.3</td>
</tr>
</tbody>
</table>

\[
y = \text{Percent Viable} \\
x = \text{Exposure Time} \\
slope = \frac{\text{rise}}{\text{run}} = \frac{(y_1 - y_2)}{(x_1 - x_2)} \\
y' = \text{intercept} = y - \text{(slope} \times x)
\]

<table>
<thead>
<tr>
<th>X</th>
<th>Y</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>57.2</td>
</tr>
<tr>
<td>2</td>
<td>44</td>
</tr>
<tr>
<td>3</td>
<td>50</td>
</tr>
</tbody>
</table>

\[
slope = -3.3 \\
y' = 110
\]
**EPIOCULAR™ BIOASSAY**

**EXPERIMENT DATE:** 27-Feb-13  
**TEST MATERIAL:** 0.3% TRITON®-X-100  
**ET50 =** 30.3 Minutes

<table>
<thead>
<tr>
<th>TIME (Minutes)</th>
<th>PERCENT VIABLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>94.0</td>
</tr>
<tr>
<td>16</td>
<td>79.4</td>
</tr>
<tr>
<td>45</td>
<td>24.6</td>
</tr>
</tbody>
</table>

\[ y = \text{Percent Viable} \]
\[ x = \text{Exposure Time} \]
\[ \text{slope} = \frac{\text{slope}}{\text{run}} = \frac{(y_2 - y_1)}{(x_2 - x_1)} \]
\[ y \text{ intercept} = y (\text{slope} \times x) \]

<table>
<thead>
<tr>
<th>X</th>
<th>Y</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>15.0</td>
</tr>
<tr>
<td>2</td>
<td>45.0</td>
</tr>
<tr>
<td>3</td>
<td>30.289575</td>
</tr>
</tbody>
</table>

\[ \text{slope} = \frac{-1.726687}{50} \]

\[ y \text{ intercept} = 102.3 \]

**0.3% TRITON®-X-100**  
27-Feb-13
HUMAN CUMULATIVE IRRITATION PATCH TEST

TKL STUDY NO. [Redacted]

CONDUCTED FOR: [Redacted]

DATE OF REPORT:

January 24, 2013
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APPENDICES

I SUMMARY TABLES
II DATA LISTINGS
III INFORMED CONSENT DOCUMENT
IV PROTOCOL / PROTOCOL AMENDMENT

Version 1.0
SIGNATURES

This study was conducted in compliance with the requirements of the protocol and TKL's Standard Operating Procedures, and in the spirit of GCP ICH Topic E6.\(^1\) The report accurately reflects the raw data for this study.

Jonathan S. Dosik, MD  
Principal Investigator  
1/22/13  
Date

Kathleen Georgean  
Director, Dermatologic Safety Testing  
1/23/13  
Date

Michelle Medina  
Manager, Dermatologic Safety Testing  
1/23/13  
Date

STATEMENT OF QUALITY ASSURANCE

This report has been reviewed by the TKL Research, Inc (TKL) Corporate Quality Assurance Department and the report accurately reflects the raw data for this study.

Quality Assurance  
1/24/13  
Date

\(^1\) ICH Topic E6 “note for the guidance on Good Clinical Practices (CPMP/ICH/135/95)” – ICH Harmonised Tripartite Guideline for Good Clinical Practices having reached Step 5 of the ICH Process at the ICH Steering Committee meeting on 1 May 1996.  
Version 1.0
TITLE OF STUDY
Human Cumulative Irritation Patch Test

SPONSOR

STUDY MATERIALS
Facial Moisturizer
Face cream with 1.6% polysilicone-11

DATE STUDY INITIATED
October 22, 2012

DATE STUDY COMPLETED
October 29, 2012

DATE OF REPORT
January 24, 2013

INVESTIGATIVE PERSONNEL
Jonathan S. Dosik, MD - Dermatologist
Principal Investigator
Kathleen Georgeian
Director, Dermatologic Safety Testing
Michelle Medina
Manager, Dermatologic Safety Testing

CLINICAL SITE
TKL RESEARCH, INC
1 Palmer Terrace
Carlstadt, NJ 07072

Version 1.0
SUMMARY
Face cream with 1.6% polysilicone-11

...were evaluated neat to determine their ability to cause irritation to the skin of volunteer subjects with normal skin using a 7-day semi-occlusive cumulative irritation patch study. Distilled water served as a negative control and 0.75% SLS served as a positive control. Thirty-eight (38) subjects completed the study.

The dermatologist was present on the final study day for evaluation.

This study determined the following irritation scores and associated classifications:

<table>
<thead>
<tr>
<th>Irritation Scores</th>
<th>Cumulative Irritation Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>Overall Average Skin Grade (N=39 Enrolled)</td>
</tr>
<tr>
<td>SLS 0.75%</td>
<td>117.5</td>
</tr>
</tbody>
</table>

Face cream with 1.6% polysilicone-11
Distilled Water

Source: Table 4, Appendix 1, and Data Listing 3, Appendix II

Under the conditions employed in this study, the subjects showed no evidence of irritation to Face cream with 1.6% polysilicone-11

Version 1.0
1.0 OBJECTIVE
The objective of this study was to assess the potential of the test substances to elicit human skin irritation by repetitive topical application.

2.0 RATIONALE
Cumulative irritancy patch testing is a modified primary irritancy patch test that can detect weak irritants, which require multiple applications to cause a skin reaction. These reactions are due to direct damage to the epidermal cells and no immunologic (allergic) mechanism is involved. This procedure may detect so-called "fatiguing substances" which are mild irritants that cause more strongly positive reactions with successive multiple skin exposure.

3.0 STUDY DESIGN

3.1 Study Population
A sufficient number of healthy subjects were enrolled to provide a minimum of 30 completed subjects.

3.1.1 Inclusion Criteria
Individuals eligible for inclusion in the study were those who:

1. Were male or female, between the ages of 18 and 65;
2. Were in general good health as determined by the Medical and Dermatological History Questionnaire (Appendix A of Protocol, see Appendix IV);
3. Read, understood, and signed an informed consent (IC) agreement after being advised of the nature of the study;
4. Were willing to refrain from using lotions, creams, powders, or other skin preparations on the skin in the test area for the duration of the study;
5. Were willing to refrain from exposing skin sites to the sun or going to tanning beds for the duration of the study; and
6. Were willing to refrain from swimming and using hot tubs for the duration of the study.

3.1.2 Exclusion Criteria
Individuals excluded from participation in the study were those who:

1. Had clinically significant active dermatitis or skin disease anywhere on the body (excluding facial acne);
2. Had a history of psoriasis, eczema, or skin cancer;
3. Had a condition or were taking medication(s) which, in the judgment of the Investigator or Designate, made the subject ineligible or placed the subject at undue risk;
4. Had received treatment (chemotherapy, radiation, immune suppressant medications) for any type of cancer within the last 6 months;
5. Had a mastectomy or axillary lymph nodes removed;
6. Had an autoimmune or immune deficiency disease (eg, lupus, myositis, Crohn's disease, autoimmune thyroid diseases, autoimmune hepatitis);

Version 1.0
7. Were taking any immunosuppressant medication;
8. Had insulin-dependent diabetes;
9. Had asthma or any other chronic respiratory condition requiring daily therapy;
10. Were taking or using any antihistamines or systemic/topical anti-inflammatory medications (eg, ibuprofen, corticosteroid) on a routine or frequent basis. Maximum acceptable dosage should be determined by written laboratory guidelines;
11. Used a topical anti-inflammatory in the patch area within the last 2 weeks;
12. Were receiving allergy injections, expected to start injections before the conclusion of the study, or had the final injection within a week of the study start;
13. Were participating in another dermal study of any kind;
14. Were participating in any clinical study, which, in the judgment of the Investigator, would have potentially affected responses in either study;
15. Had a confirmed skin allergy as a result of participation in a patch study;
16. Had a known sensitivity or allergy relating to the substance(s) being evaluated;
17. Had a known sensitivity or allergy to adhesives, surgical tapes, bandages, etc; and/or
18. Had scars, moles, sunburn, tattoos, etc. in the patch area.

3.1.3 Informed Consent
A properly executed IC document was obtained from each subject prior to entering the study. The signed IC document is maintained in the study file. In addition, the subject was provided with a copy of the IC document (see Appendix III).

