Safety Assessment of Glycerin Ethoxylates as Used in Cosmetics

Status:	Draft Final Report for Panel Review
Release Date:	November 13, 2020
Panel Meeting Date:	December 7-8, 2020

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.; Lisa A. Peterson, Ph.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. Previous Panel member involved in this assessment: James G. Marks, Jr., M.D. The Cosmetic Ingredient Review (CIR) Executive Director is Bart Heldreth, Ph.D. This safety assessment was prepared by Alice Akinsulie, former Scientific Analyst/Writer, and Preethi Raj, Senior Scientific Analyst/Writer, CIR.

1620 L Street, NW, Suite 1200 ◇ Washington, DC 20036-4702 ◇ ph 202.331.0651 ◇ fax 202.331.0088 ◇
cirinfo@cir-safety.org

Cosmetic Ingredient Review

Commitment & Credibility since 1976

Memorandum

To: Expert Panel for Cosmetic Safety Members and Liaisons
From: Preethi S. Raj, Senior Scientific Analyst/Writer, CIR
Date: November 13, 2020
Subject: Safety Assessment of Glycerin Ethoxylates as Used in Cosmetics

Enclosed is the Draft Final Report on the Safety Assessment of Glycerin Ethoxylates as Used in Cosmetics (identified as *glyeth122020rep* in the report package). This is the fourth time the Panel is reviewing the report on these 8 ingredients. At the June 2020 meeting, the Panel expressed concerns about low level reactions occurring in HRIPT studies in the absence of fully disclosed experimental details. Thus, the Panel issued a Tentative Report with an insufficient conclusion, requesting full experimental details for previously received summaries, or, newly completed HRIPT experimental data, at or above maximum concentrations of use, with n ≥ 100 participants.

In response to the stated data needs, the following were submitted and have been incorporated (highlighted in yellow in the report):

1. Two new Glycereth -26 HRIPTS, with full experimental details:
    a. KGL, Inc. 2007. Individual results for an HRIPT on a product containing 3% Glycereth-26 (*glyeth122020data1*)
    b. Anonymous. 2005. Individual results for an HRIPT on a product containing 8.75% Glycereth-26 (*glyeth122020data2*)
2. Experimental details and clarification for previously submitted data
    a. Personal Care Products Council. 2020. Glycerin Ethoxylates: Clarification and Individual Data for HRIPT Study Summaries with PCPC Memos 7 and 8 (*glyeth062020data3)*

Comments on the Tentative Report, received from Council after the June 2020 meeting, have been addressed (*glyeth122020pcpc*).

Also included in this package for your review:

- *glyeth122020flow*: flow chart
- *glyeth122020hist*: history
- *glyeth122020min:* meeting minutes
- *glyeth122020prof*: data profile
- *glyeth122020FDA*: 2020 FDA VCRP frequency of use data
- *glyeth122020strat*: search strategy

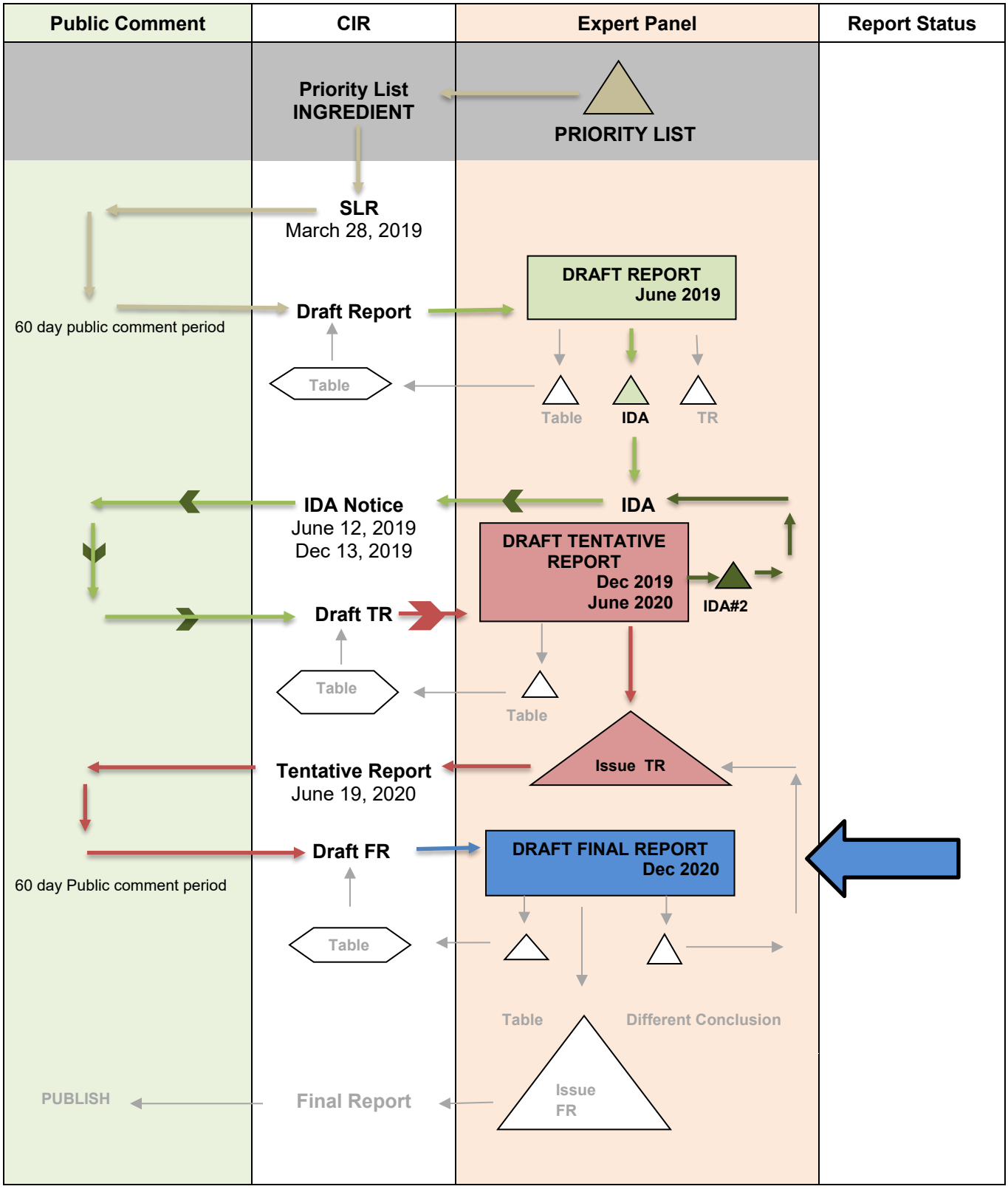
After reviewing these documents, if the available data are deemed sufficient to make a determination of safety, the Panel should identify any additional matters to be addressed in the Discussion and then issue a Final Report with a safe as used, safe with qualifications, or unsafe conclusion. If, however, the available data remain insufficient, the Panel should issue a Final Report with a conclusion of insufficient data, discussing the rationale therein.

1620 L Street, NW Suite 1200, Washington, DC 20036
(Main) 202-331-0651 (Fax) 202-331-0088
(email) cirinfo@cir-safety.org (website) www.cir-safety.org

SAFETY ASSESSMENT FLOW CHART

INGREDIENT/FAMILY Glycerin Ethoxylates

MEETING December 2020



CIR History of:

Glycerin Ethoxylates

Scientific Literature Review (SLR) was issued: March 28, 2019

The CIR sought the following during the 60-day public comment period:

- Method of manufacture
- Impurities
- Dermal absorption
    - If absorbed, also requested systemic toxicity data

Data for two HRIPT studies and an in vitro ocular irritation assay were received from the Council and incorporated into the report.

Draft Report was presented at the 151st Expert Panel Meeting: June 6-7, 2019

Upon initial review of this ingredient, the Panel found the data insufficient to determine safety. The results of a concentration of use survey conducted by the Council in 2018 indicated that Glycereth-26 is used at up to 1% in body and hand spray formulations, which may result in incidental inhalation exposure. The Panel discussed the issue of incidental inhalation exposure from aerosol spray moisturizers, and body and hand products. The Panel also asked to see data from similar alkoxylated ingredients for potential inference.

These observations resulted in the Panel issuing an Insufficient Data Announcement for the following:

- Method of manufacture
- Impurities
- Inhalation toxicity

The Panel noted that if sufficient manufacturing and impurities data are found, they may able to make a safety evaluation in the absence of inhalation data.

After the mail date for the 151st Expert Panel Meeting, CIR received Council comments, new concentration of use, and the following industry data to be incorporated in the upcoming report:

- Glycereth-26
    - 2019 HRIPT on product containing 3% Glycereth-26
    - 2019 Certificate of Analysis
    - 2017 Safety testing summary, including studies on the following:
        - Acute oral toxicity
        - Ocular irritation
        - Dermal irritation
    - 2007 ocular irritation assay summary
- Glycereth-7
    - 2019 HRIPT on product containing 0.68% Glycereth-7

Draft Tentative Report was presented at the 153rd Expert Panel meeting: December 9-10, 2019

The Panel deemed that their previous data insufficiency requests were satisfied because:

- the described method of manufacture addressed the family of ingredients,
- the Glycereth-26 certificate of analysis confirmed minimal impurity levels,
- and the revised Glycereth-3 inhalation toxicity study reassured respiratory safety.

However, the Panel found the available HRIPT summaries to provide insufficient information. Thus, the Panel requested full experimental details (issued a second insufficient data announcement) for each of these summaries, or, newly completed HRIPT experimental data, at or above maximum concentrations of use, with $n \geq 100$ participants.

The Panel was especially interested in receiving complete experimental data for an HRIPT done with the maximum reported concentration of use for the ingredient with the highest reported use, namely, 6% Glycereth-26.

After the mail date, for the 153rd Expert Panel Meeting, CIR received Council comments, new 2020 FDA frequency of use data, and the following industry data to be incorporated into the upcoming report:

- Wave 2, Glycereth-7 and Glycereth-26
    - 2019: 2 HRIPT summaries on products containing 1% and 2% Glycereth-7
    - 2019: 2 HRIPT summaries on products containing 3% Glycereth-26
- Individual-level data for 2 existing HRIPTs for Glycereth-12 and -26
    - 2014: HRIPT on product containing 0.35% Glycereth-12
    - 2016: HRIPT on product containing 5% Glycereth-26
- 1973 HRIPT summary on product containing 10% Glycereth-26, in 200 subjects

A (2nd) Draft Tentative Report was presented at the 154th Expert Panel Meeting: June 8-9, 2020

Besides discussing the incidental inhalation exposure from glycereth ingredients of smaller sizes, the Panel was wary of HRIPT summaries in which low-level reactions were reported during the induction, and sometimes challenge phase, in the absence of subject-level details. Since the Panel could not evaluate the reason for these reactions, the available data was deemed insufficient to make a determination of safety for the glycerin ethoxylates. A Tentative Report was issued with the remaining data requests:

- Full experimental details for the previously submitted sensitization summaries/studies; or
- A newly completed HRIPT, with fully-disclosed experimental data, at or above maximum concentrations of use for Glycereth-26, with $n \geq 100$ participants

After the June 2020 meeting, the following data were received:

- New irritation/sensitization data
    - July 13, 2020: HRIPT of 3% Glycereth-26, with subject-level data
    - July 21, 2020: HRIPT of 8.75% Glycereth-26, with subject-level data
- Clarification for previously submitted studies (mostly, studies with low-level reactions)
    - July 30, 2020: Packet from Council containing subject-level data for previous submissions, and accompanying clarifications

A Draft Final Report is being presented for review at the 156th Expert Panel Meeting: December 8-9, 2020

Glycerin Ethoxylates Data Profile* – December 8-9, 2020 – Preethi Raj																																
				Toxicokinetics			Acute Tox			Repeated Dose Tox			DART		Genotox		Carci		Dermal Irritation			Dermal Sensitization				Ocular Irritation		Clinical Studies	
	Reported Use	Method of Mfg	Impurities	log P	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	Phototoxicity	In Vitro	Animal	Retrospective/ Multicenter	Case Reports
Glycereth-3																													
Glycereth-7	X			X																				X					
Glycereth-8				X																									
Glycereth-12	X			X																				X		X			
Glycereth-18	X			X																									
Glycereth-20	X			X																									
Glycereth-26	X		X	X				X												X	X			X		X	X		
Glycereth-31				X																									
Read across ingredients																													
"Ethoxylated glycerols"		X	X	X			X	X	X						X				X	X						X	X		
Propoxylated nitrilotriethanol											X			X	X														
Propoxylated glycerol															X								X						

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

[Glycerin Ethoxylates]

Ingredient	CAS #(generic)	InfoB	SciFin	PubMed	TOXNET	FDA	EU	ECHA	IUCLID	SIDS	ECETOC	HPVIS	NICNAS	NTIS	NTP	WHO	FAO	NIOSH	FEMA	Web
Glycereth-3	31694-55-0	✓	0/9	0/674	✓	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	✓
Glycereth-7	31694-55-0	✓	0/7	0/205	NR	NR	✓	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	✓
Gycereth-8	31694-55-0	✓	0/1	0/173	NR	NR	✓	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	✓
Glycereth-12	31694-55-0	✓	NR	0/79	NR	NR	✓	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	✓
Glycereth-18	31694-55-0	✓	0/1	0/41	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	✓
Glycereth-20	31694-55-0	✓	1/3	0/93	NR	NR	✓	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	✓
Glycereth-26	31694-55-0	✓	1/129	0/18	✓	NR	✓	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	✓
Glycereth-31	31694-55-0	✓	NR	0/26	NR	NR	✓	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	✓
Glycerin Ethoxylate	31694-55-0	NR	1/225	0/7	NR	NR	NR	✓	NR	NR	NR	✓	NR	NR	NR	NR	NR	NR	NR	✓

***NR – No results were found; Check mark - Data available; 0/0 – relevant/hits**

Web Search

1,2,3-Propanetriol, ethoxylated
Ethoxylated glycerine
Ethoxylated glycerol
Glycereth-3; Glycereth-7; Glycereth-8; Glycereth-12; Glycereth-18; Glycereth-20; Glycereth-26; Glycereth-31
Glycerol poly(oxyethylene) ether
Glycerol polyoxyethylene ether
Glycerol, ethoxylated
Lupranol VP 9209
Alkoxylated alcohols
Acute inhalation toxicity → Glycereth-26
Propoxylated nitrilotriethanol toxicity
Impurities of ethoxylated compounds
Ethoxylated compounds and lung toxicity
Case reports
Composition of alkoxylated alcohols
PEG ethers of glycerin
Acute toxicity; Repeated dose toxicity; Subacute toxicity; Short-term toxicity; Subchronic toxicity; Chronic toxicity; Adverse health effects; Hypersensitivity; Sensitization; Carcinogenicity; Genotoxicity; Mutagenicity; Dermal absorption; Dermal penetration; Dermal irritation; Developmental toxicity; Reproductive toxicity; In vitro toxicity; Ocular effects; Oral exposure; Phototoxicity; Photosensitivity

Typical Search Terms

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

LINKS

Search Engines

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

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

Pertinent Websites

- wINCI - http://webdictionary.personalcarecouncil.org

- FDA databases http://www.ecfr.gov/cgi-bin/ECFR?page=browse
- FDA search databases: http://www.fda.gov/ForIndustry/FDABasicsforIndustry/ucm234631.htm;,
- EAFUS: http://www.accessdata.fda.gov/scripts/fcn/fcnnavigation.cfm?rpt=eafuslisting&displayall=true
- GRAS listing: http://www.fda.gov/food/ingredientspackaginglabeling/gras/default.htm
- SCOGS database: http://www.fda.gov/food/ingredientspackaginglabeling/gras/scogs/ucm2006852.htm
- Indirect Food Additives: http://www.accessdata.fda.gov/scripts/fdcc/?set=IndirectAdditives
- Drug Approvals and Database: http://www.fda.gov/Drugs/InformationOnDrugs/default.htm
- http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/UCM135688.pdf
- FDA Orange Book: https://www.fda.gov/Drugs/InformationOnDrugs/ucm129662.htm
- OTC ingredient list: https://www.fda.gov/downloads/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cder/ucm135688.pdf
- (inactive ingredients approved for drugs: http://www.accessdata.fda.gov/scripts/cder/iig/

- HPVIS (EPA High-Production Volume Info Systems) - https://ofmext.epa.gov/hpvis/HPVISlogon
- NIOSH (National Institute for Occupational Safety and Health) - http://www.cdc.gov/niosh/
- NTIS (National Technical Information Service) - http://www.ntis.gov/
- NTP (National Toxicology Program) - http://ntp.niehs.nih.gov/
- Office of Dietary Supplements https://ods.od.nih.gov/
- FEMA (Flavor & Extract Manufacturers Association) - http://www.femaflavor.org/search/apachesolr_search/

- EU CosIng database: http://ec.europa.eu/growth/tools-databases/cosing/
- ECHA (European Chemicals Agency – REACH dossiers) – http://echa.europa.eu/information-on-chemicals;jsessionid=A978100B4E4CC39C78C93A851EB3E3C7.live1
- ECETOC (European Centre for Ecotoxicology and Toxicology of Chemicals) - http://www.ecetoc.org
- European Medicines Agency (EMA) - http://www.ema.europa.eu/ema/
- IUCLID (International Uniform Chemical Information Database) - https://iuclid6.echa.europa.eu/search
- OECD SIDS (Organisation for Economic Co-operation and Development Screening Info Data Sets)- http://webnet.oecd.org/hpv/ui/Search.aspx
- SCCS (Scientific Committee for Consumer Safety) opinions: http://ec.europa.eu/health/scientific_committees/consumer_safety/opinions/index_en.htm
- NICNAS (Australian National Industrial Chemical Notification and Assessment Scheme)- https://www.nicnas.gov.au/

- International Programme on Chemical Safety http://www.inchem.org/
- FAO (Food and Agriculture Organization of the United Nations) - http://www.fao.org/food/food-safety-quality/scientific-advice/jecfa/jecfa-additives/en/
- WHO (World Health Organization) technical reports - http://www.who.int/biologicals/technical_report_series/en/

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

JUNE 2019 PANEL MEETING – INITIAL REVIEW/DRAFT REPORT

Belsito Team – June 6, 2019

DR. BELSITO: Okay. And then Glycerin Ethoxylates. So we need manufacture and impurities, right?

DR. SNYDER: Yes.

DR. LIEBLER: Yep.

DR. BELSITO: We need absorption, distribution, metabolism?

DR. LIEBLER: Yes.

DR. BELSITO: Regarding the DART study, it says that concentration of test article -- this is page 11 in the PDF. "Concentration of test article and days of dosing were not specified." But it was performed according to the OECD guidelines, so the days of dosing would be specified by those guidelines. Right?

And then it says the doses of 0, 100, 300, and 1000 milligrams per kilogram bodyweight. We have the doses and we would know the days of application, of gavage, based on OECD. So, I think that sentence needs to go out.

Dan, we're using read across for ethoxylated glycerol?

DR. LIEBLER: Yeah. I thought that was fine.

DR. BELSITO: Okay.

DR. LIEBLER: It's fine. It kind of covers the lower mass range of these ingredients. But those are the ones, I think, where one might have more concern about possible toxicity because those could be absorbed to some extent dermally. They'd have more extensive absorption in the gut. So, safety with those on both dermal and oral endpoints, I think, is likely to be quite predictive for the whole group.

DR. BELSITO: What about sensitization?

DR. LIEBLER: I think it's appropriate for sensitization because the fundamental chemical feature of this is a polyethoxylated core piece.

None of the parts of this family of molecules has any real propensity for reaction with proteins, nor could any reasonable metabolites -- I mean, I suppose aldehydes produced from any of these alcohols could be protein reactive. But certainly, the parents aren't. Not all aldehydes are really good protein modifiers. Most of the aldehydes we look at, or RIFM for example, aren't sensitizers.

DR. BELSITO: Right. Okay.

DR. LIEBLER: So, I was very comfortable with it. In fact, I'd go further to say that the eco read across material, the propoxylated nitrilotriethanol, I think that was also reasonable as read across materials. It's a nitrogen-containing compound in the core, but the overall structure is very similar. It's a polyethoxylated molecule that presents a very similar overall structure, and it presents the polyethoxylated part of the molecule well.

In fact, while we're on the topic of read across and analogs, this is something I think I'd like to see us do more. But we've reviewed a lot of polyethoxylated ingredients with different core molecules that are polyethoxylated. And I think it would be helpful to cite the safety conclusions from some of those reports. Because, in general, these have been very safe. Even if the core part of the molecule isn't the same structure, essentially we're talking about very similar overall chemical presentations.

We could use them -- I think read-across isn't quite the word, but weight-of-evidence that we could cite somewhere in the report; a paragraph on -- maybe in the introduction -- that we've reviewed the following related families of chemicals. And then, in the discussion, the Panel noted that previous safety assessments containing structurally related polyethoxy, you know, materials have -- provide further weight-of-evidence support for the safety of these. I mean, these are low toxicity.

DR. BELSITO: Okay. So, then, that brings me back. Since the DART and genotox are okay, do we need absorption, distribution, and metabolism?

DR. SNYDER: No.

DR. LIEBLER: No.

DR. BELSITO: Okay. But we still need method of manufacturing and impurities?

DR. SNYDER: Yes. We got nothing there.

DR. BELSITO: So, that's the only insufficiency?

DR. SNYDER: Yep.

DR. BELSITO: We're going to add a paragraph in the introduction of the discussion about other polyethoxylated ingredients that we found safe.

DR. SNYDER: Right.

DR. BELSITO: And we're going to discuss that we don't need the ADME data because the DART and genotoxicities are fine.

DR. LIEBLER: We already have good --

DR. BELSITO: However, we need to know the manufacturing and impurities, and we're going insufficient just for that.

DR. LIEBLER: I do think the low molecular weight members of this family will be absorbed a little bit. Under 500 molecular weight, there will be a little dermal absorption. But we know, from the oral endpoints, that these have a very favorable safety profile. So, I'm not concerned about dermal absorption, systemic tox. And I don't think there's any mechanistic reason to be concerned about sensitization with these.

DR. BELSITO: Well, I mean, we have sensitization studies that are above -- I think at 0.35. And the max leave-on is 0.25.

DR. SNYDER: We actually have 0.5.

DR. LIEBLER: Yeah. So, I think once we have method of manufacture and impurities, we're on the way to the finish line with these. I think that'd be fine.

DR. BELSITO: Okay. Anything else on these?

Marks Team – June 6, 2019

DR. MARKS: Next is glycerin ethoxylates. Let's see here. So this is a draft report on these eight glycerin ethoxylate ingredients. So this is the first review. They are a combination of polyethylene glycose PEGs -- PEG 4, et cetera -- plus glycerin, which has been reviewed previously and found to be safe.
Tom and Ron, and Ron the surrogate, are these eight ingredients okay, or is there any one that you feel shouldn't be included in this?

DR. SLAGA: I thought they all could be included.

DR. SHANK: I don't know why nitrilotriethanol is included in use for read across. I'm looking to see if Dr. Hill addresses that, and I don't see it. So I guess the chemists think that's okay.

DR. MARKS: So in the report, they use the safety of that as a read across. Is that what you're saying?

DR. SHANK: Yes.

DR. MARKS: And we don't have Bart here to say.

DR. SHANK: No.

DR. MARKS: What was your sense, Alice, why that was included?

MS. AKINSULIE: The ECHA dossier was prepared for ingredients on ethoxylated glycerol, but the test materials specifically were read across constituents.

DR. MARKS: So you're questioning whether it should even be in the report?

DR. SHANK: Right.

MS. FIUME: We also found it interesting when it was included. But it's in here because if ECHA gives it to us, we present it to you to weigh in on.

DR. SHANK: If the chemists can say it makes no difference, then I guess it didn't seem to fit for me. But we can discuss that tomorrow.

DR. MARKS: So do you want me to mention it, Ron? When Wilma asks for comments after, you'll just bring that up?

DR. SHANK: I'll be happy to, yes.

DR. MARKS: Great. I had the sensitization data were okay for these ingredients.
Tom, Ron, any needs?

DR. SLAGA: I didn't have any needs. Irritation is not a problem and genotoxicity not a problem.

DR. SHANK: Okay. I didn't think there was very much tox data here, so I have a 28-day dermal tox on glycereth-26 because that one has the greatest number of uses and the highest concentrations. Skin penetration -- and if it's absorbed, then we need genotox in DART. These are used in inhalable products, so we need inhalation tox data.

MS. FIUME: Any specific study time length on inhalation tox?

DR. SHANK: I'd have to look at the table --frequency of use table. Okay. So it's used in powders and sprays at 2 to 4 percent. That's glycereth-26. That's the only one.

MS. FIUME: So just a generic request for inhalation tox without any specific timeframe included?

DR. SHANK: I would do just an acute toxicity, because this would be an incidental spray with exposure a few seconds at a time.

MS. FIUME: Thank you.

DR. SHANK: So I don't see any long term tox needs.

DR. MARKS: And Ron, just to be clear, the previous reviews of the PEGs and glycerin you don't think could be used as a substitute for needing these -- the 28-day? Since they were safe, you don't think that could be used as a proxy for the safety of, if I heard you correctly, the glycereth-26 is the prototype. We want the 28-day dermal tox, the inhalation tox, and the skin penetration data and, if absorbed, genotox and DART.

DR. SHANK: Possibly DART, yes.

DR. MARKS: So I just want to be clear that you couldn't use those previous safety of the -- since this is a combination of PEGs and glycerin, that wouldn't substitute for the combined? I'm asking that from a point of –

DR. SHANK: I don't think so. Perhaps the chemists can convince me.

DR. MARKS: No, that's fine. I just want to clarify.

DR. SLAGA: I assumed that we could use it, but that's just me.

DR. SHANK: PEGs by themselves or glycerin by themselves, okay. But now, this is a much bigger molecule.

DR. MARKS: Okay. I'll put in there -- if that comes up tomorrow, I'll mention those. Do I have that correct, Ron? Needs

are glycereth-26. That's the prototype -- 28-day dermal tox, the inhalation tox, and a skin penetration; if absorbed, then genotox and DART. And then we'll see where it goes from there.

DR. SHANK: Okay.

DR. SLAGA: The 26 Ron picked because of concentration of use?

DR. SHANK: Right.

DR. MARKS: It's the highest concentration, highest use. 379 uses and the highest leave-on is 6 percent.

DR. SLAGA: A lot of times we usually ask for the one that's lower, smaller.

DR. MARKS: Yes. I thought of that, too, Tom. I agree.

DR. SHANK: Do you want both?

DR. SLAGA: There's a 3, 12, 24, and 26.

DR. MARKS: Yeah. The 3 there are no uses. The 7 is 80 uses at 1 percent. But I like your approach to ask for 26. And we'll see. We'll see what the -- I like how you, Ron, defer to the chemists. If Dan feels we can use the PEGs and the glycerin individually as a read across, so to speak, for the combination, then maybe we'll go from there. But I'll bring this up so that it's a discussant point tomorrow, Ron, and let you weigh in.

DR. SLAGA: Okay.

DR. BERGFELD: Can you just clarify the situation here? This is reopened, is it not?

DR. MARKS: No, this is the first review.

DR. BERGFELD: The first -- but we looked at the components. Those are the propylene ethyl glycol PEGs in 2010. I see. So this is just another ingredient using some of the stem ingredients.

DR. MARKS: Exactly. Yeah. This is glycerin plus PEGs. And did I say that right? Ethoxylates?

DR. SHANK: Ethoxylates.

DR. MARKS: I guess it depends on whether you're from Boston or Philly. Okay. So I'm going to put second insufficient data announcement, and we'll see what the other team -- if they come to a different conclusion, we'll have a discussion and then resolve that. But for now, an ISA.
Does that sound good, Tom?

DR. SLAGA: Yeah.

DR. MARKS: It's fine with me. Okay. And we took into consideration Ron Hill's comments. Okay. So I will presumably second tomorrow an insufficient data announcement. And I mentioned the needs previously.

Full Panel – June 7, 2019

DR. BELSITO: Okay, so this is the first time we're looking at these glycerin ethoxylates. There was a good amount of data. It would appear that the low molecular weight members could be absorbed a bit. But there was good oral data, and the DART and genotoxicity data were good.

Dan felt that we should add in a paragraph in the introduction and discussion indicating that we've reviewed other polyethoxylated ingredients and found them safe as used. And, I suspect Ron Shank may object, we just thought we needed method of manufacture and impurities. But given the DART and genotox data, do we want to just say safe as used instead?

DR. BERGFELD: Dan, you want to respond?

DR. LIEBLER: Method of manufacture and impurities are insufficient. And I'm sure we can come up with something.

DR. BERGFELD: Ron Shank?

DR. MARKS: I'd like to hear, is this a motion for an insufficient data announcement?

DR. BELSITO: We said insufficient for method of manufacture and impurities.

DR. MARKS: Right. So, we second that insufficient data announcement. We have some other insufficiencies. But, Dan, go ahead. I wanted to be clear what the motion was.

DR. LIEBLER: Yeah. That was it.

DR. MARKS: Okay.

DR. BERGFELD: Ron Shank?

DR. SHANK: I'd like to ask Dr. Liebler, is propoxylated nitrilotriethanol a good proxy for these?

DR. LIEBLER: It is to the extent that it's essentially a relatively unreactive internal core that serves as a scaffold for these polyethoxylated chains. So, I would use it with some explanation in the discussion, why we were able to rely on it. There's also, although you didn't ask, the other read-across proposed in the report was the mixture of ethoxylated glycerols. And I thought that that was an appropriate read-across as well.

DR. SHANK: Okay. Thank you.

DR. LIEBLER: Just to the extent that these molecules are essentially a little core, in this case glycerol with these polyethoxylated antennas hanging off them. So, the other molecules that present that structure, I think, are an appropriate read-across in the right context.

DR. SHANK: Do you feel these will not be absorbed -- penetrate?

DR. LIEBLER: Oh, I think the lower molecular ones will be absorbed to some extent. The lower molecular ones are under 500 molecular weight, so that we'd probably have some modest absorption.

DR. SHANK: Okay, so, I thought we needed some toxicology data. Choosing glycereth-26 for the tox studies 28-day dermal, skin penetration if it's absorbed, and then if it is absorbed genotox and possibly DART. These compounds can be inhaled, so we'd need inhalation toxicology data.

DR. BELSITO: So, you're not buying the read-across?

DR. SHANK: I didn't, but I really have to defer to our chemist, so if he's happy that we can read across the tox data, then I will accept that. But I didn't accept it on my own.

DR. LIEBLER: Here's my thinking. For dermal application, so we'll set aside the respiratory for the moment, for the dermal application the low molecular weight compounds are more likely to be absorbed. We have tox data for glycereth-3, and then that ethoxylated glycerol. There were the acute tox studies, and these were very low toxicity. And then for the short-term we had the propoxylated nitrilotriethanol, that read across from the ECHA dossier that you just asked about. And my feeling is that this is essentially a surrogate for a polyethoxylated molecule. And those molecules were fine in both the DART and the short-term oral.

And then we've got a very much bigger body of data for other polyethoxylated molecules that we've absorbed, where we've got some pretty innocuous core decorated with these polyethoxy chains. And, I thought that those data could be brought into the report to provide weight of evidence to support the safety profile of these overall because they really look pretty non-toxic.

Now the respiratory, I haven't been thinking about that too much, if you wanted to elaborate on your concerns about that. I don't think we have too much to go on.

DR. SHANK: Just that they are used in products that could be inhaled, and they don't have inhalation toxicology data.

DR. LIEBLER: So we can leave that on the list of insufficiencies, see what we get, and then deal with that next time.

DR. SHANK: Okay. I would put it on the insufficient list, inhalation data.

DR. BERGFELD: Okay, are we going to do that? Paul, did you have something to say?

DR. SNYDER: No, I was just going to second Ron's concern. I had the same concern until our team meeting when Dan assured me that it was a good read-across. And it also gave me some comfort that both the DART study and the short-term study, there was no observed adverse effect level, with the highest dose tested at 1,000. So that gave me another level of comfort that there's probably no signal there.

DR. SHANK: Yes, right.

DR. BERGFELD: Curt?

DR. KLAASSEN: I agree.

DR. BERGFELD: You agree. So, where do we stand with this? We have the insufficient data announcement going out. And, would you please read what the insufficiencies are that you've got?

MS. AKINSULIE: Sure. So we have the 28-day dermal...

DR. BERGFELD: 28-day dermal?

