Safety Assessment of Fluoropolymers as Used in Cosmetics

Status: Draft Report for Panel Review
Release Date: February 9, 2018
Panel Date: March 5-6, 2018
Memorandum

To: CIR Expert Panel Members and Liaisons
From: Wilbur Johnson, Jr.
Senior Scientific Analyst
Date: February 9, 2018
Subject: Draft Report on Fluoropolymers

A Scientific Literature Review (SLR) on Fluoropolymers was issued on January 8, 2018. The attached use concentration data (fluoro032018data1 and fluoro032018data2) that are included in this draft report were received from the Personal Care Products Council (Council) prior to issuance of the SLR. Data relating to the skin irritation and sensitization potential and ocular irritation potential of formulas containing PTFE (fluoro032018data3) and report comments (fluoro032018pcpc1) were received from the Council after the SLR was issued. These data are included in the draft report, and the Council’s comments have been addressed.

Additionally, a memorandum with report comments (fluoro032018pcpc2) was received from the Cosmetic Ingredient Review (CIR) Science and Support Committee of the Council. This memorandum states that further justification for the current grouping of ingredients for review (generated by CIR staff) in this safety assessment is needed. Furthermore, the memorandum states that the appropriateness of using data on one ingredient to support the safety of other ingredients in the safety assessment is not clear and requires further discussion within the report, that is, if all of the other ingredients remain in a single report. These issues will need to be addressed by the Panel.

Also included in this package for your review are the Draft Report (fluoro032018rep), the CIR report history (fluoro032018hist), Flow chart (fluoro032018flow), Literature search strategy (fluoro032018strat), Ingredient data profile (fluoro032018prof), and 2017 FDA VCRP data (fluoro032018FDA).

No studies on PTFE, or other fluoropolymers that are being reviewed, relating to inhalation toxicity potential have been identified in the published literature. The National Toxicology Program (NTP) has evaluated the carcinogenicity of tetrafluoroethylene, the monomer that is used in the synthesis of PTFE, and the NTP’s conclusion is stated in the Carcinogenicity section of the safety assessment for the Panel’s consideration.

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. If the available data are insufficient, the Panel should issue an Insufficient Data Announcement (IDA), specifying the data needs therein.
CIR History of:

Fluoropolymers

A Scientific Literature Review (SLR) on Fluoropolymers was issued on January 8, 2018.

**Draft Report, Teams/Panel: March 5-6, 2018**

The draft report contains use concentration data on the fluoropolymers that were received from the Council. Skin irritation and sensitization data and ocular irritation data on formulas containing PTFE were also received, and these data are included in the draft report as well. Report comments that were received from the Council have been addressed. Comments relating to the need for further justification for the grouping of ingredients that are being reviewed in this safety assessment were received from the CIR Science and Support Committee of the Personal Care Products Council.
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PTFE

- Acrylates/Methoxy PEG-23 Methacrylate/Perfluorooctyl Ethyl Acrylate Copolymer
- Behenyl Methacrylate/Perfluorooctyl-ethyl Methacrylate Copolymer
- C6-14 Perfluoroalkylethyl Acrylate/HEMA Copolymer
- Hexafluoropropylene/tetrafluoroethylene Copolymer
- PEG-10 Acrylate/Perfluorohexylethyl Acrylate Copolymer
- Polychlorotrifluoroethylene
- Poly(perfluorooxymethyl)hexylmethacrylate Difluorocetyl PEG Dlisisostearate
- Poly(perfluorooxymethyl)hexylmethacrylate Difluorocetyl PEG Ether
- Polyfluorooxymethylhexylmethacrylate Difluorohydroxyethyl Ether
- Poly(perfluorooxymethyl)hexylmethacrylate Difluoromethyl Ether
- Stearyl Methacrylate/Perfluorooctyl-ethyl Methacrylate Copolymer

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### Search Strategy

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

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

InfoBase (self-reminder that this info has been accessed; not a public website) - [http://www.personalcarecouncil.org/science-safety/line-infobase](http://www.personalcarecouncil.org/science-safety/line-infobase)

Scifinder (usually a combined search for all ingredients in report; list # of this/# useful) - [https://scifinder.cas.org/scifinder](https://scifinder.cas.org/scifinder)


Toxnet databases (usually a combined search for all ingredients in report; list # of this/# useful) – [https://toxnet.nlm.nih.gov/](https://toxnet.nlm.nih.gov/) (includes Toxline; HSDB; ChemIDPlus; DAR; IRIS; CCRIS; CPDB; GENE-TOX)


EU (European Union); check CosIng (cosmetic ingredient database) for restrictions and SCCS (Scientific Committee for Consumer Safety) opinions - [http://ec.europa.eu/growth/tools-databases/cosing/](http://ec.europa.eu/growth/tools-databases/cosing/)


HPVIS (EPA High-Production Volume Info Systems) - [https://ofmext.epa.gov/hpvis/HPVISlogo](https://ofmext.epa.gov/hpvis/HPVISlogo)


NTIS (National Technical Information Service) - [http://www.ntis.gov/](http://www.ntis.gov/)

NTP (National Toxicology Program ) - [http://ntp.niehs.nih.gov/](http://ntp.niehs.nih.gov/)


FEMA (Flavor & Extract Manufacturers Association) - [http://www.femaflavor.org/search/apachesolr_search/](http://www.femaflavor.org/search/apachesolr_search/)

Web – perform general search; may find technical data sheets, published reports, etc

ECETOC (European Center for Ecotoxicology and Toxicology Database) - [http://www.ecetoc.org/](http://www.ecetoc.org/)

**Botanical Websites, if applicable**

Dr. Duke’s [https://phytochem.nal.usda.gov/phytochem/search](https://phytochem.nal.usda.gov/phytochem/search)


GRIN (U.S. National Plant Germplasm System) - [https://npgsweb.ars-grin.gov/gringlobal/taxon/taxonomysimple.aspx](https://npgsweb.ars-grin.gov/gringlobal/taxon/taxonomysimple.aspx)


**Fragrance Websites, if applicable**


Distributed for comment only -- do not cite or quote
RIFM (the Research Institute for Fragrance Materials) should be contacted

Qualifiers
Absorption
Acute
Allergy
Allergic
Allergenic
Cancer
Carcinogen
Chronic
Development
Developmental
Excretion
Genotoxic
Irritation
Metabolism
Mutagen
Mutagenic
Penetration
Percutaneous
Pharmacokinetic
Repeated dose
Reproduction
Reproductive
Sensitization
Skin
Subchronic
Teratogen
Teratogenic
Toxic
Toxicity
Toxicokinetic
Toxicology
Tumor
Safety Assessment of Fluoropolymers as Used in Cosmetics

Status: Draft Report for Panel Review
Release Date: February 9, 2018
Panel Date: March 5-6, 2018

The 2018 Cosmetic Ingredient Review Expert Panel members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Ronald A. Hill, Ph.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; James G. Marks, Jr., M.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The CIR Executive Director is Bart Heldreth, Ph.D. This report was prepared by Wilbur Johnson, Jr., M.S., Senior Scientific Analyst.

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INTRODUCTION

The safety of the following 13 fluoropolymers in cosmetics is reviewed in this Cosmetic Ingredient Review (CIR) safety assessment.

PTFE
Acrylates/Methoxy PEG-23 Methacrylate/Perfluoroctyl Ethyl Acrylate Copolymer
Acrylates/Perfluorohexylethyl Methacrylate Copolymer
Behenyl Methacrylate/Perfluorooctylethyl Methacrylate Copolymer
C6-14 Perfluoroalkylethyl Acrylate/HEMA Copolymer
Hexafluoropropylene/Tetrafluoroethylene Copolymer
PEG-10 Acrylate/Perfluorohexylethyl Acrylate Copolymer
Polychlorotrifluoroethylene
Polyperfluoroethoxymethoxy Difluoroethyl PEG Disostearate
Polyperfluoroethoxymethoxy Difluoroethyl PEG Ether
Polyfluoroethoxymethoxy Difluorohydroxyethyl Ether
Polyperfluoroethoxymethoxy Difluoromethyl Ether
Stearyl Methacrylate/Perfluorooctylethyl Methacrylate Copolymer

According to the web-based International Cosmetic Ingredient Dictionary and Handbook (wINC Industry Dictionary), these fluoropolymers are reported to have the following functions in cosmetics: bulking agents, slip modifiers, film formers, viscosity increasing agents, dispersing agents, skin conditioning agents, skin protectants, and hair conditioning agents. Most of the ingredients have the film former function in common. Additionally, these ingredients share in common a fluorinated organic polymer backbone, wherein at least some of the carbon atoms in that backbone are perfluoronated. The non-fluorinated monomers utilized in the synthesis of the copolymers in this report, have also been utilized in the synthesis of ingredients the Panel has previously assessed for safety. The monomers comprising these fluoropolymers that have been evaluated for safety by the CIR Expert Panel are presented in Table 1.

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

CHEMISTRY

Definition and General Characterization

The definitions, structures, and functions in cosmetics of these ingredients are presented in Table 2. These ingredients share in common a fluorinated organic polymer backbone, wherein at least some of the carbons in that backbone are perfluoronated.

\[ \text{Figure 1. Fluoropolymers – wherein R and R' are fluorine, other monomers, or end-capping units} \]

For instance, PTFE is a perfluoronated homopolymer, comprising only carbon and fluorine.

\[ \text{Figure 2. Polyfluorotetraethylene (PTFE)} \]
However, most of these ingredients are copolymers and/or are end-capped.

![Figure 3. Polyafluoroethoxymethoxy Difluorohydroxyethyl Ether – comprising 2 perfluoronated monomers and end-capping units](image)

As will any polymeric ingredient, the number of monomeric repeat units (and thus polymeric size) and degree of linearity (i.e., branched or straight) have the potential to greatly impact the physical characteristics (e.g., matter phase, hardness, etc.) imbued on the moiety. Accordingly, size, distribution, and connectivity variations, as used in cosmetic ingredients, are important considerations for understanding the nature of these materials. For example, while PTFE is typically supplied as a very large, linear, solid polymer, one supplier indicates that a Polychlorotrifluoroethylene trade name material is defined as follows: a nonflammable fluid composed of chlorotrifluoroethylene oligomers of different carbon chain lengths (C₅ to C₉), primarily 6 (trimers) and 8 (tetramers) carbons.