3.2 DESCRIPTION OF STUDY
3.2.1 Outline of Study Procedures
The study extended over a 7-consecutive day period with 4 product applications and evaluations. On Day 1, the study material was applied to the back under conditions described in Section 3.3.4. Twenty-three hours (±1 hour) later the patches were removed. Twenty to 40 minutes after patch removal the sites were evaluated, the responses recorded, and identical patches applied to the same sites. This was repeated daily for a total of 7 days, including Saturdays and Sundays.

3.2.2 Study Flow Chart

<table>
<thead>
<tr>
<th>Day</th>
<th>Activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Obtained informed consent, reviewed completed medical screening form, applied patches</td>
</tr>
<tr>
<td>2, 3, 4, 5, 6</td>
<td>Staff removed patches, graded, applied patches</td>
</tr>
<tr>
<td>7</td>
<td>Staff removed patches, graded</td>
</tr>
</tbody>
</table>

3.2.3 Definitions Used for Grading Responses
Responses were graded using the following numeral equivalents.

<table>
<thead>
<tr>
<th>Response</th>
<th>Numerical Equivalent</th>
</tr>
</thead>
<tbody>
<tr>
<td>No apparent cutaneous involvement</td>
<td>0</td>
</tr>
</tbody>
</table>

Version 1.0
The maximum obtainable individual score was a 4.0. Should a reaction of 2.0 have occurred at any point during the study, further patch application on that subject would have been terminated with respect to the product involved. An "NP" symbol and a score of 2.0 would be assigned to all subsequent days.

For each test substance, the average of all inclusive scores was calculated for each completed grade day and reported as the average skin grade for that particular day. An overall average skin grade was calculated (i.e., the sum of the daily average skin grades divided by the number of study days) for each test substance.

The Cumulative Irritation Index (CII) was calculated by dividing the total score by the sums of the highest possible score multiplied by the number of subjects multiplied by the number of days.

3.2.4 Evaluation of Responses

All responses were graded by a trained dermatologic evaluator meeting TKL's strict certification requirements to standardize the assignment of response grades.

3.3 Study Material

3.3.1 Storage, Handling, and Documentation of Study Material

Receipt of the material used in this study was documented in a general logbook, which serves as a permanent record of the receipt, storage, and disposition of all study material received by TKL. On the basis of information provided by the sponsor, the study material was considered reasonably safe for evaluation on human subjects. A sample of the study material was reserved and will be stored for a period of 6 months. All study material is kept in a locked product storage room accessible to
clinical staff members only. At the conclusion of the clinical study, the remaining study material was discarded or returned to the Sponsor and the disposition documented in the logbook.

3.3.2 Nature of Study Material

Identification: Facial Moisturizer  Face cream with 1.6% polysilicone-11
Amount Applied: 0.2 g

Special Instructions: Prior to the first application of product, the sites were wiped with 70% isopropyl alcohol. All Patches were prepared upon the subjects' arrival and were used within 15 minutes from patch preparation.

3.3.3 Application of Study Material

Study material was applied to patches as instructed. Patches were applied in a randomized schedule to the infrascapular area of the back, either to the right or left of the midline, or to the upper arm.

3.3.4 Description of Patch Conditions

Material evaluated under occlusive patch conditions is applied to a 2 cm x 2 cm Webril™ pad attached to a non-porous, plastic film adhesive bandage (3M medical tape). The patch is secured with hypoallergenic tape (Micropore), as needed.

Material evaluated under semi-occlusive patch conditions is applied to a 2 cm x 2 cm Webril™ pad. The pad is affixed to the skin with hypoallergenic tape (Micropore).

4.0 INTERPRETATION

Cutaneous irritation accounts for the majority of cases of contact dermatitis. Reactions consist of local inflammatory responses characterized by erythema and/or edema, or an erosive reaction characterized by local tissue destruction or necrosis. These reactions are due to direct damage to the
epidermal cells and require no prior sensitization. No immunologic (allergic) mechanism is involved.

To qualify as an "irritant", a substance should evoke inflammation on initial exposure (primary irritation) or on repeated exposure to an identical site (cumulative irritation). An irritant substance will cause dermatitis if it is permitted to act in sufficient concentration for a sufficient length of time. Irritant reactions may develop in all subjects, although individual susceptibility varies greatly.

Cumulative irritancy patch testing can detect weak irritants that require multiple applications to produce skin irritation. During and after first contacts with weak irritants, no visible skin alterations are observed. After repeated contact, the skin gradually becomes erythematous; drying and cracking occur; and later, oozing, crusting, and erosion may develop. An eczematous reaction with papules, vesicles, and edema may also develop.

The procedure employed is a modification of that described by Dr. B. M. Lanman\(^1\) at the Joint Conference on Cosmetic Sciences, April 21-23, 1968 in Washington, DC, and further modified by Phillips, et al\(^2\) and Berger, et al.\(^3\)

### 5.0 PROTOCOL
See Protocol - Appendix IV.

### 6.0 DOCUMENTATION AND RETENTION OF DATA
The case report forms (CRFs) are designed to identify each subject by subject number and initials, and to record demographics, examination results, adverse events (AEs), and end of study status. Originals or copies of all CRFs, correspondence, study reports, and all source data will be kept on hard-copy file for a minimum of 20 years from completion of the study. Storage is maintained either at a TKL facility in a secured room accessible only to TKL employees, or at an offsite location which provides a secure environment with burglar/fire alarm systems, camera detection and controlled temperature and humidity. Documentation will be available for the Sponsor’s review on the premises of TKL.

### 7.0 RESULTS & DISCUSSION
Thirty-nine (39) subjects between the ages of 20 and 65 were enrolled and 38 subjects completed the study (see Tables 1 and 2 in Appendix I and Data Listings 1 and 2 in Appendix II). The following table summarizes subject enrollment and disposition.

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Number enrolled:</td>
<td>39</td>
</tr>
<tr>
<td>Number discontinued:</td>
<td>1</td>
</tr>
<tr>
<td>Lost to follow-up:</td>
<td>1</td>
</tr>
<tr>
<td>Number completed:</td>
<td>38</td>
</tr>
</tbody>
</table>

Source: Table 1, Appendix I

The dermatologist was present on the final study day for evaluation.

There were no AEs reported.

Version 1.0
The Sponsor's Test Substance Information contained incorrect product descriptions. A protocol amendment was issued on January 8, 2013 with instruction to change the incorrect product descriptions to the correct descriptions provided in the protocol amendment. A copy of the protocol amendment is included in Appendix IV.

A summary of response data are provided in Table 3, Appendix I. A Cumulative Irritation Index by product is provided in Table 4. Individual dermatological response grades are provided in Data Listing 3, Appendix II.

This study determined the following irritation scores and associated classifications:

<table>
<thead>
<tr>
<th></th>
<th>Irritation Scores</th>
<th>Cumulative Irritation Index</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total</strong></td>
<td>117.5</td>
<td>0.1090</td>
</tr>
<tr>
<td><strong>Overall Average Skin Grade</strong></td>
<td>0.4361</td>
<td></td>
</tr>
<tr>
<td>(N=39 Enrolled)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>SLS 0.75%</td>
<td>117.5</td>
<td>0.1090</td>
</tr>
<tr>
<td>Face cream with 1.6% polysilicone-11</td>
<td>1.5</td>
<td>0.0056</td>
</tr>
<tr>
<td>Distilled Water</td>
<td>1.0</td>
<td>0.0038</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.0009</td>
</tr>
</tbody>
</table>

Source: Table 4, Appendix I, and Data Listing 3, Appendix II

8.0 CONCLUSION

Under the conditions employed in this study, the subjects showed no evidence of irritation to...

9.0 REFERENCES


APPENDIX I

SUMMARY TABLES
**Table 1: Summary of Subject Enrollment and Disposition**

<table>
<thead>
<tr>
<th>Description</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects enrolled</td>
<td>39</td>
</tr>
<tr>
<td>Subjects completed all phases</td>
<td>38 (97.4)</td>
</tr>
<tr>
<td>Total subjects discontinued</td>
<td></td>
</tr>
<tr>
<td>Lost to follow-up</td>
<td>1 (2.6)</td>
</tr>
</tbody>
</table>

Note: All percentages are relative to total subjects enrolled.

See data listing 1 for further detail.

