Alkyl PEG Ether

CIR EXPERT PANEL MEETING
DECEMBER 13-14, 2010

ADMINISTRATIVE

Cosmetic Ingredient Review
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Memorandum

To: CIR Expert Panel Members and Liaisons

From: Monice M. Fiume MMF
Senior Scientific Analyst/Writer
Bart A. Heldreth, Ph.D., Chemist BAH

Date: November 18, 2010

Subject: Final Report (Draft) on Alkyl PEG Ethers

At the June 2010 meeting, the CIR Expert Panel issued a tentative report that encompassed the entire family of Alkyl PEG Ethers used in cosmetics. Additional concentration of use data were received and incorporated into the report. Technical comments from the Council were received and addressed. Additional data were considered as described below. And a draft final report has been prepared for your review.

As you recall, this report was originally brought forward as a possible re-review of laureth-4 and laureth-23. In preparing that re-review document, it was realized that there is a large number of ingredients that are very similar to one another. Therefore, a grouping of ingredients based on structural and functional similarities was created, and the Panel agreed to re-review laureth-4 in order to include these ingredients. Many of the ingredients included in this family have been reviewed previously, as have many of the components of these ingredients, and the information included in those original reports is used to support the safety of the entire Alkyl PEG Ether family. While not a new approach, this was the first time an ingredient family of this size was created.

In the draft report presented to the Panel in June, summaries from the original reports on previously reviewed ingredients, as well as from reports on components, were included in text and in a table. Per the request of the Panel, all that information is now contained in table format only. (See Table 2b.)

A Scientific Committee on Consumer Products (SCCP) opinion paper exists for laureth-9. The information summarized in the SCCP paper is on alcohol ethoxylates analogous to laureth-9. This information has been added to the report. The information is summarized under the subheading 'Laureth-9', but the test product will be given as described in the SCCP paper – i.e., by the average alkyl chain length (C) and by the average alcohol ethoxylate number (AE), e.g. $C_{12\text{-}15}AE_7$. The new information that has been added (as well as any other new information) is designated by vertical lines on both sides of text.

Information from a SIDS document on PEG-3 Methyl Ether has also been added to the review.

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At the June meeting, the Panel stated that the botanical boiler plate should be included in the Discussion, since some ingredients have plant sources. While plants are the source of some components in the ingredients of this report, it appears that alkyl PEG ethers are produced as a result of significant processing, and as such are not expected to contain residual pesticides or heavy metals. We made the judgment that the boilerplate was not needed.

You will note that the boiler plates for animal- and tallow-derived ingredients have been updated to reflect current guidelines.

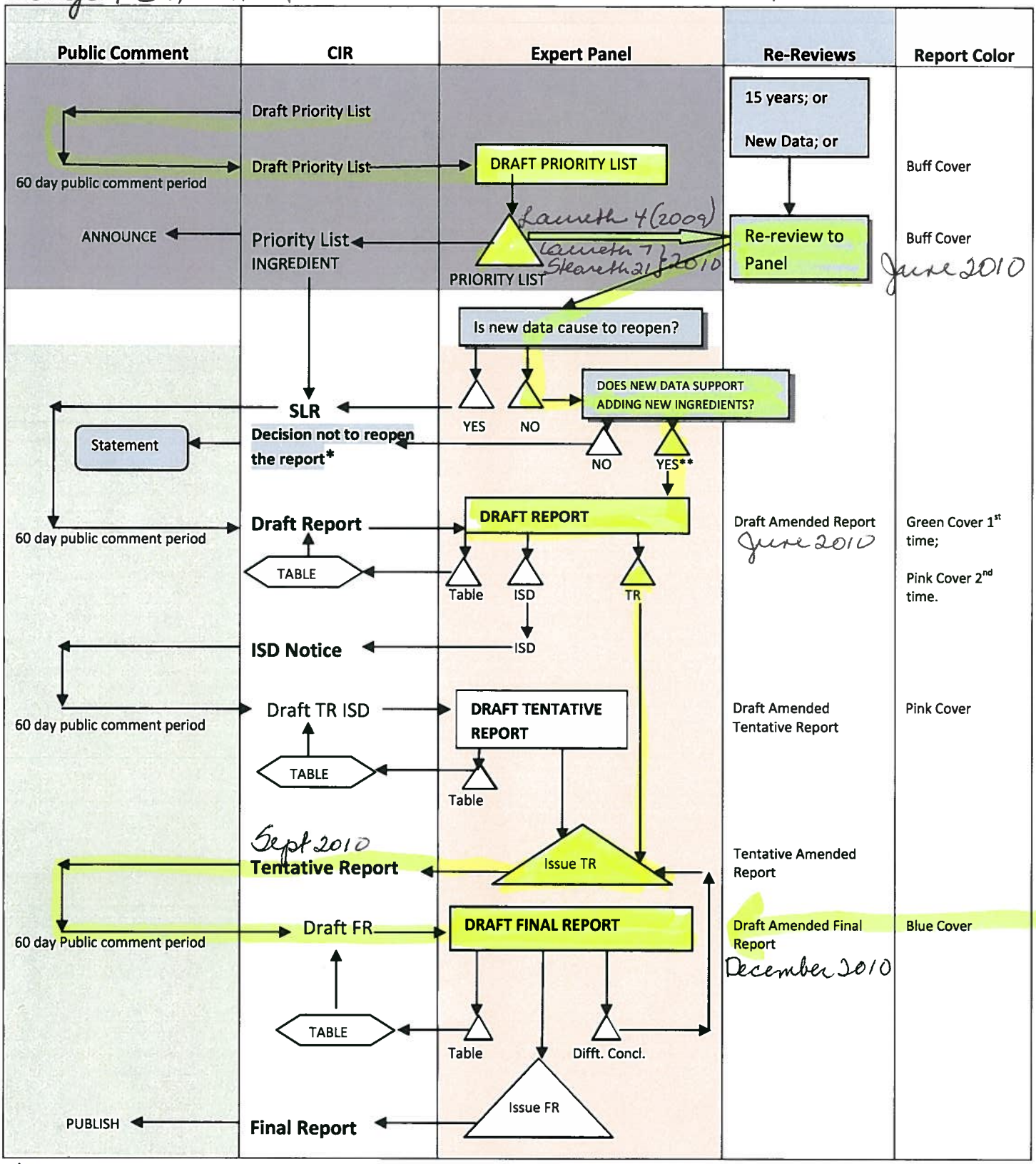
The Panel should vote to issue the Final Report on the Alkyl PEG Ethers.

The following information is being provided:

1. additional concentration of use data
2. Council comments on the June draft report
3. Council comments on the Tentative Report
4. Data profile for the Alkyl PEG Ethers

SAFETY ASSESSMENT FLOW CHART

Alkyl PEG Ethers — December 2010



*The CIR Staff notifies of the public of the decision not to re-open the report and prepares a draft statement for review by the Panel. After Panel review, the statement is issued to the Public.

**If Draft Amended Report (DAR) is available, the Panel may choose to review; if not, CIR staff prepares DAR for Panel Review.

△ Expert Panel Decision

▭ Document for Panel Review

⇨ Option for Re-review

History - Alkyl PEG Ethers

June 28-29, 2010

Laureth-4 and laureth-23 were brought forward to the Panel for a decision as to whether or not to rereview this report. In preparing that re-review document, it was realized that there is a large number of ingredients (369) that are very similar to one another. Therefore, a grouping of ingredients based on structural and functional similarities was created, and the Panel agreed to re-review laureth-4 in order to include these ingredients. Many of the ingredients included in this family were previously reviewed, as were many of the components of these ingredients. The information included in those original reports is used to support the safety of the entire Alkyl PEG Ether family.

The Panel agreed to rereview laureth-4 and laureth-23. Additionally, a Tentative Report was issued with the conclusion that the alkyl PEG ethers safe in the present practices of use and concentration described in this safety assessment when formulated to be non-irritating. Were ingredients in this group not in current use to be used in the future, the expectation is that they would be used in product categories and at concentrations comparable to others in this group. This assessment is also intended to address future alkyl PEG ether cosmetic ingredients that vary from those ingredients recited herein only by the number of ethylene glycol repeat units

The Panel did state that available data regarding biohandling and biotransformation of branched chains would be useful.

December 13-14, 2010

Information on compounds analogous to laureth-9 were added to the report.

Alkyl PEG Ethers Data Profile* – Dec 2010 – Writers, Monice Fiume and Bart Heldreth (includes data in original assessments)															
	Cosmetic Use	ADME/ Absorption	Animal Tox- Oral – Acute	Animal Tox – Drml - Acute	Animal Tox – Inhal-Acute	Animal Tox- Oral – Rptd	Animal Tox – Drml - Rptd	Animal Tox – Inhal-Rptd	An. Irrt/Sens	Ocular Irr.	Repro/Dev - Dermal	Repro/Dev	Genotox	Carc	Clin . Data
PEGs (component)		X	X	X		X	X		X	X	X	X	X	X	X
Arachideth-20															
Beheneth-2															
Beheneth-5															
Beheneth-10	X														
Beheneth-15															
Beheneth-20	X														
Beheneth-25	X														
Beheneth-30	X														
Behenyl Alcohol			X							X					
C9-11 Pareth-3									X	X					
C9-11 Pareth-4															
C9-11 Pareth-6	X		X	X			X		X	X	X		X		
C9-11-Pareth-8	X								X	X					
C9-15 Pareth-8															
C10-16 Pareth-1															
C10-16 Pareth-2															
C11-13 Pareth-6															
C11-13 Pareth-9															
C11-13 Pareth-10															
C11-15 Pareth-3	X														
C11-15 Pareth-5	X														
C11-15 Pareth-7	X														
C11-15 Pareth-9	X														
C11-15 Pareth-12															
C11-15 Pareth-15															
C11-15 Pareth-20															
C11-15 Pareth-30															
C11-15 Pareth-40	X														
C11-21-Pareth-3															
C11-21-Pareth-10															
C12-13 Pareth-1															
C12-13 Pareth-2			X	X					X	X					
C12-13 Pareth-3	X								X	X					
C12-13 Pareth-4															
C12-13 Pareth-5															
C12-13 Pareth-6															
C12-13 Pareth-7	X								X	X					X
C12-13 Pareth-9															
C12-13 Pareth-10															
C12-13 Pareth-15															
C12-13 Pareth-23	X														
C12-13 Pareth – chain length not specified			X	X					X	X					
C12-14 Pareth-3	X														
C12-14 Pareth-5															
C12-14 Pareth-7															
C12-14 Pareth-9															
C12-14 Pareth-12	X														
C12-15 Pareth-2															
C12-15 Pareth-3	X								X	X					
C12-15 Pareth-4															
C12-15 Pareth-5															
C12-15 Pareth-7	X								X	X					X
C12-15 Pareth-9	X								X	X					
C12-15 Pareth-10															
C12-15 Pareth-11															
C12-15 Pareth-12	X									X					
C12-16 Pareth-5															
C12-16 Pareth-7	X														
C12-16 Pareth-9	X														
C13-15 Pareth-21															
C14-15 Pareth-4															
C14-15 Pareth-7						X			X	X					
C14-15 Pareth-8															
C14-15 Pareth-11									X	X					

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	Cosmetic Use	ADME/ Absorption	Animal Tox- Oral – Acute	Animal Tox – Drml - Acute	Animal Tox – Inhal-Acute	Animal Tox- Oral – Rptd	Animal Tox – Drml - Rptd	Animal Tox – Inhal-Rptd	An. Irrt/Sens	Ocular Irr.	Repro/Dev - Dermal	Repro/Dev	Genotox	Carc	Clin . Data
C14-15 Pareth-12															
C14-15 Pareth-13									X	X					
C20-22 Pareth-30															
C20-40 Pareth-3	X														
C20-40 Pareth-10	X														
C20-40 Pareth-24															
C20-40 Pareth-40	X														
C20-40 Pareth-95	X														
C22-24 Pareth-33															
C30-50 Pareth-3															
C30-50 Pareth-10															
C30-50 Pareth-40															
C40-60 Pareth-3															
C40-60 Pareth-10															
C11-15 Sec-Pareth-12															
C12-14 Sec-Pareth-3															
C12-14 Sec-Pareth-5	X														
C12-14 Sec-Pareth-7	X														
C12-14 Sec-Pareth-8															
C12-14 Sec-Pareth-9															
C12-14 Sec-Pareth-12															
C12-14 Sec-Pareth-15															
C12-14 Sec-Pareth-20															
C12-14 Sec-Pareth-30															
C12-14 Sec-Pareth-40															
C12-14 Sec-Pareth-50															
Capryleth-4															
Capryleth-5															
Ceteareth-2	X														
Ceteareth-3	X														
Ceteareth-4	X														
Ceteareth-5	X														
Ceteareth-6	X														
Ceteareth-7	X														
Ceteareth-8															
Ceteareth-9															
Ceteareth-10	X														
Ceteareth-11															
Ceteareth-12	X														
Ceteareth-13															
Ceteareth-14															
Ceteareth-15	X								X	X					X
Ceteareth-16	X														
Ceteareth-17															
Ceteareth-18															
Ceteareth-20	X	X													
Ceteareth-22	X														
Ceteareth-23															
Ceteareth-24															
Ceteareth-25	X														
Ceteareth-27															
Ceteareth-28															
Ceteareth-29															
Ceteareth-30	X														
Ceteareth-33	X														
Ceteareth-34															
Ceteareth-40															
Ceteareth-50															
Ceteareth-55	X														
Ceteareth-60	X														
Ceteareth-80															
Ceteareth-100	X														
cetyl, stearyl, and./or cetearyl alcohol (component)		X	X	X	X	X	X		X	X			X	X	X
Ceteth-1	X														
Ceteth-2	X		X				X		X	X					

Alkyl PEG Ethers Data Profile* – Dec 2010 – Writers, Monice Fiume and Bart Heldreth (includes data in original assessments)															
	Cosmetic Use	ADME/ Absorption	Animal Tox- Oral – Acute	Animal Tox – Drml - Acute	Animal Tox – Inhal-Acute	Animal Tox- Oral – Rptd	Animal Tox – Drml - Rptd	Animal Tox – Inhal-Rptd	An. Irrt/Sens	Ocular Irr.	Repro/Dev - Dermal	Repro/Dev	Genotox	Carc	Clin . Data
Ceteth-3	X														
Ceteth-4															
Ceteth-5															
Ceteth-6	X														
Ceteth-7															
Ceteth-10	X		X				X		X						
Ceteth-12	X														
Ceteth-13															
Ceteth-14															
Ceteth-15	X														
Ceteth-16	X														
Ceteth-17															
Ceteth-18															
Ceteth-20	X		X										X		
Ceteth-23															
Ceteth-24	X														
Ceteth-25	X														
Ceteth-30	X														
Ceteth-40															
Ceteth-45															
Ceteth-150															
Ceteth – unspecified chain length			X												
cetyl alcohol (component)			X	X	X		X		X	X			X		X
Cetoleth-2															
Cetoleth-4															
Cetoleth-5															
Cetoleth-6															
Cetoleth-10															
Cetoleth-11															
Cetoleth-15															
Cetoleth-18															
Cetoleth-20															
Cetoleth-22															
Cetoleth-24															
Cetoleth-25	X														
Cetoleth-30															
oleyl alcohol (component)		X		X					X				X		X
Coceth-3															
Coceth-5															
Coceth-6															
Coceth-7	X														
Coceth-8	X														
Coceth-10	X														
Coceth-20															
Coceth-25															
coconut alcohol (component)															
Deceth-3	X														
Deceth-4															
Deceth-5	X														
Deceth-6															
Deceth-7	X														
Deceth-8	X														
Deceth-9	X														
Deceth-10															
Decyltetradeceth-5															
Decyltetradeceth-10															
Decyltetradeceth-15															
Decyltetradeceth-20															
Decyltetradeceth-25															
Decyltetradeceth-30															
Hexyldeceth-2															
Hexyldeceth-20															
Hydrogenated Dimer Dilinoleth-20															
Hydrogenated Dimer Dilinoleth-30															
Hydrogenated Dimer Dilinoleth-40															

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Hydrogenated Dimer Dilinoleth-60															
Hydrogenated Dimer Dilinoleth-80															
Hydrogenated Laneth-5															
Hydrogenated Laneth-20															
Hydrogenated Laneth-25															
Hydrogenated Talloweth-12															
Hydrogenated Talloweth-25															
Isoceteth-5															
Isoceteth-7															
Isoceteth-10	X														
Isoceteth-12															
Isoceteth-15															
Isoceteth-20	X														
Isoceteth-25	X														
Isoceteth-30															
Isodeceth-4															
Isodeceth-5															
Isodeceth-6	X														
Isolaureth-3															
Isolaureth-6	X														
Isolaureth-10															
Isomyreth-3															
Isomyreth-9															
Isostearеth-2	X														
Isostearеth-3															
Isostearеth-5	X														
Isostearеth-8															
Isostearеth-10	X														
Isostearеth-12															
Isostearеth-15															
Isostearеth-16															
Isostearеth-20	X														
Isostearеth-22															
Isostearеth-25															
Isostearеth-50															
isostearyl alcohol (component)			X						X	X					X
Laneth-5	X		X						X	X					X
Laneth-10															
Laneth-15	X														
Laneth-16	X		X						X	X					X
Laneth-20	X														
Laneth-25	X		X						X	X					X
Laneth-40	X														
Laneth-50															
Laneth-60															
Laneth-75															
cholesterol (component)		X				X			X			X	X	X	X
alcohol ethoxylates		X	X		X	X		X	X		X		X		X
Laureth-1	X	X													
Laureth-2	X														
Laureth-3	X	X													
Laureth-4	X		X	X			X		X	X	X				X
Laureth-5	X								X						
Laureth-6	X	X													
Laureth-7	X														
Laureth-8	X														
Laureth-9	X	X	X	X		X	X		X	X		X	X	X	X
Laureth-10	X	X													
Laureth-11	X														
Laureth-12	X														
Laureth-13															
Laureth-14	X														
Laureth-15															
Laureth-16	X														
Laureth-20	X														

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	Cosmetic Use	ADME/ Absorption	Animal Tox- Oral – Acute	Animal Tox – Drml - Acute	Animal Tox – Inhal-Acute	Animal Tox- Oral – Rptd	Animal Tox – Drml - Rptd	Animal Tox – Inhal-Rptd	An. Irrt/Sens	Ocular Irr.	Repro/Dev - Dermal	Repro/Dev	Genotox	Carc	Clin . Data
Laureth-21	X														
Laureth-23	X		X	X					X	X					X
Laureth-25	X														
Laureth-30	X														
Laureth-38															
Laureth-40															
Laureth-50															
Laureth – chain length not specified									X				X		
Methoxy PEG-7															
Methoxy PEG-10															
Methoxy PEG-16	X														
Methoxy PEG-25															
Methoxy PEG-40															
Methoxy PEG-100															
methyl alcohol		X	X	X	X			X		X	X	X			X
Myreth-2															
Myreth-3	X														
Myreth-4	X														
Myreth-5															
Myreth-10	X														
myristyl alcohol (component)			X	X	X				X	X					X
Noneth-8															
Octyldodeceth-2															
Octyldodeceth-5															
Octyldodeceth-10															
Octyldodeceth-16	X														
Octyldodeceth-20	X														
Octyldodeceth-25	X														
Octyldodeceth-30															
octyl dodecanol (component)			X	X					X	X					X
Oleth-2															
Oleth-3															
Oleth-4															
Oleth-5															
Oleth-6															
Oleth-7															
Oleth-8	X														
Oleth-9															
Oleth-10	X		X						X	X					
Oleth-11															
Oleth-12	X														
Oleth-15	X														
Oleth-16	X														
Oleth-20	X					X			X	X					
Oleth-23															
Oleth-24															
Oleth-25	X														
Oleth-30	X														
Oleth-35															
Oleth-40															
Oleth-44															
Oleth-45															
Oleth-50	X														
Oleth-82	X														
Oleth-100															
Oleth-106	X														
Oleth – chain length not specified						X									
oleyl alcohol (component)		X		X					X				X		X
Palmeth-2															
PEG-16 Cetyl/Oleyl/Stearyl/Lanolin Alcohol Ether															
lanolin alcohol (component)			X						X	X					X
cholesterol (component)		X				X			X			X	X	X	X
PEG-Cetyl Stearyl Diether															
PEG-4 Distearyl Ether	X														
stearyl alcohol (component)		X	X				X		X	X			X	X	X

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PEG-4 Ditallow Ether															
PEG-15 Jojoba Alcohol															
PEG-26 Jojoba Alcohol															
PEG-40 Jojoba Alcohol															
Jojoba Alcohol (component)			X				X		X				X		X
PEG-3 Methyl Ether		X	X	X	X	X	X		X	X		X	X		X
PEG-4 Methyl Ether															
PEG-6 Methyl Ether															
PEG-7 Methyl Ether				X			X						X		
PEG-7 Propylheptyl Ether	X														
PEG-8 Propylheptyl Ether	X														
Steareth-1															
Steareth-2	X		X						X	X					X
Steareth-3															
Steareth-4	X		X												
Steareth-5															
Steareth-6	X														
Steareth-7	X														
Steareth-8															
Steareth-10	X		X						X	X					X
Steareth-11															
Steareth-13															
Steareth-14															
Steareth-15	X														
Steareth-16	X														
Steareth-20	X		X				X		X	X					
Steareth-21	X														X
Steareth-25	X														
Steareth-27															
Steareth-30	X														
Steareth-40															
Steareth-50	X														
Steareth-80															
Steareth-100	X														
Steareth-200	X														
stearyl alcohol (component)		X	X				X		X	X			X	X	X
alcohol ethoxylates													X	X	
Steareth-60 Cetyl Ether															
Talloweth-4	X														
Talloweth-5	X														
Talloweth-6	X														
Talloweth-7															
Talloweth-18															
Talloweth – chain length not specified							X								
Trideceth-2															
Trideceth-3	X														
Trideceth-4															
Trideceth-5	X														
Trideceth-6	X														
Trideceth-7	X														
Trideceth-8	X														
Trideceth-9	X														
Trideceth-10	X														
Trideceth-11	X														
Trideceth-12	X														
Trideceth-15															
Trideceth-18															
Trideceth-20															
Trideceth-21															
Trideceth-50															
Undeceth-3	X														
Undeceth-5	X														
Undeceth-7															
Undeceth-8															

Alkyl PEG Ethers Data Profile* – Dec 2010 – Writers, Monice Fiume and Bart Heldreth (includes data in original assessments)															
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Undeceth-9															
Undeceth-11	X														
Undeceth-40															
Undecyleneth-6															

*"X" indicates that data were available in a category for the ingredient; it is not an indication of positive or negative findings
Alternate shading indicates a related set of ingredients

Updated Search – 09-21-10 – last 12 mos entries only

Sebacic 09-21-10 10 hits/0 useful
111-20-6 OR 184706-97-6 OR 109-43-3 OR 110-40-7 OR 122-62-3 OR 359073-59-9 OR 10340-41-7 OR 7491-02-3 OR 69275-01-0 OR 17265-14-4 OR 478273-24-4 OR (DICAPRYL AND CAPRYL AND SEBACATE) OR (DIISOSTEARYL AND SEBACATE)

Malonic-Succinic-Glutaric 09-21-10 74 hits/0 useful
141-82-2 OR 105-53-3 OR 110-15-6 OR 2922-54-5 OR 150-90-3 OR 106-65-0 OR 123-25-1 OR 2915-57-3 OR 2530-33-8 OR 14491-66-8 OR 93280-98-9 OR 925-06-4 OR 110-94-1 OR 1119-40-0 OR 71195-64-7 OR (DIISOSTEARYL AND GLUTARATE)

Adipic 09-21-10 23 hits/0 useful
124-04-9 OR 627-93-0 OR 141-28-6 OR 103-23-1 OR 106-19-4 OR 105-99-7 OR 105-97-5 OR 26720-21-8 OR 155613-91-5 OR 110-33-8 OR 141-04-8 OR 57533-90-1 OR 58262-41-2 OR 59686-69-0 OR 27178-16-1 OR 33703-08-1 OR 108-63-4 OR 6938-94-9 OR 62479-36-1 OR 155613-91-5 OR 85117-94-8 OR 16958-92-2 OR (ALKYL AND ADIPATE) OR (DIHEXYLDECYL AND ADIPATE)

Azelaic-Dodecanedioic 09-21-10 10 hits/3 possibly useful
123-99-9 OR 9619-43-3 OR 52457-54-2 OR 17265-13-3 OR 27825-99-6 OR 132499-85-5 OR 693-23-2 OR 131252-83-0 OR 129423-55-8

October 26, 2010 – identified a SIDS document on PEG-3 Methyl Ether (now included in text)

TRANSCRIPTS/MINUTES

Clinical observations? So we just need to clarify what that -- what you mean by different activity measurements.

DR. HELDRETH: Okay.

DR. BELSITO: Any other comments? Okay. So we're going safe as used. And again, anything that Bart needs to put into the discussion that isn't currently there? No? We're happy with it? Okay. Good.

Okay. It's 10:30. Why don't we take a 10-minute break and regroup at 10:40.

(Recess)

DR. BELSITO: Have we reassembled?

SPEAKER: Yes.

DR. BELSITO: Okay. So now we're ready and we've been refortified to take on the gorilla, alkyl PEG ethers. And this is a list of about 367 ingredients that we're being asked to look at. So before we even start I guess my question is to Dan and the other members of my team, is the grouping okay? Any comments on that, Dan?

DR. LIEBLER: I didn't have any concerns. I'm paging through my notes here to refresh my memory. But I don't -- I don't think so.

DR. KLAASSEN: I thought it was great.

DR. LIEBLER: Yeah, my first note is reaction schemes in the text. I love it.

DR. BRESLAWEC: Just want to point out for the record we don't see --

SPEAKER: Oh, sorry.

DR. BRESLAWEC: I would like to point out for the record that you don't see one writer analyst reviewer here, you see three. There's a reason for that. Monice coordinated and was the head person on the report, but it involved a lot of other staff.

DR. BELSITO: Okay. Okay, so at least our team says keep the seatbelts on. We're going to keep all 367 chemicals in this report.

So if we're okay with the family and since we've done so many of these reports before, and if you looked at all of the data, we really certainly have lots of data, then is it a little bit presumptuous of me to say that these are safe as used when formulated not to be irritating and move on?

DR. LIEBLER: It's not presumptuous.

DR. BELSITO: I mean, if you're comfortable with the chemical grouping, I'm comfortable with the conclusion. I mean, because we've already looked at a number of these that are included in here. Otherwise, in the discussion there are animal sources for lanolin so we need the animal boilerplate. I didn't make a note if there are any plant sources. I didn't see any, but it's a huge document. I may have missed them. If there are any plant sources we need that. And then there's notes about penetration enhancements so we need that usual boilerplate in our discussion. That's the only comments I had.

DR. LIEBLER: First of all, I'd like to say from a chemistry perspective the organization was excellent. Very nice. And the explanation at the beginning of the report explaining the chemistry and incorporating those reaction schemes into the text was very nice for readability. So that was very good, and my compliments to you guys. You may want to number the schemes though so you can refer to them, just like you would, you know, in a manuscript, scheme 1A or scheme 1, 2, 3, 4.

DR. BELSITO: Page 17, under octyldodecanol, the second line, "30 percent A. Solution." Is that supposed to be aqueous solution?

MS. FIUME: Yes.

DR. BELSITO: And then some minor comments, but I guess this is the point now when we need to look at how the use information is given. So I will open that up for discussion for our group. I think for me I definitely like it. I mean, literally, in this report it probably would save me five hours of going through and tallying what's a dermal leave-on and what's the range for that and what's a rinse-off and what's the range for that. And what's a lipstick and is there an aerosol use in having to go through each

one in looking for hairspray and foot spray. I mean, I think it's wonderful. I would agree with comments that Dan and Curt made that electronically the old format I think should still be available. So it will involve making the old tables and take a little bit of time for the reader. And then that should be available for us to look at -- or the writer, rather. It should be available for us to look at, but not be in the published documents. This is so much easier. And then agree with the comments from the Council that you need to split off rinse-offs into something like diluted prior to application or not diluted. And so that would be like shampoos and things versus a vaginal douche.

DR. BERGFELD: Do you have a comment?

DR. ANSELL: No.

DR. BELSITO: So I like those comments. And then Dave had a very interesting point about, you know, when we get to things that are used as pH adjusters would be very different than used as a hair straightener. I don't know how we'll deal with that, but I guess we'll deal with that when we have to deal with it.

The only issue is, I guess, in terms of how do you explain to the public that you have the total number for leave-on and rinse-offs is the total number, but the total number that will appear in the paragraph for the different types of uses may be greater than N because a lipstick would be counted twice, both as a dermal and as a possible absorption. And maybe what you could do there is do a leave-on and a rinse-off. And then I do like the idea of putting a heading below, you know, so you have types of use broken down into leave-on, rinse-off, rinse-off without dilution, or however you wanted to do that. And then number and concentration of use. And then what you probably could do would be to do that as, you know, dermal yadda, yadda, yadda so the N is the same. But then below it put Special Categories of Use. And sort out, you know, the I, the possible ingestion, the possible inhalation in the baby so that, you know, it makes a little bit more sense to someone that that is not going to be the total N, but you're captured the N in terms of types of use and then number and concentration of uses. Those will be the Ns and then below a third category, you know, which are the specials.

Yes, Wilma.

DR. BERGFELD: I was thinking just asterisk them and put down that you can -- under the asterisk you could state that uses may be shared between product lines or something, rather than to do all that detail. That would account for the difference in number.

DR. BELSITO: So what you're suggesting is an asterisk that would say that the total number here may be greater because a single product would be included under two different categories such as a baby lotion would be under both dermal and baby lipstick would be under both possible ingestion and dermal?

DR. BERGFELD: Something like that. I think we can work on that to make it as brief as possible.

DR. BRESLAWEC: Something along the lines of ingredients may be used in more than one category?

DR. BERGFELD: Yeah.

MS. FIUME: Dr. Belsito, can I ask -- because I just need to get clarification on the other way we used to do it. AS I pulled this in, I have an Excel spreadsheet that lists by ingredient everything that came from FDA. Would that be satisfactory to show you what the exact categories are rather than putting them in a table?

DR. BELSITO: Yeah. I mean, I'm fine with that. I think that it would be nice for the panel to look at that. But in terms of -- and see so that we're comfortable that we're getting representative data for each of the individual ingredients we're looking at. I think that was Ron and Paul's concern that when it's condensed like this we don't really have information on, you know, in the dermal category the different categories or products that might be being used

and where we're getting report. And that's the kind of information we would like to see before we're comfortable signing off on it. In terms of the types of information that eventually we want in assessing the safety, these tables address it. You know, I want to know am I looking at something that's used 27 percent in lipstick? You know, what are the leave-on concentration ranges for sensitization, irritation that I'm worried about that I want to see good data? So, you know, I think these tables are wonderful. But, yeah, I mean, an Excel spreadsheet is fine.

DR. BRESLAWEC: We may want to play with something in that, maybe provide you with both formats or both for a while and see if there's anything that you feel is missing from the new use tables. Maybe be able to draw that in. Because I just don't think you have any real familiarity with using this. And if you find yourself going back to the spreadsheet or the raw data routinely for the same type of information then we need to do something to put that in. So we may be playing with both formats for a while if that's all right with you.

DR. BELSITO: I think that's great, and I think that, you know, Monice answered Rachel's criticism before. And if you look on page 102 in Table 5 you see that for steareth-2 that in the original report there are 107 uses. There are now 593. In the original report it was used in leave-ons less than or equal to 10 percent and rinse-offs at less than or equal to 5 percent. So we are capturing in generality the type of data that we got from the individual reports at least for, you know, is it significantly increased in usage? We got that. Has it significantly changed in concentrations? We have that. So, I mean, again I think that, you know, the way these tables are organized is great. The only information we're not getting is broken down in a dermal category how many areas are blank. And are we getting it just all of this range for a face cream or are we getting it for body lotions, et cetera, et cetera. And that's what the detailed map I think would assure us. Just scanning down and seeing that we're getting numbers in all the general categories, I almost don't need to look at the numbers. Just get a sense that they're there, you know, and then use your tables because that's what I did before on my own.

MS. FIUME: And then, just so we know as we progress with these tables, in Table 6, just because it was easier, we do list the total number of uses per category. Is that information you would still like to see in the report so you have an idea?

DR. BERGFELD: Yes.

DR. KLAASSEN: Yes.

DR. BERGFELD: (inaudible) impact.

DR. BELSITO: Yeah. I mean, I think that's good. But now that you're on to Table 6, the concentration of uses for all the laureths are blank there, so.

DR. BRESLAWEC: The same situation as with the other report. This was a huge number. It overwhelmed the system and they're responding as rapidly as they possibly can.

DR. BELSITO: Okay. And then the only comment that I have is in the report we had data on laureth-4 and there were some neurotoxicity issues that I don't think are real issues given absorption and that. But laureth-4 is not listed here so I'm assuming there are no uses for it. It's page 106 of the document.

MS. FIUME: Lauret-4 is actually on page 101 because it was previously reviewed. Table 5 is all the previously reviewed reports.

DR. BELSITO: Oh.

MS. FIUME: And Table 6 is the newly added reports.

DR. BELSITO: Okay. Didn't catch that.

DR. ANSELL: Before we leave Table 6, the total 36,000, is that formulations reported using any one of these ingredients or is that the total number of leave-on products in the entire database representing all possible ingredients?

DR. BRESLAWEC: It's the total number of all possible ingredients, leave-on and rinse-off.

DR. ANSELL: Irrespective of whether they contain this ingredient or not?

DR. BRESLAWEC: Correct. That is a total -- that's the -- what you're comparing to. So a total of 36,808 reported product uses for ingredients. Laureth-1 is used in one of those reports. So that's the overall.

DR. BELSITO: So the FDA has in their databank for the VCRP system has a total of 23,788 leave-on cosmetics?

DR. BRESLAWEC: Correct.

DR. BELSITO: Okay. So that's our universe.

DR. BRESLAWEC: That would be your universe of what we have. It may not be the spectrum of the totality of the universe, but it's just what's available to the FDA at a given point in time.

DR. BELSITO: Right. Somehow that needs to be explained because I had the same question as Jay, whether it was for all products in the table or for the universe of VCRP, so.

DR. BRESLAWEC: This is the same number that you used to see in parenthesis in the old table. You'd say see category of use and then you'd see a number in parenthesis.

DR. BELSITO: Yeah. I don't know how you make that clear to a reader, but somehow it almost needs to be broken out of the table and always be a separate table, like 6A, 6B or something, you know, where 6A is total number of, you know, cosmetic ingredients in the VCRP by category. And then 6B is total number for the specific chemicals under review. Because otherwise it's very -- I mean, I didn't know what the heck it meant either.

DR. ANSELL: Yeah. Although I don't object to its presence, I'm curious as to what we can interpret from that. You know, certainly if that number were of these ingredients we could tell that the laureth-4 is, you know, the big one, but how it compares to everything in the databases is far from clear what we can interpret from that.

DR. BRESLAWEC: We have the same concern. And that's why we presented it with that piece of information when Christina did the presentation and without because we weren't sure whether you were getting anything out of that number. And if you're not then maybe get rid of it, you know.

DR. BELSITO: Any other comments about how we're going to be reporting frequency and concentration of use?

DR. SNYDER: My only comment is that it's a work in progress and we just have to see how it works. You just have to see a report and see how the new data works. And I think we've accomplished a lot of that today to make it more useful to us as reviewers.

DR. BRESLAWEC: As Christina said, we really are very much seeking your input and guidance on this. It's not going to work unless it works for you and gives you the kind of information that you need.

DR. BELSITO: I think it's great. Okay, so we're happy with the groupings and we're going to -- we're happy with the tables. We're expecting that PCPC will fill in some of the concentrations of use. And we'll check to make sure in the discussion that there are no botanical sources. If there are I'll put that boilerplate in. There are animal sources for lanolin so that boilerplate needs to go in. And Table 6, we're getting rid of the universe listings and we're going with the safe as used when formulated not to be irritating.

DR. BRESLAWEC: Okay. Because this is a re- review, you have an option to reopen or you can accept this as a draft report.

DR. BELSITO: We're reopening, accepting it as a draft, and going safe as used. Moving it to a final.

DR. BERGFELD: Don, do you think in your discussion, because this is a new way of dealing with so many ingredients, that we ought to have some kind of small statement?

DR. BELSITO: Give me an example of a small statement that you want.

DR. BERGFELD: Well, that there were 300 -- what was it -- 364 ingredients that related chemically that fell into the alkyl PEG ethers, many of which had been reviewed before and were found to be safe. And then we could possibly say that these were, I'm going to say, were condensed, but these were grouped together in one large report or one review report.