**Chemical and Physical Properties**

Fluoropolymers such as PTFE and its copolymers are noted for high thermal stability. PTFE is a white translucent to opaque solid, ranging in molecular weight from 400,000 to 10,000,000 Daltons (Da). The densities of PTFE (2.25 g/cm³) and Polychlorotrifluoroethylene (2.10 to 2.15 g/cm³) are similar. According to the following values, the melting points of fluoropolymers can vary: Polychlorotrifluoroethylene (210 to 215°C), Hexafluoropropylene/Tetrafluoroethylene Copolymer (270°C), and PTFE (320 to 330°C). PTFE decomposes at 315 to 375°C, whereas, the decomposition of Polychlorotrifluoroethylene begins at ~ 220°C. Properties of fluoropolymers are presented in Table 3.

**Method of Manufacture**

**PTFE**

PTFE is prepared by the polymerization of tetrafluoroethylene. Because PTFE is poorly soluble in practically all solvents, the polymerization occurs as an emulsion in water. Alternatively, polymerization is carried out using a surfactant, such as perfluorooctanoic acid (PFOA).

**Polychlorotrifluoroethylene**

After polymerization, Polychlorotrifluoroethylene is endcapped with chlorine, so that the final product is a mixture of structural isomers where the terminal carbon atoms may have either one or two chlorine atoms.

**Composition**

**PTFE**

PTFE is composed of at least 20,000 C₂F₄ monomer units linked into very long unbranched chains.

**Polychlorotrifluoroethylene**

Polychlorotrifluoroethylene, a perhalogenated hydrocarbon, consists mainly, according to one supplier, of C-6 and C-8 oligomers of chlorotrifluoroethylene end-capped with chlorine and referred to as trimer and tetramer, respectively. Specifically, Polychlorotrifluoroethylene consists mainly of trimers (55%) and tetramers (45%) of chlorotrifluoroethylene.

Polychlorotrifluoroethylene has also been reported to comprise chlorotrifluoroethylene oligomers of different carbon chain lengths (C₅ to C₉), primarily six (trimer) and eight (tetramer) carbons. According to yet another source, Polychlorotrifluoroethylene is a polymer of chlorotrifluoroethylene, usually including vinylidene fluoride, characterized by repeating structure (CF₂-CCl).
Impurities

Impurities data on the fluoropolymers reviewed in this safety assessment were not found in the published literature, nor were these data submitted.

USE

Cosmetic

The safety of the fluoropolymers is evaluated based on data received from the United States (U.S.) FDA and the cosmetics industry on the expected use of this ingredient in cosmetics. Use frequencies of individual ingredients in cosmetics are collected from manufacturers and reported by cosmetic product category in FDA’s Voluntary Cosmetic Registration Program (VCRP) database. Use concentration data are submitted by the cosmetics industry in response to surveys, conducted by the Personal Care Products Council (Council), of maximum reported use concentrations by product category.

According to 2017 VCRP data, PTFE is reported to be used in 377 cosmetic products (355 leave-on and 22 rinse-off products). The results of a concentration of use survey conducted in 2017 indicate that PTFE is being used at concentrations up to 13% in leave-on products (mascara) and at concentrations up to 2.4% in rinse-off products (hair bleaches). Further use frequency and concentration of use data are presented in Table 4.

According to VCRP and Council survey data, the remaining 12 fluoropolymers in this safety assessment are not currently being used in cosmetic products in the U.S.

Cosmetic products containing PTFE may be applied to the skin and hair or, incidentally, may come in contact with the eyes (at maximum use concentrations up to 13% for PTFE in mascara) and mucous membranes (at maximum use concentrations up to 0.44% PTFE in other oral hygiene products). Ingredient use in oral hygiene products may result in incidental ingestion. Products containing PTFE may be applied as frequently as several times per day and may come in contact with the skin or hair for variable periods following application. Daily or occasional use may extend over many years.

PTFE is reported in the VCRP as being used in powders (dusting and talcum, excluding aftershave talc) and in face powders, which may result in incidental inhalation exposure. According to the Council survey, PTFE is being used in face powders at maximum use concentrations ranging from 0.5% to 3%. Conservative estimates of inhalation exposures to respirable particles during the use of loose powder cosmetic products are 400-fold to 1000-fold less than protective regulatory and guidance limits for inert airborne respirable particles in the workplace.

Noncosmetic

Fluoropolymers are used in a wide variety of thermal and electrical applications because of their low heats of combustion, low rates of flame spread, high resistance to ignition and inherent chemical resistance.

PTFE

PTFE is ubiquitous in materials that are commonly used in cooking (e.g., coatings for cookware), due to its thermal stability and non-stick properties. It is included on the list of resinous and polymeric coatings that FDA has determined may be safely used as the food-contact surface of articles intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food (21CFR175.300). PTFE is also included on the list of polymers categorized as exemptions from the requirement of a tolerance (i.e., after meeting the criteria specified for defining a low-risk polymer), whereby this categorization relates to use as an inert ingredient in a pesticide chemical formulation (40CFR180.960).

The increased use of synthetic polymeric materials (e.g., PTFE) as construction materials for homes, in furniture, carpeting, and draperies, as packaging material and in aircraft or automobiles has been reported.

PTFE membrane filters have been used in the collection of particulate matter (i.e., nano or ultrafine particulate matter fraction). Diffusion cells that are used in some in vitro percutaneous absorption experiments are made of PTFE. PTFE skin graft chambers have been used to isolate wounds and prevent epidermal heating from the skin edge. Flexible PTFE feeding tubes have been used in oral carcinogenicity studies.
Other non-cosmetic uses of PTFE include: hookup and hookup-type wire in electronic equipment; computer wire, electrical tape, electrical components and spaghetti tubing; seals and piston rings, basic shapes, bearings, mechanical tapes, and coated glass fabrics; tubing and sheets for chemical laboratory and process work; lining vessels; for gaskets and pump packings, sometimes mixed with graphite or glass filters; electrical insulator, especially in high frequency applications; filtration fabrics; protective clothing; and a prosthetic aid.

**Hexafluoropropylene/Tetrafluoroethylene Copolymer**

Hexafluoropropylene/Tetrafluoroethylene Copolymer is included on the list of perfluorocarbon resins that FDA has determined may be safety used as articles or components of articles intended to contact food, subject to the provisions that are stated in the CFR (21CFR177.1550).

**Polychlorotrifluoroethylene**

Polychlorotrifluoroethylene has been used as a hydraulic fluid for aircraft. Other non-cosmetic uses include: chemical piping, gaskets, tank linings, connectors, valve diaphragms, wire and cable insulation, and electronic components. This polymer is included on the list of fluorocarbon resins that FDA has determined may be safely used as articles intended for use in contact with food (21CFR177.1380).

**TOXICOKINETIC STUDIES**

**Dermal Penetration**

Dermal penetration data on the fluoropolymers reviewed in this safety assessment were not found in the published literature, nor were these data submitted.

**Absorption, Distribution, Metabolism, and Excretion**

**Animal**

**Oral**

**Polychlorotrifluoroethylene**

Repeated oral dosing of 4 Rhesus monkeys with Polychlorotrifluoroethylene (hydraulic fluid) at a dose of 0.725 g/kg resulted in venous concentrations of chlorotrifluoroethylene trimer and tetramer reaching 2.0 mg/l and 1.8 mg/l, respectively, by 1 day after dosing. At 2 weeks, liver concentrations of trimer and tetramer were 70 mg/l and 100 mg/l, respectively.

**Inhalation**

**Polychlorotrifluoroethylene**

In F344 rats (10 males, 10 females) exposed by inhalation to Polychlorotrifluoroethylene (oil, 0.250 mg/liter; 6 h per day, 5 days per week), blood concentrations were 0.9 mg/l for chlorotrifluoroethylene trimer and 2.0 mg/l for chlorotrifluoroethylene tetramer. Liver concentrations were 20 mg/l and 54 mg/l, respectively.

Groups of Fischer 344 rats (number not stated) were exposed to Polychlorotrifluoroethylene (mixture of trimeric and tetramer oligomers with minor amounts of other chain lengths) either for a single 6-h exposure (0.25, 0.5, or 1 mg/liter) (males and females) or daily 5 days/week, 6 h/day, for 13 weeks (0.01, 0.25, or 0.5 mg/liter) (males). A physiologically-based pharmacokinetic (PB-PK) model was developed using blood, tissue, and urinary Polychlorotrifluoroethylene concentrations measured post-exposure. Relative concentrations of trimer and tetramer in venous blood, liver, and fat after a single 6-h exposure were proportional to inhaled concentrations. The tetramer accumulated, preferentially, with multiple exposures. Components of Polychlorotrifluoroethylene were metabolized to carboxylic acids, with the release of fluoride. Polychlorotrifluoroethylene oligomers were not detected in feces, but were readily quantitated, in small amounts, from urine samples. Urinary elimination of Polychlorotrifluoroethylene favored the trimer, which was detectable for the full 2 weeks post-exposure that urine samples were collected. Blood concentrations of trimer and tetramer, respectively, were: 0.662 and 0.566 mg/liter (at 7 minutes), 0.427 and 0.349 mg/liter (at 1 h), and 0.068 and 0.072 mg/liter (at 1 day) after exposure to 0.25 mg/liter for 6 h.

