Safety Assessment of Polyfluorinated Polymers as Used in Cosmetics

Status: Draft Tentative Report for Panel Review
Release Date: May 11, 2018
Panel Date: June 4-5, 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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Memorandum

To: CIR Expert Panel Members and Liaisons
From: Wilbur Johnson, Jr.
Senior Scientific Analyst
Date: May 11, 2018
Subject: Draft Tentative Report on Polyfluorinated Polymers

The safety of the following 12 polyfluorinated polymers in cosmetics is reviewed in this Cosmetic Ingredient Review (CIR) safety assessment. An Insufficient Data Announcement (IDA) with the following data requests was issued at the March 5-6, 2018 CIR Expert Panel meeting.

- Method of manufacture and impurities data
- Skin sensitization data on PTFE at the highest maximum use concentration of 13%

To date, the following data have been received from the Personal Care Products Council (Council) in response to the IDA:

1) 24 h patch test on an eye shadow containing 12% PTFE (skin irritation test) (*fluoro062018data1*);
2) HRIPT on an eye shadow containing 6% PTFE (skin sensitization test) (*fluoro062018data1*); and
3) impurities data on PTFE (*fluoro062018data2)*.

These data are included for the Panel's review and are summarized and highlighted in the text of the draft Tentative Report on Polyfluorinated Polymers. A determination as to whether the data received satisfy the Panel's request for skin sensitization and impurities data will need to be made.

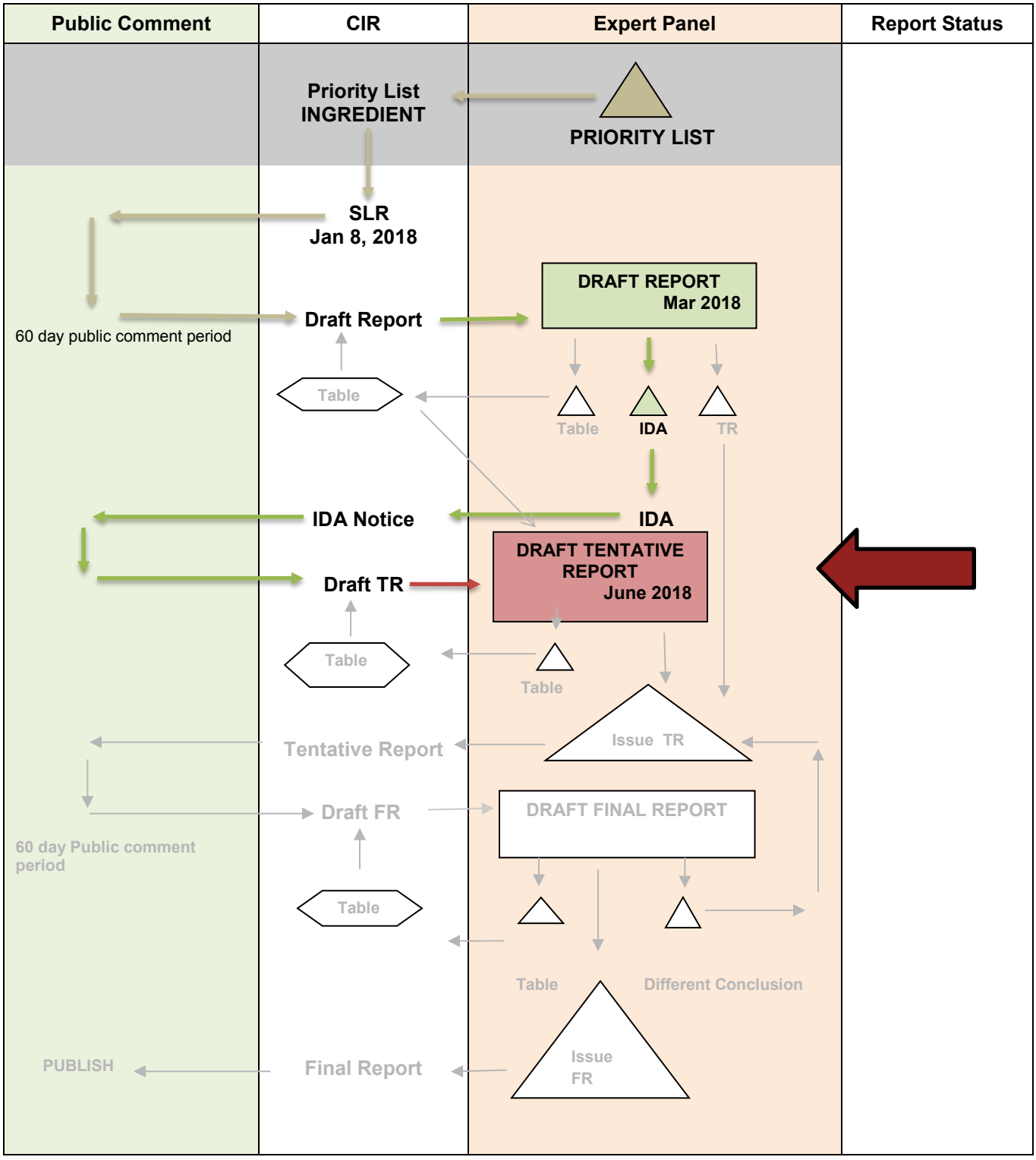
Also included in this package for your review are the draft Tentative Report (*fluoro062018rep)*, the CIR report history (*fluoro062018hist*), flow chart (*fluoro062018flow*), literature search strategy (*fluoro062018strat*), ingredient data profile (*fluoro062018prof*), 2018 FDA VCRP data (*fluoro062018FDA*), minutes from the March 5-6, 2018 CIR Expert Panel meeting (*fluoro062018min*), and comments that were received from the Council prior to the March 2018 Panel meeting (*fluoro062018pcpc)*.

In that all of the data requested by the Panel have not been received, the Panel may consider issuing a Tentative Report with an insufficient data conclusion. The Panel also has the option of issuing a Tentative Report with a safe as used, safe with qualifications, or unsafe conclusion, if deemed appropriate after further review of the available data.

SAFETY ASSESSMENT FLOW CHART

INGREDIENT/FAMILY Polyfluorinated Polymers

MEETING June 2018



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.

The Panel issued an Insufficient Data Announcement (IDA) for the following 12 polyfluorinated polymer (Polyfluorinated Polymers is new name for this ingredient group) ingredients:

Fluoropolymers
PTFE
Hexafluoropropylene/Tetrafluoroethylene Copolymer

Fluorinated-Side-Chain Polymers
Acrylates/Perfluorohexylethyl Methacrylate Copolymer
Behenyl Methacrylate/Perfluorooctylethyl Methacrylate Copolymer
C6-14 Perfluoroalkylethyl Acrylate/HEMA Copolymer
Stearyl Methacrylate/Perfluorooctylethyl Methacrylate Copolymer

Fluorinated Polyethers
Acrylates/Methoxy PEG-23 Methacrylate/Perfluorooctyl Ethyl Acrylate Copolymer
PEG-10 Acrylate/Perfluorohexylethyl Acrylate Copolymer
Polyperfluoroethoxymethoxy Difluoroethyl PEG Diisostearate
Polyperfluoroethoxymethoxy Difluoroethyl PEG Ether
Polyfluoroethoxymethoxy Difluorohydroxyethyl Ether
Polyperfluoroethoxymethoxy Difluoromethyl Ether

The Panel determined that Polychlorotrifluoroethylene should be deleted from the group because the properties of this chemical are very different from the other polyfluorinated polymers under review. Furthermore, following a discussion relating to similarities and differences in chemistry within this ingredient group, the Panel determined that these ingredients should be sub-divided into fluoropolymers, fluorinated-side-chain polymers, and fluorinated polyethers, as indicated above.

The Panel identified the following data needs:

- Method of manufacture and impurities data
- Skin sensitization data on PTFE at the highest maximum use concentration of 13%

Draft Report, Teams/Panel: June 4-5, 2018

The following data were received in response to the IDA that was issued at the March 2018 Panel meeting, and have been added to the draft tentative report:

- Single-insult (24 h) patch test on an eye shadow containing 12% PTFE (skin irritation test)
- HRIPT on an eye shadow containing 6% PTFE (skin sensitization test)
- Impurities data on PTFE

Data Profile on Polyfluorinated Polymers for June 4th-5th, 2018 Panel – Wilbur Johnson

	Dermal Penetration			Nail Penetration	Penetration Enhancement	ADME					Acute Toxicity			Short-Term Toxicity	Sub-Chronic Toxicity	Chronic Toxicity	DART		Genotoxicity	Carcinogenicity	Other Relevant Studies		Dermal Irritation*	Dermal Sensitization		Ocular Irritation *		Clinical Studies	Case Reports		Epidemiology Studies
	In Vivo -Animal	In Vitro-Human	In Vivo-Human	In Vitro-Human	In Vitro-Animal	In Vitro-Human Dermal	Animal-Dermal	Animal-Oral	Animal-Inhalation	Human-Oral	Animal-Dermal	Animal-Oral	Animal-Inhalation	Animal	Animal	Animal	In Vitro	In Vivo	In Vitro/In Vivo	In Vivo	In Vitro	In Vivo-Animal	Animal/Human/In vitro	Animal	Human	In Vitro	Animal	Human-Subcutaneous	Human-Dermal	Human-Inhalation	Human
PTFE												X	X			X		X	X	X			X		X	X	X	X		X	
Acrylates/Methoxy PEG-23 Methacrylate/Perfluorooctyl Ethyl Acrylate Copolymer																															
Acrylates/Perfluorohexyleth-yl Methacrylate Copolymer																															
Behenyl Methacrylate/Perfluorooctyl-ethyl Methacrylate Copolymer																															
C6-14 Perfluoroalkylethyl Acrylate/HEMA Copolymer																															
Hexafluoropropylene/Tetra-fluoroethylene Copolymer																															
PEG-10 Acrylate/Perfluorohexylethyl Acrylate Copolymer																															
Polychlorotrifluoroethylene								X	X			X	X	X	X	X							X	X			X				
Polyperfluoroethoxymethoxy Difluoroethyl PEG Diisostearate																															
Polyperfluoroethoxymethoxy Difluoroethyl PEG Ether																															
Polyfluoroethoxymethoxy Difluorohydroxyethyl Ether																															
Polyperfluoroethoxymethoxy Difluoromethyl Ether																															
Stearyl Methacrylate/Perfluorooctyl-ethyl Methacrylate Copolymer																															

X = data

[Fluoropolymers – 11/9/17;1/18/18; 4/19/18]

Ingredient	CAS #	InfoBase	SciFinder	PubMed	TOXNET	FDA	EU	ECHA	IUCLID	SIDS	HPVIS	NICNAS	NTIS	NTP	WHO	FAO	ECET -OC	Web
Polytetrafluoroethylene (PTFE)	9002-84-0	1/1	1489/59	15/7	3957/10	Yes	No	No	6/0	No	No Report	No Report	No	Yes	No	No	No	
Acrylates/Methoxy PEG-23 Methacrylate/Perfluorooctyl Ethyl Acrylate Copolymer		1/1	0/0	0/0	0/0	No	No		No	No	No	No Report	No	No	No	No	No	
Acrylates/Perfluorohexylethyl Methacrylate Copolymer	1557087-30-5	1/1	2/1	0/0	0/0	No	No	No	No	No	No	No Report	No	No	No	No	No	
Behenyl Methacrylate/Perfluorooctylethyl Methacrylate Copolymer		1/1	0/0	0/0	0/0	No	No	No	No	No	No	No Report	No	No	No	No	No	
C6-14 Perfluoroalkylethyl Acrylate/HEMA Copolymer		1/1	1/0	0/0	0/0	No	No	No	No	No	No	No Report	No	No	No	No	No	
Hexafluoropropylene/Tetrafluoroethylene Copolymer	25067-11-2	1/1	73/7	1/1	0/0	No	No	No.	1/0	No	No Report	No Report	No	No	No	No	No	
PEG-10 Acrylate/Perfluorohexylethyl Acrylate Copolymer		1/1	0/0	0/0	0/0	No	No	No	No	No	No	No Report	No	No	No	No	No	
Polychlorotrifluoroethylene	9002-83-9	1/1	66/18	34/7	10/5	No	No	No	No	No	No Report	No Report	No	No	No	No	No	
Polyperfluoroethoxymethoxy Difluoroethyl PEG Diisostearate		1/1	0/0	0/0	0/0	No	No	No	No	No	No	No Report	No	No	No	No	No	
Polyperfluoroethoxymethoxy Difluoroethyl PEG Ether	162492-15-1	1/1	1/0	0/0	0/0	No	No	No	1/0	No	No	No Report	No	No	No	No	No	
Polyperfluoroethoxymethoxy Difluoroethyl PEG Diisostearate		1/1	0/0	0/0	0/0	No	No	No	No	No	No	No Report	No	No	No	No	No	
Polyperfluoroethoxymethoxy Difluorohydroxyethyl Ether	88645-29-8	1/1	2/0	0/0	0/0	No	No	No	1/0	No	No	No Report	No	No	No	No	No	
Stearyl Methacrylate/Perfluorooctylethyl Methacrylate Copolymer		1/1	1/0	0/0	0/0	No	No	No	No	No	No	No Report	No	No	No	No	No	

Search Strategy

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

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

LINKS

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

FDA databases – http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm (CFR); then,
list of all databases: http://www.fda.gov/ForIndustry/FDABasicsforIndustry/ucm234631.htm; then,
http://www.accessdata.fda.gov/scripts/fcn/fcnnavigation.cfm?rpt=eafuslisting&displayall=true (EAFUS);
http://www.fda.gov/food/ingredientspackaginglabeling/gras/default.htm (GRAS);
http://www.fda.gov/food/ingredientspackaginglabeling/gras/scogs/ucm2006852.htm (SCOGS database);
http://www.accessdata.fda.gov/scripts/fdcc/?set=IndirectAdditives (indirect food additives list);
http://www.fda.gov/Drugs/InformationOnDrugs/default.htm (drug approvals and database);
http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/UCM135688.pdf (OTC ingredient list);
http://www.accessdata.fda.gov/scripts/cder/iig/ (inactive ingredients approved for drugs)

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

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

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

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

Day 1 of the March 5-6, 2018 CIR Expert Panel Meeting – Dr. Belsito's Team

Polyfluorinated Polymers

DR. LIEBLER: Fluoropolymers. More polymers.

DR. BELSITO: Fluoropolymers. Okay so this is the first time we're also looking at this. And we got data in Wave two. Dan, first question, grouping?

DR. LIEBLER: Yeah, I thought these were all appropriate. But the one that I thought that could probably be deleted from the report is the polychlorotrifluoroethylene, which is in the middle of the list in the introduction. And this apparently is not a large molecule.

It may have similar uses, but it has a small enough molecular weight that I think absorption and distribution is an issue. Whereas with the rest of these, it's not at all an issue. It's fluorinated molecule, but it does not provide read across to any of the others.

DR. BELSITO: This is Polychlorotrifluoroethylene?

DR. LIEBLER: Correct.

DR. ANSELL: We would suggest that this is actually three separate families.

DR. LIEBLER: Yes.

DR. ANSELL: That you have the fluorinated polymers consisting of fully fluorinated materials. That you have materials where only the side chains is fluorinated, and have variable compositions of the non-fluorinated, the carbon backbones. And then you have fluorinated polymers consisting of ethers, ether languages.

DR. LIEBLER: Right.

DR. ANSELL: And we would suggest that they be treated as three separate chemistries.

DR. LIEBLER: I made a note of the same thing because I noticed the three themes. But I felt that they were presented to us, so I thought that the council had already kind of thought that that would be fine, to present them together.

I'm certainly willing to consider them together. I can see the different chemistries, but the uses and the chemical physical properties are pretty similar across these.

DR. ANSELL: None of the other two families are used in cosmetics.

DR. SNYDER: No suppliers.

DR. LIEBLER: Well -- okay, they're in the dictionary. If you want them reviewed -- I mean, from a purely chemical, biology standpoint, which is what I can respond to, I have no problem with reviewing these together. If there's a sort of review priorities reason to include or not include some of these, then that's fine -- and I won't argue.

But they could go together in a report, except for the one that I recommended to be deleted. I basically volley it back to you and say, decide and then tell us what you want me to review.

DR. HELDRETH: Since we depend on the Voluntary Cosmetic Registration Program for telling us whether or not these ingredients are in use or not, I think it's best not to delete ingredients solely on the fact that they might not be listed this year in the VCRP.