DR. BELSITO: Sure. I mean, I think for all of these re-reviews where we've opened them to add other ingredients, I mean, I think there should be sort of maybe a standard boilerplate first paragraph as to what was originally reviewed, what's being added in, and the rationale for the inclusion of the new ingredients. And that's going to largely be crafted by I presume Bart and Dan and Ron, the chemists, because that's what's driving the additions is the chemical structural similarities. So, you know, you three get together and draft those -- that first paragraph for us. I mean, but I think that should be standard for all re-reviews that are open to add things on as to the rationale as to why we did it. Sure.

DR. BERGFELD: Thank you. And it's better said than I said it. But I think it should occur in the discussion. I'm not sure it should occur in the introductory portion, but it could occur there, also.

DR. BELSITO: Yeah. I mean --

DR. BRESLAWEC: Monice. No, I'm sorry.

DR. BELSITO: Go ahead.

DR. BRESLAWEC: Monice and Bart, do you want to mention methyl?

DR. LIEBLER: We're really talking about a new sort of inclusion boilerplate, if you will, that we'll use common language to describe rationale for including larger groups, additional groups of chemical substances in these reports. And I think it would be pretty easy for us to come up with something. Because we'll almost always have the same reasons for including.

MS. FIUME: In Council's comments, they were wondering whether or not the PEG methyl ethers, methoxy PEG ethers belong in this report because they have a different function. I'll actually just read what they said. It will probably be easiest.

"Please consider removing the PEG methyl ethers and methoxy these ingredients are all defined as having an average number of ethylene oxide units that have the potential of containing methoxyethanol and methoxydiglycol, both in the dictionary. Both methoxyethanol and methoxydiglycol are not permitted for use in Europe and both are developmental toxicants. As indicated on page 6, the functions reported for the methyl ingredients, which is solvents and humectants, are different than the functions reported for the majority of the other ingredients included in this report."

And then they wanted to know if the methyl group ingredients are removed from the report, the CIR Expert Panel should be asked if a statement that extends the report conclusion to other alkyl PEG ethers in the same families as in this report added to the dictionary in the future should be added to this report, similar to what was done in the propylene glycol report. So I guess it's actually two --

DR. BRESLAWEC: Two separate issues.

MS. FIUME: Two separate issues.

DR. BELSITO: Okay. Well, I think that, yeah, it would be great that we do that and should there be in the future PEG X that falls above whatever that it's automatically to be concluded as safe. So I would say that, you know, it's probably a no-brainer to say, yeah, definitely to the second part. For the first part of your question I guess I'll see to Dan and ask him.

DR. LIEBLER: I'd like to hear that one more time, just the first suggestion.

MS. FIUME: As these ingredients are all defined as having an average number of ethylene oxide units that have the potential of containing methoxyethanol and methoxydiglycol, both are in the dictionary, both methoxyethanol and methoxydiglycol are not permitted for use in

cosmetics in Europe. And both are developmental toxicants. As indicated on page 6, the functions reported for the methyl ingredients, which are solvents and humectants, are different than the functions reported for the majority of the other ingredients included in this report.

DR. LIEBLER: Right. And the compound class we're talking about here -- I'm just trying to find myself.

DR. BRESLAWEC: They're PEG-3 methyl ether.

DR. LIEBLER: PEG methyl ethers.

DR. BRESLAWEC: PEG-4 methyl ethers. PEG-7.

DR. ANSELL: The concern was raised that the --

SPEAKER: Microphone, please.

DR. ANSELL: The concern which was raised was that the PEG ethers may have present methoxyethanol or potentially methoxydiglycol and that one suggestion was that to address the potential impurities that they simply be eliminated from the report. Alternatively, since it's well known that they may be present and industry is well aware of their presence that a statement be added simply noting the concern if these materials were to be present. And I think that's more consistent with what our recommendation would be today.

DR. BERGFELD: So what you said is you'd like to keep this ingredient group that's been requested to be removed and just clarify it in the discussion?

DR. ANSELL: That's what we think today.

DR. KLAASSEN: Okay. I just -- I think the issue here is that ethylene glycol ethers, the very, very small ones, can be developmental toxicants and testicular toxicants. And I think what's being said here is that there could be some of that contaminant when they make some of these chemicals. And so the bottom line is that we should, you know, maybe just put in there in regard to purities or impurities that it does not contain these. That's basically what you're saying, Jay, right?

DR. ANSELL: Right.

MS. FIUME: Then for a point of clarification on the bottom of page 5 of the report, the last paragraph, and then also on page 22, which is the first summary paragraph under Reproductive and Developmental Toxicity, is that enough to cover the concern?

DR. KLAASSEN: (inaudible)

DR. BELSITO: So it says --

SPEAKER: Microphone, please.

DR. BELSITO: Page 5 or page 6 with the PEG methyl ethers. First of all --

DR. KLAASSEN: On page 5, what she had referenced to is the presence of 1,4-dioxane and the unreacted ethylene oxide. And that's kind of a different issue. But, you know, that is an important point and should go into the discussion. It turns out that, you know, 1,4- dioxane and ethylene oxide are carcinogens, but, you know, there's just tiny amounts here. And as long as that's in the discussion.

Then if you go to page 22.

DR. BELSITO: Well, page 6, though --

DR. KLAASSEN: Okay.

DR. BELSITO: -- is component ingredients. You have the PEG methyl ethers on page 6. Is that not where you should put the issue of the small glycols?

DR. LIEBLER: That seems like a logical place to put that.

DR. BELSITO: Right here?

DR. KLAASSEN: Yeah.

DR. BELSITO: So we could put that restriction there and then your next one was on reproductive toxicity?

DR. KLAASSEN: Correct. Page 22. Which says -- the summary there at the top in italics says, "Overall it was found that metabolites of ethylene glycol monoalkyl ethers are reproductive and developmental toxicants -- toxins. In general, however, the metabolites of concern are not expected to be formed in cosmetic formulation that contain polymers of ethylene glycol." I

think that's fine. I think it could be maybe made a little bit more -- I think it's only the very, very short esters that are reproductive toxicants.

Also as a general point for the writers, while we say the word "toxins," most toxicologists use the word "toxins" only for "god-made chemicals." That is a snake venom-type things. A synthetic chemical we usually do not call toxins. We call them toxicants or just chemicals. Developmental toxicants, not toxins. But that's kind of minutia, maybe.

DR. LIEBLER: So I would just like to return to Don's suggest. Is that on, I guess it's page, hang on, yeah, page 6, under PEG methyl ethers we add a line. There's one line there right now. But we add a line indicating that these may be contaminated with these compounds, the methoxyethanol, the methoxydiglycol. Maybe that's not the place to put it, but I think we could deal with Council's objection by noting the presence of these compounds, just as we note the possible presence of the dioxane in the ethylene oxide.

DR. BELSITO: I guess, I don't know, where are you getting the information? Because it's not in any of the reports that we have that these compounds will be there. In fact --

DR. ANSELL: Well, and that really is the issue. Is that there was simply an interest in adding it as a note.

DR. BELSITO: But do you have information that they're there and industry specifically goes and removes them? Or is your concern that they could be there and industry should monitor for them?

DR. ANSELL: They should be aware that these materials have a potential toxicity and assure that the products are --

DR. BELSITO: So your concern is that they have be absolutely certain that industry know this and make sure that none of that is in their product?

DR. ANSELL: That's right. We're suggesting something exactly along the lines of ethylene oxide and dioxane.

DR. BELSITO: Right. Not that it's in their products and they need to remove it; just that it --

DR. ANSELL: No.

DR. BELSITO: Okay. So then actually I'm not sure where that would go. Maybe just you could put under PEG methyl ethers that -- I guess in the discussion. It doesn't really make sense to put it under page 6 there simply because it doesn't -- it's not known to be in that product.

DR. SNYDER: It's not new data.

DR. BELSITO: It's just a hypothetical thing. So I guess in the discussion put that hypothetical that the panel was --

DR. SNYDER: The potential for these impurities --

DR. BELSITO: -- was concerned about the potential for the impurities to exist in formulation and Industry should be aware that they shouldn't exist or something.

DR. SNYDER: Yeah. I think Discussion

DR. BELSITO: Just in the discussion, yeah.

DR. BERGFELD: So you're not going with the removal of the methyl group?

DR. BELSITO: No. No. We're not going with the removal of the PEG ethers. We are going with insertion into the discussion that we're concerned about a theoretical possibility that these could be present in the manufacturing -- as a result of the manufacturing process and Industry should be aware of this and assure that it's not in their formulations. And I guess in terms of wordsmithing, however you want to do it, but I think that the theoretical potential is very important because we have no information that they're actually in product.

DR. LIEBLER: I think you could simply, in the discussion you could refer to those compounds as well as the dioxane and ethylene oxide all together because this is basically the same issue. These compounds should not or these

impurities should not be present in the -- in products formulated with these ingredients.

DR. BELSITO: So those are dioxane and small chain ethylene oxide?

DR. LIEBLER: They were captured throughout the report.

DR. BELSITO: Okay.

DR. LIEBLER: Right. They appear in different places in the report. Since the discussion isn't written yet.

DR. BELSITO: Right.

DR. LIEBLER: When the discussion is written it would be good to have a sentence or two that captures that information.

DR. BELSITO: And capturing it, why don't we create a list of exactly what chemicals we want to capture. Dioxane, ethylene glycol.

DR. LIEBLER: Dioxane, ethylene oxide, and then the two compounds we've just been referring it.

DR. BELSITO: And just give us -- give me the precise name of those compounds again.

DR. LIEBLER: Well, there's actually five impurities that we're concerned about. The 1,4-dioxane, ethylene oxide, butylated hydroxyanisol (BHA), formaldehyde, and peroxide that we've discussed in the document. So we probably should have a paragraph that addresses all of those in the discussion.

DR. BELSITO: And then the last two are the dimethyl --

DR. LIEBLER: Methoxyethanol and methoxy -- was it methoxyglycol?

DR. BRESLAWEC: Methoxydiglycol.

DR. LIEBLER: Diglycol.

DR. ANSELL: PEG 1 and PEG 2.

DR. BELSITO: Methoxy --

DR. BRESLAWEC: Ethanol.

DR. BELSITO: Ethanol.

DR. BRESLAWEC: And methoxy --

DR. BELSITO: Diglycol.

DR. HELDRETH: And then those 2 impurities are only of concern for the PEG methylene, not the rest of the PEG (inaudible).

DR. LIEBLER: Correct.

DR. BELSITO: Okay. Anything else on this?

DR. SNYDER: Yes. The carcinogenicity section on page 25 of the current report I think is a good example of what as these reports grow and they become a synthesis of other reports, that we have to make sure that we capture and accurately reflect all of the data. So we have limited carcinogenicity data, but if we go to page 901 of the steareth report in the back, there actually was a study in that report on polyethylene -- polyoxymethylene alkyl ether. There was a carcinogenicity study. It was negative and we don't even mention that. So we need to bring that probably forward into this report.

Additionally, on the ceteth report in the back also on page 166, we refer to the PEG-8 report in this document saying that -- making the statement that PEG-8 was non-carcinogenic when administered orally, intraperitoneally and subcutaneously in various test animals. But actually, if you go and read that summary of the carcinogenicity data, all of the carcinogenicity data in the PEG-8 report was only when it was used as a solvent control. So those were not studies designed to evaluate carcinogenicity of PEG-8. And so we're kind of misrepresenting that data. So we have to be very, very careful about that because once we kind of start propagating that misinformation, we need to put it in the correct accurate context of what the study design was. It wasn't a study designed to look at carcinogenicity. Those were just the solvent controls. And so we make sure that we do that.

And it's the same thing in the other report in the Oleth report. On page 22 and 23 there's data also that we haven't really brought in to this report. And so if we're using all of those previous reports to substantiate this report, we have to be careful that we're capturing data, particularly when there's data gaps. And I consider the carcinogenicity section here to be

rather limited data that we need to capture all that we have and capture it accurately.

It was kind of quick. Did you capture all of that?

DR. BRESLAWEC: I assume you have comments in your document that expands on that.

DR. SNYDER: Yeah.

DR. BRESLAWEC: Thank you.

~~DR. BELSITO: Other comments? Okay. Propylene glycol and polypropylene glycols. We're going to Blue 2, that's a final. Oh, and Monice, on the last one, you got that -- the if new ingredients come into the dictionary, that boilerplate we're adding, okay?~~

~~DR. BERGFELD: Can we discuss if new ingredients come into the dictionary with the emphasis being put onto a couple of these reports?~~

~~DR. BELSITO: Sure.~~

~~DR. BERGFELD: You really want to put an X where it's unlimited?~~

~~DR. BELSITO: Yeah, because by and large the toxicity is the lower molecular weights. I~~

~~DR. MARKS: Or reaffirmed. (Laughter) At any rate, it's minor. I think the intent is obvious.~~

DR. MARKS: Alkyl PEG ethers, Buff 3. This is a fun one. Maybe.

So, in 1983, the CIR published a conclusion that laureths 4 and 23 are safe. This is beginning a re-review. And when we re-review this, the issue is do we expand it to this large group of alkyl PEG ethers, which number 368 ingredients.

And, in addition to that, we have the new formatted "Use and Concentration" tables, too. So we should comment about that. That begins on page 101.

So let's first make a decision whether or not we want to reopen this with the intent of making a marked expansion in a number of ingredients.

And if we use the criteria before, when we do these re-reviews, it should be -- quote-unquote -- "no-brainers," in terms of adding

ingredients. So we get into this issue of read-across safety data.

So what's the sense? Ron, Ron and Tom?

DR. SLAGA: Well, I think we have to reopen it just to give it a try, and see what -- what to put in.

DR. MARKS: Reopen and see what we should put in was Dr. Slaga's comment.

Ron? Do you want to reopen it, Ron Shank? Or --

DR. SHANK: Yes.

DR. MARKS: Okay.

DR. HILL: I think I had "could be reopened," too. But it seems like opening Pandora's box.

DR. MARKS: Okay. Well, again, as Tom said, we can reopen and always go back and not. We can close it again. So, do you want to proceed to this long list of simple alkyl PEG ethers? And there's mixtures of these simple ethers. And there are -- I hate to say this, Ron Hill, but there are branched-chains, too. And then there

are sterols.

So there's -- Bart was having fun with this, I bet, looking at all the chemistry.

So I'm looking at, let me see --

MS. WEINTRAUB: Dr. Marks, I just had one (inaudible) comment here. My understanding is that we've reviewed some of these things before. So what are we doing? You know, I understand, you know -- I know -- I do understand what we're doing. I do understand the desire to be more efficient, do more work when the ingredients are related. But when we've already done that?

DR. BRESLAWEC: Well, Monice can tell you exactly what number of the ones that we're looking at we've actually already reviewed. And I don't know the number offhand.

DR. SHANK: 82.

DR. BRESLAWEC: 82. And the total number is --

DR. SHANK: 369.

DR. BRESLAWEC: 369. So we've essentially evaluated the safety of parts of each

of these groups, which are very similar, but (inaudible) that probably don't matter that much, they're named differently. The dictionary has given them different names. And yet they're all the same chemical structures.

We're trying to step back a little bit and look at all the ingredients in our purview. And when we approach their review, try to approach them in a chemically and toxicologically and scientifically justifiable way. And this is one such attempt.

These chemicals are, in our opinion, very similar. They're sub-groups, but they're all very similar. They've had different names.

We've reviewed and determined the safety of critical ingredients in each of these groups. And now we'd like to just step back and try to have this group together in a logical way.

MS. WEINTRAUB: And moving forward -- so for these different sort of sub-parts in this whole group that we have reviewed again, does that mean that that, sort of, in our office wouldn't

happen again? If they are part of --

DR. BRESLAWEC: Well, I think that it was determined that they're a part of this whole group. So I think that -- in doing that, that's when the Panel needs to make that determination.

So, are these groups similar enough that they can be grouped together? And are the data in each of the groups supportive enough of their safety?

That's what -- we think that the structure, the logical structure is in place. We think that there are data in place. But it's the Panel's decision to let us know if they think that approach makes sense, and if these ingredients are safe for use in cosmetics.

We're trying to develop, and put forth, a number of new approaches. And until we get some feedback from the Panel, we don't know which ways we're going. So this is really a very open question.

We think what we've proposed is justifiable. But it's not our decision to make.

DR. HILL: Yes, I mean, I will say that I've encountered on a number of occasions in these books, statements that they're structurally similar. And "similar" has no meaning when you get down to biology. Only you can conclude "similar" if you know that the biohandling is similar, that small-molecule impurities or metabolites are identical and related. It's basically a word that doesn't mean anything.

And I'm very attuned to the idea of "structurally similar," because this spring I taught a graduate class, and that's a concept that's been hammered heavily from a (inaudible) thematics point of view in the drug discovery process, and that was the focus of this course. And so people were doing data base searches, and identifying structures that were similar -- and, at face value they were, in fact, similar. But biologically, not at all.

And so what you would really want to know is, is the biohandling consistent, if they're all molecular weight 5000 and above, or -- well,

1500 and above you probably have no worries as long as there's no means of ingesting much.

But, again, there needs to be some similarity from a biological point of view to define "similar."

So I'm troubled by the use of "structurally similar" wherever it occurs, because I'm looking at, say -- "Okay. In what way?" And I'm not sure that question is being always asked in a way that makes scientific sense.

And, on that score, it's well and good that the Panel can provide input. But when we have a book that has 300-and-some ingredients, and we have two weeks to look at it, or three weeks to look at it, or less time to look at it, I'm not sure we had adequate time to -- and then the process dictates that something moves forward.

So the best was at least when we're looking at the ingredient lists today, and we're seeing what might be put into that group, we at least have the opportunity then to have some input into "this makes sense to group this," and this

doesn't. So that's better.

But we get a book and a 60-day timeframe, or whatever it is for the next meeting, it's troublesome to try to get one's mind around how similar or dissimilar.

And, again, if it's a group of polymers, and everything is 1500 molecular weight and above, I'd feel one way about it. As long as we can see there aren't impurity issues -- process impurities or whatever -- that still need to be addressed. But in some other cases, things that look similar on paper, because of vast differences in biohandling, vast differences in the biological substrates, where any toxic effects from a molecular toxicology standpoint might be exerted, then "similar" is no longer similar.

DR. BRESLAWEC: I think we've tried to make a point, when it's chemically similar, to say that it's chemically similar. And we're, you know, very much aware of the toxicological and how it acts biologically aspect of it. And it's essential that that be --

DR. HILL: Because at a level we don't chemically similar -- it (inaudible) we don't, really. What we care about is are there fragments in the molecule that have some biological meaning. That's what we care about.

And so, again, that's -- that's molecular toxicological similarity, which is what we really need to be concerned about. What's the biohandling like? What are the likely substrates biologically for sensitization? Or tumor growth promotion, or transformation of cells? Or any teratogenic effects -- like that.

And I don't always see that logic captured. And, again, "chemical similarity" has no meaning if we're talking about safety evaluation from where I sit -- other than the vapor pressure is the same and we could inhale it or we couldn't. That's pretty much, chemically -- and log P. I mean, if you talk about physical chemical properties.

DR. BRESLAWEC: From the perspective -- Dr. Marks, I'll stop if you -- from the

perspective of grouping ingredients together for the purpose of review, we think that chemical similarity is a very good place to start.

DR. MARKS: Okay. So, shall we proceed? When you look on page 119 -- the report's number page -- the previous reports -- they're pretty much all similar. Safe. There's a couple caveats, but it would pretty easy if we want to include them in this large document, the way I see it. "Safe as used," the denatured alcohol was the one for methyl alcohol.

So shall we actually take a look at these groups and decide? Is that the best way to go, is just to go down the different groups and say, "Yes, there are no concerns within that group," and proceed that way? Take the rest of the afternoon to do it, as far as individuals.

DR. SHANK: Individually, yes.

DR. MARKS: So if you go on --

DR. SHANK: Table 4.

DR. MARKS: Table 4? Or Table 1?

DR. SHANK: Okay.

DR. MARKS: Which one do you want to -- it doesn't matter.

DR. SHANK: Well, in 4, you see the structures.

DR. MARKS: Yes, okay. Well, we can do it by 4.

DR. SHANK: Or Table 9.

DR. MARKS: Yes, Table 1 is shorter. We can refer to the structure.

So if we go on page 71 -- this is the alcohol PEG ethers. And we don't have -- I'm going to assume that none of these have any caveats from the previous. Is there anything in here? There's a lot of ingredients, but is there any reason that there should be concern about these? Based on the safety -- again, doing cross --

DR. SHANK: "These," meaning all of them? Or --

DR. MARKS: Yes, all of them on page 71, and --

DR. SHANK: 72, 73 and 74?

DR. MARKS: Yes. We have mixtures. 73 would be partially unsaturated. I'm going to hold off for a second on branched, because at least this morning, Ron Hill, you raised issues about branched compounds.

So how about these alkyl PEG esters, and the ethers, and the mixtures, the pareths.

DR. SHANK: Are the pareths the only the only ones that are branched?

DR. MARKS: Pardon? The pareths. Because of irritation? Or --

DR. SHANK: Just because they have a branch? We have a methyl group.

DR. MARKS: So that would be -- on page 73, that whole group of pareths. And your concern there, Ron? Because --

DR. SHANK: I'm not concerned.

DR. MARKS: Oh, okay. Okay. Good.

DR. SLAGA: I basically -- well, I didn't study each one individually, but I like the chemical summary. There's enough similarity.

Granted, you know, biology is the

endpoint here. But this is a logical way, chemically, to look at it.

DR. SHANK: I think if you have polymers of ethylene oxide, and if the number of moles of ethylene oxide is 12 or 13 or 14 -- I understand what Dr. Hill is saying, but that kind of similarity, I think, is very easy to accept.

And most of these are just that, where -- and there's a variation on the number of moles of ethylene oxide.

DR. HILL: Let me just say, in follow-up to my -- maybe you could call it a diatribe -- is that I thought all the molecules in this report belong in this group.

So then the question is simply how do we capture the data in such a way that we -- what I lose, when the groups get this large, is to what extent are we -- not only to what extent are we relying on read-across data, but basically, what I'm going to need to do is make a table with 360 molecules in it and look at dermal sensitization, carcinogenicity, chronic oral tox -- for all of

these.

And, ideally, it would be one of these nice PDF tables with the mini-structures in there. But when you click on it or drift over it, you can open it up and actually see the full-size structure.

But I guess what I'm looking for is a monster spreadsheet or a monster table that allows one to determine what is actually the nature of the read-across that we're looking at.

Are there any branched-chains that have been considered? If so, what?

And then, from a toxicological standpoint, we're back down to what I talked about earlier, which is when somebody did a tox evaluation on a particular endpoint, what was the material that was actually studied. Because if the mixture was studied, then you can at least presume that if there was going to be any hit, it would show up.

On the other hand, if somebody's got a toxicology study where they've studied a purer

compound, and then we want to extrapolate it to this mixture that has these other branchings and so forth, then I'm troubled.

And so that's the sort of thing, in reviewing, from my perspective, so we can make a confident conclusion "safe," or a confident conclusion we're lacking data, when we're actually doing read-across, from a toxicology standpoint, does that read-across make sense? Biologically?

And so, like I say, what I find myself doing, sort of done with some of these, is just trying to make a big table. Here are all the molecules. Here's dermal sensitization. Here is dermal penetration. Here is -- something's known or not.

And some of these books do have that kind of a table -- not quite that way, but the equivalent of that. I mean, you can't easily make such a monster table. But, effectively, in order --

DR. SHANK: We have -- Table 11 is just --

DR. HILL: Right. Right. And I like that table. And I guess that's -- and I did think it was excellent, myself, as well. That kind of thing is very helpful, because you can see what compounds were evaluated, what kinds of studies were done. So, yeah.

But now we're looking at 360-some of them. So actually --

DR. SHANK: Well, this is for the 80-some -- 82.

DR. MARKS: Right.

DR. HILL: Right.

DR. SHANK: And that's the read-across base.

DR. MARKS: Right.

DR. SHANK: To incorporate the other.

DR. HILL: Right.

DR. MARKS: Other --

DR. SHANK: I haven't (inaudible) 241 (inaudible).

DR. MARKS: Okay. So getting back. So we have a lot of safety data, since about -- what?

-- (inaudible), something like that, that we've already reviewed.

Is there anything -- again, going back to -- I'm now on page 73 -- we talked about the branched alcohol. That's, I think, the last one.

How about the sterol and the dialkyl ethers? Is there any concern there about that group?

We're almost -- and that's the last -- and they're small numbers of ingredients in those. But, again, can we use cross, read-across data for sterol-containing PEG ethers? And the same with the dialkyl PEG ethers?

DR. SHANK: Are you saying "sterol" or "stearyl."

DR. MARKS: Sterol, S-T-E-R-O-L. That's on page 74, Ron. Still on Table --

DR. SHANK: Sterol.

DR. MARKS: Yes.

DR. HILL: Okay, I was looking at page 98.

DR. MARKS: I'm on page 74, Table 1,

still, at the end of Table 1.

DR. SHANK: And you're saying "sterol."

DR. MARKS: That's what it is up there.

DR. SHANK: "Stearyl." Well --

DR. MARKS: Sterol.

DR. SHANK: One is the poly-ring structure, like cholesterol and hormones and stuff.

DR. MARKS: Right.

DR. SHANK: That's not here.

DR. MARKS: And is that --

DR. SHANK: But you're saying --

DR. MARKS: It says, "Sterol-containing PEG ethers." Is that incorrect?

DR. HILL: No, that's correct. The laneths -- the structure's on page 98.

DR. SHANK: Oh, okay.

DR. MARKS: So any concerns about those?

DR. SHANK: But we did the laneths. I mean --

DR. MARKS: Yes.

DR. SHANK: -- I know, because we have

data on those.

DR. MARKS: Right. So all these -- so we can reopen and include all these ingredients. And where we don't have prior reports we can use safety assessments, we can just do read-across.

DR. SHANK: That's where I am.

DR. HILL: Yes, with the caveat that the only branched one I see in the summary of the previous reports is isostearyl -- which presumably is a mixture. I'm just pointing that out.

DR. EISENMANN: So what type of data would you like to see? Anything on branched.

I mean, before, you were discussing dermal.

DR. HILL: Well, let me see --

DR. EISENMANN: Your focus was dermal. Is that still your focus?

DR. HILL: I'm guessing we will find that the vast majority is that's the only route of exposure. I mean, I suppose we'll see them -- and these are really widely used. So, I mean, I suppose we could see them in mouthwashes or

toothpastes or -- but still, I'm guessing mostly dermal or mucous membrane exposures, right.

So, I'm still looking to see what else was there before. Because I don't see hexyldeseths, for example. Maybe they're there and I missed them. Not there.

DR. MARKS: So, Ron Hill, would you just want to continue with all these ingredients, but the branched alkyl PEG ethers? You raise a little red flag on that?

DR. HILL: Yeah, but, I mean, I'm of the general mindset that if they're out there on the market, then we should -- because this is -- we're at 1983 was the original report, if I'm not mistaken.

So anything that's known about, really, (inaudible) -- I mean, these large molecular weights, 11, 23, you know, above 330 -- yes, I'd be interested in what might be known about what happens to these things.

DR. MARKS: In Table 5, is that organized in the same way? It looks like -- at

first I thought it was going to be alphabetical. But then I see it begins with laureth-4 and -23, of course. And then we go into -- this is page 101. Then we go to page 106, and we capture other laureths.

MS. FIUME: Page 106 starts Table 6. The difference between the two of them is Table 5 are the ingredients that have been previously reviewed. They have historical data. Whereas Table 6 are all the new ingredients.

DR. MARKS: And that's in -- so that addresses the question this morning about -- I think, Rachel, you had, the old use and concentration data, in Table 5. Okay.

We can come back to these branched alkyl PEG ethers. Why don't move on in terms of the comments about -- they were favorable. I think everybody was favorable on doing this new presentation of the data tables with "leave- on," "rinse-off," and then switching to "important exposures" -- eye, inhalation, ingestion, dermal, et cetera.

Any comments? Further comments, looking at this?

DR. SLAGA: I think it's a very nice way to look at it.

DR. SHANK: I have one -- on the "use" tables, the new format, "leave on," "rinse-off," et cetera. They have "dermal," then under dermal is "deodorant, underarm." Why is that different from dermal?

MS. FIUME: I just know that from the past reports, and I think it may have propylene glycol, that Dr. Belsito was concerned because these deodorants could be an occluded type of application, rather than a moisturizer on the skin. So I didn't want to lose that information.

DR. SHANK: Okay.

MS. FIUME: But we're open to any comments --

DR. SHANK: I just wondered why.

MS. FIUME: That was why.

DR. SHANK: That stuck out from all of the others, and I wondered what's your reason.

MS. FIUME: (inaudible)

DR. SHANK: Okay. Thank you.

DR. HILL: Yes, he had some statements in one of the transcripts -- and I have no recollection of which one -- on that subject, and difference in dermal penetration characteristics in the underarm, compared to other areas of skin.

MS. FIUME: Yes. I remember (inaudible) propylene glycol. But he actually referenced a previous, I think it might have been a publication by Dr. Anne Marie Api.

DR. HILL: Yes, it was the quantitative risk assessment presentation, and he was talking about that (inaudible).

MS. FIUME: Yes.

DR. MARKS: Further comments about the --

DR. SHANK: In the actual report there's a lot of this italicized summaries. Can't that just be replaced by a table -- what is it, Table 11? Just refer to Table 11, that the previous data is summarized in Table 11? And then you

don't need any of this italicized material.
You can read it much -- in the tabular form, you can read it much faster. Just a suggestion for consideration.
The discussion should have the caveat that some of these can increase skin penetration of other ingredients, and that the ingredients shouldn't contain 1,4-dioxane or ethylene oxide.
And then --
DR. SLAGA: That will be in the discussion.
DR. SHANK: In the discussion. And then the standard aerosol boilerplate.
DR. HILL: One thing I noted --
DR. MARKS: Monice, I'll let you continue writing. I'll put, Ron, just your comments there.
DR. SHANK: Okay.
DR. MARKS: They're quite appropriate in the discussion. You'll have that, Monice. I'm going to Put Ron Shank's discussion points.
MS. FIUME: Dr. Marks, tomorrow would

you mind mentioning -- I don't -- I'm more than happy to take the italics out, but I would just not like to do it without its being discussed (inaudible) panel (inaudible).
DR. MARKS: Right. So we can bring that up tomorrow.
DR. HILL: What I was going to say -- this is coming out of some -- what? -- 1983 report, and there was one place I noticed it, but think there are others.
If you look at page 12 of the report, which is book page 47. And I know we had this whole "we don't convert units" discussion, but it says, "The percutaneous LD50 of laureth-9 was.93 ml/kg." But laureth-9 is probably not a liquid. So that probably means that they made a solution of some particular percent, and then that number traces to that solution, I'm guessing.
And so that's totally uninformative, as to what the actual dose was. And so I don't if, parenthetically -- in some other places it is in milligrams per kilogram, and maybe this is a

liquid, and maybe this is neat.
MS. FIUME: I will check it.
DR. HILL: And also, if there's any information as to -- and this I encountered a lot of places in reports we've seen on dermal penetration, is the size of the area of skin that is actually dosed matters, when you consider the equations for flux -- passive diffusion flux, or even not passive. The size of the exposed skin matters. And if that can be indicated -- I think we started doing that in some cases.
It may not always be available. In fact, I'm sure it's not always available.
DR. MARKS: Any other comments?
DR. HILL: There's a place where -- I'll just make note of this -- "animal toxicology data were not available on cetearyl alcohol." But that's just actually a mixture of two other alcohols that there was data on.
So, unless would be proposing some positive or negative synergy, that could at least be mentioned so you don't have that red-flag

statement. This is page 10 of the report, on cetearyl alcohol. That's a mixture of two that are actually listed on -- ones on that page, right below, cetyl. And stearyl's on the next page.
And that might apply to cetear -- it probably does apply to ceteareths, too. So -- you have a red flag where we really don't need it, if you just make the comment that these are -- it's a mixture of these other two ingredients, and those have been tested.
DR. MARKS: Okay. Any other comments? So, tomorrow I will make a motion that we reopen this 1983 report on laureths-4 and -7, with the express purpose of expanding it into the alkyl PEG ethers, of which there are 368 ingredients. A number of them, 82 to be exact, were reviewed already. And we would proceed forward to having a draft toward the expectation that we're going to have a "safe" --
DR. HILL: Kevin Fries is not in here, is he? But, Bart, you might take note of this.
These come at a cost, but in the drug

creation process, there are multiple vendors that have these software packages where you have a molecule, and then, basically, annotation. So data from everything from -- well, say, metabolism in cells expressing certain P450s, to what's been learned about toxicology, to what's been learned in preclinical pharmacology assessments in a variety of species, et cetera. So it provides a way of making these monster tables that I'm talking about, where you have multiple molecules and multiple characteristics that are basically annotated in.

And I don't know -- I'm not talking about this month, or even maybe this year, but somewhere down the line people could begin to think about using the software that's already out there to provide a way to create these monster tables in a way that we could actually access and use. Probably it demands having laptops in her -- to discuss, and easily see where we're relying on read-across, and what read- across data we're relying on.

DR. HELDRETH: That is something that we're already considering.

DR. HILL: Okay.

DR. HELDRETH: And working on down the road. I mean, it's going to take awhile. But eventually it will be a beautiful map of the structures, and you can just hover over it, and you'll have all the details you want. But we're just not there yet in development.

DR. HILL: And, again, I was just pointing it out, because I figured you were already thinking about it. It's just to note that other people have grappled with similar issues, and the technology's probably there to grapple. I'm sure at a cost, but I think that cost has come down a lot from what it was 15 years ago.

DR. BRESLAWEC: Dr. Marks?

DR. MARKS: Yes.

DR. BRESLAWEC: I want to point out -- this is certainly for the Panel's discretion -- that the Panel could consider this a draft report, and evaluate it as such, and choose to propose to

issue a tentative amended safety report on this if they wish to.

DR. SLAGA: I think I have the same issue. We're reopening a report called "laureth-4," and changing the title -- is that correct? Isn't that a new procedure for us?

DR. BRESLAWEC: We have done this in the past.

DR. SLAGA: We have?

DR. BRESLAWEC: We've done it with trimoniums, where we reopened the cetrimonium.

DR. SLAGA: (inaudible)

DR. BRESLAWEC: Yes. It was called "cetrimonium, steartrimonium," and we renamed it "trimonium." So that's not unusual.

DR. SLAGA: That's also this (inaudible).

DR. BRESLAWEC: But this would be the case here, too.

DR. SLAGA: Before June 2010, we hadn't done that.

DR. BRESLAWEC: I think we did that the

last time, with the trimoniums.

DR. SLAGA: And that's still an active document.

DR. BRESLAWEC: It's still an active document.

DR. SLAGA: Have we concluded a document where we've actually rereviewed something and changed the name at the top of it?

SPEAKER: (inaudible)

DR. BRESLAWEC: I don't know the answer to that.

MS. BECKER: The myristates we changed -- reopened to add and change the name.

DR. SLAGA: Okay. Thank you.

DR. MARKS: Do you like the new name? Yes.

DR. HILL: We might have done that with the hydrotropes. Is that one completed?

DR. BRESLAWEC: That one? Yes. Well, we've been, I think, doing it more than before.

DR. HILL: Okay.

DR. BRESLAWEC: But that's based on my

level of knowledge historically.

DR. HILL: In that regard, do you think you've captured most of the data that's out there to be captured?

MS. FIUME: For this report? I did an extensive search on all of the ingredients.

DR. HILL: That's what I got.

MS. FIUME: I did note that there is one item, steareth-3, that I did not bring in on carcinogenicity which I will add.

But otherwise, as far as I could find -- I did put my search strategy. I've searched all the data bases. And as far as I can find, this is the information available. When I did my search, I did start at whatever the old report was. I might go back a year or two to make sure I captured anything that may have been missing from that report. So the in-depth information was from whenever the original report was issued -- on the ingredients that were reviewed.

If it was new laureth, then I did a complete search. It's generally pretty much

(inaudible).

DR. HILL: Okay, so let me be blunt --

MS. FIUME: Did I miss something?

DR. HILL: -- and say -- no. I have this book in my possession, maybe a little over three weeks, maybe it's as much as four, but a little over three weeks. And this is again, it's a situation where a lot of information to get one's head around to reach a conclusion.

And the usual procedure is -- I mean, I can go out and get the book online, but I lose whatever I've written in the book until I get the book back -- which, in this case, would probably be about five weeks. And then I have another compressed timeframe to look.

So, I don't know, I was going to write a note in the cover of this one, "Please send the book back to me just as soon as you're finished looking through my comments," or something like that.

MS. FIUME: And --

DR. HILL: I don't know. I mean, this

is something for discussion, to talk about. Because I have to leave my book, but I won't see it again until it gets sent back. I can pull up online and go through, which is fine.

MS. FIUME: From my aspect, I made my comments. I take care of all comments as soon as the Panel meeting is over. So, I'm done with it.

DR. HILL: And I'm not proposing to give FedEx more money. It can go in snail mail.

DR. MARKS: Did you have another comment?