Simulation indicated that the lung was a significant route of elimination for both trimer and tetramer, though elimination of trimer by this route was relatively greater than tetramer, but was not measured directly. Metabolism and
excretion played only minor roles in the elimination of Polychlorotrifluoroethylene. The greater retention of tetramer relative to trimer is due to its long retention in fat, higher blood/air partition coefficient, particularly after subchronic exposure to 0.25 and 0.50 mg Polychlorotrifluoroethylene/liter, and its lower rate of metabolism.\textsuperscript{25}

In another study, male Fischer 344 rats (number not stated) were exposed to 250 mg/m\textsuperscript{3} Polychlorotrifluoroethylene via inhalation in 690 l chambers. Exposures were conducted 6 h/day, 5 days/week, for 13 weeks (64 exposures over a 90 day test period).\textsuperscript{11} After 90 days exposure, one group of test animals was placed in metabolism cages for 24 h urine and feces collection over a 14 day period. A second group was killed 48 h post-exposure by carbon dioxide inhalation. Urine collected from a rat exposed to via inhalation was esterified and analyzed for carboxylic acid metabolites. Four chromatographic peaks were identified as methyl esters of chlorotrifluoroethylene trimer carboxylic acids. Liver homogenate obtained from a rat exposed to Polychlorotrifluoroethylene was esterified and analyzed for carboxylic acid metabolites of Polychlorotrifluoroethylene. Three chromatographic peaks were identified as methyl esters of chlorotrifluoroethylene tetramer carboxylic acids. In the mass spectrum of the first methyl ester of the chlorotrifluoroethylene tetramer carboxylic acid isolated from rat liver, chlorofluorocarbon fragments were observed.

**TOXICOLOGICAL STUDIES**

**Acute Toxicity Studies**

**Oral**

**PTFE**

According to an English abstract from a Chinese publication, the oral LD\textsubscript{50} values for 2 types of PTFE in mice and rats were 12.5 x 10\textsuperscript{3} mg/kg and 2.5 x 10\textsuperscript{3} mg/kg in mice and 6.25 x 10\textsuperscript{3} mg/kg, and1.25 x 10\textsuperscript{3} mg/kg in rats.\textsuperscript{26} Pertinent details are not included in the abstract.

**Polychlorotrifluoroethylene**

The acute oral toxicity of undiluted Polychlorotrifluoroethylene was evaluated using 10 fasted male Sprague-Dawley rats.\textsuperscript{27} A single dose of 9.2 g/kg (dose volume = 5 ml/kg) was administered by gavage. Dosing was followed by a 14-day observation period. None of the animals died.

The acute oral toxicity of undiluted Polychlorotrifluoroethylene was evaluated using 10 fasted Fischer 344 rats (5 males, 5 females).\textsuperscript{28} The rats were dosed (method not stated) at a limit of 5 g/kg and observed for 14 days. Weight gain was normal during the observation period. None of the animals died.

**Short-Term Toxicity Studies**

**Oral**

**Polychlorotrifluoroethylene**

The short-term oral toxicity of a Polychlorotrifluoroethylene trade name material and its components was evaluated. A general definition of this trade name material is stated in the Definition and General Characterization section of the report, however, the characterization of the trade name materials tested in this study is more precise. Four test groups of Fischer 344 rats (16 rats/group) were dosed by gavage for 2 weeks, with the following substances at a daily dose of 1.25 g/kg: Polychlorotrifluoroethylene containing a 55:45 ratio of trimer and tetramer (both chlorotrifluoroethylene oligomers); Polychlorotrifluoroethylene containing 95% trimer, pure tetramer, and pure trimer.\textsuperscript{2} Four rats per treatment group were killed after 1, 3, 7, and 14 doses. Rats dosed with either Polychlorotrifluoroethylene containing a 55:45 ratio of trimer and tetramer or pure tetramer demonstrated significant weight losses, increased liver weights, increased rates of liver fatty acid \(\beta\)-oxidation, pronounced hepatomegaly and altered hepatocellular architecture, and elevated serum liver-associated enzymes. Rats dosed with either Polychlorotrifluoroethylene containing 95% trimer or only pure trimer demonstrated a significant increase in liver weight and moderate liver histopathologic changes. Compositional analyses of the ratio percentage of trimer to tetramer present in Polychlorotrifluoroethylene (55:45) were found to be altered when measured in the liver (32:68).

The toxicity of a Polychlorotrifluoroethylene trade name material (defined in Definition and Characterization section of the report) characterized as consisting primarily of oligomers with 3-4 monomer units was evaluated in this study.\textsuperscript{23} The material was administered to 4 Rhesus monkeys, by gavage, for 15 days at a daily dose of 0.725 g/kg. At 15 days, liver sections were analyzed for palmitoyl Co-A \(\beta\)-oxidation rates or by electron microscopy. Despite the observed reduced food intake in monkeys, there were no statistically significant changes in animal weights. An increased blood urea nitrogen
(BUN) at 15 days was the only clinical pathological abnormality that was observed. Increased triglycerides and glycogen depletion were also reported. There also were no significant changes in hematology parameters. Minor changes in the hepatocytes were observed, i.e., mild to moderate mitochondria swelling in both control and treated animals. There was no evidence of peroxisomal proliferation. The difference between the mean number of peroxisomes for control primate liver, 2.5 ± 0.33 and exposed primate liver, 3.3 ± 0.42, was not statistically significant.

**Subchronic Toxicity Studies**

**Inhalation**

**Polychlorotrifluoroethylene**

Subchronic inhalation exposure experiments (13 weeks) conducted on male Fischer 344 rats at Polychlorotrifluoroethylene concentrations of 50 mg/m³ and 250 mg/m³ have shown concentration-dependent liver and kidney weight increases. Hepatic peroxisome proliferation was found in the 250 mg/m³-exposed group.

To determine the potential subchronic inhalation toxicity of Polychlorotrifluoroethylene, male and female F-344 rats were exposed to air only or to 0.25, 0.50, or 1.00 mg/l of Polychlorotrifluoroethylene in 65 6-h inhalation exposures over a 90-day period. A dose-dependent depression in body weight gains was noted in male rats only. Serum alkaline phosphatase, aspartate aminotransferase, and alanine aminotransferase activities examined at the conclusion of the study indicated a treatment-related effect in the male test rats, but not the female test rats. Concentration-related increases (p < 0.07) in relative kidney and liver weights occurred in both sexes of rats at all test concentrations. The male rats had slight to minimal hyaline droplet formation in the kidney proximal tubule epithelium. Pronounced cytomegaly of hepatocytes was the predominant lesion recognized.

**Oral**

No toxic effects or abnormalities were observed during macroscopic or microscopic examination of male and female weanling rats (number and strain not stated) fed diets containing finely ground 25% PTFE resin for 90 days.

**Chronic Toxicity Studies**

**Oral**

**PTFE**

The chronic oral toxicity of PTFE was evaluated using 6 Swiss mice. The mice were fed a standard diet supplemented with PTFE (concentration not stated) for 6 months. Normal growth was reported; however, the animals developed spotty loss of fur, skin lesions, and a 50% loss of weight. A control group (fed standard diet only) was included in the study, but results for this group were not reported.

**Polychlorotrifluoroethylene**

A repeated-dose gavage study, using groups of 12 male Fischer 344 rats, was initiated to determine the relative contributions of the corresponding C₆ (trimer) and C₈ (tetramer) acid metabolites to the toxicity of Polychlorotrifluoroethylene. Test animals were dosed once per week for various time periods up to one year. A depression (p < 0.05) in mean body weight occurred in the highest dose tetramer acid (2.16 mg/kg) group. An increase in hepatic peroxisomal β-oxidation activity was found in the 2.16 mg Polychlorotrifluoroethylene tetramer acid/kg dose group at the 3-, 6-, and 9-month sacrifice periods. An increase in relative liver weight was observed in this dose group. Hepatocellular cytomegaly was a common finding in the higher dose tetramer acid groups but not in the trimer-treated groups.

**DEVELOPMENTAL AND REPRODUCTIVE TOXICITY STUDIES**

**Oral**

**PTFE**

According to an English abstract from a Chinese publication, the results for 2 types of PTFE were negative in a teratogenicity study. Study details are not included in the abstract.
GENOTOXICITY STUDIES

In Vitro

PTFE

According to an English abstract from a Chinese publication, two types of PTFE were negative in the Ames test at doses up to 10,000 µg/plate in the following *Salmonella typhimurium* strains, with and without metabolic activation: TA98, TA100, and TA1535. Study details are not included in the publication abstract.

In Vivo

PTFE

In the same abstract, 2 types of PTFE were reported to be negative in the micronucleus test. Study details are not included in the publication abstract.

CARCINOGENICITY STUDIES

Inhalation

Tetrafluoroethylene (PTFE Monomer)

Because tetrafluoroethylene is used primarily in the synthesis of PTFE, it is important to note that the National Toxicology Program (NTP) has evaluated the safety of tetrafluoroethylene in inhalation carcinogenicity studies involving F344/N rats and B6C3F1 mice. Groups of 60 male F344 rats were exposed (inhalation) to 156, 312, or 625 ppm tetrafluoroethylene, and groups of 60 female F344 rats were exposed (in inhalation chamber) to 312, 625, or 1250 ppm tetrafluoroethylene, 5 days per week (6 h per day) for 104 weeks. Groups of 58 male and 58 female B6C3F1 mice were exposed (in inhalation chamber) to 312, 625, or 1250 ppm tetrafluoroethylene 5 days per week (6 h per day) for 95 to 96 weeks. NTP’s conclusion is stated as follows: “Under the conditions of these 2-year inhalation studies, there was clear evidence of carcinogenic activity of tetrafluoroethylene in male F344/N rats based on increased incidences of renal tubule neoplasms (mainly adenomas) and hepatocellular neoplasms. There was clear evidence of carcinogenic activity of tetrafluoroethylene in female F344/N rats based on increased incidences of renal tubule neoplasms, liver hemangiosarcomas, hepatocellular neoplasms, and mononuclear cell leukemia. There was clear evidence of carcinogenic activity of tetrafluoroethylene in male and female B6C3F1 mice based on increased incidences of liver hemangiomas and hemangiosarcomas, hepatocellular neoplasms, and histiocytic sarcomas”.

The subcutaneous and intraperitoneal carcinogenicity studies on PTFE summarized below are presented in Table 5 (size of implants tested included).

Subcutaneous

PTFE

The following results were reported in carcinogenicity studies in which PTFE was implanted subcutaneously (s.c.) in mice of the following strains: 89 random-bred female Swiss mice (fibrosarcomas: 11 of 89 mice), groups of random-bred male and female Swiss mice (fibrosarcomas: 8 of 89 mice; 1 of 61 mice; 23 of 103 mice; 10 of 53 mice; 7 of 54 mice; and 4 of 40 mice), 19 male and 27 female inbred C5BL mice (sarcomas: 4 of 20 females and 4 of 15 females that retained implant), 10 male and 20 female random-bred, CTM albino mice (sarcomas: 18 of 40 females; 9 of 40 males), 38 BALB/c female mice (fibrosarcomas: 17 of 38 mice), 38 C3Hf/Dp female mice (fibrosarcomas: 36 of 38 mice), and 39 C57BL/He female mice (fibrosarcomas: 12 of 39 mice).

