
Safety Assessment of Glyceryl Acrylates as Used in Cosmetics

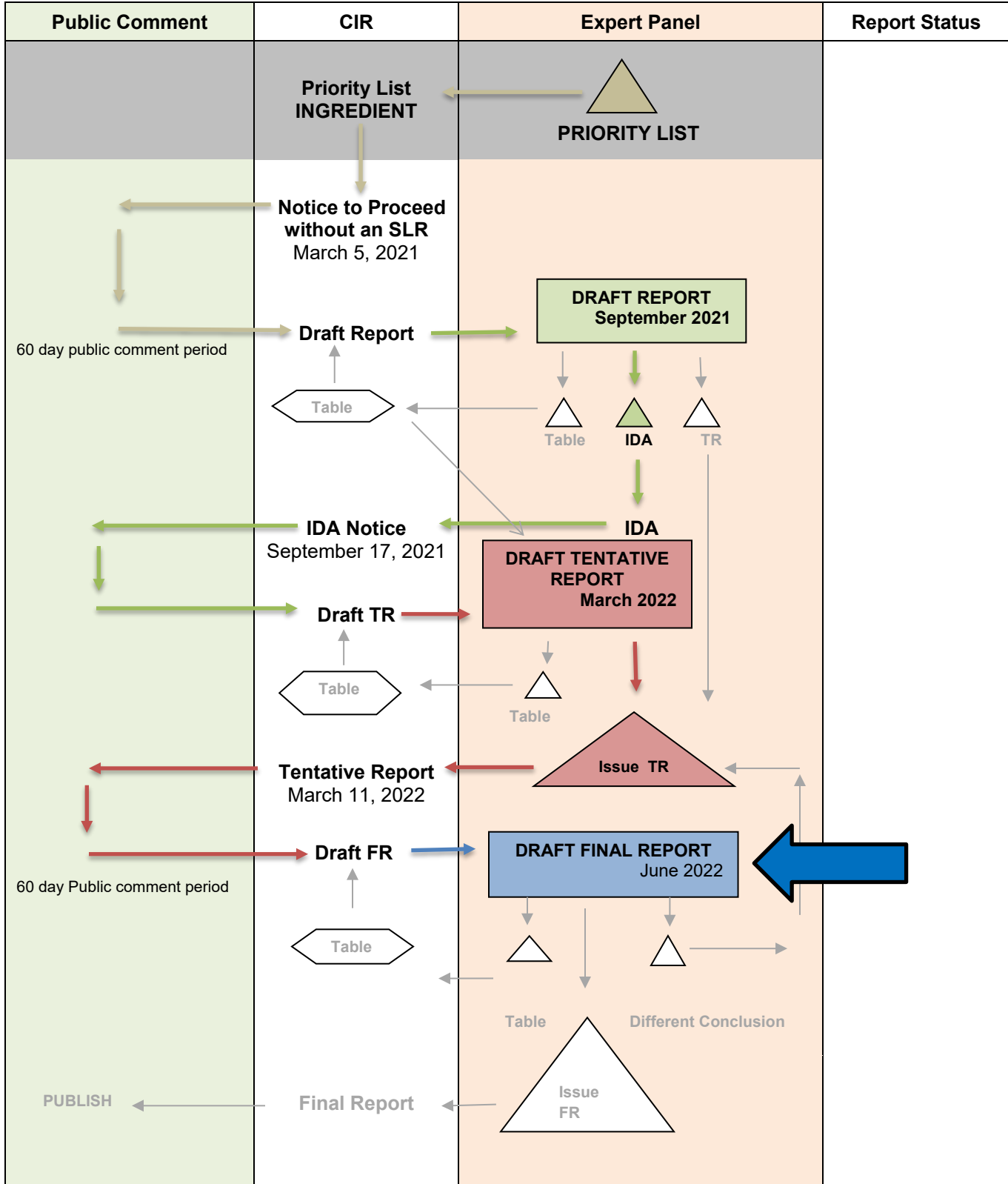
Status: Draft Final Report for Panel Review
Release Date: May 23 , 2022
Panel Meeting Date: June 16-17, 2022

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

SAFETY ASSESSMENT FLOW CHART

INGREDIENT/FAMILY Glyceryl Acrylates

MEETING June 2022





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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Regina Tucker, M.S., Scientific Analyst/Writer, CIR
Date: May 23, 2022
Subject: Safety Assessment of Glyceryl Acrylates as Used in Cosmetics

Enclosed is the Draft Final Report of the Safety Assessment of Glyceryl Acrylates as Used in Cosmetics. (It is identified in this report package as *report_GlycerylAcrylates_062022*.) At the March 2022 meeting, the Expert Panel for Cosmetic Ingredient Safety (Panel) issued a Tentative Report for public comment with the conclusion that the 4 glyceryl acrylate ingredients reviewed in the safety assessment are safe in the present practices of use and concentration.

No new data were received or found. Comments on the Tentative Report that were provided from the Council (*PCPCcomments_GlycerylAcrylates_062022*), as well as CIR responses to these comments (*response-PCPCcomments_GlycerylAcrylates_062022*) are included in this packet. Changes to the language involving the inhalation exposure boilerplate and use in airbrush delivery systems have been **highlighted** to aid the Panel's review.

Also included in this packet are the report history (*history_GlycerylAcrylates_062022*), a data profile (*dataprofile_GlycerylAcrylates_062022*), the search strategy (*search_GlycerylAcrylates_062022*), transcripts of previous meeting (*transcripts_GlycerylAcrylates_062022*), flow chart (*flow_GlycerylAcrylates_062022*), and VCRP data (*VCRP_GlycerylAcrylates_062022*).

The Panel should carefully consider the Abstract, Discussion, and Conclusion presented in this report. If these are satisfactory, the Panel should issue a Final Report.



Memorandum

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

FROM: Alexandra Kowcz, MS, MBA
Industry Liaison to the CIR Expert Panel

DATE: March 22, 2022

SUBJECT: Tentative Report: Safety Assessment of Glyceryl Acrylates as Used in Cosmetics
(release date March 11, 2022)

The Personal Care Products Council respectfully submits the following comments on the tentative report, Safety Assessment of Glyceryl Acrylates as Used in Cosmetics.

Introduction – Please correct: “are both reported function in cosmetics as a skin-conditioning agents” (add “to” before function, delete “a”)

Cosmetic Use – Please correct: “3 of these 4 ingredients are also used in products are reported to be used in formulations that come in contact with mucous membranes” (delete “are reported to be used in formulations”)

Acute, Oral – Please correct: “fore” to “for”

Effect on Burn-Wound Healing – If available, please state the concentration of Glyceryl Polyacrylate in the oil-in-water emulsion.

Table 5 – It is not clear why the concentrations are in the first column for all studies except reference 7 and reference 4. It would be better if the concentrations were in the Concentration column. The material tested in reference 7 was the ingredient as sold to the cosmetics industry. It was tested undiluted. Although only limited information on the HRIPT was provided in reference 4, they did state: “did not indicate potential for dermal irritation or allergic contact sensitization” which should be added to the Results column of Table 5. Please check the reference numbers in this table as some of the higher numbers appear to be incorrect, e.g., 27 should be 25.

Glyceryl Acrylates - June 2022 – Regina Tucker	
Comment Submitter: Personal Care Products Council	
Date of Submission: March 22, 2022	
Comment	Response/Action
Introduction – Please correct: “are both reported function in cosmetics as a skin-conditioning agents” (add “to” before function, delete “a”)	Addressed
Cosmetic Use – Please correct: “3 of these 4 ingredients are also used in products are reported to be used in formulations that come in contact with mucous membranes” (delete “are reported to be used in formulations”)	Addressed
Acute, Oral – Please correct: “fore” to “for”	Addressed
Effect on Burn-Wound Healing – If available, please state the concentration of Glyceryl Polyacrylate in the oil-in-water emulsion.	Concentration of Glyceryl Polyacrylate not available. Paragraph has been updated with “concentration not available” to reflect its absence.
Table 5 – It is not clear why the concentrations are in the first column for all studies except reference 7 and reference 4. It would be better if the concentrations were in the Concentration column. The material tested in reference 7 was the ingredient as sold to the cosmetics industry. It was tested undiluted. Although only limited information on the HRIPT was provided in reference 4, they did state: “did not indicate potential for dermal irritation or allergic contact sensitization” which should be added to the Results column of Table 5. Please check the reference numbers in this table as some of the higher numbers appear to be incorrect, e.g., 27 should be 25	Concentrations are in the first columns for all studies except reference 7 and reference 4 because the ingredient is a product containing only a percentage of the select glyceryl acrylate. All other comments have been addressed.

CIR History: Glyceryl Acrylates

SLR NTP: March 2021

A Scientific Literature Review (SLR) Notice to Proceed (NTP) was issued

Concentration of use data and the limited safety test data that were identified in the published literature were incorporated into the draft report. No other data were received.

Draft Report: September 2021

The Panel issues an Insufficient Data Announcement, with the following data needs:

For all except Glyceryl Polymethacrylate:

- Method of manufacture data

For all 4 ingredients:

- Molecular weights and impurities, including residual monomers
 - Depending on the data received (especially residual monomer content), 28-d dermal toxicity, skin penetration data, and other toxicity endpoints may be needed
- Genotoxicity data
- Skin irritation and sensitization data at maximum use concentration

Draft Tentative Report: March 2022

The following unpublished data were received, and have been incorporated into the report:

- concentration of use data for Glyceryl Polyacrylate
- toxicology summary on Glyceryl Acrylate/Acrylic Acid Copolymer ((impurities, acute oral toxicity, skin, ocular, and mucosal membrane irritation)
- summary data on Glyceryl Polyacrylate (molecular weight and impurities, genotoxicity, and skin irritation and sensitization
- Maximization assay for a product containing 7.7% Glyceryl Polymethacrylate.
- Human patch test for a product containing 7.7% Glyceryl Polymethacrylate.
- Maximization assay for a product containing 0.586% Glyceryl Poly Acrylate/Acrylic Acid Copolymer.
- Human patch test for a product containing 0.586% Glyceryl Polyacrylate/Acrylic Acid Copolymer.
- Insult patch test for a product containing 0.5% Glyceryl Polyacrylate.