If there's other reason -- you know, like you're saying, they don't belong together, or there's some scientific rationale for why we should be deleting them, that's great. Follow your heart on that. But just deleting them because they're not currently listed in the VCRP, I think is not an appropriate pathway to go about.

DR. ANSELL: Well, we do believe, then, they need to be reviewed as three separate families.

DR. HELDRETH: And we can easily separate them out. We've done that before.

DR. ANSELL: Because that how you're going to find the chemistry listed. That's how OECD group these materials.

DR. HELDRETH: We've done that in other reports.

DR. LIEBLER: I mean, if you want to do that, that's fine with me, and I can respond to it in the report. I'm just telling you. I think I reviewed this around the same time I reviewed the methacrylates, which was a complete dog breakfast of chemistry.

And this is a little tidier in terms of the groupings, you know, kind of clearly separating out. On the other hand, you've got these polymers with very similar functions and similar overall likely biological properties. That's why I was okay with including them. And if there are other reasons to do them separately, I'm fine with that too.

DR. HELDRETH: My understanding is part of industry's issue with this, is the nomenclature and the way they viewed these ingredients as being different. For example, I think one suggestion is that really only PTFE and the hexyl methyl fluoro/tetra-fluoroethyl one are actually polyfluoro compounds, and they would actually

call it the other ones, fluorinated, something else polymers.

DR. LIEBLER: I was going to suggest a title change.

DR. HELDRETH: We can definitely do a title change.

DR. LIEBLER: To polyfluorinated polymers.

DR. ANSELL: Poly and perfluorinated. Because there's a nomenclature to these materials.

DR. LIEBLER: Okay. Anyway, but that depends now on what the hell is in this report, too. Like I said decide, and then call us.

DR. ANSELL: Well, that is our recommendation, is that these be grouped, consistent with the industry guidelines, the way these are grouped.

DR. BELSITO: Okay. So, I'm not a chemist. What are we agreeing to do here, split this into three reports?

DR. HELDRETH: My understanding -- my suggestion, I should say, is to keep it as one report, but separate out the chemistry. Separate out so that it's clear that there's some differences between these different compounds. Have the PTFE and the other true perfluorinated polymer be a group; and have the other two groups, as industry has suggested. And make a title change that accurately reflects the way the industry views these ingredients so that in the end the report is useful to those folks.

DR. BELSITO: And in so doing we're still getting rid of polychlorotrifluoroethylene?

DR. HELDRETH: Yes.

DR. BELSITO: Okay, so that goes?

DR. HELDRETH: Yes. I mean, beforehand, just looking at the definition of it, there's an X next to how many monomer units are there. So, we have no idea, is this huge, is this little?

But in putting this report together, we were able to find data that let us know that it's really tiny and it's actually a liquid. And so, I agree. I think it should absolutely be done now that we know that information.

DR. KLAASSEN: Since we do have some data on it.

DR. LIEBLER: I'm fine with that outcome, if that's all right with council.

DR. SNYDER: So, we're insufficient, right?

DR. LIEBLER: Well, we're still going to be insufficient.

DR. SNYDER: Is the bottom line.

DR. LIEBLER: Yeah.

DR. BELSITO: What are we changing the name of the report to?

DR. LIEBLER: Polyperfluorinated polymers.

DR. ANSELL: Poly and perfluorinated.

DR. BELSITO: So, poly --

DR. LIEBLER: How about polyfluorinated and perfluorinated polymers?

DR. BELSITO: Polyfluorinated and fluorinated?

DR. LIEBLER: And perfluorinated.

DR. HELDRETH: Typically, when we're naming polymers up, we're talking about the monomer. The monomers that are imparting fluorine to the end polymer are perfluorinated. Not all the monomers in some of those examples have a fluorine; but the ones that do are perfluorinated.

So, I mean, we're going to have to define what we mean by perfluorinated if we're not going to just call them all perfluorinated.

DR. BELSITO: What are you suggesting, Bart?

DR. HELDRETH: We could just either go with Dan's original suggestion of polyfluorinated ingredients, and not worry about discriminating between per and not per. Or just call them all polyperfluorinated ingredients.

DR. LIEBLER: I've always thought of per as meaning every C-H bond is a C-F bond.

DR. ANSELL: Correct.

DR. LIEBLER: And that's obviously only true of the fluorinated monomer contributors. Whereas the other contributors, like the acrylates and the methacrylates, et cetera, those are not.

I think, talking about these molecules, it's better to just say polyfluorinated then per anything. Because the polymer is not perfluorinated for sure. Okay, Bart, so I guess back to polyfluorinated polymers?

DR. HELDRETH: Or just polyfluorinated ingredients. Because otherwise, I think we're kind of saying poly twice.

DR. LIEBLER: Well, we're saying poly about the fluorination and then they're also polymers.

DR. HELDRETH: Okay. Okay. Now I see what you're saying. Okay.

DR. ANSELL: Polymers are fluorinated monomers.

DR. BELSITO: So, our title is now polyfluorinated polymers?

DR. LIEBLER: Yes.

DR. BELSITO: We got rid of the perfluorinated?

DR. LIEBLER: Correct.

DR. BELSITO: Okay. Polyfluorinated. On Page 11 of the PDA, are any of you concerned regarding individual components that maybe present as residues?

DR. SNYDER: Monomers. We have no impurities.

DR. BELSITO: Right. We have no impurities. So, that's an insufficiency.

DR. SNYDER: Right. We know that one monomer causes some issues.

DR. LIEBLER: We got acrylates and we got the fluoro monomers. So, we need those.

DR. BELSITO: Okay. And what about this tetrafluoroethylene carcinogenicity study, Page 16?

DR. SNYDER: That's why we have the impurities.

DR. BELSITO: Okay.

DR. SNYDER: Because that's a monomer, right?

DR. BELSITO: Okay. But could we go safe and just limit the impurities? Or we just don't know what to limit them to?

DR. LIEBLER: I say we ask for impurities and then we can handle this in the discussion.

DR. BELSITO: Okay. And what did you all think of those sarcomas, not relevant?

DR. SNYDER: Well, hemangiosarcomas, and stuff, I think, are probably relevant to liver toxicity and not a true carcinogenicity.

DR. BELSITO: Okay. Now these are used in aerosolized products. Is any of that going to concern you regarding respiration?

DR. LIEBLER: Not with these polymers, no.

DR. BELSITO: Okay. So, insufficient for impurities, sensitization at maximum concentration of use 13 percent.

DR. LIEBLER: Right. Yes. Method of manufacture.

DR. BELSITO: Method of manufacture.

DR. LIEBLER: And I think for the chemistry section, at the beginning, where you've got these sort of minimalist representation of the structures, I think we need to take another run at this; to see if we can represent the families of structures somehow, to represent the fact that these are three different groups.

You should have some common features, but that also have some distinct structure. I'll let you guys put your heads together and think about how to represent that.

DR. HELDRETH: And have an example of each.

DR. LIEBLER: Yeah. You've done very well with other chemistry like that with polymers. But these really minimal C-F things don't tell you anything, so.

DR. KLAASSEN: There's a general issue I'd like to bring up. And I don't know how relevant this is. There's a major environmental problem with these fluorinated compounds. One of the problems of these things is they don't break down. And so, there's been two chemicals that have been extensively studied, and that's perfluorodecanoic acid and perfluorooctanoic acid.

And these compounds, when they get in the animal they concentrate in the liver and they really increase the size of a liver, like in the order of three to four times the normal size of the liver. And they are PPARalpha agonist, et cetera.

Well, these compounds were originally used to make Teflon, so when you fry your eggs they don't stick. And they've also been used as scotch guard. You spray your upholstery with scotch guard. And these chemicals have kind of a crazy characteristic that they don't have much water solubility or lipid solubility. And so, things don't stick to them.

But the real problem is that they get into the environment and the same thing happens. And two weeks ago, in the state of Minnesota, 3M was sued -- the state of Minnesota sued 3M for making these fluorinated compounds, and 3M has to pay them $850 million.

And the same thing has happened with DuPont that makes these polyfluorinated compounds, and they are now paying $350 million. So, we've got over a billion dollars in suits, largely for environmental and they can't be used anymore.

Some of these compounds that we're looking at here have some similarities. And I don't know how much. And I guess I see most of the concern, largely, from an environmental -- especially at the dose we're going to be using -- than the biological affect.

But anyhow, I just wanted to make sure that I put this on the table and that everybody was aware

of the social concern of the fluorinated compounds at this time in history.

DR. BELSITO: I mean, we've dealt that with another propellant where we felt that environmentally it was not safe. In fact, I think it's been banned either by EPA or by some European regulatory agencies. And we basically ended up saying from a human health perspective, it's safe as used. But environmental effects of these materials are not within our purview.

I think we can say the same thing for these materials. We're looking at it in terms of direct effects on human health, not long-term effects on the environment and subsequent effects on human health.

DR. LIEBLER: The molecules that Curt was talking about, and these, share the fact that they are highly fluorinated?

DR. KLAASSEN: Right.

DR. LIEBLER: Now that we've gotten rid of that one smaller molecule, these are all really large molecules which will not be absorbed. They're not going to have that kind of bioaccumulation and bio-persistence aspect to them that the perfluorodecanoic and perfluorooctanoic have, which are indeed a problem.

It's also true, I think, that these are going to be persistent in the environment to the extent that they are present in the environment. They're going to be more resistant to degradation in part because of the fluorination. On the other hand, these also consist of a lot of non-fluorinated carbon structure as well.

I think this still falls outside of the purview of this panel to the extent that these get in the environment. They may or may not be more persistent than other polymeric materials. Definitely, probably more stable -- or less stable -- than the fluorooctanoic and decanoic acids.

I don't think that example of the octanoic and decanoic perfluoro compounds represents something that we need to point to as a toxicity risk or hazard for these molecules. If we want to mention it in the discussion, we can probably say that we're aware of that, but these are distinct because of their large molecular weights, lack of capacity for absorption, and leave it at that.

DR. KLAASSEN: I'm happy with that. But I think we should somehow mention that we are aware of these compounds. And I was wondering if any of these things might be metabolized. You know, when you get these -- I don't know what molecular weight we're talking about on some of these chemicals and how big they really are.

DR. LIEBLER: Many, many thousands.

DR. KLAASSEN: These are all in the many thousands?

DR. LIEBLER: Yeah. They're in the range where you can't even get them in the solution for an enzymes to be able to chew on them if that could happen.

DR. ANSELL: The issue with the PFOAs is really the heritage issue, and they're no longer used in the manufacturing process. My understanding is it was a voluntary cessation with the EPA where the industry was completely out of them by, I think, 2012.

So, while certainly we can discuss what would be appropriate language, but I don't think it's relevant to the cosmetic ingredients that's used to manufacture today.

MR. JOHNSON: The concern that you mentioned related to cancer, right? Perfluorooctanoic cancer?

DR. KLAASSEN: Well, they do a number of things. There's even developmental toxicity. So, there's a lot of different toxicities.

I hesitated about bringing this up because I know it's kind of more environmental than human health affect. But I guess I would like to -- if we could put the one sentence in the discussion, that'd keep me happy.

DR. BELSITO: I mean, basically, get the discussion from the propellant.

DR. KLAASSEN: So, the people that read that know that we at least know that.

DR. BELSITO: Right.

DR. LIEBLER: What did you find?

MR. JOHNSON: I guess, the fact that cancer was mentioned, is there any concern about residual monomer, because tetrafluoroethylene is a carcinogen?

DR. LIEBLER: That's why we want residuals. I think these are going to be --

DR. BELSITO: We're asking for method of manufacture and impurities.

DR. KLAASSEN: They should be able to clean them up if they try.

DR. BELSITO: And sensitization at 13 percent. So, we're not going final with these. I guess the only other thing I need to know is, what are the three groups we're doing here?

DR. KLAASSEN: The top half, the middle and the bottom half.

DR. SNYDER: It's on Page 38 of the PDF.

DR. BELSITO: Page 38 of the PDF.

DR. SNYDER: From the PCPC standpoint.

DR. BELSITO: PCPC standpoint, 38. Okay.

DR. LIEBLER: Page 38 of the PDF.

DR. BELSITO: The fluoropolymers, the side-chain fluoropolymers and the perfluoropolyethers. Okay. So, we're keep it as one report, but we're going to look at three categories.

DR. KLAASSEN: Three categories.

DR. SNYDER: Makes sense.

DR. LIEBLER: Yeah. It's fine.

DR. BELSITO: And we're getting rid of that small molecular weight doodad. The report needs to be a little reorganized, Wilbur, and then we're insufficient for manufacturer, impurities and sensitization at 13 percent.

MR. JOHNSON: The sensitization data refer to all of the ingredients in the safety assessment, or just --

DR. BELSITO: There's only one that -- the ones that use that 13 percent. There's only one that's used, right?

MR. JOHNSON: Yes. It's one ingredient in there. That's fine.

DR. BELSITO: Anything else? Okay.

MR. JOHNSON: I guess what I was asking, Dr. Belsito, in that we only have use frequency and concentration of use data on the PTFE --

DR. BELSITO: Right. That's the one that's used at 13 percent. That's the one we need.

MR. JOHNSON: So, you don't need any sensitization data on any of the other chemicals in the report?

DR. BELSITO: No.

MR. JOHNSON: Okay. Thank you.

Day 1 of the March 5-6, 2018 CIR Expert Panel Meeting – Dr. Marks'Team

Polyfluorinated Polymers

Fluoropolymers. Wilbur has sent us a draft report on the fluoropolymers dated February 9th of this year. This is the first time we've seen these ingredients, and the first question of course, are the ingredients okay? The Council has questioned the group, so we need to address that. Then we'll go on to what are the needs.

I guess the first issue is the ingredients itself. Let me get my notes. Tom, Ron, your comments about -- the ingredients are on page 24.

DR. HILL: I worked from the table on page 22 and 23. Table 2, which had all the definitions.

DR. MARKS: I did 24 because it's all on one page.

DR. HILL: That's 24.

DR. MARKS: No, it isn't.

DR. HILL: I think probably you were looking the same place I was, 22, 23.

DR. MARKS: Yeah, okay. Actually, the one I was looking at, Ron Hill, was page five where it has the various tests that were done on all of the ingredients.

DR. HILL: What we call the read across table?

DR. MARKS: Yes.

DR. HILL: They're probably in a different order than in Table 2 aren't they?

DR. MARKS: Council's point -- let's see if I have that memo.

DR. EISENMANN: What we discovered was that there is a group -- the people that make these compounds have classified them a certain way, and we're not following that classification. If you want to leave all the ingredients in the report, the term, fluoropolymers, they are using for polymers that consist of carbon only backbones with chlorines directly attached to this backbone. So, they're using it for a specific group of polymers and we only have two of those in this report.

And then the other groups they have as side-chain fluorinated polymers and perfluoropolyethers. If they're all left in this report, it would be nice to have them organized in the same way that the industry is organizing these polymers, and to call it fluorine-containing polymers, or something else other than fluoropolymers.

But whether or not you really want to put them all, we thought we might want to reconsider that too because really only one has uses. It's very likely all the others, other than PTFE and perhaps the other fluoropolymer in here, would probably be insufficient. Which is fine, but it just means keeping track of a bunch of insufficient data ingredients.

DR. HELDRETH: Right, and the rationale for initially putting this group together wasn't, per se, for there to be read across because with polymers, much like botanicals, it is really not something that's usually very effective. But the idea was that if these are large molecules, that what we're worried about are contaminants or leftover monomers or similar impurities. That's what this group shares in common, is having these fluorinated monomers and these small fluorinated molecules often hit a lot of red flags.

That was the idea behind having these ingredients grouped together as fluoropolymers; although, we're happy to change the nomenclature if it better represents these groupings to the industry.

DR. HILL: So, do you want me to tell you what I think we should do? We need to look at page 22 and 23. I apologize, but they're in a different order than on page five.

I also pretty much concur with the fluoropolymer group. I think we should keep Teflon, which is the first one, PTFE. The hexafluoropropylene, tetrafluoroethylene -- although it's not clear that it's in use and we won't be getting any data. So, that's the second one on page 23.

And then two down from that is the polychlorotrifluoroethylene, and that's really a fluoropolymer with chlorine end-capping, and I thought that that could stay in this group. The only caveat is that Teflon, which is a solid, is a very different beast than this polychlorotrifluoroethylene, which is small molecular weight liquid with only a couple of things in there. We really have disparate data. And then a third one where we will have no data, because as far as I can tell it's not out there in use.