When PTFE was implanted s.c. in carcinogenicity studies involving rats, the following results were reported: 15 rats of unknown strain (malignant sarcomas: 4 of 15 rats), 65 male and female weanling Wistar rats (sarcomas: 2 of 65 rats), 2 groups of Wistar rats, number per group unknown (sarcomas: 8 of 34 rats and 6 of 32 rats that survived minimum latent period), 39 male Evans rats (no tumors), 40 male Evans rats (no tumors).
Intraperitoneal

PTFE

When PTFE (rod or powder form) was implanted intraperitoneally (i.p.) in rats, the results were as follows: 16 weanling Wistar rats (no sarcomas; fibroadenoma: 1 of 16 rats tested with rods) and 17 weanling Wistar rats (sarcomas: 2 of 17 rats; fibroadenoma: 1 of 17 rats tested with powder; fibrosarcomas: 2 of 17 rats tested with powder).\textsuperscript{34,43}

**OTHER RELEVANT STUDIES**

Muscle Necrosis

PTFE

A PTFE patch was implanted (size of implant not stated) in the muscle of rabbits.\textsuperscript{44} At specified time intervals, ranging from 24 h to 12 weeks following implantation, the rabbits were killed. The paravertebral muscles were isolated and dissected to recover the implanted material and adjacent tissue. Each site was examined grossly for signs of tissue reaction and the appropriate score was recorded. The implant and adjacent tissue were removed and prepared for microscopic examination. The initial type of necrosis exhibited by rabbit skeletal muscle in response to the physical injury of implant insertion, and the chemical injury sustained by the toxic qualities of the implant, was coagulative necrosis. Coagulative necrosis was soon followed by liquefactive necrosis. The necrotic debris was removed, partly by phagocytic macrophages and giant cells. Fibrosis immediately adjacent to and completely surrounding the implant was observed. In addition to regenerating and encapsulating, fatty infiltration was associated with the repair process. PTFE caused an occasional to mild eosinophilic infiltrate at each time interval investigated.

Inflammatory Response

PTFE

Three populations, each consisting of two mongrel dogs, 5 New Zealand White rabbits, and 10 BALB/c mice, were injected with PTFE particulate (total particulates (42%) size = 485 ± 200 nm; total particulates (30%) size = 7000 to 25,000 nm) in a glycerine carrier and were followed for a period of 1 week, 3 months, 6 months, and 1 year.\textsuperscript{45} Mice received 1 subcutaneous dorsal injection each, rabbits received two subareolar injections each, and dogs received 3 subareolar injections each in addition to 2 periurethral injections. Histologic examination of the biopsy sites revealed a persistent chronic inflammatory reaction with progressive growth of the involved tissue volume. In addition to giant cells and macrophages, lymphocytes became apparent at 3 months and comprised up to 40% of the cellular infiltrate by 1 year. Plasma cells were also noted at the 1-year period in the rabbit model.

A material consisting of 72% PTFE and 28% zinc oxide by volume was implanted (size of implant not stated) in the mandibles of 13 guinea pigs.\textsuperscript{46} Seven animals were killed at intervals of 4 weeks and 12 weeks after surgery, and tissue sections were prepared. Mild-to-moderate inflammation was observed at 4 weeks, but the inflammation was predominantly moderate in intensity. In regions where the material appeared to be loosely dispersed or poorly condensed, a round cell infiltrate was present with active phagocytosis of the material by multinucleated giant cells. The inflammatory response at 12 weeks was predominantly mild. The material was surrounded by a moderately thick fibrous capsule with very few inflammatory cells, except for tissue samples in which the material appeared to be poorly condensed. In areas where the material was loosely condensed, active phagocytosis and chronic inflammation persisted and were characterized by the presence of macrophages, plasma cells, and multinucleated giant cells.

**DERMAL IRRITATION AND SENSITIZATION STUDIES**

Irritation

**Animal**

Polychlorotrifluoroethylene

The skin irritation potential of Polychlorotrifluoroethylene (concentration not stated) was evaluated using 6 female New Zealand White rabbits.\textsuperscript{27} The test substance (0.1 ml) was applied to both intact and abraded skin sites that were covered with an occlusive patch for 4 h. The test sites were evaluated at 1 h and 1, 2, 3, and 7 days using the Draize scale. The test substance was classified as non-irritating (primary dermal irritation index = 0).

**Human**
PTFE

The skin irritation potential of a formula containing 7.6% PTFE was evaluated in a 48-h semi-occlusive patch test involving 26 subjects. The dose per cm² was not stated. Skin irritation was not observed (primary irritation index (PII) = 0).47

Sensitization

Animal

Polychlorotrifluoroethylene

The skin sensitization potential of Polychlorotrifluoroethylene was evaluated using 10 male Hartley albino guinea pigs.27 A topical induction application of the test substance (0.1 ml) was made 4 times over a 10-day period. The induction application site and dose/cm² were not stated. During the challenge phase, the test substance (0.1 ml) was applied to the flank. The challenge site was scored for edema and erythema at 24 h and 48 h using the Draize scale. A sensitization response was observed in 30% of the animals tested, and the test substance was classified as having mild sensitization potential.

Human

PTFE

The skin sensitization potential of a formula containing 2.89% PTFE was evaluated in a human repeated insult patch test (HRIPT, occlusive patches) involving 107 subjects. The dose per cm² and duration of patch application were not stated. There was no evidence of dermal irritation or sensitization.47

OCULAR IRRITATION/TOXICITY STUDIES

In Vitro

PTFE

The ocular irritation potential of a formula containing 2.89% PTFE was evaluated in the in vitro Epiocular eye irritation test. An ET₅₀ of > 24 h (no eye irritation potential) was reported.47

Animal

PTFE

To investigate the effects of focal implantation of expanded PTFE episcleral implants (i.e., explants or exoplants) on surrounding ocular tissues, an experimental and histopathological study was performed.48 Twenty-seven Fauve de Bourgogne rabbits eyes were implanted for a period of 3–11 months with PTFE episcleral implants. A newly formed capsule constantly encased the implants. Only 2 severe complications observed, i.e., 2 eyes had an endcapsular acute inflammation and could not be included in the study. Finally, 25 eyes were studied histopathologically. Neither intrusion nor extrusion of episcleral implants was observed. The inner surface of the capsule was often covered with numerous giant cells, i.e., a foreign-body granuloma developed against the irregular outline of the episcleral implants. The sclera was both thinned and invaginated under the episcleral implants.

Polychlorotrifluoroethylene

Polychlorotrifluoroethylene (0.1 ml) was instilled into the conjunctival sac of each of 9 female New Zealand White rabbits.27 Contralateral eyes served as controls. The eyes of 3 rabbits remained unrinised. Reactions were scored according to the Draize scale. The test substance was classified as practically non-irritating.
CLINICAL STUDIES

Other Clinical Reports

PTFE

The cellular tissue response to subcutaneously implanted PTFE (laminated to aluminum oxide; 5 x 10 mm implant blocks) was evaluated using 7 healthy volunteers. PTFE was implanted s.c. in the iliac crest region. After 1, 2, 4, 12, and 26 weeks, respectively, the implants with surrounding soft tissue were removed for histological and immunohistochemical examination using a panel of antibodies to various leukocyte markers. After 1 week, there were signs of edema, slight vessel proliferation, and fibroblast proliferation. At 2 weeks, a foreign body reaction with giant cells and some decomposed microfragmented implant material dominated the peri-implant picture. At 4 weeks, there were only some giant cells seen, the reaction having been mostly lymphohistiocytic. In one specimen, eosinophils were detected. At 12 weeks, the vessel proliferation, fibroblast proliferation, and foreign body reactions were decreasing, but there was still a slight lymphohistiocytic reaction. Thus, PTFE implants primarily induced a slight foreign body reaction, leaving only a slight lymphohistiocytic reaction at 26 weeks. The authors noted that the study provided no clues to a toxic, allergic, or traditional immunological pathogenesis of the tissue reaction induced by PTFE.

OCCUPATIONAL EXPOSURE

PTFE

The percentage retention at 24 h of 4µm PTFE particles (aerodynamic diameter of ~6 µm) in the alveoli was studied using 29 healthy male volunteers. Students/workers at a university (11 total) inhaled 4.2 ± 0.7 and 4.3 ± 0.8 µm (mean ± SD) PTFE particles and the workers from a battery factory (18 workers) inhaled 3.9 ± 0.4 µm PTFE particles. Inhalation of the test particles resulted from 10 to 20 maximally deep inhalations. Radioactivity in the lungs was measured after inhalation. The 24-h retention correlated significantly with the first second of the forced expiratory volume (FEV1) and the forced vital capacity (FVC), and persisted when the subjects were divided into different categories according to profession and smoking habits. It was noted that the results suggest that exposure to particles larger than a few microns in workers with large FEV1 values may result in a greater risk for systemic toxic effects, when compared to workers with small FEV1 values.

Clinical phenomena in employees exposed to fumes from the processing of PTFE have been reported. After exposure to the fumes, there is a latent period of a few hours and then a feeling of general malaise, aching muscles, a sense of oppression behind the mid-chest, a dry throat, and a cough followed, by shivering and profuse sweating. The symptoms abate after 24 hours, with no after-effects. Seven cases were described, which included the 4 employees regularly working in the PTFE section of a fabrication works. Two cases were seen during the acute phase of the illness; x-ray examination of the chest revealed no abnormalities. One case had marked conjunctival congestion. Two employees working on a "dispersion process" (process similar to paint spraying, using PTFE dispersed in 10% chromic acid) complained of skin irritation.