Comments on the Draft Tentative Report were received from the Personal Care Products Council

April 2022

The report has been revised to include comments that were received from the Council

June 2022

Panel reviews Draft Final Report

Glyceryl Acrylates Profile - June 2022 - Writer, Regina Tucker (and previously, Wilbur Johnson)

				Toxico-kinetics	Acute Tox			Repeated Dose Tox			DART	Genotox		Carci	Dermal Irritation			Dermal Sensitization			Photo-tox	Ocular Irritation		Mucous Membrane Irritation		Clinical Studies	
	VCRP	Method of Mfg	Impurities	Dermal Penetration ADME	Dermal Oral	Inhalation	Dermal Oral	Inhalation	Dermal Oral	In Vitro In Vivo	Dermal Oral	In Vitro Animal Human	In Vitro Animal Human	In Vitro Animal Human	In Vitro Animal Human	In Vitro Animal Human	In Vitro Animal Human	In Vitro Animal Human	In Vitro Animal Human	In Vitro Animal Human	In Vitro Animal Human	In Vitro Animal Human	In Vitro Animal Human	In Vitro Animal Human	In Vitro Animal Human	In Vitro Animal Human	In Vitro Animal Human
Caprylyl Glycol/Glycerin/Polyacrylic Acid Copolymer	0																										
Glyceryl Acrylate/Acrylic Acid Copolymer	295		X		X					X				X	X			X				X		X			
Glyceryl Polyacrylate	119		X							X								X									
Glyceryl Polymethacrylate	142	X																X				X					

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

GLYCERYL ACRYLATES

Ingredient	CAS #	InfoBase	SciFinder	PubMed	TOXNET	FDA	EU	ECHA	IUCLID	SIDS	HPVIS	NICNAS	NTIS	NTP	WHO	FAO	ECE-TOC	Web
Glyceryl Acrylate/Acrylic Acid Copolymer		Yes		0		No	0	0	0	0	0	0	0	0	0	0	0	Yes
Glyceryl Polymethacrylate	146126-21-8 28474-30-8	Yes		8		No	0	0	0	0	0	0	0	0	0	0	0	Yes
Caprylyl Glycol/Glycerin/Polyacrylic Acid Copolymer		Yes		0		No	0	0	0	0	0	0	0	0	0	0	0	Yes
Glyceryl Polyacrylate**	104365-75-5	Yes		1		No		0	0	0	0	0	0	0	0	0	0	Yes

** Glyceryl Polyacrylate search: 1999 forward; ingredient added to group at September 2021 Panel meeting

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>

SciFinder (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,

<https://www.fda.gov/food/food-additives-petitions/substances-added-food-formerly-eafus> (Substances added to Food);

<http://www.fda.gov/food/ingredientspackaginglabeling/gras/default.htm> (GRAS);

<https://www.fda.gov/food/generally-recognized-safe-gras/gras-substances-scogs-database> (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/>

SEPTEMBER 2021 PANEL MEETING – INITIAL REVIEW/DRAFT REPORT

Belsito Team – September 13, 2021

DR. BELSITO: Glyceryl Acrylates. So this is the first time that we're reviewing the three ingredients in the report, and it's reported to be used in 286 cosmetic products, mostly leave-ons. Glyceryl Acrylates have the greatest reported use frequency. We got concentrations of use and so we need to look and see where we are with this grouping and data. So, my first question is to you, Dan, are you okay with the grouping?

DR. SNYDER: Yeah.

DR. BELSITO: Particularly Caprylyl Glycol.

DR. SNYDER: Which report are you on, Don, sorry, which report?

DR. LIEBLER: Glyceryl Acrylates, Paul. Glyceryl Acrylates. Let us know when you got it.

DR. SNYDER: I got it.

DR. LIEBLER: Okay.

DR. SNYDER: Thanks.

DR. LIEBLER: So, with respect to the question of the grouping, yes, I'm okay with the grouping. And, furthermore, there was a suggestion in the Council memo that we add Glycerol Polyacrylate, and I'm okay with that, at least in terms of the chemistry. I think it's probably due for a re-review, but if there's any programmatic issue, Monice can fill us in. Monice, anything to consider there?

MS. FIUME: So it is actually scheduled for re-review next year as part of the Glycerol monoesters, I believe, report. I forget.

MR. JOHNSON: Yeah, that's right.

MS. FIUME: Yes, but, Wilbur, you looked back at the original document, and you stated there are no data on that ingredient in that original document, is that correct?

MR. JOHNSON: You're right, no safety test data.

MS. FIUME: Yes. So, adding that ingredient, if it fits better here than there, is great, would be fine. But just be aware that there are no data to pull from the old report on Glycerol Polyacrylate itself.

DR. SNYDER: If the absence of data is the basis to include in this report, that's fair, because there's no data on this whole group.

DR. LIEBLER: So, the question I have is about the other report that the Glyceryl Acrylates are currently in, you said that was Glycerol esters?

MR. JOHNSON: Glycerol Monoesters.

DR. LIEBLER: Monoesters. Are those polymers?

MS. FIUME: Let me grab the report.

MR. JOHNSON: No.

DR. LIEBLER: It doesn't sound like they're polymers, and if they're not, if that was like an orphan polymer thrown in with a bunch of non-polymers, it probably belongs in this report instead.

MR. JOHNSON: Mm-hmm.

MS. FIUME: It's a compilation of Glycerol monoesters.

DR. LIEBLER: Yeah, Glyceryl Polyacrylate is a polymer, so --

DR. ANSELL: Yeah, I think the point here is not the amount of data, but whether this is the right family.

DR. LIEBLER: Yeah.

DR. ANSELL: And we believe it is.

DR. BELSITO: No, I was being facetious, Jay, sorry.

DR. LIEBLER: It sure sounds like it is.

DR. BELSITO: Dan, you want to add Glyceryl Polyacrylate to this report?

DR. LIEBLER: That's correct. That's the Council's suggestion. Jay, if I've got that right, the feeling that it belongs more in this report than in the Glycerol monoesters.

DR. ANSELL: That's right.

DR. LIEBLER: Okay. I agree with that.

DR. BELSITO: Okay.

DR. LIEBLER: So, to get back to my assessment of this, so, the groupings are fine, the ingredients are fine with the additional Glyceryl Polyacrylate. And, then, this is insufficient for method of manufacture and impurities. And, most importantly, we need molecular weight information. These are polymers, so they should be high molecular weight. If they are, you know, greater than like 5,000, there will be no dermal absorption and the systemic endpoints really won't be needed.

We would need residual monomer and then, the other data needs that we would have to consider. Don, you can take the lead on that. But, anyway, I think insufficient method of manufacture and impurities, and residual monomer.

DR. BELSITO: And you said molecular weight?

DR. LIEBLER: Yeah. We don't need chapter and verse on method of manufacture. A sentence or two would probably be adequate. It's molecular weight range characterization. You know, even broad numbers would be adequate. We just need to verify that these are high molecular weight molecules.

DR. BELSITO: Okay, so manufacturing, impurities, molecular weight, and residual monomer.

DR. LIEBLER: Yep. I mean, these are, if you look at the uses, humectant, viscosity increasing agent, this is hallmarks of polymers, film formers, and so forth. So I think that we'll -- it won't be too hard for industry to provide the information we need to focus this report appropriately.

DR. BELSITO: Okay. And so, then, I'm assuming if we get that and there isn't any significant residual monomer and they're high molecular weight, we really don't need the toxicogenic studies because in the discussion we can assume that they won't be absorbed, is that correct?

DR. LIEBLER: That's correct. So that circumvents the whole 28-day dermal and all that stuff. And then it's sensitization, irritation.

DR. BELSITO: Okay. And, then I had a question on PDF page 12, the effect on burn wound healing? How long were they treated and were only the wounds assessed or were there any other tox endpoints that were looked at? Because that would give us some additional toxicity data. I'm assuming none of that was, in fact, reported, I didn't have time to look at the individual reference.

MR. JOHNSON: No, Dr. Belsito, just, you know, as stated here, you know, beginning on Day 0 until healing was complete.

DR. BELSITO: Okay.

DR. SNYDER: We don't even know the concentration of the Glycerol Polymethacrylate in the cream.

DR. BELSITO: Right.

MR. JOHNSON: Yeah.

DR. SNYDER: This is not very informative.

DR. BELSITO: Okay. So, then, again, with the lack of developmental and repro, if we have the residual monomer and the molecular weights, we don't have to worry about that. So, in the discussion, we would have the respiratory boilerplate. So I had insufficient. We needed, as Dan mentioned, manufacturing, impurities, molecular weight, residual monomer. We need mutagenicity. We need irritation and sensitization at 1.9 percent for the polymethacrylate, which is the most frequently used in the highest concentration of use. And that's what I have for insufficiencies. Does anyone have others?

DR. SNYDER: Well, we just have to qualify that insufficiency, because if there's molecular weights that would suggest that it is absorbed, then we need the 28-day dermal.

DR. BELSITO: Okay. So, then depending on molecular weight in residual monomer?

DR. SNYDER: Correct.

DR. LIEBLER: That's right.

DR. BELSITO: Let me just add that. Anything else on this?

MR. JOHNSON: Dr. Belsito, you said irritation and sensitization data at what concentration?

DR. BELSITO: One point nine for the Polymethacrylate.

MR. JOHNSON: For the Polymethacrylate. Okay.

DR. LIEBLER: And, if we bring in Glyceryl Polyacrylate and it's got uses, if it's higher then, you know, we need to key off of that one.

DR. BELSITO: Right.

MS. FIUME: Typically, the request will go out at maximum concentrations of use.

DR. BELSITO: Okay.

MS. FIUME: Is that wording okay, or --

DR. BELSITO: That's perfect.

MS. FIUME: Okay.

DR. LIEBLER: Yeah.

DR. BELSITO: That would cover the Glycerol if it's used at a higher --

DR. SNYDER: Wouldn't that also be qualified with the monomer content? If we have one that has a high monomer content?

DR. BELSITO: Yeah, but I mean, you would pick that up if, well, I guess -- so, depending upon molecular weight and residual monomer, we may need 28-day dermal toxicity and possibly other endpoints?

DR. SNYDER: Sensitization data or irritation data, yeah.

DR. LIEBLER: Yeah. The monomer usually is not any issue at all. I mean, we need to document it if we can.

If the method of manufacture indicates that the polymer is produced and then describes any sort of use wash or clean up steps, then that's going to mitigate our need for hard data on residual monomer because the acrylates are very volatile.

DR. BELSITO: Right.

DR. LIEBLER: So any residual monomer, you know, is going to evaporate and is going to be removed by wash steps in the cleanup of these. So, depending on what else we get, we can kind of audible on how we handle the monomer, but I don't anticipate it's going to be a problem for us such that we would need data on the monomer per se.

DR. BELSITO: Okay. Any other comments?

MR. JOHNSON: Yeah, Dr. Belsito, you said depending on the molecular weight and residual monomer data, 28-day dermal toxicity data may be needed, any additional data needs based upon that?

DR. BELSITO: Possibly sensitization and irritation, if there's significant monomer.

MR. JOHNSON: Okay. Thank you.

DR. LIEBLER: And, I don't know, I just want to make a comment here, and Jay might be able to tell me. If we're really short on data with these and we need it, this might be an example where there might be other acrylate polymers that have similar alcohol hydroxyl functional substituents. I don't know if, you know, we probably don't have any in vivo endpoint -- I mean, any, you know, we don't have -- we'll probably not going to have repeat dose and DART and so forth, but I guess, when we look at the data we have, we can consider whether we need any kind of read across.

DR. ANSELL: Yeah, I guess if the question is, are there other members which could contribute data? I mean, we can look at that.

DR. LIEBLER: Okay.

DR. ANSELL: You know, this is the first review. Other than the Polyacrylate, I didn't really have any comments about ingredient additions, but relevant data from other materials would be a good question.

DR. LIEBLER: Okay.

DR. BELSITO: Anything else? Okay.