MS. FIUME: I did. We received counsel comments last week, and there are two issues that I want to make sure you're aware of. The first -- I'll just read it as they have it. "Please consider removing PEG-3 methyl ether, PEG-4 methyl ether, the PEG methyl ethers and methoxy PEG from this report. As these ingredients are all defined as having an average number of ethylene oxide units, they have the potential of containing methoxyethanol, and methoxydiglycol, both of which are in the dictionary.

"Both methoxyethanol and methoxydiglycol are not permitted for use in cosmetics in Europe, and both are developmental toxicants.

"As indicated on page 6, the functions reported for the methyl ingredients which are solids and humectants are different than the functions reported for the majority of the other ingredients included in this report."

So that was one item brought up by the counsel for the Panel's input.

DR. EISENMANN: I mean, the -3 has been tested. So if we know -- and so I don't know if we've had a chance and see the purity of what the -3 is, you know, and the tests that were done. That information is available.

So I have gone back to the companies who list a supplier and tried to get -- they're in Japan, and I haven't heard anything.

You know, if the definition could be changed, equal -3, you're all right. You know, because it's an average. We're most concerned about the -3 and the -4.

MS. FIUME: The purity of that ingredient, according to the test paper read, that was very -- 99.9, or 98.7 percent pure. So, I mean, if they're using the pure, which it may be, because I looked on their website, and they're using the name "triethylene glycol" (inaudible) rather that PEG-3. So -- I mean, you could also handle it that way that, you know, you expect it to be the purity, same purity as what was tested.

You could deal with it that way, too, without (inaudible).

DR. SHANK: And this group said that this is a developmental toxicant?

MS. FIUME: The methoxy ethanol and methoxy diglycol.

DR. SHANK: But those are impurities.

MS. FIUME: They are possible impurities. They're not even, I don't believe, definite impurities, right? Are they definite impurities?

DR. EISENMANN: Well, it's defined as an average of 3. So those two small ones, that

leaves it open to having the smaller ones in. Actually, you know, I would love to get in touch with the company and find out. Maybe we need to change the definition.

DR. SHANK: We've already considered that in the original documents.

DR. EISENMANN: Those, we didn't have a report originally on those compounds.

DR. BRESLAWEC: You have considered something very similar, with --

DR. SHANK: We've considered these impurities in other ingredients before, as impurities. But the compounds were tested for reproductive toxicity, developmental toxicity, and the results were negative, indicating that the impurity was at an acceptable level, it was not --

DR. EISENMANN: I don't think you've done the methyl. I have no concern with the larger ones. It's only the methyls.

DR. SHANK: Methoxyethanol?

DR. EISENMANN: Yes.

DR. SHANK: We considered that.

DR. EISENMANN: Yes, as reproductive -- for ethoxyethanol, the conclusion is "unsafe." You haven't reviewed methoxyethanol. And it's (inaudible), special report. So I'm fine with saying the -3 is, you know, safe -- you know, based on the purity of the material as tested. And that if cosmetic ingredients are that purity, then you're okay.

MS. FIUME: In the past we have made statements that -- it's on the bottom of page 5, "In past assessments CIR has acknowledged the possible presence," and it names the impurity, and, "The Panel has stated that cosmetic preparations should not contain these impurities."

So it has been handled in the past. This could very easily go in the discussion.

DR. MARKS: Well, that's what Ron mentioned right in the beginning, that the discussion should include that sort of thing in it -- the ethylene oxide and the dioxane. You mentioned both of those, Ron.

DR. SHANK: I had those, but I didn't

have methoxy ethyl.

DR. BAILEY: So you're proposing that (inaudible) stated in the (inaudible)?

MS. FIUME: Into the discussion.

DR. MARKS: So do we have that captured, between those? So the ethylene oxide, the dioxane. And then you would include also, in that, Ron, the methoxy?

DR. SHANK: Well, that note there says methoxyethanol has an impurity.

DR. MARKS: Mm-hmm.

MS. FIUME: And then I just wanted to point out the other comment. It says, "If the methyl group ingredients are removed from the report."

"Regardless, the CIR Expert Panel should be asked if a statement that extends the report conclusions to other alkyl PEG ethers in the same family that's in this report, according to the dictionary, in the future should be added to this report?"

Let me re-read that. That didn't sound

right. Basically, they're asking you to do something like we did in the propylene glycol report, that is, make a statement that if additional ingredients of the same families are added, with just a different chain length, just a different length, would they also be covered by the conclusion?

DR. MARKS: Are you talking about the sum?

DR. EISENMANN: What you've done for PEGs and PPGs. So if you add another stearic-N that's not currently in the dictionary, that it would be covered. But it would have to be in the same group.

So it's a little more complicated in that, you know, it wouldn't say another chain length that you hadn't reviewed.

DR. HILL: Yes, because what we just did was actually the number of monomer units in a long polymer.

DR. EISENMANN: Right.

DR. HILL: And that didn't have anything

to do with what might have been there on the end.

DR. EISENMANN: Right. So the ends would have to be the same as what you've already reviewed.

DR. HILL: Right.

DR. BAILEY: So, basically, you could say that the conclusion would be any additions to the groups in this report, where you have blah, blah, blah-X, would be --

DR. HILL: Additional (inaudible) repeating units, basically.

DR. BAILEY: (inaudible) that's important. Something that would link it back to those groups. That shouldn't be difficult.

DR. HILL: I would be good with that.

DR. MARKS: So do you want to -- how do you specifically want to do that, John? It's in that letter. So that's an important discussion point tomorrow, I think, when we reopen it.

DR. BAILEY: Right. It would be an addition to the conclusion, you know, just like we've done for the others (inaudible). But, you

know, within the scope of the groups considered in this report, you know, the addition of other substances where n varies, or something like that. I don't know. We'd have to play with the words.

DR. MARKS: Do you want to give me that for tomorrow?

DR. BAILEY: Yes --

DR. MARKS: Or do you want me to just -- you want to give me that tomorrow, and I'll go ahead and.

DR. BAILEY: Well, maybe Monice and I can work on it.

DR. MARKS: Okay, so we want to extend it --

DR. BAILEY: (inaudible) just makes sense.

DR. MARKS: -- future alkyl PEG ethers, essentially.

And, really, the only difference basically is the alcohol gets larger or whatever. That n would be any alcohol.

DR. BAILEY: Right.

DR. HILL: Well, I think what we were talking about was additional monomer units to the polymeric portion. So, in other words, if the number of glycol units was expanded, that would be okay.

But it shouldn't be construed that you could now add some exotic new, highly-branched and unusual alkyl terminal group.

DR. MARKS: How did you say that? You said "monomers."

DR. HILL: Yes.

DR. MARKS: But simple.

DR. HILL: Link them by added monomer units in the polymeric portion, is what I was trying to capture.

DR. MARKS: Okay. Well, I'll -- if you could get me, Monice, John, how you would phrase that, at least that will be a beginning point. And we won't be surprised to see it.

Now, we need to go back to your suggestion as to whether we go to a draft amended report, or we issue a tentative amended report.

And I think there is so much discussion, so many large -- such a large number of ingredients, and also the new way with the use tables formatted, that I think we prefer to see a draft amended report, rather than leap right into a tentative.

But I'll leave -- I'm usually the one that likes to push things forward, and I'm sort of holding up. So, Ron, Ron and Tom, how would you like -- do you want to see the next as not just a draft but with the idea that this would be the tentative amended report?

And then, I guess, the next meeting would be to issue the final. So we only get one look at this tentative amended.

DR. BRESLAWEC: I don't think that we would have the time to make the changes necessary, and to get 60 days' worth of comments on it before the next, August, meeting.

So if you issued a tentative report, you'd have ample time to look at it, and maybe issue a final in December, which would sure be nice.

DR. SHANK: Given that option, needing the 60 days.

DR. BRESLAWEC: The next meeting, you will not see this again, no matter what you do.

(Laughter) It's not going to happen.

DR. HILL: We're salivating over having 360 --

DR. MARKS: So, how do you want me to propose this? In our flow sheet, this would be the draft amended report. Yes.

DR. HILL: That's fine.

DR. BRESLAWEC: But you'd want to issue a draft report. Because what you would say is, this is, in fact, the draft report.

DR. MARKS: Well, that's what I'm asking.

DR. BRESLAWEC: That's what you're asking, right.

DR. BAILEY: But if this isn't going to be on the table until December, it gives everybody lots of time to do what we need to do. It gives

you the option, until December, to go one or go the other way -- which I think would be a better place to be. See which way it goes.

DR. MARKS: So, which way? Do you think it should be a draft amended report? Or a tentative amended report?

DR. BAILEY: Tentative. I think tentative. Because then you have the option in December to make it a -- what? -- a tentative final?

DR. BRESLAWEC: Not a tentative final.

DR. MARKS: That would be a final. So what we see in -- although we could do a lot of discussion, in point of fact, it wouldn't make any significant -- anything other than editorial changes, that's the final.

DR. BRESLAWEC: But, again, the point is that you would have ample time. I mean, we would not wait until 30 days before the meeting to mail this one. That's not the intent.

DR. HILL: The only downside I could see to that is -- okay, so the next -- this one we

would consider as a tentative?

DR. BRESLAWEC: You'd be issuing a tentative.

DR. MARKS: No, this is a draft.

DR. BRESLAWEC: This is a draft. You'd be issuing a tentative. It would be published. It would have 60 days for public comment.

DR. HILL: Okay.

DR. BRESLAWEC: We take the comments that have come in. We incorporate them into a draft final report. That's what would be sent to you.

You would discuss in December. If you like it, fine. If you don't, it shows up again in March. I mean, that's --

DR. HILL: Well, okay, so what I'm trying to clarify is simply with what level of certainty does the conclusion have to be --

DR. MARKS: So here's the step we're taking now, if we do that. We're right here, to where this would be the draft report. And the next report we see is basically would be the draft

final report, and there would not -- you know, obviously, we could change it any way we want. But what Halyna is suggesting, as I understand, is just skip this, the revisions of this, to the draft.

DR. BRESLAWEC: I think you have to, in making that decision, I would suggest that you look at the information. And if you feel it is adequate to constitute a draft report, proceeding with the strategy.

If you think there is additional information out there that you want to reconsider in a draft report, then you ask us to issue a draft report.

If you think that the information in here is probably what exists, then, based on the search strategy, and your discussion and your concern for the safety, then you certainly can issue a tentative report.

DR. HILL: We just had the discussion a few -- a short while ago as to what I would like to see additional, that I doubt is public domain

so it wouldn't have shown up in the search strategy.

So, I mean, if I had to write a conclusion right now, in my mind "insufficient data," would include some of these ingredients. And it may land that way. In which case you --

And that's the trouble with grouping. I mean, it's a fundamental trouble with grouping in that if there's some of them that are insufficient, and others that are quite sufficient, abundantly sufficient, then you're stuck -- you know what I'm saying? You can't say, "These are good, these are not."

DR. BRESLAWEC: Actually, we've issued --

DR. HILL: Or can we?

DR. BRESLAWEC: Yes.

DR. HILL: Okay.

DR. MARKS: So you want the next rendition? This is going to be a draft tentative amended report?

DR. EISENMANN: But you need a

conclusion.

DR. MARKS: You need a conclusion. We've got to say -- that's exactly right. And we haven't seen the extent of the discussion, although we have the points.

DR. SLAGA: Yes, we almost have to have, tomorrow, discussion to do that. We can't do it right now.

DR. MARKS: So I think what my sense is -- and particularly with the other changes -- we would reopen with the idea that the next document we see is the draft amended report. And all of these things will be included by then.

And we don't have to have the conclusion for that, although we're leaning toward "safe" for all these, with the exception of Ron, and what you said. I think that's where we'll get to the specifics.

Does that sound okay?

DR. SHANK: It does to me.

DR. MARKS: Let's see. Okay. It's where we're leading.

Okay, we'll see how the discussion goes tomorrow. Since I'm the one that makes the motion, after I move to reopen it, then we will see how it goes.

Any other comments? Okay. I kind of like the idea. I want to see the table. ~~Okay, next one is Methyl Acetate, Simple Acetate Esters and Relevant Metabolites, Pink 2. A draft tentative report of this was issued at the April meeting of this year, with an Insufficient Data Announcement for cetyl acetate at the highest concentration use in lipstick.~~

~~We got more data, and now I think that's safe. And so we could issue a tentative report, these ingredients as "safe as used."~~

~~DR. SLAGA: Good.~~

~~DR. MARKS: Any comments?~~

~~DR. SLAGA: Not here.~~

~~DR. EISENMANN: Just, my material -- you know, the butoxyethanol has a different conclusion. If you want to write a separate conclusion for the acetate to make it reflect that~~

Belsito?

DR. BELSITO: This is a review of stearyl heptanonoate and related stearyl alkynoates. In April we reaffirmed the conclusion for stearyl heptanonoate as safe as used but agreed to proceed with opening the document to add five additional stearyl alkanoates, stearyl caprylate, stearyl palmitate, stearyl stearate, stearyl behenate and stearyl olivate. We have included all of those, looked at the data and felt that the data was sufficient for the stearyl heptanoate and the add-ons safe as used, and that's a motion.

DR. BERGFELD: Is there a second?

DR. MARKS: Second.

DR. BERGFELD: Is there any discussion about this document and these ingredients? Seeing none I'll call for those in vote. All those in favor of approval? Thank you. Unanimous. Re-Reviews. Alkyl PEG ethers. Dr. Marks?

DR. MARKS: In 1983 the CIR published a report on laureth-4 and -23 finding that they were

safe. This is a re-review of that report and what we received was a large draft including expansion to the alkyl PEG ethers. There were over 300, about 368 of these ethers, that this draft report included, and a large number of those had been previously reviewed and had conclusions of safe, 82 to be exact. So our team felt that we should reopen and I'll move that we reopen this report with the purpose of issuing a draft amended report that included the original laureth-4 and -23 but expanded to include this large number of alkyl PEG ethers. Within this document we saw the new use table format and we've commented about that before and we like that as long as we have the backup more detailed tables which we will have access to.

We also felt that perhaps as we've done with the PEGs and the polyethylene glycols, that we could expand the conclusion in the future to extend to alkyl PEG ethers, the monomers that were not mentioned in this 368, and it could be something to the effect that this assessment is intended to address future alkyl PEG ether

cosmetic ingredients that vary from these in this assessment only in the number of ethylene glycol repeat units. So we move to reopen and to expand.

DR. BERGFELD: Second?

DR. BELSITO: When you reopen have you decided whether there is additional data or you're thinking this would be safe as used when formulated not to be irritating?

DR. MARKS: We actually felt it would be a draft amended report so we'd like to see the next draft with it and then subsequently have the tentative draft amended report with a conclusion. Yes, safe and not irritating would certainly be acceptable.

DR. BELSITO: My group felt that with all the data we had, first of all, we'd like to congratulate the triumvirate of writers who put this together, Monice, Christina and Bart. This was really truly fantastic, probably the best document I've ever seen for a first draft for such a cumbersome document. We felt we probably could go ahead safe as used when formulated not to be

irritating.

In Table 6 we liked the new approach to presenting how these ingredients were used. We were all a little confused about the first table which was the totality of all cosmetic ingredients, not the totality of cosmetic products containing these ingredients and we had recommended that that be deleted from tables. We're not really interested in how many cosmetics that exist that are hair sprays, we're interested in how many hair sprays would contain these ingredients, so that as just minor tweak.

Then we thought in the discussion in these PEGs there had been discussions about various contaminants in all the documents that preceded them. The specific ones that came up were 1, 4-dioxane, ethylene oxide, BHA, formaldehyde, peroxides, methoxyethanol and methoxy diglycol, and those just needed to be brought in to the documents, particularly the discussions, and we agree with the expansion of PEG-X going into the future.

DR. SNYDER: Second.
DR. BERGFELD: You're seconding it? We have one motion and then we have another motion. There was no second on yours so this is a second to move forward as safe. I'd like to ask you if that's agreeable?
DR. MARKS: Yes. It was safe to be nonirritating. The only other editorial comment we had was that in the text there was a lot of duplication of Table 11 on page 119. We really like Table 11 so we would suggest saving print and text by just referring to Table 11. It's a great table. That's the one where previously reviewed ingredients are summarized quite nicely.
DR. BERGFELD: Since this is a pivotal document, I would like to go around the room and ask all the panel members if they have any specific comments. I'll start with Curt.
DR. KLAASSEN: I loved reading this document. It was very nice. Overall it's very good, so no problem.
DR. SNYDER: I concur with other

previous comments and I think that it is a good example of how we can handle a large number of ingredients very thoroughly.
DR. LIEBLER: I could try and come up with a different way of saying that, but it's terrific work by the staff and it really helps us deal with complex families of compounds.
DR. HILL: I think most of my concerns and issues were expressed yesterday to the writers. The only thing that I noted in particular at the risk of sounding like a broken record is the only laureth with a branch chain that's specifically cited in terms of toxicology in this table is isostearyl which is probably the omega-1 group, but there are others that we're considering here. So if we don't have any data, I have to carefully consider what we can infer lacking any information on the ADME and I need to go and look in great detail at what's here on the biotransformation because there are molecular weights in the lower end where we could expect systemic exposure and definitely penetration

through skin.
The other thing, and I think we made this clear, to capture in the conclusion where we talk about future polymers that we were only talking about the addition of monomers at that end and not substantive changes to what's on the end of the molecules.
DR. SHANK: The report is in very good shape, the table is extremely helpful and I like the report.
DR. SLAGA: The same. The staff did a superb job on this.
MS. WEINTRAUB: I think it was a very impressive job and as you said and I'm reiterating, the quality of all of the reports is really exceptional. I really like this format. I thought it was very accessible and clear.
DR. KATZ: I really don't have anything else to add. Everybody has gone around the room and said the same thing.
DR. BERGFELD: I want to ask Ron Hill what we're to do with your concern.

DR. HILL: At this point I have no idea other than I'm tossing it out there. If there is any additional data out in the industry world as to what's known about the biohandling, specifically the biotransformation and anything that might be generated thereby that we might like to see that data. It would help in the deliberations.
DR. ANDERSEN: I think, Ron, that is exactly the benefit of offering those comments, that it's out there now and if there are data that can further inform that, the industry would be well advised to make that available.
DR. BERGFELD: I'm trying to remember if we've voted on this because we've had so much discussion.
DR. ANDERSEN: No, we haven't yet.
DR. BERGFELD: I'd like to call for the vote then. All those in favor please indicate by raising your hands. Thank you. A pivotal document for us for the future.
~~Then Dr. Andersen, the review summaries~~

Laureths 4 & 23
From the August 1982 minutes.

~~"On the basis of the available information, the Panel concludes that Isostearic Acid is safe as a cosmetic ingredient in the present practices of use and concentration."~~

~~There was a general discussion on the adequacy of comedogenic testing and the significance of this effect on users of cosmetic products. The panel agreed to include a paragraph in the report's Discussion Section to highlight this problem.~~

~~Subject to minor revisions and the addition of a Discussion Section, the document will be announced as a Tentative Report for a 90-day comment period.~~

3. Laureths -4 and -23

The following conclusion of the report was unanimously approved:

"On the basis of the available information presented in this report, the Panel concludes that Laureth -4 and Laureth -23 are safe as cosmetic ingredients in the present practices of use and concentration."

Subject to minor revisions, the document will be announced as a Tentative Report for a 90-day comment period.

4. ~~Potassium Coco Hydrolyzed Animal Protein (PCHAP) and TEA-CHAP~~

~~Dr. Bergfeld requested that this report be referred back to her Team for review at the October meeting. They will then evaluate the newly-submitted clinical data and include them in the text of the report. (The clinical data were submitted in response to the Insufficient Data Report of March 24, 1981)~~

~~Dr. Bergfeld complimented the data presentation submitted by CTFA.~~

Ceteareths
From the April 1997 meeting.

~~is safe as used in cosmetic formulations.~~

~~Dr. Belsito proposed revising the last sentence of the report discussion to read as follows: Noting that Bisabolol is used in baby products, the Panel cautioned formulators to the possibility of increased absorption of other ingredients, especially those whose safety was based on their lack of dermal absorption, also contained in the formulation. This revision (in bold print) was approved by the Panel.~~

Ceteareths-2, -3, -4, -5, -6, -7, -8, -9, -10, -11, -12, -13, -14, -15, -16, -17, -18, -20, -22, -23, -24, -25, -27, -28, -29, -30, -33, -34, -40, -50, -55, -60, -80 and -100

Dr. Andersen recalled that a Final Report with a safe as used conclusion on this group of ingredients was issued at the December 1996 Panel meeting. He also noted that because two other Ceteareths (-9 and -14) listed in the International Cosmetic Ingredient Dictionary were, inadvertently, not included in this safety assessment, an executive decision to add these ingredients to this review was made.

The Panel agreed that Dr. Andersen had acted appropriately and formally approved the addition of Ceteareths-9 and -14 to the Final Report on Ceteareths.

Dr. Andersen also brought to the Panel's attention that the report conclusion contains the following two caveats: (1) Ceteareths should not be used on damaged skin and (2) Ceteareths should not be used under conditions under which N-nitroso compounds can form. He acknowledged that the basis for the first caveat is established in the report discussion. However, after further evaluation of the available data, there does not appear to be a need for concern about the formation of

nitrosamines or nitrosamides relative to the use of these polymers in cosmetics.

The Panel unanimoulsy agreed that the caveat relating to nitrosamine formation should be deleted from the Final Report conclusion, and voted in favor of issuing a Tentative Amended Final Report on Ceteareths for public comment. At the end of the 90-day comment period, the Panel will issue an Amended Final Report.

~~REPORTS ADVANCING TO THE NEXT LEVEL~~

~~Acid Violet 43~~

~~Dr. Belsito noted that additional data on this ingredient, largely derived from FDA's files on External D&C Violet No. 2 (FDA's certified form of Acid Violet 43) were received. However, he stressed that the Panel is not reviewing the safety of Ext. D& C Violet No. 2, but, the safety of Acid Violet 43, as it is used in hair dyes.~~

~~Dr. Belsito also said that his Team determined that the available data remain insufficient for evaluating the safety of Acid Violet 43 in cosmetics, and that the following data are needed: (1)1997 concentration of use data and (2) absorption under conditions of use; if absorption occurs, then a 28-day dermal toxicity study as well as a reproductive toxicity study will be needed.~~

~~Dr. Schroeter noted that his Team determined that a 28-day dermal toxicity study would not be needed, after considering the negative short-term dermal toxicity study (guinea pigs) on a hydrophilic ointment containing 0.1 or 1.0% Acid Violet 43. Applications were made over a three-week period in this study. Dr. Schroeter's Team also requested reproductive and developmental toxicity data (i.e., if absorption occurs),~~

Ceteareths
Taken from the September 1996 meeting.

~~Sodium Sulfate~~

~~Drs. Belsito and Schroeter noted that there had been no response to the informal data request that was issued at the December 11-12, 1995 Panel meeting.~~

~~The Panel voted unanimously in favor of issuing an Insufficient Data Announcement on Sodium Sulfate with the following data requests:~~

~~(1) Human skin irritation study at concentration of use~~
~~(2) Concentrations of use~~

Ceteareths-2, -3, -4, -5, -6, -7, -8, -10, -11, -12, -13, -15, -16, -17, -18, -20, -22, -23, -24, -25, -27, -28, -29, -30, -33, -34, -40, -50, -55, -60, and -100

Dr. Belsito noted that at the March 4-5, 1996 Panel meeting, his Team informally requested a human dermal irritation and sensitization study and that the Schroeter Team also had several data requests. It was also requested that studies from the CIR Final Reports on Cetyl and Stearyl Alcohol be added to the current Draft Report on Ceteareths. In that no response to the informal data request was received, Dr. Belsito's Team determined that the present report is insufficient and that concentration of use data and dermal irritation and sensitization data (at use concentrations) are needed for completion of this safety assessment.

Dr. Shank proposed a safe as used conclusion for the Ceteareths, based on the data included in the CIR Final Report on Steareths published in 1988. The Expert Panel concluded that Steareths-2, -4, -6, -7, -10, -11, -13, -15, and -20 are safe in the present practices of use and concentration. Present practices of use meant that

Steareths were used at concentrations up to 25%. However, Dr. Shank noted that the Steareths were tested for irritancy at concentrations up to 60.0% in this report.

Dr. Schroeter agreed that the data on Steareths could be used to declare the Ceteareths safe as used, with the following caveats included in the report discussion: (1) Ceteareths increase dermal absorption; (2) there should be elimination of the production of nitrosating agents; (3) it is a mild irritant at higher concentrations of use; and (4) the standard boilerplate on ethylene glycol developmental and reproductive toxicity.

Dr. Bergfeld noted that the data on Steareths referred to by Dr. Schroeter are not included in the present report on Ceteareths.

Dr. Schroeter said that the data on Steareths will have to be incorporated into the report discussion as justification for the proposed safe as used conclusion on the Ceteareths.

Dr. Belsito said that it should also be noted in the report discussion that the Ceteareths have skin penetration enhancement properties. He also recalled that Ceteareth-20 is used in baby lotions and wanted to know how this observation should be handled in the present report.

Dr. Schroeter noted that the skin penetration enhancement properties of the Ceteareths are probably more noteworthy in terms of infant exposure, in that infants have a higher surface area to body mass ratio. He said that this area of concern with respect to adults and children should also be addressed in the report discussion as a cautionary item.

Dr. Belsito agreed with the Schroeter Team's proposal that the Ceteareths be declared safe as used and that statements relating to the following be made in the report discussion: (1) As was noted for the Polyethylene Glycols previously reviewed by CIR, use of the Ceteareths (which are polyethylene glycol ethers of cetearyl alcohol) should be limited to normal skin; (2) CIR boilerplate on ethylene glycol teratogenicity; (3) skin penetration enhancement property of Ceteareths; and (4) Ceteareths should not be used in cosmetic products in which N-nitroso compounds may be formed.

The Expert Panel unanimously concluded that Ceteareths-2, -3, -4, -5, -6, -7, -8, -10, -11, -12, -13, -15, -16, -17, -18, -20, -22, -23, -24, -25, -27, -28, -29, -30, -33, -34, -40, -50, -55, -60, and -100 are safe as used, with the caveats delineated in the preceding paragraph for inclusion in the report discussion.

Dr. Bergfeld noted that upon completion of the report discussion and inclusion of data from the report on Steareths, the Tentative Report on this group of ingredients will be reviewed by the Panel (mail review) prior to public announcement.

~~Peppermint Oil~~

~~Dr. Schroeter noted that an informal data request on Peppermint Oil was issued at the March 4-5, 1996 Panel meeting. With the exception of the RIFM (Research Institute For Fragrance Materials) monograph on Peppermint Oil that was received, there was no response to the informal data request that was issued. Thus, the Panel voted unanimously in favor of issuing an Insufficient Data Announcement on Peppermint Oil with the following data requests:~~

Taken from the December 1996

~~concludes that Propylene Glycol Dicaprylate, Propylene Glycol Dicaprylate/Dicaprate, Propylene Glycol Dicocoate, Propylene Glycol Dipelargonate, Propylene Glycol Isostearate, Propylene Glycol Laurate, Propylene Glycol Myristate, Propylene Glycol Oleate, Propylene Glycol Oleate SE, Propylene Glycol Dioleate, Propylene Glycol Dicaprate, Propylene Glycol Diisostearate, and Propylene Glycol Dilaurate are safe as cosmetic ingredients in the present practices of use.~~

Ceteth -1, -2, -3, -4, -5, -6, -10, -12, -14, -15, -16, -20, -24, -25, -30, and -45

The Panel voted unanimously in favor of issuing a Final Report with the following conclusion: Based on the available data, the CIR Expert Panel concludes that Ceteths -1, -2, -3, -4, -5, -6, -10, -12, -14, -15, -16, -20, -24, -25, -30, and -45 are safe in the present practices of use.

~~Oleth -2, -3, -4, -5, -6, -7, -8, -9, -10, -11, -12, -15, -16, -20, -23, -25, -30, -40, -44, and -50~~

~~Dr. Belsito noted that Oleth-11 was added to the review of this group of ingredients after issuance of the Tentative Report at the March 4-5, 1996 Panel meeting. He also said that the report discussion should contain a statement to the effect that the Oleths may enhance the permeability of other ingredients through the stratum corneum.~~

~~There was no opposition to Dr. Belsito's comments.~~

~~The Panel voted unanimously in favor of issuing a Final Report with the following~~

Ceteths Taken from June 1996 meeting.

on December 13,1994. Concentration of use and chemical characterization data were received in response to this announcement, as well as a commitment to supply the remaining data requests, listed as follows: 28-day dermal toxicity study, skin penetration data, and genotoxicity data.

The Panel voted unanimously in favor of tabling the Tentative Report on PCA and Sodium PCA, pending receipt of the studies that have been promised.

Ceteth-1, -2, -3, -4, -5, -6,-10, -12, -14, -15, -16, -20, -24, -25, -30, and -45

Dr. Bergfeld asked Dr. Belsito to incorporate the Panel's discussion on ethylene glycol into his comments on the Ceteths.

Dr. Belsito said that the Panel, in its discussion of a number of ingredients that were potentially contaminated by ethylene glycol during production, became concerned with the reproductive toxicity of ethylene glycol. Therefore, a separate document was compiled, in which the reproductive toxicity of ethylene glycol and its ethers (particularly 2-Methoxyethanol and 2-Ethoxyethanol) is evaluated. Based on the data in this document, it was felt that the reproductive toxicity for these chemicals was not of concern relative to use in cosmetic products. It was postulated that the level of contamination (with ethylene glycol and its ethers) of the various chemicals that the Panel will be studying would not be significant. Furthermore, Dr. Belsito said that the Panel determined that the CIR document on ethylene glycol and its ethers is of significance, and that it should be published as a separate document (special report). Thus, where applicable, this report could be referenced in the discussion section of

other ingredient reports.

Dr. Bergfeld asked the Panel to vote on the proposal that the CIR document on the reproductive toxicity of Ethylene Glycol and its ethers be issued as a special report.

Dr. Andersen noted that if the issuance of this document as a special report is approved, the announcement of this report will be followed by a 90-day comment period.

Dr. Schroeter suggested that a summary of data in the special report be included in the documents that require such information for completion of the safety assessment.

Dr. Bergfeld indicated that the Panel is highly impressed with the organization and content of the special report on ethylene glycol (and its ethers) reproductive toxicity.

The Panel unanimously approved the issuance of this special report, with the understanding that a summary paragraph will be developed and incorporated into other ingredient reports for which information on the reproductive toxicity of ethylene glycol and its ethers is relevant.

Dr. Bergfeld asked Dr. Belsito to proceed with his comments on Ceteths.

Dr. Belsito noted that the lower molecular weight Ceteths triggered the Panel's concern about Ethylene Glycol toxicity in terms of reproductive and teratogenic toxicity. He said that the Panel's review of the data on Ethylene Glycol indicates that reproductive and teratogenic toxicity are not concerns relative to the safety assessment of the Ceteths.

Dr. Belsito also said that the following data were received in response to the Insufficient Data Announcement that was issued on May 23, 1995: (1) Concentration of

use data, (2) Ocular irritation data, (3) Primary skin irritation data, and (4) Four-week subacute dermal toxicity data. Additionally, the Panel has been able to extract the data on PEGs and cetyl alcohol (from CIR Final Reports) for incorporation into this review, in that the Ceteths are ethers of cetyl alcohol and polyethylene glycol. Dr. Belsito said that this information has allowed his Team to arrive at a conclusion of safe as used.

Dr. Slaga agreed that the report on Ceteths now has data that are sufficient for determining that these ingredients are safe as used in cosmetics.

Dr. Shank said that he is still concerned that the Panel does not have good impurities data on the Ceteths. He said that there are a number of intermediates with genotoxic potential that are formed during the production of chemicals. Thus, genotoxicity data should not be deleted from the Panel's original list of data needs.

Dr. Bergfeld wanted to know whether Dr. Shank's concern could be addressed in the report discussion.

Dr. Shank said that a caveat to the effect that the finished product should contain a negligible concentration of potentially genotoxic intermediates could be added to the report discussion.

Dr. Belsito asked if the concern is that during the process of manufacturing the Ceteths, there will be additional contaminants beyond those that are present in polyethylene glycol and cetyl alcohol.

Dr. Shank said that ethylene oxide, not PEGs, is used in the manufacture of the Ceteths. Cetyl alcohol is reacted with ethylene oxide, and a variety of oxidation products (as impurities) result, some of which have genotoxic potential. He reiterated

that a statement referring to this potential problem could be included in the report discussion.

Dr. Bailey said that one of the contaminant concerns relative to ethoxylated surfactants is the presence of 1,4-dioxane, which is a carcinogen. He noted that the level of this contaminant can be controlled, and that the Panel may want this to be stated in the report summary. He also said that based on ongoing research at FDA, 1,4-dioxane is found in some products at fairly high levels, indicating that the raw materials themselves are not treated to remove the contaminant.

Dr. Bergfeld said that Dr. Bailey's concerns should also be addressed in the report discussion.

Dr. Belsito recalled that Dr. Bailey's concern (contamination) is also raised in the report on PEGs, and that this information has been incorporated into the report on Ceteths. He also mentioned that the other caveat that was raised with respect to PEGs is the restriction relating to use only on normal, undamaged skin. This restriction is also included in the report on Ceteths.

Dr. Bergfeld confirmed that the two concerns, ethylene oxide and 1,4-dioxane contamination and use on damaged skin will be retained in the report discussion on Ceteths.

Dr. Belsito said that it should also be mentioned in the discussion that the Ceteths will not be sufficiently respirable to induce toxicity via this route of exposure. In other words, this factor was considered, but is not believed to be of concern.

The Panel unanimously concluded that Ceteths-1, -2, -3, -4, -5, -6, -10, -12, -14, -

15, -16, -20, -24, -25, -30, and -45 are safe as used and also approved the additions to the report discussion that were discussed. A Tentative Report on this group of ingredients will be announced to the public.

Oleth-2, -3, -4, -5, -6, -7, -8, -9, -10, -12, -15, -16, -20, -23, -25, -30, -40, -44, and -50

Dr. Schroeter stated that his Team concluded that the data on Oleths are insufficient for arriving at a conclusion on the safety of this group of ingredients. He indicated that the following data are needed for completion of this safety assessment: (1) Dermal sensitization on Oleth-2 at concentration of use, (2) Chemical and physical properties (including stability and molecular weights), (3) 28-day dermal toxicity on Oleth-2, and (4) Two genotoxicity assays (one using a mammalian system) on Oleth-2; if results are positive, a dermal carcinogenesis study using NTP methods may be needed.

Dr. Belsito's Team recommended that, as was done in the evaluation of Ceteths, information could be extracted from the CIR reports on PEGs and Oleyl Alcohol. He also said that the general caveats raised in the report discussion on the Ceteths (i.e., use on normal skin only, and 1,4-dioxane and other potential impurities) are also applicable to the Oleths. With this in mind, Dr. Belsito's Team concluded that the Oleths are safe as used.

In consideration of Dr. Belsito's comments, Dr. Schroeter agreed that Oleths could be considered safe as used.

The Panel unanimously concluded that Oleths-2, -3, -4, -5, -6, -7, -8, -9, -10, -12,

Ceteth
Taken from March 1996
meeting

~~the distribution of Nonoxynols in Nonoxynol-9 is a fairly flat distribution, with no peak at Nonoxynol-9.~~

~~The Panel unanimously concluded that the Nonoxynols reviewed in the current report (Nonoxynols -1 through -8) are safe as used in rinse-off products and safe for use in leave-on cosmetic products at concentrations up to 5%, and voted unanimously in favor of issuing a Tentative Report with this conclusion. The 5% limitation is based on human skin irritation and sensitization data.~~

~~Dr. Bergfeld confirmed with Dr. Andersen that the Panel's discussion on Nonoxynols and the new skin penetration data submitted by Clairol, Inc. will be included and referenced in the Tentative Report that will be issued.~~

Ceteth -1, -2, -3, -4, -5, -6, -10, -12, -14,
-15, -16, -20, -24, -30, and -45

Dr. Belsito stated that his Team determined that once the concern over teratogenicity has been resolved such that ethylene glycol teratogenicity is no longer a concern, the Team will be able to rule on the safety of Ceteths and will be able to conclude that they are safe at concentrations up to 3% in leave-on cosmetic products and safe as used in rinse-off products.

Dr. Belsito also said that his Team still wants to obtain the report on the teratogenicity of ethylene glycol and a number of other chemicals that are based on ethylene glycol or polyethylene glycol after it has been completed, such that this document can be reviewed before a conclusion on the safety of Ceteths is reached.

With this in mind, Dr. Belsito proposed tabling the Draft Report on Ceteths.

Dr. Schroeter noted that additional data on the genotoxicity and chemical characteristics of Ceteths are still needed, and also proposed tabling the Draft Report on Ceteths, pending review of the report on ethylene glycol teratogenicity.