DR. EISENMANN: Actually, I think there are some old data in this 1967 summary of data that Wilbur found towards the end.

DR. HILL: It's really a Teflon analog polymer with an extra carbon stuck in there. If you look at, on page 22, number two, three, four, and then the first one on the top of the next page, those are all acrylates and they ought to go in the acrylate group that we're about to start working on. There is no reason why they don't fit

there other than the fluorines, and fluorines on alkyl chain are inert. That's why you put them there.

The only time we have fluorine issues -- I grant you, we might have a discussion about what's used to put that fluorine there back in process. But by the time you get to polymers, we're looking at things that are inert. But they definitely fit in the acrylate polymers group that we're about to start working on, I believe.

Just to telescope on that a little bit, I'm of the mind to put all the acrylate stuff that -- everything together and end up with a monster group and so there will just be one, two, three, four more fitting in there. And also, the third one down on page 23 is also an acrylate. It's a PEG-10 acrylate, perfluorohexylethyl, so what. The fact that there are fluorines in there still keeps it with the acrylate group from where I sit.

And then on the bottom of page three -- well and in fact, the last one on page 23 can also get over to the acrylate group because it fits there. We've got a methacrylate even though it's an octamethyl methacrylate copolymer, it fits there.

And then the four before that, they should all go with the PEG esters and ethers group, which unfortunately we just worked on not too long ago. I would be in favor of just putting those aside and the next time that comes up for re-review, putting them in there because I didn't see anything that red flags those for me.

I would propose we have a group of three, even though it will be a disparate group, one of which is not in use. We put one, two, three, four, five of them over to the acrylates group because they fit there. One, two, three, four, five, six, and then we have four others that we shuffle to the PEG ether and esters group because they fit there.

DR. MARKS: So, the lead is the polytetrafluorethylene?

DR. HILL: Yes.

DR. MARKS: And then what were the other two that you mentioned?

DR. HILL: The other two would be the hexafluoropropylene, tetrafluoroethylene copolymer even though --

DR. MARKS: Hexafluoropropylene, tetra --

DR. HILL: Fluroethylene copolymer. And then that third one would be the polychlorotrifluoroethylene.

DR. MARKS: So, that's one more -- two down from the --

DR. HILL: The fluoropolymers group probably won't like that because there is chlorine in the backbone, but it would be a reason for not putting that -- actually, reviewing it separately would seem to be a reasonable option in this case.

DR. HELDRETH: Historically, we've had some proposed groupings in the past of polymers; and those ones that were fluorinated, in some way, were removed from the report because they were fluorinated.

DR. HILL: If that happened since I've been on the panel, I can't imagine why.

DR. MARKS: So, Carol, what is -- you mentioned right in the beginning grouping by direct attachment to the carbon atom by fluoride and the side chain fluoride, the industry recommendation. How does this fit into that? Because this obviously -- now we're down to two or three ingredients with the polytetrafluorethylene being the lead. Obviously, that's the one that has the uses. It has almost 400 uses, 377 I had at this point. What's your sense?

DR. EISENMANN: Well, we haven't really discussed this with the CIR SSC. When I sent emails out to suppliers, on some of those other compounds, they said they're not fluoropolymers, so they don't belong in this report.

DR. HILL: I agree.

DR. EISENMANN: Which is the response. I would assume that that would be fine to put them in the other report, if you're okay with having fluorinated polymers in with the acrylate copolymer group. I mean, that's your prerogative.

DR. HILL: I can't come up with a good reason why not to, because the acrylates for me are going to be the thing that will have my attention.

DR. EISENMANN: As far as the chlorinated compound, as far as I know that has no uses in cosmetics. I mean, you can't use read across from the other two; is it really worth reviewing? I don't know. I mean, it's in the dictionary, but it's quite different from the other ones.

DR. HILL: If there are no reported cosmetic uses, my feeling is we drop that out, keep Teflon and that other one even though it's no longer reported to be in use. You said there's some older data from the '60's?

DR. EISENMANN: Yes.

DR. MARKS: Tom, what do you think? Do you like the way --

DR. EISENMANN: Because then you could call the report fluoropolymers.

DR. HILL: And they are fluoropolymers.

DR. SLAGA: I thought it looked fine this way, with the fluoropolymers -- I mean, there's a general theme, so I go with Bart, to mean that -- I can see Ron's point, but, I mean, that acrylate group is big already.

DR. HILL: I think it's going to get much bigger because my feeling on the acrylates is everything that was raised -- we have to decide about the PVP, which we'll discuss later; everything ought to go in one monster report of about 100 things, and then deal with it all. So, to add five more is nothing from where I sit.

DR. MARKS: Let me see what Ron Shank says. Page 13, metabolism. Does this mean that the polymer at 400 thousand to -- it looks like 10 million molecular weight was metabolized or broke down; or were the trimers and tetramers entrapped in the polymer?

All of these studies seem to indicate that these large polymers are absorbed from the GI tract and lungs. If so, then systemic tox studies are needed. Now we're into, what are the needs? So, we'll get to that in a minute.

DR. HILL: The point is there though, while we're on that, is that all the data there is for that one small polychlorotrifluoroethylene. It's very different from the rest of them because it's trimers and tetramers. So, they're small. That's why he apparently didn't catch that distinction.

DR. MARKS: Page 13 inhalation, where there is exposure to whole body or nose only. Whole body would lead to ingestion due to licking of the fur. Nose only could lead to ingestion if the particulate were large enough. Page 15, chronic oral study. Questions the 50 percent loss of body weight is not normal growth. Page 15, Chinese tetragenicity study, can we get the details. And then let me see, sensitization in animals. Isn't PCTE a solid? Need definition of this substance.

DR. HILL: And the answer is, no, it's a liquid with relatively small molecules.

DR. MARKS: Okay. Sensitization in humans. Was the test substance a cosmetic formulation or formula? Then he talks about even though this isn't a discussion, that polymers are large enough to preclude dermal penetration, oral and pulmonary exposure indicates these molecules are unrelated. Monomers can be absorbed.

It's not certain that the read across using PTFE for all of the other polymers is valid. Need data on dermal penetration, metabolism of all the polymers. That's of course if we -- including obviously, 28-day dermal tox or genotox.

Page 23, Table 3, can the boiling point of polychlorotrifluoroethylene be lower of the melting point?

I guess going back, Ron Shank didn't mention about the ingredients. So, we sort of a divergence here of -- Ron Hill, I hear you would really like to see polytetrafluoroethylene and then perhaps two other ingredients and --

DR. HILL: I think it should probably be just the one and keep that chlorotrifluoro out.

DR. MARKS: So, two ingredients. Tom, do you feel strongly about all versus just limiting it?

DR. SLAGA: Come again?

DR. MARKS: Do you feel strongly about including all of these ingredients versus limiting it to two? And then Ron Hill, I'll ask you to comment on that, the two, and where you would put the others.

DR. SLAGA: I have no problem going this way or splitting some of them.

DR. MARKS: Let's move forward with the split at this point. The two ingredients. We'll see what the Belsito team, how they react to that.

Then what needs do we have? We'll assume those two ingredients. Obviously, we have lots of data on the polytetrafluoroethylene. And then we also have it on a polychlorotrifluoroethylene, but was that going to be -- that was not going to be included.

DR. HILL: My suggestion would be ditch it. It's different and not in use.

DR. MARKS: So, what needs do we have? Do we need -- for those two? I had, I'd like to see sensitization on the PTFE, particularly since you say it's a liquid, it's not a solid.

DR. HILL: That's the PTC -- the one with the chlorine.

DR. MARKS: No, polytetrafluoroethylene.

DR. HILL: No, that's Teflon. So, it's either coated on something or it's a polymer. It's Teflon. You're familiar with Teflon tape?

DR. MARKS: Sure. So, it's a solid?

DR. HILL: It's a solid.

DR. MARKS: That's what I -- okay. We don't need, presumably, we don't --

DR. HILL: I think with those two, I'm pretty sure it will be safe as used. I didn't have any data

needs for Teflon that we didn't already have.

DR. MARKS: Tom? Do we have the impurities then on that? We should. It's Teflon. There should be plenty out there.

DR. SLAGA: I didn't have any data needs. I was going to go with -- I mean, they're such large polymers and you worry about the monomers, but the impurities, you know, obviously the PT -- PE is carcinogenic, but it's not mutagenic. In an inhalation study, I had some concern there; but on the skin it's so large that it's really not going to penetrate unless selectively the monomers get on. It could be formulated to be non-irritating and non-sensitizing.

DR. MARKS: No, I don't think we'll end up with that. We do have one sensitization study, but that's at 2.9 percent. I don't know how they do that if it's a solid.

DR. HILL: That's worth asking; because obviously, if you have something finely powdered and put it in the wrong -- you can get irritation, right, I guess, but --

DR. MARKS: Well, that was okay at 2.9. Since it's a solid you would think even though it's used up to a concentration of 13 percent, you wouldn't think it would be an irritant or a sensitizer.

DR. HILL: No, and if you look at what they have written under carcinogenicity -- and I don't have a problem with it, but the data on inhalation is for the monomer. I mean, I realize I've occasionally raised, in the polymer, how much monomer is likely to be retained. In this particular case, I don't have that concern. I just don't. It's very small molecular weight, extremely volatile. Any conceivable production process of this material is not going to be there.

MR. JOHNSON: Just one question. Considering that tetrafluoroethylene monomer is carcinogenic, still based upon, I guess, your understanding that the monomer would not be present --or a negligible amount would be present, you're not concerned about carcinogenicity?

DR. HILL: I am not -- vanishingly negligible. I don't think you take that study out, but I think you make it in lights that this is dealing with the monomer and then -- I think if the Teflon industry would like to supply us with some nice language explaining why -- better than I just did -- why it's not going to be there. But we're talking about a monomer that's a gas.

We could put the physical chemical characteristics of that monomer in, along with the table, just to indicate it's not an ingredient, but this is what the monomer is like.

DR. MARKS: And that would be in the discussion.

DR. HILL: And then you could put it in the discussion. We don't have any data on any of the rest of these, that's the other thing. But if you put them in with acrylates, for example, then I believe we can do read across on almost everything.

And the other ones are in the -- the only stray cats would be those four that really should go in the PEG ethers and PEG esters report, and we've put those to bed recently, so they wouldn't come up again for a while. But honestly, I don't have any problem with that because of the nature of those molecules. That's my way of thinking.

DR. MARKS: So, let me just be sure I understand here, Ron. The two you would include now, this is PTFE and the hexafluoropropylene tetrafluoroethylene copolymer, is that correct?

DR. HILL: Correct.

DR. MARKS: Let me get rid of this one.

DR. HILL: I'm sorry it's on a different page.

DR. MARKS: That's okay.

DR. EISENMANN: One quick question, do you want a little genotoxicity of the monomer in there; just because it's positive carcinogenicity, you might put a little bit of negative genotoxicity? I think there's a little -- you can almost put the summary from the NTP report on genotoxicity and that might be enough. That also would help because it's negative.

DR. HILL: I would say, yes, for sure.

MR. JOHNSON: Can I make a comment? Reading from the NTP report, it states that the multiplicity of hepatocellular neoplasm and the development of liver hemangiosarcomas, and the significant increase in histiocytic sarcomas in the liver, suggest that metabolizing enzymes in the liver may have produced unique tetrafluoroethylene metabolites; which may have played a role, perhaps through as yet undetected genotoxic events, in the development of the marked increase in tumors in the liver.

DR. HILL: And so, I agree with that. In fact, with that monomer, there are known routes of metabolism to get to acid fluoride sorts of molecules that are going to tag DNA proteins like that. That would only apply to the monomer. So, we can retain that information, honestly, as much as you want.

But the point is, there isn't going to be any monomer in any of these finished Teflons. And again,

I would solicit information from -- if we want to do an information needs -- information from industry, clearly explaining why there won't be vanishingly, negligently small amount of the stuff in any finished Teflon. If anybody has any reason to suspect otherwise, we should get that information too.

I agree with you, but those kinds of metabolism routes are known; and the kinds of molecules that can be reactive, that can cause the effects that are observed, are known from long years of experience with general anesthetics that had fluorines or fluorines and chlorines. That's not stunning.

MR. JOHNSON: I know Carol mentioned the negative genotoxicity data, but this seems to suggest that some metabolite may in fact be genotoxic.

DR. HILL: Yes, I think they're not -- for the monomer, I don't think you'll find that it's negative. But I don't see that that's cause for concern.

DR. HELDRETH: Just for the record, I would prefer that we stick to the PTFE name and not use the Teflon name, because while all Teflon may be PTFE, not all PTFE is Teflon. If we could stick to that name it would be much preferred.

DR. HILL: I agree.

DR. HELDRETH: Also, not necessarily -- you see the structure for PTFE, it's the C2F4 and then an X. That X may be a smaller or larger value than what's used in the commercial product Teflon.

DR. HILL: All right. Then we have insufficient information to get an idea about the range that's in the commercial products for that polymer.

DR. HELDRETH: We have one representative molecular weight range, and that's provided in the report. So, that gives the panel the opportunity to say --

DR. HILL: We're going to assume that that's the molecular weight?

DR. HELDRETH: Correct.

DR. MARKS: Yeah. I like that too. We're reviewing based on that. So, tomorrow, move that these two ingredients that we've just been discussing are safe? Tom?

DR. SLAGA: I agree.

DR. MARKS: The PTFE and the hexafluoropropylene tetrafluoroethylene copolymer. We're going to limit it to those two ingredients in this report. We're going to move forward with a tentative report with a safe conclusion.

MR. JOHNSON: Dr. Marks, no qualification, just safe in the present practices of use?

DR. MARKS: Yes.

DR. DEWAN: So, as I'm seeing, some of these products are used in baby products and may come in contact with eyes. And if you look at the ocular studies that were submitted, all of them showing some kind of irritation. So, do you have any concerns with the eye irritation?

DR. MARKS: Yes, maybe. I have that 20 percent in wave two and 2.8 percent for -- I think that's animal, ocular irritation was okay. Is that correct, Wilbur? Where is it? So, to me, the ocular irritation wasn't a concern at the use concentration.

MR. JOHNSON: Right, there was ocular irritation, but it cleared with 24 hours.

DR. MARKS: Yes, exactly. It was not significant. That's what I meant when I said it was okay. And that was wave two information, so that wouldn't be on the original memo from Wilbur.

DR. HILL: I think it is important to make sure that we have a good look and write that well, because one place for sure this stuff is used is in mascaras, and some eye shadows I think.

DR. MARKS: Any other comments? Nope. Again, I'll reiterate I'm going to move tomorrow that we have a tentative report on two ingredients and the conclusion will be safe as used. We'll see what the Belsito team comes up with. I suspect it will be different.

Day 2 of the March 5-6, 2018 CIR Expert Panel Meeting - Full Panel

Polyfluorinated Polymers

DR. MARKS: This is the first time we've seen the fluoropolymers. And our team, when we looked at it, we wanted to limit the report to just two ingredients. The PTFE and the hexafluoropropylene /tetrafluoroethylene copolymer. I'll let Ron Hill go into the chemistry of that. And we felt that limiting it to those two, that we could move forward with a tentative report, safe.

DR. BERGFELD: Is that a motion?

DR. MARKS: Yes.

DR. BERGFELD: Is there a second or a comment?

DR. BELSITO: We felt that looking at all of the various fluoropolymers, that we did want to remove one from the group, which was a low molecular weight, the polychlorotrifluoroethylene. We also agreed with the council's comments about sort of dividing this into three different groups, but keeping it, at least initially, into one report.

I'm trying to find exactly -- the categories would be fluoropolymers, side chain, fluorinated polymers and perfluoropolyethers. We are also recommending a change in the title of the report, which would become fluoropolymers as their title.

And then, beyond that, in terms of the reorganization into the three different groups that I had mentioned, we felt that the data were insufficient, and we wanted -- what do we want? Impurities --

DR. LIEBLER: I think it was method of manufactures --

DR. BELSITO: And impurities. And sensitization at 13 percent. Yeah. Method of manufacture, impurities and sensitization at 13 percent. We wanted to drop one ingredient, split it into the three chemical groups, rename the report, and sensitization at 13 percent and look at it again.

DR. LIEBLER: Just to clarify and suggest a new title, it was polyfluorinated polymers.

DR. BELSITO: Oh, I got it wrong.

DR. BERGFELD: Any discussion from Mark's team. Ron hill?

DR. HILL: I totally disagree with that approach. The compounds where we've got fluorine on the carbon backbone, extensively, that are not tetrafluoroethylene polymers, or we have one that's an analog of tetrafluoroethylene/hexafluoropropylene.