Cohen Team – September 13, 2021

DR. COHEN: Okay. We'll move on to glyceryl acrylates. This is a draft report. This is the first time we're reviewing this. This assessment is for three derived chemicals. They're used as skin conditioning agents, humectants, and viscosity increasing agents. We have max use reported of 1.9 percent in a leave-on product. We have frequency of use reported. It looks like we

don't have method of manufacturing and impurities. No acute, short-term tox data, no DART, no genotox, and we need irritancy and sensitization at max use. And, Lisa, can we read across this list?

DR. PETERSON: I don't know. Probably some. Let's just go -- there is a method of manufacturing in the report for the glyceryl polymethacrylate.

DR. COHEN: Oh yes. Well --

DR. PETERSON: I think there's a box that needs to be checked, but I do think that -- so the caprylyl glycol/glycerin/polyacrylic acid copolymer, there's no uses. So, again, one could say why should it be in here? There's no data. But my concern about impurities is the presence of unreacted monomers.

DR. COHEN: Yeah.

DR. PETERSON: And so I would want impurities on all. Clearly, probably the method of manufacturing could be read across, but I think we should ask for the one for the 286, the glyceryl acrylate/acrylic acid copolymer. But I thought, yeah, method of manufacturing and impurities. And I thought we could maybe drop the third one.

DR. COHEN: Drop?

DR. PETERSON: Because there's no uses. This gets to the conversation we had earlier. There are no uses. There's no data.

DR. BERGFELD: We don't have to drop it right away. (Inaudible).

DR. SLAGA: (Inaudible) report, though.

DR. PETERSON: Yes. You could ask for this.

DR. HELDRETH: So you mean for caprylyl glycol/glycerin/polyacrylic acid copolymer?

DR. COHEN: Yeah.

DR. HELDRETH: Yes, we have nothing in VCRP, but we did get survey data back suggesting there's at least one use because we got 0.2 percent concentration use in a leave-on.

DR. PETERSON: Okay. I missed that. Then, yes, we need method of manufacturing and impurities. Again, the reason for the impurities is the unreacted starting material would have some irritation or since tissue toxicity is related with it.

DR. SHANK: Can we use the Panel's 2018 report on acrylate copolymers, about 126 of them found to be safe? Can we use that to satisfy some of the toxicology needs for the current compounds? Maybe Lisa and Dan can discuss that tomorrow. If you can, then we don't need all of these toxicology studies. If we cannot, then there are quite a few needs.

DR. COHEN: So that was an acrylate copolymer report in 2018?

DR. SHANK: 2018, yes. There were 126 copolymers reviewed and found to be safe.

DR. COHEN: So that's a bit of a read-across question, no?

DR. SHANK: Yeah.

DR. PETERSON: You mean the glyceryl is not going to -- one might think you could read across unless I'm not seeing -- to me the big issue with these compounds is the presence of the starting material present in the final product, that polymers are going to be huge.

DR. COHEN: So that's the basis for your impurities ask?

DR. PETERSON: Yes.

DR. COHEN: You want to know if there's monomer in there, and then that changes the whole discussion quite a bit.

DR. PETERSON: Well, it's going to impact a lot of things, but yes. But it's worth having a conversation with Dan.

DR. COHEN: Ron, would you go as far as suggesting that the copolymer report of 2018 would obviate the need for sensitization and irritancy data on these?

DR. SHANK: If the chemist agreed that that report can be used for read across.

DR. PETERSON: So is it possible -- I guess I can search for that report and --

DR. SHANK: Okay. If you go on to the CIR site under ingredients, it is listed there as acrylate copolymers.

DR. COHEN: So one question then, could this be an addendum or an update to the existing report? Why is it its own report at this point?

DR. SHANK: That's a good question. That's basically what I was asking. Why weren't these included in 2018? And maybe the question is there are significant differences in the copolymers -- of the monomers, which could be various impurities, like

Dr. Peterson has asked for. But I don't know enough about how these things are put together and cleaned up before they're sold as a polymer.

DR. COHEN: Wilbur or Bart, do we have any insight why this came as a separate report and not 127 through 129 on the other copolymer report? I just don't know.

MR. JOHNSON: I would have to yield to Bart's expertise on that, Dr. Cohen.

DR. COHEN: Bart, are you on?

DR. HELDRETH: I'm here. Off the top of my head, I don't see why it couldn't have been, but maybe this glyceryl functional group was considered to make it different enough to leave them out of this report. But I'm not sure that that --

DR. PETERSON: Yeah. So I'm looking at the report, the other report. And they are mostly all hydrocarbons. They don't have the free alcohol, although there is one that has a carboxylic acid.

DR. COHEN: Oh, glycol.

DR. PETERSON: But there aren't structures for everything, and there's a lot of names. It's going to take time. I mean, there's 126 of them.

DR. HELDRETH: Right.

DR. PETERSON: So there's a lot of structures there to go through. But my guess is that -- well, there's a penta -- a three -- there are some polyols there -- diol; there's some ethylene glycol.

DR. COHEN: So perhaps we can come out with an IDA with the asks that we discussed, which are method of manufacturing for two of the three, impurities for all three, tox DART, genotox for all of them, irritancy and sensitization, and open for a discussion on whether there's a reason to just update the 2018 report and not have this as a separate report. So we can announce the IDA but consider another pathway.

DR. SHANK: Yeah. I like that.

DR. SLAGA: Sounds good.

DR. COHEN: All right, and then the two teams can -- the chemists can hash it out a little bit.

MR. JOHNSON: Excuse me, Dr. Cohen, will you list those data needs again, please?

DR. COHEN: Sure. So we need method of manufacturing for two of the three. We have it for glyceryl polymethacrylate. We need impurities on all three. We need acute and short-term tox, DART, and maybe genotox. And we need irritancy and sensitization at max use.

DR. SHANK: Probably skin penetration if it's available because if these don't -- they're big -- so if they don't penetrate the skin, the epidermis, then you don't need the systemic tox.

DR. COHEN: So that would be direct skin penetration data, not just molecular weight devoid of impurities we worry about?

DR. SHANK: Yes. We have log Kow -- sorry, I was reading something else -- data. Anything that could be used to judge the ability of these to cross the skin.

DR. COHEN: Got it.

MR. JOHNSON: Dr. Cohen, you said genotoxicity data maybe?

DR. COHEN: Well, Tom, would you want the genotox?

DR. SLAGA: Yes. Especially if there's some impurities like the monomer.

DR. COHEN: Okay. Take out "maybe."

MR. JOHNSON: Okay. Thank you.

Full Panel – September 14, 2021

DR. BELSITO: This is the first time we're looking at three ingredients in this report. The SLR was issued on March 5th. We received VCRP data; it's reported to be used in 286 cosmetic products, mainly leave-ons. Three Glyceryl Acrylates are reviewed. Of the three, Glyceryl Acrylate has the greatest reported use frequency. And, in terms of use concentration, Glyceryl Polymethacrylate is the max at 1.9 in leave-on products.

So, looking at the data, our group found that the information was insufficient. We need manufacturing for all -- we need manufacturing except for Polymethacrylate. We need impurities for all three, and depending upon these, other endpoints like reproductive and developmental toxicity may be needed. We need mutagenicity data. We need irritation and sensitization at maximum concentration of use, which is 1.9 for the Polymethacrylate. And depending on molecular weight and residual monomer, we may need 28-day dermal and oscillate sensitization and irritation if that monomer is present in significant amounts.

DR. COHEN: So, I can second that, Don; we really align very well on that. So, without reiterating everything you just said, we have an alternative pathway we thought you might consider, which is, there was an Acrylate Copolymer report of 2018, which assessed the safety of 126 acrylate copolymers some of which were polyols in that report. Would we consider adding an addendum of that report, or we have the other pathway which was exactly how you articulated it.

DR. BERGFELD: Do you have a comment on that, Don?

DR. BELSITO: So it was a 2008 report, David?

DR. COHEN: 18.

DR. BELSITO: So that's not going to be up for re-review until 2033. So, why would we want to open up that whole thing to add these three ingredients?

DR. SHANK: It's not to open it up but to use it as a read across.

DR. LIEBLER: So the data could be --

DR. BELSITO: So Dan and Lisa are going to have to comment on the potential for read across there, I can't.

DR. LIEBLER: Yeah, so, Ron, it's a good idea in that the data for these other copolymers, that would be structurally analogous, could be very useful read across if there are data insufficiencies for this group.

The issue initially here is that even though it's strongly implied that these are polymers, we don't have any information that would confirm their high molecular weight and other sort of basic characterization that we would need anyhow even if we were using read across to fill data gaps. So, we still need that basic information on these.

And then the Council also suggested putting in Glyceryl Polyacrylate, which, as I understand it, was sort of an orphan in a previous report of lower molecular weight glyceryl esters. And it seems like it would belong in this report, so I thought that that would make sense to bring that one in as well.

DR. SHANK: Okay.

DR. PETERSON: I agree with that.

DR. BERGFELD: So it looks like it'll be a stand-alone document? Is that correct?

DR. SNYDER: Yeah, but the suggestion to possibly bring in data for read across is a good one.

DR. BERGFELD: And, David, you agree and your team agrees?

DR. COHEN: Yeah, we agree with Dan's suggestion and Don's motion.

DR. BERGFELD: Okay. So it's quite a long list of needs, and the scientific writer is, who?

MR. JOHNSON: It's Wilbur.

DR. BERGFELD: Oh, it's Wilbur?

MR. JOHNSON: Yes.

DR. BERGFELD: Wilbur, are you clear?

MR. JOHNSON: No, because I don't think I see in Teams the need for skin penetration data was mentioned, and if that occur then developmental and reproductive toxicity data may be needed. So I'm just wondering whether or not that should be stated in that way in this particular need.

DR. LIEBLER: Wilbur, what we really need first is chemical properties definitions. If these are more than 5,000 molecular weight, as I expect they are, the polymers, then we don't need skin penetration; it's not going to penetrate. And then it basically will boil down to irritation and sensitization.

DR. BERGFELD: Okay, any addition to that?

MR. JOHNSON: So just chemical properties particularly molecular weight data are needed.

DR. LIEBLER: Correct.

MR. JOHNSON: And irritation and sensitization data at the maximum use concentration.

DR. LIEBLER: Yeah, if we can get residual monomer that would be very helpful as well.

DR. BERGFELD: So you're asking for impurities.

DR. LIEBLER: Correct.

DR. BELSITO: Yes. So, Wilbur, what we need is manufacturing for the Acrylate/Acrylic Acid Copolymer and the Caprylyl Glycol/Glycerin/Polyacrylic Acid Copolymer. So, we need manufacturing for those two. We need impurities for all three, particularly residual monomer. And then depending upon the molecular weight and levels of residual monomer, we may need a 28-day dermal or other skin-penetration data on them.

And then, in addition, we're looking for sensitization and irritation for significant monomer, if that exist. Otherwise, if they're high molecular weight compounds, they're not going to penetrate the skin, really the only thing we'd be interested in would be potentially irritation. But we can ask for sensitization.

MR. JOHNSON: Dr. Belsito, (audio skip) skin irritation and irritation for significant monomer?

DR. BELSITO: No, well, there are two separate parts to it, Wilbur. We're asking -- although we may not really need it at this point it's a first look -- we're asking for sensitization and irritation at the max concentration of use, which is 1.9 percent for the Polymethacrylate.

MR. JOHNSON: Uh-huh.