DR. MARKS: No, I don't think so, because we're reassured, as Dan explained. Really it's method of manufacture, impurities, and then an inhalation is the three I've got.

DR. BERGFELD: Three things?

MS. AKINSULIE: Okay.

DR. BERGFELD: Okay.

DR. MARKS: Is that correct, Don?

DR. BELSITO: Yeah, I mean I just wanted to raise the point that we're now -- I mean, previously we were using the respiratory boilerplate when we didn't have inhalation. And now it looks like we've gotten rid of that boilerplate and we'll ask for inhalation.

DR. BERGFELD: Ron Shank, saying yes?

DR. SHANK: I say yes.

DR. BERGFELD: See what's out there?

DR. SNYDER: It's kind of a change in our strategy, I think.

DR. BELSITO: Yeah, I mean that's...

DR. BERGFELD: Paul, want to comment?

DR. SNYDER: Well, I mean it's -- it is a significant deviation from what we've done. Previously we used the boilerplate to obviate the inhalation issue. But, again, if we have composition impurities then we would know whether we felt there was any issue with inhalation.

DR. LIEBLER: The thing about the boilerplate was that it essentially gave us an out if you will that the particle sizes were not going to be respirable. And, now we basically have had discussions at the last several meetings where there's been ambiguity about that question. And we feel that we can't necessarily always just rely on that accretion.

So if we ask for respiratory data and we get back data indicating that the particles in any of the products that we would review would be not respirable, then we would have specific information to that effect and then we could bypass the inhalation tox study.

DR. SNYDER: I think in the instances that we're asking for it, is that we have either case studies or we have evidence that there's inhalation toxicity. And so therefore, that's a bigger driver then just using the template to get around that.

In this instance I don't see anything -- but I don't have the impurities or composition. So, if we get that and we don't see anything of concern, and then I think we should just go with our boilerplate like we have, less we'll be changing our strategy for aerosolized products.

DR. BELSITO: I think, in which case, we need another look at the respiratory boilerplate to decide where we're going to go with that.

DR. SHANK: We didn't do that with the polyaminopropyl biguanide.

DR. BELSITO: We didn't do that because there was a respiratory signal. That's what Paul is saying.

DR. SHANK: But you don't know with this, there are no data.

DR. KLAASSEN: But the other, there was data.

DR. SHANK: Inhalation data?

DR. KLAASSEN: Yeah.

DR. SHANK: Where?

DR. KLAASSEN: Well, we knew for the other compounds.

DR. SHANK: Oh, yes.

DR. KLAASSEN: We knew that there was a signal there.

DR. SHANK: Yes.

DR. KLAASSEN: And, I understand what you're saying. But it is a marked change in our philosophy.

DR. SHANK: Well we may end up using the boilerplate. But since it's going out for insufficient, I would like to add a request for inhalation data.

DR. KLAASSEN: Okay.

DR. BERGFELD: Appears okay.

DR. BELSITO: So method of manufacture, impurities, and inhalation.

DR. BERGFELD: And, you're seconding that?

DR. MARKS: Oh, yes.

DR. LIEBLER: Just to come back to the boilerplate issue, I mean, if we have a boilerplate and we sort of decide whether or not to use it. On a case-by-case basis we need to take a careful look at the boilerplate and think more about how we approach this.

Because you're right, Ron, to begin with here we have nothing. And I think we have greater doubts about whether we can assume that any particles that would contain this ingredient would not be respirable. And so, that leaves us with having to ask for the data. And then we may get data that satisfy -- we may get an inhalation tox study -- or we might get data that indicate that we will not have respirable particles with this ingredient once we get more data. But I still think our boilerplate might need another look, and we kind of left that hanging.

DR. BERGFELD: Bart wishes to speak.

DR. HELDRETH: I mean, possibly the panel won't consider it sufficient, but there is some inhalation tox data in this report. Glycereth-3 has an inhalation study as does the read-across item, the ethoxylated glycerol; the PDF Page 11 of the report. Maybe it's not sufficient information, but there is some inhalation and tox information there.

DR. SNYDER: No, I don't see -- where?

DR. LIEBLER: To the top.

DR. SNYDER: Table 4 -- oh, there is on Table 4, yeah.

DR. LIEBLER: Yeah, and the top of the PDF 11, under ethoxylated glycerol, the last paragraph before short-term toxicity studies.

DR. SHANK: Yeah, there's something wrong with that study. The females gained -- let's see. In seven hours they gained -- went from 178 grams of body weight to 266. I don't think so.

DR. KLAASSEN: They bulked up.

DR. SHANK: Unless it's -- it's just not right.

DR. SNYDER: I didn't see that. That's buried underneath all that.

DR. LIEBLER: Yeah, that's like rat superheroes.

DR. BERGFELD: Are we able to move on? We have our insufficient list. And we have had a vote.

DR. SHANK: I think we can move on.

DR. BERGFELD: I want to make sure we have a vote. All those in favor of this insufficient data announcement? Thank you. Unanimous. All right, if there's anything to be added, certainly that can be added later, until Bart or Monice have added it.

Going on to the next ingredient, which is Dr. Marks, on BHT.

DECEMBER 2019 PANEL MEETING – SECOND REVIEW/DRAFT TENTATIVE REPORT

Belsito Team – December 9, 2019

DR. BELSITO: Okay. Glycerin ethoxylates. Preethi.

At the last meeting, we, again, issued an IDA for glycereth-26. We wanted a certificate of analysis, safety testing summary, topical application for ocular irritancy. Oh, our IDA was for manufacturing, impurities and inhalation. And we received certificate of analysis. We received an EpiOcular study. We received an HRIPT.

DR. SNYDER: Six of them.

DR. BELSITO: We did not receive anything on inhalation toxicity. And for glycereth-7, we also got an HRIPT at 0.68.

DR. SNYDER: There were four additional HRIPTs in Wave 2.

DR. BELSITO: Right.

DR. LIEBLER: So, we have inhalation tox acute for glycereth-3 on PDF 19. It's not yellow highlighted as new data. And let's see, is glycereth-3 one of the ingredients in our list?

DR. SNYDER: No.

PREETHI RAJ: It is.

DR. LIEBLER: Oh, it's not -- oh, it is, yeah. Glycereth-3, -7, -8, -12, et cetera.

So it's not highlighted as new data, but I don't -- was this in here last time?

MS. RAJ: It was. I think it was just misinterpreted in the sense that -- do I have to turn this on?

DR. LIEBLER: Yeah.

DR. BELSITO: Yeah.

MS. RAJ: Thanks. I think it was just misinterpreted in that like for the acute inhalation exposure, the rat's weight increased dramatically, but that was because there was a 14-day observation period.

DR. LIEBLER: Oh, because they grew, too.

MS. RAJ: Yeah.

DR. LIEBLER: Okay. And my logic for this is that if you're going to have inhalation tox on any of them, this is the one to have because it's the lowest molecular weight, and the highest likelihood of producing an inhalation tox effect.

MS. RAJ: Okay. And I think when you all had put the IDA out last time, you had said that you had wanted method of manufacture, impurities, and inhalation tox data. But if you got method of manufacture and impurities, that you would probably waive the need for inhalation tox data is what you had said.

DR. LIEBLER: Well, we've got the method of manufacture -- well, we already kind of had method of manufacture for the family, which is, I think, is okay.

And then we had the description of the new data for glycereth-26. It's at about PDF 18 with the yellow highlight. This satisfies any concern I would have about defining the composition and impurities. So, I think we're --

MS. RAJ: Okay.

DR. LIEBLER: That data need is met as far as I'm concerned.

MS. RAJ: You mean the --

DR. BELSITO: So, the certificate of analysis was good enough for you?

DR. LIEBLER: Yes.

MS. RAJ: For method of manufacturer?

DR. LIEBLER: Well, the method of manufacturer above is a general description for this family, which I think is adequate.

MS. RAJ: Okay.

DR. BELSITO: So, the fact that we were assured about dioxin and methylene oxide levels, and the certificate of analysis is what you was concerned about?

DR. LIEBLER: Yeah. Right. That's exactly what I was looking for.

DR. BELSITO: Okay. So it's used at --

DR. SNYDER: 39.5 percent rinse-off, 6 percent leave-on.

DR. BELSITO: Right. And we have three percent HRIPT in Wave 2. And we don't have anything that approaches 6 percent. We have a five percent in 55.

I was okay with it, but we don't have six percent in a leave-on. We have five percent in 55 subjects. But I've never seen these sensitized. And I'm not concerned, I'm just pointing that out. And rinse-offs are usually like a one to ten dilution so that, I think, we're covered for the rinse-offs.

DR. LIEBLER: And we'll have the discussion.

DR. BELSITO: Yeah.

DR. LIEBLER: Yeah.

MS. RAJ: How did you feel about the HRIPT where there were 38 low-level reactions, but they called it a non-sensitizer?

DR. BELSITO: This was in Wave 2?

MS. RAJ: Yes.

DR. BELSITO: Let me go to Wave 2 data.

MS. FIUME: PDF Page 11.

DR. LIEBLER: One of these summaries.

DR. BELSITO: Yeah.

MS. FIUME: And then for glycereth-7, the reactions were also seen in a different study during challenge. There were low-level reactions during challenge in 11 subjects out of 211.

DR. BELSITO: Okay. So for the glycereth, the HRIPT for the 26 at 3 percent. The low-level reactions occurred in the rinse-off product. The leave-on product under occlusion resulted in no low-level reaction. So, I interpret those as irritant from the vehicle, a matrix effect.

MS. FIUME: Okay.

DR. BELSITO: So, it didn't bother me.

MS. FIUME: Okay.

DR. BELSITO: I mean, because there were no reactions at all with the -- well, wait a minute. It said, number of subjects exhibiting low-level reactions during induction, there were 38.

MS. FIUME: Um hmm.

DR. BELSITO: Oh, I missed that. Number of subjects exhibiting a high level, zero. Number of subjects in low level at challenge, zero. Yeah. Okay. I wish they would define a low-level reaction.

DR. LIEBLER: Well, that just underscores the problem with these summaries.

DR. BELSITO: Low level. Okay, grading scale interpretation, low-level reactions, zero or one, which is really weird because zero is nothing. So, how can you include a low-level reaction as zero, when the zero is no reaction? It makes no sense.

So it has to be -- because otherwise, everyone would have a low-level reaction, right, if they have either a zero or a one?

DR. LIEBLER: I think this is Russian disinformation.

DR. BELSITO: Yeah. I think this is -- yeah. So, you have to assume low-level reactions are one, which is minimal erythema, barely perceptible.

DR. SNYDER: All on induction.

DR. BELSITO: What?

DR. SNYDER: All on induction.

DR. BELSITO: Yeah. I mean, that's just irritation. So, I don't see that as sensitization.

MS. FIUME: What about on PDF Page 12?

DR. BELSITO: Of Wave 2?

MS. FIUME: Of Wave 2. In the first study, the way it is written, I actually --

DR. BELSITO: Wait. I need to figure out how to rotate this, counterclockwise.

MS. FIUME: View. If you go to view.

DR. BELSITO: Yeah, I know, I'm just being funny. Okay. This is glycereth-7 now.

MS. FIUME: The way the comments were written, it was unclear if there was no primary dermic irritation potential, but there was potential and sensitization potential observed. Or if that was all included within the same. There was no -- because there is a semicolon.

So, it would almost read as the cumulative irritation and sensitization potential was observed, being that a semicolon was used. But there were 11 subjects with low-level reactions during the challenge.

So, I wasn't sure on the comments how to interpret the conclusion.

MR. GREMILLION: It says that there's 11 that exhibited low level, but then it says there was no irritation. Is that the question, to kind of reconcile this?

DR. BELSITO: Well again, this is a rinse-off product and now its occlusive testing.

DR. BERGFELD: Oh, occlusive didn't have anything.

DR. BELSITO: And the funny thing is that -- this is sort of counterintuitive. Because with a rinse-off, occlusive, they had two subjects with low-level reactions during induction; and with the leave-on they had four. And then during challenge, they had none with the leave-on, and 11 with the rinse-off.

DR. SNYDER: All irritation?

DR. BELSITO: That's all irritation; but again, I think that -- I've never seen problems with glycereths in terms of sensitization or, in fact, really irritation.

But the question is, do we stand our ground and say that we're not accepting data like this, where we don't have individual data supplements and know who the company is that did the testing? Which is what we --

DR. SNYDER: I mean, we can clearly see that some of the ones that had the irritation and induction, were also some of the ones that had irritation at challenge. That was the useful information, wasn't it?

DR. BELSITO: Yeah, but the quirky thing here is that, again, the leave-on product, you would expect to see more low-level reactions during induction, where you're putting it on, taking it off, putting it on, taking it off, with a wash-off; and they saw two. And with the leave-on, they saw four.

And then at the challenge -- so now they've gone two weeks, and nothing's been put on their back, you get 11 in the rinse-off product, and none in the leave-on. Which I can believe is irritation, but I mean, it just -- it's quirky.

I would just like to see, you know, who -- what were the numbers for each subject. Like was there one particular person that kept popping up, or was this 11 different people --

DR. BERGFELD: Well, you only had two, though, that had induction problems. So, the rest would assume that they didn't have that.

DR. BELSITO: No, I understand. But it would be nice to see if it was the same person who had the four different -- you know, like, one panelist out of 199 had a little bit of erythema at each of the induction patches.

DR. BERGFELD: We have nine new people.

DR. BELSITO: Well, nine new people -- but you know what I mean? I just can't believe someone would test a rinse-off product, in an HRIPT, under occlusion. I mean, we don't do use tests in rinse-off products. You do a use test or ROAT in a leave-on product.

MS. DEWAN: If you do a patch test on a wash-off product, then what's the purpose? It wouldn't really --

DR. BELSITO: Well, we do a patch test. We don't do an HRIPT. So, we used to dilute them to try and read through irritation. We'd do like one to two, one to five, one to ten, and we would occlude them.

An Goossens, a decade, ago looked at doing what was called semi-occlusive patching to rinse-off products but as-is. The purpose behind that is, is that a lot of the sensitizers are things like fragrances and preservatives. And when you start diluting them, you dilute them down beyond their ability to induce a positive patch test. So, a negative patch test is meaningless to a product as is.

And even when you test a leave-on as is, a negative reaction does not rule out the potential for an allergic reaction to the product, when it's used someplace repeatedly other than the back.

But we don't put it on, take it off, put it on, take it off, put it on, take it off.

MS. DEWAN: Thank you.

DR. BELSITO: I don't know. I mean, expert opinion that it's not an issue for sensitization. But how do we -- I mean, I guess we're already making our comment back to industry on other ingredients that we're looking at, that this type of report of sensitization, irritation is not sufficient for us.

So, maybe we don't need to make that point for this one. We have another one that will get through to industry. Will that be a general industry comment across the board, or will it just be back to whatever company was involved with the report we looked at this morning?

MS. EISENMANN: Well, we'll get back to the company that provided these reports, yeah.

DR. SNYDER: But going forward, we definitely want to see the data like we had previously.

DR. BELSITO: Right.

DR. LIEBLER: I think in the last incidence --which ingredient was it that we first pointed this out with this morning?

DR. SNYDER: Pomegranate.

MS. FIUME: Christina, it was pomegranate?

DR. SNYDER: Pomegranate?

MS. FIUME: The summary data?

DR. LIEBLER: Was it a pomegranate summary?

MS. BURNETT: Oh, it was coconut.

DR. LIEBLER: Oh, coconut. Okay. So, the coconut suppliers are going to get notice that we need better documentation, right? But not everybody else who supplies ingredients in this space. So, I don't think one is much notice to anybody except the manufacturers of the ingredient that we cited. So I think we may need to simply notify everybody who gives us these, starting now, and when we get them --

DR. BELSITO: Okay, so they --

DR. LIEBLER: -- notify them right away, that the panel's not going to take this.

DR. BELSITO: Carol, can we let whoever supplied this data know that it really didn't suffice, completely, our needs for sensitization?

DR. LIEBLER: And this isn't really --

DR. BELSITO: And that this was one that went through expert judgment more than the data they provided.

DR. LIEBLER: Right. And this is a really good example of why that summary is inadequate.

DR. BELSITO: Yeah.

DR. LIEBLER: Because there are things that we're forced to speculate about, about the data that we need to know about.

DR. BELSITO: Yeah. And it's very helpful. You know, when you see, like, four reactions and it's all in this same person out of 199, that's easy to discount. There was something going on with that individual.

DR. SNYDER: What about the fact that it's max concentration of use is 6 percent, and we only have data at 3 percent; and we got quirky results at three percent?

DR. LIEBLER: All the more reason.

DR. BELSITO: So, do you want to go insufficient for sensitization and irritation? I don't have a problem.

DR. LIEBLER: I mean, if we go insufficient then that's going to force them to respond substantively. And word can go back to them that they can respond substantively by providing us better quality data in support of the --

DR. BELSITO: So, sensitization and irritation for glycereth-26 and -7 at concentration of use?

DR. LIEBLER: Yeah.

DR. BELSITO: And not just summary data?

DR. LIEBLER: Right.

DR. HELDRETH: Alternatively, I can make a point of it in the post-meeting announcement to put it out there for anybody interested. And certainly all the companies that submit information to the panel see this that an HRIPT study is something that the panel finds quite useful but a summary like this often has its drawbacks.

DR. BELSITO: Yes.

DR. HELDRETH: And then it gets to everyone.

DR. LIEBLER: I think that would be helpful, but it still may not reach -- I think, it may not reach everybody we need it to reach. And in this case, we have a specific need for this ingredient family.

DR. KLAASSEN: It's a good time to start.

DR. LIEBLER: Right.

DR. BELSITO: Okay. So, insufficient for sensitization.

MS. RAJ: And would this be for just glycereth-26 or, I guess, whichever ingredients you're able to get?

DR. BELSITO: Glycereth-26 is the maximum concentration of use, so glycereth 26 at 6 percent maximum concentration of use in a leave-on.

DR. BERGFELD: Unless they can come back and demonstrate the details of that study. Is that a comment that can be made in the minutes?

DR. KLAASSEN: I mean they have the data, most likely.

DR. BELSITO: Of course they have the data.

MS. EISENMANN: See, for something that's large like glycereth-26 they're not testing the -- these are -- a lot of it is finished product testing and not ingredient testing. Because it's large, they're not going to test the ingredient on its own.

So, I'm not sure you're going to get -- I mean, you've got glycereth-26 at what, 3 percent?

DR. BELSITO: Three.

MS. EISENMANN: And well, there's a small study at 5 percent on 55 subjects. I don't know if you're going to get -- I don't know the molecular weight, at what point glycereth-7 would be absorbed or 3 or --

DR. LIEBLER: Yeah, I mean, I think the smaller ones might be absorbed a little bit just into the stratum -- or just through the stratum corneum enough that you couldn't exclude a possibility of any sensitization.

MS. EISENMANN: But they're not used as much.

DR. LIEBLER: The thing is, I think that they could have satisfied us with a clear report on the study that was done, so that we could interpret this. Right now, we're speculating about what the report is because all we have is the summary. If we had the report, we'd probably be on to the next ingredient right now.

MS. EISENMANN: But do -- well, that is the summary --

DR. BELSITO: We have the 5 percent, 55 subjects for glycereth-26. Again, just a summary, we don't see the actual details. And it says, the test material did not demonstrate a potential for eliciting dermal irritation or allergic contact sensitization. That's PDF Page 21.

DR. LIEBLER: I mean, it's a draft tentative report. We can go back out and get the reports.

DR. HELDRETH: Yeah, procedurally, since the panel asked for manufacture, impurities, and inhalation last time in an IDA, this is a new data request. So, essentially, if you were going to go insufficient here, instead of coming out with a tentative conclusion with that, it would be a second IDA.

DR. LIEBLER: Yeah, that's what we need. Because the data they submitted, even though we didn't ask for it, raised new questions.

DR. BELSITO: Well, we asked for summary of an HRIPT on product containing 3 percent, and for the 26th. And the summary for the glycereth-7 at 0.68. And, I guess, what we got was a summary. And what we thought we were going to get was the study.

DR. LIEBLER: And the thing is, the summary indicates that there have to be study data, it's just not being shared with us.

DR. BELSITO: I understand, but we didn't ask for the study data, we asked for the summary, and that's what they gave us. So, I don't know, procedurally, what we do here, but it puts us on notice that we don't ask for summaries anymore.

DR. LIEBLER: Right. But from here on, we do the right thing, which is get the data we need to be confident in our conclusions.

DR. BELSITO: So, what are we doing with this?

DR. SNYDER: I think it's more your call. Do you think the 5 percent and a 55 is sufficient for 6 percent max use? I'm okay with it, but I'll go with what the dermatologists on the panel think.

DR. BELSITO: Yeah, I think it's fine. But again, I'm just concerned because, you know, we're going back to the coconut people and saying, we want the hard data; and we're not going back to these people and doing the same thing.

DR. LIEBLER: I think we issue an IDA and we communicate back to them here's how -- easily how you can address it.

DR. BELSITO: So, we don't need the inhalation anymore?

DR. LIEBLER: No.

DR. BELSITO: So then the IDA is at 6 percent or -- which would be the maximum concentration for glycereth-26. Or is it the experimental results for the HRIPT on the 26 at 3 and the 7 at 0.68?

DR. SNYDER: The HRIPT at 6 percent will easily clear. We could clear it if we have the data to understand the quirky results and the other test, where we tried to decipher whether it was irritation and not sensitization. So we have a comfort level there; is that not right?

DR. BELSITO: Yeah.

DR. SNYDER: So, it'd be either/or.

DR. BELSITO: So, insufficient for sensitization of glycereth 26 at a maximum concentration of 6 percent, or the experimental details for the HRIPT performed on the three percent material, right? And the experimental details for the 7 performed on the 0.68.

DR. SNYDER: For all HRIPT studies in the report?

DR. BELSITO: Well, we don't have the details for the five percent. I mean, we don't have the actual experimental details, we just have the summary saying that there was no evidence. Rather than in the other one where we're told that there was low level --

DR. LIEBLER: Right. So, we have to get away from those.

DR. BELSITO: So basically, if you look at the sensitization and irritation data we had, it just said a product containing five percent glycereth-26 was done in 55 subjects, and the test material did not demonstrate a potential for eliciting dermal irritation or allergic contact sensitization.

It doesn't say anything about reactions or anything. And that was the conclusion of the other study, too. But they just happened to say that there were these low-level reactions, eight subjects. The researchers concluded the test material did not induce significant dermal irritation or allergic contact sensitization.

If we hadn't had that sentence put in about low-level reactions, we would have never asked for it. We don't know whether there were low-level reactions in the 5 percent. We just know the conclusion.

DR. SNYDER: Well, I think we just ask, and then go from there and see what we get, and we'll hear what the other team says and then --

DR. BELSITO: Okay. So -- and if that was the same for asking for the details for the -7, it's -- they stated there were some low-level reactions.

So, if we're going to ask for the experimental details for the 7 and the 26 at three percent, do we want the details for the 12 and the 26 at five percent?

DR. SNYDER: Well, the 12 I'm not worried about, because that was a very low level, like 0.68 or something like that percent or something, very low.

DR. BELSITO: 7 was 0.68, 12 was 0.35.

DR. SNYDER: Yeah, I mean, the 55 at 5 I'd like to know.

DR. BELSITO: Okay.

DR. SNYDER: If that was super -- if that was -- there were no induction reactions, and that was under all the right (inaudible) conditions --

DR. BELSITO: But it was only 55 subjects.

DR. SNYDER: Well, I know, but -- and then --

DR. BELSITO: Normally, you ask for a hundred at least.

DR. SNYDER: Right. I don't remember seeing so many HRIPTs that had these low-level reactions before. Usually they're just clean.

DR. BERGFELD: Occasionally, we've had them in the beginning but not in the end.

DR. BELSITO: Well, often times we weren't told that data. We just had a summary statement that said, boom, there was no evidence of irritation or sensitization just as we have for the five percent.

MS. EISENMANN: I think it depends on what company is doing the study. Some companies report low-level reactions more carefully than other companies, is what I think. And I also think that location of where the study is done makes a difference too. If it's done it Texas where it's nice and hot during the summer, they might have more low-level reactions, than if it's done in New Jersey in the winter.

DR. BELSITO: When your skin is dry and irritated and cracked.

MS. EISENMANN: Well, maybe in the winter, fall, spring, you know what I mean. You understand.

DR. SNYDER: Well, I mean, maybe we're over-interpreting the data. We should just go with the summary that says it was negative.

DR. LIEBLER: We're over-interpreting a summary of the data.

DR. SNYDER: Right.

DR. LIEBLER: That's the problem.

DR. SNYDER: Right.

DR. LIEBLER: We have a summary of the data that doesn't tell us enough. So we're forced to over-interpret it because there are uncertainties that suggest there might be a problem.

DR. BELSITO: And it's not tested at the maximum concentration of use. But clinically, glycereths have not been a problem.

DR. SNYDER: Well, I think that our insufficient data announcement should be very specific that we -- the preference would be to have an HRIPT done at maximum concentration of use and minimum of n equals 100, right?

DR. BELSITO: I'm fine with whatever you guys want to do. So, you want an HRIPT, n of 100), glycereth-26 at six percent. And you want to see the hard data of what goes with that study.

DR. SNYDER: Well, I think it's an either/or. If they give us new data at the highest concentration of use, with adequate numbers of subjects, then I'm clear. If we get data at the -- experimental data that we then can make valid interpretation of these low-level reactions, then we might clear it also.

DR. BELSITO: So, you no longer are requesting the individual data for glycereth-7? You just want insufficient for sensitization of glycereth-26 at maximum concentration of six percent in an HRIPT of a hundred. Or you want the experimental data for the HRIPT on the three percent; is that right? Isn't that what you just said?

DR. SNYDER: Yeah, I mean, otherwise if we don't ask for that then we have to say it's sufficient right now. It's either sufficient right now as it stands, 55 subjects at seven percen,t glycereth-26. And some other ones at the 7 and three percent level, or --

DR. BELSITO: 26, glycereth-26 was 55 at five percent --

DR. SNYDER: Right.

DR. BELSITO: -- and 102 at --

DR. SNYDER: Three.

DR. BELSITO: -- three percent.

DR. SNYDER: So we have to make a decision of what we're comfortable with. If we're comfortable with that data, which is quite a bit of sensitization data with very little --

DR. BELSITO: I told you that I'm comfortable.

DR. SNYDER: Okay.

DR. BELSITO: The question is, do we set a precedent and let this company sneak by when we're not doing it for the coconut people?

DR. BERGFELD: Well, you're really asking for them to give you the details on the three percent and giving them an option to do a new study.

DR. BELSITO: What we're really asking for, going forward, is, yes, those kind of details. For this material because of other things that surround it, we're not as concerned by the abbreviated study data. However, for other materials, we could be, but in general we find it insufficient to get a study like this, an HRIPT, when we've asked for data without the actual data to back it up.

Although in retrospect, I don't know how often we've looked at actual data. We've often times relied on summaries just like what we're getting for the five percent. You know, there was -- it was tested.

DR. BERGFELD: But you didn't have a question of the results. This is a question of the results that were recorded.

DR. BELSITO: I know, but typically we've seen individual data only when we specifically said, okay, it's insufficient for this endpoint, and give us the data. We haven't seen them with the original reports. We've just -- with the first SLR, you don't send us all of that data. It's only when we turn around and say, oh, we want this data. So very frequently we have passed on sensitization with the type of information that we got for the five percent without asking to see the individual data.

MS. FIUME: Having done quite a few of these reports, I think historically we did receive the entire studies. Because our data submission size would be very hard, because there would be a table that included --

DR. BELSITO: So, you would get it all, but we would just --

MS. FIUME: Every single --

DR. BELSITO: -- see the summary?

MS. FIUME: Well, and often you would get all of them too because sometimes we would question the summary that was in the write up --

DR. BELSITO: Right.

MS. FIUME: -- didn't match the --

DR. BELSITO: If there were reactions, yeah.

MS. FIUME: Yes.

DR. BELSITO: Okay. You're right. Okay. So then my assumption was not totally correct. If your writers looked at it and had concerns, they would send all of the data together in the package we saw, yeah. Because sometimes we do get full studies and sometimes we don't.

MS. FIUME: Right.

MR. GREMILLION: Okay. I just wanted to ask if you -- you'll say this is sufficient, but then say in general it's not sufficient to have this kind of data. Would that really send a message that you --

DR. BELSITO: No, that's what I'm saying.

MR. GREMILLION: Yeah.

DR. LIEBLER: Yeah, that's what worried me about doing. Look, I'm where I was all along on this. We have data that suggests that there might be a problem. That the summary of the data is -- does not enable us to interpret it. We should get the actual report of the study. If we have to issue an IDA to do that, then we have to issue an IDA to do that.

DR. BELSITO: Okay.

DR. LIEBLER: So, let's just do it.

DR. BELSITO: So, it's insufficient for sensitization of glycereth-26 at maximum concentration of six percent, or the experimental details for each subject for the HRIPT on the three percent.

And do we want similarly for the glycereth-7, even though it was a lower concentration, now that's more penetrable that also gave quirky data?

DR. KLAASSEN: Yes.

DR. BELSITO: Okay. So, then we want experimental details for the glycereth-7 at 0.68. Okay?

DR. KLAASSEN: You need to make clear --

DR. BELSITO: Capisce?

DR. KLAASSEN: -- that the experimental details needs a results. I mean, some people can --

DR. BELSITO: Well, we did say summary. Okay.

DR. KLAASSEN: Exactly.

DR. BELSITO: Are we done? Anything more on glycereth?

MS. RAJ: Well, since you all, you know, obviously want more details, maybe this is a little premature. But I just wanted to get your feedback on what I presented so far, in the discussion, as far as bringing in some language from previous reports.

Because I know you had said that you wanted weight of evidence from previously reviewed ingredients. So, I just wanted to make sure, you know, I'm in line with your thinking. And if you have anything to add, please do share.

DR. BELSITO: I thought it was fine.

DR. LIEBLER: Yeah, I added a sentence in your discussion section, basically saying that just to state that the panel felt that other families of structurally analogous ingredients, previously reviewed, could be used to provide read-across and weight of evidence support for the safety assessment. And I indicate exactly where that goes in my edited copy.

MS. RAJ: Okay. Thank you.

DR. BELSITO: That's it? Okay.

Marks Team – December 9, 2019

DR. MARKS: At any rate, we're here for reviewing a draft tentative report on glycerin ethoxylates. At the June meeting, the panel issued an insufficient data announcement for method of manufacture, impurities, and inhalation tox data on these. And they are listed in Preethi -- am I saying that correctly?

MS. RAJ: Preethi.

DR. MARKS: Pree-three.

MS. RAJ: No, Preethi. My friend says is like pretty with a lisp.

DR. MARKS: These are your friends?

MS. RAJ: I don't -- no, no, she's a lady. And I'm fine with ladies saying that; men I am not. But you're fine. It's okay.

DR. MARKS: Preethi. I'm not a linguist, so it'll take me a while. Please excuse me.

MS. RAJ: No worries.

DR. MARKS: Okay. So are we going to -- so we're at a point of issuing a tentative report that -- let me see? I didn't see where we had gotten any of this.

MS. RAJ: No.

DR. MARKS: And that's oftentimes in the memo, helpful, no new data.

DR. SLAGA: In Wave 2, didn't we get some --

DR. SHANK: HRIPT.

DR. MARKS: Yeah. But not the method of manufacture or the impurities. We didn't get that, did --?

MS. RAJ: There was a certificate of analysis for glycereth-26, which I was wondering if you all thought that qualified as some sort of method of manufacturing data.

DR. PETERSON: Say that again.

MS. RAJ: So, for glycereth-26, in the -- well not Wave 2, but prior, like an interim data from the council -- or industry, I guess. There was a certificate of analysis for glycereth-26, which kind of listed some, I guess, various values, which I wasn't sure would qualify as method of manufacturing in some capacity.

DR. HELDRETH: It's really --

DR. MARKS: What page is this?

DR. HELDRETH: So, this is -- the actual submitted information is PDF Page 36. It's really a property information, so chemical-physical properties. I don't think there's any methodologies there. So you have things like acid value, hydroxyl value.

DR. SLAGA: Would that serve for the impurities?

MS. RAJ: Oh, yeah.

DR. PETERSON: But not the method of analysis, not the method of manufacturer, but the impurities.

DR. ANSELL: But isn't the reason we need a method is to identify what are the potential impurities? The manufacturing in and of itself is not of interest. It's whether --

MS. RAJ: There are impurities?

DR. ANSELL: Yeah.