An investigation concerning human exposure to PTFE took place at a fabricating plant that employed 130 persons. Air levels of PTFE ranging from 0 to 5.48 mg/m³ were found. Urinary fluoride levels were investigated as an index of PTFE exposure, because carbonyl fluoride, a pyrolysis product of PTFE, is metabolized and excreted as inorganic fluoride ion. Spot urine samples and occupational histories relating to polymer fume fever were obtained from 77 workers. All urine values were below the level at which systemic effects are reported to occur. Analyses of the results (analysis of variance method) demonstrated that the mean urinary fluoride level among workers who had one or more years of exposure to PTFE (workers also had experienced 1 or more reported episodes of polymer fume fever) was significantly higher ($P < 0.01$) than that among employees with less than one year or more of exposure and no history of polymer fume fever. Additional exposure beyond one year and additional polymer fume fever episodes did not result in further elevation of urine fluoride levels.

SUMMARY

The safety of 13 fluoropolymers in cosmetics is reviewed in this CIR safety assessment. According to the Dictionary, these fluoropolymers are reported to have the following functions in cosmetics: bulking agents, slip modifiers, film formers, viscosity increasing agents, dispersing agents, skin conditioning agents, skin protectants, and hair conditioning agents. Most of the ingredients have the film former function in common.

According to 2017 VCRP data, PTFE is reported to be used in 377 cosmetic products (355 leave-on and 22 rinse-off products). The results of a concentration of use survey conducted by the Council in 2017 indicate that PTFE is being used at concentrations up to 13% in leave-on products (mascara), the greatest use concentration that is being reported for PTFE, and
at concentrations up to 2.4% in rinse-off products (hair bleaches). Use of the remaining 12 fluoropolymers in cosmetics is not reported in VCRP or Council survey data.

The repeated oral dosing of Rhesus monkeys with Polychlorotrifluoroethylene (hydraulic fluid) resulted in venous concentrations of chlorotrifluoroethylene trimer and tetramer and concentrations of both in the liver. The same was true for F344 rats after repeated inhalation exposure to the oil, and urinary elimination of Polychlorotrifluoroethylene favored the trimer. Polychlorotrifluoroethylene oligomers were not detected in the feces. Components of Polychlorotrifluoroethylene were metabolized to carboxylic acids, with the release of fluoride. A PBPK model was developed for Fisher 344 rat inhalation exposure to Polychlorotrifluoroethylene, and the lung was found to be a significant route of elimination for both the trimer and tetramer, favoring the trimer. There was greater retention of the tetramer.

LD₅₀ values for PTFE of 12.5 x 10³ mg/kg and 2.5 x 10³ mg/kg (mice, both values) and 6.25 x 10³ mg/kg and 1.25 x 10³ mg/kg (rats, both values) have been reported. Information on the mouse/rat strain and number of animals is not included in the study summary. In acute oral toxicity studies in which 10 Sprague-Dawley rats and 10 Fischer 344 rats received a single oral dose of 9200 mg/kg and doses up to 5000 mg/kg Polychlorotrifluoroethylene, respectively, none of the animals died.

No acute inhalation toxicity studies on PTFE or any other fluoropolymers have been identified in the published literature.

In a short-term oral toxicity study involving groups of 16 Fischer 344 rats, animals dosed with either Polychlorotrifluoroethylene containing a 55:45 ratio of trimer and tetramer or pure tetramer demonstrated significant weight losses, increased liver weights, increased rates of liver fatty acid β-oxidation, pronounced hepatomegaly and altered hepatocellular architecture, and elevated serum liver-associated enzymes. Rats dosed with either Polychlorotrifluoroethylene containing 95% trimer or only pure trimer demonstrated a significant increase in liver weight and moderate liver histopathologic changes. In a short-term (15-day) oral toxicity study involving 4 Rhesus monkeys, increased BUN at 15 days was the only clinical pathological abnormality that was observed. Minor changes in the hepatocytes were observed (i.e., mild to moderate mitochondria swelling in both control and treated animals), and there was no evidence of peroxisomal proliferation.

In a chronic oral toxicity involving 6 Swiss mice fed a standard diet supplemented with PTFE (concentration not stated) for 6 months, growth was normal, but the animals developed spotty loss of fur, skin lesions, and a 50% loss of weight. No toxic effects or abnormalities were observed during macroscopic or microscopic examination of male and female weanling rats (number and strain not stated) fed diets containing finely ground 25% PTFE resin for 90 days.

Subchronic inhalation exposure experiments conducted on male Fischer 344 rats at 50 mg/m³ and 250 mg/m³ have shown concentration-dependent liver and kidney weight increases. Hepatic peroxisome proliferation was found in the 250 mg/m³-exposed group. In another inhalation study, F-344 rats were exposed to Polychlorotrifluoroethylene at concentrations up to 1.00 mg/l over a 90-day period. Concentration-related increases (p < 0.07) in relative kidney and liver weights occurred in both at all test concentrations. Male rats had slight to minimal hyaline droplet formation in the kidney proximal tubule epithelium. Pronounced cytoemgaly of hepatocytes was the predominant lesion observed.

A chronic, 1-year, gavage study using groups of 12 male Fisher 344 rats, was performed to determine the relative contributions of the C₆ (trimer) and C₈ (tetramer) acid metabolites to the toxicity of Polychlorotrifluoroethylene. A depression (p < 0.05) in mean body weight occurred in the highest dose tetramer acid (2.16 mg/kg) group. An increase in hepatic peroxisomal β-oxidation activity and an increase in liver weight were found in the 2.16 mg Polychlorotrifluoroethylene tetramer acid/kg dose group. Hepatocellular cytoemgaly was a common finding in the higher dose tetramer acid groups, but not in the trimer-treated groups.

According to an English abstract from a Chinese publication, the results for 2 types of PTFE were negative in a teratogenicity study. Study details are not included in the abstract.

According to an English summary from a Chinese publication, 2 types of PTFE were negative in the Ames test at doses up to 10,000 µg/plate in the following Salmonella typhimurium strains, with and without metabolic activation: TA98, TA100, and TA1535 and 2 types of PTFE were negative in the micronucleus test. Study details are not included in the abstract.

When PTFE was implanted s.c. or i.p. in rats of different strains, tumor formation around the implantation site was observed. The same was true for PTFE implanted s.c. in mice of different strains. The tetrafluoroethylene monomer , used in the synthesis of PTFE, was found to be carcinogenic in mice and rats in an NTP inhalation carcinogenicity study.
In a study in which PTFE particulate in a glycerine carrier was injected into 2 mongrel dogs, 5 New Zealand White rabbits, and 10 BALB/c mice, histologic examination of the biopsy sites revealed a persistent chronic inflammatory reaction. Mild to moderate inflammation was observed in a group of 13 guinea pigs after implantation of a material consisting of 72% PTFE and 28% zinc oxide.

Polychlorotrifluoroethylene was classified as non-irritating to the skin (abraded and intact) of 6 New Zealand white rabbits in a 4-h patch test. The same was true for a formula containing 7.6% PTFE in a 48-h patch test involving 26 subjects. In an HRIPT involving 107 subjects, a formula containing 2.89% PTFE did not cause dermal irritation or sensitization.

Polychlorotrifluoroethylene was classified as practically non-irritating to the eyes of 9 female New Zealand White rabbits. At histopathologic examination of the eyes of 25 Fauve de Bourgogne rabbits with PTFE episcleral implants, a foreign-body granuloma developed and the sclera was both thinned and invaginated under the implant. A formula containing 2.89% PTFE was classified as having no ocular irritation potential in the in vitro Epiocular eye irritation test.

A foreign-body reaction (slight lymphohistiocytic reaction) was observed in 7 healthy volunteers implanted s.c. with PTFE.
### Table 1. Monomer Components of Fluoropolymers

<table>
<thead>
<tr>
<th>Monomer</th>
<th>CIR Review Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acrylic Acid</td>
<td>Not Reviewed</td>
</tr>
<tr>
<td>Methacrylic Acid</td>
<td>Published Final Report – Conclusion: Safe as used as a nail primer by trained professionals, but there are insufficient data for retail use by consumers.(^{53})</td>
</tr>
<tr>
<td>Butyl Methacrylate</td>
<td>Published Final Report – Conclusion: Safe as used in nail enhancement products when skin contact is avoided. Products containing this ingredient should be accompanied with directions to avoid skin contact, because of the sensitizing potential of methacrylates.(^{54})</td>
</tr>
<tr>
<td>Methyl Methacrylate</td>
<td>Scientific Literature Review issued on 1-13-2003 – Determined not to be an ingredient; report terminated (although data are available).(^{44})</td>
</tr>
<tr>
<td>Ethoxymethyl Methacrylate</td>
<td>Published Final Report – Conclusion: Safe as used in nail enhancement products when skin contact is avoided. Products containing this ingredient should be accompanied with directions to avoid skin contact, because of the sensitizing potential of methacrylates.(^{54})</td>
</tr>
<tr>
<td>Propyl Methacrylate</td>
<td>Not Reviewed</td>
</tr>
<tr>
<td>Ethyl Acrylate</td>
<td>Not Reviewed</td>
</tr>
<tr>
<td>Butyl Acrylate</td>
<td>Not Reviewed</td>
</tr>
<tr>
<td>sec-Butyl Methacrylate</td>
<td>Not Reviewed</td>
</tr>
<tr>
<td>t-Butyl Methacrylate</td>
<td>Published Final Report – Conclusion: Safe as used in nail enhancement products when skin contact is avoided. Products containing this ingredient should be accompanied with directions to avoid skin contact, because of the sensitizing potential of methacrylates.(^{54})</td>
</tr>
<tr>
<td>Stearyl Methacrylate</td>
<td>Not Reviewed</td>
</tr>
</tbody>
</table>

### Table 2. Definitions, idealized structures, and functions of the ingredients in this safety assessment.\(^{1}\) (CIR Staff)