DR. BELSITO: And then if there's significant residual monomer, we may want to -- and say the Polymethacrylate doesn't have significant residual monomer, but the Acrylate/Acrylic Acid Copolymer does, then we would want information on sensitization and irritation for that specific residual monomer.

What we really need right now are the impurities, molecular weight, and residual monomers, sensitization, irritation for the Polymethacrylate at highest concentration of use. And then depending upon this information, other toxicity endpoints may be needed.

MR. JOHNSON: Okay. Just one more point of clarification. The skin sensitization and irritation data are on the Polymethacrylate only, or for all three ingredients?

DR. BELSITO: No, right now at the finished product it's for the Polymethacrylate at 1.9 percent.

MR. JOHNSON: Okay, thank you.

DR. LIEBLER: And, Wilbur, I can add that if you can't get irritation and sensitization on any of these, we can still consider the previous report that Ron Shank mentioned where we have a structurally analogous polymer that we can consider. And that we would need to take a look at that, at the structures and data for those. But that's a possibility to address a data gap for the skin endpoints.

MR. JOHNSON: Okay, thank you.

DR. BELSITO: Monice?

DR. BERGFELD: Wilbur should do that right away?

MS. FIUME: I just have a question. Since Glyceryl Polyacrylate has been added, for the purposes of the conversation of the data needs, is that ingredient included with all of the data needs, does that amend the list at all for the IDA if we're adding that ingredient to the report?

DR. LIEBLER: We don't know what the data are for it, so if it has all those data -- I don't know if it has all those data needs or if it comes with data that supported it you can look at that and decide which ones are still needed.

MS. FIUME: Okay. Yeah, I do know the previously report --

MR. JOHNSON: Dr. Liebler, they're --

MS. FIUME: Go ahead, Wilbur.

MR. JOHNSON: I was just going to say that in the -- Glyceryl Polyacrylate is included in the report on glyceryl monoesters. And, that report does not include any safety test data on Glyceryl Polyacrylate.

DR. LIEBLER: Okay. So it's part of the data needs then.

MS. FIUME: Thank you.

MR. JOHNSON: Okay, thank you.

DR. BERGFELD: Monice, do you have something else?

MS. FIUME: Nope, that was it.

DR. BERGFELD: So, we're going out for an insufficient data announcement, and I think we've clarified what the needs are and what we're requesting. Does anyone else have a comment about that before we call the vote? Okay, going to call the vote then, those opposing? Abstaining? Unanimously accepted IDA report on this ingredient.

MARCH 2022 PANEL MEETING – SECOND REVIEW/DRAFT TENTATIVE REPORT

Cohen Team March 11, 2022

Dr. David Cohen

Let's move on to glyceryl acrylates. And Regina was down one member. Our chemist isn't here.

And our team will hopefully come back to full play soon. So glyceryl acrylates were reviewed in September. At that point, we had three ingredients. At that meeting we thought it was appropriate to add glyceryl polyacrylate, so it's in this safety assessment now. I think some notable issues were max use of glyceryl polyacrylate, which was reported at 2%. Many years ago is now reported at .99%. We issued an IDA asking for method of manufacturing for all except glyceryl Poly methacrylate. And molecular weights and impurities, including residual monomers. A dermal tox depending on the data we received, genotoxic. Skin sensitization and irritation and in the second wave, there was a letter from WVE about some acrylate copolymers and sprays so, I just want to ask the team weather those were relevant to this particular set of chemicals and whether there were any pulmonary tox implications. So there's a lot of questions I threw out there. Ron, you want to start?

Dr. Ron Shank

OK, We have enough data on the glyceryl. Acrylate acrylic acid copolymer.

To say it's safe as used and I would like to read it, use it for read across.

Dr. David Cohen

Yeah.

Dr. Ron Shank

But I, we need to see what Dr. Liebler says that if he agrees with that. If he agrees with that, then they're all safe as used. There was a question about the acrylic acid, which is a irritant corrosive agent. But the level into the copolymers was less than five PPM, which would be. Non irritating concentration. And when it's formulated to be even less, if I don't think acrylic acid is a problem if all of the molecular weights are above 10,000, then no more systemic toxicity data is needed. We have skin irritation and sensitization data. At the maximum concentrate use concentration or even above.

Dr. David Cohen

Yep.

Dr. Ron Shank

And their negative for three of them. No data for the capital glycol. Glycerin, polycrylic acid, but I'd use read across. So I see they're all safe for use in cosmetics?

Dr. Thomas Slaga

Yeah, I Tom. We had a lot of data, good bit of data including not only your irritation and sensitization, but genotoxicity for two of the compounds and, as Ron mentioned its very large molecules. And I'm I wasn't sure if we could read across, but it looked like I thought we could. But like Ron said, to, we wait for one of the chemist to make a statement. I also had the if there is read across, then we're they're all safe.

Dr. David Cohen

That we have a try factor because I had a safe as used as well. Really the issue for sensitization is going to be in the monomers, right? And well, that will have that.

Dr. Thomas Slaga

Right. In the discussion.

Dr. David Cohen

Yep, it will have that in the discussion. I found some pub Med date on glyceryl methacrylate is a potential sensitizer, but that's going to be in its monomeric form. And these are large molecules. So was there anything I'm not quite sure we got every piece of information, but I thought we had enough in here to move this along as safe as used.

Dr. Ron Shank

I agree.

Dr. Thomas Slaga

I agree too.

Dr. David Cohen

So I'm going to, yeah.

Dr. Ron Shank

There. There was a question about the 2003 report on glycerol monoesters. Should that information be there? And those are small molecules, and they're not a quick acid derivatives. So I don't think they belong in the report. I don't remember where that came from. Probably in the cover letter.

Dr. David Cohen

OK, so an issue I before we finish on this, I'll go out as safe as used and I'll ask for an opinion from the Belsito side on read across. But were reading across and we were intending to read across.

Dr. Thomas Slaga

Right.

Dr. Ron Shank

Yes.

Dr. David Cohen

All along, even though we had any addition. Of a fourth constituent, the WVE letter. Where they these chemicals? And is there any Pulmonary issue? Even if these are in Airbrushes.

Dr. Ron Shank

Well, there are. I would handle that with the boiler plate.

Dr. Thomas Slaga

Right.

Dr. David Cohen

Which boilerplate?

Dr. Ron Shank

The one we just the well, I call it, I shouldn't call it a boilerplate. A reference to the inhalation resource document. The one we just finished.

Dr. David Cohen

Right, so, but at times we used to split conclusion for airbrush, right? We just did it. Right. But this one look, the question is, are the acrylates that were listed the acrylic acrylates octylacrylamide copolymer.

Right, that's, that's not necessarily this is it? So all I'm getting at is, are we going to do a split conclusion with airbrushes or as in this situation the Pulmonary toxicology doesn't warrant that and we can reference the new resource document that we have?

Dr. Ron Shank

Let me look.

Dr. Wilma Bergfeld

While he's looking. You no longer wanted molecular weights?

Dr. David Cohen

Yeah, that was one of the things Wilma that we didn't get but we got, we have it for glyceryl. Polyacrylate. It's over 500,000 daltons.

Dr. Wilma Bergfeld

Well, it could go to the discussion and their large molecular weight.

Dr. David Cohen

And. Yeah, I think we were assuming that all of these are going to be pretty big.

Dr. Thomas Slaga

Right.

Dr. David Cohen

They're all big polymers.

Dr. Wilma Bergfeld

But we'd ask for it. So I think we should put in discussion. We had one and assumed all the others were similar.

Dr. David Cohen

Ah. Yeah. Thank you.

Dr. Bart Heldreth

Yeah, the acrylates octylacrylamide copolymer is, it is an ingredient in a different report altogether.

Dr. David Cohen

Yeah, that's why I wasn't sure these were relevant.

Dr. Bart Heldreth

It's the final report that we're going to get to later in the day, the 4th from the end, acrylamide, acrylate copolymers. It's the one that that exists in.

Dr. David Cohen

OK. OK. Sure. OK. So could we move on as a,

Dr. Ron Shank

Well, while we're here.

Dr. David Cohen

OK.

Dr. Ron Shank

Of the current draft discussion has this phrase about aerosol products. That 95 to 99% of them are too big to be respired. And that actually does not agree anymore with our inhalation resource document because we now know that there are Cosmetic products that contain smaller respirable things.

So I would just ask the panel to consider removing that 95 to 99% limitation. The rest of it's OK. But to say that 95 to 99% are not respirable.

Dr. David Cohen

It doesn't harmonize anymore.

Dr. Ron Shank

It doesn't harmonize is a good way to put it. Thank you.

Dr. Thomas Slaga

Right.

Dr. Wilma Bergfeld

To be specific.

Dr. Ron Shank

And that's in the barley report. It's in the Rosa Damascus, Santa, it's on the porterlaka. The glucosamine. The acrylamide acrylate its in six of the reports. And I'm not seeing change anything other than eliminate that range of 95 to 99%. We can discuss that with the other team tomorrow.

Dr. David Cohen

Carol, you have your hand raised.

Carol Eisenmann (PCPC)

Did on mute. From what I hear, inhalation background document you're saying you're not covering that that the data on airbrush products, it's insufficient. So I don't an individual reports, I'm not sure why you need to go into airbrush products at all. When did you don't have any information on them? The reports cover what the uses that are described and so far we haven't gotten anybody to say they're using it and the VCRP doesn't cover airbrush suits. So you're don't necessarily have to go into airbrush products in at each and every report and for the product categories that are covered those product categories, the particle size is our most so particle sizes are large. There are some data on the report that your inhalation background document does go into. So I don't know if you really truly want to remove the 95 to 90, because that's not about airbrush products. That's about the products for which it was measured. You could make it clear that it's for what product categories that was for and have to read it again to see if it specifically says what product categories. But you have the inhalation background document that says the data on airbrush is insufficient. Then you can refer to that.

Dr. Ron Shank

It. It's not. It's not just airbrushes anymore.

Dr. David Cohen

Right. I thought other devices were able to make smaller particles now.

Carol Eisenmann (PCPC)

But still only a small percentage is this the small particles.

Dr. Wilma Bergfeld

What are you suggesting they say?

Carol Eisenmann (PCPC)

They prefer.

Dr. Wilma Bergfeld

Or say nothing.

Dr. Ron Shank

It's up to the panel.

Dr. David Cohen

No, but Carol, what were you? What were you going to come? What would you? What would your suggestion be for that?

Carol Eisenmann (PCPC)

Well, I think referring to your document is probably the best thing to do, because then you can change that document. And then it without having to change the individual reports.

Dr. Wilma Bergfeld

So you would say within the inhalation information is inaccurate. It's insufficient then. And refer to the document.

Carol Eisenmann (PCPC)

Right, especially for the airbrush product you referred to that document.

Dr. David Cohen

The question is Ron, is it really 95 to 99% or not responsible? Still.

Dr. Ron Shank

We don't know that that that was based on. Old information. Maybe even 20 years ago. When we first started to consider. A particle size in aerosolized in sprays and such. And the technology to measure smaller particles were lacking. Now, both the technology to measure the smaller molecules accurately is available and apparently manufacturers or using nanotechnology to make intentionally smaller molecules that's covered very nicely in the new resource document. So all I'm saying is I don't see it's useful to put in that. 95 to 99% range. Leave the rest of it alone. That's fine.