Both Teams agreed to delete the following items that were received from the list of data requests in the Insufficient Data Announcement: (1) Concentration of use, (2) Dermal irritation and sensitization on Ceteth-2 at concentration of use, (3) 28-day dermal toxicity on Ceteth-2, and (4) Ocular toxicity, if available. The preceding data items have been incorporated into the Draft Report on Ceteths, and the following data on Ceteths are still needed: (1) Physical and chemical characteristics (including stability), (2) Two genotoxicity assays on Ceteth-2 (one using a mammalian system); if results are positive, a dermal carcinogenesis study using NTP methods is needed; and (3) A review of literature addressing the teratogenic potential of ethylene glycol and ethylene glycol ethers will be conducted and included in the report. Teratogenicity testing of this ingredient may be required.

Dr. Belsito asked if the mutagenicity data from the reports on Polyethylene Glycols and Cetyl Alcohol would satisfy the Panel's request for mutagenicity data.

Dr. Schroeter indicated that these mutagenicity data would not satisfy the Panel's data request.

Ms. Fise said that, according to her notes from the previous Panel meeting, a portion of the Panel's discussion on Ceteths related to damaged skin. Specifically, comments indicated that the Panel's conclusion on the safety of Polyethylene Glycols

(PEGs) needs to be qualified to state that cosmetic formulations containing PEGs should not be used on damaged skin. She also wanted to know if some type of qualification relating to use in baby products had also been made.

Dr. Belsito recalled that the issue of teratogenicity was raised during the Panel's discussion on Ceteths. Based on his recollection, Dr. Klaassen suggested that in addition to paying attention to reproductive toxicity, that the Panel also should pay attention to the fact that children have a larger body surface area, and, perhaps, the Panel should further consider this. Dr. Belsito expressed the view that there was no need to restrict the Ceteths in baby care products, but agreed to indicate that this is another area that the Panel should think about and be sensitive to.

Dr. Andersen said that the reference relating to Polyethylene Glycols (PEGs) that Ms. Fise was referring to is included in the report that the Panel issued on PEGs -6 through -20M in 1992. This report was published in the *Journal of the American College of Toxicology* in 1993. He also said that in the report discussion, concerns about sensitization and nephrotoxicity in burn patients treated with a PEG-based antimicrobial were raised, which represent data on adverse effects in a severely compromised population.

Dr. Bergfeld said that it should be recorded in the minutes that concerns regarding teratogenicity and potential effects in children (who have a larger body surface area) were raised in evaluating the safety of Ceteths.

The Panel voted unanimously in favor of tabling the report on Ceteths.

In summarizing the Panel's discussion, Dr. Bergfeld noted that mutagenicity data

and data on physical and chemical properties of the Ceteths are still needed. There is also the need to further clarify CIR's ongoing review of ethylene glycol reproductive toxicity and include this review in the report on Ceteths.

Oleth -2, -3, -4, -5, -6, -7, -8, -9, -10, -12, -15,
-16, -20, -23, -25, -30, -40, -44, and -50

~~Dr. Schroeter noted that an Insufficient Data Announcement was issued at the August 1995 Panel Meeting. He said that his Team recognizes the concentration of use and ocular irritation data that were received, but still sees the need to issue an insufficient data conclusion. It was noted that the following data are still needed in order for the Panel to complete its safety assessment:~~

~~(1) Dermal irritation and sensitization on Oleth -2 at concentration of use~~
~~(2) Chemical and physical properties (including stability and molecular weights)~~
~~(3) 28-day dermal toxicity on Oleth -2~~
~~(4) Two genotoxicity assays (one using a mammalian system) on Oleth -2, if results are positive, a dermal carcinogenesis study using NTP methods may be needed~~
~~(5) A review of literature addressing the teratogenic potential of ethylene glycol and ethylene glycol ether will be conducted and included in the report. Teratogenicity testing on this ingredient may be required~~

~~Dr. Bergfeld said that the Panel is reviewing five or six ingredient reports that require an insert on ethylene glycol reproductive toxicity, including the report on Oleths. She said that it is important as the Panel reviews these ingredients that it also be determined which data are still needed.~~

~~Dr. Andersen said that the CIR review on ethylene glycol will be a concerted effort on the part of the CIR staff, with Dr. Klaassen's assistance.~~

Laneth-10 Acetate
Taken from the July 1980 meeting.

~~eliminated. The information will appear in full in the Laneth-10 report and will be cross-indexed in Laureth. With regard to the data that were needed to reach a conclusion about the Laureth-23 Group, the Panel members agreed to request additional phototoxicity tests at higher concentrations. The public statement of the need for such tests will be made immediately, and persons interested in submitting results will have one year to do so and 90 days in which to notify CIR of their intent.~~

~~2. TEA-Lauryl Sulfate. Drs. Bergfeld, Hoffmann, and Roudabush presented their report on TEA-Lauryl Sulfate. This Team decided at its last meeting that the ingredient is most likely an irritant. It also causes problems with regard to percutaneous absorption. The Team concluded that the data on TEA-Lauryl Sulfate are not sufficient for a determination of either safe or unsafe. Dr. Schroeter concurred that the ingredient is well-known in the dermatologic community as an irritant. Mr. McNerney indicated that formulations in which TEA-Lauryl Sulfate is used take the irritancy of the material into consideration and adjust the formulations to minimize the potential for irritation. However, Dr. Bergfeld pointed out that according to the data which industry has submitted, formulations containing TEA-Lauryl Sulfate have still produced irritancy. After discussion, the Panel decided to request additional studies on the pure ingredient, not on formulations. The need for testing and the types of studies required will be stated in a public announcement. Persons wishing to submit results will have 90 days to notify CIR of their intent and the time required to complete their studies.~~

~~3. p-Hydroxyanisole. Dr. Bergfeld presented to the Panel a review of the previously considered report on p-Hydroxyanisole. She began by noting that the present document was still the fourth draft, the same version that had come up in the March 1980 meeting.~~

~~Dr. Bergfeld stressed that p-Hydroxyanisole produces a condition in which melanocytes are destroyed resulting in depigmentation of the exposed skin. Dr. Bergfeld then reminded the Panel of her correspondence with Dr. Pathak and reiterated her earlier recommendation that p-Hydroxyanisole be judged unsafe. Dr. Montagna agreed in principle. Dr. Schroeter suggested that the Panel might reach a decision of incomplete and await more data. His proposal was adopted. Drs. Montagna and Bergfeld will outline the additional tests that would be requested. These will be announced by CIR, and 90 days will be allowed for a response to the request. Dr. Roudabush did not participate in the discussion.~~

~~Notice of Insufficient Data Report is attached and made part of these minutes.~~

4. Laneth-10 Acetate. Drs. Bergfeld, Hoffmann, and Roudabush presented their report on Laneth-10 Acetate to the Panel. The Team and part of the Panel had previously agreed that this ingredient was safe. Some problems had arisen, however, over the clinical data that were reported. The animal studies on Laneth-10 were extensive. The human ones were limited but did support the laboratory results. Dr. Fine had previously mentioned some objections to the recording of clinical data in this report. His comments

have since been incorporated into the present draft. When Dr. Beyer called for the vote on the draft Tentative Report on Laneth-10, all but one Panel member expressed the opinion that the ingredient is safe. After a review by mail of the document which will incorporate suggestions made in the discussion, Laneth-10 Acetate will be issued as a Tentative Report for a 90-day public comment period.

~~5. Cetearyl Octanoate. Dr. Montagna briefly reviewed the history of this report, pointing out that at the March Panel meeting it was deemed incomplete and that industry has since submitted more data. After the full Panel discussed some aspects of the new data, the question of sufficiency was taken up at a Team session. Following a Team meeting, the full Panel was advised that the Team considered the response from industry to be sufficient on all counts. All but one Panel member concurred. The dissent was due to the lack of at least one subchronic (90 day) toxicity study. The newly-submitted data will be used to write a Second Technical Analysis, which the Team will consider at its September meeting.~~

~~6. Testing Guidelines. To open the discussion, Dr. Elder summarized his memo on how CIR could develop a procedure by which guidelines for testing might be established. The guidelines would come from the adequately documented tests (both published and unpublished) that are contained in the CIR files. Furthermore, Dr. Elder suggested that the CIR staff gradually build up these guidelines from industry's methodologies. Industry has long been working at such testing, and a document including industry's methods would be useful.~~

~~Agreeing with Dr. Elder about the need for guidelines, Dr. Bergfeld proposed that each Panel member could review the old ones in his area of specialization and work up new ones. She also suggested that CIR might utilize the specific testing protocols which the North American Contact Dermatitis Group has already developed.~~

~~A general discussion about industry's role in the review process ensued when Dr. Beyer mentioned the possibility of the Panel's collaborating with this group to develop a mutually useful checklist. According to Mr. McNerney, industry would like not only to make this particular joint effort, but also to become more involved with the basic work of the Expert Panel. He said that industry is interested in having the Team meetings opened to its representatives, who would make presentations regarding Technical Analysis. Dr. Bergfeld objected to the notion of such involvement on the grounds that industry would wait for the opportunity to submit its data at the meetings, rather than earlier in written form. Dr. Elder pointed out that the practice of industry's presenting information on a given ingredient at a Panel meeting prior to the initiation of a report was discontinued because of a lack of interest on the part of industry. The Procedures do now allow an industry representative, Mr. McNerney, to participate in the Team meeting on an ingredient.~~

Oleths

Taken from the December 1996.

~~concludes that Propylene Glycol Dicaprylate, Propylene Glycol Dicaprylate/Dicaprate, Propylene Glycol Dicocoate, Propylene Glycol Dipelargonate, Propylene Glycol Isostearate, Propylene Glycol Laurate, Propylene Glycol Myristate, Propylene Glycol Oleate, Propylene Glycol Oleate SE, Propylene Glycol Dioleate, Propylene Glycol Dicaprate, Propylene Glycol Diisostearate, and Propylene Glycol Dilaurate are safe as cosmetic ingredients in the present practices of use.~~

~~Ceteth-1, -2, -3, -4, -5, -6, -10, -12, -14, -15, -16, -20, -24, -25, -30, and -45~~

~~The Panel voted unanimously in favor of issuing a Final Report with the following conclusion: Based on the available data, the CIR Expert Panel concludes that Ceteths -1, -2, -3, -4, -5, -6, -10, -12, -14, -15, -16, -20, -24, -25, -30, and -45 are safe in the present practices of use.~~

Oleth -2, -3, -4, -5, -6, -7, -8, -9, -10, -11, -12, -15, -16, -20, -23, -25, -30, -40, -44, and -50

Dr. Belsito noted that Oleth-11 was added to the review of this group of ingredients after issuance of the Tentative Report at the March 4-5, 1996 Panel meeting. He also said that the report discussion should contain a statement to the effect that the Oleths may enhance the permeability of other ingredients through the stratum corneum.

There was no opposition to Dr. Belsito's comments.

The Panel voted unanimously in favor of issuing a Final Report with the following

conclusion: Based on the available data, the CIR Expert Panel concludes that Oleths -2, -3, -4, -5, -6, -7, -8, -9, -10, -11, -12, -15, -16, -20, -23, -25, -30, -40, -44, and -50 are safe in the present practices of use.

~~Hydroxystearic Acid~~

~~The Panel voted unanimously in favor of issuing an Amended Final Report with the following conclusion: On the basis of the animal and clinical data included in this report, the CIR Expert Panel concludes that Hydroxystearic Acid is safe as a cosmetic ingredient in the present practices of use.~~

~~AHA Update~~

~~Dr. Andersen said that he anticipates the review of AHAs and the issuance of a Tentative Final Report on this group of ingredients at the December 16-17, 1996 Panel meeting. He noted that this plan is dependent on receiving the results of the tests that are being conducted by industry and FDA, respectively.~~

~~Dr. Bronaugh said that FDA's studies are on target. The necessary dosing prior to beginning the skin penetration study has begun, and the skin penetration data should be available in time for the December Panel meeting.~~

~~Dr. McEwen said that the initial industry study requested by the Panel relates to the effects of UV light after chronic use of products containing AHAs. The application and sample testing phases have been completed, slides are now being evaluated, and the data will be made available to the Panel in mid-November.~~

Oleth
Taken from the June 1996 meeting

~~15, -16, -20, -24, -25, -30, and -45 are safe as used and also approved the additions to the report discussion that were discussed. A Tentative Report on this group of ingredients will be announced to the public.~~

Oleth-2, -3, -4, -5, -6, -7, -8, -9, -10, -12, -15, -16, -20, -23, -25, -30, -40, -44, and -50

Dr. Schroeter stated that his Team concluded that the data on Oleths are insufficient for arriving at a conclusion on the safety of this group of ingredients. He indicated that the following data are needed for completion of this safety assessment: (1) Dermal sensitization on Oleth-2 at concentration of use, (2) Chemical and physical properties (including stability and molecular weights), (3) 28-day dermal toxicity on Oleth-2, and (4) Two genotoxicity assays (one using a mammalian system) on Oleth-2; if results are positive, a dermal carcinogenesis study using NTP methods may be needed.

Dr. Belsito's Team recommended that, as was done in the evaluation of Ceteths, information could be extracted from the CIR reports on PEGs and Oleyl Alcohol. He also said that the general caveats raised in the report discussion on the Ceteths (i.e., use on normal skin only, and 1,4-dioxane and other potential impurities) are also applicable to the Oleths. With this in mind, Dr. Belsito's Team concluded that the Oleths are safe as used.

In consideration of Dr. Belsito's comments, Dr. Schroeter agreed that Oleths could be considered safe as used.

The Panel unanimously concluded that Oleths-2, -3, -4, -5, -6, -7, -8, -9, -10, -12,

-15, -16, -20, -23, -25, -30, -40, -44, and -50 are safe as used. A Tentative Report on this group of ingredients will be announced to the public.

PEG-2, -3, -5, -10, -15, and -20 Cocamine

~~Dr. Belsito noted that, except for concentration of use data, there are a number of prior data requests for which no response has been received. He also said that though data from the CIR report on PEGs have been incorporated into this safety assessment, there are still concerns relating to the cocamine moiety (i.e. the presence of amines). Such concerns led Dr. Belsito's Team to believe that the current document is somewhat insufficient for determining safety. Specifically, the physical and chemical purity and chemical characteristics (particularly, in terms of the partition coefficient in lipids, how much will penetrate the skin), and the genotoxicity of PEG-2 Cocamine in a mammalian system are of concern.~~

~~Dr. Schroeter concurred with the data needs that were expressed by Dr.Belsito's Team and indicated that 28-day dermal toxicity data on PEG-2 Cocamine and dermal irritation and sensitization data on PEG-2 Cocamine, at the concentration of use, are also needed.~~

~~Dr. Belsito's Team determined that the two studies mentioned by Dr. Schroeter are not needed because a 28-day dermal toxicity study on PEG-15 Cocamine is included in the present report. The Belsito Team determined that these data satisfy the Panel's prior requests for dermal toxicity and dermal sensitization data. Dr. Belsito reiterated that his Team's present concerns relate to the amine portion of the PEG~~

Oleth
Taken from March 1996 meeting.

~~and data on physical and chemical properties of the Ceteths are still needed. There is also the need to further clarify CIR's ongoing review of ethylene glycol reproductive toxicity and include this review in the report on Ceteths.~~

Oleth -2, -3, -4, -5, -6, -7, -8, -9, -10, -12, -15, -16, -20, -23, -25, -30, -40, -44, and -50

Dr. Schroeter noted that an Insufficient Data Announcement was issued at the August 1995 Panel Meeting. He said that his Team recognizes the concentration of use and ocular irritation data that were received, but still sees the need to issue an insufficient data conclusion. It was noted that the following data are still needed in order for the Panel to complete its safety assessment:

(1) Dermal irritation and sensitization on Oleth -2 at concentration of use
(2) Chemical and physical properties (including stability and molecular weights)
(3) 28-day dermal toxicity on Oleth -2
(4) Two genotoxicity assays (one using a mammalian system) on Oleth -2; if results are positive, a dermal carcinogenesis study using NTP methods may be needed
(5) A review of literature addressing the teratogenic potential of ethylene glycol and ethylene glycol ether will be conducted and included in the report. Teratogenicity testing on this ingredient may be required

Dr. Bergfeld said that the Panel is reviewing five or six ingredient reports that require an insert on ethylene glycol reproductive toxicity, including the report on Oleths. She said that it is important as the Panel reviews these ingredients that it also be determined which data are still needed.

Dr. Andersen said that the CIR review on ethylene glycol will be a concerted effort on the part of the CIR staff, with Dr. Klaassen's assistance.

Dr. Bergfeld noted that, eventually, the review on ethylene glycol reproductive toxicity will be inserted under the heading **Reproductive and Developmental Toxicity** in the report on Oleths as well as all of the other documents for which this review is required.

The Panel voted unanimously in favor of tabling the Draft Report on Oleths.

Sodium Alpha-Olefin Sulfonates

~~Dr. Belsito said that since the last Panel meeting, information and protocols indicating that the sultone contaminants in Sodium Alpha-Olefin Sulfonates could be reliably measured at lower concentrations than the Panel had originally been made to believe had been received. Therefore, the conclusion on Sodium Alpha-Olefin Sulfonates has been changed slightly and should now read as follows: Based on the available data, the CIR Expert Panel concludes that Sodium Alpha-Olefin Sulfonates (of chain lengths C_{14-16}, C_{12-14}, C_{14-18}, and C_{16-18}) to be safe as used in rinse-off products and safe up to 2% in leave-on products, with the sultone concentration of any formulation limited to: gamma sultones ≤ 10 ppm; chlorosultones ≤ 1 ppm; and unsaturated sultones ≤ 10 ppb .~~

~~The Panel voted unanimously in favor of the above conclusion.~~

~~Dr. Bergfeld asked for any comments concerning the report text and discussion.~~

~~Dr. Schroeter said that since the unsaturated sultones may be found in formulations at a concentration of 10 ppm, a bioassay may have to be used to determine negative sensitization of the unsaturated sultone. He said that this should~~

Steareths
Taken from November 1987 meeting.

Sorbic Acid

Dr. Bergfeld reported that her team was recommending a standard safe conclusion for Sorbic Acid and Potassium Sorbate with a discussion noting that these ingredients are mild dermal irritants but do not appear to be sensitizers. She noted that the discussion also included a recommendation that Sorbic Acid be buffered when used in cosmetic formulations, although now it was uncertain if this was necessary.

Dr. Schroeter stated that his team agreed with the Bergfeld team's conclusion; however, he did not concur with the discussion. He considers Sorbic Acid a weak sensitizer and his team agreed the discussion could be deleted. His team also recommended deleting the carcinogenicity studies in which subcutaneous injection was the route of administration; all concurred.

The Panel then unanimously agreed to delete the discussion and approved a standard safe conclusion. It was noted that the papers referenced in the section entitled "Reactions with Nitrite" were to be sent to Drs. Shank and Hoffmann for their comments. The tentative final report will shortly be announced for a 90-day comment period.

Steareths

Dr. Schroeter reported that data available on Steareths-2, -10, and -20 were considered sufficient for a decision to be made on the entire Steareth group including Steareths-4, -6, -11, -13, and -15 (some data were available on Steareth-15) because of chemical similarity. He noted that an alcohol ethoxylate of unspecified chain length was found to be non-mutagenic in three separate studies and because of structural similarities, his team considered the data on this ethoxylate sufficient not to require mutagenic testing. These points were set forth in the discussion of the report. Dr. Schroeter then recommended a standard safe conclusion for the Steareth group.

Mr. Eiermann inquired as to the possibility of 1,4-dioxane as an impurity. Dr. Elder noted that previous reports on ethoxylates had included a statement to that effect and that a similar statement would be added to the Steareth report. Dr. Hoffmann requested that the statement read "Information was not available as to the possible presence of trace quantities of 1,4-dioxane or other impurities in the Steareth compounds."

The Panel then unanimously approved Dr. Schroeter's recommendation of a standard safe conclusion for the Steareths. The tentative final report will shortly be announced for a 90-day comment period.

Adjournment

The Expert Panel meeting adjourned at approximately 1:00 p.m., June 23, 1987. The next meeting of the Expert Panel is scheduled for November 16-17, 1987.

Respectfully submitted,

Elizabeth M. Santos
Senior Scientific Analyst

Attachments: Meeting agenda (June 22-23, 1987)
Proposal to include "5-Bromo-5-Nitro-1,3-Dioxane" on the priority list, submitted by D. Hoffmann (June 19, 1987)

sensitization, and the specific reports can be generated.

APPROVAL OF FINAL REPORTS

Reproductive and Developmental Toxicity of Ethylene Glycol and Its Ethers (Special Report)

The Panel unanimously approved the Special Report on Ethylene Glycol and its ethers, with the editorial changes (e.g. section entitled Implications replaced with the title, Discussion) that were noted, the addition of a brief discussion of the Panel's findings, and a final conclusion, which reads as follows: Metabolites of ethylene glycol monoalkyl ethers are reproductive and developmental toxins. In general, the metabolites of concern are not expected to be formed in cosmetic formulations that contain polymers of ethylene glycol.

Dr. Andersen noted that this report will be referenced in each case where the presence of ethylene glycol and/or its monoalkyl ethers may be a safety issue.

PEG-2, -3, -5, -10, -15, and -20 Cocamine

The Panel voted unanimously in favor of issuing a Final Report with an insufficient data conclusion. The data that are needed for completion of this safety assessment are listed in the report discussion as follows:

(1) Physical properties and chemical impurities, especially nitrosamines
(2) Genotoxicity in a mammalian system; if the results are positive, then a dermal carcinogenesis study using NTP methods may be needed
(3) 28-day dermal toxicity study using PEG-2 Cocamine
(4) Dermal sensitization data on PEG-2 Cocamine

REPORT

Draft Amended Final Report

Alkyl PEG Ethers

November 18, 2010

The 2010 Cosmetic Ingredient Review Expert Panel members are: Chairman, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; Ronald A Hill, Ph.D. James G. Marks, Jr., M.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The CIR Director is F. Alan Andersen, Ph.D. This report was prepared by Monice M. Fiume, Senior Scientific Analyst/Writer and Bart Heldreth, Ph.D., Chemist, CIR.

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ABSTRACT

The CIR Expert Panel assessed the safety of Alkyl PEG Ethers used in cosmetics. These 369 ingredients function in cosmetics primarily as surfactants. The undeceths, laneths, and hydrogenated laneths also function as skin conditioning agents, the oleths as fragrance ingredients, and the *sec*-pareths as emulsion stabilizers. Some do not function as surfactants. For example, the PEG methyl ethers function as solvents and humectants, and the PEG propylheptyl ethers as emulsion stabilizers. The Panel reviewed the relevant animal and clinical data from both previous CIR reports as well as that found in an updated search. The Panel concluded that the Alkyl PEG Ethers are safe as used when formulated to be non-irritating, and the same applies to future alkyl PEG ether cosmetic ingredients that vary from those ingredients recited herein only by the number of ethylene glycol repeat units.

INTRODUCTION

This report assesses the safety of alkyl PEG ethers as used in cosmetics. Most of the alkyl PEG ethers included in this review function in cosmetics as surfactants. The undeceths, laneths, and hydrogenated laneths also function as skin conditioning agents, undecyleneth-6 as a cosmetic biocide, the oleths as fragrance ingredients, and the *sec*-pareths as emulsion stabilizers. Some do not function as surfactants. The PEG methyl ethers function as solvents and humectants, the PEG propylheptyl ethers as emulsion stabilizers, steareth-60 cetyl ether as a viscosity increasing agent, and PEG-4 ditallow ether as a skin conditioning agent.

Many of the ingredients have previously been reviewed by the Cosmetic Ingredient Review (CIR) Expert Panel, including laureth-4 and laureth-23.[1] In 1983, the Expert Panel concluded that these ingredients are safe as cosmetic ingredients in the present practices of use and concentration. This report was initiated as a re-review of the safety of laureth-4 and laureth-23.

The laureths are members of the alkyl PEG ethers family, which consists of compounds that are the reaction products of an alkyl alcohol, in this case lauryl alcohol, and one or more equivalents of ethylene oxide. While the naming conventions used in the *International Cosmetic Ingredient Dictionary and Handbook* for the alkyl alcohols of different chain lengths make them seem like very different entities, they are actually very similar – both in structure and function. Therefore, the entire family of alkyl PEG ethers is included in this rereview. The list of cosmetic ingredients that belongs to this family is quite extensive and is given in Table 1.

Some alkyl PEG ethers have been previously reviewed by the CIR. These ingredients were reviewed as a family based on the alkyl alcohol, for example, the ceteths. Those that have been previously reviewed are identified in Table 1. (Often the ingredient group was incomplete in the original safety assessment. For example, ceteth-7 was not included in the original ceteth report.)

In addition to the simple alkyl PEG ethers, this report also includes mixtures of simple alkyl PEG ethers, partially unsaturated alkyl PEG ethers, branched alkyl PEG ethers, sterol-containing PEG ethers, and dialkyl PEG ethers. These ingredients are also listed in Table 1.

While the number of ingredients in this report may seem overwhelming, the Panel has already dealt with a number of these ethers as individual families based on an individual alkyl chain length, as stated above. Many of the constituents of the alkyl PEG ethers have been reviewed by CIR. Similarities of this large group are explained in the Chemistry section.

Much of the determination of safety of the ingredients included in this new alkyl PEG ethers group is based on the use of the existing safety assessments of previously reviewed ingredients,[1-6] as well as the assessments that exist for some of the base components of these ethers. [7-16] However, this is not a novel approach. CIR has already set a precedent in using existing information on chemically similar ingredients, as evidenced in the ceteareth review,[2] as well as using safety assessments of base components, as evidenced in the reviews on the ceteths[3] and oleths,[4] to determine safety of an ingredient

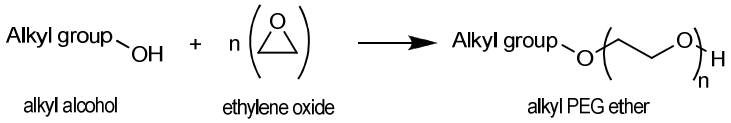
family that does not, itself, have complete safety data. Based on these precedents, use of existing safety assessments can be used in the absence of specific data, making a determination of safety possible for all of these ingredients. The previously reviewed ingredients, and component ingredients used to evaluate safety, are listed in Table 2a. **Summaries of information from the reports on previously reviewed ingredients and from component ingredients, as well as the conclusions and important discussion items, are summarized in Table 2b**.

CHEMISTRY

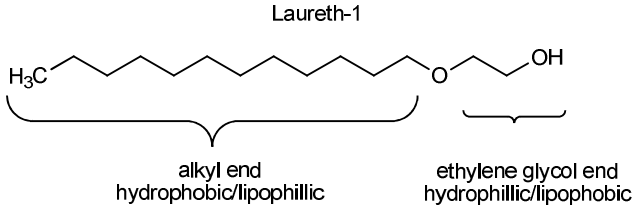
Definition and Structure

Alkyl PEG Ethers

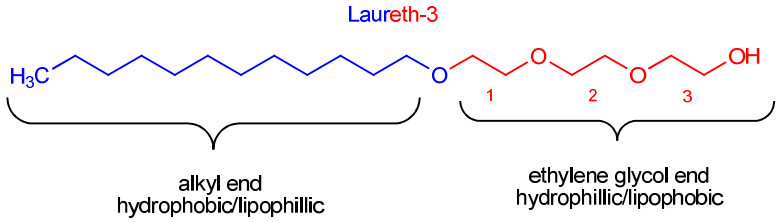
An alkyl PEG ether is the reaction product of an alkyl alcohol and one or more equivalents of ethylene oxide.[17]



Laureth-1 represents one of the simplest ingredients in this review, as the reaction product of lauryl alcohol and one equivalent of ethylene oxide:



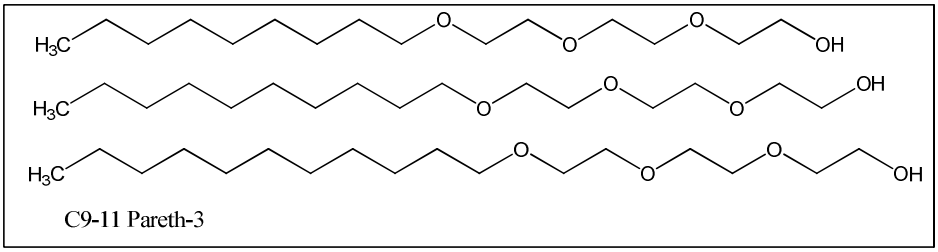
Laureth-3 (i.e. a lauryl chain attached to a polyethylene glycol chain, with an average of 3 ethylene glycol units) differs from laureth-1 by the addition of two ethylene glycol units:



Each of the methoxy PEGs and PEG methyl ethers (two International Nomenclature Cosmetic Ingredient (INCI) naming conventions that both mean a methyl group attached to a variable length PEG chain); capryleths (8 carbon chain with a variable PEG); noneths (9 carbon chain with a variable PEG); deceths (10 carbon chain with a variable PEG); undeceths (11 carbon chain with a variable PEG); laureths (12 carbon chain with a variable PEG); trideceths (13 carbon chain with a variable PEG); myreths (14 carbon chain with a variable PEG); ceteths (16 carbon chain with a variable PEG); steareths (18 carbon chain with a variable PEG); arachideth-20 (20 carbon chain with a 20 unit PEG chain); and beheneths (22 carbon chain with a variable PEG) follow this simple structural motif, as shown above for laureth-3 (and in more detail in Table 3).

Alkyl PEG Ether Mixtures

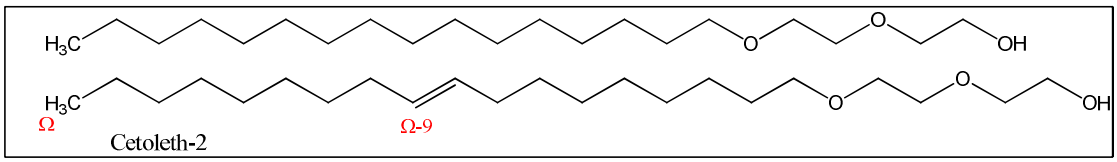
Each of the ceteareths (mixture of 16 and 18 carbon chains with a variable PEG); pareths (mixture of variable length carbons chains with a variable PEG); and hydrogenated talloweths (mixture of 14, 16, and 18 carbon chains with a variable PEG) are mixtures of the above simple structures. For example, C9-11 pareth-3 is a mixture of noneth-3, deceth-3 and undeceth-3.



C9-11 Pareth-3

Partially Unsaturated Alkyl PEG Ethers

Also included in this review are partially unsaturated straight chain ingredients. These include undecyleneth-6 (omega-1 (Ω-1) unsaturated 11 carbon chain with a 6 unit PEG); oleths (Ω-9 unsaturated 18 carbon chain with a variable PEG); cetoleths (mixture of 16 carbon chain and Ω-9 unsaturated 18 carbon chains with a variable PEG); coceths (mixture of 6, 8, 10, 12, 14, 18, Ω-9 unsaturated 18, Ω-6 unsaturated 18, and 20 carbon chains with a variable PEG); palmeth-2 (mixture of 14, 16, 18, Ω-6 unsaturated 18, and Ω-6 unsaturated 18 carbon chains with a 2 unit PEG); talloweths (mixture of 14, 16, Ω-9 unsaturated 16, 18, Ω-9 unsaturated 18, Ω-6 unsaturated 18, and Ω-3 unsaturated 18 carbon chains with a variable PEG); and PEG jojoba alcohols (mixture of Ω-9 unsaturated 18, Ω-9 unsaturated 20, and Ω-9 unsaturated 22 carbon chains with a variable PEG). For example, cetoleth-2 is a mixture of ceteth-2 and oleth-2.

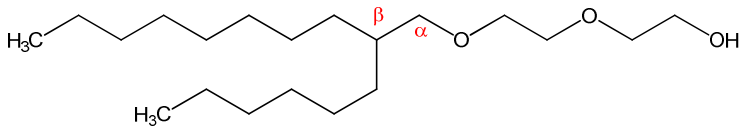


Cetoleth-2

Although the above Ω-9 unsaturated chain is drawn as the *trans* isomer, the *cis* isomer is also possible and actually more likely if the parent alcohol was obtained from natural sources.

Branched Alkyl PEG Ethers

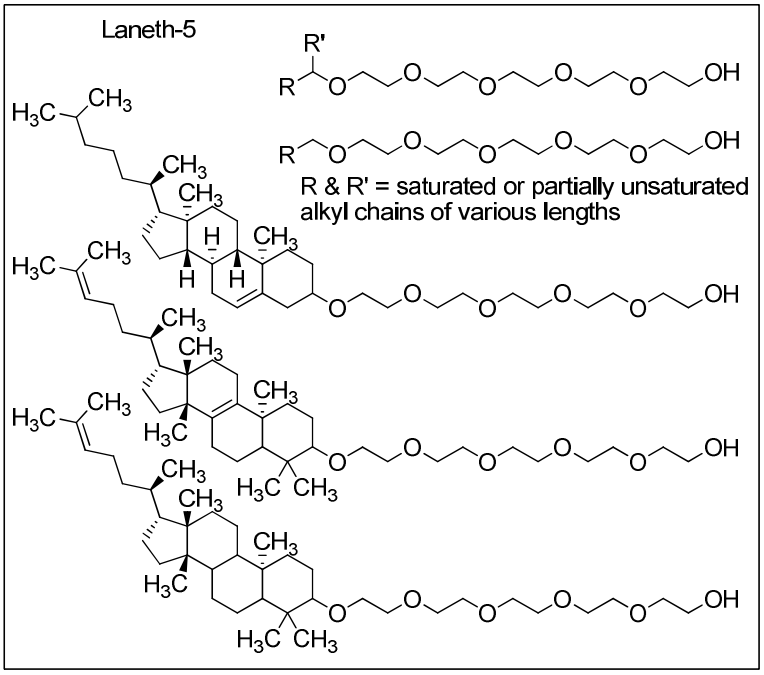
Another structural variation within the ingredients of this review is branching. The branched ingredients included in this review are the isodeceths (mixture of various branched 10 carbon chains with a variable PEG); isolaureths (mixture of various branched 12 carbon chains with a variable PEG); isomyreths (mixture of various branched 14 carbon chains with a variable PEG); isoceteths (mixture of various branched 16 carbon chains with a variable PEG); isosteareths (mixture of various branched 18 carbon chains with a variable PEG); *sec*-pareths (mixture of variable length, alpha-branched (α-branched) carbons chains with a variable PEG); PEG propylheptyl ethers (3 carbon chain beta-substituted (β-substituted) 7 carbon chain with a variable PEG); hexyldeceths (6 carbon chain β-substituted 10 carbon chain with a variable PEG); octyldodeceths (8 carbon chain β-substituted 12 carbon chain with a variable PEG); and decyltetradeceths (10 carbon chain β-substituted 14 carbon chain with a variable PEG). For example, hexyldeceth-2 is as shown:



Hexyldeceth-2

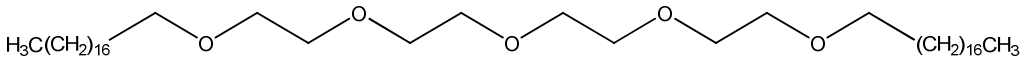
Sterol-Containing PEG Ethers

Another grouping of ingredients within this review contains PEG ethers of sterols. These ingredients consist of the laneths (mixture of various length saturated and partially unsaturated alkyl chains, cholesterol, lanosterol and dihydrolanosterol with a variable PEG) and the hydrogenated laneths (mixture of various length saturated alkyl chains and dihydrocholesterol with a variable PEG). For example, laneth-5 is as shown:



Dialkyl PEG Ethers

The final grouping of ingredients within this review consists of dialkyl PEG ethers. Structurally, these ingredients consist of a PEG chain, capped at *each* end with an alkyl group. These ingredients include hydrogenated dimer dilinoleths and PEG-4 distearyl ether (two INCI naming conventions that both mean a variable PEG capped at each end with a saturated 18 carbon chain); PEG cetyl stearyl diether and steareth-60 cetyl ether (two INCI naming conventions that both mean a variable PEG capped at one end with a saturated 18 carbon chain and at the other end with a saturated 16 carbon chain); PEG-4 ditallow ether (a 4 unit PEG independently capped at each end with one of a 14, 18, 18, Ω-9 unsaturated 18, Ω-6 unsaturated 18, or Ω-3 unsaturated 18 carbon chain); and PEG-16 cetyl/oleyl/stearyl/lanolin alcohol ether (a 16 unit PEG independently capped at each end with a variable length saturated or partially unsaturated alkyl chain, cholesterol, lanosterol or dihydrolanosterol). For example, PEG-4 distearyl ether is as shown:



PEG-4 Distearyl Ether

Physical and Chemical Properties

The physical and chemical properties of the alkyl PEG ethers are summarized in Table 3.[18] These ingredients range from viscous liquids to amorphous solids, and from highly water soluble to highly lipid soluble.

UV Absorption

While no UV absorption data were available, the ingredients included in this review would not be expected to have any meaningful ultraviolet (UV) absorption. None of these ingredients contain metals or halogens. Except for the partially unsaturated alkyl PEG ethers and the sterol-containing PEG ethers, these ingredients also do not possess any π-bonds. The π-bonds in the partially unsaturated alkyl PEG ethers and the sterol-containing PEG ethers are not part of any conjugated systems. No heteroatoms participate in these π-bonds. Accordingly, the likelihood of any of these ingredients to absorb light within the UV spectrum, at a detectable molar absorptivity, is extremely low.