Generated on 11/07/12:12:23 by DIPS/SAS / Uses: FINAL PRODUCT = R
Table 2: Summary of Subject Demographics
All Enrolled Subjects

<table>
<thead>
<tr>
<th>Age</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>16 (41.0)</td>
</tr>
<tr>
<td>N (%) 18 to 44</td>
<td></td>
</tr>
<tr>
<td>N (%) 45 to 64</td>
<td>21 (53.8)</td>
</tr>
<tr>
<td>N (%) 65 and up</td>
<td>2 (5.1)</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>47.3 (12.8)</td>
</tr>
<tr>
<td>Median</td>
<td>48.4</td>
</tr>
<tr>
<td>Range</td>
<td>20.9 to 65.7</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gender</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>14 (35.9)</td>
</tr>
<tr>
<td>N (%) Male</td>
<td></td>
</tr>
<tr>
<td>N (%) Female</td>
<td>25 (64.1)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Race</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Black</td>
<td>3 (7.7)</td>
</tr>
<tr>
<td>Caucasian</td>
<td>21 (53.8)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>15 (38.5)</td>
</tr>
</tbody>
</table>

See data listing 2 for further detail.

Generated on 11/07/12:12:23 by DEMOSMY.SAS / Uses: DEMOGS
PRODUCT = R
Table 3: Summary of Dermatologic Response Grades
Number of Subjects by Product

Product = __Face cream with 1.6% polysilicone-11__

<table>
<thead>
<tr>
<th>Response</th>
<th>Reading No.</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
<td>39</td>
<td>39</td>
<td>39</td>
<td>37</td>
<td>37</td>
<td>37</td>
<td></td>
</tr>
<tr>
<td>0.5</td>
<td></td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Average skin grade</td>
<td></td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.01</td>
<td>0.01</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>Total evaluable</td>
<td></td>
<td>39</td>
<td>39</td>
<td>39</td>
<td>38</td>
<td>38</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>Number absent</td>
<td></td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Number discontinued</td>
<td></td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

Overall Average Skin Grade: 0.01

Note: 'Total evaluable' includes subjects with no patch applied.
Generated on 11/07/12:12:23 by SUMMARY15.SAS / Uses: RESPONSE, PRODLIST, FINAL
PRODUCT = R
Memorandum

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

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

DATE: July 23, 2019

SUBJECT: Polysilicone-11

Summary Information: Polysilicone-11

Molecular Weight: >1 million Daltons in the form of an elastomer rubber, amorphous polymer

Safety Testing on blends containing Polysilicone-11

**Acute Oral**
Blend: 6% Polysilicone-11 + 94% Cyclotetrasiloxane
Test lab: Product Safety Labs 725 Cranbury Road East Brunswick, New Jersey 08816
FHSA ACUTE ORAL TOXICITY LIMIT TEST
Five Male and Five Female Sprague Dawley Rats
Administered, undiluted as received.
Protocol No.001/P203 Agency, FHSA/CPSC Date: September 26, 1991
Conclusion: LD₉₀ >5g/kg

**Primary Skin Irritation**
Blend: 6% Polysilicone-11 + 94% Cyclotetrasiloxane
Test lab: AMA Labs, 216 Congers Rd, New City NY 1095
Date: September 30, 1991
Six New Zealand Albino rabbits
Administered undiluted, 0.5g / 2.5cm² patch, intact vs abraded skin
Conclusion: Not a primary irritant

**Acute Eye Irritation**
Blend: 6% Polysilicone-11 + 94% Cyclotetrasiloxane
Test lab: Product Safety Labs 725 Cranbury Road East Brunswick, New Jersey 08816
FHSA Primary Eye Irritation Test
Date: September 7, 1991
Six New Zealand Albino rabbits
Administered undiluted, 0.1 ml
Conclusion: Minimally irritating

**Irritation/Sensitization**
Blend: 11% Polysilicone-11 + 89% Cyclopentasiloxane
Test lab: AMA Labs, 216 Congers Rd, New City NY 1095
Repeat Insult patch test (hRIPT) - 50 human panelists, product undiluted, 9 inductions
Date: January 8, 2007
Conclusion: Not irritating or Sensitizing

**Gene Mutation test on Bacteria**
Blend: 14% Polysilicone-11 + 47% Dimethicone + 39% Cyclopentasiloxane
Test lab: Litron Labs, 1351 Mt Hope Avenue, Suite #207; Rochester NY 14620
AMES SCREENING ASSAY - Bacterial cell lines (Salmonella typhimurium strains TA98 and TA100; tested with and without metabolic activation)
Doses tested: 50, 100, 500, 1000 and 5000 μg of the blend/plate
Date: November 15, 2002
Conclusion: Not mutagenic

Cytotoxicity
Blend: 14% Polysilicone-11 + 47% Dimethicone + 39% Cyclopentasiloxane
Test lab: AMA Labs, 216 Congers Rd, New City NY 1095
AGAR DIFFUSION CYTOTOXICITY TEST cell lines
Date: December 16, 2006
Conclusion: Not cytotoxic
Memorandum

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

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

DATE: August 5, 2019

SUBJECT: Polysilicone-11

Method of Manufacture and Impurities: Polysilicone-11

Polysilicone-11 (Cyclosiloxanes, dimethyl, polymers with dimethyl, methyl hydrogen siloxanes and vinyl-group terminated dimethylsiloxanes) is manufactured in cosmetic grade D5 (cyclopentasiloxane) solvent, preferable from low D4 (cyclotetrasiloxane) feedstock using a hydrosilation catalyst. It is a very pure addition reaction, with no impurities being formed during the reaction.

By virtue of additions, the product contains, generally <20 ppm platinum catalyst from hydrosilation.
Memorandum

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

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

DATE: August 6, 2019

SUBJECT: Polysilicone-11

Consumer Product Testing Co. 2017. 48 Hour patch test (lipstick containing 1.8% Polysilicone-11).
FINAL REPORT

CLIENT:

ATTENTION:

TEST: 48 Hour Patch Test
Protocol No.: CP-1.02

TEST MATERIAL: LIPSTICK containing 1.0% Polysilicone-11

EXPERIMENT
REFERENCE NUMBER:

Reviewed by: Richard R. Eisenberg, M.D.
Medical Director
Board Certified Dermatologist

Approved by: Michael Caswell, Ph.D., CCRA, CCRC
Vice President, Clinical Evaluations

Approved by: Joy Frank, R.N.
Executive Vice President, Clinical Evaluations

This report is submitted for the exclusive use of the person, partnership, or corporation to whom it is addressed, and neither the report nor the name of those Laboratories nor any member of its staff, may be used in connection with the advertising or sale of any product or process without written authorization.

70 New Dutch Lane • Fairfield, New Jersey 07004-2514 • (973) 808-7111 • Fax (973) 808-7234
QUALITY ASSURANCE UNIT STATEMENT

Trial Number:

The Consumer Product Testing Company, Incorporated (CPTC) Quality Assurance Unit (QAU) is responsible for auditing the conduct, content and reporting of all clinical trials that are conducted at CPTC.

This trial has been conducted in accordance with the Declaration of Helsinki, the ICH Guideline E6 for Good Clinical Practice, the requirements of 21 CFR Parts 50 and 56, other applicable laws and regulations, CPTC Standard Operating Procedures, and the approved protocol.

The CPTC QAU has reviewed all data, records, and documents relating to this trial and also this Final Report. The following QAU representative signature certifies that all data, records, and documents relating to this trial and also this Final Report have been reviewed and are deemed to be acceptable, and that the trial conforms to all of the requirements as indicated above.

All records and documents pertaining to the conduct of this trial shall be retained in the CPTC archives for a minimum of ten (10) years. At any time prior to the completion of the tenth archival year, a Sponsor may submit a written request to the CPTC QAU to obtain custody of trial records once the CPTC archive period has been completed. This transfer shall be performed at the Sponsor's expense. In the absence of a written request, trial-related records shall be destroyed at the end of the CPTC archive period in a manner that renders them useless.

William Cavaliere
Quality Assurance Representative

10/6/2017
Date
Objective: To determine by epidermal contact the primary irritation potential of a test material.

Participants: Fifty-two (52) subjects, male and female, ranging in age from 20 to 68 years, who qualified were selected for this evaluation. Fifty (50) subjects completed this study. The remaining subjects discontinued their participation for various reasons unrelated to the use of the test material.

Inclusion Criteria:

a. Male and female subjects, age 16 to 79 years.
b. Absence of any visible skin disease which might be confused with a skin reaction from the test material.
c. Prohibition of use of topical or systemic steroids and/or antihistamines for at least seven days prior to study initiation.
d. Completion of a Medical History Form and the understanding and signing of an Informed Consent Form.

c. Considered reliable and capable of following directions.

Exclusion Criteria:

a. Ill health.
b. Under a doctor's care or taking medication(s) which could influence the outcome of the study.
c. Females who are pregnant or nursing.
d. A history of adverse reactions to cosmetics or other personal care products.