<table>
<thead>
<tr>
<th>Ingredient CAS No.</th>
<th>Definition &amp; Structures</th>
<th>Function(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTFE 9002-84-0</td>
<td>PTFE is the polymer of tetrafluoroethylene that conforms to the formula: (\text{C}_2\text{F}_4)(^x)</td>
<td>Bulking Agents; Slip Modifiers</td>
</tr>
<tr>
<td>Acrylates/Methoxy PEG-23</td>
<td>Acrylates/Methoxy PEG-23 Methacrylate/Perfluorooctyl Ethyl Acrylate Copolymer is a copolymer of methoxy PEG-23 methacrylate, perfluorooctyl ethyl acrylate, and one or more monomers of acrylic acid, methacrylic acid or one of their simple esters.</td>
<td>Film Formers</td>
</tr>
<tr>
<td>Methacrylate/Perfluorooctyl Ethyl Acrylate Copolymer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acrylates/Perfluorohexylethyl Methacrylate Copolymer 1557087-30-5</td>
<td>Acrylates/Perfluorohexylethyl Methacrylate Copolymer is a copolymer of perfluorohexylethyl methacrylate, and one or more monomers consisting of acrylic acid, methacrylic acid, or one of their simple esters.</td>
<td>Film Formers</td>
</tr>
<tr>
<td>Behenyl Methacrylate/Perfluorooctylethyl Methacrylate Copolymer</td>
<td>Behenyl Methacrylate/Perfluorooctylethyl Methacrylate Copolymer is a copolymer of behenyl methacrylate and perfluorooctylethyl methacrylate monomers.</td>
<td>Film Formers; Viscosity Increasing Agents - Nonaqueous</td>
</tr>
</tbody>
</table>

\(^{1}\) Distributed for comment only -- do not cite or quote
<table>
<thead>
<tr>
<th>Ingredient CAS No.</th>
<th>Definition &amp; Structures</th>
<th>Function(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C6-14 Perfluoroalkylethyl Acrylate/HEMA Copolymer</td>
<td>C6-14 Perfluoroalkylethyl Acrylate/HEMA Copolymer is a copolymer of 2-(perfluoro(C6-14 alkyl)) ethyl acrylate and 2-hydroxyethyl methacrylate monomers.</td>
<td>Dispersing Agents; Nonsurfactant; Skin-Conditioning Agents; Emollient; Slip Modifiers; Viscosity Increasing Agents - Nonaqueous</td>
</tr>
<tr>
<td>Hexafluoropropylene/Tetrafluoroethylene Copolymer 25067-11-2</td>
<td>Hexafluoropropylene/Tetrafluoroethylene Copolymer is a copolymer of hexafluoropropylene and tetrafluoroethylene monomers.</td>
<td>Film Formers; Skin-Conditioning Agents - Emollient; Slip Modifiers</td>
</tr>
<tr>
<td>PEG-10 Acrylate/Perfluorohexylethyl Acrylate Copolymer</td>
<td>PEG-10 Acrylate/Perfluorohexylethyl Acrylate Copolymer is a copolymer of PEG-10 acrylate and perfluorohexylethyl acrylate monomers.</td>
<td>Film Formers</td>
</tr>
<tr>
<td>Poly(chlorotrifluoroethylene) 9002-83-9</td>
<td>Poly(chlorotrifluoroethylene) is the polymer of chlorotrifluoroethylene that conforms generally to the formula:</td>
<td>Film Formers; Skin-Conditioning Agents - Occlusive</td>
</tr>
<tr>
<td>Polyperfluoroethoxymethoxy Difluoroethyl PEG Disostearate</td>
<td>Polyperfluoroethoxymethoxy Difluoroethyl PEG Disostearate is the diester of isostearic acid and Polyperfluoroethoxymethoxy Difluoroethyl PEG Ether.</td>
<td>Skin Protectants; Hair Conditioning Agents; Skin-Conditioning Agents - Emollient; Slip Modifiers; Viscosity Increasing Agents - Nonaqueous</td>
</tr>
<tr>
<td>Polyperfluoroethoxymethoxy Difluoroethyl PEG Ether 162492-15-1</td>
<td>Polyperfluoroethoxymethoxy Difluoroethyl PEG Ether is the polymer that conforms generally to the formula:</td>
<td>Hair Conditioning Agents; Skin-Conditioning Agents - Miscellaneous; Skin-Conditioning Agents - Occlusive</td>
</tr>
<tr>
<td>Polyperfluoroethoxymethoxy Difluorohydroxyethyl Ether 88645-29-8</td>
<td>Polyperfluoroethoxymethoxy Difluorohydroxyethyl Ether is the polymer that conforms generally to the formula:</td>
<td>Hair Conditioning Agents; Skin-Conditioning Agents - Miscellaneous</td>
</tr>
<tr>
<td>Polyperfluoroethoxymethoxy Difluoroethyl Ether 161075-02-1</td>
<td>Polyperfluoroethoxymethoxy Difluoroethyl Ether is the polymer that conforms generally to the formula:</td>
<td>Solvents</td>
</tr>
<tr>
<td>Stearyl Methacrylate/Perfluorooctylethyl Methacrylate Copolymer</td>
<td>Stearyl Methacrylate/Perfluorooctylethyl Methacrylate Copolymer is a copolymer of stearyl methacrylate and perfluorooctylethyl methacrylate monomers.</td>
<td>Film Formers; Viscosity Increasing Agents - Nonaqueous</td>
</tr>
</tbody>
</table>
### Table 3. Chemical and Physical Properties of Fluoropolymers

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (Daltons)</td>
<td>400,000 to 10,000,000</td>
<td>5</td>
</tr>
<tr>
<td>Physical form and/or color</td>
<td>White translucent to opaque solid</td>
<td>4</td>
</tr>
<tr>
<td>PTFE is available in the following 3 forms: (1) granular for molded parts and for extruding thick-walled tubing and rods; (2) coagulated dispersions (also referred to as fine powders), for extruding thin sections; and (3) aqueous dispersions, for coating, impregnation and preparation of fibers and films. Filled polymers are also available; these are generally made by mixing fillers such as glass fiber, graphite, molybdenum disulfide, metal oxides or ceramics and finely-divided granular PTFE. Reprocessed scrap and off-grade material is also used.</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Density (g/cm³)</td>
<td>2.25</td>
<td>6</td>
</tr>
<tr>
<td>Solubility</td>
<td>No substance that will dissolve the polymer has been found</td>
<td>5</td>
</tr>
<tr>
<td>Melting point (°C)</td>
<td>320-330</td>
<td>6</td>
</tr>
<tr>
<td>Decomposes (°C)</td>
<td>315 to 375 and up to 500.</td>
<td>9, 53</td>
</tr>
</tbody>
</table>

When heated, depending on the temperature of thermal decomposition, a variety of oxidized products containing fluorine, carbon, and oxygen may be released. At temperatures ranging from 315 to 375 and up to 500, PTFE decomposition products are primarily the monomer tetrafluoroethylene, perfluoroisopropylene, and other C4-C5 perfluoro-compounds, and an unidentified waxy fume.

The burning of PTFE produced a significant amount of carbon dioxide (~6000 ppm), a small amount of carbon monoxide (~60 ppm), and some carbon tetrafluoride (amount not stated). Carbonyl fluoride was not detected in the combustion product gas. However, it was suspected that carbonyl fluoride may have been decomposed to form carbon dioxide and carbon tetrafluoride during the thermal equilibrium of the combustion product gas.

#### Hexafluoropropylene/Tetrafluoroethylene Copolymer

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melting Point (°C)</td>
<td>270</td>
<td>6</td>
</tr>
<tr>
<td>Polychlorotrifluoroethylene</td>
<td></td>
<td>7</td>
</tr>
<tr>
<td>Color</td>
<td>Colorless</td>
<td>7</td>
</tr>
<tr>
<td>Density (g/cm³)</td>
<td>2.10 to 2.15</td>
<td>7</td>
</tr>
<tr>
<td>Refractive index</td>
<td>1.43</td>
<td>7</td>
</tr>
<tr>
<td>Melting Point (°C)</td>
<td>210 to 215</td>
<td>8</td>
</tr>
<tr>
<td>Boiling Point (°C)</td>
<td>140 to 190</td>
<td>8</td>
</tr>
<tr>
<td>Decomposes (°C)</td>
<td>220 (in pyrolysis process, fusion and decomposition starting temperature); ~ 600 (rapid pyrolysis)</td>
<td>8</td>
</tr>
</tbody>
</table>

### Table 4. Frequency and Concentration of Use According to Duration and Type of Exposure.12,13

<table>
<thead>
<tr>
<th>Exposure Type</th>
<th># of Uses</th>
<th>Conc. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Totals/Conc. Range</td>
<td>377</td>
<td>0.11-13</td>
</tr>
<tr>
<td>Duration of Use</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leave-On</td>
<td>355</td>
<td>0.11-13</td>
</tr>
<tr>
<td>Rinse off</td>
<td>22</td>
<td>0.15-2.4</td>
</tr>
<tr>
<td>Diluted for (bath) Use</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Exposure Type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eye Area</td>
<td>249</td>
<td>0.11-13</td>
</tr>
<tr>
<td>Incidental Ingestion</td>
<td>1</td>
<td>0.44</td>
</tr>
<tr>
<td>Incidental Inhalation- Sprays</td>
<td>13*</td>
<td>NR</td>
</tr>
<tr>
<td>Incidental Inhalation- Powders</td>
<td>31</td>
<td>0.6-3</td>
</tr>
<tr>
<td>Dermal Contact</td>
<td>345</td>
<td>0.11-12</td>
</tr>
<tr>
<td>Deodorant (underarm)</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Hair - Non-Coloring</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Hair-Coloring</td>
<td>NR</td>
<td>2.4</td>
</tr>
<tr>
<td>Nail</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Mucous Membrane</td>
<td>1</td>
<td>0.44</td>
</tr>
<tr>
<td>Baby Products</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>

NR = Not Reported; Totals = Rinse-off + Leave-on + Diluted for Bath Product Uses.