MS. RAJ: But Bart, the council, remember, their comments that we got right before the meeting, they said that they felt that that information fit in the, I think, chemical and physical properties, not in the impurities, which was interesting, I thought.

DR. HELDRETH: It's up to the panel how they want to use it.

DR. MARKS: So Ron, Tom, Lisa, move forward with still insufficient for method of manufacture and impurities versus safe? Ron, you had comments the last time about that, which is on page 14 in the minutes.

Do you want to reiterate those for Lisa? I think it'd be helpful.

DR. SHANK: Well, my position was this is a -- these are single chemicals. And if there were impurities that had significant toxicity, that would have been indicated in the toxicology studies. So I felt it wasn't necessary to have the impurity data.

But the other team felt very strongly that, if you don't know what the impurities are, we're missing significant data. So, we see it differently. And if they want the impurity data, I won't object.

DR. MARKS: Okay. Good.

DR. ANSELL: And the impurity data that's most of concern, with ethoxylates, is the presence of dioxane. So, that we monitor very closely, and you now have the dioxane levels.

DR. PETERSON: Dioxane? Or ethylene dioxide.

DR. ANSELL: And EO. Although, EO is so reactive you don't really see EO per se. But you do see the 1,4-dioxane, which is something we manage very carefully and have recommended, as a Council, that it be controlled to less than ten PPM.

MS. LORETZ: Recommended under the international ICCR. It's far beyond us, actually.

DR. ANSELL: Right. Canadian, Brazilian, European, U.S., and --

DR. SHANK: Japan.

DR. ANSELL: Do I have five? And Japan.

DR. HELDRETH: It's a rather volatile chemical. Isn't that correct? They're easy to get rid of if you make an effort to --

DR. ANSELL: It is volatile, and it can be managed. I'm not sure easy is the right word.

DR. HELDRETH: Okay. There's no methodologies.

DR. ANSELL: Yeah. Yeah. And it's something we've been tracking for decades with FDA. And ten PPM in the final product is what we manage, and this was less than five an in a raw material, which is then diluted itself.

DR. MARKS: So tomorrow -- I'm sorry.

DR. ANSELL: No, I was just going to finish. So, we feel that we've address the manufacturing, impurity issue.

DR. SHANK: At the September meeting, I raised a concern about the inhalation data for --

DR. MARKS: Yeah. I'm going to get to that. So are we going to -- we're seconding it, the tentative report? But are we -- I gather, Ron --

DR. SHANK: I'll remain silent.

DR. MARKS: Yeah. If the Belsito team says insufficient for method of manufacture and impurities, we're going to go ahead and second that. Jay, even though you bring up a very important point -- did we capture that either in the discussion at all, this issue with the dioxanes?

MS. RAJ: There's some boilerplate language. Let me see, that is on Page 24. But you'll see it's pretty short mention there.

DR. HELDRETH: Yeah. We usually say -- since there are no methodologies to get rid of it and industry is well aware that this is an issue. We usually put in a statement to the effect of industry should continue to use, you know, basically good manufacturing procedures to --

DR. MARKS: That's under the draft -- which paragraph is that under?

MS. RAJ: The second to last of the discussion.

DR. MARKS: Oh, yeah. Dioxane and ethylene oxide impurities -- yeah. Okay. Super. So we'll see how that runs out.

And actually, Preethi brought up -- she wanted us to also comment about the discussion, since I don't know if this is the first one you've written --

DR. HELDRETH: Yeah.

DR. MARKS: -- but close to it.

MS. RAJ: Yes.

DR. MARKS: So, we'll get to overall comments on the discussion in a minute. Ron, thank you for bringing up the respiratory because that was my next point I wanted to bring up, is the potential respiratory toxicity.

MS. RAJ: Yes. And since you just finished talking about the method of manufacture and impurities, I just wanted to remind you that you had said that if you found sufficient method of manufacture and impurities, you would, I guess, waive the need for inhalation data. That's what you had said before, so just reminding you all.

DR. SHANK: Well, we have inhalation data. It was just misinterpreted the first time.

MS. RAJ: Yeah.

DR. MARKS: Oh, okay.

DR. SHANK: It said that the rats gained half their bodyweight in seven hours or something like that. And I said I didn't think that was correct. And it wasn't.

MS. RAJ: But now you're satisfied?

DR. SHANK: I'm fine.

DR. MARKS: So, all we do is use the inhalation tox resource document is that --

DR. SHANK: Yes.

DR. MARKS: We include that. Okay.

DR. SHANK: With that dioxane and ethylene oxide paragraph, why do we say, "Therefore more data are required for clarity?"

MS. RAJ: Where are you looking?

DR. SHANK: What more data do we want? It's the second to the last paragraph in the discussion.

MS. RAJ: Yes, I see that. I think that's, I guess, going along with what I just explained. Because I had understood that until you felt satisfied with the method of manufacture, and impurities, that you would want inhalation data.

DR. HELDRETH: So now that we have --

DR. SHANK: But this is on the impurities.

MS. RAJ: Yeah. Well, the post-meeting announcement last time, there were three IDA requirements. There was method of manufacture, impurities and inhalation data.

DR. SHANK: Yes. Right.

DR. PETERSON: And you got the impurity information, but not the manufacturers, right?

DR. SLAGA: Right.

DR. SHANK: But we don't need more -- we don't need clarity, do we, on the --

DR. ANSELL: I think the method of manufacture is requested to determine whether there's a potential for unreactive materials or reaction products, which would be of concern. We feel that, for ethoxylated products, the chemistry is well-known, and the ingredients of concern are the potential for the formation of 1,4-Dioxane.

We have established international standards for what are appropriate residuals. And these materials, even unformulated, would fall below the concern level for the international standards set for 1,4-Dioxane. So we believe that that responds to the concern of residuals and method of manufacture.

DR. SHANK: Okay. But we don't need more data for clarity on 1,4-Dioxane?

DR. ANSELL: No, no -- that's --

DR. SHANK: That's what it says.

DR. ANSELL: I think those two sentences are --

DR. SHANK: The other impurities maybe, but --

MS. RAJ: We can modify that.

DR. SHANK: Okay.

MS. RAJ: So, how would you like that worded?

DR. SHANK: Just say more data are sought on other impurities for clarity.

MS. RAJ: Okay. Thank you.

DR. ANSELL: Well, no. This is very specific to the 1,4-dioxane. I would suggest that the modification is -- rather than saying the Panel was concerned with the possible presence, that the Panel is aware of the possible presence and, therefore, recommends that we continue to use all the necessary procedures to limit the 1,4-dioxane impurities.

MS. RAJ: Okay. Thanks.

DR. ANSELL: Yeah. So, first sentence and then the second sentence align.

DR. SHANK: Yeah. Right.

DR. PETERSON: And then you have the report on the certificate of analysis for the --

MS. RAJ: Glycereth-26.

DR. PETERSON: Yup. That says that it's really low.

MS. RAJ: When you say "it" you mean impurities?

DR. PETERSON: Yeah. The 1,4-dioxane was less than 0.0001 percent.

MS. RAJ: Yeah. Okay.

DR. MARKS: So Ron, you would be -- you would be okay going on with a safe conclusion?

DR. SHANK: I would.

DR. MARKS: Yeah. And Tom?

DR. SLAGA: I would, too.

DR. SHANK: They'll want impurities.

DR. SLAGA: Well, we -- we had -- that's what we wanted when we said flag for the time before, wasn't it?

DR. SHANK: Well, we had the concern about the inhalation.

DR. SLAGA: Inhalation, right.

DR. SHANK: These rats gained a whole lot of weight really fast.

DR. MARKS: Well, we'll see what the Belsito team moves tomorrow. And if they still want the insufficient for method of manufacture, we will not dispute it. We've had that long discussion before.

I wanted to comment about Wave 2, W2. So we didn't discuss -- we talked about method of manufacture, the impurities and inhalation.

But the new data on Wave 2 were sensitization data. So, the 2 percent glycereth-7 was HRIPT. And the 3 percent glycereth-26, both were fine. However, in one of the HRIPTs, with the glycereth-26, 38 subjects had a, quote/unquote, low level reaction with induction but not with challenge.

When I compare it with the other HRIPTs, 3 percent and 5 percent, which had been done previously, they were okay. So, I don't know if this was a leave-on product they had there, that those 38 reactions were just a mild irritant reaction to that particular formula in leave-on.

To me, it didn't create a big alert. And again, the formatting was fine. I was able to take a look and see.

MS. RAJ: Is this something you would allude to in the discussion?

DR. MARKS: No, I don't feel compelled to allude to it.

DR. SHANK: Well, they concluded -- I found it very confusing.

DR. MARKS: Yeah.

DR. SHANK: One concentration was negative, and another concentration even lower, potential sensitizer. And I didn't know how to interpret that.

DR. MARKS: They didn't -- in the end, they didn't categorize this as a potential sensitizer. They didn't call it a sensitizer. Correct?

MS. RAJ: Yes, correct.

DR. MARKS: So, I think they interpreted it as just being mild irritation. That's what I suspect with it.

DR. SHANK: Okay.

DR. MARKS: I mean, we could mention it in the discussion if you think that would be helpful. But with two other studies and the other ingredients being negative as far as sensitization, and with this not being -- with the lab that did this interpreting it as a non-sensitizer, then I was fine as a non-sensitizer.

DR. SHANK: Okay. Good.

DR. MARKS: And I didn't think we needed to have some sort of caveat, formulate to be non-irritating, either.

DR. SHANK: Good.

MS. RAJ: Okay.

DR. MARKS: So is that okay, Ron?

DR. SHANK: Yes.

MS. RAJ: So, would you say something to the effect that there was a study, a sensitization study, where you saw some low-level reactions? You weren't sure of the nature of the product, like if it was leave-on?

DR. MARKS: It was a leave-on.

MS. RAJ: Okay. It was a leave-on.

DR. MARKS: Because they had one that was -- the other one that was in there was not a leave-on.

MS. RAJ: Right. But that basically the lab did not classify it as a sensitizer, so that's why you're not concerned?

DR. MARKS: Correct. That and the other ones with the same ingredient, the glycereth-26, the other HRIPTs which were negative.

So, I think with those others that were negative, even though -- you're right, Ron, one was the same concentration, 3 percent. But then there was a 5 percent, higher concentration, which was okay. That was from the original data.

We always put in the data we have. I don't know that we have to speculate that, perhaps, this was a mild irritant in the induction phase or not.

DR. SHANK: Okay.

MS. RAJ: Okay.

DR. MARKS: But I think the investigator is saying it's non-sensitizing, that's important.

DR. SHANK: Yeah.

DR. MARKS: Because otherwise then we're trying to explain -- and they didn't -- and what I saw, they didn't try to explain what the reactions were. It came to the conclusion non-sensitizing.

MS. RAJ: Yeah.

DR. MARKS: Okay. Any other comments?

MS. RAJ: I was hoping, if you had anything you'd like to add in the discussion about the nature of previous reports, which Dr. Liebler had said he wants to use as weight of evidence for safety of these ingredients.

Because, again, me being very new here, I looked at, I guess, all these -- there were about like 20 reports referenced from before -- and it seems to be practice to usually draw on, or kind of use, the safety of similar ingredients from the past as, like, a substantiation for, like, the presently reviewed ingredients being safe. So, do you have any language for that?

DR. SHANK: I didn't go back and look at those earlier reports.

MS. RAJ: I do have -- I mean, I'm not -- obviously, it's has to be coming from you. But to jog your memory, I was looking at there were laurates, stearates, cetates, PEG, cetyl alcohol, oleates, laneth-10 acetate. So, they kind of had a nice paragraph here.

It said, the alcohol ethoxylates -- this is paraphrased. There PEG metabolites are noncarcinogenic and relatively innocuous when given orally. Various alcohol ethoxylate preparation are nontoxic when inhaled, and do not inhibit ciliary movement in vitro. Ingredients are relatively innocuous when administered orally, acutely, and subchronically. They are not mucosal irritants.

Some are slight to moderate skin irritants, but are not sensitizers. Negative for teratological, multiple generation, and mutagenic potential. So, is that kind of what gives you -- ?

DR. SHANK: Okay. I guess that would be helpful.

DR. MARKS: It's long-winded. I didn't like "relatively." I guess it depends. That to me is a little bit --

MS. RAJ: Okay.

DR. HELDRETH: I think Preethi already has something to this effect in her draft discussion. If you look on PDF Page 24, the second full paragraph. "The Panel noted." That may be sufficient. It's up to the panel if you think we should expand upon that or not.

MS. RAJ: Yeah. That I took from Dr. Liebler's comments. But I'd love to see if you have anything to add to that.

DR. MARKS: See, I like that, because you kind of --

MS. RAJ: I feel like there's quite a bit of language across these reports, about how it's -- because of the chemical structure.

But again, me not being a chemist and kind of knowing everything, it kind of feels a little vague in that, okay, it's because of the chemical structure. But what is so safe about this chemical structure? So, should there be more explanation there? I'm not sure.

DR. PETERSON: I actually, like -- I mean, I like how that paragraph reads.

MS. RAJ: Okay.

DR. PETERSON: Because the difference is this methyl group or change in the --

DR. MARKS: And in my mind, even though we -- it's helpful we have these read across or related -- the chemistry, it's these ingredients stand on their own with the data we have in this report.

DR. SHANK: I thought so.

DR. MARKS: So, this is nice background, but the ingredients themselves stand. If we had the method of manufacture, it would be easy. It'd be a safe.

MS. RAJ: Okay. And there was some language on previous reports about how the toxicity is inversely proportional to the length of alkyl chains. Or I guess maybe in this case, you could say the ethoxylation values, like, just the size of the molecule.

Also the fact that glycereth-26 is the one that's, I guess, the most used, does that maybe also maybe provide some assurance for the panel?

DR. ANSELL: They're all useful to model and extrapolate, but in the presence of actual data, I don't think we need to spend a lot of time talking about how we might have derived the data were it not --

MS. RAJ: Okay.

DR. ANSELL: But I do think those concepts are foundational in terms of the safety assessment of cosmetics, the ability to rely on materials that are --

MS. RAJ: Do you think the inverse line, though, about the size of the molecule and toxicity is worth putting in the discussion?

DR. ANSELL: It's really not toxicity. It's, I mean, there's certain surface-active properties that may affect irritation.

DR. SHANK: I don't think it's necessary to have that.

DR. PETERSON: I agree. It reads pretty well, pretty clear.

DR. MARKS: Okay. Any other comments, Preethi?

MS. RAJ: Yes. Let's see. That's mostly what I wanted to ask you. You seemed to have addressed everything.

DR. MARKS: Good. Any other comments, Ron and Lisa? So, tomorrow, our team will be seconding a tentative report motion, and we'll see what the conclusion is. It's going to be either insufficient or safe, and we'll see. Okay. Let me go ahead and close this.

Full Panel – December 10, 2019

DR. BELSITO: Okay, so at the June 2019 meeting we issued an IDA for method of manufacture, impurities, inhalation toxicity. And we received a certificate of analysis. We received some safety testing, an EpiOcular irritation assay, and some summaries of HRIPTs on a product containing 3 percent. We also received a summary of a HRIPT on a product containing 0.68 percent for glycereth-7.

We felt that these were still insufficient. We were not happy with the summary statements of the HRIPT; perhaps this was our fault for asking for a summary. But, there is some quirky data where there were low-level reactions during the induction phase. And, it's not clear to us if those were occurring in just one of the subjects, which you could easily discount, or whether it was occurring in different subjects which would raise other issues.

And so, going forward, when we ask for HRIPTs, we would like to see the individual data. And going forward means starting with these ingredients.

So, we are happy with the certificate of analysis and the ocular irritation, but we felt that it was insufficient. We would like to see the individual data on the actual HRIPT studies that were performed. Or, since glycereth-26 is used at a maximum concentration of six percent in leave-ons, a new HRIPT at six percent for glycereth-26.

We recognize that expert opinion would say these are not sensitizers; however, expert opinion is sometimes wrong as we've discussed previously in this meeting. And so, we would actually like to see the data, particularly, given that twinkling that's going on in these studies.

DR. BERGFELD: Again, this is at issue the validation of the abbreviated summaries of the testing that we've been discussing. Jim, do you have a comment?

DR. MARKS: Yeah, we concur that a tentative report should be issued with an insufficient data. And I wondered what happened with the method of manufacture and impurities. Did I over --?

DR. BELSITO: Dan felt that the certificate of analysis that we received was adequate. Well, I'll let him address that.

DR. LIEBLER: Yeah, with this, you know, it's a typical polymer situation. And with these we're worried about -- with this type of polymer we're worried about dyoxane and ethylene oxide. And they provided this data, very low for glycereth-26, which I think is probably reasonably representative of the group. So, I felt that our data need on that was met.

DR. MARKS: Interesting. So, our team would concur since the last meeting we thought we could move forward with a safe conclusion, so. We had that discussion about method of manufacture and impurities.

Concerning the sensitization, Don, I think the study you're talking about was a three percent glycereth-26, which the investigators concluded in this one HRIPT where they had 38 subjects had low-level reaction with induction of a leave-on. But in the end, on challenge, had no reactions and concluded that this was not a sensitizer.

We had two other HRIPTs at three percent, and then another one at five percent, and acknowledge that the five percent is not at the use concentration of six percent. But those were okay.

I was wondering, I agree, we don't have the details whether the leave-on was a mild irritant in the induction phase, and that's why they saw these low-level reactions. But certainly to be safe, I'm fine with moving forward with an insufficient -- we actually are concurring, going forward without a method of manufacture and impurities. But now we just do insufficient, forgetting the details of that study.

DR. BELSITO: Yeah, I mean, we also discussed the fact that the 5 percent was said to be non-sensitizing, but again we didn't have individual data for that one either.

And, you know, had this been a surfactant, or you know, something that we know has a tendency to irritation, like iodopropynyl butylcarbamate or methyldibromo glutaronitrile, I might easily dismiss these quirky reactions, even if they were occurring in five separate individuals, or how many. But, you know, the glycereths typically aren't irritants. You know, they're very well tolerated. So, I just wasn't certain -- you know, the tests that were done on the rinse-offs I had no problems with.

DR. MARKS: Exactly.

DR. BELSITO: You know, but it was the leave-ons that bother me. And, in fact --

DR. MARKS: Yes, it was that one leave-on.

DR. BELSITO: Yeah. For glycereth-26, I think there were more, you know, low-level reactions in the leave-on product then there was in the rinse-off product.

DR. MARKS: Yes, which you would expect perhaps the opposite way.

DR. BELSITO: Exactly the opposite. So, you know, I just --

DR. MARKS: No, I'm concurring, Don, insufficient and a tentative report. In this case the only insufficient is clarifying the HRIPTs.

DR. BELSITO: Right.

DR. MARKS: And I don't know if "quirky" is a scientific word, but I like it.

DR. BERGFELD: Any other discussion?

DR. HELDRETH: Yeah, so procedurally, since the panel put out an insufficient data announcement on this report for three issues that are now resolved, and we're making a new data request, this should actually go out as a second IDA, instead of a tentative report.

DR. BERGFELD: Okay.

DR. BELSITO: That's fine.

DR. HELDRETH: And then it'll come back as a tentative report again at the next meeting.

DR. MARKS: Yeah, and did we mention that the inhalation tox data, did you mention that that we got that and that was okay?

DR. BELSITO: Right. Yes.

DR. MARKS: Because that was one of the insufficient data needs in the last go round with these ingredients. Okay.

DR. BERGFELD: All right? Seeing no other questions, I'll call the vote on that then, a tentative IDA again going out. All those in favor, please indicate yes. Consensus is met, unanimous.

Moving on to the next ingredient, Methicones, Dr. Marks.

JUNE 2020 PANEL MEETING – THIRD REVIEW/DRAFT TENTATIVE REPORT

Belsito Team – June 8, 2020

DR. BELSITO: Okay. So glycerin ethoxylates. Let's see. At the December meeting, the panel deemed that the available HRIPT summaries provided insufficient information, especially on the low-level reactions during induction. And we issued an IDA for all of the experimental details for each of the summaries or newly completed HRIPT experimental data at maximum concentration of use in more than 100 patients. We are interested in receiving the actual experimental data for HRIPT done with the maximum reported concentration of use, which was 6 percent for Glycerel-26.

We got details of the previous HRIPTs readout summaries on a product containing 0.35 percent Glycerel-12, individual results, with a 5 percent Glycerel-26 HRIPT on a 10 percent aqueous Glycerel-26. But actually, a lot of the data was redacted from the material we got on Glycerel-26. I don't understand that. What was the deal there, Bart? I mean, it was just blacked out. There was really no data given.

DR. HELDRETH: I don't know. That's as received.

DR. BELSITO: Yeah. So we got data only for those studies in the original report that were entirely negative. The studies that I had questions on where there were these iffy reactions going on, we got none of the individual data on that, which is what I wanted. So they didn't give us what we asked for. They gave us the individual data on the studies that were clean.

So I'm not sure that what I was asking for has been met. And I still have concerned about sensitization. And I thought the data was very quirky if you look. They gave us the clean data. They didn't give us the dirty data.

DR. SNYDER: Yeah. I thought the same thing. We were asking for clarification of the data we already had, not for new data.

DR. BELSITO: Right. Yeah. And they gave us the individual responses for the HRIPTs on the studies that were clean. The studies where they were getting these reactions during the induction phase and these low-level reactions at challenge we didn't get. And the only one that they gave us everything was redacted. I mean, if you look, all of that -- it's on PDF page 56. All of

that information is redacted. It's just the summary. I think, from my standpoint, I'm still asking for the same data or a new HRIPT, which they didn't give us. I don't know what -- Curt, Paul, Dan?

DR. LIEBLER: Yeah. I mean, I think the situation is really not supportable. We can't use these to support our assessments.

DR. BELSITO: Paul?

DR. SNYDER: I felt the same way. We didn't get the data we asked for. We wanted to see if we could ferret out why there were quirky results, and we didn't get that data.

DR. LIEBLER: We got an assurance. We didn't get data.

DR. BELSITO: Curt?

DR. KLAASEN: Can we go back and ask them again? Or we just make it not satisfactory.

DR. BELSITO: Where are we here, Bart? I mean, isn't this we -- wouldn't this be a tentative final "insufficient for sensitization at the highest concentration of use"?

DR. HELDRETH: Yes. So apparently we have -- it's a draft tentative report for panel review. So if you have a conclusion to make, yes, it would be issued as a tentative report of the whatever conclusion. So there would be one more bite at the apple -- one more time the panel would see this. And if nothing changes, they would go final at that next meeting.

DR. BELSITO: Okay. I mean, I'm good with that. I don't understand what's going on with the sensitization. And they didn't answer our question. And then just in terms of the report, I agree with all the suggestions the council made for edits. I didn't have any problems with that. Did any of you have issues with suggested edits from council?

DR. SNYDER: I did not.

DR. LIEBLER: So I do have -- hang on a second. I'm writing this down here. I did add several edits regarding the use of the read-across chemicals in several places in this report. And I have some language I wanted to show. I don't know if I can share screen, Bart?

DR. HELDRETH: I should have you set up as a presenter. Let me double check and make sure. Yes, you're set up as a presenter. So if you hover your mouse in the center of the screen, there should be an arrow pointing up.

DR. LIEBLER: I'm sharing. Open system preferences -- Oh, shit. Sorry, this is going to require me to leave the meeting and come right back. I'm going to do that. Hang on a second.

DR. HELDRETH: Okay.

DR. LIEBLER: Be right back. Okay. I'm back. You can hear me?

DR. BELSITO: Yes.

DR. LIEBLER: And I'm going to share, and this time it should work. Share desktop, good. Oh, damn it. It's not letting me do it.

DR. HELDRETH: We see your desktop.

DR. LIEBLER: Oh, you see my desktop? Okay. Good, good. Thank you. Okay. So there are several places in this report in which, for example, propoxylated nitrilotriethanol is use. It's under short-term tox, read-across for ethoxylated glycerol. So I thought it would be good for us to begin to employ some common sentence or two to introduce this. This is something that we typically do in the RIFM reports to signal what the rationale is briefly for using a read-across.

And so I just want to show you the one example here. My comment -- I don't know if you guys can see this. It says, "Oral short-term toxicity data were not found for glycerin ethoxylates. However, data for propoxylated nitrilotriethanol were reported" -- with a reference -- "which enabled evaluation of short-terms toxicity. The read-across analog is a similar structure to glycerin ethoxylates with a small core structure modified with propoxy groups. These molecules are predicted to have similar absorption distribution metabolism and chemical reactivity to glycerin ethoxylates. And these compounds are expected to have similar toxicological profiles."

So I've done that in several places in this report. I got this in the DART. I've got another one in genotox. I've got another one in dermal irritation, skin sensitization, et cetera. So this is certainly open to further editing, wordsmithing. I didn't run this by Lisa because we had completed our evaluation of priorities and so forth. And this was in the run-up to the March meeting, which of course got cancelled. And I just sort of set this aside.

But I would propose that we have this kind of language every time we trot out a read-across material candidate in the report. What do you guys think?

DR. HELDRETH: I think that's fantastic. We've been wanting to have some explanation on the reports there, and getting it from you, the experts, is definitely the best way.

DR. LIEBLER: Okay. Now, I didn't try and do any kind of summary of the read-across at the end of the report, which I think we should work on next -- which would be some table that has -- oh, well, actually, I did propose that we have a table with the structure. I think I -- yeah. Okay. I suggested having a new Table 3, so before the frequency of use data that has the structure of the read-across molecules.

And, you know, the RIFM reports, I'm sure you've seen, have extensive outputs on things like Tanimoto structure similarity scores, which I think may be a lot less useful in the CIR chemicals. But we can consider those, along with perhaps other information about the chemicals that we are using as read across to support the assertion that these are chemically and likely toxicologically similar. But we can talk about doing that. At least for this report, I would suggest having a table with the structures.

DR. HELDRETH: We can absolutely do that. We can add any tox-endpoint information that you want in there as well. I think we drafted something to that effect a couple of years ago when we were first starting to try to make a read-across explanation a little more quantitative. But we can put whatever you like.

DR. LIEBLER: Let's take another look at what you drafted. You've seen certainly RIFM reports and what our format is there. I think we don't necessarily need everything that's in those RIFM tables. And in fact, some of that information may not be either relevant or available. But I think we can do something similar. And that ought to be just a standard part of our reports whenever we do any read-across.

DR. SNYDER: Dan, I really like this approach that you're taking here. I think we do maybe need to wordsmith a little bit in the caveat that would be expected the read would have a similar profile. But also, it seems like we could use this language also when we have a concern for when an analog that has toxicity and we don't have data. Is that correct? We could use a similar language to say we're asking for very specific data when we don't have data. And we don't think that the read-across gives us some cause for concern.

DR. LIEBLER: So you're talking about using a read-across and saying this read-across chemical causes this deleterious effect.

DR. SNYDER: And we have no data in where that endpoint is before. Therefore, that gives us even more justification for asking for that endpoint.

DR. LIEBLER: Yeah. Well, that's an interesting question because normally we use read across in general to support the chemical that we're reviewing, or we don't use it. In other words, if we don't read-across that can support the chemical, then we don't use it. That's not to say we're trying to obscure a possible hazard or risk. That's an interesting question. Because the read-across analogs, when we have a system up and going, it's really the result of a systematic search for chemical analogs that can support safety. I don't know if we have a precedent for looking for chemical analogs that would indicate hazard. Maybe the closest --

DR. SNYDER: So I guess my question is -- so when you do that search -- so you come up with ten analogs. And nine of them support safety, but one of them doesn't. So what do you do in that situation?

DR. LIEBLER: Well, if we --

DR. SNYDER: I mean, we can't just cite the nine that do and exclude the one that doesn't. You see what I'm saying?

DR. LIEBLER: Right. I think if there are analogs, then we basically need to carefully examine what are the structural relationships? What is the toxicity? What are the possible explanations for the toxicity? And how appropriate is the read-across analog? I think that we, in general, -- I mean, with the RIFM panel, we look for read-across analogs that have safety data indicating safe use, or we don't even bring them into the discussion. Because I think if you go looking for other chemicals that are structurally related but introduce hazard, you're not really sure if that hazard is relevant to the target chemical that you're studying. I guess it depends on the rules you would apply to assess the chemical similarity.

The other thing is in your example, if you had nine versus one, you would have to do what we often do with genotox in vitro assays, where we've got one positive test and a bunch of negatives. We look at what are the possible causes for that. We don't want to ignore it, but it doesn't mean that the nine are wrong. We basically need to address why we think that happened and draw a conclusion based on the whole body of evidence.

But I think that when we're doing read across, whether you agree or not, I guess, to put it in other terms, we're not going out looking for trouble. We're really looking for supporting safety data.

DR. SNYDER: I was just thinking more from a standpoint of transparency and documenting exactly what we did and why we came to a particular conclusion.

DR. LIEBLER: I think the best answer to that is to have as systematic an approach as possible. So with the RIFM inventory where most of our read-across comes from within that inventory as oppose to chemicals outside of that, we have the entire inventory clustered based on chemical similarity and the rationale for applying endpoints. In fact, we just published a paper in *Chem Research and Toxicology* on that about a month ago. And I would -- maybe Bart could at least send around the reference

if not the paper because I think it's a good illustration of the overall rationale of grouping for chemical similarity, which then guides the choice of read-across analogs.

DR. HELDRETH: Yes, I'll be happy to send it around. We at CIR already bought a copy of it. I read through it. It's quite wonderful.

DR. BELSITO: Okay. Any other comments about those introductory statements sort of justifying our read-across? Does Jay have a comment there? I see a Jay Ansell with a --

DR. ANSELL: Yeah, I've been raising my hand, but I guess -- so on our side, we strongly support that. I'm not sure editorially whether it should be included as a reference to each data point. But certainly a summary to looking for appropriate analogs would be greatly appreciated, and we think it should come as a part of the reports.

In terms of the question about the nine versus one, it's all baked in to determining what structural alerts are. And so if you had a material which had a data point which was of concern, it would be all considered whether it's an appropriate analog. And so in doing a full integrated assessment, if it had a component which had been determined to be a hazard, it would become part of the read-across.

DR. BELSITO: Any other comments?

MS. RAJ: Thank you everyone for that great suggestion, Dr. Liebler and panel at large. Would those same sentiments, or I guess the language, be echoed in the discussion as well? Because I know we have like a short paragraph right now in the draft discussion explaining, I guess, why the read-across ingredients are there. It's the third paragraph on -- I think that's page 40.

DR. LIEBLER: Well, one thing you might do here is adapt the language from one of these sections that I use that I pointed to -- maybe adapt some of that language. My intention is that, essentially, becomes sort of a boilerplate pattern that we could work from. And then that could also be used in discussions.

DR. BELSITO: I mean, but basically that third paragraph just said we thought it was appropriate, or we considered. What Dan is saying is we really should be giving its explanations as to why we felt they were important for those endpoints. So a summary in the discussion like that I think is okay, as long as you could go back into the paper and see why we thought those read across -- or those materials were adequate read-across for those endpoints. That's my feeling. I don't think we need to go over it again in the discussion.

DR. SNYDER: Right. Yeah. I think we just need language here that says "as appropriate for read-across or data gap," something.

MS. RAJ: Okay. Because it sounds like the introductory paragraph that you are suggesting, Dr. Liebler, isn't necessarily going to change for each of those sections where we use it, right?

DR. LIEBLER: Yeah.

MS. RAJ: Like it's not that the language isn't going to be specific to that section?

DR. LIEBLER: Right. I mean, I basically just cut out "ocular irritation" and put "skin sensitization." Or I cut out "reproductive and developmental" and put in "repeat dose." In what you can say -- if you adapt theses for the discussion, you can say "Data were not found for several endpoints for glycerin ethoxylates. However, data for several read-across analogs including blab, blab, blab, and these molecules were predicted to have similar features, et cetera, and were expected to have similar toxicological profiles. Or the panel felt that these could be evaluated in the absence of data for the target." Something like that.

MS. RAJ: Okay. Thank you.

DR. LIEBLER: We're just expanding this paragraph a little bit.

MS. RAJ: Okay. Thank you. And at this point, I guess, I agree with your sentiments about the HRIPTs. I guess how would you all want me to maybe reflect that in the discussion?

DR. BELSITO: I think that, you know, from my perspective, basically, we asked for the individual data on the particular studies where that data was quirky. And we did not get the individual responses for those studies. The ones that we got -- the individual responses we got were for the studies that were totally clean. So, you know, what we're asking for specifically, which would be nice, is the HRIPT on Glycerel-26 that was completely -- all of the information was redacted out of it. It's all black -- all of the individual results. We didn't see any of them.