You put fluorine on these chains because that creates inertness. Looking at one, two, three, four, five of them, they belong in the acrylates reports. There's really nothing, other than those fluorines on those chains, to separate them from the acrylates that we're looking at, and the one we're going to discuss next.

And then there's four others that belong in the PEG esters and PEG ethers report; and there's nothing really unique about them, from the fact that they have fluorines, to not have them in that other category. And I didn't see any urgency in getting those other four reviewed.

I can tell you which ones are which, if we want to know in Table two. But I didn't see any urgency in getting those reviewed unless there was somebody that had an issue for getting them reviewed. We could just wait until PEG esters and ethers came back up; and put those fluorinated compounds in there and review them together with them when they come up in due course.

That was my take on it. For me, the only one that fit was PTFE, polytetrafluoroethylene, and in common, the hexafluoropropylene, which is no longer in use, or we don't think it's in use, and unlikely to be used again. But all the issues there would be in common.

The commonality is that they have the low molecular weight monomer that we do have some toxicology data for; even though with PTFE, what I believe is, and my insufficiency was, some assurance at the processing to give us whatever is showing up in cosmetic ingredients is going to eliminate that very volatile gas, that's the monomer in that particular case.

That was my logic. These others are clearly going to be made by disparate processes, have different concerns; and five of them are acrylates, they should go in the acrylates reports and be reviewed along with those.

DR. BERGFELD: I wonder if we could hear what Ron Shank said, please. Comment, maybe, while you're looking. Do you have it?

DR. MARKS: Oh, yeah. I have it right here. It's extensive. And I'm not --

DR. BERGFELD: Well, highlight it.

DR. MARKS: I read all this yesterday. Metabolism. Does this mean that the polymer -- it is on page 13 of this PDF. Polymer of 400,000 to 10 million molecular weight was metabolized or broke down. I don't

think -- let me see is this, discussion.

He doesn't talk about the chemistry per se and the various grouping. Of course, that memo came out, we just saw that yesterday. And so, Ron didn't have the privilege of seeing that and discuss dividing it into groups.

This is a first review, I think we could move forward and we're going to have at it again. So, I probably wouldn't spend a great deal of time. If you strongly feel keep all the ingredients in, we'll keep all the ingredients in --

DR. LIEBLER: We can kick them out --

DR. MARKS: Huh?

DR. LIEBLER: We can kick them out later.

DR. MARKS: Yeah. Exactly. That's what I'm saying. You've heard our rationale and we'll have another crack at it and decide whether we want to kick them out. The sensitivity data on PTFE, as Ron Hill mentioned, the monomers is gas. We felt there'd be small concentrations that could be handled in the discussion. But let's see if we get sensitization for it. Always, it's better to have the hard data.

I think, if our teams okay, I'll second the motion.

DR. BERGFELD: You're the one that made it.

DR. HILL: I'm not okay. I don't like that.

DR. MARKS: Oh. I'll withdraw that motion.

DR. BERGFELD: Thank you.

DR. HILL: I don't like that approach. I'm not okay with it.

DR. BERGFELD: What don't you like, Ron?

DR. HILL: Of course, with the acrylates that are moving forward, the same information request will go to industry. What do we know about that chemistry of these things? Potential for impurity, low molecular monomers, all of that will go, of course, forward. But to me, waiting and saying, okay we didn't get any data -- they just don't belong together.

I could see making this into three separate reports and reviewing them that way. But they don't go together. The chemistry used to create the fluorinated molecules in those acrylates is very different than what's used to create the polytetrafluorethylene in terms of manufacturing them. And similarly, with the perfluoroethoxymethoxy, that group that are PEG esters and ethers.

The chemistry used to put the fluorines in there is going to be very different than it is in creating these polytetrafluorethylenes. They just don't go together chemically. The concerns don't overlap to me in any regard. There's going to be no overlap.

And I think, in this case, the idea of putting them together administratively, just because they have fluorine in there doesn't make any sense for me, chemically or biologically. So, I'm not good with that approach of just keeping them.

DR. BELSITO: We did ask to split them into three groups within the report.

DR. HILL: I don't think that's sufficient. I'm just saying. For me, I don't like it.

DR. BELSITO: You can look at it and say, let's make it three reports.

DR. HILL: Then that would be fine with me. If we want to make three reports, that'll be fine with me.

DR. BELSITO: So, we'll see the data next time.

DR. MARKS: I think what Ron Shank would say is, let the chemist duke it out and then we'll take care of it from a toxicologic point of view. He mentioned that about one of the other group of ingredients. Bart, I guess I'd be interested to hear your take.

DR. BERGFELD: I just asked him, he was shaking his head.

DR. MARKS: Your take at this point. I know we're going to have another hit at it. But, I'd be very interested in your take on this grouping and respond to Ron Hill's concern about the chemical.

DR. HELDRETH: Certainly, I bend to the expertise of the panel. You certainly are the experts. It is your prerogative to make the choice on this.

From my perspective on the staff side, it just looks like we're choosing which bins these things go in. I don't see it affecting how we approach the safety assessment, whether we put them in an acrylates report or put them here or separate them out. Whichever seems like the most efficient root for this panel; whichever seems like the easiest pathway to get these safety assessments completed, I'm for.

DR. BERGFELD: Dan, you want to make a comment?

DR. LIEBLER: Yeah. I acknowledge that there are very distinct differences in the chemistry between the groupings here. I was looking, as I read this report -- particularly as I read the memo from the CIR

Science and Support Committee -- for some kind of clear smoke signal. Clear smoke signal; that's probably not the best thing to say.

Anyway, a clear signal. We disagree with these grouping, or we agree with the groupings of all of these together in the report. I didn't see that.

We had an extended discussion back and forth with Jay, during our session, where we talked about the pros and cons of including these together or not. And I ended up basically saying, several times, make up your mind. Because I think we can handle them scientifically either way.

The way that they're presented to us now -- you know, I acknowledge the differences in the chemistry. I think there are also some overwhelming similarities, driven mainly by the fact that these are very big molecules, which are essentially not going to be absorbed and not going to be metabolized. The differences in the chemical structure of the polymers, probably are going to be less important than the potential residual monomers, the issues that we usually have with polymers and impurities.

So, you know, if we end up deciding to split them out later, okay, I won't -- you know, I'm not going to -- I don't feel so strongly that they must be together. On the other hand, I don't feel strongly that they must be separated into three groups. And if these end up getting parsed out into other reports, you won't hear me objecting. Because it's obvious that the thing that's driving this is the PTFE and the other one that has the very similar structure.

I just wanted to make clear that I agree -- acknowledge some of the points on the chemistry. And I'm really looking for some guidance really from the council, and from CIR staff, as to how to best proceed. Because we can review the safety either way you cut it.

DR. HILL: I think the reason that I so forcefully stated that I'd like to see them separated is because, I don't want there to be any impression later that we dropped a set of ingredients because there's no data. Because I'm not sure we're going to get the data, but maybe we will get the data we're looking for.

There's just no commonality. And since we're looking at what to put in the acrylates report, I thought at least let's move the acrylates, which clearly have common issues. There'll still be a subgroup within the acrylates report because there's going to be something unique to putting the fluorines on these particular side chains. But we have the opportunity to put them in that other report, that we don't know what we're doing with yet until we discuss in a moment what we're doing.

I thought at least move those. And I think if you put the -- we can keep the PEG ethers and esters in there, but they don't belong. I'd like to see a separate report. I will argue, sort of to the death, on making a separate report for those four that don't belong with these others. That's my take on it.

DR. HELDRETH: Would it be acceptable to the panel, as a whole, to move forward with this report with the ingredients in, as is, except for the deletion of the polychlorotrifluoroethylene? And effectively separate the ingredients within the report, quite clearly, demonstrating the different chemistries of the three different groups?

And making sure that the sections are separate so that it's quite obvious that read across cannot be done from one to the other? And lay it out in such a format that it would be very easy to parse it out if the data that we get, or don't get, in the future directs us to do so? Would that be an acceptable pathway?

DR. HILL: Okay.

DR. MARKS: Yes.

MR. GREMILLION: Can I ask a question? Is that something you've done before, dividing within a report?

DR. BERGFELD: Yes.

DR. HILL: No often, but some. The polysaccharides were an example, noteworthy, in recent years that I can think of. I don't see what the upfront downside is in creating three different reports and handling them that way from the get go so that's it's clear.

And one of the reasons I was brought onto the panel was to advise about -- I mean, it was made very clear to me at the get go -- was to advise about creating groupings. And in this particular case, I feel very strongly those three basic groups that's in there, plus the low molecular weight one we're kicking out anyway, which we should, don't belong together as a group.

I agree that sometimes, administratively, that's the reason for creating the group, but ultimately, we're looking for safety assessment and how the chemistry relates to the biology in terms of assessing safety. And that's my take on that.

DR. HELDRETH: Further to your question, Mr. Gremillion, very often on molecule will have two, three or four different chemical aspect to it. And each one of those aspects may lend it to be grouped with one set of ingredients. And one of the other aspects may lend it to be grouped with another set of ingredients.

It's very common that one ingredient may be properly grouped in more than one situation. In cases like this where there seems to be some disparity within the grouping, even though there are some similarities, it's often useful if we separate them out and call out those differences so that when we're making the safety assessment, we're sure not to cross over those lines.

MR. GREMILLION: Sure. And that makes perfect sense to me. Our concern would be here a review of the safety of PTFE. I think that's seems to be driving this delay because of the broad grouping.

DR. BERGFELD: Wilbur has something,

MR. JOHNSON: Yeah. I'd like to call the panel's attention to PDF page 33. PTFE is used in face powders at concentrations up to 3 percent. And not knowing the content of residual monomer, or other components in PTFE, are inhalation toxicity data needed?

DR. BELSITO: We're asking for impurities, so I think we'll find that out.

DR. BERGFELD: Any other comments? I'm going to have to have the motion restated. We've had Dr. marks withdraw his motion, so it's Dr. Belsito's motion to put in place.

DR. BELSITO: Okay. Let me pop up my comments again. We are eliminating perchlorofluorethylene from this report. We are keeping them together, but we are renaming the report polyfluorinated polymers. We are going with council's suggestion to split this in terms of looking at the methods of manufacture, et cetera, into three different groups. And those would be -- I'm trying to find it here.

DR. BERGFELD: Can Wilbur help you?

MR. JOHNSON: I can read them. Yeah. The fluoropolymers, the side chain fluorinated polymers and the perfluoropolyethers.

DR. BELSITO: Thank you, Wilbur.

MR. JOHNSON: You're welcome.

DR. BELSITO: Then we're going to go insufficient for method of manufacture and impurities, and if possible, sensitization at 13 percent. And that was it.

DR. BERGFELD: Is that agreeable, Dr. Marks?

DR. MARKS: Second.

DR. BERGFELD: Second. Any further discussion or comment?

DR. MARKS: So, this would be an insufficient data announcement.

DR. BERGFELD: Thank you. Seeing none, call to question? All those in favor of this conclusion? Thank you. Unanimous.

Safety Assessment of Polyfluorinated Polymers as Used in Cosmetics

Status: Draft Tentative Report for Panel Review
Release Date: May 11, 2018
Panel Date: June 4-5, 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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ABSTRACT: The Cosmetic Ingredient Review (CIR) Expert Panel (Panel) reviewed the safety of polyfluorinated polymers, which function as bulking agents, slip modifiers, film formers, viscosity increasing agents, dispersing agents, skin conditioning agents, skin protectants, and hair conditioning agents in cosmetic products. The Panel reviewed relevant data relating to the safety of these ingredients under the intended conditions of use in cosmetic formulations, and the issuance of a conclusion is expected.

INTRODUCTION

The safety of the following 12 polyfluorinated polymers in cosmetics is reviewed in this safety assessment.

Fluoropolymers
- PTFE
- Hexafluoropropylene/Tetrafluoroethylene Copolymer

Fluorinated-Side-Chain Polymers
- Acrylates/Perfluorohexylethyl Methacrylate Copolymer
- Behenyl Methacrylate/Perfluorooctylethyl Methacrylate Copolymer
- C6-14 Perfluoroalkylethyl Acrylate/HEMA Copolymer
- Stearyl Methacrylate/Perfluorooctylethyl Methacrylate Copolymer

Fluorinated Polyethers
- Acrylates/Methoxy PEG-23 Methacrylate/Perfluorooctyl Ethyl Acrylate Copolymer
- PEG-10 Acrylate/Perfluorohexylethyl Acrylate Copolymer
- Polyperfluoroethoxymethoxy Difluoroethyl PEG Diisostearate
- Polyperfluoroethoxymethoxy Difluoroethyl PEG Ether
- Polyfluoroethoxymethoxy Difluorohydroxyethyl Ether
- Polyperfluoroethoxymethoxy Difluoromethyl Ether

According to the web-based *International Cosmetic Ingredient Dictionary and Handbook* (wINCI *Dictionary*), these polyfluorinated polymers 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.[1] (See Table 1). 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 perfluorinated. 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 polyfluorinated polymers that have been evaluated for safety by the CIR Expert Panel are presented in Table 2.

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 1.[1] These ingredients share in common a fluorinated organic polymer backbone, wherein at least some of the carbons in that backbone are perfluoronated. PTFE is a perfluoronated homopolymer, comprising only carbon and fluorine. Together with Hexafluoropropylene/Tetrafluoroethylene Copolymer, these two ingredients comprise the fluoropolymers sub-group.

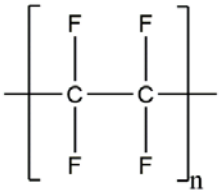


Figure 1. PTFE (Polyfluorotetraethylene)

Certain other polyfluorinated polymer ingredients can be classified as fluorinated-side-chain polymers. These ingredients comprise polyacrylates with polyfluorinated side-chains. For example, Acrylates/Perfluorohexylethyl Methacrylate Copolymer is a copolymer of acrylates and methacrylate, wherein the methacrylic acid residues are esterified with perfluorinated, branched chains.

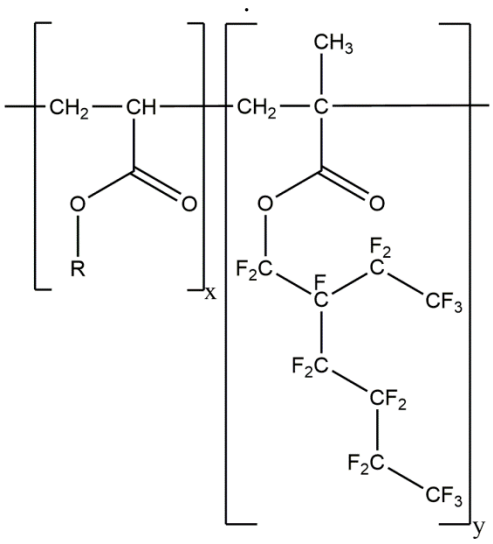


Figure 2. Acrylates/Perfluorohexylethyl Methacrylate Copolymer – wherein R is methyl, ethyl, propyl, or butyl.

And the rest of these polyfluorinated polymers in this report, comprise a fluorinated polyethers sub-group. This sub-group of ingredients comprises copolymers ethers and fluorinated monomers. In some cases, Polyperfluoroethoxymethoxy Difluorohydroxyethyl Ether for example, these fluorinated polyethers also comprise end-capping units.

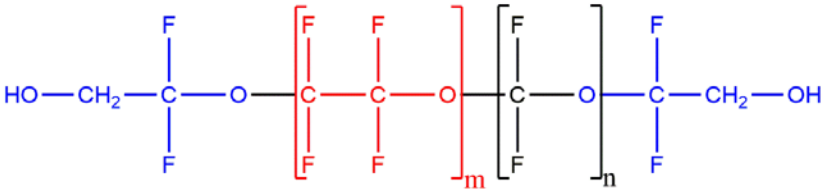


Figure 3. Polyperfluoroethoxymethoxy Difluorohydroxyethyl Ether – comprising 2 perfluorinated monomers and end-capping units

As with 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.

Chemical and Physical Properties

Polyfluorinated polymers such as PTFE are noted for high thermal stability.[2] PTFE is a white translucent to opaque solid,[3] ranging in molecular weight from 400,000 to 10,000,000 Daltons (Da).[4] The density of PTFE is 2.25 g/cm^3.[5] According to the following values, the melting points of polyfluorinated polymers can vary: Hexafluoropropylene/Tetra-fluoroethylene Copolymer (270°C),[5] and PTFE (320 to 330°C).[5] PTFE decomposes at 315 to 375°C.[6] Properties of polyfluorinated polymers are presented in Table 3.