Method of Manufacture

Alkaline catalysis is by far the most common method of manufacture of alkyl PEG ethers, although acid catalysis is known.[17] The initiation of the alkaline catalyzed synthesis of alkyl PEG ethers consists of the addition of ethylene oxide to a dry solution of the appropriate alcohol (e.g., stearyl alcohol is used to synthesize steareths) with an alkali earth metal (e.g., potassium hydroxide) or alkoxide (e.g., sodium methoxide). The reaction continues to propagate (i.e., continues to add additional units of ethylene glycol to the alcohol) until the available ethylene oxide is consumed and/or the reaction is terminated by the addition of an acid (e.g., hydrochloric acid). Dioxane (1,4-diethylene dioxide; 1,4-dioxane) is commonly formed as a byproduct. Finally, a finishing step is commonly employed via the addition of one or more oxidizing agents (e.g., hydrogen peroxide) or antioxidants/stabilizers (e.g., butylated hydroxytoluene (BHT) or α-tocopherol (vitamin E)).

Impurities

PEG Methyl Ethers

Since PEG methyl ethers, or methoxy PEGs, are defined as having an average number of ethylene oxide units, they have the potential of containing toxicants, methoxyethanol and methoxydiglycol.[19] In past assessments, CIR has acknowledged the possible presence of 1,4-dioxane and unreacted ethylene oxide (a gas), both toxic chemicals, which are possible oxidation products in alkyl PEG ethers.[2-4] PEG-3 methyl ether has a purity of approximately 90-96% by volume; major impurities and/or unreacted starting material include tetraethylene glycol monomethyl ether, diethylene glycol, methoxydiglycol, and triethylene glycol.[20] Production samples of PEG-7 methyl ether typically contain a combined concentration of 0.02-0.05% of ethylene glycol and 0.1% of water.[21]

Stability

Laureths

Samples of laureth-5 and laureth-8 were assayed for peroxide and formaldehyde content under various conditions.[22] Production samples of laureth-3 and laureth-5 were subjected to 8 months of daylight and contact with air, and resulted in impurities of formaldehyde as high as 3000 µg/g (i.e. 3000 ppm or 0.3%).[22,23] However, these are *not* typical storage conditions.

In four newly opened samples of laureth-5, the formaldehyde content ranged from 0.4-6 µg/g, while the peroxide content ranged from 0-11 mEqv/kg. In a newly opened sample of laureth-8, the formaldehyde content was 2 µg/g, and the test for peroxide content was negative. Only a minor increase was seen when the products were refrigerated for 2 yrs, but surfactants are normally stored at room temperature; they generally become semi-solid if stored in temperatures below their melting point. Autoxidation occurred in daylight and in darkness. One sample of undiluted laureth-5 had a formaldehyde content of 1289 µg/g after 10 mos of storage in the dark, and the test for peroxide content was positive. The highest formaldehyde and peroxide contents were observed in a sample of undiluted laureth-5 that was exposed to daylight for 8 mos and was handled, i.e. stirred for 1 h, 4x/day, to simulate use conditions. In that sample, the formaldehyde content was 2950 µg/g and the peroxide content was 1087 mEqv/kg.

USE

Cosmetic

Laureth-4, laureth-23, and the majority of the PEG alkyl ethers included in this review function in cosmetics as surfactants.[24] Generally, within each family, although there may be exceptions, the lower chain length ingredients mostly function as surfactant – emulsifying agents, and as the chain length increases, the ingredients function as surfactant – solubilizing agents and/or surfactant – cleansing agents. Some of the ingredient families have other functions, in addition to being surfactants. The undeceths, laneths, and hydrogenated laneths also function as skin conditioning agents, undecyleneth-6 is also a cosmetic biocide, the oleths are also fragrance ingredients, and the *sec*-pareths also function as emulsion stabilizers.

A few of the ingredients included in this rereview are not reported to function as surfactants at all. The PEG methyl ethers and methoxy PEGs function as solvents and humectants. The PEG propylheptyl ethers function as emulsion stabilizers, steareth-60 cetyl ether functions as a viscosity increasing agent, aq. and non-aq., and PEG-4 ditallow ether functions as a skin conditioning agent, occlusive.

There are 369 ingredients named in this report. Of those, 61 have been reviewed previously, and 49 of those previously reviewed are currently in use. There are 99 ingredients being reviewed for the first time that are reported to be used. Currently 221 ingredients have no reported cosmetic use.

The original safety assessment on laureth-4 and laureth-23 stated that, in 1981, according to data supplied to the Food and Drug Administration (FDA) as part of the Voluntary Cosmetic Registration Program (VCRP), laureth-4 was used in 202 formulations at concentrations of ≤0.1-25% and laureth-23 was used in 218 cosmetic formulations at concentrations of ≤0.1-5%.[1] Since that time, the frequency of use has more than doubled for laureth-4 and nearly doubled for laureth-23. VCRP data obtained recently report that laureth-4 is used in 441 formulations and laureth-23 is used in 404 formulations.[25] Many of the ingredients that have been reviewed previously have increased in frequency of use, a few have decreased in use, and it appears that ceteth-29 is no longer being used. The biggest increase in frequency of use was for steareth-2, which was used in 107 formulations in 1986, but is currently reported to be used in 593 cosmetic formulations. The ingredients with the greatest frequency of use, according to VCRP data, are ceteareth-20, with 955 uses, laureth-7, with 932 uses, and steareth-21, with 891 uses.

The Personal Care Products Council (the Council) conducted concentration of use surveys for the alkyl PEG ethers.[26,27] The concentrations of use of laureth-4 and laureth-23 are similar to those at the time of the original safety assessment. According to these surveys, many of the ingredients included in this review are used at concentrations of <5%. The ingredient with the highest concentration of use is C12-13 pareth-3, at 32% in a product that will be diluted and at 25% in dermal preparations. Laureth-4 and isoceteth-20 are used in leave-on products at concentrations up to 21%, and steareth-20 is used in leave-on products at up to 20%. The ingredients used at the highest concentration in formulations applied near the eye or that could possibly be ingested are, respectively, ceteth-9, which is used at 18% in an eyeliner, and ceteareth-10, which is used at 11% in a lipstick.

The frequencies and concentrations of use are summarized in Tables 4a and 4b. Table 4a includes current and historical information for all ingredients previously reviewed by CIR. (Some of these ingredients now have no reported uses.) Table 4b includes all previously-unreviewed ingredients that have been identified as in-use by either VCRP data[25] or the Council survey.[26] Table 4c is a listing of ingredients not reported to be used.

Many alkyl PEG ethers are used in products that may be inhaled, and effects on the lungs that may be induced by aerosolized products containing this ingredient are of concern.

The aerosol properties that determine deposition in the respiratory system are particle size and density. The parameter most closely associated with deposition is the aerodynamic diameter, d_a, defined as the diameter of a sphere of unit density possessing the same terminal settling velocity as the particle in question. In humans, particles with an aerodynamic diameter of ≤ 10µm are respirable. Particles with a d_a from 0.1 - 10µm settle in the upper respiratory tract and particles with a d_a < 0.1 µm settle in the lower respiratory tract.[28,29]

Particle diameters of 60-80 µm and ≥80 µm have been reported for anhydrous hair sprays and pump hairsprays, respectively.[30] In practice, aerosols should have at least 99% of their particle diameters in the 10 – 110 µm range and the mean particle diameter in a typical aerosol spray has been reported as ~38 µm.[31] Therefore, most aerosol particles are deposited in the nasopharyngeal region and are not respirable.

In some previous safety assessments, such as that of ceteareths,[2] it was concluded that ingredients that contained a PEG moiety should not be used on damaged skin because of potential increased dermal penetration of the PEG moiety and associated renal toxicity. Based on new data, the concern about increased PEG dermal penetration exists only for severely burned skin and not for abnormal skin seen in cases, for example, of atopic dermatitis. The need to avoid use of PEG containing medications is now well understood in the burn treatment community and the caveat regarding use of cosmetic products containing PEGs on damaged skin was removed for PEGs and PEG-containing ingredients.

All of the ingredients included in this review are listed in the European Union (EU) inventory of cosmetic ingredients.[32] The Scientific Committee on Consumer Products (SCCP) opinion paper exists for laureth-9 and was initiated due to concern that laureth-9 has an anesthetic effect.[33] While not restricted according to the EU, the SCCP concluded that laureth-9 does not pose a risk when used at ≤3% in leave-on products and ≤4% in rinse-off products. The information summarized in the SCCP paper was on alcohol ethoxylates analogous to laureth-9, but each compound was not clearly defined. Therefore, for the purpose of this CIR assessment, the information will be summarized under the subheading 'Laureth-9', but the test product will be given as described in the SCCP paper – i.e., by the average alkyl chain length (C) and by the average alcohol ethoxylate number (AE), e.g. $C_{12\text{-}15}AE_7$.

Non-Cosmetic

Alkyl PEG ethers are especially useful as solvents for lacquers, paints, varnishes, dyes, inks, resins, cleaning formulations, and liquid soaps.[34] In addition, alkyl PEG ethers have utility as coupling solvents for a variety of chemical specialties, and they are used as intermediates in the production of plasticizers and other solvents. Laureths, ceteths, oleths, and talloweths are listed as indirect food additives.[35] Laureth-7 is reported to have spasmogenic action on veins,[36] although it is not approved for sclerosant use in the United States.[37] PEG methyl ethers are frequently used in adhesives, lubricants, inks, soaps, and detergents.[21] PEG methyl ethers are also used as components in hydraulic brake fluid.[38]

GENERAL BIOLOGY

Absorption, Distribution, Metabolism, and Excretion

Laureths

Non-Human

Female Colworth Wistar rats, number per group not given, were used to determine the pharmacokinetics of compounds analogous to laureth-9.[33] [^{14}C]Labeled $C_{12}AE_3$, $C_{12}AE_6$, and $C_{12}AE_{10}$ were each administered orally by gavage, intraperitoneally, and subcutaneously, and the rats were then place in metabolism cages for 4 days for collection of feces, urine, and expired air. Radioactivity was primarily recovered in the urine, with 49.8-87.5% being recovered by this route. The amount of radioactivity recovered in the feces, expired air, and carcass ranged from 2.1-19.9%, 4.1-14.2%, and 0.8-

4.9%, respectively. Total recovery was near 100%. Route of administration did not affect the proportions of the compounds recovered in the urine, feces, and air, but proportions did increase with longer ethoxylate length. There was some indication that the longer ethoxylate chain compounds may be excreted via the bile or excreted into the intestines by other routes. For each test substance, two distinct polar metabolites were identified in the urine, with no parent compound. (These metabolites were not identified.)

[^{14}C]Labeled $C_{12\text{-}15}AE_6$ and $C_{12\text{-}15}AE_7$ were administered orally to Cox CD rats, number not specified. More than 75% of the dose was absorbed rapidly, and approximately 50% of the absorbed dose was excreted in the urine. The greatest levels of radioactivity were found in the urine, feces, and expired air, while recovery in the tissues was negligible.

Human

The absorption, distribution, and excretion of orally administered radiolabeled $C_{12}AE_6$ and $C_{13}AE_6$, compounds that are analogous to laureth-9, were examined using groups of 6 male subjects.[33] The subjects were given capsules containing 50 mg of the test substance. Blood, urine, feces, and air samples were taken at various intervals after dosing. The majority of the radioactivity, 75%, was eliminated in the urine within 24 h after dosing. Fecal recovery was 5%, and 4% was recovered in expired air. The amount of radioactivity recovered in the blood was <1%. A total of 83-89% of the radioactivity was recovered within 144 h of dosing. The distribution and excretion of each test compound was similar, but the metabolic product of each compound was a defined function of carbon chain length. The longer carbon chain ethoxylates produced more metabolic CO_2 and less urinary elimination products. The degradation of ether linkages and oxidation of the alkyl chain to form lower molecular weight PEG-like compounds and carbon dioxide and water appeared to be the major degradation pathway of alcohol ethoxylates.

Percutaneous Absorption

Laureths

Animal

In dermal metabolism studies with hairless mice treated with 0.25% solutions in ethanol, the percutaneous absorption, after 4 hours, was 22.9% for laureth-1, 15.5% for laureth-3, 10.4% for laureth-6, and 2.1% for laureth-10.[39] Absorbed laureths were rapidly metabolized to carbon dioxide, and excreted with expired air. With increasing number of ethylene oxide units, the percentage in expired air was decreased, and the amount excreted in feces and urine increased.

The absorption of compounds analogous to laureth-9 was evaluated.[33] [^{14}C]Labeled $C_{12}AE_3$, $C_{12}AE_6$, and $C_{12}AE_{10}$ were applied to female Colworth Wistar rats as 1% solutions in a series of wash and rinse procedures. It was stated that a considerable proportion of the administered dose penetrated the skin, and that the short chain ethoxylates were absorbed more readily than the longer chain ethoxylates, but details of the studies were not provided. After a single 5 min wash with 1% w/v $C_{12}AE_3$ and 1% w/v $C_{12}AE_6$, 4-5 μg/cm^2 penetrated, while in a similar study using $C_{12}AE_{10}$, only 0.85 μg/cm^2 penetrated rat skin. For all three test compounds, penetration was proportional to longer durations of contact and multiple applications. The highest penetration rate, 8.4 μg/cm^2, was observed after 20 min of contact to $C_{12}AE_3$.

Solutions of 0.5 mg [^{14}C]labeled $C_{12\text{-}15}AE_6$ and $C_{12\text{-}15}AE_7$ were applied to a 20 cm^2 shaved area on the backs of Cox CD rats. The animals were restrained to avoid ingestion and were placed in metabolism cages. Samples were collected at 24, 48, and 72 h. By 72 h, approximately 50% of the dose was absorbed. Approximately 50% of the absorbed [^{14}C] was excreted in the urine. The highest concentrations of radioactivity were found in the urine, feces and expired air. Radioactivity in the tissues was negligible.

Human

The absorption of compounds analogous to laureth-9 was evaluated using human subjects.[33] A solution of 100 mg [^{14}C]labeled $C_{12}AE_6$, as a 50/50 ethanol/water solution, was applied to a 90 cm^2 area of the skin of 2 male subjects for 8 h. The test site was protected by a non-occlusive metal shield. After repeated washing, the area was tape-stripped 10 times. Blood samples, urine and feces, and expired air were collected at various intervals. The majority of the radioactive solution, i.e. 73.9 and 87.5%, was removed by cleansing the application site with alcohol-soaked gauze. Less than 2% of the radioactivity was detected in the urine, and measurable amounts were not found in the feces or expired carbon dioxide. Low levels of radioactivity, 0.14, 0.02, and 0.01 µg/g at 8, 12, and 24 h, respectively, were found in the blood of one subject. The total radioactivity recovered was 82.4% for one subject and 94.7% for the other.

The percutaneous absorption of laureth-9 through damaged skin was evaluated using 22 atopic dermatitis patients.[39] The patients were treated with a bath oil containing laureth-9 either by bathing in diluted product or by applying the oil onto the skin for 8 h after showering. Percutaneous penetration was quantified by measuring laureth-9 blood concentrations and urinary excretion rates. Blood concentrations were 0.015-0.021 µg/ml after both types of application. The calculated absorption was 0.0017% after bathing and 0.0035% following the after-shower application.

PEG-3 Methyl Ether

In an *in* vitro study, epidermal samples, separated from human whole abdominal skin, were mounted in a glass diffusion apparatus and used to determine the diffusion of undiluted PEG-3 methyl ether (99.9+% purity) through skin.[40] The epidermal damage caused by exposure to PEG-3 methyl ether was also determined. Six samples were used. The *in vitro* diffusion rate of PEG-3 methyl ether through human epidermal skin samples (expressed in units of µg of test chemical diffusing through 1 cm^2 of skin surface per hr) was 34 ± 7.7 µg/cm^2/hr, indicating that PEG-3 methyl ether would not readily penetrate the skin. The diffusion barrier function of the skin was slightly diminished after 12 h of exposure to PEG-3 methyl ether.

Penetration Enhancement

Laureths

Laureth-9 was reported to promote drug absorption and increase bioavailability of high molecular weight compounds following nasal administration (the specific drugs for which bioavailability might be increased were not identified).[41] It appeared as if 1% laureth-9 induced damage to the nasal mucosa and that was the basis for the potential increased bioavailability. The damage was not observed 4 h after dosing, but was apparent after 24 and 48 h.

Oleths

Oleths have been reported to increase permeability of isolated stratum corneum in *in vitro* studies.[42] (Details were not provided.)

Ceteareths

No effect was found on the stratum corneum, by one study group, for ceteareth-20, while another group reported that percutaneous absorption of piketoprofen was increased in rabbits following topical application of aqueous and anhydrous creams containing 2%, 3% or 5% ceteareth-20.[42]

Spermicidal Activity

Laureths

The spermicidal activity of laureth-9 was investigated *in vitro* using three semen samples.[43] The concentration of laureth-9 immobilizing human spermatozoa within 20 sec ranged from 1:1200-1:3000 and within 2 min ranged from 1:1500-1:3500.

ANIMAL TOXICOLOGY

Acute (Single Dose) Toxicity

The acute toxicity studies are summarized in Table 5.

Oral

Laureths

The acute oral toxicity of laureth-9 was evaluated using groups of 10 male albino Swiss Webster mice.[43] The oral LD_{50} values after 24 h and 7 days were 3300 and 3050 mg/kg, respectively. In rats, the oral LD_{50} ranged from 1642-4900 mg/kg/bw using analogs of laureth-9, applied neat.[33] For a 50% solution of the analogs in corn oil, the oral LD_{50} ranged from >2000 to 2500 mg/kg/bw for male rats and from 1000-2000 mg/kg/bw for female rats. The oral LD_{50} of laureth-9 in beagles was 1650 mg/kg bw, and in monkeys it was 6700 mg/kg/bw.

Ceteths

The acute oral toxicity of an undiluted ceteth (avg. chain length not specified) was determined using fasted ddY mice.[44] The oral LD_{50} was 2880 mg/kg for males and 2602 mg/kg for females.

PEG Methyl Ethers

PEG-3 methyl ether (purity not specified) has an LD_{50} of ≥11.3 g/kg in rats.[20] The oral LD_{50} of PEG-7 methyl ether was >16 ml/kg for the rat.[21] (Details not provided.)

C9-11 Pareths

The acute oral toxicity of C9-11 pareth-6 was determined using groups of 5 male and 5 female Fischer 344 rats.[45] The groups of animals were dosed by gavage with 320-3260 mg/kg of the test material. The combined LD_{50} was calculated as 1378 mg/kg C9-11 pareth-6.

The oral LD_{50} values of various C9-11 pareths for rats, which range from 1000-2900 mg/kg, are stated in Table 5.[46]

C12-13 Pareths

The acute oral toxicity of a C12-13 pareth (avg. chain length not specified) was determined.[47] Groups of 4 male and 4 female Wistar albino rats were dosed by gavage with 5 or 10 g/kg of the test material. One female of the 5 g/kg group, and 2 males and 3 females of the 10 mg/kg, group died by day 11. The oral LD_{50} was approximately 10 g/kg.

The acute oral toxicity of C12-13 pareth-2 was also determined.[48] Four male and 4 female rats were dosed by gavage with 10 g/kg. One female died on day 4, and the LD_{50} was >10 g/kg. The oral LD_{50} values of various C12-13 pareths for rats, which range from 4600-7600 mg/kg, are stated in Table 5.[46]

C12-15 Pareths

The oral LD_{50} values of various C12-15 pareths for rats, which range from 1600-5600 mg/kg, are stated in Table 5.[46]

C14-15 Pareths

The oral LD_{50} values of various C14-15 pareths for rats, which range from 1000-2700 mg/kg, are stated in Table 5.[46]

Dermal

Laureths

The percutaneous LD_{50} of laureth-4 was 0.93 ml/kg for male rabbits and 1.78 ml/kg for females rabbits.[49] (Details not specified.) Pulmonary lesions were found within 3 days of a single dermal application. In rats, the potential for neuro-toxicity was observed within 48 h of a single dermal dose. (Details not specified.)

For analogs of laureth-9, applied neat, the dermal LD_{50} was >2000 mg/kg bw for rats and rabbits.[33] The dermal LD_{50} in rats of a 40% solution in corn oil was >920 mg/kg.

PEG Methyl Ethers

The acute dermal toxicity of PEG-3 methyl ether (purity not specified) was 7.1 ml/kg (7.4 g/kg) in New Zealand white rabbits.[20] The percutaneous LD_{50} of PEG-7 methyl ether was >16 ml/kg for the rabbit.[21] (Details not provided.)

C9-11 Pareths

The acute dermal toxicity of C9-11 pareth-6 was determined using 4 male and 4 female New Zealand white (NZW) rabbits.[45] A dose of 2.0 g/kg was applied under a 4 in x 4 in occlusive patch to the shaved back of the animals. Mild to moderate irritation was observed at patch removal, and mild and moderate edema were still observed after 14 days. The dermal LD_{50} was >2.0 mg/kg C9-11 pareth-6. The dermal LD_{50} values of various C9-11 pareths, which range from 2000-5000 mg/kg for rabbits and 2000-4000 mg/kg for rats, are stated in Table 5.[46]

C12-13 Pareths

The acute dermal toxicity of a C12-13 pareth was determined.[47] Two g/kg of the undiluted test material were applied under occlusion to shaved dorsal skin of 4 male and 4 female Wistar albino rats. The dermal LD_{50} was >2.0 g/kg.

The acute dermal toxicity of C12-13 pareth-2 was determined as described above.[48] One, 2, or 4 g/kg of the test article was applied for 24 h to groups of 4 male and 4 female rats. One female of the 2 g/kg group died on day 6 and all 4 males and 1 female died by day 14. The dermal LD_{50} was >2 g/kg and approximately 4 g/kg.

The dermal LD_{50} values of various C12-13 pareths, which range from 2000-3300 mg/kg for rabbits, are stated in Table 5.[46]

C12-15 Pareths

The dermal LD_{50} values of various C12-15 pareths, which range from 2300-5000 mg/kg for rabbits, are stated in Table 5.[46]

C14-15 Pareths

The dermal LD_{50} values of various C14-15 pareths, which range from 2500-5000 mg/kg for rabbits and is >5000 mg/kg for rats, are stated in Table 5.[46]

Inhalation

PEG Methyl Ethers

In two separate studies, rats were either exposed to 200 mg/l PEG-3 methyl ether (purity not specified) for 1 h or exposed to concentrated vapor for 8 h.[20] All animals survived both studies, and the LC_{50} value was not established in either study.

Other

Laureths

The acute intravenous (i.v.) toxicity of laureth-9 was evaluated using groups of 10 male albino Swiss Webster mice.[43] The i.v. LD_{50}, after 24 h and 7 days, was 100 mg/kg.

A single intratracheal dose of 100 µl/animal of 1% laureth-9 was administered to 12 male Sprague-Dawley rats in order to examine the toxic effects on the lungs.[50] A negative control group of 12 rats was dosed with water. Four rats were killed at 1, 3, or 7 days after dosing. Moderate pulmonary lesions were observed in the bronchi, bronchioles and alveoli of the test animals, but not controls, at each time period.

Repeated Dose Toxicity

Oral

Laureths

Oral toxicity of compounds analogous to laureth-9 was evaluated in a number of repeated dose studies.[33] Groups of 6 Colworth Wistar rats, 3 per gender, were fed 0.023 – 1.5% $C_{12-14}AE_7$, $C_{12-15}AE_7$, and $C_{12-15}AE_{11}$ in the diet for 21 days. A group of 6 male and 6 female rats was used as the control group. With all test compounds, growth was decreased in the 0.75 and 1.5% groups; changes in plasma protein concentration and organ weights were associated with this effect. The liver appeared to be the major target organ, but it was stated that changes seemed to be indicative of an adaptive response rather than a true adverse effect. The lowest observable effect level (LOEL) was 0.75% in the diet for all the test compounds. The no-observable adverse effect level (NOAEL) was 0.375% in the diet for these compounds, corresponding to 502 mg/kg bw $C_{12-14}AE_7$, 459 mg/kg bw $C_{12-15}AE_7$, and 519 mg/kg bw $C_{12-15}AE_{11}$.

Groups of Colworth Wistar rats, number per group not specified, were fed 0.03 – 1.0% active material $C_{12-15}AE_7$ and $C_{12-14}AE_7$ in the diet for 90 days. (Active was not defined.) With both compounds, body weight gains were significantly decreased in male and female rats fed doses >0.25%. Relative liver to body weights were significantly increased in males fed 0.5 and 1.0% and in females fed 0.25, 0.5, and 1.0% of the test materials. Upon microscopic examination, hepatocytic enlargement was noted in the livers. No effects were observed in reproductive organs. The NOAEL for these compounds was 0.125% in the diet, which corresponded to 102 mg/kg bw/day $C_{12-15}AE_7$ and 110 mg/kg bw/day $C_{12-14}AE_7$.

$C_{14-15}AE_7$ was fed to groups of 6 male and 6 female Wistar rats at concentrations of 300-10,000 ppm of active ingredient for 90-days. The control group was compromised of 12 male and 12 female rats. Body weights were decreased in males of the 10,000 ppm group and females of the 3000 ppm group. Relative liver to body weights were increased in males and females of the 3000 and 10,000 ppm groups and in females of the 1000 ppm group; the relative spleen to body weight was increased in males of the 10,000 ppm group. Microscopically, no compound-related effects were seen at any dose level. The dietary NOAEL was 300 ppm, corresponding to 15 mg/kg bw $C_{14-15}AE_7$.

In another 90-day study, $C_{14-15}AE_7$ was also fed to groups of 20 male and 20 female albino rats at concentrations of 0.1, 0.5, and 1% in the diet. Five rats/gender were killed for necropsy on day 28. No treatment-related changes in body weights, feed intake, organ weights, clinical chemistry, or hematology were observed. The NOAEL was 1% $C_{14-15}AE_7$, corresponding to 700 mg/kg bw for males and 785 mg/kg bw for females.

In a 2-yr study, rats, number per group not specified, were fed 0.1, 0.5, and 1% $C_{12-13}AE_{6.5}$ and $C_{14-15}AE_7$ in the diet. Reduced feed consumption, resulting in decreased body weight gains, was observed in the 0.5 and 1% females and 1% males. Relative liver, kidney, and brain to body weights were increased in the 0.5 and 1% female groups, an increased relative heart to body weight was observed in the 1% female group, and increased relative liver to body weights were observed in the 1% male group. The incidence of focal myocarditis was greater in treated males than in controls. No other treatment-related lesions were observed. The NOAEL was 0.1%, corresponding to 50 mg/kg bw/day.

$C_{14-15}AE_7$ was fed to rats, number per group not specified, at concentrations of 0, 0.1, 0.5, and 1% in the diet for 2 yrs. Body weights were decreased for females of the 0.5 and 1% groups and for males of the 1% group. Relative liver, kidney, heart, and thyroid/parathyroid gland to body weights were observed in the high dose group. The only significant microscopic finding was focal myocarditis in all test groups; this lesion was observed at 13 mos but not at 2 yrs. The NOAEL was 0.5%, corresponding to 190 and 162 mg./kg bw/day for female and male rats, respectively.

Deceths

Groups of 5 female NZW rabbits were dosed orally by gavage with 2 ml/kg of 0.12, 0.25, 0.50, 0.75, or 1.0 g/kg deceth (avg. chain length not specified) for 13 days.[51] The negative control group was dosed with distilled water. The deaths that occurred were: 1 rabbit dosed with 0.12 g/kg (day 8; thought to be gavage error); all 5 rabbits dosed with 0.25 g/kg (days 2-12); 4 rabbits dosed with 0.5 g/kg (days 2-14); 4 rabbits dosed with 0.75 g/kg (days 2-14); and all 5 rabbits dosed with 1.0 g/kg (days 2-6). The majority of the mortality was a result of respiratory distress. A number of signs of toxicity, such as post-dose inactivity, clonic convulsions, and respiratory distress, were observed occasionally in the 2 lower dose groups and frequently in the higher dose groups. Severe body weight loss was noted in the highest dose group, and slight to moderate body weight loss was observed in the other groups. Feed consumption was significantly decreased at some point for all groups.

PEG Methyl Ethers

Sprague-Dawley rats (number/gender/group not specified) were given 0, 0.75, 1.6, 3.9, and 8.0 g/kg/day PEG-3 methyl ether (purity not specified) in the drinking water for 14 days.[20] PEG-3 methyl ether was mildly to moderately toxic at 4 g/kg and severely toxic at ≥8 g/kg. A NOAEL of 1.6 g/kg/day was assigned.

Groups of 15 male and15 female Sprague-Dawley CD rats were given drinking water containing target doses of 0, 400, 1200, and 4000 mg/kg/day PEG-3 Methyl Ether (98.7% purity) for 91 days.[20] One female of the high dose group died during the study. No treatment-related clinical signs of toxicity, alterations in functional observational battery, or gross microscopic lesions in the nervous system were found. Statistically significant increases in absolute liver weights were observed in males of the high dose group; increased relative liver weights were also observed in males of this group. Microscopically, hepatocellular cytoplasmic vacuolization and/or hypertrophy were seen in the livers of high-dose males; the severity of these lesions was mostly minimal to mild, although some had moderate or marked vacuolization. Minimal or mild hepatocellular hypertrophy was seen in 10 high dose females. Treatment-related mild to moderate degeneration and/or minimal to moderate atrophy of the seminiferous tubules was observed in males of the high dose group. The researcher stated that a possible contributing factor in the development of testicular lesions was low-level contamination with 2-methoxyethanol (0.02-0.04%), which is a testicular toxicant. For liver effects, the researchers assigned a NOAEL of 400 mg/kg/day and a lowest observable adverse effect level (LOAEL) of 1200 mg/kg/day PEG-3 methyl ether. For testicular effects, the researchers assigned a NOAEL of 1200 mg/kg/day and LOAEL of 4000 mg/kg/day. However, it was noted that the Environmental Protection Agency (EPA) reviewed the information and determined that the LOAEL for testicular effects in this study is between 400 and 1200 mg/kg/day.

C14-15 Pareths

Groups of 12 male and 12 female Wistar rats were fed diet containing 300, 1000, 3000, or 10,000 ppm C14-15 pareth-7 for 13 weeks.[52] A control group of 24 males and 24 females was given untreated feed. All the animals were killed at the termination of dosing. Treatment-related clinical signs were not observed during the study. Mean body weights of males of the 10,000 ppm and females of the 3000 and 10,000 ppm groups and feed consumption of males and females of the 10,000 ppm group were statistically significantly decreased compared to controls. Differences were noted for some hematol-ogical and clinical chemistry values compared to controls, and increases in mean liver weights (3000 and 10,000 ppm males and females and 1000 ppm females), spleen weights (10,000 ppm males), and kidneys (1000 ppm females) were recorded. No microscopic lesions were observed. Therefore any observed differences in organ weights and clinical chemistry and hematology values that were observed were not attributed to dosing and not considered toxicologically significant.

Oleths

A short-term oral study was performed in groups of 3 male and 3 female rats that were dosed by gavage with 0, 100, 300, and 1000 mg/kg/day of an unspecified oleth.[53] One male and 1 female died after 2 doses of 1000 mg/kg, and as a result the high dose was reduced to 750 mg/kg/day. Two additional high dose males died after the 3rd or 4th dose, and 2 additional females in moribund condition were killed after 7 doses. A mid-dose male was killed after receiving 17 doses due to signs of toxicity. Generally, the organs and tissues appeared normal at necropsy. (No other study details were given.)

Dermal

Laureths

The dermal toxicity of laureth-4 was evaluated using groups of female Sprague-Dawley rats.[49] Doses of 495, 990, and 1980 mg/kg undiluted laureth-7 (at dose volumes of 0.5, 1.0, and 2.0 ml/kg, respectively) were applied to the clipped skin of the rats for 5 days during wk 1 and for 4 days during wk 2. The test sites were occlusively wrapped for at least 6 h, and the application site was rinsed when the wrap was removed. The controls were dosed with 2.0 ml of water. Erythema and edema were not observed in this study. Exfoliation was observed for animals of all test groups. Excoriation and/or fissures were observed for 2, 7, and 11 animals of the low, mid, and high dose groups, respectively. Microscopic lesions, such as acanthosis and hyperkeratosis, were also reported. All test groups had an increase in the incidence of abnormal gait. This finding was not considered neurotoxicologically significant since there were no other neurotoxicological observations. No other treatment-related clinical signs of toxicity were observed.

A dose of 2 ml/kg bw of 2.5% aq. $C_{14\text{-}15}AE_7$, a compound analogous to laureth-9, was applied 5 days a wk, 6 h/day, for 13 wks to groups of 3 male and 3 female rabbits.[33] Three test animals died during the study; death was attributed to an infectious disease (also observed in the controls) and the stress of treatment. Moderate localized dermal irritation, as evidenced by erythema and edema, was observed in all test groups.

PEG Methyl Ethers

Groups of 5 rats/gender were dosed dermally with 0, 1000, 2500, or 4000 mg/kg/day PEG-3 methyl ether (purity not specified), 6 h/day.[20] Nine applications were made during a 12-day period. No treatment-related adverse effects were observed. Slight scabbing or crusting was noted at the test site of a few mid or high dose males and females. Clinical chemistry and hematological and urinalysis values that were statistically significantly different from control values were reported, but these effects were not considered by the researchers to be treatment-related. The NOAEL was determined to be 4000 mg/kg/day for this study.

A group of 5 male and 5 female NZW rabbits was used to determine the dermal toxicity of PEG-3 methyl ether (99.9+% purity).[20,40] A dose of 1000 mg/kg/day was applied neat to the shaved skin (size of test area not specified) on the back of each animal, 6 h/sday, 5 days/wk for 3 wks, under an occlusive covering; the animals were restrained during dosing. Six h after application, the site was rinsed. The negative control group of 10 animals was sham-treated. The test sites were scored for dermal irritation immediately prior to dosing. All animals were killed within 24 h of the last dose.

No animals died during the study. The only observation made related to testing was the incidence of erythema and edema due to dermal application of PEG-3 methyl ether. Slight erythema and edema was first observed for 1 animal on day 6. Erythema was observed for all animals on day 9 and continued until study termination. Edema was observed in some, but not all, animals, and it resolved completely by day 18. According to microscopic examination, the lesions were primarily trace acanthosis. No other significant toxicological findings were reported during the study or at necropsy.

The toxic potential of undiluted PEG-3 methyl ether (99.23% purity) was evaluated by applying doses of 0, 400, 1200, or 4000 mg/kg bw to a shaved site on the backs of 10 rats/gender/group for 6 h/day, 5 days/wk, for 13.[20] The test

material was uniformly spread on a 12 cm^2 area under a semi-occlusive covering. Additional groups of 5 rats/gender/dose were used for interim evaluations. There were no indications of systemic toxicity, and the researchers did not consider testicular effects in one high dose and one mid-dose male to be test-article related. (Dermal effects were not described.) The researchers assigned a NOAEL of 4000 mg/kg bw/day PEG-3 methyl ether. However, it was noted that the EPA reviewed that data and, based on testicular effects in 2 males, the assigned an NOAEL of >400 and<1200 mg/kg bw.

The dermal toxicity of PEG-7 methyl ether was evaluated in 14-day and 28-day studies using CD(SD)BR rats.[21] In the 14-day study, 10 males and 10 females were dosed dermally with 5000 mg/kg undiluted PEG-7 methyl ether. The test site was clipped of hair, and applications were made 5 days/wk. The application site was not occluded, but a collar was placed on the animals just prior to dosing until study termination. Controls were handled similarly, except no applications were made. In the 28-day study, groups of 15 male rats were dosed dermally with 1250, 2500, or 5000 mg/kg undiluted PEG-7 methyl ether, 5 days/wk.

No mortality was recorded. In the 28-day study, slight to moderate erythema and slight to moderate desquamation were observed for some animals. In the 14-day study, the mean absolute weight of the spleens of males were significantly decreased and the mean and absolute relative thymus gland to body weight ratios of test males and females were slightly, but not significantly, decreased compared to controls. In the 28-day study, the mean absolute body weights of the high dose animals and the mean testes weights of the low dose group was significantly decreased compared to the controls. No microscopic lesions were reported for any test group, and as such the researchers found that it was unlikely that there was any biological significance associated with the changes in organ weights.

The same researchers also examined the dermal toxicity of PEG-7 methyl ether in a 9-day study and 90-day study using NZW rabbits. In the 9-day study, the dorsal surfaces 5 male rabbits/group were clipped free of hair, and the rabbits were dosed with 1.0 ml of a solution of 50% PEG-7 methyl ether in 0.1% methyl cellulose in distilled water or with undiluted PEG-7 methyl ether. After 6 h, the test site was wiped. Five applications were made during wk 1, and 4 were made during wk 2. The application site was not occluded, but a collar was placed on the animals daily, prior to dosing, until the site was wiped. Vehicle was applied to animals in the negative control group. No mortality was recorded. Barely perceptible erythema and slight to moderate desquamation was observed. No significant differences in organ or body weights were observed as compared to controls.