So we got no sense as to was it one or two patients that kept having this? Or was it different patients that suggested, well, that was just something unusual happening? I mean, I don't think it changes anything. We didn't get the data we asked for. So either they do a new HRIPT on Glycerel-26 at the highest concentration, which I believe is 6 percent --

MS. RAJ: Yes.

DR. BELSITO: -- or we get the individual data on that very old study that they gave us but redacted all the data from.

Just a few other comments within the document, on PDF page 37, the last paragraph, it's important to say that the time of the readings -- it says, "No visible skin changes occurred upon challenge." So I mean, it was immediate, and it was 24 and 48 hours after -- that the study was. But again, all of that was -- the individual data was redacted from it. And then -- did you follow that? Where I was?

MS. RAJ: Yes. I'm looking at that, Dr. Belsito. So I'll check that study, but, as you said, I feel like some details of these studies may not be available. But I will check.

DR. BELSITO: No, they said that the readings were done at 24 and 48 hours. So they did have that information. You can check it, but I'm pretty sure that's what they said.

MS. RAJ: Okay.

DR. BELSITO: And then on PDF page 39, the route and vehicle, this is the third paragraph in a pilot study on Wistar rats who received propoxylated nitrilotriethanol. It doesn't say by what route or what the vehicle was.

MS. RAJ: Okay.

DR. SNYDER: Well, it does say in water, so.

DR. BELSITO: I missed that. Yeah.

DR. SNYDER: It would correlate. Yeah.

DR. BELSITO: Pardon?

DR. SNYDER: It was (Inaudible), certainly, and within water.

DR. BELSITO: But did it say that?

DR. SNYDER: Yeah.

MS. RAJ: So are you looking --

DR. BELSITO: In water. Yeah. I see it. Okay.

MS. RAJ: This is the summary section you're pointing to, right, Dr. Belsito?

DR. BELSITO: Yes.

MS. RAJ: Okay. I can add those details in there. I'm guessing they're higher up. Thank you.

DR. BELSITO: I mean, I didn't have any other comments, other than I don't think they answered our questions. So it's still insufficient for sensitization at higher concentration of use -- either a new HRIPT or let us see the individual data. And then, the individual data may still suggest that it's insufficient. But we didn't get what we asked for. I mean, I would like to see the data on the specific studies, you know, particularly the Glycerel-26 study where you were seeing some of these patients reactive. Is everyone in agreement with that?

DR. SNYDER: I am.

DR. LIEBLER: Yeah.

DR. BELSITO: Any other comments? Okay.

DR. LIEBLER: Answer that.

DR. BELSITO: Pardon?

DR. LIEBLER: Somebody answer that.

DR. BELSITO: No. I'm not going to answer it.

DR. LIEBLER: All right.

DR. BELSITO: They know I'm in meetings. Okay. Then we move on to methicones.

Marks Team – June 8, 2020

DR. MARKS: Okay. I think we're ready to go. We have all the major players here. So we have a memo from Preethi dated February 21st. At the June 2019 meeting -- so a year ago -- the Panel issued an insufficient data announcement for method of manufacture, impurities, and inhalation toxicity. Shortly before the December 2019 meeting, we got a Wave 2 HRIPT summary, et cetera, et cetera. Let me see.

So we are at the point now that we should be issuing a tentative report. The December 2019 IDA was -- we issued it again to clarify HRIPT concerns about reactions seen in the induction phase. We got new HRIPT data with a 10 percent concentration at Glycereth-26, and that looked fine to me.

Alex, your comments didn't seem to affect the final report. So I think we're ready to move on with a tentative report with a safe conclusion, but I may be jumping the gun. Lisa, Ron, Tom, your comments and what would your proposal be for the tentative report? Hopefully, not another IDA. We've done that twice now.

DR. SHANK: If you're satisfied with the HRIPT, then I think we can go ahead and say this is safe.

DR. MARKS: Did you have any concerns, Ron? Because you always look at this and keep me honest.

DR. SHANK: No, I have some editorial things in the discussion.

DR. MARKS: Okay.

DR. SHANK: Let's see. The second to the last paragraph in the discussion on page 40 -- I think that sentence needs to be revised. We received data on the method of manufacture and impurities, and the needs of the Panel have been met. The inhalation data in the earlier report have been misinterpreted, and that's been resolved. So that eliminates the need for further inhalation data. And in the last paragraph of the discussion, the boilerplate on inhalation is unnecessary because we have inhalation toxicity data.

Let's see. The third sentence in the last paragraph, we can delete that sentence. Deposition in these regions other than the deep lung can be of toxicological significance, but they aren't in this case. So I think that last sentence would be better just deleted. And those are the only comments I have, editorial.

DR. MARKS: Okay. Excellent. Yeah. Getting back to the HRIPT on page 37 --

DR. SHANK: Yes.

DR. MARKS: -- they used 10 percent Glycereth-26 on two of the subjects. I thought it was done well. That was -- and the maximum use concentration as 6 percent. They had no changes are visible in the summary here by Preethi. And then I believe page 61 is the final conclusion by the testing laboratory, and there was no irritation seen of the subject. So, yeah. I was fine with the HRIPT, Ron.

DR. SHANK: Great.

DR. BERGFELD: Question. This is Wilma. There is mention that it's used in rinse off at 39.5 percent. Does that need to be addressed in the discussion?

DR. SHANK: For rinse off?

DR. BERGFELD: Yeah. Rinse-off cleansing agent.

DR. SHANK: Yeah.

DR. MARKS: I didn't feel strongly that way, Wilma, but we'll let others comment. I think, as a rinse off, that's much higher than the 10 percent, which the HRIPT didn't bring that up as issue before. I don't think it is. But Ron, Lisa, Tom, your comments?

DR. SHANK: Well, as a rinse off, no, that didn't concern me.

DR. MARKS: Yeah. Okay. Lisa, Tom?

DR. BERGFELD: The question I had -- should it go in the discussion?

DR. MARKS: Okay. I got you, Wilma. So it should be noted and go in the discussion that we didn't feel that with the sensitivity and irritation data we have that this should be a problem since it's a rinse off.

DR. BERGFELD: Right.

DR. MARKS: Lisa, Tom, any other comments? Otherwise, I'll move tomorrow a tentative report with a safe conclusion.

DR. PETERSON: Yeah. I support that, and Ron's suggested edits it to the discussion.

DR. MARKS: Yeah. Preethi, I'm not going to bring up the edits tomorrow unless, Ron, you feel strongly that we should mention in the full panel.

DR. SHANK: No. It's okay.

DR. MARKS: Okay.

MS. RAJ: May I ask the Panel how they felt about -- you know, in the IDA, you had requested details for some of these kind of weird results you got from the HRIPTs with the reactions at the induction level, but the data that we received -- we got that new study, and it wasn't for those studies of concern. So is the Panel okay with that?

DR. MARKS: I am.

DR. SHANK: Okay. So that's good.

MS. FIUME: Jim, can I ask a question regarding bringing up the changes in the discussion for tomorrow?

DR. MARKS: Oh, sure.

MS. FIUME: Did I understand Ron correctly that last paragraph's not needed or should be altered? Because that -- compared to what was in the draft version, that is sort of a major change to remove that whole paragraph, so that could be discussed in open session. We would appreciate that, just because it is such a big change.

DR. SHANK: Okay. The comment I had was in the last paragraph of the discussion, starting with "The Panel discussed the issue", the sentence that says, "Furthermore, droplet particles deposited in the nasopharyngeal or bronchial regions of the respiratory tract present no toxicological concerns --" They can, not in this case, but I don't think that sentence is necessary. So I would like to see that deleted. If the rest of the Panel wants to keep it in, okay. But it's not necessary to say that.

It almost implies that deposition outside of the deep lung isn't really important toxicologically, and that's not true. In this case, deposition in the nasopharyngeal bronchial regions is not a problem. So it's just it may be a toxicology sensitivity. If everybody wants to leave it in, fine.

DR. PETERSON: Now, I agree with you.

MS. FIUME: I was going to say I wasn't questioning whether it should be taken out or not. It's just, because that is because it's part of our typical boilerplate language, it's not truly simply an editorial change because it's something that's in a lot of our reports. So that was the only reason that I was asking that it be discussed in full panel tomorrow because it is a change to boilerplate language.

DR. SHANK: Okay. Well, I looked at the boilerplate for inhalation respiratory exposures, and that boilerplate begins with -- in the second paragraph, it talks about deposition in the nasopharyngeal and bronchiole regions as being important toxicologically or can have toxicological importance. So I didn't realize we say this every time. We shouldn't.

A famous example is formaldehyde. It's not a deep lung problem; it's a nasopharyngeal problem. So if we say it all the time, then I guess leave it in.

DR. MARKS: Now, Ron, I think --

DR. SHANK: But I can't believe I've missed it every time.

DR. MARKS: Hey, Ron.

DR. SHANK: Yes.

DR. MARKS: I think what you bring up as the definition of an expert is say it every time with greater -- you say the wrong thing every time with greater confidence. That's the definition of an expert. So just saying this every time in the past, somehow, perhaps, we're not right on.

So I think tomorrow what I'll do is bring it up. I'll say, Ron -- I'll ask you, Ron, to comment about your edits of deleting a sentence in the last paragraph concerning the inhalation resource document. I think that's our new terminology. We're not using boilerplate anymore.

MS. FIUME: That's correct.

DR. MARKS: And then I think what it can be done is -- although we can easily make the change. You know, it is a tentative report, so that's not a big deal. But I think going forward about future use of the inhalation boilerplate or resource document -- that perhaps that needs to be changed.

DR. BERGFELD: Can I make a --

DR. MARKS: Does that sound reasonable, Ron and Monice?

DR. SHANK: Well, in our resource document, the first thing we discussed is deposition in the nasopharyngeal and bronchiole. I think that's right. Let me look. I have it here.

DR. MARKS: While Ron's looking that up, Lisa or Tom, do you have any comments? And we've actually had this discussion several times in the past in terms of inhalation toxicity and not ignore the upper airway. Yes, Wilma?

DR. BERGFELD: Well, why can't we do a compromise? Why can't we explain why the inhalation is not of concern due to the study that was done?

DR. SHANK: Okay. That's good.

DR. PETERSON: Works for me.

DR. SHANK: So do we leave that sentence in or not?

DR. BERGFELD: Well, I think you take everything out, and you explain why you don't need it.

DR. SHANK: Maybe too much emphasis on it. Okay. You can leave it in. We'll see if Curt has any objection to it, but it's not a big deal.

DR. MARKS: Okay, Ron.

DR. SHANK: I'll withdraw my editorial.

MS. FIUME: Ron, I just want to make clear I wasn't questioning your wanting to change it. I was just asking that it was brought up tomorrow because I thought Jim said that it wasn't going to be necessarily brought up. That was my only question for that aspect of the discussion.

DR. SHANK: I see.

DR. MARKS: That's exactly right, Monice. So Ron, that was the only thing of your editorial comments that I really -- and Monice -- picked out as far as making sure that the Belsito team was aware of it.

DR. MARKS: Do you want me to --

DR. SHANK: Leave it in.

DR. MARKS: -- bring it up tomorrow or just see it, not say anything, and let you bring it up if you want to, Ron, thinking between now and tomorrow?

DR. SHANK: It's okay to leave it in.

DR. MARKS: Okay.

DR. SHANK: It's not worth taking Panel time to discuss.

DR. MARKS: Okay.

DR. SHANK: It's merely an emphasis in toxicology that really doesn't -- I'm not comfortable with that kind of a statement, but if we've been saying it all the time, I guess --

DR. PETERSON: Well, for what it's worth, I get stuck on that statement every time I read it because, without data, what do you know? And I'm not an expert in inhalation, so I just underscore, Ron, your uncomfortableness.

DR. SHANK: Thank you. Okay. I'll bring it up tomorrow and see. If Curt says I'm silly, leave it in and everybody else wants to leave it in, go ahead.

DR. MARKS: Well, you've already had Lisa say it's not silly, and I think it would good to -- I'm glad tomorrow you're going to bring it up, Ron.

DR. SHANK: Okay. I'll bring it up.

DR. MARKS: I will say our team will move that a tentative report be issued with a safe conclusion.

DR. SHANK: Okay.

DR. MARKS: And that, Ron, if I forget to mention you having a potential inhalation edit in the discussion, remind me. Don't hesitate to do that.

DR. SHANK: Okay. That's good.

MS. RAJ: I have a few questions. So is it safe to say for the inhalation toxicity as far as -- Dr. Bergfeld was saying that we should refer to the studies we have? This is in the acute tox section because I don't see -- I don't think we have inhalation anywhere else.

DR. BERGFELD: No, just there.

MS. RAJ: Okay. And Dr. Shank, what you mentioned in the discussion for, I think, that section where it says that we have method of manufacture or received method of manufacture and impurities data, therefore, we don't need inhalation data -- so it's basically just removing that last part just to say that the data needs were met?

DR. SHANK: Yes, because --

DR. MARKS: Because at the December meeting --

DR. SHANK: -- it shouldn't say --

MS. RAJ: It was misinterpreted before. Yeah. The data.

DR. SHANK: Yes. So we don't need -- the reason we don't need acute inhalation toxicology data is not because we have methods of manufacture and impurities. It's because we have some inhalation data, and it had been misinterpreted the first time.

MS. RAJ: Okay.

DR. SHANK: Not by you.

MS. RAJ: Thank you.

DR. MARKS: Okay. Any other comments?

MS. RAJ: But for the discussion though, if we are going to go -- or if the Panel's going go with the tentative safe conclusion, what kind of language would you want in the discussion to say that the existing HRIPTs assure you of safety?

DR. MARKS: Basically, that -- that we got the 10 percent, which is above the leave-on use concentration, and that was clean. It showed no evidence of sensitivity. I think Don was the one who brought up the concern about reactions seen in the induction phase in a previous study, although, in the challenge phase, it was okay. So this is reassuring based on our previous data.

And then, again, it addresses what Wilma brought up. There's a much higher concentration of rinse off, but, because it being a rinse off, we're not concerned that it's going to cause sensitivity or allergic contact dermatitis. Yeah. Any other comments? Preethi, is that okay?

MS. RAJ: I think so. If anyone else has anything to add for the discussion, I'd be glad to hear it but yep.

DR. MARKS: Okay. So tentative report safe conclusion and we'll see what happens tomorrow. Obviously, being a tentative report, we're going to get another crack at this in the draft final report. Okay. Okay. Methicones.

Full Panel – June 9, 2020

DR. MARKS: So, in June of 2019 we issued an insufficient data announcement, and then in December 2019 we got data, but we issued another insufficient data announcement that we wanted clarification of sensitivity since there was concern about reactions seen in one of the HRIPTs in the induction phase.

We got new HRIPT data in which 10 percent Glycereth-26 was clean, so our team feels we can move forward with a tentative report with a safe conclusion for these ingredients.

DR. BERGFELD: Dr. Belsito?

DR. BELSITO: Well, we were very disturbed by the fact that when you look at the report in question, that there were actually several reports that weren't totally clear. The Glycereth-26 report, in particular, I wanted to look at and look at the individual data in terms of the responders; all of that data was totally redacted from the study. And so, we felt that it was still insufficient for all the reasons we had previously asked for. I would like to see that individual data. The individual data they gave us were only on the studies that were totally clean, which is not the data we wanted.

DR. MARKS: So you didn't think the new data with the 10 percent, which is above use concentration, was satisfactory then, Don? You still want to go back and see those other conflicting studies.

DR. BELSITO: Yes. I wanted to see it and get a better sense of what was going on there. Let me just close this out and look at that new study again.

DR. MARKS: Yeah, that was on Page 37 has the summary, but on Page 61 is the actual report, the conclusion. So, if you look on Page 61, Don.

DR. BELSITO: I have it.

DR. MARKS: Good.

MS. EISENMANN: This is Carol. It's a 1973 study and I don't think that the individual data ever existed: it's a slansky study. And I think the strong point of the study is that it was 10 percent in water, so you don't have any other confounding ingredients.

DR. MARKS: Yeah, so Carol, that reinforce for me why I felt we could move forward with a safe conclusion. And I guess we haven't seen case reports of any significance, or outbreaks like we'll be discussing in a bit.

DR. BELSITO: So the amount of test material was not specified. It was secured for 24 hours, the patch was removed, contact site was retested for -- was rested for 24 hours, and there were repeats three times a week for five week, 15 applications. And then, again it was retested with an amount that wasn't specified. And, there were no visible skin changes upon challenged. And, the test was deemed a non-sensitizer. And then, the individual data for that is on Page 61, right Jim?

DR. MARKS: Yeah. Page 61 is basically the summary conclusions.

DR. BELSITO: Right.

DR. MARKS: No visible skin changes...

DR. BELSITO: And, again, there's no data on that; it's totally redacted all of that data. No visible skin changes, signifying reaction to injury, were observed in any of the 200 subjects. And, it also doesn't say --

DR. MARKS: And that was for the applications 2 through 15, so that's the induction. And then when the challenge, they saw no skin changes also. So, even though it was redacted I assumed it would be all zeros based on what -- that is what they're saying in that.

MS. EISENMANN: I don't think it was redacted, I'm not sure it ever existed. I'm not sure in 1973 they ever recorded individual data at that point. Because I did ask for the individual data and they said they did not have it.

DR. MARKS: Okay.

MS. EISENMANN: So, it's not like they're hiding something; they don't have it.

DR. MARKS: So I guess, Don, when I saw that, that the challenge, there were no skin changes and in the -- or, I mean the applications and then get it at the challenge, I was willing to accept this to support a safe conclusion. But, again, if you still have concerns I guess it would go out as a tentative report with insufficient. But, I'm not sure we're going to get much more, but, you know... Ron, I'm certainly willing to go along with your feelings.

DR. BELSITO: I mean, what are Dan, Curt, Paul...? And, I just don't like seeing a study where I don't see any of the individual data, and I just get someone's summation that there was no evidence of "injury".

DR. SNYDER: Well, we didn't really have an issue with this study, because it was clear. It was those other HRIPTs that had quirky results we were concerned about, and you wanted to better understand why they were, you know, not as clean as this study.

DR. BELSITO: Right, exactly. And, we did not get the individual data on those studies that we asked for.

DR. LIEBLER: Yeah, that's what I think we need to be expecting. We need those data; that's the issue.

DR. MARKS: So, it wouldn't have mattered if we had this study right off the get-go; this was added since then, Carol submitted this data since the IDA was issued. So, you still want to --

DR. BELSITO: You know, when I look at studies, sensitization studies in particular, and I see some quirky stuff going on during the challenge, I like to look at the individual data and, you know, if it's one or two particular people, they may just have hypo-irritable skin or whatever. But, if it's popping up in different groups, I think then that raise a little bit of a red flag for me. And, in this submission that we have, it's what, 47 years old, it just has a summary statement of the results, we have no individual data, I mean, it's just not totally comfortable, but again, as you say, there aren't really -- you don't see Glycereth-26 popping up as notorious contact allergen. On the other hand, we never thought that alkyl glucosides were contact allergens until people started testing them, and who's testing Glycereth-26. I mean, I still would like to see that data. I'll let my other team members talk.

DR. LIEBLER: I agree.

DR. MARKS: Okay. I'll withdraw the motion. So, Don, do you want to propose it? This would be a tentative report with an insufficient conclusion.

DR. BELSITO: Yes. So, we want to see the actual data for the previously submitted HRIPTs, the one on 5 percent Glycereth-26, and the one -- I'm sorry, those were the ones that were clean.

MS. RAJ: Dr. Belsito, this is Preethi, I think you're referring to, so there was a two percent Glycereth-7, three percent Glycereth-26, and then a three percent Glycereth-26 rinse-off, and then a leave-on. Those were the four, I guess, questionable sensitization studies.

DR. BELSITO: Exactly, yes. I wanted to see the individual data on those studies.

DR. BERGFELD: Jim, you want to respond with a second or other discussion?

DR. MARKS: Oh, yeah. I have already withdrawn, yes, I second that motion.

DR. BERGFELD: Okay. Are there any other needs that might be added to this discussion?

DR. LIEBLER: Wilma, I have a comment, maybe we can cover it after the vote, I guess. I just want to (audio skip), okay?

DR. BERGFELD: Okay. I'll come back to you. Any other discussion or comment regarding the vote?

MS. RAJ: Dr. Shank, did you want to bring up your comment on the sentence in the inhalation explanation in the discussion?

DR. SHANK: No.

MS. RAJ: No. Okay.

DR. BERGFELD: All right. Now, we're going to call the vote. All those in favor of that of the conclusion of insufficient with the insufficiencies being described as details of various studies, indicate by raising your hand. Anyone opposing, please be verbal. None? Unanimous, then.

And now, I understand there are a couple of discussion points or comments. Is it Dan, and then Ron?

DR. LIEBLER: Sure, so this is one of the first reports where we've made extensive use of some read-across of molecules. And, I made some edits to the report to introduce essentially what I hope will be the beginnings of some boilerplate language we can use when we introduce a read-across chemical. And, I have these before each of the sections where we do this. And I'm just going to read one of them just to give you a flavor for it. And, maybe we can send these around to the Panel so they can see these. These can certainly be wordsmith, or if you'd like Lisa and I to go back and forth on this a little bit more, but this is my sort of opening gambit on this. This is based on the RIFM language.

So, for ocular irritation, for example, I say, the ocular irritation data were not found for Glycerin Ethoxylates. However, data for ethoxylated glycerol were reported for -- and then provide a reference -- which enabled the evaluation of ocular irritation. The read-across analog is a mixture of compounds identical to glycereth ethoxylates. These molecules are predicted to have similar absorption, distribution, metabolism, and chemical reactivity to Glycerin Ethoxylates, and these compounds are expected to have similar toxicological profiles.

So I have, you know, sort of cut and paste variations of that for several other endpoints for which we use read-across molecules. And I would propose that in our reports going forward we make this a standard practice, when we introduce read-across molecules, at the place where we trot them out.

And then, in addition to that, I suggested adding a new Table 3, which would simply have the structures of the read-across molecules, next to the target molecule so that the reader can see for themselves the similarities. We can eventually build this out with more information about the chemical/physical properties of the read-across molecules themselves, compared to the target substances.

Those of you who have looked at RIFM reports know that these can be very extensive, you don't need to start that way, but it provides documentation for the rational application of the read-across molecules in our reports.

DR. BERGFELD: Wonderful addition, thank you so much. Thank you, Lisa, also. Ron Shank, do you have a comment?

DR. SHANK: No.

DR. BERGFELD: Any comments regarding the read-across information and the development of this new addition to our documents?

DR. SHANK: No, not at this time.

DR. BERGFELD: All right, I'm going to call the vote -- oh, I did call the vote. Everybody voted, excuse me. We're going to end the discussion and we're going to move on to the next ingredient, which is Tris Citrate, Dr. Belsito.

Safety Assessment of Glycerin Ethoxylates as Used in Cosmetics

Status: Draft Final Report for Panel Review
Release Date: November 13, 2020
Panel Meeting Date: December 7-8, 2020

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.; Lisa A. Peterson, Ph.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. Previous Panel member involved in this assessment: James G. Marks, Jr., M.D. The Cosmetic Ingredient Review (CIR) Executive Director is Bart Heldreth, Ph.D. This safety assessment was prepared by Alice Akinsulie, former Scientific Analyst/Writer, and Preethi Raj, Senior Scientific Analyst/Writer, CIR.

1620 L Street, NW, Suite 1200 ♢ Washington, DC 20036-4702 ♢ ph 202.331.0651 ♢ fax 202.331.0088 ♢
cirinfo@cir-safety.org

DRAFT ABSTRACT

The Expert Panel for Cosmetic Ingredient Safety (Panel) assessed the safety of 8 glycerin ethoxylates, as used in cosmetic formulations. All of these ingredients are reported to function in cosmetics as skin-conditioning agents, and most are also reported to function as viscosity-decreasing agents. The Panel reviewed relevant data relating to the safety of these ingredients. The Panel concluded that the available data are insufficient to make a determination of safety that the ethoxylated glycerin ingredients are safe under the intended conditions of use in cosmetic formulations.

INTRODUCTION

This is a safety assessment of the following 8 glycerin ethoxylates as used in cosmetic formulations:

Glycereth-3	Glycereth-18
Glycereth-7	Glycereth-20
Glycereth-8	Glycereth-26
Glycereth-12	Glycereth-31

According to the web-based *International Cosmetic Ingredient Dictionary and Handbook* (wINCI; *Dictionary*), all of these ingredients are reported to function in cosmetics as skin-conditioning agents, and most are reported to function as viscosity decreasing agents (Table 1).[1]

The rationale for this grouping of ingredients stems from the fact that these ingredients are structurally-related as polyethylene glycol ethers of glycerin. The Expert Panel for Cosmetic Ingredient Safety (Panel) has reviewed the safety of other similar, structurally-related, families of ingredients. In 2010, the Panel issued a final report on the safety of polyethylene glycols (PEGs); the Panel concluded that the PEGs are safe in the present practices of use and concentration.[2] In 2015, the Panel issued a safety assessment on glycerin, with the conclusion that glycerin was safe as a cosmetic ingredient in the practices of use and concentration described in the safety assessment.[3] Additionally, the Panel has issued safety assessment reports of structurally-related polyethoxylated compounds, such as alkyl PEG ethers and PEGs cocamine, in which it was concluded that these ingredients are safe in the present practices of use and concentration.[4,5] These reports are available on the Cosmetic Ingredient Review (CIR) website (https://www.cir-safety.org/ingredients).

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 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.

Much of the data included in this safety assessment was obtained from robust summaries submitted to the European Chemicals Agency (ECHA) by companies as part of the REACH chemical registration process.[6] The REACH dossier was prepared for ingredients with the generic CAS No. 31694-55-0 (identified as glycerol, ethoxylated in the dossier), but the specific identities of the ingredients were not discerned; the identification of the test article in each study was provided as a trade name, and those trade names were not found in the *Dictionary*. However, because these data were included as part of the REACH dossier on ethoxylated glycerols, they are included in this safety assessment as potential read-across. Additionally, data for read-across chemical analogs of ethoxylated glycerols, such as propoxylated nitrilotriethanol, have been included, when appropriate. If it is known that a test substance is a cosmetic ingredient, then the INCI name is used; otherwise, a generic term that identifies that test substance (e.g., ethoxylated glycerol) is used.

CHEMISTRY

Definition and Structure

These ingredients are polyethylene glycol ethers of glycerin, as depicted in **Figure 1**.

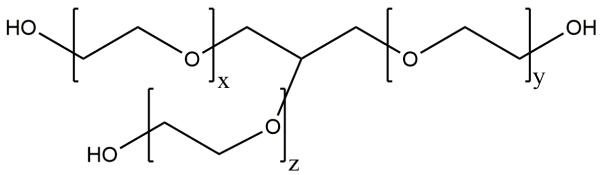


Figure 1. Glycerin ethoxylates, wherein the average ethoxylation value equals x + y + z (e.g., x + y + z = 3 in the case of Glycereth-3)

The definition of each ingredient, as given in the *Dictionary*, is provided in Table 1. This group of ethoxylated glycerin ingredients is identified by the CAS No. 31694-55-0.[1] For the data summarized herein as ethoxylated glycerol, the REACH

dossier describes the average ethoxylation value as between 1 and 6.5, inclusive of 1 and 6.5. Thus, the average ethoxylation value for ethoxylated glycerol may be described as $1.0 \leq x + y + z \leq 6.5$ for the test material evaluated in those summaries. While ethoxylated glycerin is not precisely defined as a cosmetic ingredient, comparing this range of average ethoxylation values to those of the ingredients in this report, Glycereth-3 (i.e., $x + y + z = 3$) falls in that range. Accordingly, structurally, ethoxylated glycerol is a suitable candidate for a read-across source to these ingredients, especially Glycereth-3. Justifications for the use of propoxylated nitriloethanol, propoxylated glycerol, and ethoxylated glycerol as read-across sources are provided in Table 2, and such use is described in the body of the report.

Chemical Properties

Ethoxylated glycerin is a non-volatile (vapor pressure 0.0000389 hPa at 20 ºC), slightly viscous liquid at room temperature, and it is fully miscible with water.[6] Physical and chemical properties of glycerin ethoxylates are presented in Table 3.

Method of Manufacture

These ingredients, in general, are the products resulting from the reaction of glycerin and ethylene oxide.[7] Glycerin ethoxylates belong to the chemical class of alkoxylated alcohols which are also polyether alcohols (specifically, polyethylene glycol ethers of glycerin). Polyether alcohols are often formed from the reaction of an alcohol with an alkylene oxide, such as ethylene or propylene oxide.[1] Since the ether formed from the reaction of one molecule of an alcohol with one molecule of the alkylene oxide is also an alcohol, the reaction with the alkylene oxide can continue until the latter is consumed.

Alkaline catalysis is a common method of manufacturing ethoxylated glycerols, as seen in the manufacturing of alkyl PEG ethers.[4] The initiation of the alkaline catalyzed synthesis of ethoxylated glycerin consists of the addition of an alkoxide, such as ethylene oxide, to a dry solution of the appropriate alcohol (e.g., glycerin). The reaction continues to propagate (i.e. continues to add additional units of ethylene oxide to the alcohol) until the available ethylene oxide is consumed or the reaction is terminated by the addition of an acid. The finishing step consists of adding one or more oxidizing agents (e.g., hydrogen peroxide) or antioxidants/stabilizers (e.g., butylated hydroxytoluene (BHT) or α-tocopherol (vitamin E)).

Impurities

A previous Panel safety assessment of the chemically similar alkyl PEG ethers confirms that dioxane (1,4-dioxane) and ethylene oxide can be present as reaction by-products.[4]

Glycereth-26

In a certificate of analysis provided by a manufacturer, it was noted that Glycereth-26 contained < 0.0005% 1,4-dioxane, < 0.0001% ethylene oxide, 0% free glycerin, and 0.05% water.[8]

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. Use frequencies of individual ingredients in cosmetics are collected from manufacturers and reported by cosmetic product category in the FDA Voluntary Cosmetic Registration Program (VCRP) database. Use concentration data are submitted by the cosmetic industry in response to a survey, conducted by the Personal Care Products Council (Council), of maximum reported use concentrations by product category.

These ingredients are used in a variety of rinse-off and leave-on cosmetics products. According to 2020 VCRP survey data, Glycereth-26 is reported to be used in 437 formulations, and Glycereth-7 is reported to be used in 80 formulations (Table 4).[9] The three other in-use ingredients are reported to be used in 21 formulations or less. The results of the concentration of use survey conducted by the Council in 2018, and updated in 2019, indicate Glycereth-26 has the highest maximum concentration of use, at 39.5% in skin cleansing products.[10] The highest concentration of use reported for products resulting in leave-on dermal exposure is 6% Glycereth-26 in eye lotion formulations.

Uses were reported in the VCRP for Glycereth-20, but no concentration of use was reported for this ingredient in response to the industry survey. The three ingredients not reported to be in use by both the VCRP and industry survey, are Glycereth-3, -8, and -31.

A few of the glycerin ethoxylate ingredients could be used in products that may be incidentally ingested or come into contact with mucous membranes; for example, Glycereth-7 is reported to be in 67 lipstick formulations (concentration of use data were not reported for this category) and Glycereth-18 is reported to be used in bath soaps and detergents at a maximum concentration of 0.3%. Additionally, these ingredients have been reported to be used in products that may come into contact with the eyes; for example, Glycereth-26 is reported to be used at up to 6% in eye lotions. Moreover, these ingredients are reported to be used in spray products that could possibly be inhaled. Glycereth-26 was reported to be used at up to 1% in body and hand spray formulations. In practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters > 10 μm, with propellant sprays yielding a greater fraction of droplets/particles < 10 μm

compared with pump sprays.[11,12] Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and thoracic regions of the respiratory tract and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.[13,14]

The ingredients named in the report are not restricted from use in any way under the rules governing cosmetic products in the European Union.[15]

Non-Cosmetic

Ethoxylated glycerol is used in a number of non-cosmetic applications such as modelling clay adhesives, sealants, polymer preparations and compounds, coatings, and paints.[6]

TOXICOKINETICS STUDIES

Toxicokinetic data (such as dermal penetration and absorption, distribution, metabolism, and excretion data) were not discovered in the published literature, and unpublished data were not submitted.

TOXICOLOGICAL STUDIES

Acute Toxicity Studies

The acute dermal, oral, and inhalation studies summarized below are described in Table 5.