Method of Manufacture

PTFE

PTFE is prepared by the polymerization of tetrafluoroethylene.[3] Because PTFE is poorly soluble in practically all solvents, the polymerization occurs as an emulsion in water.[7] Alternatively, polymerization may be carried out using a surfactant, such as perfluorooctanoic acid (PFOA). More recent information relating to the manufacture of PTFE is as follows: "The ammonium salts(in some cases also the sodium salts) of long chain PFCAs such as PFOA and PFNA have been applied as processing aids (emulsifiers) at low concentrations around 0.5 wt%) in the polymerization of certain polyfluorinated polymers (i.e., PTFE, FEP, PFA, and PVDF) and fluoroelastomers. After 2006, many fluoropolymer manufacturers in China, Japan, Western Europe and the United States started to replace the salts of long-chain PFCAs with the salts of short-chain PCFAs (such as PFHxA) or other nonperfluoroalkyl alternatives (such as polyfluoroalkyl ether carboxylic acids) for fluoropolymer manufacturing."[8]

Composition

PTFE

PTFE is composed of at least 20,000 C_2F_4 monomer units linked into very long, unbranched chains.[3]

Impurities

According to a chemical supplier, all commercial grades of PTFE contain some trace level of perfluorooctanoic acid (PFOA) and perfluorooctyl sulfonate (PFOS).[9] The incidental content is detectable in the ppb range. The supplier also noted that, in 2017, the European Union (EU) published measures to regulate PFOA and its salts and related substances under Annex XVII of Registration, Evaluation, Authorization, and Restriction of Chemicals (REACH). The new law (EU 2017/1000) will be implemented in phases, starting July 4, 2020. Under this new law, trace content of PFOA will be regulated to < 25 ppb, and, trace content of PFOA-related substances, regulated to < 1000 ppb.

USE

Cosmetic

The safety of the polyfluorinated polymers is evaluated based on data received from the United States (U.S.) FDA and the cosmetics industry on the expected use of these ingredients in cosmetics. Use frequencies of individual ingredients in cosmetics are collected from manufacturers and reported by cosmetic product category in FDA's Voluntary Cosmetic Registration Program (VCRP) database.[10] 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.[11]

According to 2018 VCRP data, PTFE is reported to be used in 365 cosmetic products (343 leave-on and 22 rinse-off products).[10] 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).[11] Further use frequency and concentration of use data are presented in Table 4.

According to VCRP and Council survey data, the remaining 12 polyfluorinated polymers 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 [fragrance] 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.[12,13,14]

The ingredients reviewed in this safety assessment are not restricted from use in any way under the rules governing cosmetic products in the European Union.[15]

Noncosmetic

Polyfluorinated polymers (e.g., PTFE and Tetrafluoroethylene/Hexafluoropropylene Copolymer) 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.[16]

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.[17] 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).[18] Diffusion cells that are used in some *in vitro* percutaneous absorption experiments are made of PTFE.[19] PTFE skin graft chambers have been used to isolate wounds and prevent epidermal heating from the skin edge.[20] Flexible PTFE feeding tubes have been used in oral carcinogenicity studies.[21]

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.[3]

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).

TOXICOKINETIC STUDIES

Dermal Penetration

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

Absorption, Distribution, Metabolism, and Excretion

Absorption, distribution, metabolism, and excretion data on the polyfluorinated polymers reviewed in this safety assessment were not found in the published literature, nor were these data provided.

TOXICOLOGICAL STUDIES

Acute Toxicity Studies

Dermal

PTFE

Results relating to the acute dermal toxicity of PTFE are presented in a study evaluating the skin irritation potential of this ingredient.[22] Skin irritation data from this study are summarized later in this report. The test substance (powder, 0.5 g) was applied to abraded and intact skin of the trunk (cm^2 area not stated) of 6 New Zealand White rabbits for 24 h. None of the animals died, and no clinical signs or behavioral alterations were observed during the study.

Oral

PTFE

The acute oral toxicity of 2 anticohesive coating materials containing PTFE was evaluated using 4 groups of Kunming mice (10 males and 10 females per group).[23] One of the materials contained 60% PTFE, and the other material contained 68% to 73% PTFE. Both materials were administered by gavage. The two 60% PTFE groups received doses of 12.5×10^3 mg/kg and 25×10^3 mg/kg, respectively. The two 68% to 73% PTFE groups received doses of 2.5×10^3 mg/kg and 5×10^3 mg/kg, respectively. Dosing was followed by a 1-week observation period, and LD_0 (dose at which no animals are expected to die) values were determined. The LD_0 values were determined to be 12.5×10^3 mg/kg (for 60% PTFE material) and 2.5×10^3 mg/kg in mice (for 68% to 73% PTFE material).

The acute oral toxicity of 2 anticohesive coating materials containing PTFE was evaluated according to the same procedure (stated above) using 4 groups of Wistar rats (10 males and 10 females per group).[23] The two 60% PTFE groups received doses of 6.25×10^3 mg/kg and 18.8×10^3 mg/kg, respectively. The two 68% to 73% PTFE groups received doses of 1.25×10^3 mg/kg and 3.75×10^3 mg/kg, respectively. The LD_0 values were determined to be 6.25×10^3 mg/kg (for 60% PTFE material) and 1.25×10^3 mg/kg (for 68% to 73% PTFE material).[23]

A low molecular weight PTFE resin (fluorotelomer, chemical characterization data not included) was administered orally to rats (strain and dosing method not stated) at doses as high as 17 g/kg.[24] None of the animals died, and there were no clinical effects or organ changes that were related to test substance administration.

Short-Term Toxicity Study

Dermal

Polyperfluoroethoxymethoxy Difluorohydroxyethyl Ether

Results relating to the short-term dermal toxicity of Polyperfluoroethoxymethoxy Difluorohydroxyethyl Ether are presented in a guinea pig maximization test in which the test substance was injected/applied topically to 10 guinea pigs during a 7-day period.[25] Skin sensitization data from this study are summarized later in this report. No mortalities occurred and there were no signs of general toxicity in any of the animals tested.

Inhalation

PTFE

Spray inhalation experiments on a low molecular weight PTFE resin (fluorotelomer, chemical characterization data not included) were performed using 4 rats (strain not stated).[24] The rats were exposed for 9 days (3 times per day) to a 20% dispersion of the fluorotelomer in dichloro(fluoro)methyl (CCl_2F)—chlorodifluoromethyl radical ($CClF_2$) from a pressurized container. After spraying, the jars were sealed and exposure to the dispersion was continued for 15 minutes. A total of 26 exposures were performed. During exposure, uncoordination, labored breathing, and irritation of the nose were observed. It was noted that these signs were primarily due to propellants and the dispersing agent (not stated). Recovery occurred immediately after exposure, and it was noted that there was no evidence of pathology that could have been attributed to exposure.

Subchronic Toxicity Studies

Oral

PTFE

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 .[26]

Three types of PTFE resin (chemical characterization data not included, 25% in the diet) were fed to male and female rats (strain and number per group not stated) for 90 days.[24] After feeding with each type of PTFE resin, there were no adverse effects on growth rate or behavior and there was no microscopic evidence of tissue changes. However, a slight shift in the distribution and number of white blood cells was observed. Also, feeding with 1 of the 3 types of resin (unsintered PTFE resin) caused an increase in the size of the liver (relative to body weight). This finding was not accompanied by any histological abnormality.

Chronic Toxicity Studies

Oral

PTFE

The chronic oral toxicity of PTFE was evaluated using 6 Swiss mice.[27] The mice were fed a standard diet supplemented with PTFE (concentration not stated) for 6 months. 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.

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY STUDIES

Oral

PTFE

The teratogenicity of 2 anti-cohesive coating materials containing PTFE (one containing 60% PTFE, and the other containing 68% to 73% PTFE) was evaluated using groups of 10 Wistar rats (5 males and 5 females per group).[23] The positive control, N,N'-methylene bis -(2-amino-1,3,4-thiadiazole), was administered to a group of 12 rats (6 males and 6 females), and the negative control (soybean oil) was administered to a group of 10 rats (5 males and 5 females). The 60% PTFE material was administered at dose of 6.25×10^3 mg/kg, and the 68% to 73% PTFE material was administered at a dose of 1.25×10^3 mg/kg. The positive and negative controls were administered at doses of 0.5 mg/kg and 5 mg/kg, respectively. All materials were administered once daily on gestation days 7-16. The results for both PTFE materials were classified as negative.

GENOTOXICITY STUDIES

In Vitro

PTFE

Two anti-cohesive coating materials containing PTFE (one containing 60% PTFE, and the other containing 68% to 73% PTFE) were negative in the Ames test at doses up to 10,000 µg/plate in *Salmonella typhimurium* TA98, TA100, and TA1535, with and without metabolic activation.[23]

In Vivo

PTFE

The genotoxicity of 2 anti-cohesive coating materials containing PTFE (one containing 60% PTFE, and the other containing 68% to 73% PTFE) was evaluated in the micronucleus test using groups of 10 Kunming mice (5 males and 5 females per group).[23] Cyclophosphamide served as the positive control. Doses were administered by gavage. The 60% PTFE material was administered at a dose of 12.5×10^3 mg/kg, and the 68% to 73% PTFE material was administered at a dose of 2.5×10^3 mg/kg. The positive control was administered at a dose of 60 mg/kg. Each dose was administered twice, separated by a 24-h interval. Results for both PTFE materials were classified as negative.

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 $B6C3F_1$ mice.[4] 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 $B6C3F_1$ 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 $B6C3F_1$ mice based on increased incidences of liver hemangiomas and hemangiosarcomas, hepatocellular neoplasms, and histiocytic sarcomas."

The subcutaneous (s.c.) and intraperitoneal (i.p.) 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 s.c. in mice of the following strains: 89 random-bred female Swiss mice (fibrosarcomas: 11 of 89 mice),[28,29] 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),[30,29] 19 male and 27 female inbred C5BL mice (sarcomas: 4 of 20 females and 4 of 15 females that retained implant),[29,31] 40 male and 40 female random-bred, CTM albino mice (sarcomas: 18 of 40 females; 9 of 40 males),[29,32] 38 BALB/c female mice (fibrosarcomas: 17 of 38 mice),[29,33] 38 C3Hf/Dp female mice (fibrosarcomas: 36 of 38 mice),[29,33] and 39 C57BL/He female mice (fibrosarcomas: 12 of 39 mice).[29,33]

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),[34,29] 65 male and female weanling Wistar rats (sarcomas: 2 of 65 rats),[29,35] 2 groups of Wistar rats, number per group unknown (sarcomas: 8 of 34 rats and 6 of 32 rats that survived minimum latent period),[29,36] 39 male Evans rats (no tumors),[29,37] 40 male Evans rats (no tumors).[29,37]

Intraperitoneal

PTFE

When PTFE (rod or powder form) was implanted 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).[29,38]

OTHER RELEVANT STUDIES

Muscle Necrosis

PTFE

A PTFE patch was implanted (size of implant not stated) in the muscle of rabbits.[39] 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, defined by the following particle size distribution, in a glycerine carrier: 4% of total particulate = 79.1 ± 38 nm; 24% of total particulate = 6100 ± 1000 nm; 30% of total particulate = 7000 to 25,000 nm; and 42% of total particulate = 485 ± 200 nm. The animals were observed for a periods of 1 week, 3 months, 6 months, and 1 year.[40] Mice received 1 s.c. 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 14 guinea pigs.[41] Seven animals were killed at intervals of 4 weeks and 12 weeks after surgery (i.e., total of 14 animals killed), 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 SENSITZATION STUDIES

Irritation

Animal

PTFE

The skin irritation potential of PTFE (powder) was evaluated using 6 New Zealand White rabbits (3 males, 3 females).[22] Two areas on the trunk (cm^2 area not stated) were clipped free of hair and one area of skin was abraded. The test substance (0.5 g) was applied to occlusive patches that were applied to the skin for 24 h. The test sites were examined for reactions at 24 h and 72 h after patch application. Skin reactions were not observed at intact or abraded skin sites in any of the animals tested, and PTFE was classified as a non-irritant.

A 20% dispersion of the fluorotelomer in $CCl_2F—CClF_2$ (defined in Short-Term Inhalation toxicity section) was applied to the skin of 10 guinea pigs (strain not stated).[24] The method and duration of test substance application and dose per cm^2 were not stated. When the $CCl_2F—CClF_2$ evaporated, the material hardened and moderate mechanical irritation was observed. There was no evidence of sensitization in any of the animals tested.

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.[42] The dose per cm^2 was not stated. Skin irritation was not observed (primary irritation index (PII) = 0).

A single-insult (24h), semi-occlusive patch test on an eye shadow containing 12% PTFE was performed using 15 subjects.[43] The location of the patch and dose per cm^2 are not stated in this study. Skin irritation was not observed in any of the subjects tested (PII = 0).

Sensitization

Animal

PTFE

A 20% dispersion of the fluorotelomer in $CCl_2F—CClF_2$ (defined in Short-Term Inhalation toxicity section) was applied to the skin of 10 guinea pigs (strain not stated).[24] The method and duration of test substance application and dose per cm^2 were not stated. There was no evidence of sensitization in any of the animals tested.

Polyperfluoroethoxymethoxy Difluorohydroxyethyl Ether

The skin sensitization potential of Polyperfluoroethoxymethoxy Difluorohydroxyethyl Ether was evaluated in the maximization test using 15 male Dunkin Hartley albino guinea pigs (10 test animals and 5 controls).[25] On day 0, the 10 test animals received the following 3 pairs of intradermal injections: Freund's complete adjuvant (FCA) emulsion (0.1 ml), Polyperfluoroethoxymethoxy Difluorohydroxyethyl Ether (concentration not stated, 0.1 ml), and Polyperfluoroethoxymethoxy Difluorohydroxyethyl Ether in FCA (0.1 ml). Similarly, the 5 control animals received the following 3 pairs of intradermal injections: FCA emulsion (0.1 ml), petrolatum oil vehicle (0.1 ml), and vehicle in FCA (0.1 ml). On day 6, the animals were treated topically with 10% sodium lauryl sulfate in vaseline oil (0.5 ml). On day 7, the same area was treated with applications of undiluted Polyperfluoroethoxymethoxy Difluorohydroxyethyl Ether or the vehicle for 48 h using an occlusive patch. The test sites were observed for signs of skin irritation 24 h after patch removal. At challenge on day 20, an occlusive patch containing 75% Polyperfluoroethoxymethoxy Difluorohydroxyethyl Ether or the vehicle was applied for 24 h to animals of the 2 groups. Sites were observed for any reactions at 24 h after patch removal and at 24 h later.

The injection of the test substance (in vehicle) caused slight irritation (number of animals not stated). Reactions were not observed after injection of the vehicle alone. At 24 h post-removal of the 48-h occlusive patch, signs of slight irritation (erythema) were observed at sites treated with the test substance. None of the animals had a positive reaction after treatment with the test substance during the challenge phase. Also, no skin reactivity was observed in the negative control group. The authors concluded that Polyperfluoroethoxymethoxy Difluorohydroxyethyl Ether did not appear to possess sensitizing capacity in this study.[25]

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 cm^2 and duration of patch application were not stated. There was no evidence of dermal irritation or sensitization.[42]

In another HRIPT, the skin sensitization potential of an eye shadow containing 6% PTFE was evaluated in 111 subjects. Approximately 0.01 to 0.04 g of the product was applied to an occlusive patch that was placed on the back (left side; cm^2 area not stated) of each subject.[44] The patch remained in place for 24 h. This procedure was repeated for a total of 9 induction patch applications over an approximately 3-week period. The challenge phase was initiated after a 2-week non-treatment period. An occlusive patch containing 0.2 g of the product was applied to the right side of the back (new site) for 24 h. Reactions were scored at the time of patch removal and at 48 h and 96 h after patch application. Two subjects had a low-level (±; faint minimal erythema) reaction during the induction, and the same was true for 2 other subjects during the challenge phase. It was concluded that the eye shadow did not induce skin sensitization in any of the subjects tested.

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 ET_{50} of > 24 h (no eye irritation potential) was reported.[42]

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.[45] PTFE episcleral implants were inserted (for a period of 3–11 months) into the eyes of 27 Fauve de Bourgogne rabbits. A newly formed capsule constantly encased the implants. Only 2 severe complications were observed, i.e., 2 eyes had an endocapsular 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.