In the 90-day study, groups of 10 male and 10 female rabbits were dosed, 5 days/wk, with 1.0 ml of a solution of 50% PEG-7 methyl ether in 0.1% methyl cellulose in distilled water or with undiluted PEG-7 methyl ether. The application site was not occluded, but a collar was placed on the animals daily, prior to dosing, until the site was wiped. Vehicle was applied to animals in the negative control group. No mortality was recorded. Barely perceptible erythema and slight to moderate desquamation was observed. No significant differences in organ or body weights were observed as compared to controls. Mild acanthosis was observed for 3 females dosed with undiluted PEG-7 methyl ether. This lesion was not considered toxicologically significant.

C9-11 Pareths

Groups of 20 Fischer 344 rats, 10 per gender, were exposed dermally to 0.5 ml/kg of 0, 1, 10 or 25% w/v aq. C9-11 pareth-6, 3 days/wk for 13 wks.[45] The test site was shaved, but the application site was not covered. Each week the test site was evaluated for irritation. None of the animals died during the study. No toxicologically significant differences in feed consumption, body weights, or clinical signs were noted for the test groups as compared to controls. Irritation scores were 0 for all animals. Dry and flaking skin was observed in the 10 and 25% dose groups, and females of these groups had an increase in discoloration at the test site. Microscopically, the epidermal thickening with hyperkeratosis observed for the skin at

the treatment site appeared to be a physiologic response to an irritant, rather than a toxic effect. Differences in organ weights, such as relative kidney to body weights in the high dose group, were not considered treatment-related since no renal lesions were observed. Differences in clinical chemistry values were also not considered treatment-related.

Talloweths

Applications of 2 ml/kg of a 0.5% solution of a talloweth (chain length not specified) in deionized water was applied to the shaved backs of 9 male and 9 female NZW rabbits.[54] The applications were made 5 times/wk for 13 wks, followed by a 4-wk recovery period. A group of 9 male and 9 female rabbits were dosed with deionized water and was used as the negative control group. The animals were placed in collars for 7 h to minimize ingestion, and the test sites were rinsed when the collars were removed. The application site was evaluated daily for irritation.

Slight irritation was observed at the test site during dosing, but the skin was almost completely normal at the end of the recovery period. At the 4-wk interim sacrifice, moderate epidermal hyperplasia, hyperkeratosis, and inflammatory infiltrates were observed microscopically, and after 13 wks, slight to moderate hyperplasia was reported. After the 4-wk recovery period, there were no specific microscopic findings. There were no toxicologically significant findings.

Dermal Irritation

The dermal irritation studies are summarized in Table 6.

Laureths

A Draize test was performed to determine the dermal irritation of laureth-9.[43] Laureth-9 was applied undiluted or as a 15 or 20% aq. solution under occlusion to the intact and abraded skin of rabbits (number, strain, and gender not specified). The test sites were scored 24 and 72 h after application. A slight irritant effect was observed on intact and abraded skin 24 h, but not 72 h, after application of the 15 and 20% solutions. Using undiluted laureth-9, slight irritation was reported at the intact sites and moderate irritation at the abraded sites at both the 24 and 72 h readings.

The dermal irritation potential of a number of test substances analogous to laureth-9 was determined.[33] $C_{14\text{-}15}AE_7$, 0.5 ml at 10, 25, or 100%, was not irritating when applied to rabbits under a semi-occlusive patch for 4 h; the PII was 1.7. Following a 4 h occlusive application to rabbit skin, undiluted $C_{12\text{-}14}AE_{10}$ and undiluted $C_{13}AE_6$ were moderately irritating, and undiluted $C_{13}AE_{6.5}$ and undiluted $C_{12\text{-}14}AE_6$ were severely irritating. A 24 h occlusive application of $C_{14\text{-}15}AE_7$ was severely irritating to rabbit skin, producing slight to moderate erythema and moderate to severe edema.

The dermal irritation of a contraceptive aerosol formulation containing 20% laureth-9 was also determined in a Draize study.[43] The formulation was applied using occlusive patches to intact and abraded skin of 4 rabbits, and the sites were scored 24 and 72 h after application. The aerosol formulation containing 20% laureth-9 was a mild irritant.

One-tenth g of a mixture containing a laureth (chain length unspecified; composition percentage not stated) was applied to the shaved dorsal skin of 6 male albino rabbits.[55] The test site was occluded for 24 h, and the site was evaluated upon removal and after 2 and 5 days. It was concluded that the laureth tested was a strong irritant, causing necrotic skin for 2 of the test animals.

PEG Methyl Ethers

Two g/kg PEG-3 methyl ether (purity not specified) was applied to intact and abraded skin of 5 New Zealand white rabbits, and the site was covered for 24 h.[20] With intact skin, erythema, but not edema, was seen in 4 rabbits. With abraded skin, erythema and edema were both seen in 1 rabbit. (A conclusion regarding irritation potential was not given.)

PEG-3 methyl ether (purity not specified), 0.1 ml, was applied uncovered to the skin of 5 rabbits for 24 h.[20] PEG-3 methyl ether caused minimal irritation, with an irritation score of 2/10 at 24 h,

C9-11 Pareths

The primary dermal irritation potential of undiluted C9-11 pareth-6 was evaluated in a Draize test using 3 male and 3 female NZW rabbits.[45] Two g/kg were applied to a 1" square of gauze, and the gauze was applied to the shaved backs of the animals under an occlusive patch for 24 h. The test site was scored at patch removal after 24 and 72 h. The PII was 5.3/8, and C9-11 pareth-6 was classified as "moderately irritating".

The dermal irritation potentials of undiluted C9-11 pareth-3, C9-11 pareth-5, C9-11 pareth-6, and C9-11 pareth-8 was evaluated in Draize studies, each using 6 albino rabbits.[46] All of these ingredients were severely irritating. Some dilutions (vehicle not specified) were also tested. C9-11 Pareth-5 was non-irritating at 0.1%, minimally irritating at 1%, and slightly irritating at 10%. C9-11 Pareth-6 was non-irritating at 0.1% and slightly irritating at 1%. C9-11 Pareth-8 was minimally irritating at 0.1%, mildly irritating at 1%, and moderately irritating at 10%.

C12-13 Pareths

The dermal irritation potential of a C12-13 pareth (chain length unspecified) was evaluated in a Draize test using 3 male NZW rabbits.[47] A single occlusive patch of undiluted test material was applied to intact and abraded skin for 24 h, and the test sites were graded at 24 h, 72 h, and 7 days after application. Mean scores of 2, 2.2, and 2.5/4 for erythema and 1, 2, 2/4 for edema were reported at 24 h, 72, h and 7 days, respectively, for both intact and abraded skin. Necrosis and cracking skin was observed. The test substance was moderately irritating.

The same protocol was followed to determine the dermal irritation potential of undiluted C12-13 pareth-2 (chain length nor specified).[48] The erythema and edema scores were slightly lower, and necrosis was not observed, but this compound was also classified as moderately irritating.

The dermal irritation potentials of undiluted C12-13 pareth-3 and C12-13 pareth-7 were evaluated in a Draize study using 6 albino rabbits.[46] C12-13 pareth-3 was severely irritating and C12-13 pareth-7 was mildly to severely irritating. Dilutions of C12-13 Pareth-7 (vehicle not specified) was non-irritating at 0.1%, mildly irritating at 1%, and moderately irritating at 10%.

C12-15 Pareths

The dermal irritation potentials of undiluted C12-15 pareth-3, C12-15 pareth-7, and C12-15 pareth-9 were evaluated in Draize studies, each using 6 albino rabbits.[46] C12-15 pareth-3 was moderately to extremely irritating, C12-15 pareth-7 was moderately irritating, and C12-15 pareth-9 was severely irritating. Some dilutions (vehicle not specified) were also tested. A 50% solution of C12-15 pareth-12 was minimally irritating. At concentrations of 0.1 and 1%, C12-15 pareth-7 was mildly irritating, while at 10%, it was moderately irritating. C12-15 pareth-9 was non-irritating at concentrations of 0.1 and 1%.

C14-15 Pareths

The dermal irritation potentials of undiluted C14-15 pareth-7, C14-15 pareth-11, C14-15 pareth-13, and C14-15 pareth-18 were evaluated in Draize studies, each using 6 albino rabbits.[46] C14-15 pareth-7 was severely irritating, C14-15 pareth-11 was moderately to severely irritating, C14-15 pareth-13 was moderately irritating, and C14-15 pareth-18 was mildly irritating. Some dilutions (vehicle not specified) were also tested. C14-15 Pareth-7 was minimally irritating at 0.1%, mildly irritating at 1%, and moderately irritating at 10%. C14-15 pareth-11 was non- irritating at 0.1%, slightly irritating at 1%, and moderately to severely irritating at 10%. C14-15 Pareth-18 was non-irritating at 0.1%, minimally irritating at 1%, and slightly irritating at 10%.

Dermal Sensitization

Sensitization studies are summarized in Table 6.

Laureths

The sensitization potential of laureth-5 was examined in a modified cumulative contact enhancement test that was performed without adjuvant stimulation at induction and with closed epidermal challenge.[22] At induction, occlusive applications of 200 mg of 10% aq. laureth-5 were made to the shaved backs of 15 Dunkin-Hartley guinea pigs on days 0, 2, 7, and 9 of induction. Water was used for induction with the negative control group. The challenge was performed on day 21, and 15 µg of 0, 0.1, 1, and 5% aq. laureth-5 was applied to the shaved left flank for 24 h using Finn chambers. The test sites were evaluated 48, 72, or 96 h after application. Laureth-5 did not produce a sensitization reaction. However, confluent erythema was seen in 1 test and 2 control animals at 48 h and in 2 test and 1 control animal at 72 h and 1 test and 1 control animal with the 1% induction and at 96 h in 1 test and 1 control animal with the 5% challenge.

Groups of 7 male guinea pigs were dosed intracutaneously with a 0.02% aq. solution of laureth-9 or a 0.1% solution of an aerosol contraceptive formulation containing 20% laureth-9, to determine the sensitization potential.[43] The injections were made 3 times per wk for a total of 10 applications. The first dose volume was 0.05 ml, and the subsequent injections were 0.1 ml. A control group was injected with distilled water. Two wks after the last induction injection, 0.05 ml of the corresponding test or control solution was given as a single injection. A small, transient raised area was observed after test and control injections. Neither laureth-9 solution produced direct or delayed sensitization reactions.

The sensitization potential of a number of test substances analogous to laureth-9 was determined.[33] In Magnusson-Kligman guinea pig maximization tests in which intradermal induction used concentrations of 0.05-0.2%, dermal induction used concentrations of 20-100%, and challenge was with concentrations of 15-60%, the compounds were non-sensitizing. In Buehler studies using guinea pigs, the products were applied undiluted during induction and at 50% aq. at challenge. Again, no sensitization was observed.

C9-11 Pareths

The sensitization potential of a 1% aq. solution of C9-11 pareth-6 was evaluated using the Buehler method.[45] Induction patches of the negative, positive, or irritant controls or the test article were applied to the clipped skin on the back of 4 groups of 5 male and 5 female Dunkin-Hartley albino guinea pigs. The occlusive patches were applied 1 day/wk, 6 h/day, for 3 consecutive weeks. The rest period duration was not stated. Signs of sensitization were scored 24 and 48 h after the challenge applications. C9-11 pareth-6 did not produce a sensitization reaction.

C 9-11 Pareth-3, C9-11 pareth-5, C9-11 pareth-6, and C9-11 pareth-8 were not sensitizers in guinea pigs studies.[46] (Technique used not specified.)

C12-13 Pareths

The dermal sensitization potential of a C12-13 pareth (chain length not specified) was evaluated with a Magnusson-Kligman maximization study.[47] The test group consisted of 10 male and 10 female guinea pigs, while the negative control group had 5 animals per gender. A dose of 0.50% w/v was used for the intradermal induction, 50% w/v for topical induction, and 25% w/v for the topical challenge patch. Corn oil was used as the vehicle. Erythema was scored immediately and 24 and 48 h after removal of the challenge patch, and trace erythema was observed for 1 female test animal at each reading. It was concluded that the test material was a very weak sensitizer in guinea pigs.

The dermal sensitization potential of C12-13 pareth-2 (chain length not specified) was evaluated using the same procedure.[48] In this study, the intradermal induction dose was 0.1% w/v, the topical induction used undiluted test material, and the topical challenge dose was 50% w/v. None of the guinea pigs had an erythematous response, and the test material was not considered to be a sensitizer.

C12-13 Pareth-3 was not a sensitizer in guinea pigs , and, C12-13 pareth-7 had either low sensitization potential or was negative for sensitization.[46] (Details not given.)

C12-15 Pareths

C12-15 Pareth-3, C12-15 pareth-7, and C12-15 pareth-9, concentrations not specified, were not sensitizers in guinea pig studies.[46] (Details not given.)

C14-15 Pareths

C14-15 Pareth-7, C14-15 pareth-11, C14-15 pareth-13 and C14-15 pareth-18, concentrations not specified, were not sensitizers in guinea pig studies.[46] (Details not given.)

Ocular Irritation

Ocular irritation studies of alkyl PEG ethers are summarized in Table 7.

Laureths

Laureth-9, 5% aq., was not irritating and had an anesthetic effect on the cornea of rabbit eyes.[39] (The methodology used to determine the anesthetic effect was not described.)

The ocular irritation potential of a number of test substances analogous to laureth-9 was determined using rabbits.[33] The compounds were instilled neat or in varying concentrations. Undiluted compounds were moderately to severely irritating. A 10% aq. solution was moderately irritating, while 0.1-1.0% aq. solutions were non-irritating to rabbit eyes. (Additional details are provided in Table 7.)

PEG Methyl Ethers

The ocular irritation potential of PEG-3 methyl ether (purity not specified) was evaluated in rabbit eyes using various concentrations and volumes of the test material.[20] PEG-3 methyl ether was slightly irritating to rabbit eyes, with an irritation score of 1/10.

C9-11 Pareths

Draize studies in rabbits were used to evaluate the ocular irritation potential of some C9-11 pareths. Undiluted C9-11 pareth-3, C9-11 pareth-5, C9-11 pareth-6, and C9-11 pareth-8 were severely irritating to rabbit eyes.[46] With rinsing, C9-11 pareth-3 was mildly irritating, while C9-11 pareth-6 was still moderately to severely irritating. Dilutions (vehicle not specified) were also evaluated. C9-11 Pareth-5, C9-11 pareth-6, and C9-11 pareth-8 were all non-irritating at 0.1% and were non- to slightly irritating at 1%. A 1% solution of C9-11 pareth-5 was moderately irritating. (Number per group not specified.)

C12-13 Pareths

Undiluted C12-13 pareth-3 was moderately to extremely irritating and C12-13 pareth-7 was severely irritating to rabbit eyes in Draize studies.[46] With rinsing, C12-13 pareth-7 was minimally irritating. At 0.1 and 1% (vehicle not specified), it was non-irritating, and, at 10%, it was moderately irritating.

The ocular irritation potential of a C12-13 pareth was evaluated using 3 NZW rabbits.[47] The test material, 0.2 ml, was instilled into the lower conjunctival sac of one eye, and the eye was not rinsed. The undiluted test material was mildly irritating to rabbit eyes. In a study evaluating the ocular irritation potential of C12-13 pareth-2, this test material was defined as non-irritating.[48]

C12-15 Pareths

In Draize studies, undiluted C12-15 pareth-3 was severely irritating, undiluted C12-15 pareth-7 was moderately irritating, and undiluted C12-15 pareth-9 and C12-15 pareth-12 were severely to extremely irritating to rabbit eyes.[46] With

rinsing, undiluted C12-15 pareth-7 was mildly to moderately irritating. Undiluted C12-15 pareth-7 produced no to mild irritation.

C14-15 Pareths

Undiluted C14-15 pareth-11 and C14-15 pareth-13 were severely irritating and undiluted C14-15 pareth-18 was minimally to mildly irritating to rabbit eyes in Draize studies.[46] With rinsing, C14-15 pareth-7 was mildly irritating. At 0.1%, C14-15 pareth-7, C14-15 pareth-11,and C14-15 pareth-18 were non-irritating. At 1% (vehicle not specified), these ingredients were non- to mildly irritating, and at 10% C14-15 pareth-7 was mildly irritating and C14-15 pareth-18 was practically non-irritating, but C14-15 pareth-11 was severely irritating.

Oleths

In a Draize test, 5% Oleth-20 (vehicle not specified) produced very mild, transient conjunctival redness and chemosis in rabbit eyes.[56]

Mucosal Irritation

Laureths

The effect of laureth-9 on the nasal mucosa was examined using male Sprague-Dawley rats.[41] Twenty-five ml of 1% laureth-9 was placed into the left nostril of each test animal, while saline was instilled into the nostril of the negative controls. (Number of animals not given.) Two to 4 test animals and one control were killed 4 h or 2, 3, 4, 5, 7, or 10 days after dosing, and the nasal mucosal tissues were examined. Four h after dosing, swelling was observed, but there were no changes in the nasal epithelium. Severe damage was observed on day 2, with shedding of necrotic epithelium. Regeneration of the epithelium started by day 3, and there was evidence of basal cell regrowth by day 4. The epithelium was completely regenerated between days 7-10.

A single dose of 5 ml undiluted laureth-9 was instilled into the vagina of 2 dogs.[43] No irritation was observed in the cervical or vaginal mucosa of either dog on day 0 or 3. The researchers performed a second study in which 5 ml of a 15% aq. solution of laureth-9 was instilled once daily for 5 days. Again, no mucosal irritation was observed.

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

Dermal

C9-11 Pareths

A two-generation reproductive study was performed using Fischer 344 rats to examine whether C9-11 pareth-6 had any effect on reproductive parameters.[45] The F_0 groups, consisting of 30 males and 30 females, were exposed dermally to 1 ml/kg of 0, 1, 10 or 25% w/v aq. C9-11 pareth-6 for 119 days prior to mating. The test site was shaved, but the application sites were not covered. The test material was not applied during mating to avoid ingestion. For the second generation, after 133 days of dosing, groups of 20 males and 20 females per test group were mated. For both generations, the application sites were evaluated for irritation. The male rats of both generations were killed following mating. Gross necropsies were performed on all F_0 and F_1 parents and on 5 pups/gender/dose.

There was no mortality in the F_0 generations, and deaths that did occur in the F_1 generation were not attributed to treatment. No irritation was observed for any of the animals, but dry flaking skin was observed in the 10 and 25% dose groups. For effects on body weight, 10% was a no-effect level and 25% C9-11 pareth-6 caused a minimal decrease in body weights over the study. There were no compound-related effects on maternal body weights in any test group. No toxicologically significant effects were observed regarding organ weights, mating indices, fertility indices, or mean gestational length,

and dermal administration of the test compound did not have an effect on the growth or development of the offspring. A decrease in the number of sperm in the high dose F_0 males was not considered treatment-related or toxicologically significant.

Oral

Laureths

The reproductive and teratogenic toxicity of compounds analogous to laureth-9 was evaluated.[33] Groups of 25 gravid female rabbits were dosed orally with 0, 50, 100, or 200 mg/kg bw $C_{12}AE_6$ on days 2-16 of gestation, and the animals were killed and necropsied on day 28 of gestation. In the 100 and 200 mg/kg groups, ataxia and a slight decrease in body weights was evidence of maternal toxicity. No effects on reproductive parameters were noted. Nine control animals and 1 test animal died during the study. Based on maternal toxicity, the NOAEL was >50 mg/kg bw/day.

Groups of 25 male and 25 female CD rats were used to evaluate the reproductive toxicity of $C_{14-15}AE_7$ in a two-generation study. The animals were fed a diet containing 0, 0.05, 0.1, and 0.5% of the test article (equivalent to approximately 0, 25, 50, and 250 mg/kg bw/day). In three test groups, males and females were given treated feed throughout the study; in another three groups, females only were dosed, and dosing was performed on days 6-15 of gestation. (Additional details regarding study and dosing regimen were not provided.). No compound-related differences in fertility, gestation, or viability indices were observed, and the NOAEL for reproduction with dietary administration of $C_{14-15}AE_7$ was >0.5% (equivalent to 250 mg/kg bw/day).

In addition, effects on the F_C generation, i.e. offspring from the third mating of the F_0 and F_1 parenteral generation, were examined. Gravid female rats were necropsied and examined on either day 13 or day 21 of gestation. Differences in maternal and fetal indices were observed in the test groups compared to the controls, but these effects were not considered test-compound related. Parental female rats and pups of the high-dose group had reduced body weight gains. In the 0.5% continuous feeding test group, increased mean liver weights of males and females of the P_1 generation and an increase in relative liver to body weights of males of the 0.5% continuous feeding group of the P_2 generation at 60 days were considered compound-related. The NOAEL for maternal and developmental toxicity was 50 mg/kg bw/day.

The reproductive toxicity of $C_{12}AE_6$ was evaluated in a similar study, and the animals were fed 0, 25, 50, or 250 mg/kg bw/day of the test article in the diet. No treatment-related effects on behavior, appearance, survival, or fertility were observed in any of the test groups. Parental and offspring weight gain was reduced in the 250 m/kg group. In the 250 mg/kg group, statistically significant increases in embryo lethality and soft tissue anomalies were observed, and in the 50 mg/kg group, a statistically significant decrease in mean fetal liver weights was observed. None of these effects were considered test article-related. The NOAEL for reproduction was >250 mg/kg bw/day, and the NOAELs for maternal and developmental toxicity were 50 mg/kg bw/day $C_{12}AE_6$ in the diet.

PEG Methyl Ethers

In a modified Chernoff-Kavlock test, groups of 10 gravid Alpk:AP Wistar rats were dosed daily by gavage with 250 or 1000 mg/kg PEG-3 methyl ether (99.9+%) at a volume of 10 ml/kg on days 7-16 of gestation.[40] The negative control group of 10 gravid rats was given 10 ml/kg water and the 2 positive control groups were dosed with 50 and 250 mg/kg methoxyethanol. The dams were allowed to deliver their pups. Treatment-related effects were not seen in either the dams or the pups as a result of dosing with 250 or 1000 mg/kg PEG-3 methyl ether, as compared to the negative controls. All dams of the negative control and PEG-3 methyl ether groups delivered live fetuses. None of the positive control animals delivered any litters.

Groups of gravid CD (SD) rats (number not stated) were dosed orally by gavage with 0, 300, 1650, or 3000 mg/kg PEG-3 methyl ether on day 6 of gestation to post-natal day (PND) 21.[57] The litters were culled to 8 pups on PND 4, and 1

male and 1 female pup from each litter was killed on PNDs 22 and 68. The only maternal dose-related effects reported were increased length of gestation and in increase in kidney weight at the highest dose. Birth weight of females in the mid dose group and males and females in the high dose group were significantly increased compared to controls. However, post-natal weight gains were decreased at various times. No effects on motor activity were observed.

The developmental toxicity of PEG-3 methyl ether (99.27% purity) was evaluated using rats and rabbits.[38] Gravid Crl:CD (SD) BR rats, 25 per group, were dosed orally by gavage with 625, 1250, 2500, or 5000 mg/kg on days 6-15 of gestation, and the animals were killed on day 20 of gestation. A negative control group was given deionized water by gavage. In the high dose group, clinical signs of toxicity, such as decreased motor activity, excess salivation, ataxia, and impaired righting reflex, were statistically significantly increased and occurred with the first or second dose of 5000 mg/kg PEG-3 methyl ether. One rat in this group, which was actually non-gravid, died on day 13; no treatment-related effects were seen at necropsy. No signs of toxicity were seen in the other dose groups. Maternal body weights, gravid uterine weights, and feed consumption were statistically significantly reduced in the high dose group, and feed consumption was statistically decreased in the 2500 mg/kg group on days 12-16 of gestation. Pregnancy rates were not affected, but embryo lethality was statistically significantly increased in the high dose group. Fetal body weights were statistically significantly decreased in the 2500 and 5000 mg/kg group and slightly decreased in the 1250 mg/kg group. The incidence of gross external, soft tissue, or skeletal fetal malformations was not affected at any dose level. Doses of ≥1250 mg/kg PEG-3 methyl ether did cause significant increases in reversible delayed ossification. The maternal and developmental no-observable effect levels (NOELs) for rats were 625 mg/kg/day PEG-3 methyl ether. The NOAEL for maternal toxicity in the rat was 1250 mg/kg/day.

Gravid NZW rabbits, 20 per group, were also dosed orally with PEG-3 methyl ether. Doses of 250, 500, 1000, or 1500 mg/kg were given by stomach tube on days 6-18 of gestation, and the animals were killed on day 29 of gestation. A negative control group was dosed with deionized water. In the high dose group, clinical signs of toxicity, such as decreased motor activity, labored breathing, reddish brown staining of the anogenital area and a red substance in the cage, appeared near the end of dosing, and the incidence was statistically significant. Mortality was also statistically significantly increased for this group; 8 does died during days 17-21 of gestation. Gastric ulcerations, observed at necropsy, were also statistically significantly increased for this group. Treatment-related effects were not seen in the other dose groups, but one doe of the 1000 mg/kg groups died on day 18 of gestation.

Maternal weight gain was decreased for the high dose group during dosing, but a rebound effects occurred during the post-treatment period, leading to significantly increased body weight gains. The average uterine weight was decreased in the high dose group as compared to controls. Feed consumption was decreased throughout dosing. Again, a rebound effect was seen post-dosing, and feed consumption was increased in the 500 mg/kg group and statistically significantly increased in the 1000 and 1500 mg/kg groups. Oral administration of PEG-3 methyl ether did not affect pregnancy rates, average number of corpora lutea or implantation sites, or mean fetal body weights, and it did not cause any gross external, internal soft tissue, or skeletal malformations. Decreased live litter sizes and increased resorption rates in the 1000 and 1500 mg/kg groups occurred, but were not statistically significant. Fetal and/or litter incidence of two common skeletal variations, angulated hyoid alae and reversible delayed ossification of the xiphoid, were statistically significantly increased in the 1500 mg/kg group. For rabbits, the maternal and developmental toxicity NOELs were 250 and 1000 mg/kg/day PEG-3 methyl ether, respectively. The NOAEL for maternal toxicity was 500 mg/kg/day, and the presumed NOAEL for developmental toxicity was 1500 mg/kg/day.

Groups of 64 gravid female Sprague-Dawley rats were dosed orally, by gavage, with 0, 300, 1650, or 3000 mg/kg/day PEG-3 methyl ether (99.2% purity) on days 6-21 of gestation in a study of developmental neurotoxicity.[20] The pups were delivered, litters were culled on day 4, and the offspring were observed in a number of tests. One male and one female pup from each litter were killed on post-natal days (PNDs) 22 and 68. In maternal animals, no dose-related patterns of clinical signs of toxicity or mortality were noted, and there were no significant differences in body weights between test and control animals. Kidneys weights of maternal rats were statistically significantly increased in high dose dams compared to controls. A maternal NOAEL of 1650 mg/kg bw was assigned.

The length of gestation was statistically significantly increased in animals of the high dose group; however, the researchers found the biological significance of this questionable. Body weights of female pups of the mid and high dose groups and male pups of the high dose group were significantly greater than controls at PND 0. At PND 68, male pups of the high dose group weighed statistically significantly less than controls. Male pup development, determined by time of testes descent, was significantly advanced in pups of the mid and high dose groups; no treatment-related effects for this observation were found at necropsy. Behavioral evaluations did not find any dose-related effects on motor activity or active avoidance. A significant effect on auditory startle response parameters was noted; the significance of this finding was not clear to the researchers. The researchers assigned an NOEL of 300 mg/kg for offspring, while EPA assigned an NOAEL of 300 mg/kg for teratogenicity.

GENOTOXICITY

Laureths

Laureth (chain length not specified) was tested in a number of genotoxicity studies. In an Ames study, laureth (3-333 µg/plate) was negative with and without activation.[58] In a standard transformation assay with BALB/c-3T3 cells, laureth (tested at 0.00132-0.0417 and 0.00625-0.0250 mM) was inactive.[59] Using Chinese hamster ovary (CHO) cells, laureth did not induce sister chromatid exchanges (concentrations of 3.08-10.8 µg/ml with or 0.308-3.08 µg/ml without metabolic activation) or chromosomal aberrations (5-50 µg/ml with or without activation).[60] In a L5178Y mouse lymphoma cell mutation assay (0-50 nl/ml with and 0-40 nl/ml without activation), the results were suggestive of a lack of mutagenic activity; one test without metabolic activation produced questionable results, and one with metabolic activation had inconclusive results.[61] In a mouse bone marrow micronucleus assay, laureth was not genotoxic when tested at doses of 31.25-125 mg/kg.[62]

Compounds that are analogous to laureth-9 were not mutagenic in the Ames test at concentrations of ≤5000 µg/plate or clastogenic in a chromosomal aberration assay using CHO cells at concentrations of ≤25 µl/ml, with or without metabolic activation.[33] *In vivo*, 1.7 g/kg of a 20% solution and 2.5 g/kg active ingredient of a 10% solution did not induce chromosomal aberrations in Chinese hamsters. A dose of 1000 mg/kg was not clastogenic in Wistar rats.

PEG Methyl Ethers

The mutagenicity and genotoxicity of aq. PEG-3 methyl ether (99.23% purity) was evaluated in an Ames test using four strains of *S. typhimurium* at concentrations ≤5000 µg/plate with and without metabolic activation, in an HGPRT forward mutation assay in CHO cells at concentrations of ≤5000 µg/plate with and without metabolic activation, and in an *in vivo* mouse micronucleus test at concentrations of ≤5000 mg/kg.[20] The results were negative in all three studies. Expected results were seen with appropriate negative and positive controls.

The mutagenic potential of PEG-7 methyl ether was evaluated using an Ames assay.[21] Concentrations of 1-110 mg/plate were tested using five strains of *Salmonella typhimurium*, with and without metabolic activation. PEG-7 methyl ether was not mutagenic at any dose.

C9-11 Pareths

The mutagenic potential of ≤1 mg/plate C9-11 pareth-6 was evaluated in an Ames test using *S. typhimurium* strains TA98, TA100, TA1535, TA1537, and TA1538 in the presence and absence of metabolic activation.[45] The appropriate positive controls were used with each strain to validate the study. Toxicity occurred at higher concentrations (actual doses not specified) in all strains, but there were no mutagenic responses to C9-11 pareth-6, with or without metabolic activation.

CARCINOGENICITY

Laureths

The carcinogenic potential of compounds analogous to laureth-9 was evaluated.[33] Groups of 65 rats/gender were fed a diet containing 0, 0.1, 0.5, and 1% $C_{14-15}AE_7$ for 2 yrs. At 1 yr, 14-15 animals per gender were killed and necropsied. No compound-related changes were seen in behavior or appearance at any time. Survival rate was comparable between test and control animals. Body weight gains were significantly decreased in females of the 0.5 and 1.0% groups and males of the 1% group. At necropsy, no differences in relative or absolute organ weights were observed between test and control animals. There was no evidence of a carcinogenic effect.

$C_{12-13}AE_{6.5}$ was fed to 100 Sprague-Dawley rats at concentrations up to 1% in feed for 2 yrs. Feed consumption, and correspondingly, body weight gain, was reduced for females fed 0.5 or 1% and for males fed diets containing 1% of the test compound. No microscopic effects were seen, and $C_{12-13}AE_{6.5}$ was not carcinogenic.

CLINICAL ASSESSMENT OF SAFETY

Dermal Irritation/Sensitization

Laureths

In a retrospective (Jan-Apr 1996) European study of allergic contact response, only 1 of 475 patients had an allergic contact reaction to laureth-4.[63] From 1992 to 1999, 3186 patients were patch tested with 0.5% laureth-9.[64] Based on 72 h readings, 0.94% had questionable (erythematous) reactions, and 0.88, 0.97, and 0.25% had slightly irritating, weakly positive, and strongly positive reactions, respectively. For 6202 patients that were patch tested with 3% laureth-9, 1.79, 0.48, 1.77, and 0.34% of the subjects had questionable, irritating, weakly positive, and strongly positive reactions, respectively. For the 649 patients patch tested with both concentrations, the concordance was moderate.

Clinical dermal irritation testing was performed with test substances that were analogous to laureth-9.[33] In a 3-patch application test using 10 subjects, undiluted or 25% aq. $C_{14-15}AE_7$ was applied under occlusive patches for 4 h on 3 alternate days. Slight to negligible irritation was observed. In a 24 h occlusive patch test with 8 subjects, a 10% aq. solution of $C_{12-13}AE_{6.5}$ was slightly irritating.

A human repeat insult patch test (HRIPT) was completed with 51 subjects to determine the sensitization potential of aerosol cream preparations containing 10, 15, and 20% laureth-9.[43] During induction, occlusive patches were applied for 24 h to the anterolateral surface of the upper arm, 3 times/wk for 3 wks. Challenge patches were applied 16 days after removal of the last induction patch, and those patches were left in place for 24 h.

During induction, reactions were observed for all 3 preparations with patches 3-9. Most of the reactions were mild (1+). A 2+ reaction was recorded for some subjects after the third 20% formulation patch and after the sixth patch for all formulations. Following the ninth application, all formulations produced 1+ to 3+ reactions. This was interpreted as skin

fatigue. At challenge, 12% of the subjects had a mild reaction to the 10 and 15% formulations, while 18% had a mild reaction to the 20% solution. These numbers decreased to 4 and 6%, respectively, by day 3. None of the subjects had reactions that were indicative of sensitization.

HRIPTs were performed with test substances that were analogous to laureth-9.[33] In an HRIPT performed using 108 subjects, 24-h induction patches with 0.3 ml of 5, 10, or 25% aq. $C_{12-15}AE_7$ and $C_{12-15}AE_9$ were applied 3 times/wk for 9 wks. A 24-h challenge patch was applied after a 2-wk non-treatment period. During induction, patches with 25% of the test materials caused very slight primary skin irritation, with slight erythema seen in 6/108 subjects induced with 25% $C_{12-15}AE_7$ and in 15/108 subjects induced with 25% $C_{12-15}AE_9$. At induction with 5%, very slight erythema was seen in 1 and 5 subjects for $C_{12-15}AE_7$ and $C_{12-15}AE_9$, respectively. Upon challenge, there was no evidence of sensitization with either compound.

In the same HRIPT, induction patches containing 0.3 ml of 5 or 15% aq. $C_{12-13}AE_{6.5}$ and $C_{12-15}AE_{12}$ were applied to 12 subjects per test material. With both induction concentrations of $C_{12-15}AE_6$, 1 subject developed mild erythema. Erythema was not observed with $C_{12-15}AE_6$. Upon challenge, there was no evidence of sensitization with either test substance.

$C_{12-15}AE_{6.5}$ and $C_{12-15}AE_9$, using patches containing 1% aq. solution, were evaluated in another HRIPT witn 12 subjects following the same protocol. Very slight primary skin irritation was observed with $C_{12-13}AE_{6.5}$, with very slight erythema observed for one subject at 4 different readings. $C_{12-15}AE_9$ did not produce any irritant effects. Upon challenge, there was no evidence of sensitization with either compound.

A study was reported in which subjects wore patches containing 2.5% aq. $C_{14-15}AE_7$ (144 subjects) or $C_{12-13}AE_{6.5}$ (165 subjects) for up to 3 wks, with challenge following a 17 day non-treatment period. Skin hyperactivity was observed in one subject exposed to $C_{12-13}AE_{6.5}$.

Steareths

The effect of steareth-2, steareth-10 and steareth-21 was evaluated on normal and damaged skin.[65] The test compounds were applied at a concentration of 5% w/v in a water/mineral oil (50:50) mixture. Vehicle was used for the control. Fifty µl of each test compound and the control were applied to normal skin of the volar forearm of 20 subjects for 48 h. An aluminum chamber was used for application. Upon removal, the sites were washed. For the second part of the study, the skin of 27 subjects was irritated using sodium lauryl sulfate prior to application of the test material. The chambers were removed after 17 h, and the sites were washed. At 24 h after patch removal, the sites were examined for irritation based on the presence of erythema, the transepidermal water loss (TEWL; measured with an evaporimeter), and microvascular blood flow (measured with a laser Doppler flowmeter).

Erythema was similar between the control and the test sites for both normal and damaged skin. With normal skin, TEWL was statistically significantly increased for all three steareths as compared to the controls. Skin blood flow was similar. With irritated skin, TEWL was statistically significantly decreased with stearth-2 and steareth -21 when compared to controls. Again, skin blood flow was similar to control values.