The dermal LD_{50} of ethoxylated glycerol in male and female Wistar rats was > 5000 mg/kg.[6]

The oral LD_{50} of ethoxylated glycerol tested at concentrations of 1 - 50% was > 10 ml/kg in male and female Fischer 344 rats.[6] In female Wistar rats, the oral LD_{50} of ethoxylated glycerol was > 2000 mg/kg. In another oral toxicity study, the LD_{50} of ethoxylated glycerol in Sprague-Dawley rats was > 10,000 mg/kg. In an acute oral toxicity study of Glycereth-26, the LD_{50} was determined to be > 5000 mg/kg in male and female albino rats.[16]

In an acute inhalation toxicity study, performed in accordance with Organization for Economic Co-operation and Development test guideline (OECD TG) 403, no mortality was observed when male and female rats were exposed (whole body) to an aerosol of 3.575 mg/l of ethoxylated glycerol for 8 h.[6] In an inhalation study of ethoxylated glycerol, performed in accordance with OECD TG 403, in which rats were exposed to 0.178 mg/l of the test article for 7 h, no mortalities were observed.[6] Similarly, no mortalities were observed in rats following exposure (whole body) to 0.143 mg/l of the ethoxylated glycerol for 7 h as a vapor.

Short-Term Toxicity Studies

Oral short-term toxicity data were not found for the glycerin ethoxylates reviewed in this report. However, data for propoxylated nitrilotriethanol were reported [6] which enabled read-across evaluation of short-term toxicity. This read-across source is of similar structure to glycerin ethoxylates, with a small core structure modified with propoxy groups. These molecules are predicted to have similar absorption, distribution, metabolism, and chemical reactivity to glycerin ethoxylates and these compounds are expected to have similar toxicological profiles.

Oral

Propoxylated nitrilotriethanol (a read-across source)

A pilot study was performed using 2 male and 2 female Wistar rats.[6] Animals were administered a propoxylated nitrilotriethanol (with molar equivalents of 3.2 propoxyl) at doses of 0, 65, 160, 400, and 1000 mg/kg, for 2 wk. (No other details were provided). No clinical findings or relevant effects on body weight development were observed.

In a short-term oral exposure study, a propoxylated nitrilotriethanol (MW ~ 340 g/mol) in water was administered once daily by gavage to Wistar rats (5 per sex) at doses of 0, 100, 300, and 1000 mg/kg for 31 d in accordance with OECD TG 407.[6] No mortality was observed in either sex. There was no effect observed upon hematological, clinical biochemistry, or macroscopic examination at any dose. The histopathological evaluation revealed slightly more pronounced hypertrophy of the follicular cell epithelium in the thyroid gland of females of the high dose. Biochemical analysis revealed significantly low plasma creatinine concentrations in males dosed with 1000 mg/kg and higher levels in all groups of treated females. Based on these results, the no-observable-adverse-effect-level (NOAEL) was considered to be 1000 mg/kg bw/day.

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY STUDIES

Developmental and reproductive toxicity data were not found for the glycerin ethoxylates reviewed in this report. However, data for propoxylated nitrilotriethanol were reported,[6] which enabled evaluation of developmental and reproductive toxicity. The read-across source is of similar structure to glycerin ethoxylates, with a small core structure modified with propoxy groups. These molecules are predicted to have similar absorption, distribution, metabolism and chemical reactivity to glycerin ethoxylates and these compounds are expected to have similar toxicological profiles.

Oral

Propoxylated nitrilotriethanol (a read-across source)

A reproductive/developmental toxicity screen test was performed in accordance with OECD TG 421.[6] Groups of 12 male and 12 female Wistar rats were administered a propoxylated nitrilotriethanol (average MW 280 g/mol) in water at doses of 0, 100, 300, and 1000 mg/kg bw, by gavage. Typically, in a study following this TG, females are dosed throughout the study; however, that was not stated in the summary. The rats in each dose group were allowed to deliver. Body weights were determined daily during pregnancy, and dams were examined shortly after birth and on day 4 postpartum. Transient salivation was noted in both sexes of the parental rats dosed with 1000 mg/kg. Slight body weight loss occurred in females of the 1000 mg/kg dose group during lactation, and marginal body weight gains were noted during the premating period at all doses. Neither significant embryotoxic or teratogenic effects, nor abnormalities, were noted, and no effects on reproductive performance were observed. Four pups from the F_1 generation developed filiformed tip at 1000 mg/kg, compared to 3 pups in the control group. No-observable-effect-levels (NOELs) were determined to be 100 mg/kg in females and 300 mg/kg in males, based on increased incidence of salivation. During the premating phase, a statistically significant body weight increase, compared to the control group, was observed in the 1000 mg/kg female group. However, the NOAEL was determined to be 1000 mg/kg, as a slight body weight reduction in females within the highest dose group (1000 mg/kg bw/day) was not considered adverse.

GENOTOXICITY STUDIES

Genotoxicity data were not found for the glycerin ethoxylates reviewed in this report. However, data for ethoxylated glycerol, propoxylated glycerol and propoxylated nitrilotriethanol were reported,[6] which enabled evaluation of genotoxicity. These read-across sources are mixtures of compounds similar or identical to glycerin ethoxylates. These molecules are predicted to have similar absorption, distribution, metabolism and chemical reactivity to glycerin ethoxylates and these compounds are expected to have similar toxicological profiles.

In Vitro

Glycereth-3 (ethoxylated glycerol, a read-across source)

The mutagenicity of ethoxylated glycerol was evaluated in an Ames test, performed in accordance with OECD TG 471.[6] *Salmonella typhimurium* strains TA 1535, TA 1537, TA 98, and TA 100 and *Escherichia coli* WP2 were studied with and without metabolic activation. The test article, dissolved in water, was administered at concentrations of 0, 33, 100, 333, 1000, 2500, and 5000 µg/plate. Appropriate positive and negative controls were used. The test article did not produce any mutagenic effects.

Propoxylated glycerol (a read-across source)

In a mammalian chromosomal aberration study performed in accordance with OECD TG 473, a propoxylated glycerol was considered to be non-clastogenic to human lymphocytes with or without metabolic activation.[6] (No other details were provided.)

Propoxylated nitrilotriethanol (a read-across source)

Chinese hamster lung fibroblasts (CHL) V79 cells were used in a mammalian cell gene mutation assay (hypoxanthine-guanine phosphoribosyl transferase (HGPRT) test) to evaluate the mutagenicity of a propoxylated nitrilotriethanol (average MW 265 g/mol) in ethanol.[6] Cells were treated with the test article at concentrations of 400, 800, 1200, 1600, 2000, 2400, and 2800 µg/ml without metabolic activation and 42, 84, 168, 336, 672, 1344, and 2688 µg/ml with metabolic activation. Appropriate positive and negative controls were used. The test article did not induce mutagenic effects in the presence or absence of metabolic activation.

CARCINOGENICITY STUDIES

Carcinogenicity studies were not found in the published literature, and unpublished data were not provided.

DERMAL IRRITATION AND SENSITIZATION STUDIES

The dermal irritation and sensitization studies summarized below are described in Table 6.

In an vitro study, performed in accordance with OECD TG 439, it was determined that no irritation occurred when 30 µl of ethoxylated glycerol was applied undiluted to a reconstructed three-dimensional human epidermis model (EpiDerm™).[6]

In a study using methods comparable to OECD TG 404, no edema or erythema occurred when 1 ml of ethoxylated glycerol was applied to the shaved skin of 2 Vienna white rabbits, under occlusion.[6] The test article was considered to be non-irritating to rabbit skin. Three male and 3 female rabbits had single applications of 0.5 ml of Glycereth-26 applied under an occlusive patch on both abraded and non-abraded sites; the test article was deemed to have no irritation potential.[16] In a

Buehler test, performed in 10 male and 10 female Dunkin Hartley guinea pigs, in accordance with OECD TG 406, propoxylated glycerol was shown to be a non-sensitizer.[6]

An undiluted leave-on spray formulation containing 1.68% Glycereth-7 was tested in an occlusive human repeat insult patch test (HRIPT) in 199 subjects.[17-19] No participants withdrew due to adverse reactions; 4 subjects exhibited low-level reactions; the test material did not induce dermal sensitization. A rinse-off, cleanser formulation containing 2% Glycereth-7 was tested in a similar occlusive HRIPT in 211 subjects.[18,19] Two subjects exhibited low-level reactions during induction, and 11 subjects exhibited low-level reactions during challenge. An occlusive HRIPT of a mascara formulation containing 0.35% Glycereth-12 was completed in 100 subjects; there were no signs of irritation or sensitization.[20] In an HRIPT of a 3% Glycereth-26 rinse-off product in 103 subjects, 5 subjects exhibited low-level reactions during induction, and 1 subject exhibited a low-level reaction during challenge. The test material was deemed a non-sensitizer. The contact sensitization potential of a topically applied formulation containing 3% Glycereth-26 was evaluated in a maximization study of 27 subjects.[21] No instances of contact allergy or irritation were observed during the challenge scorings, and the test substance was deemed a non-sensitizer. A leave-on product containing 3% Glycereth-26 was tested in an HRIPT in 200 subjects; 27subjects exhibited low-level reactions during induction.[17,19] The researchers concluded that the test material did not induce significant dermal irritation or allergic contact sensitization. Low level reactions were observed during the induction phase of an HRIPT, completed in 200 subjects, evaluating a leave-on product containing 3% Glycereth-26.[19,22] Twenty-four subjects exhibited low-level reactions, and 1 subject exhibited a high-level reaction during induction; the researchers concluded that the test material did not induce dermal sensitization. A product containing 5% Glycereth-26 was tested in an HRIPT on 55 subjects; the test material did not demonstrate a potential for eliciting dermal irritation or allergic contact sensitization.[23] A modified semi-occlusive HRIPT of a shaving oil formulation containing 8.75% Glycereth-26 was completed in 221 subjects.[24] Faint erythema was noted following removal of the initial 24-h application on 11 subjects and in 1 subject following the challenge application, however, these effects dissipated within 24 h. The test material was not found to be a skin irritant or sensitizer. An HRIPT of a 10% aqueous solution of Glycereth-26 was performed in 200 subjects.[25] No visible skin changes were observed, and test substance was deemed a non-sensitizer.

OCULAR IRRITATION STUDIES

The ocular irritation studies summarized below are described in Table **7**.

The potential irritation of ethoxylated glycerol was studied in a bovine corneal opacity and permeability (BCOP) test conducted according to OECD TG 437.[6] It was concluded the test substance does not cause serious eye damage. In an EpiOcular™ assay, a 20% aqueous dilution of a product containing 0.35% Glycereth-12 (actual test concentration, 0.07% Glycereth-12) was tested using 100 µl; the estimated Draize ocular irritation score of the test material at 100% was predicted to be 0, and it was classified to be non-irritant.[26] The ocular irritation potential of undiluted Glycereth-26 (100 µl) was evaluated in vitro in an EpiOcular™ human cell assay.[27] The ET_{50} (time to reduce tissue viability as measured using a 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay) was > 4 h for Glycereth-26; this was predicted to be non-irritating in the BCOP test, and it was classified as not irritating. In another eye irritation test evaluating ethoxylated glycerol, in accordance with OECD TG 405 and using an EpiOcular™ three-dimensional human cornea model, the test article was considered to be non-irritating.[6]

The ocular irritation potential of ethoxylated glycerol was evaluated in 2 Vienna white rabbits using a test method that is similar to OECD TG 405.[6] Slight conjunctivae redness was observed in both animals after 10 min, 1 h, and 3 h; these effects were fully reversible within 24 h and the test article was found to be non-irritating. In another study, two Vienna white rabbits were used to test the ocular irritation potential of ethoxylated glycerol following a protocol similar to OECD TG 405.[6] Hyperemia was noted in the blood vessels of both animals. In one animal, this effect was not fully reversible within 8 d; however, a similar observation was noted in the control eye of this animal. The test article was considered non-irritating. Six rabbits were administered a single 1.8 - 2.4 g, 0.1 ml, dose of Glycereth-26, without washing, for 24 h.[16] Ocular irritation to eye mucosa, cornea, iris, and bulbar/palpebral conjunctivae was observed; however, the irritation score was 0.0, and the test article was deemed non-irritating under these test conditions.

SUMMARY

This is a safety assessment of 8 glycerin ethoxylates as used in cosmetics. These ingredients are all polyethylene glycol ethers of glycerin. All of the ingredients in this report are reported to function as skin-conditioning agents, and most are reported to function as viscosity decreasing agents. Ethoxylated glycerols, propoxylated nitrilotriethanol and propoxylated glycerol were considered structurally, and hence toxicologically, similar to glycerin ethoxylates; data for these substances are included in this safety assessment as read-across sources for these ingredients.

These ingredients are mostly used in leave-on formulations. Glycereth-26 has the highest reported frequency of use (437 formulations), and Glycereth-7 has the second greatest reported number of uses (80). Glycereth-26 has the highest concentration of use, at 39.5% in skin cleansing products. The highest concentrations of use reported for products resulting in leave-on dermal exposure is 6% Glycereth-26 in eye lotions.

The acute dermal LD_{50} of ethoxylated glycerol was calculated to be > 5000 mg/kg in Wistar rats. No acute toxicity was observed when ethoxylated glycerol was administered orally at concentrations ranging from 1 - 50% to male and female Fischer 344 rats. The oral LD_{50} was determined to be > 10 ml/kg. No evidence of toxicity was observed in an acute oral toxicity study using female Wistar rats; the oral LD_{50} of ethoxylated glycerol was determined to be > 2000 mg/kg. Similarly, no evidence of toxicity was reported when ethoxylated glycerol was administered orally to Sprague-Dawley rats, and the LD_{50} was > 10,000 mg/kg. In an acute oral toxicity study of Glycereth-26, the LD_{50} was determined to be > 5000 mg/kg dose.

Two studies were performed in accordance with OECD guidelines, in which rats were used to determine acute inhalation toxicity. Ethoxylated glycerol at a concentration of 3.575 mg/l, was tested in rats as an aerosol/mist for 8 h. No mortality occurred. The acute inhalation toxicity of ethoxylated glycerol was evaluated in a study involving rats. Animals were exposed whole-body to 0.178 mg/l, for 7 h, and 0.143 mg/l in experiment 2, for 7 h each. No mortality occurred.

In a pilot study, 2 male and 2 female Wistar rats received a propoxylated nitrilotriethanol at doses of 0, 65, 160, 400, and 1000 mg/kg, for 2 wk; no clinical findings or relevant effects on body weight development were observed. In a repeated dose toxicity study, rats (5 per sex) were administered a propoxylated nitrilotriethanol (MW ~ 340 g/mol) in water at doses of 0, 100, 300, and 1000 mg/kg for 31 d. No mortality and no clinical effects were observed in either sex of all dose groups. The histopathological evaluation revealed slightly more pronounced hypertrophy of the follicular cell epithelium in the thyroid gland of females of the high dose. Based on these results, the NOAEL was considered to be 1000 mg/kg bw/day.

A reproductive/developmental toxicity screening test was performed with 12 male and 12 female Wistar rats. Animals were administered a propoxylated nitrilotriethanol (average MW = 280 g/mol) in water at doses up to 1000 mg/kg. The rats in each dose group were allowed to deliver. Transient salivation was noted in both sexes of the parental rats dosed with 1000 mg/kg. Slight body weight loss occurred in females of the 1000 mg/kg dose group during lactation and marginal body weight gains were noted during the premating period at all doses. There were no effects on total body weights or viability of offspring, and no embryotoxic or teratogenic effects were reported. The NOAEL was > 1000 mg/kg bw/day.

Ethoxylated glycerol was not mutagenic in Ames tests at concentrations up to 5000 µg/plate, with or without metabolic activation, in S. *typhimurium* strains TA 1535, TA 1537, TA 98, and TA 100, or *E. coli* WP2. In a mammalian chromosomal aberration study, a propoxylated glycerol was not clastogenic to human lymphocytes (concentrations not reported), with or without metabolic activation. A propoxylated nitrilotriethanol was evaluated for genotoxicity in a mammalian cell gene mutation assay with CHL fibroblasts at doses of 400, 800, 1200, 1600, 2000, 2400, and 2800 µg/ml (-S9), and 42, 84, 168, 336, 672, 1344, and 2688 µg/ml (+S9) in ethanol. The test article did not induce mutagenic effects in the presence or absence of a metabolic activation system.

According to the results of an EpiDerm™ assay, ethoxylated glycerol is not expected to be irritating. In a dermal irritation study, ethoxylated glycerol was applied for 20 h to a shaved skin area of 2.5 cm x 2.5 cm on 2 Vienna white rabbits using an occlusive dressing. The test article was considered to be non-irritating to the skin. In another study, 3 male and 3 female rabbits had 0.5 ml of Glycereth-26 applied once under an occluded patch on both abraded and non-abraded sites, with no signs of irritation observed at 24 and 72 h after application. The test article was deemed to have no irritation potential. The sensitization potential of a propoxylated glycerol (MW = 300 g/mol) was evaluated in a Buehler test using 10 male and 10 female Dunkin Hartley guinea pigs. Six-h occlusive patches of undiluted test article were used for both induction (days 1, 7, and 14) and challenge. The test article was not a sensitizer.

An undiluted spray formulation containing 1.68% Glycereth-7 was tested undiluted for skin sensitization potential in an HRIPT completed in 199 subjects. Four subjects exhibited low-level reactions during induction; the test material did not induce dermal sensitization. A rinse-off product containing 2% Glycereth-7 was tested for skin sensitization potential via occlusive HRIPT, in up to 211 subjects. Two subjects exhibited low-level reactions during induction, and 11 subjects during challenge, for the rinse-off product, and the test material was deemed non-sensitizing. A mascara formulation containing 0.35% Glycereth-12 was evaluated for skin sensitization potential in an HRIPT using 100 subjects. Neither irritation nor sensitization were observed. A rinse-off product containing 3% Glycereth-26 was tested undiluted in a semi-occlusive HRIPT in 103 subjects; 5 subjects exhibited low-level reactions during induction, and 1 subject exhibited a low-level reaction during challenge; the test substance was deemed non-sensitizing. The contact sensitization potential of a topical formulation containing 3% Glycereth-26 was evaluated in a maximization study using 27 subjects. No instances of post-challenge contact allergy or irritation were observed and the test substance was deemed a non-sensitizer. A leave-on product containing 3% Glycereth-26 was evaluated in an HRIPT in 200 subjects. Twenty-seven subjects exhibited low-level reactions during induction; the researchers concluded that the test material did not induce significant dermal irritation and allergic contact sensitization. A leave-on product containing 3% Glycereth-26 was tested undiluted in an occlusive HRIPT in 200 subjects; 24 subjects exhibited low-level reactions, and 1 subject exhibited a high-level reaction, during induction; the test material did not induce dermal sensitization. The skin sensitization potential of a product containing 5% Glycereth-26 was evaluated in an HRIPT involving 55 subjects. No adverse reactions were observed, and there were no instances of dermal irritation or allergic contact sensitization. An HRIPT of a shaving oil formulation containing 8.75% Glycereth-26 was completed in 221 subjects; faint erythema that was observed in 11 subjects during induction and 1 subject following challenge resolved within 24 h, and the test material was not found to be a skin irritant or sensitizer. An HRIPT was performed in 200 subjects on a

10% aqueous solution of Glycereth-26; neither changes in skin nor signs of sensitization were observed during the induction or challenge applications.

The potential of ethoxylated glycerol to cause damage to the eyes was evaluated in vitro in a BCOP test and in an EpiOcularTM assay. The test article did not show ocular irritation potential under either the test condition. In an EpiOcularTM assay, a 20% aqueous dilution of a product containing 0.35% Glycereth-12 was predicted to not be an ocular irritant, and in the same type of assay, undiluted Glycereth-26 was predicted to be non-irritating.

The ocular irritation potential of ethoxylated glycerol was studied using rabbits. The test article was found to be non-irritating. In another study, in which 50 µl of undiluted ethoxylated glycerol was applied to the conjunctival sac of one eye of 2 white Vienna rabbits, hyperemia was noted in blood vessels of both animals. In one animal, this effect was not fully reversible within 8 d; however, a similar observation was made in the control eye; and, the test article was determined to be non-irritating. In rabbits administered single instillations of 1.8 - 2.4 g, 0.1 ml, Glycereth-26 for 24 h without washing, the ocular irritation score was 0.0, and the test article was deemed non-irritating under these test conditions.

DISCUSSION

The 8 glycerin ethoxylates reviewed in this document are structurally-related as PEG ethers of glycerin

Data for a few toxicological endpoints were not available for these ingredients; however, several endpoints for read-across sources, including acute toxicity, short-term toxicity, oral developmental and reproductive toxicity, genotoxicity, in vitro dermal irritation, animal sensitization, and animal ocular irritation, have been included this report. The Panel considered propoxylated nitrilotriethanol, propoxylated glycerol, and ethoxylated glycerol to have similar chemical and toxicological profiles to the ingredients being reviewed, and felt that these read-across sources could be utilized, as appropriate, to mitigate data gaps. Furthermore, the Panel deemed these read-across sources as representative of lower molecular weight glycerin ethoxylates, and were reassured due to their previous review of polyethoxylated ingredients.

The Panel discussed the issue of incidental inhalation exposure from formulations which are aerosolized, such as the body and hand spray formulations containing 1% Glycereth-26. The Panel noted that in aerosol products, 95% – 99% of droplets/particles would not be respirable to any appreciable amount. Furthermore, droplets/particles deposited in the nasopharyngeal or bronchial regions of the respiratory tract present no toxicological concerns. In results from an acute inhalation study of rats with an aerosol of 3.575 mg/l Glycereth-3, the smallest and most volatile of these ingredients, no mortality and no clinical or gross pathology was observed. Coupled with the small actual exposure in the breathing zone and the concentrations at which the ingredients are used, the available information indicates that incidental inhalation would not be a significant route of exposure that might lead to local respiratory or systemic effects. 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.

Finally, the Panel did not suspect any mechanistic basis for sensitization by these ingredients, as this family of polyether alcohols does not have the propensity to react with proteins, or to produce metabolites that would cause concern. However, HRIPT summaries for several ingredients reported low-level reactions during the induction, and sometimes challenge, phase. The Panel…[TBD]

CONCLUSION

The Expert Panel for Cosmetic Ingredient Safety concluded that the available data are insufficient to make a determination that the following 8 ethoxylated glycerin ingredients are safe under the intended conditions of use in cosmetic formulations.

Glycereth-3*	Glycereth-8*	Glycereth-18	Glycereth-26
Glycereth-7	Glycereth-12	Glycereth-20	Glycereth-31*

** Not reported to be in current use.*

TABLES

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

Ingredient CAS No.	Definition	Function(s)
Glycereth-3 31694-55-0 (generic)	Glycereth-3 is the polyethylene glycol ether of glycerin with an average ethoxylation value of 3. [The chemical structure of this ingredient conforms to that of Figure 1, wherein x + y + z = 3.]	Skin-Conditioning Agents - Emollient; Surfactants - Cleansing Agents; Surfactants - Emulsifying Agents
Glycereth-7 31694-55-0 (generic)	Glycereth-7 is the polyethylene glycol ether of glycerin with an average ethoxylation value of 7. [The chemical structure of this ingredient conforms to that of Figure 1, wherein x + y + z = 7.]	Skin-Conditioning Agents - Humectant; Viscosity Decreasing Agents
Glycereth-8 31694-55-0 (generic)	Glycereth-8 is the polyethylene glycol ether of glycerin with an average ethoxylation value of 8. [The chemical structure of this ingredient conforms to that of Figure 1, wherein x + y + z = 8.]	Skin-Conditioning Agents - Emollient; Skin-Conditioning Agents - Humectant; Viscosity Decreasing Agents
Glycereth-12 31694-55-0 (generic)	Glycereth-12 is the polyethylene glycol ether of glycerin with an average ethoxylation value of 12. [The chemical structure of this ingredient conforms to that of Figure 1, wherein x + y + z = 12.]	Skin-Conditioning Agents - Humectant; Viscosity Decreasing Agents
Glycereth-18 31694-55-0 (generic)	Glycereth-18 is a polyethylene glycol ether of glycerin containing an average of 18 moles of ethylene oxide. [The chemical structure of this ingredient conforms to that of Figure 1, wherein x + y + z = 18.]	Skin-Conditioning Agents - Humectant
Glycereth-20 31694-55-0 (generic)	Glycereth-20 is the polyethylene glycol ether of glycerin with an average ethoxylation value of 20. [The chemical structure of this ingredient conforms to that of Figure 1, wherein x + y + z = 20.]	Skin-Conditioning Agents - Humectant; Viscosity Decreasing Agents
Glycereth-26 31694-55-0 (generic)	Glycereth-26 is the polyethylene glycol ether of glycerin with an average ethoxylation value of 26. [The chemical structure of this ingredient conforms to that of Figure 1, wherein x + y + z = 26.]	Skin-Conditioning Agents - Humectant; Viscosity Decreasing Agents
Glycereth-31 31694-55-0 (generic)	Glycereth-31 is the polyethylene glycol ether of glycerin with an average ethoxylation value of 31. [The chemical structure of this ingredient conforms to that of Figure 1, wherein x + y + z = 31.]	Skin-Conditioning Agents - Humectant; Viscosity Decreasing Agents

Table 2. Read across justification

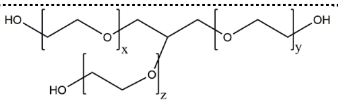
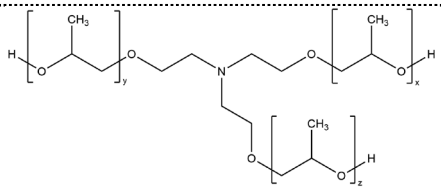
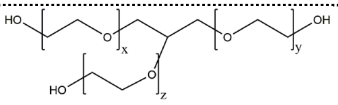
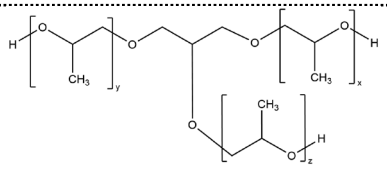
	Target Ingredient(s)	Read-Across Source
Name	***Glycerin ethoxylate ingredients***	*Propoxylated nitriloethanol*[6]
CAS No.	31694-55-0	31694-55-0
Structure		
read-across endpoints		• short-term toxicity – oral • DART, oral • genotoxicity; in vitro
justification	similar small core structure modified with propoxyl groups; molecules are predicted to have similar absorption, distribution, metabolism, chemical reactivity, and toxicological profiles	
Name	***Glycerin ethoxylates ingredients***	*Propoxylated glycerol*[6]
CAS No.	31694-55-0	31694-55-0
Structure		
read-across endpoints		• genotoxicity; in vitro • dermal sensitization; animal
justification	similar small core structure modified with propoxyl groups; molecules are predicted to have similar absorption, distribution, metabolism, chemical reactivity, and toxicological profiles	

Table 2. Read across justification

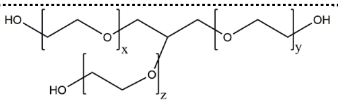
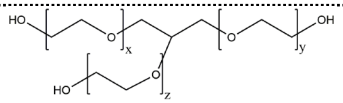
	Target Ingredient(s)	Read-Across Source
Name	***Short-chain glycerin ethoxylate ingredients, especially Glycereth-3***	*Ethoxylated glycerol*[6]
CAS No.	31694-55-0	31694-55-0
Structure		
read-across endpoints		• acute toxicity; dermal, oral; inhalation • genotoxicity; in vitro • dermal irritation; in vitro • ocular irritation; in vitro, animal
justification	mixture of compounds similar to glycerin ethoxylates; molecules are predicted to have similar absorption, distribution, metabolism and chemical reactivity to glycerin ethoxylates and these compounds are expected to have similar toxicological profiles	

Table 3. Chemical Properties

Property	Value	Reference
	Glycereth-3	
Molecular Weight (g/mol)	224.25	[28]
log P	-1.79 (estimated)	[28]
	Ethoxylated glycerol (a read-across source for Glycereth-3)	
Physical Form	clear liquid	[6]
Density (g/ml @ 20ºC)	1.163	[6]
Viscosity (mPa·s @ 20 ºC)	399	[6]
Vapor pressure (hPa @ 20ºC)	0.0000389	[6]
Melting Point (ºC)	-49.1	[6]
Boiling Point (ºC))	260	[6]
Water Solubility (g/l @ 20ºC)	1000	[6]
	Glycereth-7	
Physical Form	Yellow to amber color, mild odor	[29]
Molecular Weight (g/mol)	400.47	[28]
log P	-2.42 (estimated)	[28]
	Glycereth-8	
Molecular Weight (g/mol)	444.52	[28]
log P	-2.57 (estimated)	[28]
	Glycereth-12	
Molecular Weight (g/mol)	620.73	[28]
log P	-3.19 (estimated)	[28]
	Glycereth-18	
Molecular Weight (g/mol)	885.05	[28]
log K_{ow}	-7.19 (estimated)	[30]
	Glycereth-20	
Molecular Weight (g/mol)	972.57	[28]
log K_{ow}	-7.73 (estimated)	[30]
	Glycereth-26	
Physical Form	Yellow to amber color, mild odor	[31]
Molecular Weight (g/mol)	1237.47	[28]
log K_{ow}	-9.38 (estimated)	[30]
Acid value (mg KOH/g)	0.2	[8]
Hydroxyl value (mg KOH/g)	133.40	[8]
Ash content (following pyrolyzation)	0.04%	[8]
Specific gravity (at 25°C)	1.134	[8]
Dissociates in water (at pH, in 5% aq solution)	6.6	[8]
	Glycereth-31	
Molecular Weight (g/mol)	1457.74	[28]
log K_{ow}	-10.75 (estimated)	[30]

Table 4. Frequency (2020)[9] and concentration (2019)[10] of use data for glycerin ethoxylates

	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)
	Glycereth-7		**Glycereth-12**		**Glycereth-18**	
Totals*	**80**	**1 - 2**	**6**	**0.09 - 0.35**	**21**	**0.019 - 0.32**
Duration of Use						
Leave-On	*76*	*1*	*6*	*0.21 - 0.35*	8	*0.019 - 0.3*
Rinse-Off	*4*	*2*	*NR*	*0.09*	13	*0.3 - 0.32*
Diluted for (Bath) Use	*0*	*NR*	*NR*	*NR*	NR	*NR*
Exposure Type						
Eye Area	NR	NR	3	0.09-0.35	NR	0.019-0.036
Incidental Ingestion	67	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	6[a]; 2[b]	NR	2[b]	NR	5[a]; 1[b]	NR
Incidental Inhalation-Powder	2[b]	NR	2[b]	NR	1[b]	0.3[c]
Dermal Contact	13	1- 2	4	0.09- 0.21	21	0.036-0.32
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR
Mucous Membrane	68	NR	NR	NR	9	0.3
Baby Products	NR	NR	NR	NR	NR	NR

	Glycereth-20		**Glycereth-26**		
Totals*	**3**	**NR**	**437**	**0.3 - 39.5**	
Duration of Use					
Leave-On	*3*	*NR*	338	*0.3 - 6*	
Rinse Off	*NR*	*NR*	99	*0.9 - 39.5*	
Diluted for (Bath) Use	*NR*	*NR*	NR	*NR*	
Exposure Type					
Eye Area	NR	NR	18	2-6	
Incidental Ingestion	NR	NR	NR	NR	
Incidental Inhalation-Spray	2[a]; 1[b]	NR	5; 128[a]; 138[b]	1; 0.3-2[a]	
Incidental Inhalation-Powder	1[b]	NR	138[b]	1[c]	
Dermal Contact	2	NR	385	1-39.5	
Deodorant (underarm)	NR	NR	NR	NR	
Hair - Non-Coloring	NR	NR	50	0.3-1	
Hair-Coloring	NR	NR	1	NR	
Nail	NR	NR	NR	NR	
Mucous Membrane	NR	NR	35	NR	
Baby Products	NR	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 these products may be sprays, but it is not specified whether the reported uses are sprays.

[b] Not specified whether a powder or a spray, so this information is captured for both categories of incidental inhalation.

[c] It is possible these products may be powders, but it is not specified whether the reported uses are powders.