Test Material: LIPSTICK

Study Schedule:

<table>
<thead>
<tr>
<th>Panel #</th>
<th>Initiation Date</th>
<th>Completion Date</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>September 26, 2017</td>
<td>September 29, 2017</td>
</tr>
</tbody>
</table>

*With parental or guardian consent*

Consumer Product Testing Company, Inc., 70 New Dutch Lane, Fairfield, NJ 07004
Methodology: The upper back between the scapulae served as the treatment area. Approximately 0.2 ml of the test material, or an amount sufficient to cover the contact surface, was applied to the 1" x 1" absorbent pad portion of a clear adhesive dressing. When secured to the appropriate treatment site, this dressing formed a semi-occlusive patch.

The test material remained in contact with the skin for a total of 2 days. This site was then evaluated for gross changes. Absence of any visible skin change was assigned a zero value. The test site was re-evaluated at Day 3.

**Evaluation Criteria (Erythema and additional Dermal Sequelae):**

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
<th>Code</th>
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<tbody>
<tr>
<td>0</td>
<td>No visible skin reaction</td>
<td>E</td>
</tr>
<tr>
<td>0.5</td>
<td>Barely perceptible</td>
<td>D</td>
</tr>
<tr>
<td>1</td>
<td>Mild</td>
<td>S</td>
</tr>
<tr>
<td>2</td>
<td>Moderate</td>
<td>P</td>
</tr>
<tr>
<td>3</td>
<td>Marked</td>
<td>V</td>
</tr>
<tr>
<td>4</td>
<td>Severe</td>
<td>B</td>
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<td></td>
<td>U</td>
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<tr>
<td></td>
<td></td>
<td>Sp</td>
</tr>
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</table>

Erythema was scored numerically according to this key. If present, additional Dermal Sequelae were indicated by the appropriate letter code and a numerical value for severity.

**Adverse Events:** There were no adverse events.

**Amendments:** There were no amendments.

**Deviations:** There were no deviations.
**Results:**

The results of each participant are appended (Table 1).

Observations remained negative throughout the test interval.

Subject demographics are presented in Table 2.

**Summary:**

Under the conditions of this study, test material, LIPSTICK, indicated no potential for dermal irritation.
Table 1

**Individual Results**

**LIPSTICK**

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<thead>
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<th>Subject Number</th>
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DNC = Did not complete study
Table 1  
(continued)

Individual Results

LIPSTICK

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<th>Subject Number</th>
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Table 2
(continued)

Subject Demographics

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</table>
Memorandum

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

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

DATE:   August 19, 2019

SUBJECT: Polysilicone-11

MB Research Laboratories. 2009. MatTek EpiOcular MTT Viability Assay (98.5%
Polysilicone-11).

KGL Inc. 2009. An evaluation of the contact-sensitization potential of a topical coded product
in human skin by means of the maximization assay (liquid blend containing 24.625%
Polysilicone-11).
VOLUME I

Study Title : MatTek EpiOcular MTT Viability Assay

Test Article : RI104978, [Redacted]

Positive Control : 0.3% Triton® X-100

Negative Control : Tissue culture water (TCH₂O)

Internal Control : PC-17:1047L

Author : Michelle Piehl, Ph.D, Study Director

Study Completed On : February 4, 2009

Performing Laboratory : MB Research Laboratories

MB Research Project # : MB 09-17849.19

MB Research Protocol # : 720-03

Sponsor : [Redacted]

Citation : Michelle Piehl, Ph.D (2009)

Unpublished Report by

MB Research Laboratories
GOOD LABORATORY PRACTICES COMPLIANCE STATEMENT

This study was conducted in accordance with the Good Laboratory Practice requirements of EPA, 40 CFR 160 and 792, FDA 21 CFR 58, and as specified in Principles on Good Laboratory Practices, published by the Organization for Economic Cooperation & Development (OECD), 1997, with the following exception:

The test article characterization was not supplied by the sponsor prior to study initiation.

STUDY DIRECTOR: [Signature] 2-4-09
Michelle Plehl, Ph.D. Date
MB RESEARCH LABORATORIES
ABSTRACT

OBJECTIVE: To provide an estimate of eye irritation potential using an alternative to the Draize Rabbit Eye Test. The exposure time needed for a test article to reduce viability to 50% can be correlated to an estimated Draize Rabbit Eye Score (MMAS) or a "Predicted Irritancy Class".

METHOD SYNOPSIS: MatTek EpiOcular™ tissue samples were treated with the test articles, positive control, and internal control for various exposure times listed below. Negative controls, treated with tissue culture water, were tested at 16 minutes only. Following treatment, the viability of the tissues was determined using MTT uptake and conversion, and the absorbance of each sample was measured at 540 nm using a reference wavelength of 690 nm. The viability was then expressed as a percent of control values. The mean percent viability for each time point was used to calculate an ET₅₀, which represents the time at which the EpiOcular™ tissue viability was reduced 50% compared to control tissues.

SUMMARY/CONCLUSION:

<table>
<thead>
<tr>
<th>Test Article identity</th>
<th>Exposure Times (min)</th>
<th>ET₅₀ (min)</th>
<th>Irritancy Classification</th>
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<tbody>
<tr>
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<td>64, 256, 1200</td>
<td>725.9</td>
<td>Non-Irritating, Minimal</td>
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<td>PC-17:1047L (Internal Control)</td>
<td>64, 256, 1200</td>
<td>436.1</td>
<td>Non-Irritating, Minimal</td>
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<td>0.3% Triton® X-100 (Positive Control)</td>
<td>15, 45</td>
<td>27.5</td>
<td>Within Range (12.2 - 37.5)</td>
</tr>
</tbody>
</table>
MB Research Laboratories

Study Title : MatTek EpiOcular Assay
Project #  : MB 09-17849.19
Protocol  : 720-03

OBJECTIVE

To provide an estimate of eye irritation potential using an alternative to the Draize Rabbit Eye Test. The exposure time needed for a test article to reduce viability to 50% can be correlated to an estimated Draize Rabbit Eye Score (MMAS) or a "Predicted Irritancy Class".

TEST ARTICLE

Supplied by : [Redacted]
Test Article Characterization : Not supplied by the sponsor.
Stability : Not supplied by the sponsor.
Date Received : 01/14/09
Storage : Room temperature and humidity.

<table>
<thead>
<tr>
<th>Identity</th>
<th>Description</th>
<th>Sample Preparation</th>
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<tr>
<td>RI104978</td>
<td>Opaque lotion</td>
<td>Shaken well and used as received.</td>
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</table>

POSITIVE CONTROL

Identity : 0.3% Triton® X-100, MatTek, Lot #10509TTA
Provided by : MB Research Laboratories
Date Received : 01/27/09
Expiration Date : 08/11/09
Storage : Refrigerated at approximately 4°C.
Description : Clear liquid
Sample Preparation : Used as received.
MB Research Laboratories

Study Title: MatTek EpiOcular Assay
Project #: MB 09-17849.19
Protocol: 720-03

NEGATIVE CONTROL
Identity: Tissue culture water, Sigma, Lot #097K2343 (TCH₂O)
Provided by: MB Research Laboratories
Date Received: 04/17/08
Expiration Date: 09/09
Storage: Room temperature and humidity
Description: Clear liquid
Sample Preparation: Used as received.

INTERNAL CONTROL
Identity: PC-17:1047L, Lot #1047L
Provided by: MB Research Laboratories
Date Received: 07/09/08
Expiration Date: 04/10
Storage: Room temperature and humidity
Description: Off-white cream
Sample Preparation: Used as received.

TEST DATES
Study Initiation (date protocol signed): 01/23/09
Experimental Start Date (1st exposure to test substance): 01/28/09
Experimental Term Date (last date data collected): 01/30/09
Final Report Signed (study completion): 02/04/09
EXPERIMENTAL DESIGN

EpiOcular™ Tissue Samples:
EpiOcular™ tissues, Lot 10362 Kits L & M, were received from MatTek on 01/27/09 and refrigerated until used. Before use, tissues were incubated (37°C ± 1°C, 5% ± 1% CO₂) with assay medium (MatTek) for a one-hour equilibration. Equilibration medium was replaced with fresh medium before dosing.

Reduction of MTT:
100 µl of the test article were mixed with 1 ml of the MTT (Methyl thiazole tetrazolium) solution. A negative control, 100 µl of tissue culture water, was tested concurrently. The solutions were incubated at room temperature in the dark for 60 minutes. After incubation, the solutions were visually inspected for purple coloration, which indicates that the test article converted MTT. Since tissue viability is based on MTT conversion, direct conversion by a test article can exaggerate viability, making a test article seem less irritating than it really is. None of the test articles were found to have converted MTT and the assay continued as per the protocol.