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

Note: Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure type uses may not equal the sum total uses.
Table 5. Carcinogenicity of Implant PTFE

<table>
<thead>
<tr>
<th>Subcutaneous Implantation</th>
<th>Animals Tested</th>
<th>Test Protocol</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTFE (square sheet, 12 x 12 x 1.2 mm)</td>
<td>89 random-bred female Swiss mice</td>
<td>Implanted subcutaneously (s.c.) in left flank</td>
<td>First local tumor developed 25 weeks after implantation. Total of 11 (12.5%) fibrosarcomas found after average latent period of 54.5 weeks. IARC working group noted that because the implant was not retained in 9 mice and 70 mice remained alive at appearance of first tumor, the effective tumor incidence should be ~ 16%.33,34</td>
</tr>
<tr>
<td>PTFE</td>
<td>Random-bred Swiss mice: 89 females and 61 males (tested with 12 x 12 x 1.2 mm square PTFE implant); 103 females (tested with 15 mm diameter PTFE disk); 53 females (tested with PTFE fragment corresponding to 1 disk [size not specified]); and 54 females and 50 males (tested with 20 mm diameter PTFE disk)</td>
<td>Implanted s.c.</td>
<td>Tumors (all fibroadenomas) developed around the implant in all groups of mice, and incidences were as follows: 8 of 89 (10%), and 1 of 61(2%); 23 of 103 (22.3%; 10 of 53 (21.2%); 7 of 54 (15.2%); and 4 of 50 (8%). No similar tumors were observed in untreated mice (200 females, 100 males). Furthermore, of 50 female mice implanted with 12 x 12 x 1.2 mm square glass coverslips, 6 developed sarcomas (13.6% incidence); of 48 females implanted with fragments of glass corresponding to 1 square, 2 developed sarcomas (4.3% incidence). The average latent period for gross palpable tumors was 55 weeks. Survival rates and when experiment was terminated not reported.33,34</td>
</tr>
<tr>
<td>PTFE (15 x 1.2 mm disk)</td>
<td>Inbred C5BL mice (27 females, 19 males)</td>
<td>Implanted s.c. Mice observed for 90 weeks</td>
<td>4 local sarcomas (20%) developed in 20 females that retained the implant and were considered to be at risk at weeks 39, 47, 52, and 58. 4 local sarcomas in 15 males considered to be at risk (26%) at weeks 49, 51, 60, and 91. The tumors always developed around the disks. In a control group of 30 male and 33 female non-implanted mice, observed for 100 weeks, no sarcomas were observed; spontaneous tumors developed in 3 females and 2 males.34,36</td>
</tr>
<tr>
<td>PTFE (15 x 1.2 mm disks)</td>
<td>Random-bred CTM albino mice (40 males, 40 females)</td>
<td>Implanted s.c. into right flank. Mice observed for lifespan</td>
<td>Sarcomas (around disks) in 18 females and 9 males. Total incidence of 38% of the 69 mice still alive at the time of appearance of first tumor. No fibrosarcomas in 99 male and 98 female control mice of same strain observed for lifespan.34,37</td>
</tr>
<tr>
<td>PTFE (15 x 1.2 mm disks)</td>
<td>BALB/c mice (38 females); C3H/Db mice (38 females); and C57BL/He mice (39 females)</td>
<td>Implanted s.c. in dorsal area. Surviving mice killed at 120 weeks of age.</td>
<td>Fibrosarcomas (around disks) in 17 of 38 (44%) BALB/c mice, 36 of 38 (94%) C3H/Db mice, and 12 of 39 (30%) C57BL/He mice; mean latent periods of 78, 61, and 82 weeks, respectively. Of the 56 tumors examined histologically, 2 were rhabdomyosarcomas and the remainder were fibrosarcomas.34,38</td>
</tr>
<tr>
<td>PTFE films</td>
<td>15 rats (strain not stated)</td>
<td>Implanted s.c. in 2-year study.</td>
<td>Malignant sarcomas in 4 of 15 rats. All 15 rats survived the study.39,40</td>
</tr>
<tr>
<td>PTFE implants (4 x 5 0.16 mm)</td>
<td>65 weanling Wistar rats (males and females)</td>
<td>Implanted s.c. in abdominal wall. All rats killed within 800 days</td>
<td>2 sarcomas induced. 45 rats alive at time of appearance of first tumor (at day 659). No tumors in in 20 control animals that received glass implants and survived for 300 days.39,40</td>
</tr>
<tr>
<td>PTFE disks (plain and perforated; 15 x 0.02 mm)</td>
<td>Wistar rats (2 groups)</td>
<td>Implanted s.c. in abdominal wall</td>
<td>34 rats implanted with plain disks and 32 rats implanted with perforated disks survived the minimum latent period. 8 of 34 rats (23.5%) and 6 of 32 rats (18.7%) had sarcomas.34,41</td>
</tr>
<tr>
<td>PTFE mesh surgical outflow patches (20 x 20 mm squares) or shredded material</td>
<td>39 male Evans rats (tested with PTFE squares); 40 rats (tested with shredded material); 41 non-implanted control rats</td>
<td>Implanted s.c. Experiment terminated 19 months after implantation</td>
<td>24 of 39 rats and 23 of 40 rats were alive when experiment was terminated. 28 of 41 controls also survived. No local tumors observed in study.34,42</td>
</tr>
</tbody>
</table>
Table 5. Carcinogenicity of Implanted PTFE

<table>
<thead>
<tr>
<th>Test Substance</th>
<th>Animals Tested</th>
<th>Test Protocol</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraperitoneal Implantation</td>
<td>PTFE rods (10 x 2 x 2 mm) or powder</td>
<td>Implanted intraperitoneally (i.p.). Surviving animals killed 27 months after implantation</td>
<td>13 of 16 and 10 of 17 rats were alive after 1 year. No sarcomas in rats implanted with PTFE rods. 2 sarcomas became palpable at 354 and 476 days after implantation of PTFE powder. Extraperitoneal tumors observed after PTFE rod implantation (1 fibroadenoma in inguinal region) and after PTFE powder implantation (1 fibrosarcoma in upper leg, 1 fibrosarcoma in shoulder, and 1 inguinal fibroadenoma. In control group, 1 adenoma of testis and possible carcinoma in inguinal region observed.</td>
</tr>
<tr>
<td></td>
<td>16 weanling Wistar rats (tested with PTFE rods); 17 rats (tested with PTFE powder); 25 untreated controls</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
REFERENCES


   polychlorotrifluoroethylenes (3.1 Oils) and two chlorotrifluoroethylene (CTFE) oligomers in male Fischer 344 rats. Fundamental

   Stability. 1993;42(2):181-188.


5. National Toxicology Program. NTP Toxicology and Carcinogenesis Studies of Tetrafluoroethylene (CAS No. 116-14-3) in F344

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17. Williams, S. J., Baker, B. B., and Lee, K-P. Formation of acute pulmonary toxicants following thermal degradation of

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47. Anonymous. 2018. Summaries of studies on products containing PTFE.


### 2017 FDA VCRP Data

**PTFE**

<table>
<thead>
<tr>
<th>Code</th>
<th>Category</th>
<th>2017 Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>03A</td>
<td>Eyebrow Pencil</td>
<td>3</td>
</tr>
<tr>
<td>03C</td>
<td>Eye Shadow</td>
<td>204</td>
</tr>
<tr>
<td>03D</td>
<td>Eye Lotion</td>
<td>6</td>
</tr>
<tr>
<td>03F</td>
<td>Mascara</td>
<td>31</td>
</tr>
<tr>
<td>03G</td>
<td>Other Eye Makeup Preparations</td>
<td>5</td>
</tr>
<tr>
<td>04C</td>
<td>Powders (dusting and talcum, excluding aftershave talc)</td>
<td>1</td>
</tr>
<tr>
<td>07A</td>
<td>Blushers (all types)</td>
<td>28</td>
</tr>
<tr>
<td>07B</td>
<td>Face Powders</td>
<td>30</td>
</tr>
<tr>
<td>07C</td>
<td>Foundations</td>
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<tr>
<td>07E</td>
<td>Lipstick</td>
<td>1</td>
</tr>
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<td>07G</td>
<td>Rouges</td>
<td>2</td>
</tr>
<tr>
<td>07H</td>
<td>Makeup Fixatives</td>
<td>1</td>
</tr>
<tr>
<td>07I</td>
<td>Other Makeup Preparations</td>
<td>3</td>
</tr>
<tr>
<td>11E</td>
<td>Shaving Cream</td>
<td>3</td>
</tr>
<tr>
<td>11G</td>
<td>Other Shaving Preparation Products</td>
<td>21</td>
</tr>
<tr>
<td>12A</td>
<td>Cleansing</td>
<td>1</td>
</tr>
<tr>
<td>12C</td>
<td>Face and Neck (exc shave)</td>
<td>4</td>
</tr>
<tr>
<td>12D</td>
<td>Body and Hand (exc shave)</td>
<td>11</td>
</tr>
<tr>
<td>12E</td>
<td>Foot Powders and Sprays</td>
<td>1</td>
</tr>
<tr>
<td>12F</td>
<td>Moisturizing</td>
<td>8</td>
</tr>
<tr>
<td>12G</td>
<td>Night</td>
<td>5</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>377</strong></td>
</tr>
</tbody>
</table>

- Acrylates/Methoxy PEG-23 Methacrylate/Perfluorooctyl Ethyl Acrylate Copolymer - No Data
- Acrylates/Perfluorohexylethyl Methacrylate Copolymer - No Data
- Behenyl Methacrylate/Perfluoroctylethyl Methacrylate Copolymer - No Data
- C6-14 Perfluoroalkylethyl Acrylate/HEMA Copolymer - No Data
- Hexafluoropropylene/Tetrafluoroethylene Copolymer - No Data
- PEG-10 Acrylate/Perfluorohexylethyl Acrylate Copolymer - No Data
- Polychlorotrifluoroethylene - No Data
- Polyperfluoroethoxymethoxy Difluoroethyl PEG Diisostearate - No Data
Polyperfluoroethoxymethoxy Difluoroethyl PEG Ether - No Data

Polyperfluoroethoxymethoxy Difluoroethyl PEG Diisostearate - No Data

Polyperfluoroethoxymethoxy Difluorohydroxyethyl Ether - No Data

Stearyl Methacrylate/Perfluorooctylethyl Methacrylate Copolymer - No Data
Memorandum

TO: Bart Heldreth, Ph.D., Executive Director
   COSMETIC INGREDIENT REVIEW (CIR)

FROM: Beth A. Jonas, Ph.D.
       Industry Liaison to the CIR Expert Panel

DATE: September 28, 2017

SUBJECT: Concentration of Use by FDA Product Category: Fluoropolymers
Concentration of Use by FDA Product Category – Fluoropolymers*