Table 5. Acute toxicity studies

Test Article Concentration/Vehicle	Animals	No./Group	Dose/Protocol	LD_{50}/Results	Reference
			Dermal		
Ethoxylated glycerol; undiluted	Wistar rats	5/sex	According to OECD TG 402. Rats were dermally administered 5000 mg/kg test article; applied to a 40 cm^2 skin area and covered by a semi-occlusive dressing for 24 hours.	No mortality occurred. No systemic clinical signs were observed during clinical examination. No local effects were observed. LD_{50} is > 5000 mg/kg	6
			Oral		
Ethoxylated glycerol; in water	Fischer 344 rats	13 male and 11 females	Similar to OECD TG 401. Three females were administered 0.025 ml/kg of a 1% (v/v) solution another 3 female rats were administered 0.2 ml/kg of a 10% solution. Three male rats were administered 1.6 ml/kg of a 10% solution. Another 5 male rats were administered 3.2 ml/kg of a 50% solution. Five females were administered 6.4 ml/kg of a 50% solution and 5 males were administered 10 ml/kg of a 50% solution. Ten untreated animals were used as a negative control.	No mortality occurred and no abnormalities observed. The LD_{50} in male and female rats is > 10 ml/kg.	6
Ethoxylated glycerol; undiluted	Wistar rats	2 groups of 3 females	According to OECD TG 423. Both groups of rats were administered a maximum dosage-volume of 1.73 ml/kg, and received a 2000 mg/kg dose of the test article, via gavage	No mortality occurred. No clinical signs were observed during the observation period. The mean body weight of the test groups increased throughout the study period within the normal range. LD_{50} is > 2000 mg/kg	6
Ethoxylated glycerol; undiluted	Sprague-Dawley rats	5/sex	Similar to OECD TG 401. Five male rats were administered with 11,550 mg/kg bw and 5 female rats were exposed at a dose 10,000 mg/kg bw. Animals were observed for 14 d after administration.	No mortality occurred. Diarrhea was noted for a few hours after application; aggressiveness, convulsion and dirty fur were observed at days 3 and 4; animals fully recovered within 5 d. LD_{50} in male and female rat is > 10,000 mg/kg	6
Glycereth-26	Albino rats	5/sex	Animals were dosed orally (route of administration not specified) with 5000 mg/kg bw and were observed for 14 d for toxicity endpoints.	No mortality occurred during the observation period and the LD_{50} was determined to be > 5000 mg/kg	16
			Inhalation		
Ethoxylated glycerol	White, normal rats	3/sex	Similar to OECD TG 403. Rats were exposed to 3.575 mg/l of the test article in an aerosol/mist form for 8 hours and observed for 14 d.	No mortality or clinical signs of toxicity noted	6
Ethoxylated glycerol; no vehicle	Rats	6 animals (males and females)/ experiment	Similar to OECD TG 403. Rats were exposed (whole body) to 0.178 mg/l in experiment 1 and 0.143 mg/l in experiment 2 as a vapor for 7 h and observed for 14 d.	No mortality or clinical signs of toxicity noted.	6

Table 6. Dermal irritation and sensitization studies

Test Article	Concentration/Dose	Test Population	Procedure	Results	Reference
IN CHEMICO / IN VITRO STUDIES					
Ethoxylated glycerol	30 µl, undiluted	EpiDerm™	OECD TG 439. Single application of 30 µl of the test article to the epidermis model. Sterile PBS (30 µl) was used as the negative control. The tissues were washed with sterile PBS 1 h after the application.	Not irritating	[6]
ANIMAL					
Ethoxylated glycerol	1 ml	2 Vienna white rabbits	Comparable to OECD TG 404. Glycereth-3 (1 ml) was applied neat to shaved skin area of 2.5 cm x 2.5 cm by an occlusive dressing for 20 h, and the test sites were observed at 24 h, 48 h, and 8 d. No edema and erythema findings were observed.	Not irritating	[6]
Glycereth-26	0.5 ml	3 male and 3 female rabbits (strain not specified)	A single application of 0.5 ml of Glycereth-26 applied under an occlusive patch on both abraded and non-abraded sites. The tested areas were observed at 24 and 72 h after application. The irritation score was 0.0, and the test article was deemed to have no irritation potential.	Not irritating	[16]
Propoxylated glycerol	0.5 ml	10 male and 10 female Dunkin Hartley guinea pigs	OECD TG 406; Buehler test. Animals were patched with 0.5 ml of the undiluted test article (MW 300 g/mol) for the topical induction, using an occlusive dressing, for 6 h on d 1, 7, and 14. Challenge consisted of a topical application of 0.5 ml undiluted test article held in place by an occlusive dressing for a 6-h exposure period on day 28. Five males and 5 females served as the control group. The test article was not a sensitizer.	Not sensitizing	[6]
HUMAN					
Leave-on spray; 1.68% Glycereth-7	0.2 g	199	In an HRIPT, the test material was applied, under occlusion, for 24 to 48 h via nine, 0.2 g induction applications, made over a 3-wk induction period. After a 2-wk rest period, a 24-h challenge application was made to a previously untreated site in the same manner as the induction applications, and reactions were scored at 24, 48, 72, and 96 h after application. No participants withdrew due to adverse reactions; 4 subjects exhibited low-level reactions (a 0-1 score, on a 0-4 scoring scale) during induction. The test material did not induce dermal sensitization.	Not sensitizing	[17-19]
Rinse-off cleanser; 2% Glycereth-7	1% v/v (in tap water, effective concentration, 0.02%)	211	An HRIPT was conducted. The test material was diluted to 1% v/v with tap water (effective test concentration, 0.02%). Two subjects exhibited low-level (+/-) reactions during induction, and 11 subjects exhibited low-level (+/-) reactions during challenge. The researchers concluded that although there was no primary dermal irritation potential, cumulative dermal irritation and sensitization potential were observed. ((Individual test scores were not provided.)	Not irritating or sensitizing	[18,19]
Mascara; 0.35% Glycereth-12	0.2 g	100	The test material was applied with an occlusive, hypoallergenic patch to the infrascapular regions of the back for 9 applications. After a 14-day rest period, the same concentration and amount of the test substance was used in the challenge phase; patches were applied to a previously untested site, and reactions were scored 24 and 48 h after application. There were no signs of irritation or sensitization in those who completed the study.	Not sensitizing	[20]
Rinse-off product; 3% Glycereth-26	0.02 ml	103	The test material was applied, undiluted, under semi-occlusion, for 24 to 48 h via, nine 0.02 ml induction applications, made over a 3-wk induction period. After a 2-wk rest period, a 24-h challenge application was made to a previously untreated site in the same manner. One participant withdrew due to an adverse reaction; 5 subjects exhibited low-level reactions during induction, and 1 subject exhibited a low-level reaction ("?") at 72 h during challenge. The researchers concluded that although there was no primary dermal irritation, cumulative dermal irritation and sensitization potential was observed.	Not sensitizing	[19,22]

Table 6. Dermal irritation and sensitization studies

Test Article	Concentration/Dose	Test Population	Procedure	Results	Reference
Topical formulation; 3% Glycereth-26	0.05ml	27	A maximization study was performed in which a total of 5 induction applications were made, under occlusion, to the upper outer arm, forearm, or back of subjects. Prior to each induction application, a 24-h application of 0.05 ml of 0.25% aqueous sodium lauryl sulfate (SLS) was made, under occlusion. After removal of the SLS-pre-treatment patch, 0.5 ml of the test material was applied for 48-72 h in an induction patch. If no irritation was present after removal of the induction patch, the 0.25% aqueous SLS patch was reapplied to the same site for 24 h, followed by reapplication of a fresh induction patch with the test material to the same site. However, if irritation occurred during the induction phase, the SLS patch was not re-applied, and a second 0.5 ml patch of the test material was applied to the same site after a 24-h rest period. After a 10-d rest period, subjects were pre-treated with 0.05 ml of 5% aqueous SLS for 1 h on a novel site, prior to a 48-h challenge application, in the same manner as the induction applications. Challenge reactions were scored 15-30 min and 24 after patch removal; no instances of contact allergy or irritation were observed and the test substance was deemed a non-sensitizer.	Not sensitizing	[21]
Leave-on product; 3% Glycereth-26	20 µl	200	The test material was applied, under occlusion, for 48 to 72 h via nine, 20 µl induction applications, made over a 3-wk induction period. After a 2-wk rest period, a 24-h challenge application was made to a previously untreated site in the same manner as the induction applications, and reactions were scored at 48 and 96 h after application. No participants withdrew due to adverse reactions; 27 subjects exhibited low-level reactions (0-1 score, on a 0-7 scale) during induction, and no reactions occurred during challenge. The researchers concluded that the test material did not induce significant dermal irritation or allergic contact sensitization.	Not sensitizing	[17,19]
Leave-on product; 3% Glycereth-26	20 µl	200	The test material was applied, neat, under occlusion, for 24 to 48 h via, nice 20 µl induction applications, made over a 3-wk induction period. After a 2-wk rest period, a 24-h challenge application was made to a previously untreated site in the same manner. No participants withdrew due to adverse reactions; 24 subjects exhibited low-level reactions and 1 subject exhibited a high-level reaction during induction, no subjects exhibited any reactions during challenge. The researchers concluded that the test material did not induce dermal sensitization.	Not sensitizing	[19,22]
5% Glycereth-26	NS	55	An HRIPT was performed in which the test material was applied to a 1 in^2 absorbent pad portion of an adhesive dressing and applied to the skin under semi-occlusion for 24 h. Nine induction applications were made. After a 2-wk non-treatment period, a 24-h challenge application was made to a previously untreated site in the same manner as the induction applications, and reactions were scored 24 and 72 h after application. The test material did not demonstrate a potential for eliciting dermal irritation or allergic contact sensitization.	Not sensitizing	[23]
Shaving oil formulation; 8.75% Glycereth-26	0.15 ml	221	A modified HRIPT was performed in which the test material was applied to a 2 cm^2 absorbent pad portion of a semi-occlusive patch for 24 h. Nine induction applications were made. After a 2-wk non-treatment period, a 24-h challenge application was made to a previously untreated site in the same manner as the induction applications. Reactions to induction applications were scored both prior to, and after patch application, and at 24, 48, and 72 h after challenge application. Faint erythema was noted following removal of the initial 24-h application on 11 subjects and in 1 subject following the challenge application, however, these effects dissipated within 24 h. The test material was not found to be a skin irritant or sensitizer.	Not sensitizing	[24]
10% Glycereth-26, aqueous	NS	200	Discs of lintine paper were moistened with the test material (amount not specified) and secured to a site on the upper arm for 24 h. After 24 h, the patch was removed and the contact site was rested for 24 h. Repeated 24-h patch applications were applied 3 times/wk, for 5 wk, for a total of 15 applications. After a 2-wk non-treatment period, the challenge patch was applied on the same contact sites with the test material (amount not specified) for 24 h under occlusion. Upon removal of the challenge patch, the contact site was examined immediately and after 24 and 48 h. No visible skin changes occurred upon challenge, and test substance was deemed a non-sensitizer.	Not sensitizing	[25]

HRIPT – human repeated insult patch test; MW – molecular weight; NS- not specified; PBS- phosphate buffered saline

Table 7. Ocular irritation studies

Test Article	Concentration/Dose	Test Population	Procedure	Results	Reference
IN VITRO					
Ethoxylated glycerol	750 µl	BCOP test	OECD TG 437. Ethoxylated glycerol was applied directly to the epithelial surface of the cornea using a syringe (open chamber method) for 10 minutes. Highly deionized water was used as the negative control, and a 1% (w/v) solution of sodium hydroxide in highly de-ionized water served as the positive control (treatment group consisted of 3 corneas). The opacity and permeability assessments of the cornea were derived by an IVIS, which is used to classify the irritancy level of the test article. The calculated mean IVIS was 3.0 ± 1.2, 2.6 ± 3.3, and 184.0 ± 20.9 in the test group, the negative control group, and the positive control group, respectively. It was concluded the test substance does not cause serious eye damage in the BCOP test.	Not irritating	[6]
Ethoxylated glycerol	50 µl	EpiOcular™	OECD TG 405. Fifty µl of the undiluted test article was applied (2 tissue sample per treatment). The treated tissue was incubated for 30 minutes, washed out, and post-incubated under normal medium and culture conditions for 2 h. The negative control tissues received applications of 50 µl of highly de-ionized water. The test article was considered to be non-irritating.	Not irritating	[6]
0.35 % Glycereth-12 (20% aqueous dilution)	100 µl; effective concentration 0.07% Glycereth-12	EpiOcular™	Appropriate negative and positive controls were used. The estimated Draize ocular irritation score of the test material at 100% was predicted to be 0, and it was classified to be non-irritant.	Not irritating	[26]
Glycereth-26	100 µl	EpiOcular™, human cell assay	The cell cultures were tested in duplicate, with exposure times of 0.33, 1, 2, and 4 h. Appropriate negative and positive controls were used. The ET_{50} (time to reduce tissue viability as measured using MTT) was > 4 h for Glycereth-26; this was predicted to be non-irritating.	Not irritating	[27]
ANIMAL					
Ethoxylated glycerol	50 µl; undiluted	2 Vienna white rabbits	Similar to OECD TG 405. Undiluted Glycereth-3 was instilled into the conjunctival sac of the right eye of each animal without washing, and the eyes were observed for 8 d. The left eye of the animals remained untreated and served as a control. Slight conjunctivae redness was observed in both animals after 10 min, 1 h, and 3 h. These effects were fully reversible within 24 h. The test article was found to be non-irritating.	Non-irritating	[6]
Ethoxylated glycerol	50 µl	2 Vienna white rabbits	Similar to OECD TG 405. Undiluted ethoxylated glycerol was instilled into the conjunctival sac of one eye of each animal. The saline-treated contralateral eye served as a control. The eyes were not washed out and were observed for a total of 8 d. Hyperemia was noted in the blood vessels of both animals. In one animal, this effect was not fully reversible within 8 d; however, a similar observation was noted in the control eye of this animal. The test article was considered non-irritating.	Non-irritating	[6]
Glycereth-26	1.8-2.4g, 0.1 ml	6 rabbits (strain not specified)	The animals received a single instillation of the test article dose, without washing for 24 h. Ocular irritation to eye mucosa, cornea, iris, and bulbar/palpebral conjunctivae was observed for 7 d. However, the irritation score was 0.0, and the test article was deemed non-irritating under these test conditions.	Non-irritating	[16]

BCOP- bovine corneal opacity and permeability

IVIS – in vitro irritancy score

REFERENCES

1. Nikitakis J, Kowcz A. Web-Based *International Cosmetic Ingredient Dictionary and Handbook* (wINCI *Dictionary*). http://webdictionary.personalcarecouncil.org/jsp/IngredientSearchPage.jsp. Washington, D.C.: Personal Care Products Council. Last Updated 2020. Accessed 1/26/2020.

2. Bergfeld WF, Belsito DV, Hill RA, et. al. Final Report of the Cosmetic Ingredient Review Expert Panel of the Amended Safety Assessment of Triethylene Glycol and Polyethylene Glycols (PEGs)-4, -6, -7, -8, -9, -10, -12, -14, -16, -18, -20, -32, -33, -40, -45, -55, -60, -75, -80, -90, -100, -135, -150, -180, -200, -220, -240, -350, -400, -450, -500, -800, -2M, -5M, -7M, -9M, -14M, -20M, -23M, -25M, -45M, -65M, -90M, -115M, -160M and -180M and any PEGs > 4 as used in Cosmetics. 2010. http://www.cir-safety.org/ingredients.

3. Becker LC, Bergfeld WF, Belsito DV, et. al. Safety Assessment of Glycerin as Used in Cosmetics. 2015. http://www.cir-safety.org/ingredients.

4. Fiume MM, Heldreth B, Bergfeld WF, et al. Safety assessment of alkyl PEG ethers as used in cosmetics. *Int J Toxicol*. 2012;31(Suppl 5):169s-244s.

5. Boyer I, Burnett CL, Bergfeld WF, et al. Safety Assessment of PEGs Cocamine and Related Ingredients as Used in Cosmetics. *Int J Toxicol*. 2018;37(2_suppl):10s-60s.

6. European Chemical Agency (ECHA). REACH registration dossier: Glycerol, ethoxylated (CAS 31694-55-0). http://echa.europa.eu/registration-dossier/-/registered-dossier/13553. Last Updated 2020. Accessed 2/8/2019.

7. Hinton C, ed. *The Chemistry and Manufacture of Cosmetics. Vol. III - Ingredients.* Carol Stream, IL: Allured Publishing Company; 2002.

8. Anonymous. 2019. Certificate of analysis: Glycereth-26. Unpublished data submitted by the Personal Care Products Council on June 11, 2019.

9. U.S.Food and Drug Administration (FDA). 2020. U.S. Food and Drug Administration Center for Food Safety & Applied Nutrition (CFSAN). Voluntary Cosmetic Registration Program - Frequency of Use of Cosmetic Ingredients. Obtained under the Freedom of Information Act from CFSAN; requested as "Frequency of Use Data" January 6, 2020; received January 13, 2020).

10. Personal Care Products Council. 2019. Updated concentration of use information: Glycerin Ethoxylate. Unpublished data submitted by Personal Care Products Council on May 9, 2019.

11. Johnsen MA. The Influence of Particle Size. *Spray Technology and Marketing*. 2004;14(11):24-27.

12. Rothe H. 2011 2011. Special aspects of cosmetic spray safety evaluations: Principles on inhalation risk assessment. Unpublished data presented at the 26 September Expert Panel meeting. Washington D.C.

13. Bremmer HJ, Prud'homme de Lodder LCH, van Engelen JGM. Cosmetics Fact Sheet: To assess the risks for the consumer; Updated version for ConsExpo 4. Bilthoven, Netherlands: Netherlands National Institute for Public Health and the Environment; 2006. RIVM 320104001/2006. Pages 1-77. http://www.rivm.nl/bibliotheek/rapporten/320104001.pdf. Accessed 8/24/2011.

14. Rothe H, Fautz R, Gerber E, et al. Special aspects of cosmetic spray safety evaluations: Principles on inhalation risk assessment. *Toxicol Lett*. 2011;205(2):97-104.

15. European Commission. CosIng database;. http://ec.europa.eu/growth/tools-databases/cosing/. Last Updated 2020. Accessed 2/14/2019.

16. Anonymous. 2019. Safety testing summary: Glycereth-26. Unpublished data submitted by the Personal Care Products Council on June 11, 2019.

17. Anonymous. 2019 2019. Summary of HRIPT on leave-on products (containing 0.68% Glycereth-7 and 3% Glycereth-26). Unpublished data submitted by the Personal Care Products Council on August 27, 2019.

18. Anonymous. 2019. Summaries of Two HRIPTs (one product containing 2% Glycereth-7, one product containing 1% Glycereth-7). Unpublished data submitted by the Personal Care Products Council on November 19, 2019.

19. Personal Care Products Council. 2020. Glycerin Ethoxylates: Clarification and Individual Data for HRIPT Study Summaries with PCPC Memos 7 and 8. Details and explanations for previously submitted data provided by the Personal Care Products Council on July 28, 2020.

20. AMA Laboratories I. 2014. Summary of results: 100 human subject repeat insult patch test skin irritation/sensitization evaluation (occlusive patch) product containing 0.35% Glycereth-12. Unpublished data submitted by the Personal Care Products Council on December 19, 2019.

21. KGL, Inc. 2007. An evaluation of the contact-sensitization potential of a topical coded product in human skin by means of the maximizaiton assay (product contains 3% Glycereth-26). Unpublished data submitted by the Personal Care Products Council on July 13, 2020.

22. Anonymous. 2019. Summaries of Two HRIPTs (both products contain 3% Glycereth-26). Unpublished data submitted by the Personal Care Products Council on November 19, 2019.

23. Consumer Product Testing Co. 2016. Individual results: Repeated insult patch test/product containing 5% Glycereth-26. Unpublished data submitted by the Personal Care Products Council on December 19, 2019.

24. Anonymous. 2005. Determination of the Irritating and Sensitizing Propensities of 685310 5 on Human Skin. Unpublished data submitted by the Personal Care Product Council on July 21, 2020.

25. Food and Drug Research Laboratories Incorporated. 1973. Repeated insult patch test: Glycereth-26 (10% aqueous solution tested). Unpublished data submitted by the Personal Care Products Council on January 16, 2020.

26. Anonymous. 2019 2019. Summary information: Safety studies on Glycerin Ethoxylates (Glycereth-12 and Glycereth-26). Unpublished data submitted by the Personal Care Products Council on April 23, 2019.

27. Anonymous. 2019. Summary- Topical Application Ocular Irritation Screening Assay Using the EpiOcular Human Cell Construct. Unpublished data submitted by the Personal Care Products Council on June 11, 2019.

28. ChemDraw Pro. 13.0. Waltham, MA: PerkinElmer Inc; 2018.

29. UPI Chem. Glycereth 7. https://www.upichem.com/products/glycereth-7/. Last Updated 2014. Accessed 10/2/2019.

30. EPI Suite (for Windows)., Environmental Protection Agency. 4.0. Washington, DC.: 2012.

31. UPI Chem. Glycereth 26. https://www.upichem.com/products/glycereth-26/. Last Updated 2014. Accessed 10/2/2019.

2020 Glycerin Ethoxylates VCRP Data

CATEGORY	MAINTERM	COUNT
Glycereth-7; Total: 80		
07E - Lipstick	GLYCERETH-7	67
10E - Other Personal Cleanliness Products	GLYCERETH-7	1
12A - Cleansing	GLYCERETH-7	3
12D - Body and Hand (exc shave)	GLYCERETH-7	2
12F - Moisturizing	GLYCERETH-7	2
12I - Skin Fresheners	GLYCERETH-7	1
12J - Other Skin Care Preps	GLYCERETH-7	1
13B - Indoor Tanning Preparations	GLYCERETH-7	3
Glycereth-12; Total: 6		
03F - Mascara	GLYCERETH-12	2
03G - Other Eye Makeup Preparations	GLYCERETH-12	1
07C - Foundations	GLYCERETH-12	1
12C - Face and Neck (exc shave)	GLYCERETH-12	2
Glycereth-18; Total: 21		
07I - Other Makeup Preparations	GLYCERETH-18	1
10A - Bath Soaps and Detergents	GLYCERETH-18	9
12A - Cleansing	GLYCERETH-18	4
12C - Face and Neck (exc shave)	GLYCERETH-18	1
12F - Moisturizing	GLYCERETH-18	4
12G - Night	GLYCERETH-18	1
12J - Other Skin Care Preps	GLYCERETH-18	1
Glycereth-20; Total: 3		
12C - Face and Neck (exc shave)	GLYCERETH-20	1
12F - Moisturizing	GLYCERETH-20	2
03A - Eyebrow Pencil	GLYCERETH-26	1
Glycereth-26; Total: 437		
03A- Eyebrow Pencil	GLYCERETH-26	1
03D - Eye Lotion	GLYCERETH-26	12
03F - Mascara	GLYCERETH-26	1
03G - Other Eye Makeup Preparations	GLYCERETH-26	4
04A - Cologne and Toilet waters	GLYCERETH-26	3
04E - Other Fragrance Preparation	GLYCERETH-26	1
05A - Hair Conditioner	GLYCERETH-26	9
05B - Hair Spray (aerosol fixatives)	GLYCERETH-26	1
05E - Rinses (non-coloring)	GLYCERETH-26	1
05F - Shampoos (non-coloring)	GLYCERETH-26	27
05G - Tonics, Dressings, and Other Hair Grooming Aids	GLYCERETH-26	4
05I - Other Hair Preparations	GLYCERETH-26	8

06D - Hair Shampoos (coloring)	GLYCERETH-26	1
07C - Foundations	GLYCERETH-26	2
07F - Makeup Bases	GLYCERETH-26	1
07H - Makeup Fixatives	GLYCERETH-26	1
07I - Other Makeup Preparations	GLYCERETH-26	2
10A - Bath Soaps and Detergents	GLYCERETH-26	30
10E - Other Personal Cleanliness Products	GLYCERETH-26	5
11D - Preshave Lotions (all types)	GLYCERETH-26	1
11E - Shaving Cream	GLYCERETH-26	1
11G - Other Shaving Preparation Products	GLYCERETH-26	2
12A - Cleansing	GLYCERETH-26	14
12B - Depilatories	GLYCERETH-26	1
12C - Face and Neck (exc shave)	GLYCERETH-26	126
12D - Body and Hand (exc shave)	GLYCERETH-26	12
12F - Moisturizing	GLYCERETH-26	99
12G - Night	GLYCERETH-26	8
12H - Paste Masks (mud packs)	GLYCERETH-26	7
12I - Skin Fresheners	GLYCERETH-26	8
12J - Other Skin Care Preps	GLYCERETH-26	35
13B - Indoor Tanning Preparations	GLYCERETH-26	7
13C - Other Suntan Preparations	GLYCERETH-26	2

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

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

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

DATE: July 13, 2020

SUBJECT: Glycereth-26

KGL, Inc. 2007. An evaluation of the contact-sensitization potential of a topical coded product in human skin by means of the maximization assay (product contains 3% Glycereth-26).

FINAL REPORT dated November 2, 2007

KGL Protocol: #6389

Sample: [redacted]

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

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

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

E-mail address: ivystudies@verizon.net

[redacted]

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

Product contains 3% Glycereth-26

[redacted]

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

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

Final Report Date: **November 2, 2007**

Kays Kaidbey, M.D.
Principal Investigator

November 2, 2007
Date

FINAL REPORT

KGL PROTOCOL:

Ivy Laboratories - KGL Protocol #**6389**

[redacted]

SPONSOR STUDY:

Authorization Letter Dated: September 12, 2007

STUDY TITLE:

Evaluation of the contact-sensitizing potential of a coded topically-applied test agent.

STUDY OBJECTIVE:

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

TEST MATERIAL:

The test sample, supplied by the sponsor, was a product labeled [redacted]. The test product was tested as supplied viz., neat.

This study was conducted from September 17, 2007 through October 19, 2007

PANEL COMPOSITION:

Healthy, adult volunteers over the age of 18 years were recruited for this study. None of the subjects had a medical or dermatological illness and none were sensitive to sunlight or to topical preparations and/or cosmetics. The criteria for exclusion were:

1 - History of sun hypersensitivity and photosensitive dermatoses

2 - History of drug hypersensitivity or recurrent dermatological diseases

3 - Pregnancy or mothers who are breastfeeding

4 – History of recurrent urticaria or hives

5 - Scars, moles or other blemishes over the test site which can interfere with the study

6 - Subjects receiving systemic or topical drugs or medications, including potential sensitizers within the previous 4 weeks

7 - Other medical conditions considered by the investigator as sound reasons for disqualification from enrollment into the study.

INFORMED CONSENT:

After the protocol, reasons for the study, possible associated risks and potential benefits or risks of the treatment had been completely explained, signed, informed subject consent was obtained from each volunteer prior to the start of the study. Copies of all consent forms are on file at Ivy Laboratories (KGL, INC.).

METHOD:

Patches were applied to the upper outer arm, volar forearm or the back of each subject. The entire test was composed of two distinct phases: (1) an Induction phase and (2) a Challenge phase.

(1) **Induction Phase**:

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

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

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

(2) **Challenge Phase**:

After a ten day rest period which follows the last induction patch application, the subjects were challenged with a single application of the test material to a new skin site on the opposite arm, forearm or side of back in order to determine if sensitization had developed.

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

SCORING SCALE:

0 = not sensitized

1 = mild sensitization (viz. erythema and a little edema)

2 = moderate sensitization (erythema with infiltration, raised, spreading beyond the borders of the patch, with or without vesiculation)

3 = strong sensitization (large vesiculo-bullous reaction).

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

SENSITIZATION RATES:	**GRADES:**	**CLASSIFICATION**:
0 - 2/25	1	Weak
3 - 7/25	2	Mild
8 - 13/25	3	Moderate
14 - 20/25	4	Strong
21 - 25/25	5	Extreme

RESULTS:

A total of twenty-seven (27) healthy, female adult volunteers who satisfied the inclusion criteria were enrolled into this study. Their ages ranged from 22 to 65 years. The demographic data are shown in Table 1. All 27 subjects completed this investigation as outlined in the standard protocol. No adverse or unexpected reactions were seen in any of the panelists during the induction phase.

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

CONCLUSION:

Under the conditions of this test, the test sample labeled [redacted] does not possess a detectable contact-sensitizing potential and hence is not likely to cause contact sensitivity reactions under normal use conditions.

References:

(1) Kligman, A.M.: The Maximization Test. J.I.D., Vol. 47, No. 5, pp. 393-409, 1966.

(2) Kligman, A.M. and Epstein W.: Updating the Maximization Test for Identifying Contact Allergens. Contact Dermatitis. Vol. 1, 231-239, 1975.

TABLE 1

DEMOGRAPHIC DATA

Subject Number:	Subject Initials:	Age:	Sex:	Race:
01	P-R	59	F	C
02	P-G	45	F	C
03	R-C	52	F	C
04	J-K	48	F	C
05	K-L	39	F	C
06	K-M	41	F	C
07	J-E	29	F	C
08	T-M	62	F	C
09	G-V	37	F	C
10	M-D	43	F	C
11	K-M	40	F	C
12	E-W	61	F	C
13	A-M	65	F	C
14	J-F	49	F	C
15	D-M	46	F	C
16	K-R	33	F	C
17	R-S	26	F	C
18	V-V	45	F	C
19	R-V	22	F	C
20	K-D	45	F	C
21	E-E	38	F	C
22	A-H	22	F	C
23	L-B	50	F	C
24	D-D	26	F	C
25	A-J	41	F	B
26	S-M	49	F	C
27	L-S	65	F	C

C = Caucasian
B = Black

TABLE 2

MAXIMIZATION TESTING RESULTS

Sample: [redacted]

Subject Number:	48-Hour Grading	72-Hour Grading
01	0	0
02	0	0
03	0	0
04	0	0
05	0	0
06	0	0
07	0	0
08	0	0
09	0	0
10	0	0
11	0	0
12	0	0
13	0	0
14	0	0
15	0	0
16	0	0
17	0	0
18	0	0
19	0	0
20	0	0
21	0	0
22	0	0
23	0	0
24	0	0
25	0	0
26	0	0
27	0	0

Challenge Readings:

48-Hour Reading – October 18, 2007
72-Hour Reading – October 19, 2007

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

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

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

DATE: July 21, 2020

SUBJECT: Glycereth-26

Anonymous. 2005. Determination of the irritating and sensitizing propensities of 685310 5 on human skin (product contains 8.75% Glycereth-26).

[redacted]

[redacted]

[redacted]

DETERMINATION OF THE IRRITATING AND SENSITIZING PROPENSITIES OF 685310 5 ON HUMAN SKIN

Product contains 8.75% Glycereth-26

PREPARED FOR

[redacted]

6 December 2005

TABLE OF CONTENTS

ABSTRACT

A sample identified as **685310 5** was received by [redacted] on 15 September, 2005. The product was submitted by [redacted] for a patch test to determine whether it possesses any skin-irritating and/or sensitizing potentials.

To accomplish this, Product Investigations initiated a repeated insult patch test study on two-hundred and twenty-six adult volunteers.

The regimen called for nine twenty-four hour applications of the product, i.e. on Mondays, Wednesdays and Fridays during the first three weeks and a single twenty-four hour challenge application on a naive site on Monday of the sixth week.

During the induction phase, the skin was examined and graded when the patch was removed on Tuesday, again just prior to each subsequent application, and on Monday of Week 4. During the challenge phase, the skin was first examined shortly after the patch was removed on Tuesday. Follow-up examinations were conducted Wednesday, Thursday, Friday.

Data were acquired on two-hundred and twenty-five subjects during the Induction Phase of the regimen. No clinically significant adverse effects were detected on any of the subjects.

Data were acquired on two-hundred and twenty-one subjects during the Challenge or Diagnostic Phase of the regimen. No clinically significant adverse effects were detected on any of the subjects.

On the basis of the above-cited observations, **685310 5** was found to possess neither clinically significant skin-irritating nor skin-sensitizing propensities.

The investigator concluded that the data do not contraindicate exposure of the skin to **685310 5** for usages entailing repeated applications commensurate with those that prevailed during the course of this study.

COMPLIANCE WITH GOOD QUALITY ASSURANCE STANDARDS

In my review of the data I have found no discrepancies between the information presented in this report and the records that were kept during the conduct of this study.

[redacted]

12/6/05
Date

[redacted] III
[redacted] Assurance

[redacted]

DETERMINATION OF THE IRRITATING AND SENSITIZING P ROPENSITIES OF 685310 5 ON HUMAN SKIN

1.00 OBJECTIVES:

.01 To determine whether **685310 5** is capable of causing visible skin damage under the conditions of the regimen used in this patch test procedure.

.02 To adjudge whether the skin-damaging capability such as the test material manifests can be attributed to an irritant or sensitizing activity.

.03 To adjudge whether the data acquired in the study population provide an adequate level of confidence in the safety of the appropriate use of the test material by any consumer population.