Dosing:
At the request of the sponsor, the test articles were dosed neat. 100 µl of the test article were applied to the top of each EpiOcular™ tissue. Three exposure times (64, 256 and 1200 minutes) were chosen by the sponsor for each test article. Duplicate EpiOcular™ tissues were exposed to the test article for the specified time. At the request of the sponsor, an internal control identified as "PC-17:1047L" was used to treat duplicate tissues at 64, 256 and 1200 minutes. A negative control assay was tested in duplicate using sterile, deionized tissue culture water for 16 minutes. A positive control (0.3% Triton® X-100) was tested in duplicate at 15 and 45 minutes.

MTT Conversion:
At the end of the selected exposure periods, each EpiOcular™ tissue was rinsed with PBS, soaked for 10 minutes in assay media and transferred to a 24-well plate containing 300 µl of MTT solution (1 mg/ml Methyl thiazole tetrazolium diluted in Dulbecco’s Modified Eagle’s Medium (DMEM)), provided by MB Research. The tissues were then returned to the incubator for a three-hour MTT incubation period.

Following the MTT incubation period, each EpiOcular™ tissue was rinsed and then treated overnight with 2.0 ml of extractant solution. An aliquot of the extracted MTT formazan was measured at 540 nm using a plate reader, subtracting the absorbance at a reference wavelength of 690 nm.
MB Research Laboratories

Analysis of Data:
The mean absorbance value for each time point was calculated from the optical density (OD) of the duplicate samples and expressed as percent viability for each sample using the following formula:

\[ \% \text{ viability} = 100 \times \frac{\text{OD sample}}{\text{OD negative control}} \]

The \( ET_{50} \), the time at which the EpiOcular™ tissue viability was reduced 50\% compared to control tissues, was then determined using a macro in Microsoft Excel 5.0, provided by MatTek, using the equation:

\[ V = a + b \log t \]

Where \( V \) = percentage viability, \( t \) = time in minutes, and \( a \) and \( b \) are constants that can be determined by using the viability data for two different exposure times of the test article to the tissue. These exposure times must yield viabilities that flank 50\%.

Correlation of \textit{In vitro} and \textit{In vivo} Results:
As per MatTek, as a general guideline, the following groups can be used to assign expected \textit{in vivo} irritancy responses\(^1\) based on the \( ET_{50} \) results obtained using the EpiOcular™ MTT Viability Assay:

<table>
<thead>
<tr>
<th>Draize Score</th>
<th>Irritancy Classification</th>
<th>Example</th>
<th>EpiOcular™ ( ET_{50} ) (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Standard Method</td>
</tr>
<tr>
<td>0 - 15</td>
<td>Non-Irritating, Minimal</td>
<td>PEG-75 Lanolin, Tween(^*) 20</td>
<td>&gt; 60</td>
</tr>
<tr>
<td>16.1 - 26</td>
<td>Mild</td>
<td>3% SodiumDodecyl Sulfate</td>
<td>30-60</td>
</tr>
<tr>
<td>25.1 - 50</td>
<td>Moderate</td>
<td>5% Triton(^*) X-100</td>
<td>3-29.99</td>
</tr>
<tr>
<td>50.1 - 110</td>
<td>Severe, Extreme</td>
<td>5% Benzalkonium Chloride</td>
<td>&lt; 3</td>
</tr>
</tbody>
</table>

These groups are based on correlation with an analysis of historical animal test data\(^2\) using the following equation derived by MatTek:

\[ \text{Draize} = -4.74 + \left(101.7 \div ET_{50} \right) \]

---


RetentionPolicy:
Upon signing the final report, all raw data, supporting documentation and reports are submitted to the Archivist by the Study Director. The raw data is filed at MB Research by project number. The final report is filed at MB Research by sponsor name and MB project number.

All data generated during the conduct of this study are archived at MB Research for at least 10 years from the date of the final report. The Sponsor will be contacted in writing to determine final disposition of the records. If the Sponsor fails to respond within 90 days, the archived items will be properly discarded. Any remaining test article will be discarded upon submission of the report.
RESULTS AND DISCUSSION

The test articles provided by [redacted] were tested using the MalTek EpiOcular™ MTT Viability Assay (see Appendix A for data). At the request of the sponsor, the test articles were dosed neat. The ET<sub>50</sub> scores were converted to a Draize score grouping and irritancy classification using the Standard Method. The ET<sub>50</sub> of the positive control 0.3% Triton® X-100, was 27.5, which fell within MalTek's acceptance range of 12.2 - 37.5 minutes.

The summarized data and irritation classifications are as follows:

<table>
<thead>
<tr>
<th>Test Article Identity</th>
<th>ET&lt;sub&gt;50&lt;/sub&gt; (mL)</th>
<th>Irritancy Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>R104978</td>
<td>725.9</td>
<td>Non-Irritating, Minimal</td>
</tr>
<tr>
<td>PC-17:1047L (Internal Control)</td>
<td>438.1</td>
<td>Non-Irritating, Minimal</td>
</tr>
<tr>
<td>0.3% Triton® X-100 (Positive Control)</td>
<td>27.5</td>
<td>Within Range (12.2 - 37.5)</td>
</tr>
</tbody>
</table>

FINAL REPORT

Approved by: [Signature]
Michelle Plehl, Ph.D
Study Director
MB Research Laboratories

Study Title: MatTek EpiOcular Assay
Project #: MB 09-17849.19
Protocol: 720-03

APPENDIX A

EXPERIMENTAL DATA

<table>
<thead>
<tr>
<th>Test Article:</th>
<th>RF104978</th>
<th>dose: 100 µl</th>
<th>conc: Neat</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIME (min)</td>
<td>OD 1</td>
<td>OD 2</td>
<td>MEAN (OD)</td>
</tr>
<tr>
<td>64.0</td>
<td>1.348</td>
<td>1.571</td>
<td>1.460</td>
</tr>
<tr>
<td>256.0</td>
<td>1.550</td>
<td>1.469</td>
<td>1.510</td>
</tr>
<tr>
<td>1200.0</td>
<td>0.359</td>
<td>0.306</td>
<td>0.333</td>
</tr>
<tr>
<td>neg control</td>
<td>1.458</td>
<td>1.406</td>
<td>1.431</td>
</tr>
</tbody>
</table>

ET₅₀ (min) 725.9

Irritancy Classification: Non-Irritating, Minimal
### APPENDIX A (cont’d)

#### EXPERIMENTAL DATA (cont’d)

<table>
<thead>
<tr>
<th>Internal Control:</th>
<th>PC17:1047L</th>
<th>dose: 100 µl</th>
<th>conc: Neat</th>
<th>TIME (min)</th>
<th>OD 1</th>
<th>OD 2</th>
<th>MEAN (OD)</th>
<th>SD</th>
<th>VIABILITY %</th>
<th>ERROR %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>64.0</td>
<td>1.518</td>
<td>1.551</td>
<td>1.535</td>
<td>0.023</td>
<td>107.2</td>
<td>1.6</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>256.0</td>
<td>1.032</td>
<td>1.116</td>
<td>1.074</td>
<td>0.059</td>
<td>75.1</td>
<td>4.2</td>
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<td></td>
<td></td>
<td>1200.0</td>
<td>0.032</td>
<td>0.037</td>
<td>0.035</td>
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<td>0.2</td>
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<tr>
<td>neg control</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.456</td>
<td>1.406</td>
<td>1.431</td>
<td>0.035</td>
<td>100.0</td>
<td>2.5</td>
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</table>

**ET<sub>50</sub> (min)** 436.1

**Irritancy Classification:** Non-Irritating, Minimal

<table>
<thead>
<tr>
<th>Positive Control:</th>
<th>0.3% Triton X-100</th>
<th>dose: 100 µl</th>
<th>conc: Neat</th>
<th>TIME (min)</th>
<th>OD 1</th>
<th>OD 2</th>
<th>MEAN (OD)</th>
<th>SD</th>
<th>VIABILITY %</th>
<th>ERROR %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
<td>15.0</td>
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<td>71.5</td>
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<td>0.446</td>
<td>0.464</td>
<td>0.025</td>
<td>32.4</td>
<td>1.8</td>
</tr>
<tr>
<td>neg control</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.456</td>
<td>1.406</td>
<td>1.431</td>
<td>0.035</td>
<td>100.0</td>
<td>2.5</td>
</tr>
</tbody>
</table>

**ET<sub>50</sub> (min)** 27.5

**Irritancy Classification:** Within Range (12.2-37.5)
MB Research Laboratories

Study Title: MatTek EpiOcular Assay
Project # : MB 09-17849.19
Protocol : 720-03

QUALITY ASSURANCE EVALUATION

The Quality Assurance Unit has inspected a critical phase of this study, audited the raw data and the report and determined that the methods and results contained herein accurately reflect the raw data. A summary of the compliance inspections is presented below.