PTFE
Acrylates/Methoxy PEG-23 Methacrylate/Perfluorooctyl Ethyl Acrylate Copolymer
Acrylates/Perfluorohexylethyl Methacrylate Copolymer
Behenyl Methacrylate/Perfluorooctylethyl Methacrylate Copolymer
C6-14 Perfluoroklyl ethyl Acrylate/HEMA Copolymer
Hexafluoropropylene/Tetrafluoroethylene Copolymer
PEG-10 Acrylate/Perfluorohexylethyl Acrylate Copolymer
Polychlorotrifluoroethylene
Polyperfluoroethoxymethoxy Difluoroethyl PEG Diisostearate
Polyperfluoroethoxymethoxy Difluoroethyl PEG Ether
Polyperfluoroethoxymethoxy Difluoroxyethyl Ether
Polyperfluoroethoxymethoxy Difluoromethyl Ether
Stearyl Methacrylate/Perfluorooctylethyl Methacrylate Copolymer

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Product Category</th>
<th>Maximum Concentration of Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTFE</td>
<td>Eyebrow pencils (3A)</td>
<td>5%</td>
</tr>
<tr>
<td>PTFE</td>
<td>Eyeliner (3B)</td>
<td>0.5-6.1%</td>
</tr>
<tr>
<td>PTFE</td>
<td>Eye shadows (3C)</td>
<td>0.3-12%</td>
</tr>
<tr>
<td>PTFE</td>
<td>Eye lotions (3D)</td>
<td>0.11-3.8%</td>
</tr>
<tr>
<td>PTFE</td>
<td>Mascara (3F)</td>
<td>1-13%</td>
</tr>
<tr>
<td>PTFE</td>
<td>Hair bleaches (6G)</td>
<td>2.4%</td>
</tr>
<tr>
<td>PTFE</td>
<td>Blushers (7A)</td>
<td>2-6%</td>
</tr>
<tr>
<td>PTFE</td>
<td>Face powders (7B)</td>
<td>0.6-3%</td>
</tr>
<tr>
<td>PTFE</td>
<td>Foundations (7C)</td>
<td>0.5-3.4%</td>
</tr>
<tr>
<td>PTFE</td>
<td>Makeup bases (7F)</td>
<td>8%</td>
</tr>
<tr>
<td>PTFE</td>
<td>Other makeup preparations (7I)</td>
<td>6.7%</td>
</tr>
<tr>
<td>PTFE</td>
<td>Other oral hygiene products (9C)</td>
<td>0.44%</td>
</tr>
<tr>
<td>PTFE</td>
<td>Shaving products (11E)</td>
<td>0.15%</td>
</tr>
<tr>
<td>PTFE</td>
<td>Face and neck products (12C)</td>
<td>0.6-3.6%</td>
</tr>
<tr>
<td></td>
<td>Not spray</td>
<td></td>
</tr>
<tr>
<td>PTFE</td>
<td>Body and hand products (12D)</td>
<td>0.8-1%</td>
</tr>
<tr>
<td></td>
<td>Not spray</td>
<td></td>
</tr>
<tr>
<td>PTFE</td>
<td>Moisturizing products (12F)</td>
<td>0.5%</td>
</tr>
<tr>
<td></td>
<td>Not spray</td>
<td></td>
</tr>
</tbody>
</table>

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

Information collected in 2017
Table prepared: September 27, 2017
Memorandum

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

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

DATE: January 23, 2018

SUBJECT: PTFE

Anonymous. 2018. Summaries of studies on products containing PTFE.
## Summaries of Studies on Products Containing PTFE

<table>
<thead>
<tr>
<th>Study Type</th>
<th>Test Sample</th>
<th>Test Condition</th>
<th>Test Dates</th>
<th>Completed Subjects #</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>48 hour patch</td>
<td>formula containing 7.6% PTFE</td>
<td>neat, semi-occlusive patch</td>
<td>1/15-17/2014</td>
<td>26</td>
<td>Primary irritation index (PII) = 0, no irritation</td>
</tr>
<tr>
<td>HRIPT</td>
<td>formula containing 2.89% PTFE</td>
<td>neat, occlusive patch</td>
<td>2/18-3/25/2004</td>
<td>107</td>
<td>no dermal irritation or dermal sensitization potential</td>
</tr>
<tr>
<td>EpiOcular</td>
<td>formula containing 2.89% PTFE</td>
<td>neat</td>
<td>3/1/2006</td>
<td>not applicable</td>
<td>$ET_{20} &gt; 24$ hours, no eye irritation potential</td>
</tr>
</tbody>
</table>
Memorandum

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

FROM: Jay Ansell, Ph.D.  
Industry Liaison to the CIR Expert Panel

DATE: January 18, 2018

SUBJECT: Scientific Literature Review (SLR): Safety Assessment of Fluoropolymers as Used in Cosmetics (report posted on CIR’s website on January 8, 2018)

The Council has no suppliers listed for the following ingredients included in the SLR on fluoropolymers:
- Acrylates/Perfluorohexylethyl Methacrylate Copolymer
- Behenyl Methacrylate/Perfluorooctylethyl Methacrylate Copolymer
- Polychlorotrifluoroethylene
- Polypersfluoroethoxymethoxy Difluoroethyl PEG Diisostearate
- Stearyl Methacrylate/Perfluorooctylethyl Methacrylate Copolymer

The Council respectfully submits the following comments on the SLR, Safety Assessment of Fluoropolymers as Used in Cosmetics.

Key Issues
As it is not relevant to cosmetic use of these ingredients, the information on pyrolyzed PTFE and pyrolyzed Polychlorotrifluoroethylene should be deleted from this report.

Genotoxicity studies of the monomer tetrafluoroethylene should be added to this report. This would add insight into potential mechanisms of action for the positive NTP bioassay on tetrafluoroethylene.

A supplier has suggested that the following reference would be a helpful review of the historical data on fluoroalkene monomers and their polymers:

Additional Considerations
Introduction, Table 1 - Polypersfluoroethoxymethoxy Difluoroethyl PEG Diisostearate is listed twice as an ingredient in this report. Polypersfluoroethoxymethoxy Difluoromethyl Ether,
which was included in the concentration of use survey, is not listed as an ingredient in this report.

Acute Oral, Summary - The types of values presented in the Acute Oral section and the Summary are not the same. The Acute Oral section calls them “LD₉₀” values while the Summary calls them “LD₅₀” values. Rather than presenting the highest LD₅₀ values in the Summary, the lowest LD₅₀ values should be presented.

Short-Term, Oral - In the last paragraph (study in rhesus monkeys, reference 22), it is not necessary to state: “showed no significant indication of peroxisomal proliferation” and “There was no evidence of peroxisomal proliferation.”

Chronic, Oral, PTFE - The 90-day study does not belong in the Chronic section.

Genotoxicity, In Vitro - This section should also indicate that the information is from an abstract (reference 25).

Carcinogenicity, Inhalation - The concentrations of tetrafluoroethylene tested in the NTP bioassay need to be added to the CIR report. Please correct “tetrafluoroethylene”.

Carcinogenicity, Subcutaneous - With the sentence indicating that the subcutaneous and intraperitoneal studies are presented in Table 5, it should also state that the table includes the size of the implants tested.

Other Relevant Studies - Please indicate the size (or weight/volume) of implants in the studies (references 55, 56, 57) included in this section.

Other Clinical Reports - Please indicate the size (or weight/volume) of implants in the study (reference 60) included in this section.

Occupational Exposure - Reference 61 concerning lung exposure to PTFE particles, and reference 63 concerning urinary fluoride levels should be moved to the ADME section.

Table 2 - Reference 5, the NTP bioassay of tetrafluoroethylene is not the correct reference for some chemical/physical properties of PTFE.

Table 5 - If studies on other compounds are not found, the title of the table should be changed to “Carcinogenicity of Implanted PTFE”. The size of the material implanted should always be presented in the first column of this table.

Reference 25 - If only the abstract was reviewed, this should be stated in the reference section.

References 26 and 27 - The references are missing the journal (they have “Acute Toxicity Data” instead of the journal name). Reference 26 is from the International Journal of Toxicology.
Memorandum

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

FROM: CIR Science and Support Committee of the Personal Care Products Council

DATE: January 31, 2018

SUBJECT: Scientific Literature Review: Safety Assessment of Fluoropolymers as Used in
   Cosmetics (report released January 8, 2018)

The CIR Science and Support Committee (CIR SSC) appreciates the opportunity to comment on
the scientific literature review on polymers containing fluorine.

We believe that further justification is needed for the grouping of ingredients in this report. The
appropriateness of using data on one ingredient to support the safety of other ingredients is not
clear, and needs further discussion within the report if all of these ingredients remain in a single
CIR report. There is one other ingredient (Hexafluoroisopropylene/Tetrafluoroethylene
Copolymer) that shares the tetrafluoroethylene monomer with the lead ingredient, PTFE. If it is
not appropriate to read-across using data on PTFE to support the safety of the other ingredients in
the report, the other ingredients should not be included in the report.

The OECD/UNEP Global PFC Group published a document in 2013 entitled ‘Synthesis paper on
which includes an organization scheme for fluorine containing polymers. If all of the ingredients are retained in
the CIR report, the report should be reorganized to reflect the categories described in this document. The
document classifies fluorine containing polymers into the following three groups:

1. Fluoropolymers: “fluorinated polymers consisting of carbon only backbone with
   fluorines directly attached to this backbone”, e.g., PTFE, polyvinylidene fluoride,
   fluorinated ethylene propylene, perfluoroalkoxy polymer.

2. Side-chain fluorinated polymers: “consisting of variable compositions of
   non-fluorinated carbon backbones with polyfluoroalkyl (and possibly
   perfluoroalkyl) side chains”, e.g., fluorinated (meth)acrylate polymers, fluorinated
   urethane polymers.
3. Perfluoropolyethers: “fluorinated polymers consisting of backbones containing carbon and oxygen with fluorines directly attached to carbon.”

Therefore, based on this classification, only two ingredients in this report, PTFE and Hexafluoropropylene/Tetrafluoroethylene Copolymer should actually be considered “fluoropolymers”, suggesting that the title of the report also needs to be revised if all of the ingredients are retained in the report.