2.00 SPONSOR:

[redacted]

Project Director: [redacted]

Authorization: Dispatch Note dated 14 September, 2005

3.00 FEATURES OF THE METHOD:

.01 A modified version of the Repeated Insult Patch Test regimen was conducted under double blind conditions on a panel consisting of more than two-hundred subjects at the outset.

.02 The induction regimen called for applications of twenty-four hour durations on Mondays, Wednesdays and Fridays during Weeks Nos. 1, 2, and 3.

.03 The induction regimen called for examinations to be conducted within moments after removal of the first set of applied patching devices on Tuesday and just prior to subsequent applications of the product throughout the remainder of the Initial/Induction Phase. During this phase, the responses that were in evidence just prior to a scheduled application mandated whether applications were to be continued on the same site, switched to a new site, or terminated.

.04 The challenge regimen called for a single application of twenty-four hours duration on a naive site on Monday of Week 6. Post-application examinations were conducted within moments after removal of the patching devices on Tuesday and, subsequently, on Wednesday, Thursday, Friday, and the following Monday.

.05 The study was conducted in compliance with the standards of good clinical practices generally applicable for the protection of the privileges and well-being of individuals who participate in patch test procedures.

4.00 STUDY PRODUCT:

Product Information:	Shaving Oil
Sample №:	**685310 5**
DT#:	015665
Date of Receipt:	15 September, 2005
Form used in study:	neat
[redacted]	20089

5.00 SITE OF STUDY:

[redacted]

STAFF:

[redacted]

6.00 DATES OF STUDY:

Start: 19 September, 2005 Finish: 31 October, 2005

7.00 SELECTION OF SUBJECTS:

.01 RECRUITING:

Individuals interested in participating were recruited from local areas by telephone, flyers, and direct contact.

.02 INFORMED CONSENT:

Individuals who expressed interest in participating were given an informed consent document to read and, after they professed to have a thorough understanding of its contents and were still intent on participating, to sign. This document presented the following information:

a. The number of people that were to be enrolled in the study;
b. the intended use of the product;
c. why the product was being tested;
d. how the test was to be performed;
e. that the regimen was not intended to benefit a subject's health, well being, or quality of life.
f. The different ways that participation may be detrimental to a subject's health, well being, or quality of life.
g. that not all detrimental effects could be foreseen and made known at the time the informed consent was presented for the prospective subject's signature.
h. the commitments which a subject would have to make to ensure that meaningful data would be generated;
i. the responsibilities which a subject would assume in care of the product.
j. the rights endowed on a subject for her/his protection;
k. the avenues of recourse available to a subject who believes that she/he has been misused; and
l. the considerations a subject was entitled to receive and the conditions for receiving them.

.03 DETERMINATION OF ELIGIBILITY:

An individual's eligibility was determined by checking her/his medical history and the answers given in response to specific questions in the informed consent document against the criteria listed below.

a. Inclusion Criteria: Satisfaction of all the following items was obligatory for enrolment:
1) The candidate was between eighteen (18) and seventy (70) years of age inclusive, and
2) agreed to comply fully with the scheduled study regimen, and
3) expressed awareness that a participant would incur risks that would affect her/his well-being, and
4) denied that the stipend had induced her/him to volunteer against her/his better judgement, and
5) had assured the interviewer that she/he had read the informed consent form and had no questions about the informed consent's contents that had not been answered to her/his satisfaction, and
6) had signed the consent form willingly and without reservation.
7) was not participating in any other clinical trials.

b. Exclusion Criteria: Any one of the following items was cause for rejection:
1) The candidate had an illness that contraindicated participation; or
2) a condition that rendered the skin unsuitable for use in this study; or
3) was using dosages of medications that could alter the skin's tolerance; or
4) had a documented history of intolerance to the category of products submitted for study; or
5) was a female who was pregnant or was breast feeding an infant.

.04 PANELS NOS. [redacted]

a. Dedication: The subjects in [redacted] (111subjects) were engaged exclusively in the studies of products submitted by [redacted]

8.00 SITE INFORMATION:

.01 LOCATION:

685310 5 was assigned Band #3 on the left side of the back of each subject.

.02 IDENTIFICATION OF A CONTACT SITE:

The skin around the contact site in current use was marked at each visit. These markings enabled the technicians to locate the site for examinations and for positioning subsequently-applied devices as precisely as was feasible on the previously contacted skin in the absence of the device or other means of identification.

9.00 PATCHING DEVICES:

.01 TYPE OF DEVICE:

Partially-occlusive patching devices were used to convey the product to the skin and to maintain it on its assigned site on each subject. These devices consisted of a 2cm × 2cm absorbent pad centered on the adhesive-coated surface of a 4cm × 2cm water-impermeable plastic film.

.02 PREPARATION OF A PATCHING DEVICE:

a. The webril pad of a patching device was infused with 0.15ml of the test material.

.03 POSITIONING AND REMOVING A PATCHING DEVICE:

a. A prepared device was positioned on its designated site on each subject with the product-treated surface of the pad in contact with the skin.
b. Firm pressure was applied to the backing of the device to effect intimate contact of the pad with the skin and to bond the flanges of the device securely to the skin.
c. When the time came for removing the device, the device was peeled off the skin as gently as was feasible under the circumstances.

10.00 DATA ACQUISITION:

.01 GRADING PROCEDURE:

a. As each subject came in on a scheduled examination day, the technician examined the skin of the contact site.

i. If no adverse effect was detected, a "0" was recorded in the subject's examination record.
ii. If an adverse effect was detected, the technician entered a grade indicating her assessment of the response's intensity.

b. The subject was then sent into the patching room where the site was examined again by a second technician to ascertain independently whether or not the site should be used again. If she disagreed with the first technician's assessment, the application was held in abeyance until the issue could be resolved with the help of the supervisor and/or the investigator.
c. The supervisor or the investigator was called when a disagreement had to be resolved and when responses had to be validated, e.g. responses assigned grades ≥2 or responses showing a decrease ≥2 from the previous value.

.02 CRITERIA FOR GRADING RESPONSE INTENSITY:

Grades were assigned in accordance with the following criteria to designate the intensity of the effects elicited on the skin by the test material.

Morphology	Visible Change	Grade
Preclinical Stage	None	0
Inflammation		
Vascular Dilation:	Faint redness with poorly defined margins	1
	Redness with well-defined margins	2
Infiltration:	Redness plus well-defined edema	3
	Redness plus papules, vesicles or ulceration	4
	Extension beyond the contact area	5

.04 SITE CHANGES:

a. Switch to a Naive Site:
i. A grade 2 response appearing for the first time on a subject mandated switching the next application to a naive contact site immediately.

b. Discontinuation of Applications:
i. A grade 2 response appearing for the second time on a subject mandated immediate termination of applications for the remainder of the induction phase on the affected subject.
ii. A grade 3 response appearing on a subject mandated immediate termination of applications for the remainder of the induction phase on the affected subject.

11.00 REGIMEN FLOW CHART:

	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Week #1	Applied	Removed/Graded	Graded/Applied	Removed in clinic	Graded/Applied	Removed at home	--
Week #2	Graded/Applied	Removed in clinic	Graded/Applied	Removed in clinic	Graded/Applied	Removed at home	--
Week #3	Graded/Applied	Removed in clinic	Graded/Applied	Removed in clinic	Graded/Applied	Removed at home	--
Week #4	Graded	--	--	--	--	--	--
Week #6	Applied naive site	Removed/graded	Graded	Graded	Graded-	--	--
Week #7	--	--	--	--	--	--	--

12.00 INSTRUCTIONS BEFORE INTERRUPTIONS IN THE REGIMEN :

.01 WEEKENDS:

Before being dismissed for the weekends during Weeks 1, 2, and 3, subjects were given instructions to remove their patch at home on Saturday at a specified time, record the time of removal on the provided form, and notify the investigator without delay if the skin showed any of the following changes:

a. a substantial increase in the intensity of an already-elicited response,
b. the spread of a response beyond the area of contact, or
c. the outbreak of a rash on a hitherto unaffected site.

.02 INTERMEDIATE PHASE:

Before being dismissed for the hiatus between the phases the subjects were instructed to notify the investigator without delay if the skin showed any of the changes listed above.

13.00 REGIMEN:

.01 INITIAL/INDUCTION PHASE:

Week #1:

MONDAY:

i. As each subject presented herself/himself at the clinic, the skin of the contact site assigned to the product submitted for study was examined and ascertained to be suitable before applications were begun.
ii. A freshly-prepared device was applied on its assigned site.
iii The skin around the device was marked and the subject was instructed to return on Tuesday.

TUESDAY:

i. As each subject returned, the site-identifying marks were reinforced.
ii. The device was removed by a technician.
iii. The contact site was examined; skin status was graded; the grade was recorded.
iv. The subject was instructed to return on Wednesday.

WEDNESDAY:

i. As each subject returned, the skin of the contact site was graded. The grade was recorded.
ii. A freshly-prepared device was applied.
iii. The site-identifying marks were reinforced and the subject was instructed to return on Thursday.

THURSDAY:

i. As each subject returned, the site-identifying marks were reinforced.
ii. The device was removed by a technician and the subject was instructed to return on Friday.

FRIDAY:

i. As each subject returned, the skin of the contact site was graded. The grade was recorded.
ii. A freshly-prepared device was applied.
iii. The site-identifying marks were reinforced.
iv. The subject was dismissed with instructions to remove the device on Saturday, to record the time of removal, and to return to the clinic on the following Monday for resumption of the regimen.

Week #2 and Week #3:

MONDAY:

i. As each subject returned, the skin of the contact site was graded. The grade was recorded.
ii. The time at which the device was removed on Saturday was recorded.
iii. A freshly-prepared device was applied.
iv. The site-identifying marks were reinforced and the subject was instructed to return on Tuesday.

TUESDAY:

i. As each subject returned, the site-identifying marks were reinforced.
ii. The device was removed by a technician and the subject was instructed to return on Wednesday.

WEDNESDAY:

i. As each subject returned, the skin of the contact site was graded. The grade was recorded.
ii. A freshly-prepared device was applied.
iii. The site-identifying marks were reinforced and the subject was instructed to return on Thursday.

THURSDAY:

i. As each subject returned, the site-identifying marks were reinforced.
ii. The device was removed by a technician and the subject was dismissed with instructions to return on Friday.

FRIDAY:

i. As each subject returned, the skin of the contact site was graded. The grade was recorded.
ii. A freshly-prepared device was applied.
iii. The site-identifying marks were reinforced.
iv. The subject was dismissed with the standard instructions and told to return on the following Tuesday.

Week #4:

MONDDAY:

i. As each subject returned, the skin of the contact site was graded. The grade was recorded.
ii. The time at which the patch was removed on Saturday was recorded.
iii. a) If the subject had undergone all nine induction applications, she/he received instructions to:
i) report back to the clinic on the following Monday to receive the challenge applications, and
ii) notify the investigator without delay should any significant changes occur in the skin of the contact site.
b) If the subject had not received nine induction applications and was deficient without a valid reason, applications were continued.

.02 HIATUS/MAKE UP PHASE-

Week #'s 4 and 5:

After the examination on Tuesday, no procedures were scheduled during this week except make-up applications.

.03 CHALLENGE PHASE-

Week #6:

MONDAY:

i. As each subject returned, the skin of the designated challenge site was examined and ascertained to be free of any conditions that would have rendered it unfit for undergoing the challenge applications.
ii. A prepared device was applied on the naive site.
iii. The skin around the device was marked and the subject was instructed to return on Tuesday.

TUESDAY:

i. As each subject returned, the site-identifying marks around the contact site were reinforced.
ii. The patching device was removed by a technician.
iii. The skin of the contact site was graded; the grade was recorded.
iv. The subject was instructed to return on Wednesday.

WEDNESDAY:

i. As each subject returned, the skin of the contact site was graded; the grade was recorded.
ii. The subject was instructed to return on Thursday.

THURSDAY:

i. As each subject returned, the skin of the contact site was graded; the grade was recorded.
ii. The subject was instructed to return on Friday.

FRIDAY:

i. As each subject returned, the skin of the contact site was graded; the grade was recorded.
ii. The subject was instructed to return on the following Monday.

.04 FOLLOW-UP PHASE:

Week Nos. 7 / 8:

During the two weeks following the exit examination, the subjects were given the opportunity to relay any information concerning effects that were relevant to the characterization of the product as well as to communicate the need for treatment of persistent or newly-occurring responses.

14.00 TABULATION OF CYCLES COMPLETED:

Table Ia.

INITIAL/INDUCTION PHASE - (Weeks 1, 2, 3 and 4)					
NUMBER OF AECs REQUIRED	NO DATA ACQUIRED		DATA ACQUIRED		
	DROP OUTS	EXCUSED	EXCUSED	NON-COMPLIANT	COMPLIANT
9	1 subject	0 subjects	0 subjects	2 subjects	223 subjects

Table Ib.

CHALLENGE/DIAGNOSTIC PHASE - (WEEK 6)					
NUMBER OF AECs REQUIRED	NO DATA ACQUIRED		DATA ACQUIRED		
	DROP OUTS	EXCUSED	EXCUSED	NON-COMPLIANT	COMPLIANT
1	5 subjects	0 subjects	0 subjects	0 subjects	221 subjects

15.00 SUMMARY OF RESULTS:

Table II: MAXIMUM ASSIGNED GRADES PER INDIVIDUAL PARTICIPANT (MAGPIPs)

GRADE	TYPE OF RESPONSE	INDUCTION	CHALLENGE
0	NO VISIBLE CHANGE	214 SUBJECTS	220 SUBJECTS
1	FAINT REDNESS, UNDEFINED BORDER	11 "	1 "
2	MODERATE REDNESS, DEFINED BORDER	0 "	0 "
3	REDNESS + EDEMA	0 "	0 "
4	REDNESS + DEFINITE EDEMA and/or PAPULES	0 "	0 "
	NUMBER OF RESPONDERS	**11 SUBJECTS**	**1 SUBJECT**
	NUMBER OF SUBJECTS PATCHED	**226 "**	**221 "**
	NUMBER OF SUBJECTS PROVIDING DATA	**225 "**	**221 "**
	NUMBER PROVIDING NO DATA	**1 "**	**5 "**

Table III: WEEKLY INCIDENCE OF RESPONSES*

Week №	1			2			3			4			6			7
GRADE	M	T	W-F	M	W	F	M	W	F	M	W	F	M	T	W-F	M
1	B	11	0	0	0	0	0	0	0	0	0	0	B	1	0	--
2	B	0	0	0	0	0	0	0	0	0	0	0	B	0	0	--
3	B	0	0	0	0	0	0	0	0	0	0	0	B	0	0	--
4	B	0	0	0	0	0	0	0	0	0	0	0	B	0	0	--
TOTAL		11	0	0	0	0	0	0	0	0	0	0		1	0	--

16.00 PROTOCOL DEVIATIONS:

On Panel [redacted], two additional subjects were enrolled on Tuesday of Week One. These subjects were patched on Tuesday, Wednesday and Friday of that week

17.00 SIGNIFICANCE OF THE RESPONSES:

.01 INITIAL/INDUCTION PHASE:

No responses were noted on 214 of the 225 subjects who participated in this phase of the study. Faint (grade 1) erythema was noted following removal of the initial 24 hour application on eleven subjects. These effects disappeared within 24 hours. None of these subjects evidenced further irritation despite continued applications on the affected site. The responses noted were insufficient to categorize the product as one that possesses clinically significant skin irritating propensities.

.02 CHALLENGE PHASE:

No responses were noted on 220 of the 221 subjects who participated in this phase of the study. Transient faint (grade 1) erythema was noted following removal of the challenge application on one subject. The absence of significant responses categorizes the product as one that is devoid of clinically significant skin sensitizing propensities that can be detected under the prevailing conditions of study.

.03 FOLLOW-UP PHASE:

The investigator received no communications from any of the subjects during this period that provided a basis for altering his opinion concerning the safety of the test material.

18.00 CLINICAL RELEVANCE:

.01 Inasmuch as the test product proved to be incapable of eliciting persistent skin damage of any substantial degree, a projection can be made with a 95% level of confidence that the incidence of clinically significant skin damage that will be occasioned by the appropriate use of this product will be very low.

.02 This projection is based on these postulates:

- **a.** The regimen which the test product has undergone has proven itself to be one that affords products ample time and opportunity to exercise any latent propensities for eliciting gross skin changes.
- **b.** The regimen imposed a substantially greater degree of stress on the skin than the appropriate daily use of the test product would call for.

19.00 CONCLUSIONS:

.01 **Sample 685310 5** was found to be neither a clinically significant skin irritant nor a skin sensitizer.

.02 The data do not contraindicate exposure of the skin to the product represented by the sample identified as **685310 5** for usages entailing repeated applications commensurate with those that prevailed during the course of this study.

[redacted]

[redacted]

12 Dec 05
Date

[redacted]

	[redacted]					Sample No: 685310 5						[redacted]						Site: L3					
Subj #	INDUCTION PHASE															HIATUS/MAKEUPS					CHALLENGE PHASE					
	WEEK 1					WEEK 2					WEEK 3					WEEK 4					WEEK 6					WK-7
	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M
1	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
2	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
3	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
4	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
5	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
6	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
7	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
8	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
9	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
10	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
11	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
12	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
13	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
14	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
15	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
16	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
17	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
18	B/0	0	0		0	0		0		0	A		0		0	0		0			B/0	0	0	0	0	
19	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
20	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
21	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
22	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
23	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
24	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
25	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
26	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
27	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
28	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
29	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
30	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	

[redacted]

	[redacted]					Sample No: 685310 5					[redacted]						Site: L3					
Subj #	INDUCTION PHASE															HIATUS/MAKEUPS					CHALLENGE PHASE					
	WEEK 1					WEEK 2					WEEK 3					WEEK 4					WEEK 6					WK-7
	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M
31	B/0	1	0		0	0		0		0	0		0		0	0					B/0	1	0	0	0	
32	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
33	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
34	B/0	1	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
35	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
36	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
37	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
38	B/0	1	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
39	B/0	0	0		0	0		0		0	0		0		A	0		0			B/0	0	0	0	0	
40	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
41	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
42	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
43	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
44	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
45	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
46	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
47	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
48	B/0	1	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
49	B/0	0	0		0	0		0		A	0		0		0	0		0			B/0	0	0	0	0	
50	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
51	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
52	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
53	B/0	1	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
54	B/0	0	0		0	0		0		0	0		A		0	0		0			B/0	0	0	0	0	
55	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
56	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
57	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
58	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
59	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
60	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	

[redacted]

	[redacted]					Sample No: 685310 5					[redacted]						Site: L3					
Subj #	INDUCTION PHASE															HIATUS/MAKEUPS					CHALLENGE PHASE					
	WEEK 1					WEEK 2					WEEK 3					WEEK 4					WEEK 6					WK-7
	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M
61	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
62	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
63	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
64	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
65	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
66	B/0	0	0		0	0		A		0	0		A		0	0		0		0	B/0	0	0	0	0	
67	B/0	1	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
68	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
69	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
70	B/0	1	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
71	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
72	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
73	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
74	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
75	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
76	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
77	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
78	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
79	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
80	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
81	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
82	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
83	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
84	B/0	1	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
85	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
86	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
87	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
88	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
89	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
90	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	

[redacted] | Sample No: 685310 5 | [redacted] | Site: L3

Subj #	INDUCTION PHASE															HIATUS/MAKEUPS					CHALLENGE PHASE					
	WEEK 1					WEEK 2					WEEK 3					WEEK 4					WEEK 6					WK-7
	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M
91	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
92	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
93	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
94	B/0	0	0		0	0		0		A	0		0		0	0		0			B/0	0	0	0	0	
95	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
96	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
97	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
98	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
99	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
100	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
101	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
102	B/0	0	0		0	0		0		0	0		0		0	0					A	B/0	0	0	0	
103	B/0	0	0		0	0		0		0	A		0		0	0		0			B/0	0	0	0	0	
104	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
105	B/0	1	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
106	B/0	1	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
107	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
108	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
109	B/0	0	0		0	0		0		0	0		A		0	0		0			B/0	0	0	0	0	
110	B/0	1	0		0	0		0		0	0		0		0	0					B/0	0	0	0	A	
111	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
112	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
113	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
114		B/0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
115		B/0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	

g/g g = grade
top grade = new site
bottom grade = old site

B/0 B = Baseline
0 = Baseline grade

[redacted]

Subj #	[redacted]					Sample No: 685310 5					[redacted]					Site: L3										
	INDUCTION PHASE															HIATUS/MAKEUPS					CHALLENGE PHASE					
	WEEK 1					WEEK 2					WEEK 3					WEEK 4					WEEK 6					WK-7
	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M
1	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
2	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
3	B/0	0	0		0	0		0		0	0		0		0	0					A	A	A	A	A	
4	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
5	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
6	B/0	0	0		A	0		0		0	0		0		0	0					B/0	0	0	0	0	
7	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
8	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
9	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
10	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
11	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
12	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
13	B/0	0	0		0	0		0		0	0		0		0	0					A	A	A	A	A	
14	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
15	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
16	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
17	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
18	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
19	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
20	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
21	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
22	B/0	0	0		0	0		0		0	0		A		Dropped											
23	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
24	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
25	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
26	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
27	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
28	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
29	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
30	B/0	0	0		0	0		A		Dropped																

[redacted]

	[redacted]					Sample No: 685310 5					[redacted]						Site: L3					
Subj #	INDUCTION PHASE															HIATUS/MAKEUPS					CHALLENGE PHASE					
	WEEK 1					WEEK 2					WEEK 3					WEEK 4					WEEK 6					WK-7
	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M
31	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
32	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
33	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
34	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
35	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
36	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
37	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
38	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
39	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
40	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
41	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
42	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
43	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
44	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
45	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
46	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
47	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
48	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
49	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
50	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
51	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
52	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
53	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
54	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
55	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
56	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
57	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
58	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
59	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
60	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	

[redacted]

Subj #	[redacted]					Sample No: 685310 5					[redacted]										Site: L3					
	INDUCTION PHASE															HIATUS/MAKEUPS					CHALLENGE PHASE					
	WEEK 1					WEEK 2					WEEK 3					WEEK 4					WEEK 6					WK-7
	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M
61	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
62	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
63	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
64	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
65	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
66	B/0	Dropped		[redacted]			[redacted]		[redacted]			[redacted]		[redacted]			[redacted]		[redacted]							
67	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
68	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
69	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
70	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	A	A	A	
71	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
72	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	A	
73	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
74	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
75	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
76	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
77	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
78	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
79	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
80	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
81	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
82	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
83	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
84	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
85	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
86	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
87	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	A	0	
88	B/0	0	0	[redacted]	A	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]		B/0	0	0	0	0	
89	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	
90	B/0	0	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]		[redacted]		B/0	0	0	0	0	

[redacted] | Sample No: 685310 5 | [redacted] | Site: L3

Subj #	INDUCTION PHASE															HIATUS/MAKEUPS					CHALLENGE PHASE					
	WEEK 1					WEEK 2					WEEK 3					WEEK 4					WEEK 6					WK-7
	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M
91	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
92	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
93	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
94	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
95	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
96	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
97	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
98	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
99	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
100	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
101	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
102	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
103	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
104	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
105	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
106	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
107	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
108	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
109	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
110	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	
111	B/0	0	0		0	0		0		0	0		0		0	0					B/0	0	0	0	0	

g/g g = grade
top grade = new site
bottom grade = old site

B/0 B = Baseline
0 = Baseline grade

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

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

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

DATE: July 28, 2020

SUBJECT: Glycerin Ethoxylates: Clarification and Individual Data for HRIPT Study Summaries with PCPC Memos 7 and 8

Rinse-Off formula with 3% of Glycereth-26

- Per report among 112 subjects enrolled- 9 subjects discontinued- 103 subjects completed study

- **Number of subjects with low level reaction in Induction: 5, and** Challenge:1
    - *Please note error: the reported low- level reaction was 4 (Nov 2019 report, page 3, table 1, row 1). The correct number is 5.*

[redacted]

7.0 RESULTS AND DISCUSSION

One hundred twelve subjects between the ages of 21 and 75 were enrolled and 103 completed the study (see Tables 1 and 2 in Appendix I and Data Listings 1 and 2 in Appendix II).

The following table summarizes subject enrollment and disposition.

Number enrolled:	112
[redacted]	
Number completed:	103

Source: Table 1, Appendix I

[redacted]

A summary of response data is provided in Table 3, Appendix I. Individual dermatological response grades are provided in Data Listing 3, Appendix II.

8.0 CONCLUSION

Under the conditions employed in this study, there was no evidence of sensitization to [redacted]

[redacted]

DATA LISTING 3: DERMATOLOGIC RESPONSE GRADES
BY PRODUCT AND SUBJECT

[redacted]

Subject	Induction Reading										Challenge Phase		
No.	1	2	3	4	5	6	7	8	9	MU	48hr	72hr	96hr(*)
1	-	-	-	-	-	-	-	-	-		-	-	
2	-	-	-	-	-	-	-	-	-		-	-	
3	-	-	-	-	-	-	-	-	-		-	-	
4	-	-	-	-	-	-	-	-	-		-	-	
5	-	-	-	-	-	-	-	-	-		-	-	
6	-	-	X	-	-	-	-	-	-	N9G	-	-	
7	-	-	-	-	-	-	-	-	-		-	-	
8	-	-	-	-	-	-	-	-	-		-	-	
9	-	-	-	-	-	-	-	-	-		-	-	
10	-	-	-	-	-	-	X	-	-	-	-	-	
11	-	-	-	-	-	-	-	-	-		-	-	
12	-	-	-	-	-	-	-	-	-		-	-	
13	-	-	-	-	-	-	-	+	+		X	X	
14	-	-	-	-	-	-	-	-	-		-	-	
15	-	-	-	-	-	-	-	-	-		-	-	
16	-	-	-	-	-	X	X	X	X		X	X	
17	-	-	-	-	-	-	-	-	-		-	-	
18	-	-	-	-	-	-	-	-	-		-	-	
19	-	-	-	-	-	-	-	-	-		-	-	
20	-	-	-	-	-	-	-	-	-		-	-	

Key to Symbols:

- = No reaction

? = Minimal or doubtful response, slightly different from surrounding normal skin

+ = Definite erythema, no edema

++ = Definite erythema, definite edema

+++ = Definite erythema, definite edema and vesiculation

N9G = No ninth grading NA=Not applied NP=Not patched due to reaction achieved
X = Reading not performed due to missed visit or subject discontinuation
D = Damage to epidermis: oozing, crusting and/or superficial erosions
p = Papular response >50% NR=Data not recorded
MU = Make-up reading for missed induction visit

(*) when required

Program: DETAIL.SAS/USES: RESPONSE, PRODLIST/17FEB04:13:50:51

[redacted]

DATA LISTING 3: DERMATOLOGIC RESPONSE GRADES
BY PRODUCT AND SUBJECT

[redacted]

Subject	Induction Reading										Challenge Phase		
No.	1	2	3	4	5	6	7	8	9	MU	48hr	72hr	96hr(*)
21													
22							X						
23													
24													
25													
26	?	X	X	X	X	X	X	X	X		X	X	
27													
28		X	X	X	X	X	X	X	X		X	X	
29		X											
30													
31													
32													
33					X								
34													
35					X								
36													
37													
38													
39								X					
40													
41													
42									N9G				
43									N9G				
44													
45													
46													
47													
48						X							
49						X							
50							X						
51													
52													

(*) when required

Program: DETAIL.SAS/USES: RESPONSE, PRODLIST/17FEB04:13:50:51

[redacted]

DATA LISTING 3: DERMATOLOGIC RESPONSE GRADES
BY PRODUCT AND SUBJECT

[redacted]

Subject	Induction Reading										Challenge Phase		
No.	1	2	3	4	5	6	7	8	9	MU	48hr	72hr	96hr(*)
53	-	-	X	-	+	+	+	+	+	+	-	-	
54	-	-	-	-	-	-	-	-	-		-	-	
55	-	-	-	-	-	-	-	-	-		-	-	
56	-	-	-	-	-	-	-	-	-		-	-	
57	-	-	X	-	-	-	-	-	-	-	-	-	
58	-	-	-	-	-	-	-	-	-		-	-	
59	-	-	-	-	-	-	-	-	-		-	-	
60	-	-	-	-	-	-	-	-	-		-	-	
61	-	-	-	-	-	-	-	-	N9G		-	-	
62	?	?	-	-	-	-	-	-	-		-	-	
63	-	-	-	-	-	-	-	-	-		-	-	
64	-	-	-	-	-	-	-	X	-	-	-	-	
65	-	-	-	-	-	-	-	-	-		-	-	
66	-	-	-	-	-	-	-	-	-		-	-	
67	-	X	-	-	-	-	-	-	-	-	-	-	
68	-	-	-	-	-	-	-	-	-		-	-	
69	-	-	-	X	-	-	-	-	-	-	-	-	
70	-	-	-	-	X	-	-	-	-	-	-	-	
71	-	X	-	-	-	-	-	-	-	-	-	-	
72	X	X	X	X	X	X	X	X	X		X	X	
73	-	-	-	-	-	-	-	-	-		-	-	
74	-	-	-	-	-	-	-	-	-		-	-	
75	-	-	-	-	-	-	-	-	-		-	-	
76	-	-	-	-	-	-	-	-	-		-	-	
77	-	-	-	-	-	-	-	-	N9G		-	-	
78	X	-	-	-	-	-	-	-	-	-	-	-	
79	-	-	-	-	-	-	-	-	-		-	-	
80	-	-	-	-	-	-	-	-	-		-	-	
81	-	-	-	-	-	-	-	-	-		-	-	
82	-	X	-	-	-	-	-	-	-	-	-	-	
83	-	-	-	-	-	-	X	-	-	-	-	-	
84	-	X	-	-	-	-	-	-	-	-	-	-	

(*) when required

Program: DETAIL.SAS/USES: RESPONSE, PRODLIST/17FEB04:13:50:51

[redacted]

DATA LISTING 3: DERMATOLOGIC RESPONSE GRADES
BY PRODUCT AND SUBJECT

[redacted]

Subject	Induction Reading										Challenge Phase		
No.	1	2	3	4	5	6	7	8	9	MU	48hr	72hr	96hr(*)
85	X	-	-	-	-	-	-	-	-	-	-	-	
86	-	-	-	-	-	-	-	-	-		-	-	
87	-	-	-	-	-	-	-	-	-		-	-	
88	-	-	-	-	-	-	-	-	-		-	-	
89	-	-	-	-	X	-	-	-	?	?	-	?	
90	-	-	-	-	-	-	-	-	-		-	-	
91	-	-	X	X	X	X	X	X	X		X	X	
92	-	-	-	-	-	-	-	-	-		-	-	
93	-	-	-	-	-	-	-	-	-		-	-	
94	-	-	-	-	-	-	-	-	-		-	-	
95	-	-	-	-	-	-	-	-	-		-	-	
96	-	-	-	-	-	-	-	-	-		-	-	
97	-	-	-	-	-	-	-	-	-		-	-	
98	-	-	-	-	-	-	-	-	-		-	-	
99	-	-	-	-	-	-	-	-	-		-	-	
100	-	-	-	-	-	-	-	X	-	-	-	-	
101	-	-	-	-	-	-	-	-	-		X	X	
102	-	-	-	X	-	-	-	-	-	-	-	-	
103	-	-	-	-	-	-	-	X	-	-	-	-	
104	X	X	X	X	X	X	X	X	X		X	X	
105	-	-	-	-	-	-	-	-	-		-	-	
106	-	-	-	-	-	-	-	-	-		-	-	
107	-	-	-	-	-	-	X	-	-	-	-	-	
108	X	-	-	-	-	-	-	-	-	-	-	-	
109	-	-	-	-	-	-	-	-	-		-	-	
110	-	-	-	X	-	-	X	X	X		X	X	
111	-	-	-	-	-	-	-	-	N9G		-	-	
112	-	-	-	-	-	-	-	-	-		-	-	

(*) when required

Program: DETAIL.SAS/USES: RESPONSE, PRODLIST/17FEB04:13:50:51

Leave-On formula with 3% of Glycereth-26

- Per report among 220 subjects enrolled- 12 subjects discontinued- 208 subjects completed study (not sure if this is an error from lab), however individual subject data include details of **only 200 subjects** (although row numbers up to 212 in which 12 numbers are missing= 200 subjects) matching with below screen shot and it was mentioned in the study report that " Raw scores are standardized for 200 subjects"

- **Number of subjects with low level reaction-** ***Induction: 27*** **and Challenge: 0**
    - *Please note error: the reported low level induction reaction was 38 (Nov 2019 report, page 3, table 1, row 2). The correct number is 27.*

[redacted]

Table 1 Subject Disposition

	n
Enrolled Subjects	220
Completed Subjects	208
[redacted]	

Table 2 Summary of demographic information

		All Subjects (n=200)
Age (Years)	Mean ± Standard Deviation	57.26±6.19
	Minimum Age	34
	Maximum Age	65
Gender(%)	Female	159(79.5)
	Male	41 (20.5)

2.2 Test materials

[redacted]

Table 3 Test Material Descriptions

[redacted]

[redacted]

[redacted]

Appendix K

The raw data of [redacted]

NO.	Induction Reading																									Challenge Reading												Rechallenge Reading											
	G1			G2			G3			G4			G5			G6			G7			G8			G9			48HR				96HR				48HR				96HR									
																										OS			AS			OS			AS			OS			AS			OS			AS		
	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O
001	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
002	0	/	/	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
003	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
004	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
005	0	/	/	0	/	/	0	/	/	1	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
006	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
007	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
008	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
009	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
010	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
011	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
012	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
013	0	/	/	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
014	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
015	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
017	0	/	/	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
018	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
019	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
020	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
021	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
022	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
023	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
024	0	/	/	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
025	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
026	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/

Note1: In Induction reading, G = Grading, E = Erythema and elevated responses, S = Effects on superficial layers of the skin, O = other responses

Note2: In Challenge reading, OS = Original Site, AS = Alternate Site, E1 = Erythema Scale, E2 = Elevated Responses, O = Other Responses.