<table>
<thead>
<tr>
<th>Date of Inspection</th>
<th>Phase</th>
<th>Performed By</th>
<th>Date Inspection Results Reviewed</th>
</tr>
</thead>
<tbody>
<tr>
<td>01/28/09</td>
<td>Dose Administration</td>
<td>Whitney Williams</td>
<td>02/02/09 01/30/09</td>
</tr>
<tr>
<td>02/02/09</td>
<td>Raw data audit</td>
<td>Whitney Williams</td>
<td>02/02/09 02/02/09</td>
</tr>
<tr>
<td>02/04/09</td>
<td>Final report audit</td>
<td>Whitney Williams</td>
<td>02/04/09 02/04/09</td>
</tr>
</tbody>
</table>

Whitney Williams, B.S.
Quality Assurance Unit

Date 2/5/09

1765 Wentz Road, Post Office Box 178, Spinstersown, PA 19988
Phone: (215) 536-4110  Fax: (215) 536-1818
KGL Inc.

FINAL REPORT dated May 11, 2009
KGL Protocol: #6763
Sample: Liquid Blend

www.kgl-inc.com or www.ivylabs.com

Ivy Laboratories (KGL, INC.)
505 Parkway
Broomall, PA 19008-4204 (USA)

Telephone: [215] 387-8400
Fax: [215] 387-1046

E-mail address: ivystudies@verizon.net

Title: An Evaluation of the Contact-Sensitization Potential of a Topical Coded Product in Human Skin by means of the Maximization Assay

Sponsor:

Principal Investigator: Kays Kaldbey, M.D. (Board Certified Dermatologist)

Testing Facility: Ivy Laboratories (KGL, INC.)
505 Parkway
Broomall, PA 19008-4204 (USA)
(Phone: 215-387-8400)
(FAX: 215-387-1046)

Final Report Date: May 11, 2009

Kays Kaldbey, M.D.
Principal Investigator

"The names of Ivy Laboratories (KGL, INC.), any officer, employee, or collaborating scientist are not to be used for any advertising, promotional or sale purposes without the written consent of Ivy Laboratories (KGL INC)."
F I N A L R E P O R T

STUDY TITLE:

An assessment of the contact-sensitizing potential of a coded topically-applied test agent using a Human Maximization Assay.

KGL PROTOCOL:

Ivy Laboratories - KGL Protocol #6763

GUIDELINES FOR THE CONDUCT OF THE STUDY:

All procedures were conducted in compliance with the regulations of the Food and Drug Administration (FDA) (21 CFR 50, 56, 312) ICH-GCP Consolidated Guidelines, May 9, 1997 Federal Register) and in accordance with KGL's Standard Operating Procedures (SOP's).

STUDY OBJECTIVE:

The objective of this study was to assess the skin sensitizing potential of any preparation designed for topical use by means of the Maximization Test (see references #1 and #2).

DESIGN RATIONALE:

A repeat insult patch test wherein the test product was applied under an occlusive dressing to an SLS (sodium lauryl sulfate) pre-treated site on the upper outer arm repeatedly to the same designated area for five 48-hour induction periods followed 7-10 days later by a single challenge to a naïve skin site on the opposite outer arm.

STUDY SPONSOR:

[Redacted]

SPONSOR STUDY:

Commitment Letter dated March 25, 2009
TESTING FACILITY:
Ivy Laboratories (KGL INC.)
505 Parkway
Broomall, PA 19008-4204 (USA)
Telephone: Philadelphia - (215-387-8400) – Broomall (610-544-1715)
E-mail: ivystudies@verizon.net

PRINCIPAL INVESTIGATOR:
Kays Kaidbey, M.D. (Board Certified Dermatologist)
Medical Director, KGL, INC.
Telephone: (215) 387-8400
FAX: (215) 397-1046
E-mail address: ivystudies@verizon.net

KGL ADMINISTRATIVE STRUCTURE:
Diane Kozubal  (Panel Recruitment/Initial Screening)
Jane Chitwood  (Technician /Patch Applications/Removals/Recognize/Report AE's)
John B. Chicchi  (Evaluator)
Mary J. Massing  (Quality Assurance)

INFORMED CONSENT:
Prior to acceptance into the study, each subject was informed by the investigator or his
designee of the nature and purpose of the study, possible side-effects and any other
relevant information. The study procedures and possible risks and discomfort were
explained to each panelist during the interview using popular understandable language
and terms, and the panelists were encouraged to ask questions regarding the study. Each
interviewed panelist who qualified was then asked to read and sign the consent form prior
to enrollment. Copies of all consent forms are on file at KGL, Inc.

CONDUCTION DATES:
This study was conducted between March 30, 2009 and May 1, 2009
TEST MATERIAL:
The test product labeled Liquid Blend and coded [REDACTED] was supplied by the sponsor (1 jar) and tested as supplied viz. neat. The test product was shaken well prior to each application.

TEST PRODUCT ACCOUNTABILITY:
The test sample was received in good condition by our Quality Assurance Department. The test material was checked for (1) amount (2) product number or code (3) material container etc. The material was individually listed on a special sheet (drug/test product log form) signed by the receiver, the laboratory supervisor and the investigator (physician). The test sample was stored under ambient conditions in an inaccessible location under the supervision of the investigator.

DISPOSITION OF REMAINING CLINICAL SUPPLIES:
All remaining test material(s) will be disposed of in accordance with applicable governmental regulations following submission of the final written report or returned to the Sponsor via a traceable method, if requested.

PANEL COMPOSITION:
Healthy, adult volunteers over the age of 18 years were recruited for this study. Panelists had no blemishes, excess hair or other marks on their upper outer arms that would obscure grading of the test site. Both male and female panelists were eligible. None of the subjects had a medical or dermatological illness and none were sensitive to sunscreens or to topical preparations and/or cosmetics. A completed subject was a subject who satisfied the admission criteria and who completed the scheduled study procedures.

Inclusion Criteria:
1. Healthy adult male and female volunteers between the ages of 18 and 85 years.
2. All subjects who were willing to follow the study requirements and voluntarily gave their informed consent.
Exclusion Criteria:

1. Subjects with any significant internal diseases e.g., cardiac, pulmonary, renal, hepatic, etc.
2. History of allergy or hypersensitivity to cosmetics, toiletries or other dermatological products
3. History of recurrent dermatological diseases, e.g., psoriasis, atopic eczema, chronic urticaria
4. Pregnancy or mothers who are breastfeeding or planning a pregnancy
5. Scars, moles or other blemishes over the upper arm(s) or back which can interfere with the study
6. Subjects receiving systemic or topical drugs or medications which can interfere with delayed immunologic responses e.g., corticosteroids, non-steroidal anti-inflammatories, retinoids, immunosuppressants
7. Other conditions considered by the investigator as sound reasons for disqualification from enrollment into the study

SUBJECT ASSIGNMENT:
Volunteer subjects were screened and selected as described above and assigned a study number. The initials of each subject accepted into the study were recorded sequentially as they were enrolled.

RECORDING OF DATA:
The case report forms (CRF's) for this study were provided by the Investigator. All case report forms were completed in actual time, during each subject's visit. Copies of the CRF's will be retained by the investigator along with the original signed informed consent forms.

HANDLING OF STUDY DOCUMENTS:
All study related documents, case report forms (CRF's), original informed subject consent forms and any data generated were kept under secure lock in the technician's office for the duration of the study.
STUDY PROCEDURES:
Method and Procedures\textsuperscript{(1,2)}
Patches were applied to the upper outer arm of each subject. The entire test was composed of three distinct phases: (1) an Induction phase and (2) a Rest Phase and (3) a Challenge phase.