Dr. David Cohen

Well, if you take that one line out, it goes from inhalation toxicity data were not available and then you'd say furthermore droplet particles deposit in the nasopharyngeal and bronchial regions of the respiratory tract present no toxicologic concern. And keeps going on, so we would need to rewrite that a little bit because the English is a little awkward.

Dr. Ron Shank

A little bit. Yeah, he wouldn't say furthermore. Right.

Dr. David Cohen

But it we might say, please refer to the resource document on inhalation toxicity.

Dr. Ron Shank

That's best.

Dr. David Cohen

OK.

Dr. Ron Shank

It's a complex issue because particle size isn't the only thing.

Dr. Thomas Slaga

Right.

Dr. David Cohen

Alright, I want to make.

Dr. Wilma Bergfeld

So is that is that a recommendation for tomorrow?

Dr. David Cohen

Yeah, I'm writing it down to maybe. Well, open it up. It's in zeolites. Is it in zeolites? I don't, I don't remember.

Dr. Ron Shank

No, I don't think so. It's in barley. Glycerol acrylates. Rosa amascena. PorterlockerOleracea. Acrylamide, acrylate copolymers and glucosamine.

Dr. David Cohen

And methicones we call out with a split conclusion, right?

Dr. Ron Shank

Right.

Dr. David Cohen

So I could bring it up around Rosa Damascena because that's third on the list tomorrow.

Dr. Ron Shank

OK.

Dr. David Cohen

OK. And refer. Got it. Now. Thank you for bringing that up, because. It's, you know you think about it every time you see it and we spent a lot of time on that inhalation document which means the people behind the scenes spent 50 times more time on it. So.

Dr. Ron Shank

Right.

Dr. David Cohen

OK. So just to conclude, we're going out as safe as used for glyceryl acrylates.

Dr. Ron Shank

Good.

Belsito Team – March 11, 2022

Dr. Donald Belsito

Afternoon. OK. Dan is back so at the September 2021 meeting this report with three ingredients, we determine we added a fourth glyceryl polyacrylate. And the draft report of the 2021 meeting. We had an IDA and we asked for method of manufacture for all except the glycerol Poly methacrylate and for all four the ingredients molecular weight and impurities including residual monomer depending upon those other tox endpoints. Genotox data and skin irritation sensitization at maximum concentration of use. Because we received a bunch of data and updated VCRP, so I'm not going to list all the data. Let's look at it and see where we think we are with this.

Dr. Dan Liebler

I think the chemistry.

Dr. Donald Belsito

We also with wave 2.

Dr. Dan Liebler

Because I think the chemistry additions are very helpful on PDF 20. High molecular weight glyceryl polyacrylate. This confirms high molecular weight at low residual monomer, less than five PPM. So these are large molecules that cannot be dermally absorbed. System systemic tox endpoints are not an issue. If the sensitization's OK Don. Unsafe as used.

Dr. Donald Belsito

Sensitization is OK. I mean we have to update all of the reference sevens , and there are quite a few or actually on the glyceryl acrylate acrylic acid copolymer at 1.3 to 2%. Not neat. That was the clarification from Wave 2, we had no manufacturing data for the Poly methacrylate Dan does that bother you?

Dr. Dan Liebler

No, I mean I think that given the structures of these, we know that these are produced by common methods for, you know for polymer manufacturing. I don't really feel that it's critical to our assessment to have detailed manufacturing information on all of them. We have one on Glyceryl Poly methacrylate, which I believe is the main one and use?

Dr. Donald Belsito

We have manufacturing for Poly methacrylate, correct.

Dr. Dan Liebler

Yeah.

Dr. Donald Belsito

And what about impurities? We don't have impurities for capital glycol and glycerol Poly methacrylate.

Dr. Dan Liebler

Yeah, my logic is the same there.

Dr. Donald Belsito

OK,

Dr. Dan Liebler

OK, the main I just misspoke. The Glyceryl acrylate acrylic acid copolymer has the most uses.

Dr. Donald Belsito

Right.

Dr. Dan Liebler

Glyceryl Poly methacrylate has the second most uses 142.

Dr. Donald Belsito

OK.

Dr. Dan Liebler

I mean, if we were small, these are different small molecules, then we need, you know, detailed method of manufacture, composition, impurities on each one. But for these big polymers, I think representative data for major ingredients are enough.

Dr. Donald Belsito

OK. I'm in, Regina, under the use the second paragraph. The next to the last line that should be 2021, not 20 L 1. You see where I am.

Regina Tucker (CIR)

Yes, thank you.

Dr. Donald Belsito

PDF page 20. OK. Well, I mean that we need to correct the concentrations on the ones that say neat, not mark that throughout my book, because they appear or throughout my documents, they appear in tables as well as in the print, but it certainly covers the use I believe it was. What is the highest use here? A lot of new data, highest leave on concentration is 2%. And we have data we have ocular irritation, mucociliary, irritation, sensitization, irritation. So I mean we have that covered. So you're going safe is used Dan is that right?

Dr. Dan Liebler

Yes.

Dr. Curtis Klaassen

Yeah.

Dr. Donald Belsito

I said I was OK with the skin data. Wow, that was quicker than I thought. Curt, Paul?

Dr. Curtis Klaassen

Good.

Dr. Paul Snyder

Nothing.

Dr. Donald Belsito

OK, safe as used respiratory boilerplate.

Dr. Dan Liebler

Yep.

Dr. Donald Belsito

Airbrush boilerplate. Yeah, they're discussion here. The large size of it, we need to say something about why we're not asking for manufacturing and impurities for all of them.

Dr. Dan Liebler

Regina, did you note my comment or you want me to state that again?

Regina Tucker (CIR)

Yes, please.

Dr. Dan Liebler

So I my logic was that even though we didn't have method of manufacture on all the polymers we had it on a major, one of the major use ingredients and that the general approaches to polymer manufacturer manufacturing, excuse me, are well enough known. To satisfy our assessment, and the same is true for composition and purities.

Regina Tucker (CIR)

Thank you.

Dr. Dan Liebler

Sure.

Dr. Curtis Klaassen

We might say that we have a little read across. In the chemistry and manufacturing.

Dr. Donald Belsito

No.

Dr. Curtis Klaassen

Right.

Dr. Dan Liebler

Although I wouldn't use that term specifically because usually for read across we read across for a particular safety data endpoint.

Dr. Curtis Klaassen

Yes, I know I said that kind of as a as a joke.

Dr. Dan Liebler

I got it.

Dr. Curtis Klaassen

I'm not trying to, but it's kind of the same concept.

Dr. Dan Liebler

It is now, yeah.

Dr. Curtis Klaassen

We're not going to use word read across, but its kind of a read across.

Dr. Dan Liebler

Correct.

Dr. Donald Belsito

OK. Anything more with these glyceryl acrylate's? If not?

Dr. Curtis Klaassen

Good.

Dr. Dan Liebler

Yep. Good.

Full Panel – March 12, 2021

Dr. David Cohen

OK, so, the glyceryl acrylates were reviewed in September, which was our initial review of originally three derived ingredients. However, we added a fourth ingredient, glyceryl polyacrylate We had an insufficient data announcement with needs including molecular weight, impurities, genotoxic in irritation and sensitization. We got updated VCRP material. We received a fair amount of information. And our motion was safe as used, and we could.

Dr. Don Belsito

It's working.

Dr. Wilma Bergfeld

2nd. Any discussion regarding this ingredient group?

Dr. Don Belsito

Respiratory airbrush boiler.

Dr. Wilma Bergfeld

Yeah, that would include putting it under use as well as correctly. Each time you say that. The paragraph you wanted.

Dr. Dan Liebler -

It's.

Dr. Don Belsito

Yes.

Dr. Wilma Bergfeld

Included under use OK, any comment? Go ahead.

Dr. David Cohen

And yeah, and one other thing is that we have molecular weight for glyceryl polyacrylate at greater than 500,000 daltons. And that we're making our assessment and assumptions based on the other ones being very large polymers as well.

Dr. Dan Liebler -

I agree with that.

Dr. Ron Shank

Correct.

Dr. Wilma Bergfeld

Yep, that would go under discussion. OK.

Dr. David Cohen

Yeah.

Dr. Wilma Bergfeld

Anything else?

Dr. Don Belsito

Yeah, that that was also true for manufacturing and impurities in Dan. You can comment on that about basically. We had that for one with the major views and Dan felt that they approached the polymer manufacturing was well enough known as was the composition and impurities that would be expected. But damn am I quoting you correctly.

Dr. Dan Liebler -

That's correct.

Dr. Wilma Bergfeld

So you would put that into discussion as well.

Dr. Don Belsito

Yes.

Dr. Dan Liebler -

Yes.

Dr. Wilma Bergfeld

How you came to that determination? OK. Anything else?

Dr. Dan Liebler -

Right.

Dr. Wilma Bergfeld

Regina, do you have a comment or clarification you need?

Regina Tucker (CIR)

No, I have everything. Good morning. Thank you.

Dr. Wilma Bergfeld

So Morning. All right, I will call the question then I'll though all those opposed to the conclusion of safe Abstaining. It is approved. I was little acrylates were pro approved. Now moving onto a big one barley Dr Belsito.

Safety Assessment of Glyceryl Acrylates as Used in Cosmetics

Status: Draft Final Report for Panel Review
Release Date: May 23 , 2022
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The Expert Panel for Cosmetic Ingredient Safety members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; David E. Cohen, M.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; Allan E. Rettie, PhD.; David Ross, Ph.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; Paul W. Snyder, D.V.M., Ph.D.; and Susan C. Tilton, Ph.D. Previous Panel member involved in this assessment: Lisa A. Peterson, Ph.D. The Cosmetic Ingredient Review (CIR) Executive Director is Bart Heldreth, Ph.D. This report was prepared by Wilbur Johnson, Jr., M.S., former Senior Scientific Analyst/Writer, and Regina Tucker, M.S., Scientific Analyst/Writer, CIR.

ABBREVIATIONS

aq	aqueous
CFR	Code of Federal Regulations
CIR	Cosmetic Ingredient Review
Council	Personal Care Products Council
CPSC	Consumer Product Safety Commission
FDA	Food and Drug Administration
FHSLA	Federation of Health Science Library Associations
HRIPT	human repeated insult patch test
NR	not reported
Panel	Expert Panel for Cosmetic Ingredient Safety
PII	primary irritation index
SIOPT	single-insult occlusive patch test
SLS	sodium lauryl sulfate
VCRP	Voluntary Cosmetic Registration Program
wINCI	web-based <i>International Cosmetic Ingredient Dictionary and Handbook</i>
US	United States

ABSTRACT

The Expert Panel for Cosmetic Ingredient Safety (Panel) assessed the safety of 4 glyceryl acrylates as used in cosmetic formulations. Caprylyl Glycol/Glycerin/Polyacrylic Acid Copolymer and Glyceryl Acrylate/Acrylic Acid Copolymer are both reported to function in cosmetics as skin-conditioning agents, and Glyceryl Polyacrylate and Glyceryl Polymethacrylate as film formers. The Panel considered the available data and concluded that these ingredients are safe in cosmetics in the present practices of use and concentrations described in this safety assessment

INTRODUCTION

The safety of the following 4 glyceryl acrylates as used in cosmetics is reviewed in this safety assessment:

Caprylyl Glycol/Glycerin/Polyacrylic Acid Copolymer
Glyceryl Acrylate/Acrylic Acid Copolymer
Glyceryl Polyacrylate
Glyceryl Polymethacrylate

According to the web-based *International Cosmetic Ingredient Dictionary and Handbook* (wINCI; *Dictionary*), Caprylyl Glycol/Glycerin/Polyacrylic Acid Copolymer and Glyceryl Acrylate/Acrylic Acid Copolymer are both reported to function in cosmetics as skin-conditioning agents; Caprylyl Glycol/Glycerin/Polyacrylic Acid Copolymer is also reported to function as a humectant, and Glyceryl Acrylate/Acrylic Acid Copolymer as a viscosity increasing agent (Table 1).¹ Glyceryl Polyacrylate and Glyceryl Polymethacrylate are both reported to function in cosmetics as film formers.