[redacted]

[redacted]

The raw data of [redacted]

NO.	Induction Reading																									Challenge Reading												Rechallenge Reading											
	G1			G2			G3			G4			G5			G6			G7			G8			G9			48HR						96HR						48HR						96HR					
																										OS			AS			OS			AS			OS			AS			OS			AS		
	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O
028	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/
029	0	/	/	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/
030	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/
031	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/
032	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/
033	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/
034	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/
035	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/
036	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/
037	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/
038	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/
039	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/
041	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/
042	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/
043	0	/	/	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/
044	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/
045	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/
046	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/
047	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/
048	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/
049	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/
050	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/
051	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/
052	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/
053	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/

Note1: In Induction reading, G = Grading, E = Erythema and elevated responses, S = Effects on superficial layers of the skin, O = other responses

Note2: In Challenge reading, OS = Original Site, AS = Alternate Site, E1 = Erythema Scale, E2 = Elevated Responses, O = Other Responses.

[redacted]

[redacted]

[redacted]

The raw data of [redacted]

NO.	Induction Reading																											Challenge Reading												Rechallenge Reading											
	G1			G2			G3			G4			G5			G6			G7			G8			G9			48HR						96HR						48HR						96HR					
																												OS			AS			OS			AS			OS			AS			OS			AS		
	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O
054	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
055	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
056	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
058	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
059	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
060	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
061	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
062	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
063	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
065	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
066	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
067	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
068	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
069	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
070	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
071	0	/	/	0	/	/	0	/	/	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
072	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
073	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
074	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
075	0	/	/	0	/	/	1	/	/	1	/	/	1	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
076	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
077	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
078	0	/	/	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
079	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
080	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/

Note1: In Induction reading, G = Grading, E = Erythema and elevated responses, S = Effects on superficial layers of the skin, O = other responses

Note2: In Challenge reading, OS = Original Site, AS = Alternate Site, E1 = Erythema Scale, E2 = Elevated Responses, O = Other Responses.

[redacted]

[redacted]

The raw data of [redacted]

NO.	Induction Reading																									Challenge Reading												Rechallenge Reading											
	G1			G2			G3			G4			G5			G6			G7			G8			G9			48HR						96HR						48HR						96HR					
																											OS			AS			OS			AS			OS			AS			OS			AS		
	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O
082	0	/	/	0	/	/	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
083	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
084	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
085	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
086	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
087	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
088	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
089	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
090	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
092	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
093	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
094	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
095	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
096	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
097	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
098	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
099	0	/	/	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
100	0	/	/	0	/	/	1	/	/	1	/	/	1	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
101	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
102	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
104	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
105	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
106	0	/	/	0	/	/	0	/	/	1	/	/	1	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
107	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
108	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/

Note1: In Induction reading, G = Grading, E = Erythema and elevated responses, S = Effects on superficial layers of the skin, O = other responses

Note2: In Challenge reading, OS = Original Site, AS = Alternate Site, E1 = Erythema Scale, E2 = Elevated Responses, O = Other Responses.

[redacted]

[redacted]

[redacted]

The raw data of [redacted]

NO.	Induction Reading																											Challenge Reading												Rechallenge Reading											
	G1			G2			G3			G4			G5			G6			G7			G8			G9			48HR						96HR						48HR						96HR					
																												OS			AS			OS			AS			OS			AS			OS			AS		
	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O
109	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
110	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
111	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
112	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
113	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
114	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
115	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
116	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
117	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
118	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
119	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
120	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
121	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
122	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
124	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
126	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
127	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
128	0	/	/	0	/	/	0	/	/	0	/	/	1	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
129	0	/	/	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
130	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
131	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
132	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
133	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
134	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
135	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/

Note1: In induction reading, G = Grading, E = Erythema and elevated responses, S = Effects on superficial layers of the skin, O = other responses

Note2 :In Challenge reading, OS = Original Site, AS = Alternate Site, E1 = Erythema Scale, E2 = Elevated Responses, O = Other Responses.

[redacted]

[redacted]

[redacted]

The raw data of [redacted]

NO.	Induction Reading																									Challenge Reading												Rechallenge Reading											
	G1			G2			G3			G4			G5			G6			G7			G8			G9			48HR						96HR						48HR						96HR					
																											OS			AS			OS			AS			OS			AS			OS			AS		
	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O
136	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
137	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
138	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
139	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
140	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
141	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
142	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
143	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
144	0	/	/	0	/	/	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
145	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
146	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
147	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
148	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
149	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
150	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
151	0	/	/	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
152	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
153	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
154	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
155	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
156	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
157	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
158	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
159	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
160	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/

Note1: In Induction reading, G = Grading, E = Erythema and elevated responses, S = Effects on superficial layers of the skin, O = other responses

Note2: In Challenge reading, OS = Original Site, AS = Alternate Site, E1 = Erythema Scale, E2 = Elevated Responses, O = Other Responses.

[redacted]

[redacted]

[redacted]

The raw data of [redacted]

NO.	Induction Reading																									Challenge Reading												Rechallenge Reading											
	G1			G2			G3			G4			G5			G6			G7			G8			G9			48HR						96HR						48HR						96HR					
																											OS			AS			OS			AS			OS			AS			OS			AS		
	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O
161	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
162	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
163	0	/	/	1	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
164	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
165	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
166	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
167	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
168	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
169	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
171	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
172	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
174	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
175	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
176	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
177	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
178	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
179	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
180	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
181	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
182	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
183	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
184	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
185	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
186	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
187	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/

Note1: In Induction reading, G = Grading, E = Erythema and elevated responses, S = Effects on superficial layers of the skin, O = other responses

Note2: In Challenge reading, OS = Original Site, AS = Alternate Site, E1 = Erythema Scale, E2 = Elevated Responses, O = Other Responses.

[redacted]

[redacted]

[redacted]

The raw data of [redacted]

NO.	Induction Reading																									Challenge Reading												Rechallenge Reading											
	G1			G2			G3			G4			G5			G6			G7			G8			G9			48HR						96HR						48HR						96HR					
																											OS			AS			OS			AS			OS			AS			OS			AS		
	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O
188	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
189	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
190	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
191	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
192	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
193	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
194	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
195	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
196	0	/	/	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
197	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
198	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
199	0	/	/	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
200	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
201	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
202	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
203	0	/	/	0	/	/	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
204	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
205	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
206	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
207	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
208	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
209	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
210	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
211	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
212	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/

Note1: In Induction reading, G = Grading, E = Erythema and elevated responses, S = Effects on superficial layers of the skin, O = other responses

Note2: In Challenge reading, OS = Original Site, AS = Alternate Site, E1 = Erythema Scale, E2 = Elevated Responses, O = Other Responses.

[redacted]

Leave-On formula with 3% of Glycereth-26

- Per report among 218 subjects enrolled- 6 subjects discontinued- 212 subjects completed study (not sure if this is an error from lab or their practice to provide data on 200 subjects), however individual subject data include details of **only 200 subjects** (although row numbers up to 206 in which 6 numbers are missing= 200 subjects) it was mentioned in the study report that " Raw scores are standardized for 200 subjects".
    - Please note error: *Aug 2019 report, page 3, table 1, row 1:* the # of reported subject completed the test was 200, although the report states 212 subjects completed. Although, the individual subject data details was on 200.

- **Number of subjects with low level reaction-** ***Induction: 24*** **and Challenge: 0**
- **Number of subjects with high level reaction-** ***Induction: 1*** **and Challenge: 0**
    - *Please note error: the reported low level induction reaction was 8 (Aug 2019 report, page 3, table 1, row 1). The correct number is 24.*

[redacted]

Table 1 Subject Disposition

	n
Enrolled Subjects	218
Completed Subjects	212
[redacted]	

Table 2 Summary of demographic information

		All Subjects (n=200)
Age (Years)	Mean ± Standard Deviation	57.54±6.22
	Minimum Age	27
	Maximum Age	65
Gender(%)	Female	166(83)
	Male	34 (17)

2.2 Test materials

The study contains eleven kinds of test materials. The test materials and controls are listed in the following table (see Table 3). Finn chamber was used for each material and blank control.

Table 3 Test Material Descriptions

[redacted]

[redacted]

[redacted]

Appendix G

The raw data of [redacted]

NO.	Induction Reading																									Challenge Reading												Rechallenge Reading											
	G1			G2			G3			G4			G5			G6			G7			G8			G9			48HR						96HR						48HR						96HR					
																													OS			AS			OS			AS			OS			AS			OS			AS		
	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O
001	0	/	/	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
002	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
003	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
005	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
006	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
007	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
008	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
009	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
010	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
011	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
012	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
013	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
014	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
015	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
016	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
017	0	/	/	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
018	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
019	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
020	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
021	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
022	0	/	/	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
023	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
024	2	/	/	2	/	/	1	/	/	1	/	/	1	/	/	1	/	/	1	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
025	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
026	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/

Note1: In Induction reading, G = Grading, E = Erythema and elevated responses, S = Effects on superficial layers of the skin, O = other responses

Note2: In Challenge reading, OS = Original Site, AS = Alternate Site, E1 = Erythema Scale, E2 = Elevated Responses, O = Other Responses

[redacted]

The raw data of [redacted]

NO.	Induction Reading																												Challenge Reading												Rechallenge Reading											
	G1			G2			G3			G4			G5			G6			G7			G8			G9				48HR				96HR				48HR				96HR											
																													OS			AS			OS			AS			OS			AS			OS			AS		
	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O
027	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
028	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
029	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
030	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
031	0	/	/	0	/	/	0	/	/	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
032	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
033	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
034	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
035	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
036	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
037	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
038	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
039	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
040	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
042	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
043	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
044	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
045	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
046	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
047	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
048	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
049	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
050	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
051	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
052	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/

Note1: In Induction reading, G = Grading, E = Erythema and elevated responses, S = Effects on superficial layers of the skin, O = other responses

Note2: In Challenge reading, OS = Original Site, AS = Alternate Site, E1 = Erythema Scale, E2 = Elevated Responses, O = Other Responses.

[redacted]

[redacted]

The raw data of [redacted]

NO.	Induction Reading																									Challenge Reading												Rechallenge Reading											
	G1			G2			G3			G4			G5			G6			G7			G8			G9			48HR						96HR						48HR						96HR					
																										OS			AS			OS			AS			OS			AS			OS			AS		
	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O
053	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
054	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
055	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
056	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
057	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
058	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
059	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
060	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
061	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
062	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
063	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
064	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
065	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
066	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
067	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
068	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
069	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
071	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
072	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
073	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
074	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
075	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
076	0	/	/	0	/	/	0	/	/	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
077	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
078	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/

Note1: In Induction reading, G = Grading, E = Erythema and elevated responses, S = Effects on superficial layers of the skin, O = other responses

Note2: In Challenge reading, OS = Original Site, AS = Alternate Site, E1 = Erythema Scale, E2 = Elevated Responses, O = Other Responses.

[redacted]

The raw data of [redacted]

NO.	Induction Reading																									Challenge Reading												Rechallenge Reading											
	G1			G2			G3			G4			G5			G6			G7			G8			G9			48HR						96HR						48HR						96HR					
																											OS			AS			OS			AS			OS			AS			OS			AS		
	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O
079	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
080	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
081	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
082	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
083	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
084	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
085	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
086	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
087	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
088	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
089	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
090	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
091	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
092	1	/	/	1	/	/	1	/	/	1	/	/	1	/	/	1	/	/	1	/	/	1	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
093	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
094	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
095	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
096	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
097	0	/	/	0	/	/	0	/	/	0	/	/	1	/	/	1	/	/	1	/	/	1	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
098	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
099	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
101	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
102	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
103	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
104	1	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/

Note1: In Induction reading, G = Grading, E = Erythema and elevated responses, S = Effects on superficial layers of the skin, O = other responses

Note2: In Challenge reading, OS = Original Site, AS = Alternate Site, E1 = Erythema Scale, E2 = Elevated Responses, O = Other Responses.

[redacted]

[redacted]

[redacted]

The raw data of [redacted]

NO.	Induction Reading																											Challenge Reading												Rechallenge Reading											
	G1			G2			G3			G4			G5			G6			G7			G8			G9			48HR						96HR						48HR						96HR					
																												OS			AS			OS			AS			OS			AS			OS			AS		
	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O
105	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
106	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
107	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
108	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
109	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
110	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
111	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
112	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
113	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
114	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
115	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
116	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
117	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
118	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
119	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
120	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
121	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
122	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
123	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
124	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
125	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
126	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
127	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
128	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
130	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/

Note1: In Induction reading, G = Grading, E = Erythema and elevated responses, S = Effects on superficial layers of the skin, O = other responses

Note2 :In Challenge reading, OS = Original Site, AS = Alternate Site, E1 = Erythema Scale, E2 = Elevated Responses, O = Other Responses.

[redacted]

The raw data [redacted]

NO.	Induction Reading																											Challenge Reading												Rechallenge Reading											
	G1			G2			G3			G4			G5			G6			G7			G8			G9			48HR				96HR				48HR				96HR											
																												OS			AS			OS			AS			OS			AS			OS			AS		
	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O
131	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
132	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
133	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
134	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
135	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
136	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
137	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
138	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
139	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
140	0	/	/	0	/	/	0	/	/	0	/	/	1	/	/	1	/	/	1	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
141	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
142	0	/	/	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
143	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
144	0	/	/	0	/	/	0	/	/	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
145	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
146	0	/	/	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
147	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
148	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
149	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
150	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
151	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
152	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
153	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
154	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
155	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/

Note1: In Induction reading, G = Grading, E = Erythema and elevated responses, S = Effects on superficial layers of the skin, O = other responses

Note2: In Challenge reading, OS = Original Site, AS = Alternate Site, E1 = Erythema Scale, E2 = Elevated Responses, O = Other Responses.

[redacted]

[redacted]

[redacted]

The raw data of [redacted]

NO.	Induction Reading																											Challenge Reading												Rechallenge Reading											
	G1			G2			G3			G4			G5			G6			G7			G8			G9			48HR						96HR						48HR						96HR					
																												OS			AS			OS			AS			OS			AS			OS			AS		
	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O
156	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
157	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
158	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
159	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
160	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
161	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
162	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
163	0	/	/	0	/	/	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
164	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
165	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
166	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
167	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
168	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
169	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
170	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
171	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
172	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
173	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
174	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
175	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
176	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
177	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
178	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
179	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/
180	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/

Note1: In Induction reading, G = Grading, E = Erythema and elevated responses, S = Effects on superficial layers of the skin, O = other responses

Note2: In Challenge reading, OS = Original Site, AS = Alternate Site, E1 = Erythema Scale, E2 = Elevated Responses, O = Other Responses.

[redacted]

The raw data of [redacted]

NO.	Induction Reading																									Challenge Reading												Rechallenge Reading											
	G1			G2			G3			G4			G5			G6			G7			G8			G9			48HR						96HR						48HR						96HR					
																													OS			AS			OS			AS			OS			AS			OS			AS		
	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E	S	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O	E1	E2	O
181	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
182	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
183	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
184	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
185	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
187	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
188	0	/	/	0	/	/	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
189	0	/	/	0	/	/	1	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
190	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
191	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
192	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
193	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
194	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
195	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
196	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
197	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
198	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
199	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
200	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
201	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
202	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
203	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
204	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
205	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/
206	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	0	/	/	/	/	/	/	/	/	/	/	/	/

Note1: In Induction reading, G = Grading, E = Erythema and elevated responses, S = Effects on superficial layers of the skin, O = other responses

Note2: In Challenge reading, OS = Original Site, AS = Alternate Site, E1 = Erythema Scale, E2 = Elevated Responses, O = Other Responses.

[redacted]

Rinse-Off formula with 2% Glycereth-7

- Attached (below) redacted_adult_number of subject data page: among 236 subjects enrolled- 25 subjects discontinued- 211 subjects completed study

- Number of subjects with low level reaction: Induction: 2
- Number of subjects with low level reaction: Challenge:11

[redacted]

[redacted]

FINAL REPORT – REPEATED INSULT PATCH TEST (RIPT) [redacted]

[redacted]

[redacted] **Cleanser,** [redacted]

SUBJECTS:	A total of 236 subjects were enrolled; 211 subjects completed the test. [redacted] No subject discontinued due to test material reaction.
METHOD:	This test was conducted according to [redacted] Standard Operating Procedures (including any Sponsor alterations).
TEST DATES:	October 15, 2014 through November 21, 2014.
SCORING SYSTEM:	See Tables I-II.
RESULTS:	See Tables I-II. During the Induction Phase, two subjects exhibited low-level (±) reactions. During the Challenge, eleven other subjects exhibited low-level (±) reactions.
CONCLUSION:	In this Repeated Insult Patch Test, Test Material Cleanser, Formula [redacted] did not induce dermal sensitization in human subjects.

[redacted]

[redacted]

[redacted]

Leave-On spray formula Sub 0.68% of Glycereth-7 & Formula Base 1% of Glycereth-7 . *PLEASE NOTE: IN ERROR this formula had been submitted both in the November and the August submission as two separate tested formulations. However, it should have been reported as ONE tested formula. Explanation for the error is likely that this spray formulation (typically prepared as base and sub formula with and without the propellant) was reported twice. Glycereth 7 level being 1% in the base formula and 0.68% sub formula. We can assume for the final level of 1.68% Glycereth-7.*

- Attached redacted adult_ number of subject page: among 230 subjects enrolled- 31 subjects discontinued- 199 subjects completed study

Glycereth-7_ HRIPT_LOAdult_numbe

- Number of subjects with low level reaction- Induction: 4
- Number of subjects with low level reaction and Challenge:0

Glycereth-7_ HRIPT_LOAdult_individ

In addition to submitting the same report twice, the reported # of subjects with low level induction reaction was incorrect (3 subjects) in the Aug submission. The correct number is 4.

[redacted]

FINAL REPORT – REPEATED INSULT PATCH TEST (RIPT) [redacted]

[redacted] **Color Spray Lotion,** [redacted]

SUBJECTS:	A total of 230 subjects were enrolled; 199 subjects completed the test. [redacted] No subject discontinued due to test material reaction.
METHOD:	This test was conducted according to [redacted] Standard Operating Procedures (including any Sponsor alterations).
TEST DATES:	January 26, 2015 through March 6, 2015.
SCORING SYSTEM:	See Tables I-II.
RESULTS:	See Tables I-II. During the Induction Phase, four subjects exhibited low-level (±/1) reactions. Approximately 99% of the subjects exhibited staining of the skin. During the Challenge, no reactions were exhibited. Approximately 95% of the subjects exhibited staining of the skin.
CONCLUSION:	In this Repeated Insult Patch Test, Test Material Color Spray Lotion, [redacted] did not induce dermal sensitization in human subjects.

[redacted]

[redacted]

[redacted]

[redacted]

[redacted] Color Spray Lotion, [redacted]

TABLE II: INDIVIDUAL SUBJECT DATA

(see Scoring System, page 16)

Sub	[redacted]	Induction Reading									Challenge Reading			
		1	2	3	4	5	6	7	8	9	1	2	3	4
1		0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S
2		0	0	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
3		0	0	0S	0S	0S	0S	0S	0S	0S	0	0S	-	0
4		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
5		0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S
6		0S	0S	0S	0S	X	X	X	X	X	X	X	X	X
7		0	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S
8		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
9		0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	-	0
10		0S	0S	0	0	0	0	0S	0S	0S	0	X	X	X
11		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
12		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
13		0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S
14		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
15		0	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S
16		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
17		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
18		0	0	0S	0S	0S	0S	0S	0S	0S	0	0S	-	0
19		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
20		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
21		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
22		0	0	0	0S	0S	0S	0S	0S	0S	0	0	0S	0S
23		0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S
24		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	-	0
25		0	0	0S	0S	0S	0S	0DRS	0DRS	0DRS	0	0S	-	0

[redacted]

[redacted]

[redacted] Color Spray Lotion, [redacted]

TABLE II: INDIVIDUAL SUBJECT DATA

(see Scoring System, page 16)

Sub	[redacted]	Induction Reading									Challenge Reading			
		1	2	3	4	5	6	7	8	9	1	2	3	4
26		0	0S	0S	0S	0	X	X	X	X	X	X	X	X
27		X	X	X	X	X	X	X	X	X	X	X	X	X
28		0	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S
29		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0DRS	0DRS	0DRS
30		0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S
31		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
32		0	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S
33		0	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S
34		0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S
35		0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	-	0
36		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
37		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
38		0	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S
39		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
40		0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S
41		0	0S	0S	X	X	X	X	X	X	X	X	X	X
42		0S	0S	0S	0S	X	X	X	X	X	X	X	X	X
43		0	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	-	0S
44		0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	-	0
45		0	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S
46		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
47		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0	0S	0S
48		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0	0S	0S
49		0	0S	0S	0S	0S	0S	X	X	X	X	X	X	X
50		0S	0S	1DR	1DR	1DR	1DR	1DR	1DRS	1DRS	0S	0S	0S	0S

[redacted]

[redacted]

[redacted] Color Spray Lotion, [redacted]

TABLE II: INDIVIDUAL SUBJECT DATA

(see Scoring System, page 16)

Sub	[redacted]	Induction Reading									Challenge Reading			
		1	2	3	4	5	6	7	8	9	1	2	3	4
51		0DRS	0DRS	0DRS	0DRS	0S	0S	0S	0S	0S	0	0S	0S	0S
52		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
53		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0	0	0
54		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
55		0	0	0S	0S	0S	0S	0S	0S	0S	0	0S	-	0
56		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
57		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
58		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
59		0S	0S	X	X	X	X	X	X	X	X	X	X	X
60		0	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S
61		0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S
62		0	0S	0S	0S	X	X	X	X	X	X	X	X	X
63		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
64		0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S
65		0	0	0	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
66		0	0	0S	0S	0S	0S	0S	0S	0S	0S	0S	-	0
67		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
68		X	X	X	X	X	X	X	X	X	X	X	X	X
69		0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S
70		0	0	0	0	0DRS	0	0S	0S	0S	0	0	0	0
71		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
72		0	0	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
73		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
74		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
75		0	0	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S

[redacted]

[redacted]

[redacted] Color Spray Lotion, [redacted]

TABLE II: INDIVIDUAL SUBJECT DATA

(see Scoring System, page 16)

Sub	[redacted]	Induction Reading									Challenge Reading			
		1	2	3	4	5	6	7	8	9	1	2	3	4
76		0	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S
77		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
78		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
79		0	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S
80		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
81		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0	0	0
82		0	0	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
83		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0	0S	0S
84		0	0	0	0S	0S	0S	0S	0S	0S	0	0	0S	0S
85		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
86		0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S
87		0S	0S	0S	0S	0S	0S	0S	X	X	X	X	X	X
88		0S	0S	0S	0S	0S	0S	0	0	0	0	0S	-	0
89		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
90		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
91		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0	0	0S
92		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
93		0	0S	0S	0S	0S	0DRS	0DRS	0DRS	0DRS^	0	0	0	0
94		0	0	0	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
95		0	0	0	0S	0S	0S	0S	0S	0S	0	0S	-	0S
96		0	0	0	0S	0S	0S	0S	0S	0S	0	0	0	0S
97		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
98		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
99		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
100		0	X	X	X	X	X	X	X	X	X	X	X	X

[redacted]

[redacted]

[redacted] Color Spray Lotion, [redacted]

TABLE II: INDIVIDUAL SUBJECT DATA

(see Scoring System, page 16)

Sub [redacted]	Induction Reading									Challenge Reading			
	1	2	3	4	5	6	7	8	9	1	2	3	4
101	0	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S
102	0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
103	0	X	X	X	X	X	X	X	X	X	X	X	X
104	0	0S	0S	0S	0S	0S	0S	0S	0S	0	0	0S	0S
105	0	0	0S	0S	0S	0S	0S	0S	0S	0	0	0	0
106	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S
107	0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
108	0	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S
109	0	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S
110	0	0	0S	0S	0S	0S	0S	0S	0S	0	0S	-	0S
111	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	-	0S
112	0	0	0S	0S	0S	X	X	X	X	X	X	X	X
113	0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
114	0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
115	0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
116	0	0S	0S	0S	X	X	X	X	X	X	X	X	X
117	0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
118	0	0	0S	0S	0S	0S	0S	0S	0S	0	0	0S	0S
119	0S	0S	0S	0S	0S	0S	0S	0S	0S	X	X	X	X
120	0	0	0	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
121	0	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	-	0S
122	0S	0S	X	X	X	X	X	X	X	X	X	X	X
123	0S	0S	0S	0S	0S	0DRS	0DRS	0DRS	0DRS	0	0S	-	0
124	0	X	X	X	X	X	X	X	X	X	X	X	X
125	0	0	0S	0S	0S	0S	0S	0S	0DRS	0	0	0	0S

[redacted]

[redacted]

[redacted] Color Spray Lotion, [redacted]

TABLE II: INDIVIDUAL SUBJECT DATA

(see Scoring System, page 16)

Sub	[redacted]	Induction Reading									Challenge Reading			
		1	2	3	4	5	6	7	8	9	1	2	3	4
126		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	-	0S
127		0	0	0S	0S	0S	0S	0S	0S	0S	0S	0S	-	0
128		X	X	X	X	X	X	X	X	X	X	X	X	X
129		0S	0S	0S	0S	0DRS	0S	0S	0S	0S	0	0S	0S	0S
130		0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S
131		0	0	X	X	X	X	X	X	X	X	X	X	X
132		0	0S	X	X	X	X	X	X	X	X	X	X	X
133		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
134		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
135		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
136		0	X	X	X	X	X	X	X	X	X	X	X	X
137		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0	0S	0S
138		0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S
139		0	X	X	X	X	X	X	X	X	X	X	X	X
140		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
141		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	-	0S
142		0	0	0S	0S	0DRS	0DRS	0DRS	0DRS	0DRS	0	0S	0S	0S
143		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
144		0	0	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S
145		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
146		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0
147		0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S
148		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
149		0S	0S	0S	0S	0	0	0	0	0S	0	0S	0S	0S
150		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S

[redacted]

[redacted]

[redacted] Color Spray Lotion, [redacted]

TABLE II: INDIVIDUAL SUBJECT DATA

(see Scoring System, page 16)

Sub	[redacted]	Induction Reading									Challenge Reading			
		1	2	3	4	5	6	7	8	9	1	2	3	4
151		0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S
152		0S	0	X	X	X	X	X	X	X	X	X	X	X
153		0	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	-	0S
154		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
155		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0	0	0S
156		0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S
157		0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S
158		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0	0S	0S
159		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0	0S	0S
160		0S	0S	0S	0S	0S	0S	0S	0S	1DR	0	0S	0S	0S
161		0	0	0S	0S	0S	0S	0DRS	0DRS	0DRS	0	0	0	0
162		0	0S	0S	0S	0	0	0	0S	0S	0	0	0	0
163		0S	0	0	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S
164		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
165		0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	-	0S
166		0	0	0S	0S	0S	0S	0S	0S	0S	0	0S	-	0
167		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	-	0
168		0	0	0S	0S	0S	0S	0S	0S	0S	0	0	0	0
169		0	0	0	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
170		0	0	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
171		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
172		0	0	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
173		0	0	0	0S	0	0	0S	0S	0S	0	0S	0S	0S
174		0S	0S	0S	0S	0S	0S	0	0	0S	0	0S	0S	0S
175		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0	0S	0S

[redacted]

[redacted]

[redacted] Color Spray Lotion, [redacted]

TABLE II: INDIVIDUAL SUBJECT DATA

(see Scoring System, page 16)

Sub	[redacted]	Induction Reading									Challenge Reading			
		1	2	3	4	5	6	7	8	9	1	2	3	4
176		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0	0S	0S
177		X	X	X	X	X	X	X	X	X	X	X	X	X
178		0	X	X	X	X	X	X	X	X	X	X	X	X
179		0S	X	X	X	X	X	X	X	X	X	X	X	X
180		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	-	0
181		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	-	0S
182		0	0	0	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
183		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0	0	0S
184		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
185		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	-	0
186		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
187		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0	-	0S
188		0S	X	X	X	X	X	X	X	X	X	X	X	X
189		0	0	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
190		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	-	0
191		0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	-	0S
192		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0	-	0
193		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0	0S	0S
194		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
195		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
196		0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S
197		0	0	0	0	0	0	0	0	0	0	0	0	0
198		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0	0	0
199		0	0	0	0	0	0	0	0	0	0	0	0	0
200		0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	-	0S

[redacted]

[redacted]

[redacted] Color Spray Lotion, [redacted]

[redacted]

TABLE II: INDIVIDUAL SUBJECT DATA

(see Scoring System, page 16)

Sub	[redacted]	Induction Reading									Challenge Reading			
		1	2	3	4	5	6	7	8	9	1	2	3	4
201		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0	-	0
202		0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S
203		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0	-	0
204		0S	0S	1DRS	1DRS	1DRS	1DRS	1DRS	1DRS	0DRS	0S	0S	-	0S
205		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
206		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
207		0	0	0S	0S	0S	0S	0S	0S	0S	0S	0S	-	0
208		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	-	0
209		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
210		0DRS	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
211		0	X	X	X	X	X	X	X	X	X	X	X	X
212		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	-	0S
213		0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S
214		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	-	0
215		0	0S	0S	0S	±DRS	1DRS	1DRS	±DR	0DRS	0	0S	-	0
216		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
217		0S	0S	0S	0S	0S	0S	0S	0S	0S	-	0S	0S	0S
218		X	X	X	X	X	X	X	X	X	X	X	X	X
219		0	0	0S	0S	0S	0S	0S	0S	0S	0	0S	-	0S
220		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0	-	0
221		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
222		0S	0S	0S	0S	0S	0S	0S	0S	0S	0	0	-	0
223		0	0	0S	0	0S	0S	0S	0S	0S	0	0	0	0S
224		0	0	0	0S	0S	0S	0S	0S	0S	0	0S	0S	0S
225		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0S	0S	0S

[redacted]

[redacted]

[redacted] Color Spray Lotion, [redacted]

TABLE II: INDIVIDUAL SUBJECT DATA

(see Scoring System, page 16)

Sub	[redacted]	Induction Reading									Challenge Reading			
		1	2	3	4	5	6	7	8	9	1	2	3	4
226		0	0S	0S	X	X	X	X	X	X	X	X	X	X
227		0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S
228		0	0S	0S	0S	0S	0S	0S	0S	0S	0	0	0S	0S
229		0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	0S	-	0
230		0	0	0	0	0	0	0	0	0	0	0	0	0

[redacted]

[redacted]

[redacted] Color Spray Lotion, [redacted]

[redacted]

SCORING SYSTEM*:

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

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

[redacted]

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

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

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

DATE: July 9, 2020

SUBJECT: Tentative Report: Safety Assessment of Glycerin Ethoxylates as Used in Cosmetics (Release Date: June 19, 2020)

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

Summary - Please correct: “using in an HRIPT completed in 199 subjects”
Discussion - It would helpful to include the exposure concentrations used in the acute inhalation studies in the Discussion.