(1) **Induction Phase:**
Approximately 0.05ml of aqueous SLS (0.25\%) was applied to a designated site under a 15mm disc of Webril cotton cloth and the patch was fastened to the skin with occlusive tape for a period of 24 hours. After 24 hours, the SLS patch was removed and 0.05ml of the test material was applied to the same site before the site was again covered with occlusive tape (induction patch). The induction patch was left in place for 48 hours (or for 72 hours when placed over a weekend) following which it was removed and the site again examined for irritation. If no irritation was present, a 0.25\% aqueous SLS patch was again reapplied to the same site for 24 hours, followed by reaplication of a fresh induction patch with the test material to the same site. This sequence viz. 24 hour SLS pre-treatment followed by 48 hours of test material application was continued for a total of 5 induction exposures.

If irritation developed at any time-point during the induction phase as previously outlined, the 24-hour SLS pre-treatment patch was eliminated and only the test material was reapplied to the same site after a 24-hour rest period during which no patch was applied.

The aim during this phase of the study was to maintain at least a minimal degree of irritation in order to enhance penetration through the corneum barrier.

(2) **Rest Period:**
No exposure to the test material was made during this rest period, which lasted for 10 days after the last induction patch.
(3) **Challenge Phase:**
After a ten day rest period, the subjects were challenged with a single application of the test material to a new skin site on the opposite upper outer arm in order to determine if sensitization had developed.

Pre-treatment with SLS was performed prior to challenge. Approximately 0.05ml of a 5.0% aqueous solution was applied to a fresh skin site under a 15mm disc of Webril cotton and covered with occlusive tape. The SLS patch was left in place for one hour. It was then removed and 0.05ml of the test material was applied to the same site, as outlined above. The challenge patch was then covered by occlusive tape and left in place for 48 hours. After that period, the patch was removed and the site graded 15-30 minutes later and again 24 hours later for any reaction.

**SCORING SCALE:**
0 = not sensitized
1 = mild sensitization (viz. erythema and a little edema)
2 = moderate sensitization (erythema with infiltration, raised, spreading beyond the borders of the patch, with or without vesiculation)
3 = strong sensitization (large vesiculo-bullous reaction).

Based on these findings the number of subjects with positive responses were tabulated for the test material. The test system shown below was used to classify the allergenic potential of the test substance.

<table>
<thead>
<tr>
<th>SENSITIZATION RATES:</th>
<th>GRADES:</th>
<th>CLASSIFICATION:</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 2/25</td>
<td>1</td>
<td>Weak</td>
</tr>
<tr>
<td>3 - 7/25</td>
<td>2</td>
<td>Mild</td>
</tr>
<tr>
<td>8 - 13/25</td>
<td>3</td>
<td>Moderate</td>
</tr>
<tr>
<td>14 - 20/25</td>
<td>4</td>
<td>Strong</td>
</tr>
<tr>
<td>21 - 25/25</td>
<td>5</td>
<td>Extreme</td>
</tr>
</tbody>
</table>
ADVERSE EXPERIENCES:
No adverse experiences or unanticipated reactions were encountered or reported by any of the panelists.

RESULTS:
A total of twenty-seven (27) healthy, adult, volunteers who satisfied the inclusion criteria were enrolled into this study. There were 21 females and 6 males. Their ages ranged from 18 to 64 years. All 27 volunteers completed this investigation, as outlined in the standard protocol. The demographic data are shown in Table 1. No adverse or unexpected reactions were seen in any of the panelists during the induction phase.

The results of the challenge are shown in the enclosed table (Table 2). No instances of contact allergy were recorded at either 48 or 72 hours after the application of the challenge patches.

CONCLUSION:
Under the conditions of this test, the test sample labeled Liquid Blend does not possess a detectable contact-sensitizing potential and hence is not likely to cause contact sensitivity reactions under normal use conditions.
References:


### TABLE 1

**DEMOGRAPHIC DATA**

<table>
<thead>
<tr>
<th>Subject Number</th>
<th>Subject Initials</th>
<th>Age</th>
<th>Sex</th>
<th>Race</th>
</tr>
</thead>
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<td>01</td>
<td>C-H</td>
<td>18</td>
<td>F</td>
<td>C</td>
</tr>
<tr>
<td>02</td>
<td>L-G</td>
<td>50</td>
<td>F</td>
<td>C</td>
</tr>
<tr>
<td>03</td>
<td>E-R</td>
<td>61</td>
<td>M</td>
<td>C</td>
</tr>
<tr>
<td>04</td>
<td>V-B</td>
<td>49</td>
<td>M</td>
<td>C</td>
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<td>S-D</td>
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<td>C</td>
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<td>J-E</td>
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<td>C</td>
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<td>K-F</td>
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<td>C</td>
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<td>C</td>
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<td>S-F</td>
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<td>F</td>
<td>C</td>
</tr>
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<td>V-B</td>
<td>46</td>
<td>F</td>
<td>C</td>
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<td>R-M</td>
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<td>K-K</td>
<td>25</td>
<td>F</td>
<td>C</td>
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<tr>
<td>24</td>
<td>K-D</td>
<td>18</td>
<td>F</td>
<td>C</td>
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<tr>
<td>25</td>
<td>M-A</td>
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<td>C</td>
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<td>D-A</td>
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<td>C</td>
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<td>27</td>
<td>C-R</td>
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<td>C</td>
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</table>

C = Caucasian
TABLE 2

MAXIMIZATION TESTING RESULTS

Sample: Liquid Blend

<table>
<thead>
<tr>
<th>Subject Number</th>
<th>48-Hour Grading</th>
<th>72-Hour Grading</th>
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</thead>
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<tr>
<td>01</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>02</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
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Challenge Readings:

48-Hour Reading – April 30, 2009
72-Hour Reading – May 1, 2009
Memorandum

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

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

DATE: August 26, 2019

SUBJECT: Polysilicone-11

FINAL REPORT

CLINICAL SAFETY EVALUATION
REPEATED INSULT PATCH TEST
product containing 1.45% poly silicon 11

Sponsor

Sponsor Representative

Clinical Testing Facility

Sponsor Code:
Panel No.: 
Entry No.: 
Project No.: 

Date of Final Report

9-6-12

Fax #
SIGNATURE PAGE

CLINICAL SAFETY EVALUATION

REPEATED INSULT PATCH TEST

Laboratory Manager
Study Director

Scientific Director
Principal Investigator

Board-Certified Dermatologist
Medical Investigator

Date

5/July/12

Date

2/6/12

Date

2/6/12
QUALITY ASSURANCE STATEMENT

This study Panel No.: Entry No.: was conducted in accordance with the intent and purpose of Good Clinical Practice regulations described in 21 CFR Part 50 (Protection of Human Subjects – Informed Consent) and the Standard Operating Procedures of.

For purposes of this clinical study:

- [X] Informed Consent was obtained.
- [ ] Informed Consent was not obtained.
- [X] An IRB review was not required.
- [ ] An IRB review was conducted and approval to conduct the proposed clinical research was granted.

To assure compliance with the study protocol, the Quality Assurance Unit completed an audit of the applicable study records and report. This report is considered a true and accurate reflection of the testing methods and source data.

[Signature]
Manager, Quality Assurance

[Signature]
Date: July 2012
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4.0 CLINICAL INVESTIGATORS ................................................................... 1
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TABLE 1 - INDIVIDUAL SCORES
CLINICAL SAFETY EVALUATION

REPEATED INSULT PATCH TEST

1.0 OBJECTIVE

The objective of this study was to determine the irritation and/or sensitization potential of the test article after repeated application under occlusive patch test conditions to the skin of human subjects (non-exclusive panel).

2.0 SPONSOR

2.1 Sponsor Representative

3.0 CLINICAL TESTING FACILITY

The study was conducted by:

4.0 CLINICAL INVESTIGATORS

Study Director: [Redacted]
Principal Investigator: [Redacted], PhD, DABT, BCPE
Medical Investigator: [Redacted], Board-Certified Dermatologist

5.0 STUDY DATES

Study initiation: May 16, 2012
Final evaluation: June 22, 2012
6.0 ETHICS

6.1 Ethical Conduct of the Study

This study was conducted in accordance with the intent and purpose of Good Clinical Practice regulations described in Title 21 of the U.S. Code of Federal Regulations (CFR), the Declaration of Helsinki and/or Standard Operating Procedures.

6.2 Subject Information and Consent

This study was conducted in compliance with CFR Title 21, Part 50 (Informed Consent of Human Subjects). Informed Consent was obtained from each subject in the study and documented in writing before participation in the study. A copy of the informed Consent was provided to each subject.