In a study involving 6 New Zealand White rabbits (3 males, 3 females), PTFE (powder, 0.1 g) was instilled into the conjunctival sac of the right eye.[22] The lids were held together for ~ 3 to 4 seconds in order to prevent loss of the test substance. The eyes were rinsed at 24 h post-instillation, and observations were made for up to 72 h post-instillation. No clinical signs or behavioral alterations were observed. Conjunctival redness was observed in 4 rabbits. After 24 h, the reactions had cleared in 3 animals. The reaction had cleared after 48 h in the fourth animal. PTFE was classified as non-irritating to the eye in this study.

The ocular irritation potential of a 20% dispersion of the fluorotelomer in $CCl_2F—CClF_2$ was evaluated using rabbits (number and strain of animals and test protocol not stated).[24] The test substance caused mild conjunctival irritation, which was no longer observed in less than 72 h. Mild corneal injury was observed at 24 h, but not at 48 h. It was noted that the transient reactions observed in this study were no greater than those that were caused by $CCl_2F—CClF_2$ alone.

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.[46] 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 1week, 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 lympho-histiocytic reaction. Thus, PTFE implants primarily induced a slight foreign body reaction, leaving only a slight lympho-histiocytic reaction at 26 weeks. The authors noted that the study provided no indication of a toxic, allergic, or traditional immunological pathogenesis of the tissue reaction being elicited 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 a total; pf 29 healthy male volunteers.[47] 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 (FEV_1) 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 FEV_1 values may result in a greater risk for systemic toxic effects, when compared to workers with small FEV_1 values.

Clinical phenomena in employees exposed to fumes from the processing of PTFE have been reported.[48] 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.[49] Air levels of PTFE ranging from 0 to 5.48 mg/m^3 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 PFTE (workers also had experienced 1or 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 12 polyfluorinated polymers in cosmetics is reviewed in this CIR safety assessment. According to the *Dictionary*, these polyfluorinated polymers 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 2018 VCRP data, PTFE is reported to be used in 365 cosmetic products (343 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), which is 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 polyfluorinated polymers in cosmetics is not reported in VCRP or Council survey data.

According to a chemical supplier, all commercial grades of PTFE contain some trace level of perfluorooctanoic acid (PFOA) and perfluorooctyl sulfonate (PFOS). The incidental content is detectable in the ppb range.

PTFE (powder, 0.5 g) was applied to abraded and intact skin of the trunk of 6 New Zealand White rabbits for 24 h. None of the animals died, and no clinical signs or behavioral alterations were observed.

A low molecular weight PTFE resin (fluorotelomer, chemical characterization data not included) was administered orally to rats at doses as high as 17 g/kg in an acute oral toxicity study. None of the animals died, and there were no test substance-related clinical effects or organ changes. In other acute toxicity tests, oral LD_0 values were determined to be 12.5×10^3 mg/kg (for anti-cohesive coating material containing 60% PTFE) and 2.5×10^3 mg/kg (for anti-cohesive coating material containing 68% to 73% PTFE) in Kunming mice. Oral LD_0 values were determined to be 6.25×10^3 mg/kg (for 60% PTFE material) and 1.25×10^3 mg/kg (for 68% to 73% PTFE material) in Wistar rats.

Polyperfluoroethoxymethoxy Difluorohydroxyethyl Ether was injected/applied topically to 10 guinea pigs during a 7-day period . No mortalities occurred, and there were no signs of general toxicity.

In spray inhalation experiments, 4 rats were exposed for 9 days (3 times per day) to a 20% dispersion of a low molecular weight PTFE resin in dichloro(fluoro)methyl (CCl_2F)—chlorodifluoromethyl radical ($CClF_2$). Uncoordination, labored breathing, and irritation of the nose were observed, but there was no evidence of exposure-related pathology.

Three types of PTFE resin were fed to rats (25% in the diet) for 90 days. There were no adverse effects on growth rate or behavior, and there was no microscopic evidence of tissue changes. Feeding with 1 of the 3 types of resin (unsintered PTFE resin) caused an increase in the relative size of the liver.

In a chronic oral toxicity study 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.

Two anti-cohesive coating materials containing PTFE (60% PTFE and 68% to 73% PTFE) were not teratogenic in Wistar rats.

Results for the two anti-cohesive coating materials were negative in the Ames test at doses up to 10,000 µg/plate in the *S. typhimurium* TA98, TA100, and TA1535, with and without metabolic activation. The two materials were also negative for genotoxicity in the micronucleus test.

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.

After an occlusive patch containing PTFE powder (0.5 g) was applied to abraded and intact skin of 6 rabbits for 24 h, skin irritation was not observed. A 20% dispersion of a low molecular weight PTFE resin in dichloro(fluoro)methyl (CCl_2F)—chlorodifluoromethyl radical ($CClF_2$) was applied to the skin of 10 guinea pigs. There was evidence of what was described as mechanical irritation, but no evidence of sensitization. The skin sensitization potential of Polyperfluoroethoxymethoxy Difluorohydroxyethyl Ether in 10 guinea pigs was evaluated using the maximization test. Slight skin irritation, but no sensitization reaction, was observed.

A formula containing 7.6% PTFE was classified as non-irritating to the skin in a 48-h patch test involving 26 subjects. An eye shadow containing 12% PTFE was not irritating to the skin of 15 subjects in a 24-h patch test.

In an HRIPT involving 107 subjects, a formula containing 2.89% PTFE did not cause dermal irritation or sensitization. An eye shadow containing 6% PTFE did not induce skin sensitization in an HRIPT involving 111 subjects.

A formula containing 2.89% PTFE was classified as having no ocular irritation potential in the in vitro EpiOcular™ eye irritation test. PTFE powder (0.1 g) was classified as non-irritating to the eyes of 6 rabbits. The eyes were rinsed after instillation. Also, in rabbits, a 20% dispersion of a low molecular weight PTFE resin in dichloro(fluoro)methyl (CCl_2F) — chlorodifluoromethyl radical ($CClF_2$) caused transient mild conjunctival irritation and corneal injury. The reactions observed were no greater than those that were caused by $CCl_2F—CClF_2$ alone.

A foreign-body reaction (slight lymphohistiocytic reaction) was observed in 7 healthy volunteers implanted s.c. with PTFE.

DRAFT DISCUSSION

The Panel determined that additional data are needed for completion of the safety assessment of the polyfluorinated polymers. The complete list of data needs includes:

- Method of manufacture and impurities data
- Skin sensitization data on PTFE at the highest maximum use concentration of 13%

The Panel discussed the issue of incidental inhalation exposure from powders. PTFE is reported as being used in [fragrance] 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%. The Panel noted that 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. A detailed discussion and summary of the Panel's approach to evaluating incidental inhalation exposures to ingredients in cosmetic products is available at http://www.cir-safety.org/cir-findings.

DRAFT CONCLUSION

The CIR Expert Panel concluded that the available data are insufficient to make a determination that the polyfluorinated polymers (listed below) are safe under the intended conditions of use in cosmetic formulations.

Fluoropolymers
PTFE
Hexafluoropropylene/Tetrafluoroethylene Copolymer*

Fluorinated-Side-Chain Polymers
Acrylates/Perfluorohexylethyl Methacrylate Copolymer*
Behenyl Methacrylate/Perfluorooctylethyl Methacrylate Copolymer*
C6-14 Perfluoroalkylethyl Acrylate/HEMA Copolymer*
Stearyl Methacrylate/Perfluorooctylethyl Methacrylate Copolymer*

Fluorinated Polyethers
Acrylates/Methoxy PEG-23 Methacrylate/Perfluorooctyl Ethyl Acrylate Copolymer*
PEG-10 Acrylate/Perfluorohexylethyl Acrylate Copolymer*
Polyperfluoroethoxymethoxy Difluoroethyl PEG Diisostearate*
Polyperfluoroethoxymethoxy Difluoroethyl PEG Ether*
Polyfluoroethoxymethoxy Difluorohydroxyethyl Ether*
Polyperfluoroethoxymethoxy Difluoromethyl Ether*

*Not reported to be in current use. Were the ingredient in this group not in current use to be used in the future, the expectation is that it would be used in product categories and at concentrations comparable to others in this group.

TABLES

Table 1. Definitions, idealized structures, and functions of the ingredients in this safety assessment.[1; *CIR Staff*]

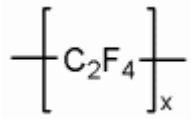
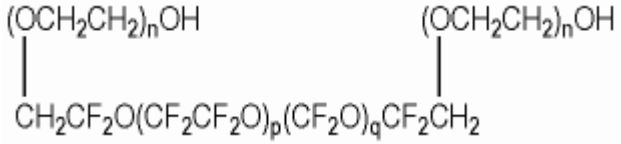
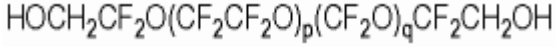
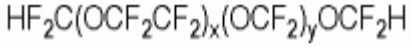
Ingredient CAS No.	Definition & Structures	Function(s)
Fluoropolymers		
PTFE 9002-84-0	PTFE is the polymer of tetrafluoroethylene that conforms to the formula: 	Bulking Agents; Slip Modifiers
Hexafluoropropylene/Tetrafluoroethylene Copolymer 25067-11-2	Hexafluoropropylene/Tetrafluoroethylene Copolymer is a copolymer of hexafluoropropylene and tetrafluoroethylene monomers.	Film Formers; Skin-Conditioning Agents - Emollient; Slip Modifiers
Fluorinated-Side-Chain Polymers		
Acrylates/Perfluorohexylethyl Methacrylate Copolymer 1557087-30-5	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.	Film Formers
Behenyl Methacrylate/Perfluorooctylethyl Methacrylate Copolymer	Behenyl Methacrylate/Perfluorooctylethyl Methacrylate Copolymer is a copolymer of behenyl methacrylate and perfluorooctylethyl methacrylate monomers.	Film Formers; Viscosity Increasing Agents - Nonaqueous
C6-14 Perfluoroalkylethyl Acrylate/HEMA Copolymer	C6-14 Perfluoroalkylethyl Acrylate/HEMA Copolymer is a copolymer of 2-(perfluoro(C6-14 alkyl)) ethyl acrylate and 2-hydroxyethyl methacrylate monomers.	Dispersing Agents - Nonsurfactant; Film Formers; Viscosity Increasing Agents - Nonaqueous
Stearyl Methacrylate/Perfluorooctylethyl Methacrylate Copolymer	Stearyl Methacrylate/Perfluorooctylethyl Methacrylate Copolymer is a copolymer of stearyl methacrylate and perfluorooctylethyl methacrylate monomers.	Film Formers; Viscosity Increasing Agents - Nonaqueous
Fluorinated Polyethers		
Acrylates/Methoxy PEG-23 Methacrylate/Perfluorooctyl Ethyl Acrylate Copolymer	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.	Film Formers
PEG-10 Acrylate/Perfluorohexylethyl Acrylate Copolymer	PEG-10 Acrylate/Perfluorohexylethyl Acrylate Copolymer is a copolymer of PEG-10 acrylate and perfluorohexylethyl acrylate monomers.	Film Formers
Polyperfluoroethoxymethoxy Difluoroethyl PEG Diisostearate	Polyperfluoroethoxymethoxy Difluoroethyl PEG Diisostearate is the diester of isostearic acid and Polyperfluoroethoxymethoxy Difluoroethyl PEG Ether.	Skin Protectants; Skin-Conditioning Agents - Emollient; Slip Modifiers; Viscosity Increasing Agents - Nonaqueous
Polyperfluoroethoxymethoxy Difluoroethyl PEG Ether 162492-15-1	Polyperfluoroethoxymethoxy Difluoroethyl PEG Ether is the polymer that conforms generally to the formula:  where n has an average value of 1 and p/q has an average value of 1.	Hair Conditioning Agents; Skin-Conditioning Agents - Miscellaneous; Skin-Conditioning Agents - Occlusive
Polyperfluoroethoxymethoxy Difluorohydroxyethyl Ether 88645-29-8	Polyperfluoroethoxymethoxy Difluorohydroxyethyl Ether is the polymer that conforms generally to the formula:  where p/q has an average value of 1.	Hair Conditioning Agents; Skin-Conditioning Agents - Miscellaneous
Polyperfluoroethoxymethoxy Difluoromethyl Ether 161075-02-1	Polyperfluoroethoxymethoxy Difluoromethyl Ether is the polymer that conforms generally to the formula: 	Solvents

Table 2. Monomer Components of Polyfluorinated Polymers

Monomer	CIR Review Status
Acrylic Acid	Not Reviewed
Methacrylic Acid	Published Final Report – Conclusion: Safe as used as a nail primer by trained professionals, but there are insufficient data for retail use by consumers.[50]
Butyl Methacrylate	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.[51]
Methyl Methacrylate	Scientific Literature Review issued on 1-13-2003 – Determined not to be an ingredient; report terminated (although data are available).[52]
Ethoxyethyl Methacrylate	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.[51]
Propyl Methacrylate	Not Reviewed
Ethyl Acrylate	Not Reviewed
Butyl Acrylate	Not Reviewed
sec-Butyl Methacrylate	Not Reviewed
t-Butyl Methacrylate	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.[51]
Stearyl Methacrylate	Not Reviewed

Table 3. Chemical and Physical Properties of Polyfluorinated Polymers

Property	Value	Reference
Fluoropolymers		
PTFE		
Molecular weight (Daltons)	400,000 to 10,000,000	4
Physical form and/or color	White translucent to opaque solid	3
	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 bibers 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.	4
Density (g/cm^3)	2.25	5
Solubility	No substance that will dissolve the polymer has been found	4
Melting point (°C)	320-330	5
Decomposes (°C)	315 to 375 and up to 500.	6,53
	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		
Melting Point (°C)	270	5

Table 4. Frequency and Concentration of Use According to Duration and Type of Exposure.[10,11]

	PTFE	
	# of Uses	Conc. (%)
Totals/Conc. Range	365	0.11-13
Duration of Use		
Leave-On	343	0.11-13
Rinse off	22	0.15-2.4
Diluted for (bath) Use	NR	NR
Exposure Type		
Eye Area	229	0.11-13
Incidental Ingestion	4	0.44
Incidental Inhalation- Sprays	15[a]	NR
Incidental Inhalation- Powders	31	0.6-3
Dermal Contact	325	0.11-12
Deodorant (underarm)	NR	NR
Hair - Non-Coloring	NR	NR
Hair-Coloring	NR	2.4
Nail	NR	NR
Mucous Membrane	4	0.44
Baby Products	NR	NR

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

[a]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.

Table5. Carcinogenicity of Implanted PTFE

Test Substance	Animals Tested	Test Protocol	Results
Subcutaneous Implantation			
PTFE (square sheet, 12 x 12 x 1.2 mm)	89 random-bred female Swiss mice	Implanted subcutaneously (s.c.) in left flank	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%.[28,29]
PTFE	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)	Implanted s.c.	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 x12 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.[30,29]
PTFE (15 x 1.2 mm disk)	Inbred C5BL mice (27 females, 19 males)	Implanted s.c. Mice observed for 90 weeks	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. [29,31]
PTFE (15 x 1.2 mm disks)	Random-bred CTM albino mice (40 males, 40 females)	Implanted s.c. into right flank. Mice observed for lifespan	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.[29,32]

Table5. Carcinogenicity of Implanted PTFE

Test Substance	Animals Tested	Test Protocol	Results
PTFE (15 x 1.2 mm disks)	BALB/c mice (38 females); C3Hf/Dp mice (38 females); and C57BL/He mice (39 females)	Implanted s.c. in dorsal area. Surviving mice killed at 120 weeks of age.	Fibrosarcomas (around disks) in 17 of 38 (44%) BALB/c mice, 36 of 38 (94%) C3Hf/Dp 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. [29,33]
PTFE films	15 rats (strain not stated)	Implanted s.c. in 2-year study.	Malignant sarcomas in 4 of 15 rats. All 15 rats survived the study.[34,29]
PTFE implants (4 x 5 0.16 mm)	65 weanling Wistar rats (males and females)	Implanted s.c. in abdominal wall. All rats killed within 800 days	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.[29,35]
PTFE disks (plain and perforated; 15 x 0.02 mm)	Wistar rats (2 groups)	Implanted s.c. in abdominal wall	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.[29,36]
PTFE mesh surgical outflow patches (20 x 20 mm squares) or shredded material	39 male Evans rats (tested with PTFE squares); 40 rats (tested with shredded material); 41 non-implanted control rats	Implanted s.c. Experiment terminated 19 months after implantation	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.[29,37]
Intraperitoneal Implantation			
PTFE rods (10 x 2 x 2 mm) or powder	16 weanling Wistar rats (tested with PTFE rods); 17 rats (tested with PTFE powder); 25 untreated controls	Implanted intraperitoneally (i.p.). Surviving animals killed 27 months after implantation	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.[29,38]

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2018 FDA VCRP Data

PTFE

03A - Eyebrow Pencil	3
03C - Eye Shadow	179
03D - Eye Lotion	6
03F - Mascara	36
03G - Other Eye Makeup Preparations	5
04C - Powders (dusting and talcum, excluding aftershave talc)	1
07A - Blushers (all types)	35
07B - Face Powders	30
07C - Foundations	6
07E - Lipstick	4
07G - Rouges	1
07H - Makeup Fixatives	1
07I - Other Makeup Preparations	2
11E - Shaving Cream	3
11G - Other Shaving Preparation Products	21
12A - Cleansing	1
12C - Face and Neck (exc shave)	4
12D - Body and Hand (exc shave)	11
12E - Foot Powders and Sprays	1
12F - Moisturizing	10
12G - Night	5
Total	**365**

Acrylates/Methoxy PEG-23 Methacrylate/Perfluorooctyl Ethyl Acrylate Copolymer - No Data

Acrylates/Perfluorohexylethyl Methacrylate Copolymer - No Data

Behenyl Methacrylate/Perfluorooctylethyl 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

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

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

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

DATE: April 9, 2018

SUBJECT: Studies on Products Containing PTFE

Anonymous. 2013. Clinical evaluation report: Human patch test of an eye shadow containing 12% PTFE.