PEG Methyl Ethers

The dermal irritation of PEG-3 methyl ether (purity not specified) was evaluated using groups of 20 subjects.[20] The test material, 0.03 ml,, was applied to the gauze center of a 3/8" x 1 ½" bandage and placed on the skin for 24 h. One h after removal, the procedure was repeated for 3 consecutive days. At 24 h,10 subjects had an erythema score of 1/4 and 3 subjects had a score of 2/4. By 72 h, 7 subjects had an erythema score of 1, and 13 subjects has an erythema score of 2. No edema was observed. The average total irritation score by 72 h was 1.65, and the test material was slightly irritating.

C12-13 Pareths

In an HRIPT, C12-13 pareth-7, tested at concentrations of 1, 5,and 15%, produced very slight irritation and was not a sensitizer.[46]

C12-15 Pareths

In an HRIPT, C12-15 pareth-7, tested at concentrations of 5, 15,and 25%, produced very slight irritation, and C12-15 pareth-9, tested at the same concentrations, produced very slight to mild irritation.[46] C12-15 Pareth-12 was very slightly (5%) or non-irritating (15%). None of the C12-15 pareths were sensitizers in human subjects.

Case Reports

Case reports are summarized in Table 8.[36,66-74] The majority of the reports are reactions to laureths, especially laureth-9. Reactions included, but were not limited to, eczema, contact dermatitis, and a pruritic rash.

SUMMARY

Laureth-4 and laureth-23 have previously been reviewed by the Cosmetic Ingredient Review (CIR) Expert Panel, and in 1983 it was concluded that both of these ingredients are safe as used as cosmetic ingredients. The laureths actually are alkyl PEG ethers - the reaction product of an alkyl alcohol, in this case lauryl alcohol, and one or more equivalents of ethylene oxide. In preparing the rereview document, it became obvious that a large number of ingredients included in the *International Cosmetic Ingredient Dictionary and Handbook* belong to this family, and should be included in this review. (See Table 1.)

Some of the alkyl PEG ethers, or at least portions of a specific family, have previously been reviewed by CIR. These ingredients are included in this assessment. Rather than summarize the data from the previous reports with the new data, all the data from previous reports are summarized in Table 2.

The ingredients in this report are comprised of alkyl PEG ethers with alkyl chain lengths ranging from 1 carbon to 22 carbons, and ethylene oxide repeat units numbering from 1 to 200. The number of ethylene oxide repeat units in each ingredient is an average (e.g. laureth-4 has an average number of ethylene oxide repeat units equal to four, but may include some laureth-5, laureth-3 etc.). There are also some ingredients in this report with known average distributions of alkyl chain length and degree of unsaturation (e.g. talloweth-4 ranges in alkyl chain length from 14 to 18 carbons, and in degrees of unsaturation from 0 to 3). Mixtures of the alkyl PEG ethers are also included. For example, the ceteareths are mixtures of 16 and 18 carbon chains and a variable PEG. Also included are unsaturated straight chain ingredients, branched compounds, PEG ethers of sterols, and dialkyl PEG ethers.

The ingredients included in this review would not be expected to have any meaningful ultraviolet absorption.

Alkyl PEG ethers are most commonly manufactured by alkaline catalysis, although acid catalysis is known. The initiation of the synthesis includes the addition of ethylene oxide to a dry solution of the appropriate alcohol, and the reaction propagates until the available ethylene oxide is consumed. Dioxane is often formed as a byproduct, and the cosmetics industry is aware of the possible presence of dioxane and the need for a purification step to remove it prior to blending into cosmetic ingredients. Formaldehyde, BHT, and/or butylated hydroxyanisole (BHA) are possible residual by-products from the manufacture of alkyl PEG ethers. The potential for methoxyethanol and methoxydiglycol to be present in PEG methyl ethers and methoxy PEGs exists.

The alkyl PEG ethers function primarily as surfactants. Generally, in each family, the lower chain length ingredients mostly function as surfactant – emulsifying agents. As the chain length increases, the ingredients function as surfactant

– solubilizing agents and/or surfactant – cleansing agents. A few of the ingredients have additional functions, and a very few do not function as surfactants at all.

The use of laureth-4 has more than doubled since 1981, with 441 uses reported recently, and the use of laureth-23 has come close to doubling, with 404 uses. The ingredients with the greatest frequency of use, according to VCRP data, are ceteareth-20, with 955 uses, laureth-7, with 932 uses, and steareth-21, with 891 uses. Many of the ingredients included in this review are used at concentrations of <5%. The ingredient with the highest concentration of use is C12-13 pareth-3, at 32% in a product that will be diluted and at 25% in dermal preparations. Laureth-4 and isoceteth-20 are used in leave-on products at concentrations up to 21%, and steareth-20 is used in leave-on products at up to 20%. The ingredients used at the highest concentration in formulations applied near the eye or that could possibly be ingested are, respectively, ceteth-9, which is used at 18% in an eyeliner, and ceteareth-10, which is used at 11% in a lipstick.

All of the alkyl PEG ethers named in this report are listed in the European Union inventory of cosmetic ingredients. Laureth-9 is not restricted, but a Scientific Committee on Consumer Products (SCCP) opinion paper does exist, stating that laureth-9 does not pose a risk when used at ≤3% in leave-on products and ≤4% in rinse-off products. Information used to reach that conclusion was on alcohol ethoxylates analogous to laureth-9, but each compound was not clearly defined. Therefore the tested products are as described in the SCCP paper – i.e., by the average alkyl chain length (C) and by the average alcohol ethoxylate number (AE), e.g. $C_{12-15}AE_7$.

In general, alkyl PEG ethers are readily absorbed through the skin of guinea pigs and rats and through the intestinal mucosa of rats. They are quickly eliminated from the body through the urine, feces, and expired air. In rats, compounds analogous to laureth-9 were rapidly absorbed and excreted in the urine after oral, intraperitoneal, or subcutaneous dosing. Two distinct polar metabolites were identified in the urine for each compound tested. The length of the alkyl chain appeared to have an effect on metabolism, with excretion of longer alkyl chains occurring at a higher proportion in expired air and less in the urine. Similar results were found following oral administration in humans. Again, the major route of excretion was the urine. The metabolic product of each compound was a defined function of carbon chain length. However, the longer carbon chain ethoxylates produced more metabolic CO_2 and less urinary elimination products. The degradation of ether linkage and oxidation of the alkyl chain to form lower molecular weight PEG-like compounds and carbon dioxide and water appeared to be the major degradation pathway of alcohol ethoxylates**.**

In dermal metabolism studies with hairless mice with 0.25% solutions in ethanol, the percutaneous absorption after 4 hours was 22.9% for laureth-1, 15.5% for laureth-3, 10.4% for laureth-6 and 2.1% for laureth-10. The absorbed laureths were rapidly metabolized to carbon dioxide. Compounds analogous to laureth-9 readily penetrated the skin of rats, and approximately 50% of the absorbed dose was excreted. Using human subjects, the majority of the dose could be wiped away from the test site after 8 h; less than 2% was found in the urine. With atopic patients, the calculated dermal absorption rate for laureth-9 was 0.0017% with diluted bath oil and 0.0035% with after-shower application. For PEG-3 methyl ether, however, *in vitro* absorption data indicated that it would not readily penetrate the skin. Some alkyl PEG ethers, such as ceteareths and oleths, have been reported to enhance the penetration of certain compounds through the skin.

Acute oral toxicity data were available for some of the laureths, PEG methyl ethers, and the C- pareth ingredients. C9-11 Pareth-8, C14-15 pareth-11, and C14-15 pareth-13 had the lowest LD_{50} values, which were 1 mg/kg in rats. Many of the LD_{50} values were in the range of 2300-3300 mg/kg, with some, such as C12-13 pareth-2, having a value >10,000 mg/kg. Dermally, the data available indicated the LD_{50} values for rats and rabbits were mostly >2000 mg/kg for these families of ingredients. Specifically for laureth-4, the dermal LD_{50} ranged from 0.93-1.78 ml/kg for rabbits, and the researchers indicat-

ed that, in rats, the potential for neurotoxicity was observed. In acute inhalation studies with PEG-3 methyl ether, an LC_{50} value was not established, as all animals survived exposure to 200 mg/l for 1 h and to concentrated vapors for 8 h.

In short-term oral studies, compounds analogous to laureth-9 had dietary NOAELs of 459- 519 mg/kg bw. Doses of ≥25 g/kg of an unspecified deceth to rabbits resulted in death. In a 14-day drinking water study, PEG-3 methyl ether was mildly to moderately toxic at 4 g/kg and severely toxic at ≥8 g/kg. For an unspecified oleth administered orally to rats, doses of ≥750 mg/kg resulted in either death or significant signs of toxicity, and 1 of 6 animals given 3000 mg/kg/day for 17 days was killed in moribund condition. However, at necropsy, the organs and tissues appeared normal. In short-term dermal studies, dosing with 495-1980 mg/kg/day undiluted laureth-4 under occlusion did not result in erythema or edema, and no toxicologically significant results were reported. For PEG-3 methyl ether, some erythema and edema were observed with occlusive applications of 1000 mg/kg/day using rats; however, one study using rats reported a NOAEL of 4000 mg/kg/day. Similar results were observed with PEG-7 methyl ether, in which ≤5000 mg/kg, unoccluded, produced slight to moderate erythema and desquamation in rats and a 50% solution applied unocclusively produced slight to moderate erythema and slight desquamation in rabbits. No results observed with any of the PEG methyl ethers were considered toxicologically significant.

In a subchronic feeding studies, compounds analogous to laureth-9 had NOAELs ranging from 50-785 mg/kg bw in feed. Decreases in body weight and increased relative liver, kidney, and heart to body weights were observed. In a 91-day drinking water study, PEG-3 methyl ether had a NOAEL of 400 mg/kd/day for liver effects. In this study, testicular effects were observed, but were attributed to contamination with 2-methoxyethanol. A dose of ≤10,000 ppm C14-15 pareth-7 produced some differences compared to controls in organ weights and clinical chemistry and hematology values, but since no microscopic lesions were observed, these were not considered toxicologically significant. In a subchronic dermal study, moderate localized erythema was observed at all doses levels in a 13-wk study of 2.5% aq. $C_{14-15}AE_7$ in rabbits. For PEG-3 methyl ether, the dermal dose NOEL was 4000 mg/kg/day. The dermal responses observed in a 13 wk studies involving application of ≤25% aq. C9-11 pareth-6 to rats (epidermal thickening with hyperkeratosis) or a 0.5% solution of an unspecified talloweth to rabbits (slight irritation, moderate epidermal hyperplasia, hyperkeratosis, and inflammatory infiltrates), were not considered toxicologically significant.

In 2-yr feeding studies with compounds analogous to laureth-9, reduced feed consumption, decreased body weights, increased relative organ to body weights were observed. The NOAEL ranged from 50-162 mg/kg bw/day.

Using rabbits, undiluted laureth-9 produced moderate irritation at abraded sites, while 10 and 20% dilutions caused slight irritation at intact and abraded sites at 24 h. The dermal irritation potentials of several compounds that were analogous to laureth-9 were determined. Under semi-occlusive conditions with a 4 h application $C_{14-15}AE_7$, 0.5 ml at 10, 25, or 100%, was not irritating to rabbit skin. Following a 4 h occlusive application to rabbit skin, undiluted $C_{12-14}AE_{10}$ and undiluted $C_{13}AE_6$ were moderately irritating, and undiluted $C_{13}AE_{6.5}$ and undiluted $C_{12-14}AE_6$ were severely irritating. A 24 h occlusive application of $C_{14-15}AE_7$ was severely irritating to rabbit skin. A contraceptive aerosol formulation containing 20% laureth-9 was mildly irritating in a Draize test. In a mixture containing an unspecified laureth, the laureth was considered to be strong irritant to rabbit skin. Non-occlusive applications of PEG-3 methyl ether caused minimal irritation to rabbit skin. Undiluted C9-11, C12-13, C12-15, and C14-15 pareths were moderately to severely irritating to rabbit skin in Draize studies, with the exception of C14-15 pareth-18, which was mildly irritating. Dilutions of these ingredients were also tested, and, generally, 0.1 and 1% dilutions were non- to mildly irritating, while 10% dilutions ranged from slightly to, mostly, moderately irritating.

The sensitization potential of a number of alkyl PEG ethers was evaluated using guinea pigs. Laureths-5 and -9, compounds analogous to laureth-9, C9-11 pareth-3, -5, -6, -8, C12-13 pareth-2, -3, and -7, C12-15 pareth-3, -7, and -9, and C14-15 pareth-7, -11, -13,and -18 were not sensitizers using guinea pigs.

A 5% aq. solution of laureth-9 was not irritating to rabbit eyes. Compounds analogous to laureth-9 were moderately to severely irritating when instilled into rabbit eyes, and a 10% solution was moderately irritating. Dilution of these compounds reduced irritancy, and 0.1-1.0% solutions were non-irritating to rabbit eyes. At varying concentrations, PEG-3 methyl ether was slightly irritating to rabbit eyes. Undiluted C9-11, C12-13, C12-15, and C14-15 pareths were moderately to extremely irritating in Draize tests using unrinsed rabbit eyes, except for C14-15 pareth-18, which was minimally to mildly irritating. Rinsing reduced irritation in some cases but not all. At concentrations of 0.1-1%, these ingredients were non- to mildly irritating, while at 10%, they were moderately to severely irritating in some cases and practically non- to mildly irritating in others. A 5% solution of Oleth-20 produced mild, transient conjunctival redness and chemosis in rabbit eyes.

Laureth-9, 1%, caused severe damage to the nasal mucosa of rats. Regeneration of the epithelium started by day 3. As a 15% aq. solution, laureth-9 was not an irritant to the vaginal mucosa of dogs.

In a two-generation reproductive study, dermal administration of ≤25% C9-11 pareth-6 did not have a toxicologically significant effect on dams or offspring. In two-generation oral reproductive studies with dietary administration of compounds analogous to laureth-9, the NOAEL for reproductive toxicity was >250 mg/kg bw/day, and the NOAELs for maternal and developmental toxicity was 50 mg/kg bw/day. Dosing with ≤1000 mg/kg PEG-3 methyl ether did not result in any treatment-related reproductive effects in rats. A dose of 3000 mg/kg PEG-3 methyl ether did result in increased length of gestation and increased maternal kidney weights. In a study in which gravid rats were dosed with ≤5000 mg/kg PEG-3 methyl ether on days 6-15 of gestation, the maternal and developmental NOELs for rats were 625 mg/kg/day, and the NOAEL for maternal toxicity was 1250 mg/kg/day. For rabbits given ≤1500 mg/kg PEG-3 methyl ether on days 6-18 of gestation, clinical signs of toxicity and mortality were statistically significantly increased for the high dose group. The maternal and developmental NOELs for rabbits were 250 and 1000 mg/kg/day PEG-3 methyl ether, respectively. The NOAEL for maternal toxicity was 500 mg/kg/day, and the presumed NOAEL for developmental toxicity was 1500 mg/kg/day. In a test for developmental neurotoxicity, no neurotoxic effects attributable to PEG-3 methyl ether were identified.

An unspecified laureth was not mutagenic or genotoxic in an Ames test, transformation assay, or mouse lymphoma assay, and it did not induce sister chromatid exchanges or chromosomal aberrations in Chinese hamster ovary cells. Compounds analogous to laureth-9 were not mutagenic in a Ames test or clastogenic in *in vitro* or *in vivo* chromosomal aberration studies. PEG-3 methyl ether was not mutagenic or gentoxic in an Ames test, forward mutation assay, or *in* vivo mouse micronucleus test. PEG-7 methyl ether and C9-11 pareth-6 were not mutagenic in Ames tests.

Compounds that are analogous to laureth-9 were not carcinogenic in feeding studies in which rats were given up to 1% in the diet for 2 yrs.

In a retrospective clinical study, only 0.97% of patients had a weakly positive and 0.25% of patients had a strongly positive reaction to 0.5% laureth-9, and only 1.77 and 0.34% had weakly and strongly positive allergic contact reactions, respectively, to 3% laureth-9. Undiluted and 25% aq. $C_{14-15}AE_7$ produced negligible to slight irritation in an occlusive 3-patch application test, and a 10% aq. solution of $C_{12-13}AE_{6.5}$ was slightly irritating when applied under an occlusive patch for 24 h. In a human repeat insult patch test (HRIPT) of formulations containing laureth-9, 12 % of subjects challenged with 10 and 15% formulations and 18% of patients challenged with formulations containing 20% laureth-9 had mild reactions. Test compounds analogous to laureth-9, evaluated in HRIPTs at concentrations of 1-25%, were not sensitizers. In HRIPTs to determine the sensitization potential of 1-15% C12-13 pareth-7 and 5-25% C12-15 pareth-7, slight or mild irritation was

observed, but the ingredients were not sensitizers to human subjects. The clinical effect of steareth-2, -10, and -21 was evaluated on normal and damaged skin. The steareths did not have an effect on dermal blood flow with either normal or damaged skin, but transepidermal water loss of damaged skin was decreased with steareth-2 and steareth-21. PEG-3 methyl ether was slightly irritating in a clinical study.

A number of case studies, primarily with laureths, particularly laureth-9, have been reported. Reactions included, but were not limited to, eczema, contact dermatitis, and a pruritic rash.

DISCUSSION

This report was initiated as a re-review of laureth-4 and laureth-23. Upon review, it was discovered there is a large number of ingredients that are very similar to one another – structurally, functionally, and toxicologically. Fundamentally, all simple alkyl PEG ethers are the reaction products of alkyl alcohols and one or more equivalents of ethylene oxide. In the past, the Panel has reviewed a number of the alkyl PEG ethers as individual groups, i.e. Ceteareths, Ceteths, Laneths, Oleths, and Steareths, and in this report, the Panel has relied to a great extent on data from these past reports. Based on the fundamental similarities between these ingredients, data available for any one ingredient or ingredient group may be extrapolated to, or in current terms, read across, to the others.

Some of the past assessments of ingredients that included a PEG moiety stated that the ingredient should not be used on damaged skin. Since an amended conclusion has been issued for the PEGs, that caveat is no longer necessary.

A concern was expressed regarding the extent of dermal absorption for certain long-chain, branched alkyl PEG ethers because of uncertainty in bio-handling of branched alkyl chains. The prevailing Panel view was that because dermal penetration of long chain alcohols is likely to be low, and the dermal penetration for alkyl PEG ethers is likely to be even lower, inferring toxicity characteristics from ingredients where toxicity data were available was appropriate.

The potential adverse effects of inhaled aerosols depend on the specific chemical species, the concentration and the duration of the exposure and their site of deposition within the respiratory system. In practice, aerosols should have at least 99% of their particle diameters in the 10 – 110 µm range and the mean particle diameter in a typical aerosol spray has been reported as ~38 µm. Particles with an aerodynamic diameter of $\leq$ 10 µm are respirable. In the absences of inhalation toxicity data, the panel determined that alkyl PEG ethers can be used safely in hair sprays, because the product size is not respirable.

Also of concern to the Expert Panel was the possible presence of 1,4-dioxane, ethylene oxide, methoxyethanol, and methoxydiglycol impurities. The Panel stressed that the cosmetics industry should continue to use the necessary procedures to remove 1,4-dioxane and ethylene oxide impurities from the ingredients before blending them into cosmetic formulations. Since methoxy PEGs are defined as having an average number of ethylene oxide units, they have the potential of containing methoxyethanol and methoxydiglycol. Cosmetic preparations should not contain these impurities. The Panel has also stated that impurities or residual by-products that may be present, such as formaldehyde, BHT, or BHA, should only be present at concentrations allowed by the Panel in past assessments.

The Panel was also concerned with the dangers inherent in using animal-derived ingredients, namely the transmission of infectious agents. The CIR Expert Panel stressed that any animal-derived ingredient must be free of detectible pathogenic viruses or infectious agents (e.g. Bovine Spongiform Encephalopathy (BSE)). Suppliers and users of these ingredients must accept responsibility for assuring that these ingredients are risk-free. Tests to assure the absence of a pathogenic agent in the ingredients, or controls to assure derivation from pathogen-free sources are two approaches that should be considered.

The CIR accepts the FDA determination, that, to assure the absence of a pathogenic agent, hydrogenated talloweth-12, hydrogenated talloweth-25, PEG-4 ditallow ether, talloweth-4, talloweth-5, talloweth-6, and talloweth-7 must be made from tallow containing a maximum level of insoluble impurities of 0.15% in weight.

The Expert Panel recognized that some of these ingredients can enhance the penetration of other ingredients through the skin. The Panel cautioned that care should be taken in formulating cosmetic products that may contain these ingredients in combination with any ingredients whose safety was based on their lack of dermal absorption data, or when dermal absorption was a concern.

The Expert Panel was also concerned that the potential exists for dermal irritation with the use of products formulated using some of the alkyl PEG ethers. The Expert Panel specified that products must be formulated to be non-irritating.

Finally, this assessment is intended to address future cosmetic use of alkyl PEG ethers that vary from those in this assessment only in the number of ethylene glycol repeat units. The Expert Panel considers that the available data would extend to additional alkyl PEG ethers that could be used in cosmetics in the future.

CONCLUSION

The CIR Expert Panel concluded that the alkyl PEG ethers, listed below, are safe in the present practices of use and concentration described in this safety assessment when formulated to be non-irritating. Were ingredients in this group not in current use to be used in the future, the expectation is that they would be used in product categories and at concentrations comparable to others in this group. This assessment is also intended to address future alkyl PEG ether cosmetic ingredients that vary from those ingredients recited herein only by the number of ethylene glycol repeat units. The ingredients reviewed in this safety assessment are:

Arachideth-20
Beheneth-2
Beheneth-5
Beheneth-10
Beheneth-15
Beheneth-20
Beheneth-25
Beheneth-30
C9-11 Pareth-3
C9-11 Pareth-4
C9-11 Pareth-6
C9-11-Pareth-8
C9-15 Pareth-8
C10-16 Pareth-1
C10-16 Pareth-2
C11-13 Pareth-6
C11-13 Pareth-9
C11-13 Pareth-10
C11-15 Pareth-3
C11-15 Pareth-5
C11-15 Pareth-7
C11-15 Pareth-9
C11-15 Pareth-12
C11-15 Pareth-15
C11-15 Pareth-20
C11-15 Pareth-30
C11-15 Pareth-40
C11-21-Pareth-3
C11-21-Pareth-10
C12-13 Pareth-1
C12-13 Pareth-2
C12-13 Pareth-3
C12-13 Pareth-4
C12-13 Pareth-5
C12-13 Pareth-6
C12-13 Pareth-7
C12-13 Pareth-9
C12-13 Pareth-10
C12-13 Pareth-15
C12-13 Pareth-23
C12-14 Pareth-3
C12-14 Pareth-5
C12-14 Pareth-7
C12-14 Pareth-9
C12-14 Pareth-12
C12-15 Pareth-2
C12-15 Pareth-3
C12-15 Pareth-4
C12-15 Pareth-5
C12-15 Pareth-7
C12-15 Pareth-9
C12-15 Pareth-10
C12-15 Pareth-11
C12-15 Pareth-12
C12-16 Pareth-5
C12-16 Pareth-7
C12-16 Pareth-9
C13-15 Pareth-21
C14-15 Pareth-4
C14-15 Pareth-7
C14-15 Pareth-8
C14-15 Pareth-11
C14-15 Pareth-12
C14-15 Pareth-13
C20-22 Pareth-30
C20-40 Pareth-3
C20-40 Pareth-10
C20-40 Pareth-24
C20-40 Pareth-40
C20-40 Pareth-95
C22-24 Pareth-33
C30-50 Pareth-3
C30-50 Pareth-10
C30-50 Pareth-40
C40-60 Pareth-3
C40-60 Pareth-10
C11-15 Sec-Pareth-12
C12-14 Sec-Pareth-3
C12-14 Sec-Pareth-5
C12-14 Sec-Pareth-7
C12-14 Sec-Pareth-8
C12-14 Sec-Pareth-9
C12-14 Sec-Pareth-12
C12-14 Sec-Pareth-15
C12-14 Sec-Pareth-20
C12-14 Sec-Pareth-30
C12-14 Sec-Pareth-40
C12-14 Sec-Pareth-50
Capryleth-4
Capryleth-5

Ceteareth-2
Ceteareth-3
Ceteareth-4
Ceteareth-5
Ceteareth-6
Ceteareth-7
Ceteareth-8
Ceteareth-9
Ceteareth-10
Ceteareth-11
Ceteareth-12
Ceteareth-13
Ceteareth-14
Ceteareth-15
Ceteareth-16
Ceteareth-17
Ceteareth-18
Ceteareth-20
Ceteareth-22
Ceteareth-23
Ceteareth-24
Ceteareth-25
Ceteareth-27
Ceteareth-28
Ceteareth-29
Ceteareth-30
Ceteareth-33
Ceteareth-34
Ceteareth-40
Ceteareth-50
Ceteareth-55
Ceteareth-60
Ceteareth-80
Ceteareth-100
Ceteth-1
Ceteth-2
Ceteth-3
Ceteth-4
Ceteth-5
Ceteth-6
Ceteth-7
Ceteth-10
Ceteth-12
Ceteth-13
Ceteth-14
Ceteth-15
Ceteth-16
Ceteth-17
Ceteth-18
Ceteth-20
Ceteth-23
Ceteth-24
Ceteth-25
Ceteth-30
Ceteth-40
Ceteth-45
Ceteth-150
Cetoleth-2
Cetoleth-4
Cetoleth-5
Cetoleth-6
Cetoleth-10
Cetoleth-11
Cetoleth-15
Cetoleth-18
Cetoleth-20
Cetoleth-22
Cetoleth-24
Cetoleth-25
Cetoleth-30
Coceth-3
Coceth-5
Coceth-6
Coceth-7
Coceth-8
Coceth-10
Coceth-20
Coceth-25
Deceth-3
Deceth-4
Deceth-5
Deceth-6
Deceth-7
Deceth-8
Deceth-9
Deceth-10
Decyltetradeceth-5
Decyltetradeceth-10
Decyltetradeceth-15
Decyltetradeceth-20
Decyltetradeceth-25
Decyltetradeceth-30
Hexyldeceth-2
Hexyldeceth-20
Hydrogenated Dimer Dilinoleth-20
Hydrogenated Dimer Dilinoleth-30
Hydrogenated Dimer Dilinoleth-40
Hydrogenated Dimer Dilinoleth-60
Hydrogenated Dimer Dilinoleth-80
Hydrogenated Laneth-5
Hydrogenated Laneth-20
Hydrogenated Laneth-25
Hydrogenated Talloweth-12
Hydrogenated Talloweth-25
Isoceteth-5
Isoceteth-7
Isoceteth-10
Isoceteth-12
Isoceteth-15
Isoceteth-20
Isoceteth-25
Isoceteth-30
Isodeceth-4
Isodeceth-5
Isodeceth-6
Isolaureth-3
Isolaureth-6
Isolaureth-10
Isomyreth-3
Isomyreth-9
Isosteareth-2
Isosteareth-3
Isosteareth-5
Isosteareth-8
Isosteareth-10
Isosteareth-12
Isosteareth-15
Isosteareth-16
Isosteareth-20
Isosteareth-22
Isosteareth-25
Isosteareth-50
Laneth-5
Laneth-10
Laneth-15
Laneth-16
Laneth-20
Laneth-25
Laneth-40
Laneth-50
Laneth-60
Laneth-75
Laureth-1
Laureth-2
Laureth-3
Laureth-4
Laureth-5
Laureth-6
Laureth-7
Laureth-8
Laureth-9
Laureth-10
Laureth-11
Laureth-12
Laureth-13
Laureth-14
Laureth-15
Laureth-16
Laureth-20
Laureth-21
Laureth-23
Laureth-25
Laureth-30
Laureth-38
Laureth-40
Laureth-50
Methoxy PEG-7
Methoxy PEG-10
Methoxy PEG-16
Methoxy PEG-25
Methoxy PEG-40
Methoxy PEG-100

Myreth-2
Myreth-3
Myreth-4
Myreth-5
Myreth-10
Noneth-8
Octyldodeceth-2
Octyldodeceth-5
Octyldodeceth-10
Octyldodeceth-16
Octyldodeceth-20
Octyldodeceth-25
Octyldodeceth-30
Oleth-2
Oleth-3
Oleth-4
Oleth-5
Oleth-6
Oleth-7
Oleth-8
Oleth-9
Oleth-10
Oleth-11
Oleth-12
Oleth-15
Oleth-16
Oleth-20
Oleth-23
Oleth-24
Oleth-25
Oleth-30
Oleth-35
Oleth-40
Oleth-44
Oleth-45
Oleth-50
Oleth-82
Oleth-100
Oleth-106
Palmeth-2
PEG-16
Cetyl/Oleyl/Stearyl/Lanolin Alcohol Ether
PEG-Cetyl Stearyl Diether
PEG-4 Distearyl Ether
PEG-4 Ditallow Ether
PEG-15 Jojoba Alcohol
PEG-26 Jojoba Alcohol
PEG-40 Jojoba Alcohol
PEG-3 Methyl Ether
PEG-4 Methyl Ether
PEG-6 Methyl Ether
PEG-7 Methyl Ether
PEG-7 Propylheptyl Ether
PEG-8 Propylheptyl Ether
Steareth-1
Steareth-2
Steareth-3
Steareth-4
Steareth-5
Steareth-6
Steareth-7
Steareth-8
Steareth-10
Steareth-11
Steareth-13
Steareth-14
Steareth-15
Steareth-16
Steareth-20
Steareth-21
Steareth-25
Steareth-27
Steareth-30
Steareth-40
Steareth-50
Steareth-80
Steareth-100
Steareth-200
Steareth-60 Cetyl Ether
Talloweth-4
Talloweth-5
Talloweth-6
Talloweth-7
Talloweth-18
Trideceth-2
Trideceth-3
Trideceth-4
Trideceth-5
Trideceth-6
Trideceth-7
Trideceth-8
Trideceth-9
Trideceth-10
Trideceth-11
Trideceth-12
Trideceth-15
Trideceth-18
Trideceth-20
Trideceth-21
Trideceth-50
Undeceth-3
Undeceth-5
Undeceth-7
Undeceth-8
Undeceth-9
Undeceth-11
Undeceth-40
Undecyleneth-6

TABLES

Table 1. Alkyl PEG Ethers group

Alkyl PEG Ethers		
Laureth-4* (CAS Nos. 9002-92-0* 68439-50-9; 5274-68-0)	Ceteth-13 (CAS No. 9004-95-9)	Steareth-21 (CAS No. 9005-00-9)
Laureth-23* (CAS No. 9002-92-0)	Ceteth-14* (CAS No. 9004-95-9)	Steareth-25 (CAS No. 9005-00-9)
Laureth-1 (CAS Nos. 9002-92-0; 4536-30-5)	Ceteth-15* (CAS No. 9004-95-9)	Steareth-27 (CAS No. 9005-00-9)
Laureth-2 (CAS Nos. 9002-92-0; 3055-93-4)	Ceteth-16* (CAS No. 9004-95-9)	Steareth-30 (CAS No. 9005-00-9)
Laureth-3 (CAS Nos. 9002-92-0; 3055-94-5)	Ceteth-17 (CAS No. 9004-95-9)	Steareth-40 (CAS No. 9005-00-9)
Laureth-5 (CAS Nos. 9002-92-0; 3055-95-6)	Ceteth-18 (CAS No. 9004-95-9)	Steareth-50 (CAS No. 9005-00-9)
Laureth-6 (CAS Nos. 9002-92-0; 3055-96-7)	Ceteth-20* (CAS No. 9004-95-9)	Steareth-80 (CAS No. 9005-00-9)
Laureth-7 (CAS Nos. 9002-92-0; 3055-97-8)	Ceteth-23 (CAS No. 9004-95-9)	Steareth-100 (CAS No. 9005-00-9)
Laureth-8 (CAS Nos. 9002-92-0; 3055-98-8)	Ceteth-24* (CAS No. 9004-95-9)	Steareth-200 (CAS No. 9005-00-9)
Laureth-9 (CAS Nos. 9002-92-0; 3055-99-0)	Ceteth-25* (CAS No. 9004-95-9)	Trideceth-2 (CAS No. 24938-91-8)
Laureth-10 (CAS Nos. 9002-92-0; 68002-97-1; 6540-99-4)	Ceteth-30* (CAS No. 9004-95-9)	Trideceth-3 (CAS No. 24938-91-8; 4403-12-7)
Laureth-11 (CAS Nos. 9002-92-0; 68002-97-1)	Ceteth-40 (CAS No. 9004-95-9)	Trideceth-4
Laureth-12 (CAS Nos. (CAS Nos. 9002-92-0; 68002-97-1)	Ceteth-45* (CAS No. 9004-95-9)	Trideceth-5 (CAS No. 24938-91-8)
Laureth-13 (CAS Nos. 9002-92-0; 68002-97-1)	Ceteth-150 (CAS No. 9004-95-9)	Trideceth-6 (CAS No. 24938-91-8)
Laureth-14 (CAS Nos. 9002-92-0; 68002-97-1)	Deceth-3 (CAS No. 26138-52-8)	Trideceth-7 (CAS No. 24938-91-8)
Laureth-15 (CAS Nos. 9002-92-0; 68002-97-1)	Deceth-4 (CAS No. 26183-52-8; 5703-94-6)	Trideceth-8 (CAS No. 24938-91-8)
Laureth-16 (CAS Nos. 9002-92-0; 68002-97-1)	Deceth-5 (CAS No. 26183-52-8)	Trideceth-9 (CAS No. 24938-91-8; 69011-36-5)
Laureth-20 (CAS No. 9002-92-0)	Deceth-6 (CAS No. 26183-52-8)	Trideceth-10 (CAS No. 24938-91-8)
Laureth-21 (CAS No. 9002-92-0)	Deceth-7 (CAS No. 26183-52-8)	Trideceth-11 (CAS No. 24938-91-8)
Laureth-25 (CAS No. 9002-92-0)	Deceth-8 (CAS No. 26183-52-8)	Trideceth-12 (CAS No. 24938-91-8; 78330-21-9)
Laureth-30 (CAS No. 9002-92-0)	Deceth-9 (CAS No. 26183-52-8)	Trideceth-15 (CAS No. 24938-91-8)
Laureth-38 (CAS No. 9002-92-0)	Deceth-10 (CAS No. 26183-52-8)	Trideceth-18 (CAS No. 24938-91-8)
Laureth-40 (CAS No. 9002-92-0)	Myreth-2 (CAS No. 27306-79-2)	Trideceth-20 (CAS No. 24938-91-8)
Laureth-50**	Myreth-3 (CAS No. 27306-79-2; 26826-30-2)	Trideceth-21 (CAS No. 24938-91-8)
Arachideth-20	Myreth-4 (CAS No. 27306-79-2; 39034-24-7)	Trideceth-50 (CAS No. 24938-91-8)
Beheneth-2	Myreth-5 (CAS No. 27306-79-2; 92669-010-7)	Undeceth-3 (CAS No. 34398-01-1)
Beheneth-5	Myreth-10 (CAS No. 27306-79-2)	Undeceth-5 (CAS No. 34398-01-1)
Beheneth-10	Noneth-8	Undeceth-7 (CAS No. 34398-01-1)
Beheneth-15	Steareth-1 (CAS No. 9005-00-9)	Undeceth-8 (CAS No. 34398-01-1)
Beheneth-20	Steareth-2* (CAS No. 9005-00-9; 16057-43-5)	Undeceth-9 (CAS No. 34398-01-1)
Beheneth-25	Steareth-3 (CAS No. 9005-00-9; 4439-32-1)	Undeceth-11 (CAS No. 34398-01-1)
Beheneth-30	Steareth-4* (CAS No. 9005-00-9; 59970-10-4)	Undeceth-40 (CAS No. 34398-01-1; 127036-24-2)
Capryleth-4	Steareth-5 (CAS No. 9005-00-9; 71093-13-5)	PEG-3 Methyl Ether (CAS No. 9004-74-4; 112-35-6)
Capryleth-5	Steareth-6 (CAS No. 9005-00-9; 2420-29-3)	PEG-4 Methyl Ether (CAS No. 9004-74-4)
Ceteth-1* (CAS No. 9004-95-9; 2136-71-2)	Steareth-7 (CAS No. 9005-00-9; 66146-84-7)	PEG-6 Methyl Ether (CAS No. 9004-74-4)
Ceteth-2* (CAS No. 9004-95-9; 5274-61-3)	Steareth-8 (CAS No. 9005-00-9)	PEG-7 Methyl Ether (CAS No. 9004-74-4)
Ceteth-3* (CAS No. 9004-95-9; 4484-59-7)	Steareth-10* (CAS No. 9005-00-9; 13149-86-5)	Methoxy PEG-7 (CAS No. 9004-74-4)
Ceteth-4* (CAS No. 9004-95-9; 5274-63-5)	Steareth-11* (CAS No. 9005-00-9)	Methoxy PEG-10 (CAS No. 9004-74-4)
Ceteth-5* (CAS No. 9004-95-9; 4478-97-1)	Steareth-13* (CAS No. 9005-00-9)	Methoxy PEG-16 (CAS No. 9004-74-4)
Ceteth-6* (CAS No. 9004-95-9; 5168-91-2)	Steareth-14 (CAS No. 9005-00-9)	Methoxy PEG-25 (CAS No. 9004-74-4)
Ceteth-7 (CAS No. 9004-95-9)	Steareth-15* (CAS No. 9005-00-9)	Methoxy PEG-40 (CAS No. 9004-74-4)
Ceteth-10* (CAS No. 9004-95-9; 14529-40-9)	Steareth-16 (CAS No. 9005-00-9)	Methoxy PEG-100 (CAS No. 9004-74-4)
Ceteth-12* (CAS No. 9004-95-9; 94159-75-8)	Steareth-20* (CAS No. 9005-00-9)	