The safety of Glyceryl Polyacrylate as used in cosmetics was previously reviewed by the Expert Panel for Cosmetic Ingredient Safety (Panel). In 2004, the Panel published a report, concluding that Glyceryl Polyacrylate is safe as a cosmetic ingredient in the present practices of use and concentration [described in that report].² Additionally, in 2018, the Panel issued a final amended report on 126 acrylates copolymers (not glyceryl) with the following conclusion, “Acrylates copolymers are safe in cosmetics in the present practices of use and concentration described in the safety assessment when formulated to be non-irritating.”³

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

CHEMISTRY

Definition and Structure

Two ingredients defined as copolymers, i.e., Caprylyl Glycol/Glycerin/ Polyacrylic Acid Copolymer and Glyceryl Acrylate/Acrylic Acid Copolymer, and two esters of glycerin, i.e., Glyceryl Polyacrylate and Glyceryl Polymethacrylate, are reviewed in this safety assessment.¹ These ingredients are each vinyl-type polymers, resulting from the esterification of acrylic acid or methacrylic acid with glycerin. The figure for Glyceryl Polymethacrylate, an ester of glycerin and polymethacrylic acid, is depicted in Figure 1.

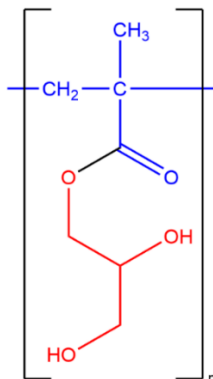


Figure 1. Glyceryl Polymethacrylate

The definitions, idealized structures, and available CAS Nos. of the glyceryl acrylates included in this safety assessment are presented in Table 1.

Chemical Properties

According to one supplier, Glyceryl Polyacrylate has a molecular weight > 500,000 Da.⁴ Properties data on a Glyceryl Acrylate/Acrylic Acid Copolymer trade name mixture, but not on the ingredient alone, were found and are presented in Table 2. This mixture (which contains 1.71 – 2.09% Glyceryl Acrylate/Acrylic Acid Copolymer, 36.5 – 44.6% glycerin, 50- 62% water, and 0.85 – 1.1% propylene glycol) is water-soluble and has a relative density of 1.15 g/ml.⁵

Method of Manufacture

Glyceryl Polymethacrylate

According to one paper, the mixing of 4-aminocarbonylazo-2-pyrimidinone with mildly acidic solutions of 1-glyceryl methacrylate resulted in polymerization to Glyceryl Polymethacrylate.⁶

Method of manufacture data on glyceryl acrylates for use in cosmetics were not found in the published literature, and unpublished data were not provided.

Impurities

Glyceryl Acrylate/Acrylic Acid Copolymer

Potential impurities of Glyceryl Acrylate/Acrylic Acid Copolymer include acrylic acid (< 5 ppm), methyl vinyl ether (< 0.5 ppm), and maleic acid (< 5 ppm).⁷

Glyceryl Polyacrylate

Glyceryl Polyacrylate may contain < 5 ppm residual acrylic acid.⁴

USE

Cosmetic

The safety of the cosmetic ingredients addressed in this assessment is evaluated based on data received from the US Food and Drug Administration (FDA) and the cosmetics industry on the expected use of these ingredients in cosmetics, and does not cover their use in airbrush delivery systems. Data are submitted by the cosmetic industry via the FDA's Voluntary Cosmetic Registration Program (VCRP) database (frequency of use) and in response to a survey conducted by the Personal Care Products Council (Council) (maximum use concentrations). The data are provided by cosmetic product categories, based on 21CFR Part 720. For most cosmetic product categories, 21CFR Part 720 does not indicate type of application and, therefore, airbrush application is not considered. Airbrush delivery systems are within the purview of the US Consumer Product Safety Commission (CPSC), while ingredients, as used in airbrush delivery systems, are within the jurisdiction of the FDA. Airbrush delivery system use for cosmetic application has not been evaluated by the CPSC, nor has the use of cosmetic ingredients in airbrush technology been evaluated by the FDA. Moreover, no consumer habits and practices data or particle size data are publicly available to evaluate the exposure associated with this use type, thereby preempting the ability to evaluate risk or safety. Therefore, airbrush application of cosmetic products is not assessed by the Panel.

According to 2022 FDA VCRP data, Glyceryl Acrylate/Acrylic Acid Copolymer has the greatest frequency of use; it is reported to be used in 295 cosmetic products, 288 of which are leave-on products (Table 3).⁸ The results of concentration of use surveys conducted by the Council, and provided to CIR in 2021, indicate that Glyceryl Polymethacrylate has the highest concentration of use; it is used at maximum use concentrations up to 1.9% in leave-on products (body and hand products).^{9,10} The frequency of use of Glyceryl Polyacrylate has increased since it was originally reviewed by the Panel; in 1998, 1 use was reported,² and in 2022, 119 uses are reported⁸ (Table 4). The maximum reported concentration of use of Glyceryl Polyacrylate has decreased slightly since the original review; in 1999, this ingredient was reported to be used at a maximum of 2% in face and neck creams, lotions, powders, and sprays,² and in 2021, it was reported to have a maximum use concentration of 0.99% in face and neck products (not sprays).¹⁰

Cosmetic products containing glyceryl acrylates may incidentally come in contact with the eyes (e.g., Glyceryl Acrylate/Acrylic Acid Copolymer at concentrations up to 0.62% in eye lotions), and 3 of these 4 ingredients are also used in products that come in contact with mucous membranes (concentrations not stated). Additionally, the potential for incidental ingestion exists with these ingredients; Glyceryl Acrylate/Acrylic Acid Copolymer is reported to be used in 12 lipstick formulations (concentration not stated). Use in baby products is also reported (e.g., Glyceryl Polyacrylate is used at up to 0.09% in baby lotions, oils, and creams.)

Some of these ingredients are used in cosmetic products that could possibly be inhaled. For example, Caprylyl Glycol/Glycerin/Polyacrylic Acid Copolymer is reported to be used at a maximum concentration of 0.2% in perfumes, and Glyceryl Polymethacrylate (concentration not reported) is reported to be used in face powders. In practice, as stated in the Panel's respiratory exposure resource document (<https://www.cir-safety.org/cir-findings>), most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and tracheobronchial regions and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount. 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.

Although products containing some of these ingredients may be marketed for use with airbrush technology, this information is not available from the VCRP or the Council survey. Without information regarding the frequency and concentrations of use of these ingredients (and without consumer habits and practices data or particle size data related to this use technology), the data are insufficient to evaluate the exposure resulting from cosmetics applied via airbrush delivery systems.

The glyceryl acrylates reviewed in this safety assessment are not restricted from use in any way under the rules governing cosmetic products in the European Union.¹¹

Non-Cosmetic

Glyceryl Polymethacrylate–collagen composite hydrogels have been developed for implantation in surgical lesions of the rat brain. Such materials provide porous matrices that can serve as support systems for growth of scar tissue and axonal growth.^{12,13} It has been noted that this technology has considerable potential for basic as well as for clinical research in central nervous system regeneration. Other reported uses of Glyceryl Polymethacrylate include autoclavable lubricant and moisturizer for medical and surgical use.¹⁴

TOXICOKINETIC STUDIES

Toxicokinetic data on glyceryl acrylates were not found in the published literature, and unpublished data were not provided.

TOXICOLOGICAL STUDIES

Acute Toxicity Studies

Oral

Glyceryl Acrylate/Acrylic Acid Copolymer

The acute oral toxicity of Glyceryl Acrylate/Acrylic Acid Copolymer was evaluated in rats (number of animals not provided).⁷ Fasted animals were dosed by gavage with up to 5 g/kg, and observed for 14 d; no mortality was reported. The oral LD₅₀ of Glyceryl Acrylate/Acrylic Acid Copolymer was > 5 g/kg in rats.

Short-Term, Subchronic, and Chronic Toxicity Studies

Repeated dose toxicity studies on glyceryl acrylates were not found in the published literature, and unpublished data were not provided.

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY STUDIES

Developmental and reproductive toxicity data on glyceryl acrylates were not found in the published literature, and unpublished data were not provided.

GENOTOXICITY STUDIES

In Vitro

Glyceryl Acrylate/Acrylic Acid Copolymer

The mutagenic potential of Glyceryl Acrylate/Acrylic Acid Copolymer was evaluated in an Ames test using *Salmonella typhimurium* TA97a, T98, TA100, and TA102, and TA1535.⁷ A concentration of 5000 µg/plate was tested with and without metabolic activation. Vehicle and positive controls were used; however, the control substances were not identified. Glyceryl Acrylate/Acrylic Acid Copolymer was not mutagenic.

Glyceryl Polyacrylate

An Ames test was conducted on 1.9% Glyceryl Polyacrylate.⁴ The test substance was not mutagenic. No details were provided.

CARCINOGENICITY STUDIES

Carcinogenicity data on glyceryl acrylates were not found in the published literature, and unpublished data were not provided.

OTHER RELEVANT STUDIES

Effect on Burn-Wound Healing

Glyceryl Polymethacrylate

Eight domestic pigs were subjected to burn wounds in the paravertebral area. Some wounds were exposed to an experimental cream, and other wounds served as air-exposed controls.¹⁵ The cream consisted of Glyceryl Polymethacrylate in an oil-in-water emulsion (concentration not stated) with the following components: fibronectin (40 ppm), proline, arginine, and glycine. Beginning on day 0 (day of wounding), the wounds were treated once daily with the cream (~ 0.2 g/wound site) to completely cover the wound until healing was complete. The wounds treated with the cream developed a soft eschar, when compared to air-exposed control wounds. Erythema was not observed after application of the cream.

DERMAL IRRITATION AND SENSITIZATION STUDIES

Dermal irritation and sensitization studies are described in Table 5, and summarized below.

In rabbits, application of an occlusive patch of 1.3 – 2% Glyceryl Acrylate/Acrylic Acid Copolymer in a water and glycerin solution for 24 h was not irritating.⁷ In clinical single insult occlusive patch tests (SIOPT), a product containing 0.586% Glyceryl Acrylate/Acrylic Acid Copolymer (23 subjects)¹⁶ and a product containing 7.7% Glyceryl Polymethacrylate (19 subjects)¹⁷ were non-irritating; the primary irritation index (PII) in each study was 0 and 0.05, respectively.