7.0 TEST MATERIAL

The test article used in this study was provided by:

It was received on May 14, 2012 and identified as follows:

<table>
<thead>
<tr>
<th>Entry No.</th>
<th>Test Article I.D.</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Pale Yellow Semi-Solid</td>
</tr>
</tbody>
</table>

8.0 TEST SUBJECTS

At least 50 male and female subjects ranging in age from 18 to 79 years were to be empanelled for this test.

The subjects chosen were to be dependable and able to read and understand instructions. The subjects were not to exhibit any physical or dermatologic condition that would have precluded application of the test article or determination of potential effects of the test article.
9.0 TEST PROCEDURE

The 9 Repeated Insult (occlusive) Patch Test (9-RIPT)\(^1\) was conducted as follows:

9.1 Induction Phase

A sufficient amount of the test article (approximately 0.1 g – 0.15 g) was placed onto a Parke-Davis Readi-Bandage\(^\circledR\) occlusive patch (approximately 25 - 38 mg/cm\(^2\) of test material) and applied to the back of each subject between the scapulae and waist, adjacent to the spinal mid-line. This procedure was performed by a trained technician/examiner and repeated every Monday, Wednesday and Friday until 9 applications of the test article had been made.

The subjects were instructed to remove the patch 24 hours after application. Twenty-four hour rest periods followed the Tuesday and Thursday removals and 48-hour rest periods followed each Saturday removal. Subjects returned to the Testing Facility and the site was scored by a trained examiner just prior to the next patch application.

If a subject developed a positive reaction of a level 2 erythema or greater during the Induction phase or if, at the discretion of the Study Director, the skin response warranted a change in site, the patch was applied to a previously unpatched, adjacent site for the next application. If a level 2 reaction or greater occurred at the new site, no further applications were made. However, any reactive subjects were subsequently Challenge patch tested.

9.2 Challenge Phase

After a rest period of approximately 2 weeks (no applications of the test article), the Challenge patch was applied to a previously unpatched (virgin) test site. The site was scored 24 and 72 hours after application. All subjects were instructed to report any delayed skin reactivity that occurred after the final Challenge patch reading. When warranted, selected test subjects were called back to the Clinic for additional examinations and scoring to determine possible increases or decreases in Challenge patch reactivity.

Dermal responses for both the Induction and Challenge phases of the study were scored according to the following 6-point scale:

0 = No evidence of any effect
+ = Barely perceptible (Minimal, faint, uniform or spotty erythema)
1 = Mild (Pink, uniform erythema covering most of the contact site)
2 = Moderate (Pink-red erythema uniform in the entire contact site)
3 = Marked (Bright red erythema with/without petechiae or papules)
4 = Severe (Deep red erythema with/without vesiculation or weeping)

All other observed dermal sequelae (e.g., edema, dryness, hypo- or hyperpigmentation) were appropriately recorded on the data sheet and described as mild, moderate or severe.

9.0 TEST PROCEDURE (CONT'D)

9.3 Data Interpretation

Edema, vesicles, papules and/or erythema that persist or increase in intensity either during the Induction and/or Challenge phase may be indicative of allergic contact dermatitis. Allergic responses normally do not resolve or improve markedly at 72-96 hours.

Exceptions to typical skin reactions may occur. These may include, but not be limited to, symptoms of allergic contact sensitivity early in the Induction period to one or more test products. When this occurs in one subject, such a reaction usually suggests either an idiosyncratic response or that the subject had a pre-exposure/sensitization to the test material or component(s) of the test material or a cross-reactivity with a similar product/component. Data for such reactions will be included in the study report but will not be included in the final study analysis/conclusion of sensitization.

10.0 RESULTS AND DISCUSSION

(See Table 1 for Individual Scores)

A total of 58 subjects (13 males and 45 females ranging in age from 19 to 73 years) were empanelled for the test procedure. Fifty-four (54/58) subjects satisfactorily completed the test procedure on Test Article: [Redacted]. Four (4/58) subjects discontinued for personal reasons unrelated to the conduct of the study. Discontinued subject data are shown up to the point of discontinuation, but are not used in the Conclusions section of this final report.

Induction Phase Summary

<table>
<thead>
<tr>
<th>Test Article</th>
<th>Induction Scores (Number of Responses)</th>
<th>Evidence of Irritation</th>
</tr>
</thead>
<tbody>
<tr>
<td>[Redacted]</td>
<td>0 0 0 0 0 Other</td>
<td>No</td>
</tr>
</tbody>
</table>

Challenge Phase Summary

<table>
<thead>
<tr>
<th>Test Article</th>
<th>Challenge Scores (Number of Responses)</th>
<th>Evidence of Sensitization</th>
</tr>
</thead>
<tbody>
<tr>
<td>[Redacted]</td>
<td>0 0 0 0 0 Other</td>
<td>No</td>
</tr>
</tbody>
</table>

There was no skin reactivity observed at any time during the course of the study.

11.0 CONCLUSIONS

Under the conditions of a repeated insult (occlusive) patch test procedure conducted in 54 subjects, Test Article: [Redacted] was "Dermatologist-Tested" and was not associated with skin irritation or allergic contact dermatitis in human subjects.
### TABLE 1

**INDIVIDUAL SCORES**

**REPEATED INSULT PATCH TEST - OCCLUSIVE**

Test Article:  

<table>
<thead>
<tr>
<th>Subj. No.</th>
<th>Induction Evaluation Number</th>
<th>Challenge Virgin Site</th>
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</thead>
<tbody>
<tr>
<td>1</td>
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<td>2</td>
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</table>

Scale:  
- 0 = No evidence of any effect  
- + = Barely perceptible (Minimal, faint, uniform or spotty erythema)  
- 1 = Mild (Pink, uniform erythema covering most of the contact site)  
- 2 = Moderate (Pink-red erythema uniform in the entire contact site)  
- 3 = Marked (Bright red erythema with/without petechiae or papules)  
- 4 = Severe (Deep red erythema with/without vesiculation or weeping)
## TABLE 1 (CONT'D)

### INDIVIDUAL SCORES

#### REPEATED INSULT PATCH TEST - OCCLUSIVE

<table>
<thead>
<tr>
<th>Subj. No.</th>
<th>Induction Evaluation Number</th>
<th>Challenge Virgin Site</th>
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<tbody>
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</table>

Scale: 0 = No evidence of any effect  
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1 = Mild (Pink, uniform erythema covering most of the contact site)  
2 = Moderate (Pink-red erythema uniform in the entire contact site)  
3 = Marked (Bright red erythema with/without petechiae or papules)  
4 = Severe (Deep red erythema with/without vesiculation or weeping)
## Concentration of Use by FDA Product Category – Polysilicone-11

<table>
<thead>
<tr>
<th>Product Category</th>
<th>Maximum Concentration of Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eye shadows</td>
<td>2.3-9.4%</td>
</tr>
<tr>
<td>Eye lotions</td>
<td>1.5-12.2%</td>
</tr>
<tr>
<td>Mascaras</td>
<td>0.59%</td>
</tr>
<tr>
<td>Other eye makeup preparations</td>
<td>0.24%</td>
</tr>
<tr>
<td>Tonics, dressings and other hair grooming aids</td>
<td>0.48%</td>
</tr>
<tr>
<td>Blushers</td>
<td>2.4-4.9%</td>
</tr>
<tr>
<td>Face powders</td>
<td>0.025-3.5%</td>
</tr>
<tr>
<td>Foundations</td>
<td>0.48-14.4%</td>
</tr>
<tr>
<td>Lipstick</td>
<td>7.2-8.8%</td>
</tr>
<tr>
<td>Makeup bases</td>
<td>0.65%</td>
</tr>
<tr>
<td>Makeup fixatives</td>
<td>1.8%</td>
</tr>
<tr>
<td>Aftershave lotions</td>
<td>1.4%</td>
</tr>
<tr>
<td>Skin cleansing (cold creams, cleansing lotions, liquids and pads)</td>
<td>0.061%</td>
</tr>
<tr>
<td>Face and neck products</td>
<td></td>
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<tr>
<td>Not spray</td>
<td>0.08-35%</td>
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<tr>
<td>Body and hand products</td>
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<tr>
<td>Not spray</td>
<td>2.5-12.5%</td>
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<td>Moisturizing products</td>
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<td>Not spray</td>
<td>0.25%</td>
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<tr>
<td>Paste masks and mud packs</td>
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<tr>
<td>Other skin care preparations</td>
<td>6.8-19.9%</td>
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<td>Suntan products</td>
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<td>Not spray</td>
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<td>Pump spray</td>
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<tr>
<td>Indoor tanning preparations</td>
<td>0.47%</td>
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Information collected in 2018
Table prepared May 31, 2018