Harrison Research Laboratories, Inc. 2017. Repeated insult patch test of an eye shadow containing 6% PTFE.

1620 L Street, N.W., Suite 1200 | Washington, D.C. 20036 | 202.331.1770 | 202.331.1969 (fax) | www.personalcarecouncil.org

[redacted]

CLINICAL EVALUATION REPORT: HUMAN PATCH TEST

This test follows the procedure described in SOP, HPT.1 **TO:** [redacted]

PRODUCT PROFILE NO: 1022166 DATE: November 25, 2013 LAB REF.: APTC-2654-13

1. TEST MATERIAL: [redacted] Eyeshadow Quads [redacted] Contains 12% PTFE

2. CONTROL MATERIAL: [redacted] Marble Baked Eyeshadow [redacted]

3. TEST PROCEDURE:

Single-Insult (24hr.) __X__ Occlusive (AllergEASE) Patch __X__ Semi-Occlusive Patch____.

4. CONCENTRATION:

Full-Strength X_____ Aqueous _____ Solution _____ Dispersion_____ Aqueous Paste_____.
Other:_____.

_____Volatiles were allowed to evaporate prior to occlusion on the patch.
_____Patch was hydrated just prior to application to skin.

5. TEST RESULTS:

TEST MATERIAL	*SUBJECTS*	*IRRITATION SCORE**									
	n	0	±	1	1+	2	2+	3	3+	4	PII
[redacted] Eyeshadow Quads [redacted]	15	15	0	0	0	0	0	0	0	0	0.00
[redacted] Marble Baked Eyeshadow [redacted]	15	15	0	0	0	0	0	0	0	0	0.00

___ Skin staining noted. Erythematous response was read "through" the Stain.

6. CONCLUSIONS:

A. There were no significant differences in irritancy observed between the Test Material (s) and the Reference Control (s). __X__.

B. _____.

Study Conducted By: [redacted] _____. Approved By: [redacted]

* SCORE
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 visibly uniform in entire contact area.
3 (Marked) = Bright red erythema with accompanying edema petechiae or papules.
4 (Severe) = Deep red erythema with vesiculation or weeping with or without edema.

+, 1+, 2+ and 3+ = Intermediate scores contributing 0.5, 1.5, 2.5 and 3.5 respectively, to the P.I.I.
P.I.I. - Primary Irritation Index - a value depicting the average skin response of the test panel as a whole. It is calculated by choosing the higher of the two Irritation Scores per panelist, adding them all together and dividing by the total number of test subjects.

CC:

HARRISON RESEARCH LABORATORIES, INC.

2497 Vauxhall Road • Union, NJ 07083
E-Mail: info@hrlabs.us.com Phone (908) 688-7600
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[redacted]

HRL Panel #17-101

Test Material #3: Shimmer Eyeshadow; [redacted] contains 6% PTFE

PURPOSE: To evaluate the potential of the Test Material, as a result of repeated applications, to induce dermal sensitization in human subjects. The subjects were scored at the first and last visit by an HRL Consulting Board-Certified Dermatologist.

IRB APPROVAL: Both the HRL Standard Protocol #100 and the Informed Consent were approved by the Clarus Institutional Review Board (CIRB) on January 20, 2016. A Sponsor-signed Protocol is retained in HRL files.

SPONSOR: [redacted]

SPONSOR AUTHORIZATION: December 20, 2016

SAFETY ASSURANCE: December 20, 2016

PRINCIPAL INVESTIGATOR: Lynne B Harrison, PhD

CO-INVESTIGATORS: Deborah R Spey, MD, FAAD
Kimberly K Ruhl, MD, PhD, FAAD
Adriana Ros, DO, FAOCD

TEST FACILITY: Harrison Research Laboratories, Inc. (HRL)
2497 Vauxhall Road
Union, New Jersey 07083

TEST MATERIAL: Test Material Shimmer Eyeshadow; [redacted] a bronze-colored powder, was received on December 22, 2016, with the following instructions: Test as received; apply approximately 0.01 - 0.04 gm of Test Material to webril of patch pre-moistened with distilled water. Patch occlusively.

- continued -

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[redacted]

HRL Panel #17-101

Test Material #3: Shimmer Eyeshadow; [redacted]

SUBJECTS:	A total of 117 subjects were enrolled; 111 subjects completed the test. One subject, #011 (HRL #29976), was discontinued by Quality Assurance. One subject, #023 (HRL #44580), was discontinued due to a Protocol violation. Four subjects discontinued due to personal reasons. No subject discontinued due to test material reaction.
METHOD:	This test was conducted according to HRL Standard Protocol #100 and HRL Standard Operating Procedures (including any Sponsor alterations).
TEST DATES:	January 4, 2017 through February 10, 2017.
SCORING SYSTEM:	See Tables I-II.
RESULTS:	See Tables I-II. During the Induction Phase, two subjects exhibited low-level (±) reactions. During the Challenge, two other subjects exhibited low-level (±) reactions.
CONCLUSION:	In this Repeated Insult Patch Test, Test Material Shimmer Eyeshadow; [redacted] did not induce dermal sensitization in human subjects. The subjects were scored at the first and last visit by an HRL Consulting Board-Certified Dermatologist.
QUALITY ASSURANCE (QA):	The QA Unit performed an in-phase audit of this study.

Kimberly K Ruhl, MD, PhD, FAAD
Co-Investigator (Dermatologist)

Debra Harrison, MA
Project Manager

Lynne B Harrison, PhD
Principal Investigator

Date: 2/21/17

[redacted]
HRL Panel #17-101
Test Material #3: Shimmer Eyeshadow; [redacted]

SUBJECTS: Each potential subject completed an HRL Subject History Form (HRL Form:SHF), including relevant medical history. (An updated Subject History Form is secured approximately every two years.) Each accepted subject was assigned a permanent HRL Identification Number. No subject was used if he or she exhibited any dermatological or other medical or physical condition that would preclude topical application of the Test Material. Upon enrollment, no subject reported using any medication that would interfere with the sensitization results. No known pregnant nor nursing women were used on this RIPT. No minor subjects were used on this RIPT.

An appropriate clearance period had elapsed since a subject was patched on a Repeated Insult Patch Test (RIPT) or a Photoallergy Test (PA) before being used in this RIPT.

Legally valid written IRB-approved Informed Consent, in conformity with: 21 CFR 50.25, Subtitle A, Protection of Human Subjects, was secured from each subject.

METHOD: Induction Phase: A webril/adhesive patch (Kendall Healthcare Products Company Patch #4022), or equivalent, was used occlusively. Approximately 0.01 - 0.04 gm of the Test Material was applied to each patch. As per HRL Standard Operating Procedures (SOP) (HRL Form:SOP/RIPT), the left side of the back was usually the test area for the Induction Phase. The subject's skin was marked with gentian violet surgical marker at the left side of the test site. The test site was recorded on the anatomical diagram of each subject's individual Data Form. In addition, at that time, the prospective placement of the Challenge test site was also recorded on the anatomical diagram.

Each subject was instructed that the patch was to remain in place and kept dry for approximately 24 hours, at which time the patch was to be removed by the subject. An approximately 24-hour period, during which no test material was applied, followed the weekday patch removals; an approximately 48-hour period followed the weekend patch removals.

Each subject returned to HRL on the appropriate day. The test site was observed by the HRL technician, and the reaction scored and recorded (see **SCORING SYSTEM**, below). The identical test site was then repatched until nine (9) Induction patchings were completed.

In accordance with HRL SOP, if a subject was unable to make up a missed patching during the same week, the subject was either patched four days the following week or was patched at the end of the Induction Phase. Any absences and make-up days are noted by the dates on the individual Data Form.

A series of nine (9) Induction patchings was completed over a period of approximately three weeks.

Rest Period: A Rest Period of approximately two weeks followed the last Induction patching; no test material was applied during the Rest Period. Subjects were instructed to notify HRL if they experienced any reaction during the Rest Period.

[redacted]

HRL Panel #17-101

Test Material #3: Shimmer Eyeshadow; [redacted]

METHOD: (continued)

Challenge Phase: At the Challenge Phase, the original Induction test site was observed and each subject queried as to whether any reaction was experienced during the Rest Period. Any reactions were recorded on the Data Form. A webril/adhesive patch (Kendall Healthcare Products Company Patch #4022), or equivalent, was used occlusively. Approximately 0.2 gm of the Test Material was applied to each patch. As per HRL RIPT SOP, the right side of the back was usually the virgin test site for the Challenge Phase.

As per HRL RIPT SOP, the Challenge patch was applied to the virgin site only. Each subject was again instructed to keep the patch on and dry.

Each subject reported to HRL approximately 24 hours later (Challenge Reading 1), at which time the patch was removed and the Challenge site scored and recorded by the HRL technician. The original test site was also observed. (See **RESULTS**, below.)

Each subject reported to HRL at approximately 48 hours (Challenge Reading 2) and approximately 96 hours (Challenge Reading 4) post-patching for additional observations; reactions were scored and recorded. HRL was closed on February 9, 2017 due to severe inclement weather. On February 8, 2017 (Challenge Reading 2), the subjects had been instructed to look at their backs on Thursday, February 9, 2017 in case HRL was closed due to the impending snowstorm. A verbal report from each subject was recorded on each subject's individual Data Form with his / her observation from February 9, 2017.

One subject, #105 (HRL #30561), missed the C4 visit due to starting the Challenge one day late. She returned to HRL on February 13, 2017 and her test site was negative. A verbal report from Subject #105 stated 'no reaction present' at what would have been Challenge Reading 4.

SCORING SYSTEM: See Tables I-II. The test sites were scored using the modified scoring scale of the International Contact Dermatitis Research Group System: Fisher, Alexander A., *Contact Dermatitis*, Lea & Febiger, Philadelphia, 2008: p 27.

RESULTS: See Tables I-II. No adverse events related to the Test Material were reported during this test. Erythema, edema, dryness, staining, peeling and hyperpigmentation / hypopigmentation are possible, expected endpoints and not considered Adverse Reactions. This test was conducted under the supervision of a Board-Certified Dermatologist, a Co-Investigator. At Challenge Reading 4, the Dermatologist participated in the scoring of the subjects. A total of 111 subjects completed the test; 22 male and 89 female. The subjects range in age from 19 to 74.

RETENTION: All original Data Forms will be retained at HRL for a period of three years, or such other time as may be required by law. A laboratory retainer bottle of the Test Material shall be retained, in ambient conditions, for at least two years, or as required by law. Return or disposal of unused Test Material shall be as per the Sponsor's instructions—to be communicated within 30 days of receipt of this Final Report. HRL shall appropriately dispose of any Test Material after six months if no Sponsor instructions have been communicated.

[redacted]
HRL Panel #17-101
Test Material #3: Shimmer Eyeshadow; [redacted]

TABLE I: SUMMARY OF REACTIONS

TOTAL NUMBER OF SUBJECTS ENROLLED: 117
TOTAL NUMBER OF SUBJECTS COMPLETED: 111

Reaction	Induction Reading									Challenge Reading			
Grade	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**1**	**2**	**3**	**4**
0	114	114	114	114	113	112	112	111	111	111	108	1	110
±	1	1	1					1	1		2		
1													
1E													
2													
2E													
3E													
4E													
-											1	110	1
N9R													
Total	115	115	115	114	113	112	112	112	112	111	111	111	111

SCORING SYSTEM:
0 = No visible reaction
± = Faint, minimal erythema
1 = Erythema
2 = Intense erythema, induration
3 = Intense erythema, induration, vesicles
4 = Severe reaction with erythema, induration, vesicles, pustules (may be weeping)
E = Edema
- = No reading
N9R = No 9th reading

[redacted]

HRL Panel #17-101

Test Material #3: Shimmer Eyeshadow; [redacted]

TABLE II: INDIVIDUAL SUBJECT DATA

(see Scoring System, page 11)

					Induction Reading									Challenge Reading			
Sub	HRL	Ini	Sex	Age	1	2	3	4	5	6	7	8	9	1	2	3	4
1	45425	EB	F	41	0	0	0	0	0	0	0	0	0	0	0	-	0
2	43331	KB	M	32	0	0	0	0	0	0	0	0	0	0	0	-	0
3	45525	IF	F	48	0	0	0	0	0	0	0	0	0	0	0	-	0
4	45711	JH	M	61	0	0	0	0	0	0	0	0	0	0	0	-	0
5	46023	SM	F	19	0	0	0	0	0	0	0	0	0	0	0	-	0
6	46024	CS	F	19	0	0	0	0	0	0	0	0	0	0	0	-	0
7	45773	JL	F	25	0	0	0	0	0	0	0	0	0	0	0	-	0
8	39333	JM	M	39	0	0	0	0	0	0	0	0	0	0	0	-	0
9	05374	KD	F	50	0	0	0	0	0	0	0	0	0	0	0	-	0
10	38625	KG	F	50	0	0	0	0	0	0	0	0	0	0	0	-	0
11	29976	CB	F	59	DISQUALIFIED BY QUALITY ASSURANCE												
12	41754	MD	M	58	0	0	0	0	0	0	0	0	0	X	X	X	X
13	37202	JB	F	53	0	0	0	0	0	0	0	0	0	0	0	-	0
14	45526	AP	M	51	±	±	±	0	0	0	0	±	0	0	0	-	0
15	45067	PP	F	49	0	0	0	0	0	0	0	0	0	0	0	-	0
16	45263	SP	F	30	0	0	0	0	0	0	0	0	0	0	0	-	0
17	42430	DV	M	45	0	0	0	0	0	0	0	0	0	0	0	-	0
18	36839	SC	F	49	0	0	0	0	0	0	0	0	0	0	0	-	0
19	44606	NC	F	21	0	0	0	0	0	0	0	0	0	0	±	-	0
20	45610	JC	F	29	0	0	0	0	0	0	0	0	0	0	0	-	0
21	37034	AG	F	53	0	0	0	0	0	0	0	0	0	0	0	-	0
22	30434	LP	F	48	0	0	0	0	0	0	0	0	0	0	0	-	0
23	44580	PC	F	57	X	X	X	X	X	X	X	X	X	X	X	X	X
24	44581	SB	M	48	0	0	0	0	0	0	0	0	0	0	0	-	0
25	39424	TS	F	30	0	0	0	0	0	0	0	0	0	0	0	-	0

[redacted]

HRL Panel #17-101

Test Material #3: Shimmer Eyeshadow; [redacted]

TABLE II: INDIVIDUAL SUBJECT DATA

(see Scoring System, page 11)