Glyceryl Acrylate/Acrylic Acid Copolymer (1.3 – 2% in a water and glycerin solution; 55 subjects; occlusive patch),⁷ a product containing 0.5% Glyceryl Polyacrylate (100 subjects; semi-occlusive patch),¹⁸ and Glyceryl Polyacrylate (1.9%; 51 subjects; patch type not specified)⁴ were not irritants or sensitizers in human repeated insult patch tests (HRIPT). Sensitization also was not observed in maximization assays with a product containing 0.586% Glyceryl Acrylate/Acrylic Acid Copolymer (25 subjects)¹⁹ and a product containing 7.7% Glyceryl Polymethacrylate (17 subjects).²⁰

OCULAR IRRITATION STUDIES

Animal

Glyceryl Acrylate/Acrylic Acid Copolymer

The ocular irritation potential of 1.3 – 2% Glyceryl Acrylate/Acrylic Acid Copolymer in a water and glycerin solution was evaluated following instillation of 0.1 ml of the test substance into the conjunctival sac of one eye of each of 6 albino rabbits; the eyes were not rinsed.⁷ The contralateral eye served as a control. Each eye was evaluated after 24, 48, and 72 h, and no signs of irritation were observed. Glyceryl Acrylate/Acrylic Acid Copolymer (1.3 – 2% in a water and glycerin solution) was not irritating to the eyes of rabbits.

MUCOUS MEMBRANE IRRITATION STUDIES

Animal

Glyceryl Acrylate/Acrylic Acid Copolymer

The vaginal mucosal irritation potential of 1.3 – 2% Glyceryl Acrylate/Acrylic Acid Copolymer in a water and glycerin solution was evaluated using groups of 6 albino rabbits.⁷ The test material (0.1 ml) was applied to the vaginal orifice of the animals, and the animals were observed 5x/d for 7 d for gross signs of edema, erythema, and excretion. For the negative controls, the tip of an empty 1.0 ml syringe was inserted. Glyceryl Acrylate/Acrylic Acid Copolymer (1.3 – 2% in a water and glycerin solution) was not irritating to the vaginal mucosa of rabbits; the mucosal irritation index was 0.

SUMMARY

The safety of 4 glyceryl acrylates as used in cosmetics is reviewed in this safety assessment. According to the *Dictionary*, Caprylyl Glycol/Glycerin/Polyacrylic Acid Copolymer and Glyceryl Acrylate/Acrylic Acid Copolymer are both reported to function in cosmetics as skin-conditioning agents, and Glyceryl Polyacrylate and Glyceryl Polymethacrylate as film formers.

The mixing of 4-aminocarbonylazo-2-pyrimidinone with mildly acidic solutions of 1-glyceryl methacrylate was reported to result in polymerization to Glyceryl Polymethacrylate. According to data submitted by industry, both Glyceryl Acrylate/Acrylic Acid Copolymer and Glyceryl Polyacrylate may contain < 5 ppm residual acrylic acid. Glyceryl Acrylate/Acrylic Acid Copolymer may also contain methyl vinyl ether (< 0.5 ppm) and maleic acid (< 5 ppm).

According to 2022 FDA VCRP data, Glyceryl Acrylate/Acrylic Acid Copolymer has the greatest frequency of use; it is reported to be used in 295 cosmetic products (288 leave-on products and 7 rinse-off products). The results of a concentration of use surveys provided by the Council in 2021 indicate Glyceryl Polymethacrylate has the highest concentration of use; it is used at maximum use concentrations up to 1.9% in leave-on products.

The acute oral toxicity of Glyceryl Acrylate/Acrylic Acid Copolymer was evaluated in rats; the test article was administered by gavage. The oral LD₅₀ was > 5 g/kg.

The mutagenic potential of Glyceryl Acrylate/Acrylic Acid Copolymer and 1.9% Glyceryl Polyacrylate were evaluated in the Ames test. Neither substance was mutagenic.

Eight domestic pigs were subjected to burn wounds in the paravertebral area. The wounds were exposed to an experimental cream that consisted of Glyceryl Polymethacrylate in an oil-in-water emulsion. Daily treatment with the cream (~ 0.2 g/wound site) was continued until wound healing was complete. Application of the cream resulted in a soft eschar, but erythema was not observed.

In rabbits, application of an occlusive patch of 1.3 – 2% Glyceryl Acrylate/Acrylic Acid Copolymer in a water and glycerin solution for 24 h was not irritating. In clinical SIOPTs, a product containing 0.586% Glyceryl Acrylate/Acrylic Acid Copolymer (23 subjects) and a product containing 7.7% Glyceryl Polymethacrylate (19 subjects) were non-irritating; the PII in each study was 0 and 0.05, respectively.

In an HRIPT, Glyceryl Acrylate/Acrylic Acid Copolymer (1.3 – 2% in a water and glycerin solution; 55 subjects; occlusive patch), a product containing 0.5% Glyceryl Polyacrylate (tested neat; 100 subjects; semi-occlusive patch), and Glyceryl Polyacrylate (1.9%; 51 subjects; patch type not specified) were not irritants or sensitizers. Sensitization also was not observed in maximization assays with a product containing 0.586% Glyceryl Acrylate/Acrylic Acid Copolymer (25 subjects) and a product containing 7.7% Glyceryl Polymethacrylate (17 subjects).

Glyceryl Acrylate/Acrylic Acid Copolymer (1.3 – 2% in a water and glycerin solution) was not irritating to rabbit eyes. It also was non-irritating when applied to the vaginal mucosa of rabbits.

DISCUSSION

This assessment reviews the safety of 4 glyceryl acrylates as used in cosmetic formulations. The Panel reviewed the available data and concluded that these ingredients are safe in cosmetics in the present practices of use and concentration described in the safety assessment.

The Panel determined that the available data were sufficient to support the safety of all 4 glyceryl acrylates. Representative data on method of manufacturing and impurities were adequate for evaluating the entire group of ingredients. Safety was further supported by the large molecular weights of these ingredients. Glyceryl Polyacrylate, for example, has a molecular weight greater than 500,000 Da. The other polymers are also very large, which precludes dermal absorption.

The Panel discussed the issue of incidental inhalation exposure resulting from these ingredients (Caprylyl Glycol/Glycerin/Polyacrylic Acid Copolymer is reported to be used at up to 0.2% in perfumes, and Glyceryl Polymethacrylate (concentrations unavailable) is reported to be used in face powders). Inhalation toxicity data were not available. However, the Panel noted that in aerosol products, the majority of droplets/particles would not be respirable to any appreciable amount. Furthermore, droplets/particles deposited in the nasopharyngeal or tracheobronchial regions of the respiratory tract present no toxicological concerns based on the chemical and biological properties of these ingredients. Coupled with the small actual exposure in the breathing zone and the low concentrations at which these ingredients are used (or expected to be used) in potentially inhaled products, the available information indicates that incidental inhalation would not be a significant route of exposure that might lead to local respiratory or systemic effects. As indicated in the respiratory exposure resource document and in the Cosmetic Use section of this report, airbrush application of cosmetic products is not assessed by the Panel. A detailed discussion and summary of the Panel's approach to evaluating incidental inhalation exposures to ingredients in cosmetic products is available at <https://www.cir-safety.org/cir-findings>.

The Panel acknowledged that some cosmetic ingredients are used in products marketed for airbrush application. However, the available data are insufficient to make a determination of safety for use of these ingredients in products that may be incidentally inhaled when applied using airbrush delivery systems. The Panel's respiratory exposure resource document (<https://www.cir-safety.org/cir-findings>) notes that airbrush technology presents a potential safety concern, and that no data are available for consumer habits and practices thereof. Thus, the data do not support the safety of the ingredients named in this report if applied via airbrush technology.

CONCLUSION

The Expert Panel for Cosmetic Ingredient Safety concluded that the following 4 glyceryl acrylates are safe in cosmetics in the present practices of use and concentration described in this safety assessment:

Caprylyl Glycol/Glycerin/Polyacrylic Acid Copolymer
Glyceryl Acrylate/Acrylic Acid Copolymer

Glyceryl Polyacrylate
Glyceryl Polymethacrylate

TABLES**Table 1.** Definitions, reported functions, and idealized structures of the ingredients in this safety assessment.^{1, CIR Staff}

Ingredient/CAS No.	Definition & Structures	Function(s)
Caprylyl Glycol/Glycerin/ Polyacrylic Acid Copolymer	Caprylyl Glycol/Glycerin/Polyacrylic Acid Copolymer is a copolymer of caprylyl glycol, glycerin, and polyacrylic acid monomers	humectant; skin-conditioning agent - emollient
<i>Drawn as a simple block-type copolymer for demonstration; other monomer connectivity patterns possible.</i>		
Glyceryl Acrylate/Acrylic Acid Copolymer	Glyceryl Acrylate/Acrylic Acid Copolymer is a copolymer of glyceryl acrylate and acrylic acid	skin-conditioning agent - humectant; viscosity increasing agent - aqueous
<i>Drawn as a simple block-type copolymer for demonstration; other monomer connectivity patterns possible.</i>		
Glyceryl Polyacrylate 104365-75-5	Glyceryl Polyacrylate is the ester of glycerin and polyacrylic acid	film former

Table 1. Definitions, reported functions, and idealized structures of the ingredients in this safety assessment.^{1, CIR Staff}

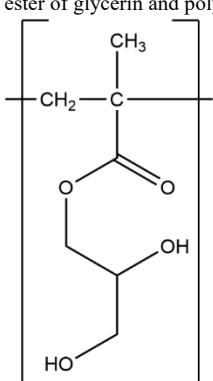
Ingredient/CAS No.	Definition & Structures	Function(s)
Glyceryl Polymethacrylate 146126-21-8 28474-30-8	Glyceryl Polymethacrylate is the ester of glycerin and polymethacrylic acid 	film former

Table 2. Chemical properties

Property	Value/Results	Reference
Glyceryl Acrylate/Acrylic Acid Copolymer trade name mixture (also containing glycerin, water, and propylene glycol)		
Form	Clear, colorless viscous gel	
Solubility	Water-soluble	
Relative density (g/ml)	1.15	
Viscosity (cps)	250,000 – 350,000	
Melting point (°C)	< 0	
Boiling point (°C)	> 100	

Table 3. Frequency (2022)⁸ and concentration (2020)^{9,10} of use according to duration and type of exposure.