					Induction Reading									Challenge Reading			
Sub	HRL	Ini	Sex	Age	1	2	3	4	5	6	7	8	9	1	2	3	4
26	41189	LS	F	74	0	0	0	0	0	0	0	0	0	0	0	-	0
27	45847	SD	F	53	0	0	0	0	0	0	0	0	0	0	0	-	0
28	44324	CN	F	74	0	0	0	0	0	0	0	0	0	0	0	-	0
29	44726	JP	F	26	0	0	0	0	0	0	0	0	0	0	0	-	0
30	20113	HA	F	51	0	0	0	0	0	0	0	0	0	0	0	-	0
31	15480	SH	F	54	0	0	0	0	0	0	0	0	0	0	0	-	0
32	45839	EG	M	47	0	0	0	0	0	0	0	0	0	0	0	-	0
33	45800	TR	F	45	0	0	0	0	0	0	0	0	0	0	0	-	0
34	36416	LE	F	45	0	0	0	0	0	0	0	0	0	0	0	-	0
35	26696	MF	F	58	0	0	0	0	0	0	0	0	0	0	0	-	0
36	24966	MB	F	51	0	0	0	0	0	0	0	0	0	0	0	-	0
37	41536	RM	M	23	0	0	0	0	0	0	0	0	0	0	0	-	0
38	43215	DP	M	21	0	0	0	0	0	0	0	0	0	0	0	-	0
39	38136	HK	F	62	0	0	0	0	0	0	0	0	±	0	0	-	0
40	45987	ED	F	30	0	0	0	0	0	0	0	0	0	0	0	-	0
41	40065	AS	F	23	0	0	0	0	0	0	0	0	0	0	0	-	0
42	44768	MC	M	72	0	0	0	0	0	0	0	0	0	0	0	-	0
43	45045	ER	F	44	0	0	0	0	0	0	0	0	0	0	0	-	0
44	06831	GP	F	56	0	0	0	0	0	0	0	0	0	0	0	-	0
45	19762	CN	F	37	0	0	0	0	0	0	0	0	0	0	0	-	0
46	26621	MI	F	49	0	0	0	0	0	0	0	0	0	0	0	-	0
47	45572	JS	M	38	0	0	0	0	0	0	0	0	0	0	0	-	0
48	44953	JD	F	40	0	0	0	X	X	X	X	X	X	X	X	X	X
49	43611	LV	F	29	0	0	0	0	0	0	0	0	0	0	0	-	0
50	45593	BD	F	71	0	0	0	0	0	0	0	0	0	0	0	-	0

[redacted]

HRL Panel #17-101

Test Material #3: Shimmer Eyeshadow; [redacted]

TABLE II: INDIVIDUAL SUBJECT DATA

(see Scoring System, page 11)

					Induction Reading									Challenge Reading			
Sub	HRL	Ini	Sex	Age	1	2	3	4	5	6	7	8	9	1	2	3	4
51	38739	LB	F	68	0	0	0	0	0	0	0	0	0	0	0	-	0
52	36901	JH	M	49	0	0	0	0	0	0	0	0	0	0	0	-	0
53	44458	RF	F	60	0	0	0	0	0	0	0	0	0	0	0	-	0
54	10794	BT	F	37	0	0	0	0	0	0	0	0	0	0	0	-	0
55	36951	NV	F	33	0	0	0	0	0	0	0	0	0	0	0	-	0
56	14892	VH	F	57	0	0	0	0	0	0	0	0	0	0	0	-	0
57	27639	CF	F	44	0	0	0	0	0	X	X	X	X	X	X	X	X
58	44913	CA	F	67	0	0	0	0	0	0	0	0	0	0	0	-	0
59	39836	ML	M	47	0	0	0	0	0	0	0	0	0	0	0	-	0
60	41597	RM	M	52	0	0	0	0	0	0	0	0	0	0	0	-	0
61	45840	CG	F	48	0	0	0	0	0	0	0	0	0	0	0	-	0
62	29772	GD	F	58	0	0	0	0	0	0	0	0	0	0	0	-	0
63	25670	SF	F	71	0	0	0	0	0	0	0	0	0	0	0	-	0
64	30324	LE	F	37	0	0	0	0	0	0	0	0	0	0	0	-	0
65	45569	SC	F	36	0	0	0	0	0	0	0	0	0	0	0	-	0
66	45880	SA	F	50	0	0	0	0	0	0	0	0	0	0	0	-	0
67	23962	HG	M	66	0	0	0	0	0	0	0	0	0	0	0	-	0
68	37205	TB	F	41	0	0	0	0	0	0	0	0	0	0	0	-	0
69	42386	DM	F	50	0	0	0	0	0	0	0	0	0	0	±	-	0
70	24904	LG	F	54	0	0	0	0	0	0	0	0	0	0	0	-	0
71	20518	MR	F	54	0	0	0	0	0	0	0	0	0	0	0	-	0
72	35211	JR	F	53	0	0	0	0	0	0	0	0	0	0	0	-	0
73	45068	AB	F	30	0	0	0	0	0	0	0	0	0	0	0	-	0
74	45671	GT	M	60	0	0	0	0	0	0	0	0	0	0	0	-	0
75	42872	LC	F	33	0	0	0	0	0	0	0	0	0	0	0	-	0

[redacted]

HRL Panel #17-101

Test Material #3: Shimmer Eyeshadow; [redacted]

TABLE II: INDIVIDUAL SUBJECT DATA

(see Scoring System, page 11)

					Induction Reading									Challenge Reading			
Sub	HRL	Ini	Sex	Age	1	2	3	4	5	6	7	8	9	1	2	3	4
76	40480	BJ	F	66	0	0	0	0	0	0	0	0	0	0	0	-	0
77	27869	NA	F	50	0	0	0	0	0	0	0	0	0	0	0	-	0
78	18738	BP	F	71	0	0	0	0	0	0	0	0	0	0	0	-	0
79	45667	BR	M	37	0	0	0	0	0	0	0	0	0	0	0	-	0
80	45904	LM	F	24	0	0	0	0	0	0	0	0	0	0	0	-	0
81	30429	LW	F	39	0	0	0	0	0	0	0	0	0	0	0	-	0
82	45805	GC	M	41	0	0	0	0	0	0	0	0	0	0	0	-	0
83	45877	RL	F	69	0	0	0	0	0	0	0	0	0	0	0	-	0
84	43593	IV	F	23	0	0	0	0	0	0	0	0	0	0	0	-	0
85	17233	GM	F	59	0	0	0	0	0	0	0	0	0	0	0	-	0
86	22589	MB	F	68	0	0	0	0	0	0	0	0	0	0	0	-	0
87	29990	TS	F	36	0	0	0	0	0	0	0	0	0	0	0	-	0
88	34934	DL	F	40	0	0	0	0	0	0	0	0	0	0	0	-	0
89	23007	BW	F	54	0	0	0	0	0	0	0	0	0	0	0	-	0
90	43425	JM	F	28	0	0	0	0	0	0	0	0	0	0	0	-	0
91	45493	KH	F	27	0	0	0	0	0	0	0	0	0	0	0	-	0
92	44821	FC	M	65	0	0	0	0	0	0	0	0	0	0	0	-	0
93	43597	LK	F	63	0	0	0	0	0	0	0	0	0	0	0	-	0
94	44753	MG	F	30	0	0	0	0	0	0	0	0	0	0	0	-	0
95	45077	LW	F	60	0	0	0	0	0	0	0	0	0	0	0	-	0
96	44859	DG	F	54	0	0	0	0	0	0	0	0	0	0	0	-	0
97	10003	LF	F	55	0	0	0	0	0	0	0	0	0	0	0	-	0
98	05633	MM	F	69	0	0	0	0	0	0	0	0	0	0	0	-	0
99	13247	PC	F	65	0	0	0	0	0	0	0	0	0	0	0	-	0
100	45011	JM	F	21	0	0	0	0	0	0	0	0	0	0	0	-	0

[redacted]

HRL Panel #17-101

Test Material #3: Shimmer Eyeshadow; [redacted]

TABLE II: INDIVIDUAL SUBJECT DATA

(see Scoring System, page 11)

					Induction Reading									Challenge Reading			
Sub	HRL	Ini	Sex	Age	1	2	3	4	5	6	7	8	9	1	2	3	4
101	45954	ST	F	40	0	0	0	0	0	0	0	0	0	0	0	-	0
102	45654	CC	F	54	0	0	0	0	X	X	X	X	X	X	X	X	X
103	40814	AL	F	46	0	0	0	0	0	0	0	0	0	0	0	-	0
104	24584	AH	M	50	0	0	0	0	0	0	0	0	0	0	0	-	0
105	30561	IE	F	53	0	0	0	0	0	0	0	0	0	0	-	0	-
106	42663	RT	M	50	0	0	0	0	0	0	0	0	0	0	0	-	0
107	30724	DE	F	57	0	0	0	0	0	0	0	0	0	0	0	-	0
108	32814	RD	F	45	0	0	0	0	0	0	0	0	0	0	0	-	0
109	33383	EG	M	48	0	0	0	0	0	0	0	0	0	0	0	-	0
110	37870	MD	F	50	0	0	0	0	0	0	0	0	0	0	0	-	0
111	40803	MA	F	41	0	0	0	0	0	0	0	0	0	0	0	-	0
112	22259	DC	F	50	0	0	0	0	0	0	0	0	0	0	0	-	0
113	45480	KC	F	21	0	0	0	0	0	0	0	0	0	0	0	-	0
114	38897	TC	F	49	0	0	0	0	0	0	0	0	0	0	0	-	0
115	03047	JB	F	71	0	0	0	0	0	0	0	0	0	0	0	-	0
116	46009	MG	F	45	0	0	0	0	0	0	0	0	0	0	0	-	0
117	44343	SM	F	26	0	0	0	0	0	0	0	0	0	0	0	-	0

[redacted]

HRL Panel #17-101

Test Material #3: Shimmer Eyeshadow; [redacted]

SCORING SYSTEM*:

0	=	No visible reaction
±	=	Faint, minimal erythema
1	=	Erythema
2	=	Intense erythema
3	=	Intense erythema, induration, vesicles
4	=	Severe reaction with erythema, induration, vesicles, pustules (may be weeping)
E	=	Edema
DR	=	Dryness
P	=	Peeling
S	=	Staining
^	=	Hyperpigmentation / Hypopigmentation
TR	=	Tape Reaction
C	=	Change of test site
N9R	=	No 9th reading
-	=	No reading
X	=	Discontinued

*International Contact Dermatitis Research Group System: Fisher, Alexander A., *Contact Dermatitis*, Lea & Febiger, Philadelphia, 2008: p 27. (Modified)

HARRISON RESEARCH LABORATORIES, INC.

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[redacted]

HRL Panel #17-101
Test Material #3: Shimmer Eyeshadow; [redacted]

QUALITY ASSURANCE MEMORANDUM

This Final Report was reviewed for accuracy and conformity with both HRL Standard Protocol #100 and HRL Standard Operating Procedures (including any Sponsor alterations) and any written communication from the Sponsor.

Inspections were accomplished by a random sampling approach and reported to the Project Manager and the Principal Investigator immediately following their completion.

Any known protocol deviations have been noted in the Final Report and/or Individual Data Form.

The raw data for this study are retained at Harrison Research Laboratories, Inc.

HARRISON RESEARCH LABORATORIES, INC.

Susan Lauck

SUSAN LAUCK
Quality Assurance Manager

QUALITY ASSURANCE UNIT

Date: 2-21-17

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

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

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

DATE: April 23, 2018

SUBJECT: PTFE

Micro Powders, Inc. 2018. PTFE products and PFOA.

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MICRO POWDERS, INC.

580 White Plains Road • Tarrytown, NY 10591 • TEL 914-793-4058 • FAX 914-472-7098 • EMAIL mpi@micropowders.com

PTFE PRODUCTS AND PFOA

There has been a great deal of publicity surrounding the issue of PFOA (perfluorooctanoic acid) and PFOS (perfluorooctyl sulfonate) in PTFE (polytetrafluoroethylene). PTFE is used either entirely or partially in the manufacture of our Fluo, Polyfluo®, Synfluo, Polysilk, PolyBlend, Propylfluo, Microslip®, and Microsilk products. The following is a summary of what we know about this subject.

All commercial grades of PTFE contain some trace level of PFOA (and fractionally lower levels of PFOS). This incidental content is detectable (if present) in the parts per billion (ppb) range. Drinking water contains up to 1 ppb of PFOA, and the human bloodstream typically contains up to 6 ppb of PFOA. In 2006, EPA and the eight major companies in the industry launched the 2010/15 PFOA Stewardship Program, in which companies committed to reduce global facility emissions and product content of PFOA and related chemicals by 95 percent by 2010, and to work toward eliminating emissions and product content by 2015. We are pleased to report that all Micro Powders PTFE grades (and combination grades) contain no intentionally added PFOA.

In 2017, the EU published measures to regulate PFOA, its salts and related substances under Annex XVII of REACH. The new law (EU 2017/1000) will be implemented in phases, starting July 4, 2020. Under this new law, trace content of PFOA will be regulated to <25 ppb, and trace content of PFOA-related substances regulated to <1,000 ppb.

Micro Powder has taken aggressive action with regards to our PTFE based products, and can now certify (well in advance of the EU regulation's effective date) that the following products comply with EU 2017/1000:

Microslip 519, Microslip 519L, Gelslip 519

Over the next few months, we will be adding other PTFE products to this list of certified grades.

Please contact us if you have any questions.

Micro Powders, Inc.

Richard Czarnecki

Richard Czarnecki
Technical Director

March 26, 2018

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

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

FROM: Alexandra Kowcz
Industry Liaison to the CIR Expert Panel

DATE: February 23, 2018

SUBJECT: Draft Report: Safety Assessment of Fluoropolymers as Used in Cosmetics (draft prepared for the March 5-6, 2018 CIR Expert Panel Meeting)

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

Key Issues

Method of Manufacture - It is no longer true that perfluorooctanic acid (PFOA) is being used to manufacture PTFE. This information appears to be cited to reference 10, Wikipedia, which is not an appropriate reference for a CIR review.

The 2013 OECD/UNEP document by the Global PFC Group entitled 'Synthesis paper on per- and polyfluorinated chemicals' (at https://www.oecd.org/env/ehs/risk-management/PFC_FINAL-Web.pdf) mentioned in the January 31, 2018 memo from the CIR SSC states (see section 1.1.14 of the OECD/UNEP document):

"The ammonium salts (in some cases also the sodium salts) of long chain PFCAs such as PFOA and PFNA have been applied as processing aids (emulsifiers) at low concentrations (around 0.5 wt%) in the polymerization of certain fluoropolymers (i.e. PTFE, FEP, PFA and PVDF) and fluoroelastomers. After 2006, many fluoropolymer manufacturers in China, Japan, Western Europe and the United States started to replace the salts of long-chain PFCAs with the salts of short-chain PFCAs (such as PFHxA) or other nonperfluoroalkyl alternatives (such as polyfluoroalkyl ether carboxylic acids) for fluoropolymer manufacturing."

Genotoxicity - As the monomer tetrafluoroethylene was positive in an NTP inhalation bioassay, the genotoxicity data for tetrafluoroethylene should also be included in the CIR report. As part of the NTP 13-week inhalation study in mice, the NTP saw no increases in

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frequencies of micronucleated erythrocytes in peripheral blood samples. The NTP also cited a review[1] that indicated that other genotoxicity studies of tetrafluoroethylene were negative. These results suggest that tetrafluoroethylene is not carcinogenic via a genotoxic mechanism indicating that exposure to possible residual monomers when PTFE is used in cosmetics would not be a concern for carcinogenicity.

Additional Considerations

Chemical and Physical Properties - Please revise: "PTFE and its copolymers" as the ingredients to which this refers is not clear. There are no other ingredients in this report that are copolymers of PTFE. There is one other ingredient in the report, Hexafluoropropylene/Tetrafluoroethylene Copolymer, that is a copolymer of tetrafluoroethylene.

Cosmetic Use - As there is more than one ingredient in this report, in the first sentence of the Cosmetic Use section, "this ingredient" needs to be corrected to "these ingredients".

Noncosmetic Use - It should be made clear that reference 17 only concerned PTFE and Tetrafluoroethylene/Hexafluoropropylene Copolymer.

ADME, Animal, Oral, Polychlorotrifluoroethylene - What was the rate of dosing of the Rhesus monkeys?

Subchronic, Oral - As this study concerns PTFE, a PTFE subheading needs to be added after the Oral subheading.

Carcinogenicity, Subcutaneous, PTFE - Please correct "fibrosbroarcomas"

Summary - Please correct: "In a chronic oral toxicity involving"

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[1]Kennedy, G.L. (1990). Toxicology of fluorine containing monomers. In Critical Reviews in Toxicology, Vol. 21, pp. 149-170. CRC Press, Boca Raton, FL.