	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)
	Caprylyl Glycol/Glycerin/ Polyacrylic Acid Copolymer		Glyceryl Acrylate/Acrylic Acid Copolymer		Glyceryl Polymethacrylate	
Totals*/Conc. Range	NR	0.2	295	0.00001-0.62	142	0.048 – 1.9
Duration of Use						
Leave-On	NR	0.2	288	0.00001-0.62	138	0.048 – 1.9
Rinse off	NR	NR	7	0.012-0.42	4	NR
Diluted for (bath) Use	NR	NR	NR	NR	NR	NR
Exposure Type						
Eye Area	NR	NR	24	0.035-0.62	9	NR
Incidental Ingestion	NR	NR	12	NR	NR	NR
Incidental Inhalation- Sprays	NR	0.2	88 ^a ;131 ^b	0.012-0.62 ^a	54 ^a ;49 ^b	NR
Incidental Inhalation- Powders	NR	NR	131 ^b ; 1 ^c	0.02-0.1 ^c	1;40 ^b	0.08-1.9 ^c
Dermal Contact	NR	0.2	278	0.00001-0.62	142	0.08-1.9
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	1	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	4	NR	NR	NR
Mucous Membrane	NR	NR	13	NR	1	NR
Baby Products	NR	NR	1	NR	NR	NR

NR = Not Reported

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

^a It is possible that these products may be sprays, but it is not specified whether the reported uses are sprays^b Not specified these products are sprays or powders, but it is possible the use can be as a spray or powder, therefore the information is captured in both categories^c It is possible that these products may be powders, but it is not specified whether the reported uses are powders

Table 4. Current and historical frequency and concentration of use of Glyceryl Polyacrylate

	# of Uses		Max Conc of Use (%)	
	2022 ⁸	1998 ²	2021 ¹⁰	1999 ²
Totals*/Conc. Range	119	1	0.008 – 0.99	0.2 – 2
Duration of Use				
<i>Leave-On</i>	110	1	0.0099 – 0.99	0.2 – 2
<i>Rinse-Off</i>	9	NR	0.008 – 0.4	0.4
<i>Diluted for (Bath) Use</i>	NR	NR	NR	NR
Exposure Type				
Eye Area	15	NR	0.25 – 0.5	NR
Incidental Ingestion	NR	NR	NR	NR
Incidental Inhalation-Spray	47 ^a ; 19 ^b	1 ^b	0.01 ^a	0.2 ^a ; 2 ^b
Incidental Inhalation-Powder	19 ^b	1 ^b	0.09 ^c	2 ^b
Dermal Contact	118	1	0.008 – 0.99	2
Deodorant (underarm)	NR	NR	NR	NR
Hair - Non-Coloring	1	NR	0.01	0.2 – 0.4
Hair-Coloring	NR	NR	NR	NR
Nail	NR	NR	NR	NR
Mucous Membrane	1	NR	NR	NR
Baby Products	NR	NR	0.0099 – 0.09	NR

NR = Not Reported

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

^a It is possible that these products may be sprays, but it is not specified whether the reported uses are sprays^b Not specified these products are sprays or powders, but it is possible the use can be as a spray or powder, therefore the information is captured in both categories^c It is possible that these products may be powders, but it is not specified whether the reported uses are powders

Table 5. Dermal irritation and sensitization studies

Test Article	Concentration/Dose	Test Population	Procedure	Results	Reference
ANIMAL					
Irritation					
Glyceryl Acrylate/Acrylic Acid Copolymer	1.3-2% in a water-glycerin solution 0.5 ml or 0.5 g	6 rabbits	Primary skin irritation testing conducted according to FHSLA, 16 CFR 1500.41. The trunk of each animal was clipped free of hair, and 2.5 cm ² patches were placed on intact and abraded skin. The trunk of each animal was wrapped with rubberized elastic cloth, and neck collars were placed on the animals. All test sites were evaluated 24 and 72 h after application.	PII = 0 not a primary irritant	7
HUMAN					
Irritation					
product containing 0.586% Glyceryl Acrylate/Acrylic Acid Copolymer	tested neat	23 subjects	SIOPT (24 h); a reference control was used (no additional details provided)	PII = 0 no irritation reported for any of the subjects	16
product containing 7.7% Glyceryl Polymethacrylate	tested neat	19 subjects	SIOPT (24 h); a reference control was used (no additional details provided)	PII = 0.05 no irritation in 18 subjects; score of 1 observed for 1 subject	17
Sensitization					
product containing 0.586% Glyceryl Acrylate/Acrylic Acid Copolymer	0.05 ml; tested neat	25 subjects	maximization assay. During induction, an occlusive patch with 0.25% aq. SLS was applied for 24 h; upon removal, an occlusive patch with test article was applied to the same site for 48 h (72 h on weekends). This sequence was repeated for a total of 5 induction exposures. After a 10-d non-treatment period, a previously-untreated site was pretreated with 1% SLS for 1 h under an occlusive patch; upon removal, a challenge patch containing the test material was applied to the site for 48 h. The challenge site was scored upon patch removal, and 24 h after removal. Protocol deviations included no SLS pretreatment prior to the last induction patch, due to a scheduling issue.	not a sensitizer; no adverse reactions were observed during the study	19
Glyceryl Acrylate/Acrylic Acid Copolymer	1.3-2% concentration in a water-glycerin solution 0.2 g	55 subjects	HRIPT. During induction, nine 24-h occlusive patches were applied (3x/wk for 3 wk). After a 2-wk non-treatment period, challenge patches were applied for 24 h to a previously untreated site on the back of each subject, and the challenge sites were evaluated 24 and 72 h after patching.	not an irritant or a sensitizer, no significant dermal reactions were observed.	7
product containing 0.5% Glyceryl Polyacrylate	0.2 ml; tested neat	100 subjects	HRIPT. Same HRIPT protocol as described above, with the exception that the patches (2 cm ²) were semi-occlusive, and challenge sites were evaluated 48 and 72h after patching	not a sensitizer During induction: 1 subject discontinued due to experiencing definite erythema and edema after the 5 th induction patch; definite erythema, no edema was reported for .9% of the subjects; minimal or doubtful response was recorded for 9.6% of the subjects	18
Glyceryl Polyacrylate	1.9%; tested undiluted	51 subjects	HRIPT (details were not provided)		4
product containing 7.7% Glyceryl Polymethacrylate	0.05 ml; tested neat	27 subjects	maximization assay. Same maximization assay protocol as described above, with the exception that 5% SLS was used for pre-treatment at challenge, and no protocol deviations occurred	not a sensitizer; no adverse reactions were observed during induction	20

Abbreviations: aq. – aqueous; CFR – Code of Federal Regulations; FHSLA - Federation of Health Science Library Associations; HRIPT – human repeated insult patch test; PII – primary irritation index; SIOPT – single-insult occlusive patch test; SLS – sodium lauryl sulfate.

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2022 VCRP data - Glyceryl Acrylates

Caprylyl Glycol/Glycerin/Polyacrylic Acid Copolymer – 0 uses

Glyceryl Acrylate/Acrylic Acid Copolymer	01B	Baby Lotions, Oils, Powders, and Creams	1	295
Glyceryl Acrylate/Acrylic Acid Copolymer	03A	Eyebrow Pencil	1	
Glyceryl Acrylate/Acrylic Acid Copolymer	03D	Eye Lotion	16	
Glyceryl Acrylate/Acrylic Acid Copolymer	03G	Other Eye Makeup Preparations	7	
Glyceryl Acrylate/Acrylic Acid Copolymer	05G	Tonics, Dressings, and Other Hair Grooming Aids	1	
Glyceryl Acrylate/Acrylic Acid Copolymer	07C	Foundations	1	
Glyceryl Acrylate/Acrylic Acid Copolymer	07E	Lipstick	12	
Glyceryl Acrylate/Acrylic Acid Copolymer	07F	Makeup Bases	2	
Glyceryl Acrylate/Acrylic Acid Copolymer	07I	Other Makeup Preparations	3	
Glyceryl Acrylate/Acrylic Acid Copolymer	08E	Nail Polish and Enamel	1	
Glyceryl Acrylate/Acrylic Acid Copolymer	08G	Other Manicuring Preparations	3	
Glyceryl Acrylate/Acrylic Acid Copolymer	10E	Other Personal Cleanliness Products	1	
Glyceryl Acrylate/Acrylic Acid Copolymer	11A	Aftershave Lotion	4	
Glyceryl Acrylate/Acrylic Acid Copolymer	11E	Shaving Cream	1	
Glyceryl Acrylate/Acrylic Acid Copolymer	11G	Other Shaving Preparation Products	2	
Glyceryl Acrylate/Acrylic Acid Copolymer	12A	Cleansing	2	
Glyceryl Acrylate/Acrylic Acid Copolymer	12C	Face and Neck (exc shave)	117	
Glyceryl Acrylate/Acrylic Acid Copolymer	12C	Face and Neck (exc shave)	1	
Glyceryl Acrylate/Acrylic Acid Copolymer	12D	Body and Hand (exc shave)	13	
Glyceryl Acrylate/Acrylic Acid Copolymer	12F	Moisturizing	81	
Glyceryl Acrylate/Acrylic Acid Copolymer	12G	Night	4	
Glyceryl Acrylate/Acrylic Acid Copolymer	12H	Paste Masks (mud packs)	1	
Glyceryl Acrylate/Acrylic Acid Copolymer	12I	Skin Fresheners	1	
Glyceryl Acrylate/Acrylic Acid Copolymer	12J	Other Skin Care Preps	18	
Glyceryl Acrylate/Acrylic Acid Copolymer	13A	Suntan Gels, Creams, and Liquids	1	
Glyceryl Polyacrylate	03D	Eye Lotion	9	119
Glyceryl Polyacrylate	03G	Other Eye Makeup Preparations	6	
Glyceryl Polyacrylate	05I	Other Hair Preparations	1	
Glyceryl Polyacrylate	10E	Other Personal Cleanliness Products	1	
Glyceryl Polyacrylate	11A	Aftershave Lotion	1	
Glyceryl Polyacrylate	11G	Other Shaving Preparation Products	5	
Glyceryl Polyacrylate	12A	Cleansing	2	
Glyceryl Polyacrylate	12C	Face and Neck (exc shave)	17	
Glyceryl Polyacrylate	12D	Body and Hand (exc shave)	2	
Glyceryl Polyacrylate	12F	Moisturizing	43	
Glyceryl Polyacrylate	12G	Night	2	
Glyceryl Polyacrylate	12H	Paste Masks (mud packs)	1	
Glyceryl Polyacrylate	12J	Other Skin Care Preps	27	
Glyceryl Polyacrylate	13A	Suntan Gels, Creams, and Liquids	2	

Glyceryl Polymethacrylate	03D	Eye Lotion	5	142
Glyceryl Polymethacrylate	03G	Other Eye Makeup Preparations	4	
Glyceryl Polymethacrylate	07A	Blushers (all types)	1	
Glyceryl Polymethacrylate	07B	Face Powders	1	
Glyceryl Polymethacrylate	07C	Foundations	2	
Glyceryl Polymethacrylate	07F	Makeup Bases	1	
Glyceryl Polymethacrylate	07I	Other Makeup Preparations	6	
Glyceryl Polymethacrylate	10E	Other Personal Cleanliness Products	1	
Glyceryl Polymethacrylate	12A	Cleansing	3	
Glyceryl Polymethacrylate	12C	Face and Neck (exc shave)	42	
Glyceryl Polymethacrylate	12D	Body and Hand (exc shave)	7	
Glyceryl Polymethacrylate	12F	Moisturizing	44	
Glyceryl Polymethacrylate	12G	Night	6	
Glyceryl Polymethacrylate	12I	Skin Fresheners	3	
Glyceryl Polymethacrylate	12J	Other Skin Care Preps	15	
Glyceryl Polymethacrylate	13C	Other Suntan Preparations	1	