Table 1. Alkyl PEG Ethers Ingredient Group (continued)

Alkyl PEG Ether Mixtures		
Ceteareth-2* (CAS No. 68439-49-6)	C9-11 Pareth-4 (CAS No. 68439-46-3)	C12-14 Pareth-12 (CAS No. 68439-50-9)
Ceteareth-3* (CAS No. 68439-49-6)	C9-11-Pareth-6 (CAS No. 68439-46-3)	C12-15 Pareth-2 (CAS No. 68131-39-5)
Ceteareth-4* (CAS No. 68439-49-6)	C9-11 Pareth-8 (CAS No. 68439-46-3)	C12-15 Pareth-3 (CAS No. 68131-39-5)
Ceteareth-5* (CAS No. 68439-49-6)	C9-15 Pareth-8 (CAS No. 157627-88-8)	C12-15 Pareth-4 (CAS No. 68131-39-5)
Ceteareth-6* (CAS No. 68439-49-6)	C10-16 Pareth-1 (CAS No. 68002-97-1)	C12-15 Pareth-5 (CAS No. 68131-39-5)
Ceteareth-7* (CAS No. 68439-49-6)	C10-16 Pareth-2 (CAS No. 68002-97-1)	C12-15 Pareth-7 (CAS No. 68131-39-5)
Ceteareth-8* (CAS No. 68439-49-6)	C11-13 Pareth-6 (CAS No. 308060-94-8)	C12-15 Pareth-9 (CAS No. 68131-39-5)
Ceteareth-9* (CAS No. 68439-49-6)	C11-13 Pareth-9 (CAS No. 308060-94-8)	C12-15 Pareth-10 (CAS No. 68131-39-5)
Ceteareth-10* (CAS No. 68439-49-6)	C11-13 Pareth-10 (CAS No. 308060-94-8)	C12-15 Pareth-11 (CAS No. 68131-39-5)
Ceteareth-11* (CAS No. 68439-49-6)	C11-15 Pareth-3 (CAS No. 68131-40-8)	C12-15 Pareth-12 (CAS No. 68131-39-5)
Ceteareth-12* (CAS No. 68439-49-6)	C11-15 Pareth-5 (CAS No. 68131-40-8)	C12-16 Pareth-5 (CAS No. 68551-12-2)
Ceteareth-13* (CAS No. 68439-49-6)	C11-15 Pareth-7 (CAS No. 68131-40-8)	C12-16 Pareth-7 (CAS No. 68551-12-2)
Ceteareth-14* (CAS No. 68439-49-6)	C11-15 Pareth-9 (CAS No. 68131-40-8)	C12-16 Pareth-9 (CAS No. 68551-12-2)
Ceteareth-15* (CAS No. 68439-49-6)	C11-15 Pareth-12 (CAS No. 68131-40-8)	C13-15 Pareth-21 (CAS No. 64425-86-1)
Ceteareth-16* (CAS No. 68439-49-6)	C11-15 Pareth-15 (CAS No. 68131-40-8)	C14-15 Pareth-4 (CAS No. 68951-67-7)
Ceteareth-17* (CAS No. 68439-49-6)	C11-15 Pareth-20 (CAS No. 68131-40-8)	C14-15 Pareth-7 (CAS No. 68951-67-7)
Ceteareth-18* (CAS No. 68439-49-6)	C11-15 Pareth-30 (CAS No. 68131-40-8)	C14-15 Pareth-8 (CAS No. 68951-67-7)
Ceteareth-20* (CAS No. 68439-49-6)	C11-15 Pareth-40 (CAS No. 68131-40-8)	C14-15 Pareth-11 (CAS No. 68951-67-7)
Ceteareth-22* (CAS No. 68439-49-6)	C11-21-Pareth-3 (CAS No. 246538-82-9)	C14-15 Pareth-12 (CAS No. 68951-67-7)
Ceteareth-23* (CAS No. 68439-49-6)	C11-21-Pareth-10 (CAS No. 246538-82-9)	C14-15 Pareth-13 (CAS No. 68951-67-7)
Ceteareth-24* (CAS No. 68439-49-6)	C12-13 Pareth-1 (CAS No. 66455-14-9)	C20-22 Pareth-30
Ceteareth-25* (CAS No. 68439-49-6)	C12-13 Pareth-2 (CAS No. 66455-14-9)	C20-40 Pareth-3 (CAS No. 246538-83-0)
Ceteareth-27* (CAS No. 68439-49-6)	C12-13 Pareth-3 (CAS No. 66455-14-9)	C20-40 Pareth-10 (CAS No. 246538-83-0)
Ceteareth-28* (CAS No. 68439-49-6)	C12-13 Pareth-4 (CAS No. 66455-14-9)	C20-40 Pareth-24 (CAS No. 246538-83-0)
Ceteareth-29* (CAS No. 68439-49-6)	C12-13 Pareth-5 (CAS No. 66455-14-9)	C20-40 Pareth-40 (CAS No. 246538-83-0)
Ceteareth-30* (CAS No. 68439-49-6)	C12-13 Pareth-6 (CAS No. 66455-14-9)	C20-40 Pareth-95 (CAS No. 246538-83-0)
Ceteareth-33* (CAS No. 68439-49-6)	C12-13 Pareth-7 (CAS No. 66455-14-9)	C22-24 Pareth-33 (CAS No. 246538-84-1)
Ceteareth-34* (CAS No. 68439-49-6)	C12-13 Pareth-9 (CAS No. 66455-14-9)	C30-50 Pareth-3 (CAS No. 246538-85-2)
Ceteareth-40* (CAS No. 68439-49-6)	C12-13 Pareth-10 (CAS No. 66455-14-9)	C30-50 Pareth-10 (CAS No. 246538-85-2)
Ceteareth-50* (CAS No. 68439-49-6)	C12-13 Pareth-15 (CAS No. 66455-14-9)	C30-50 Pareth-40 (CAS No. 246538-85-2)
Ceteareth-55* (CAS No. 68439-49-6)	C12-13 Pareth-23 (CAS No. 66455-14-9)	C40-60 Pareth-3 (CAS No. 246538-86-3)
Ceteareth-60* (CAS No. 68439-49-6)	C12-14 Pareth-3 (CAS No. 68439-50-9)	C40-60 Pareth-10 (CAS No. 246538-86-3)
Ceteareth-80* (CAS No. 68439-49-6)	C12-14 Pareth-5 (CAS No. 68439-50-9)	Hydrogenated Talloweth-12
Ceteareth-100* (CAS No. 68439-49-6)	C12-14 Pareth-7 (CAS No. 68439-50-9)	Hydrogenated Talloweth-25
C9-11 Pareth-3 (CAS No. 68439-46-3)	C12-14 Pareth-9 (CAS No. 68439-50-9)	

Table 1. Alkyl PEG Ethers Ingredient Group (continued)

Partially Unsaturated Alkyl PEG Ethers		
Undecyleneth-6	Oleth-40* (CAS No. 9004-98-2)	
Oleth-2* (CAS No. 9004-98-2; 5274-65-7; 95287-03-9)	Oleth-44* (CAS No. 9004-98-2)	Cetoleth-30 (CAS No. 8065-81-4)
Oleth-3* (CAS No. 9004-98-2; 5274-66-8; 96459-08-4)	Oleth-45 (CAS No. 9004-98-2)	Coceth-3 (CAS No. 61791-13-7)
Oleth-4* (CAS No. 9004-98-2; 5353-26-4; 103622-85-1)	Oleth-50* (CAS No. 9004-98-2)	Coceth-5 (CAS No. 61791-13-7)
Oleth-5* (CAS No. 9004-98-2; 5353-27-5)	Oleth-82 (CAS No. 9004-98-2)	Coceth-6 (CAS No. 61791-13-7)
Oleth-6* (CAS No. 9004-98-2)	Oleth-100 (CAS No. 9004-98-2)	Coceth-7 (CAS No. 61791-13-7)
Oleth-7* (CAS No. 9004-98-2)	Oleth-106 (CAS No. 9004-98-2)	Coceth-8 (CAS No. 61791-13-7)
Oleth-8* (CAS No. 9004-98-2; 26996-03-2; 27040-03-5)	Ceteth-2 (CAS No. 8065-81-4)	Coceth-10 (CAS No. 61791-13-7)
Oleth-9* (CAS No. 9004-98-2)	Ceteth-4 (CAS No. 8065-81-4)	Coceth-20 (CAS No. 61791-13-7)
Oleth-10* (CAS No. 9004-98-2)	Ceteth-5 (CAS No. 8065-81-4)	Coceth-25 (CAS No. 61791-13-7)
Oleth-11* (CAS No. 9004-98-2)	Ceteth-6 (CAS No. 8065-81-4)	Palmeth-2
Oleth-12* (CAS No. 9004-98-2)	Ceteth-10 (CAS No. 8065-81-4)	Talloweth-4 (CAS No. 61791-28-4)
Oleth-15* (CAS No. 9004-98-2)	Ceteth-11 (CAS No. 8065-81-4)	Talloweth-5 (CAS No. 61791-28-4)
Oleth-16* (CAS No. 9004-98-2; 25190-05-0)	Ceteth-15 (CAS No. 8065-81-4)	Talloweth-6 (CAS No. 61791-28-4)
Oleth-20* (CAS No. 9004-98-2)	Ceteth-18 (CAS No. 8065-81-4)	Talloweth-7 (CAS No. 61791-28-4)
Oleth-23* (CAS No. 9004-98-2)	Ceteth-20 (CAS No. 8065-81-4)	Talloweth-18 (CAS No. 61791-28-4)
Oleth-24 (CAS No. 9004-98-2)	Ceteth-22 (CAS No. 8065-81-4)	PEG-15 Jojoba Alcohol
Oleth-25* (CAS No. 9004-98-2)	Ceteth-24 (CAS No. 8065-81-4)	PEG-26 Jojoba Alcohol
Oleth-30* (CAS No. 9004-98-2)	Ceteth-25 (CAS No. 8065-81-4)	PEG-40 Jojoba Alcohol
Oleth-35 (CAS No. 9004-98-2)		

Branched Alkyl PEG Ethers		
Isodeceth-4	Isosteareth-8 (CAS No. 52292-17-8)	C12-14 Sec-Pareth-40 (CAS No. 84133-50-6)
Isodeceth-5	Isosteareth-10 (CAS No. 52292-17-8)	C12-14 Sec-Pareth-50 (CAS No. 84133-50-6)
Isodeceth-6	Isosteareth-12 (CAS No. 52292-17-8)	PEG-7 Propylheptyl Ether
Isolaureth-3 (CAS No. 39365-90-7)	Isosteareth-15 (CAS No. 52292-17-8)	PEG-8 Propylheptyl Ether
Isolaureth-6 (CAS No. 39365-90-7)	Isosteareth-16 (CAS No. 52292-17-8)	Hexyldeceth-2 (CAS No. 52609-19-5)
Isolaureth-10 (CAS No. 39365-90-7)	Isosteareth-20 (CAS No. 52292-17-8)	Hexyldeceth-20 (CAS No. 52609-19-5)
Isomyreth-3	Isosteareth-22 (CAS No. 52292-17-8)	Octyldodeceth-2 (CAS No. 32128-65-7)
Isomyreth-9	Isosteareth-25 (CAS No. 52292-17-8)	Octyldodeceth-5 (CAS No. 32128-65-7)
Isoceteth-5 (CAS No. 69364-63-2)	Isosteareth-50 (CAS No. 52292-17-8)	Octyldodeceth-10 (CAS No. 32128-65-7)
Isoceteth-7 (CAS No. 69364-63-2)	C11-15 Sec-Pareth-12 (CAS No. 68131-40-8)	Octyldodeceth-16 (CAS No. 32128-65-7)
Isoceteth-10 (CAS No. 69364-63-2)	C12-14 Sec-Pareth-3 (CAS No. 84133-50-6)	Octyldodeceth-20 (CAS No. 32128-65-7)
Isoceteth-12 (CAS No. 69364-63-2)	C12-14 Sec-Pareth-5 (CAS No. 84133-50-6)	Octyldodeceth-25 (CAS No. 32128-65-7)
Isoceteth-15 (CAS No. 69364-63-2)	C12-14 Sec-Pareth-7 (CAS No. 84133-50-6)	Octyldodeceth-30 (CAS No. 32128-65-7)
Isoceteth-20 (CAS No. 69364-63-2)	C12-14 Sec-Pareth-8 (CAS No. 84133-50-6)	Decyltetradeceth-5
Isoceteth-25 (CAS No. 69364-63-2)	C12-14 Sec-Pareth-9 (CAS No. 84133-50-6)	Decyltetradeceth-10
Isoceteth-30 (CAS No. 69364-63-2)	C12-14 Sec-Pareth-12 (CAS No. 84133-50-6)	Decyltetradeceth-15
Isosteareth-2 (CAS No. 52292-17-8)	C12-14 Sec-Pareth-15 (CAS No. 84133-50-6)	Decyltetradeceth-20
Isosteareth-3 (CAS No. 52292-17-8)	C12-14 Sec-Pareth-20 (CAS No. 84133-50-6)	Decyltetradeceth-25
Isosteareth-5 (CAS No. 52292-17-8)	C12-14 Sec-Pareth-30 (CAS No. 84133-50-6)	Decyltetradeceth-30

Table 1. Alkyl PEG Ethers Ingredient Group (continued)

Sterol-Containing PEG Ethers		
Laneth-5* (CAS No. 61791-20-6)	Laneth-25* (CAS No. 61791-20-6)	Hydrogenated Laneth-5
Laneth-10 (CAS No. 61791-20-6)	Laneth-40 (CAS No. 61791-20-6)	Hydrogenated Laneth-20
Laneth-15 (CAS No. 61791-20-6)	Laneth-50 (CAS No. 61791-20-6)	Hydrogenated Laneth-25
Laneth-16* (CAS No. 61791-20-6)	Laneth-60 (CAS No. 61791-20-6)	
Laneth-20 (CAS No. 61791-20-6)	Laneth-75 (CAS No. 61791-20-6)	
Dialkyl PEG Ethers		
Hydrogenated Dimer Dilinoleth-20	Hydrogenated Dimer Dilinoleth-80	Steareth-60 Cetyl Ether (CAS No. 9005-00-9)
Hydrogenated Dimer Dilinoleth-30	PEG-4 Distearyl Ether	PEG-4 Ditallow Ether
Hydrogenated Dimer Dilinoleth-40	PEG-Cetyl Stearyl Diether	PEG-16 Cetyl/Oleyl/Stearyl/Lanolin Alcohol Ether
Hydrogenated Dimer Dilinoleth-60		

*ingredient has been reviewed previously

**if a CAS No. is not given, there was none found

Table 2a. Previously reviewed and component ingredients

Ingredient	Conclusion	Reference
PREVIOUSLY REVIEWED		
Ceteareth-2, -3, -4, -5, -6, -7, -8, -9, -10, -11, -12, -13, -14, -15, -16, -17, -18, -20, -22, -23, -24, -25, -27, -28, -29, -30, -33, -34, -40, -50, -55, -60, -80, -100	safe as used	2
Ceteth-1, -2, -3, -4, -5, -6, -10, -12, -14, -15, -16, -20, -24, -25, -30, -45	safe as used	3
Laneth-5, -16, -25	safe for topical application	5
Laureth-4, -23	safe as used	1
Oleth-2, -3, -4, -5, -6, -7, -8, -9, -10, -11, -12, -15, -16, -20, -23, -25, -30, -40, -44, -50	safe as used	4
Steareth-2, -4, -6, -7, -10, -11, -13, -15, -20	safe as used	6
COMPONENTS		
PEGs; 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, -160M, -180M and any PEG ≥ 4	safe as used	15
Behenyl Alcohol	safe as used	12
Cetearyl Alcohol	safe as used	12
Cetyl Alcohol	safe as used	12
Cholesterol	safe as used	11
Coconut Alcohol	safe as used	14
Isostearyl Alcohol	safe as used	12
Jojoba Alcohol	safe as used	13
Lanolin Alcohol	safe for topical application	9
Methyl Alcohol	safe as used to denature alcohol	16
Myristyl Alcohol	safe as used	12
Octyl Dodecanol	safe as used	10
Oleyl Alcohol	safe as used	10
Stearyl Alcohol	safe as used	10
Special Report on Ethylene Glycol and its Ethers	it was found that metabolites of ethylene glycol monoalkyl ethers are repro. and developmental toxins; in general, however, the metabolites of concern are not expected to be formed in cosmetic formulations that contain polymers of ethylene glycol. The toxicity of the metabolites is inversely proportional to the length of the alkyl chain; e.g., 2-butoxyethanol is not a reproductive toxicant	7

Table 2b. Summaries of information provided in previous reports

Ingredient	Parameter Evaluated	Outcome	Reference
		PREVIOUSLY REVEIWED INGREDIENTS	
Ceteareths	method of manufacture	surfactants prepared by ethoxylation of fatty alcohol mixtures with ethylene oxide	2
	animal toxicology	no data	
	dermal irritation/sensitization	formulation containing 10% ceteareth-15 was minimally irritating to rabbit skin	
	ocular irritation	ceteareth-15: 10%, not irritating	
	repro/developmental toxicity	considered unlikely to cause reproductive or teratogenic effects, based on chemical and structural characteristics	
	genotoxicity	no data	
	carcinogenicity	no data	
	clinical assessment of safety	ceteareth 15: formulations w/1.35-15%, essentially non- to non-irritating	
		ceteareth-15: formulation w/1.25%, not a sensitizer	
	important Discussion items	ceteareths, particularly ceteareth-20, enhance drug absorption; care should be taken when creating formulations, especially those for use on infant skin; ceteareth preparations should not contain 1,4-dioxane or ethylene oxide, which are possible oxidation products; in that ceteareths are PEG compounds, stated that ceteareths should not be used on damaged skin – no longer applicable due to new PEGs conclusion	
	Conclusion	safe as used	
Ceteths	method of manufacture	by the ethoxylation of cetyl alcohol with the ingredient's corresponding number of moles of ethylene oxide	3
	impurities	peroxides were found in ceteth-20; peroxide formation rate, when expressed in terms of peroxide number, was inversely proportional to the concentration of ceteth-20; in terms of absolute concentration of peroxides, peroxide content was proportional to PEG concentration	
	animal toxicology	oral LD_{50} (rats): ceteth-2, >25 g/kg; ceteth-10, 2.5-3.5 g/kg; ceteth-20	
		4-wk dermal: ceteth-2 (2.5%, rabbits; 3%, rats): no systemic toxicity, moderate erythema in rabbits	
	dermal irritation/sensitization	ceteth-2: 1 and 5% , erythema and edema, ≥10%, thickening of the skin; formulation w/2.5% , minimal irritation; ceteth-10: 1 and 5%, erythema and edema, ≥10%, thickening of the skin	
	ocular irritation	ceteth-2, formulation w/2.5%, not irritating	
	repro/developmental toxicity	considered unlikely to cause reproductive or teratogenic effects, based on chemical and structural characteristics	
	genotoxicity	Ceteth-20: enhanced transposition of Tn9 in E. coli	
	carcinogenicity	no data	
	clinical assessment of safety	no data	
	important Discussion items	should not contain 1,4-dioxane or ethylene oxide, which are possible oxidation products; addressed use in inhalation products	
	Conclusion	safe as used	
Laneths	method of manufacture	lanolin alcohol can be reacted with an appropriate molar concentration of ethylene oxide in an exothermic, addition reaction to generate the desired laneth; the lanolin alcohols are melted and then agitated in the presence of ethylene oxide gas at 130-180°C; sodium methoxide may be used as a catalyst in this process; the product is refined by bleaching with hydrogen peroxide followed by vacuum stripping and filtration	5
	animal toxicology	oral LD_{50} (rats); laneth-5, ≥25 ml/kg; laneth-16, 9.33-12.2 ml/kg, 2.15 g/kg; laneth-25, >3 g/kg	
	dermal irritation/sensitization	PIIs (max=8; rabbits):laneth-5, 0.5 (10%), 0.8-1.3 (100%); laneth-16, 1.0 (10%), 1-2.43 (100%); laneth-25, 0.04 (10%), 3.83 (100%)	
	ocular irritation	laneth-5: 10%, non-irritating; 100%, non- to minimally irritating; laneth-16: 100%, non- to minimally irritating; formulations w/35%, practically non- to minimally irritating; laneth-25: 100%, minimally irritating	
	repro/developmental toxicity	no data	
	genotoxicity	no data	
	carcinogenicity	no data	
	clinical assessment of safety	laneth-5; 50%, not an irritant, mild fatiguing agent; laneth-16, 50%, not an irritant, fatiguing agent; laneth-25, 50%, not an irritant	
		laneth-5; 50%, not a sensitizer; laneth-16, 50%, not a sensitizer; laneth-25, 50%, not a sensitizer	

Table 2b. Summaries of information provided in previous reports (continued)

Ingredient	Parameter Evaluated	Outcome	Reference
	important Discussion items	Discussion not included in report	
	Conclusion	safe for topical application	
Laureths	impurities/by-products of mfg	special grades of laureth-4may have butylated hydroxyanisole (BHA) (0.05%) and citric acid (0.01%) added; laureth-23 may have BHA (0.01%) or citric acid (0.005%) added; lauryl alcohol is a mixture of fatty alcohols containing 55%-64% dodecanol and 21%-28% tetradecanol with up to 13% hexadecanol, 5% decanol, 5% octadecanol, and 0.4% octanol; the laureths may contain unreacted ethylene oxide that is not completely purged from the system; a reaction product of ethoxylation, 1,4-dioxane, may also be present in trace amounts	1
	ADME	in general, alkyl PEG ethers are readily absorbed through the skin of guinea pigs and rats and through the intestinal mucosa of rats; they are quickly eliminated from the body through the urine, feces, and expired air	
	animal toxicology	acute oral: undiluted laureth-4, practically non-toxic (rats and mice); LD_{50}: laureth-23, 7.8-9.4 g/kg (rats) and 3.5-4 g/kg (mice); acute dermal LD_{50}: >no mortality w/formulations containing ≤17% laureth-4	
	dermal irritation/sensitization	laureth-4: 100% or formulation w/1.8%, not a primary skin irritant (rabbits)	
	ocular irritation	laureth-4: 100%, moderately irritating; 10 and 20%,minimally (unrinsed) to non-irritating (rinsed); formulation w/17%, irritation scores of 33/110 at 1 h and 5/110 at 24 h; laureth-23: 100%, slight conjunctival effect; formulation w/4%, mild transient conjunctivitis and iritis	
	repro/developmental toxicity	laureth-4: 6% in 52% ethanol and water, not teratogenic or embryotoxic (rats or rabbits), not a reproductive or fetal toxicant (rats)	
	genotoxicity	no data	
	carcinogenicity	no data	
	clinical assessment of safety	laureth-4: 100%, not an irritant; laureth-23: 100%,not an irritant	
		laureth-4: 100%, not a sensitizer; laureth-23, 25%, not a sensitizer	
		laureth-4: 6% in 52% ethanol, or formulation w/1.8%, not phototoxic; laureth-23: 25% or formulations w/0.899%, not phototoxic	
	important Discussion items	no relevant items identified	
	Conclusion	safe as used	
Oleths	method of manufacture	manufactured by the ethoxylation of oleyl alcohol with the ingredient's corresponding number of moles of ethylene oxide	4
	animal toxicology	oral LD_{50}: oleth-10, >5 g//kg (rats)	
		90-day feeding study: oleth-20 (rats), no systemic toxicology; oleth-20 (dogs), hepatic lesion suggestive of a toxic etiology, 1 dog fed 0.64%	
	dermal irritation/sensitization	oleth-10: 100%, occlusive, minimally irritating; oleth-20: 10%, closed patch, primary dermal irritant; 50%, open patch, minimally irritating	
	ocular irritation	oleth-10: 100%, moderate irritant; oleth-20: 70% active, moderate irritant; 50%: moderate irritant	
	repro/developmental toxicity	considered unlikely to cause reproductive or teratogenic effects, based on chemical and structural characteristics	
	genotoxicity	no data	
	carcinogenicity	no data	
	clinical assessment of safety	oleth-10: 21 day cumulative irritation study, formulation w/3%, cumulative irritant in 3/8 subjects	
	important Discussion items	oleths may increase permeability of the stratum corneum as demonstrated *in vitro;* should not contain 1,4-dioxane or ethylene oxide, which are possible oxidation products; addressed use in inhalation products	
	Conclusion	safe as used	
Steareths	method of manufacture	are prepared by reacting ethylene oxide with stearyl alcohol	6
	animal toxicology	oral LD50 (rats):steareth-2, 16 g/kg (unspecified concentration)), ≥21 g/kg (25% in corn oil or 40% in water); formulations with ≤ 2.75% steareth-2, >5 g/kg; steareth-10, 2.9 g/kg (unspecified concentration); steareth-20, ~1.9 g/kg (unspecified concentration), ~2.1 g/kg (25% in corn oil or distilled water); formulation containing 1.5% steareth-20, >10 ml/kg	
		3 mos dermal: formulation containing 4% steareth-20 (rabbits), no systemic toxicity, some dermal irritation	

Table 2b. Summaries of information provided in previous reports (continued)

Ingredient	Parameter Evaluated	Outcome	Reference
	dermal irritation/sensitization	steareth-2, ≤60% and in formulation w/≤2.75%, mildly irritating at most; steareth-10, 60%, mild irritant; steareth-20, 60%, mild irritant, in formulations w/≤5%, moderate irritant at most	
	ocular irritation	steareth-20: unspecified concentration, moderate irritant; 60%, minimal irritant	
	repro/developmental toxicity	no data	
	genotoxicity	no data	
	carcinogenicity	a structurally undefined polyoxyethylene alkyl ether was neither a carcinogen nor a tumor promoter in a mouse skin painting study	
	clinical assessment of safety	steareth-2: 60%, not a primary irritant, formulation w/0.6%, mild irritant; steareth-10 and steareth-20, 60%, not a primary irritant steareth-2 and steareth-20: not primary sensitizers formulation w/2.7% steareth-2 and 2.25% steareth-20, not phototoxic; formulation containing 4% steareth-20, not phototoxic	
	important Discussion items	no relevant items identified	
	Conclusion	safe as used	
		COMPONENTS	
PEGs	ADME	in metabolism studies with rats, rabbits, dogs, and humans, the lower molecular weight PEGs were absorbed by the digestive tract and excreted in the urine and feces; the higher molecular weight PEGs were absorbed more slowly or not at all; e.g. PEG-8 is rapidly absorbed by the gastro-intestinal (GI) tracts of several mammalian species and excreted primarily in the urine with less excretion in the feces, and PEG-150 in water was not absorbed from the GI tract of humans	15
	animal toxicology	oral LD_{50}:15-22 g/kg (rodents), higher mol wts less toxic than lower mol wts, i.v. LD_{50}: 7.3-9.5 g/kg (rodents) 13 wk oral: PEG-8, ≤5.6 g/kg/day, no systemic toxicity (rats) inhalation: PEG-75, ≤1003 mg/m^3, little or no toxicity (rats)	
	dermal irritation/sensitization	PEGs: not irritating to rabbits or guinea pigs PEG-75: not a sensitizer	
	ocular irritation	mild, transient irritation	
	repro/developmental toxicity	no biologically significant embryotoxicity or teratogenicity	
	genotoxicity	negative: Ames assay, CHO cell mutation assay, *in vivo* bone marrow assay, dominant lethal assay, mouse forward mutation assay, SCE assay	
	carcinogenicity	PEG-8: when used as a solvent control, not carcinogenic w/oral, i.p., or s.c. admin	
	clinical assessment of safety	PEG-6, PEG-8: mild case of immediate hypersensitivity; PEG-8: not a sensitizer use of antimicrobial creams w/PEG vehicle have been associated w/renal toxicity when applied to burned skin; margin of safety (MOS) ranged from 113 to >2600	
	important Discussion items	discussed the use of PEGs with damaged or burned skin (this is no longer an issue); should not contain 1,4-dioxane or ethylene oxide, which are possible oxidation products; aerosol boiler plate	
	Conclusion	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, -160M and -180M and any PEG ≥ 4 are safe in the present practices of use and concentration	
Behenyl Alcohol	animal toxicology	no data	12
	dermal irritation/sensitization	no data	
	ocular irritation	1%, transient conjunctival irritation	
	repro/developmental toxicity	no data	
	genotoxicity	no data	
	carcinogenicity	no data	

Table 2b. Summaries of information provided in previous reports (continued)

Ingredient	Parameter Evaluated	Outcome	Reference
	clinical assessment of safety	no data	
	important Discussion items	no relevant items identified	
	Conclusion	safe as used	
Cetearyl Alcohol	animal toxicology	no data	12
	dermal irritation/sensitization	formulation w/3%, mildly irritating (rabbits)	
	ocular irritation	formulation w/3%, not irritating	
	repro/developmental toxicity	no data	
	genotoxicity	no data	
	carcinogenicity	no data	
	clinical assessment of safety	formulation w/3%: not a sensitizer	
	important Discussion items	no relevant items identified	
	Conclusion	safe as used	
Cetyl Alcohol	ADME	in general, long-chain aliphatic alcohols, such as cetyl alcohol, are oxidized to their corresponding fatty acids in mammalian tissues; in rats administered radioactive cetyl alcohol by either stomach tube or thoracic duct fistulas, most of the radioactivity was found in the thoracic duct lymph, indicating good absorption; some of the cetyl alcohol was eliminated unchanged in waste products, but most of the cetyl alcohol was oxidized to palmitic acid and incorporated into triglycerides and phospholipids	12
	animal toxicology	oral LD_{50}(rats): >8.2 g/kg; formulations w/≤4%, no toxic effects; dermal LD_{50}: >2.6 g/kg; formulation w/5%, 2 g/kg;	
		inhalation: 6-h exposure, 26 ppm (rats, mice, guinea pigs), slight irritation of mucous membranes, but no signs of systemic toxicity or mortality; 6 h exposure, 2220 mg/m^3, 100% mortality	
		short-term dermal: 20 day, 11.5%, 5x/day, exfoliative dermatitis, parakeratosis, hyperkeratosis (rabbits); 30 day, 30% in methyl alcohol and propylene glycol, dermal infiltrates of histocytes	
		3 mos dermal study: formulations w/20%, well-defined erythema, mild edema, no systemic toxicity (rabbits)	
	dermal irritation/sensitization	undiluted, minimally to slightly irritating; formulations w/2-4%, no to well-defined erythema and edema	
	ocular irritation	formulations w/≤6.36%, mostly non-irritating	
	mucosal irritation	2%: not irritating to genital mucosa of rabbits	
	repro/developmental toxicity	no data	
	genotoxicity	negative, Ames test	
	carcinogenicity	no data	
	clinical assessment of safety	100%: not irritating; formulations w/2-11.5%,:at most, mild irritants	
		formulations w/1-8.4%, not sensitizers	
		30%: 11.2% of eczema patients (pop. 330) had allergic reactions	
		formulations w/1-4%, not photosensitizers	
	important Discussion items	no relevant items identified	
	Conclusion	safe as used	
Cholesterol	ADME	found in all animals, is a membrane component and an important metabolic precursor of certain hormones, vitamins, and steroidal compounds; is a component of skin surface lipids and sebum; the normal metabolism and excretion is well understood in man and animals; upon ingestion, cholesterol is incorporated into cell membranes, further metabolized into plasma lipoproteins, bile salts, and steroid hormones, metabolized by gut bacteria, or excreted via the skin, urine, and as neutral fecal steroids.	11
	animal toxicology	4 wk oral study: 1%, reversible hepatic changes (mice)	
	dermal irritation/sensitization	undiluted, no irritating (rabbits); formulation w/1.7%, slight irritant	
	ocular irritation	formulations w/1.7-6%, at most, minimal irritants	

Table 2b. Summaries of information provided in previous reports (continued)

Ingredient	Parameter Evaluated	Outcome	Reference
	repro/developmental toxicity	s.c admin of 5-15 mg in 2 ml vegetable oil to albino rats on days 8-14 of gestation resulted in 37-57% of the pups having abnormal palates; palatal abnormalities were also observed in Sprague-Dawley rats dosed with 15 and 20 mg on days 7-14 of gestation	
		capable of crossing the placental barrier in several mammalian species, including rats, rabbits, baboons, and man. It is synthesized by the placenta as well as by the fetus	
	genotoxicity	negative, Ames test, bacterial mutagenicity/genotoxicity assay, transformation assay, mammalian cell DNA inhibition test	
		some auto-oxidation products have mutagenic activity; some metabolites induce Syrian hamster embryo cell transformation	
	carcinogenicity	not established as a promoter, cocarcinogen, or total carcinogen	
		results have varied in rat studies: not a colon cancer promoter in one study when administered after initiation with N-methyl-N'-nitrosoguanidine, it was a dietary cocarcinogen with 1,2-dimethylhydrazine, and dietary cholesterol had a protective effect in N-methyl-N-nitrosourea-induced colon cancer	
	clinical assessment of safety	formulations w/1.4-6%, not irritants, sensitizer, or photosensitizers	
	important Discussion items	Discussion not in report	
	Conclusion	safe as used	
Coconut Alcohol	animal toxicology	no data	14
	dermal irritation/sensitization	no data	
	ocular irritation	no data	
	repro/developmental toxicity	no data	
	genotoxicity	no data	
	carcinogenicity	no data	
	clinical assessment of safety	no data	
	important Discussion items	toxicity and use profiles expected to be similar to coconut oil, coconut acid, hydrogenated coconut oil, hydrogenated coconut acid; addressed use in inhalation products; possible issues with botanicals	
	Conclusion	safe as used	
Isostearyl Alcohol	animal toxicology	oral LD_{50}: >20 g/kg (rats); formulations w/25-27%, >15 g/kg	12
	dermal irritation/sensitization	formulation w/5%: mild irritant (rabbits); formulation w/25-27%: barely perceptible erythema	
		0.2-5%: not a sensitizer	
	ocular irritation	formulations w/5 and 10%, transient irritation; formulations w/25-27%, minimal to mild irritation	
	repro/developmental toxicity	no data	
	genotoxicity	no data	
	carcinogenicity	no data	
	clinical assessment of safety	100%: not irritating; formulations w/25-28%, not irritating; deodorant formulation w/ 5%, severe irritation in a 21-day cumulative study	
		25% in 95% isopropyl alcohol: not a sensitizer; formulations w/5%: sensitization reactions occurred	
	important Discussion items	no relevant items identified	
	Conclusion	safe as used	
Jojoba Alcohol	animal toxicology	oral LD_{50}: 50 ml/kg (mice)	13
		15 and 30 day dermal studies: 12.5%, some erythema and edema, very slight incrassination of the epidermal germinative zone	
	dermal irritation/sensitization	10%: not a primary skin irritant (marmots); 12.5, 25 and 50% (15 and 30-day studies): irritation scores of 0-0.5, 0.2-0.8, and 0.4-1.8	
		10%: not a sensitizer (marmots)	
	ocular irritation	12, 25, and 50%: some conjunctival reaction, cleared within 24 h; jojoba mixture w/35%, non-irritating *in vitro*	

Table 2b. Summaries of information provided in previous reports (continued)

Ingredient	Parameter Evaluated	Outcome	Reference
	repro/developmental toxicity	no data	
	genotoxicity	negative, ≤40.0 nl/plate and 35%, Ames test	
	carcinogenicity	no data	
	clinical assessment of safety	10%, 100%: not an irritant; jojoba mixture w/35%, not an irritant	
		jojoba mixture w/35%: not a sensitizer	
		10%, 100%, jojoba mixture w/35%: not phototoxic	
	important Discussion items	may be a penetration enhancer, care should be taken in formulating products that may contain this ingredient in combination with any ingredient whose safety was based on lack of dermal absorption, or when dermal absorption was of concern; addressed use in inhalation products; possible issues with botanicals	
	Conclusion	safe as used	
Lanolin Alcohol	impurities	small amounts of detergent may be present in lanolin extract from scouring of the wool; 1,4-dioxane, may also be present in trace amounts; traces of the sodium methoxide catalyst and its degradation products may remain in the finished product; antioxidants such as BHT and α-tocopherol may be present as stabilizing additives; trace metals and pesticides from the fleece may also be found	9
	animal toxicology	oral LD_{50}: 12.1 to >42.7 g/kg (rats)	
	dermal irritation/sensitization	50 or 100%: mildly irritating, at most (rabbits)	
	ocular irritation	50%: at most, a very slight irritant or mild transient irritant	
	repro/developmental toxicity	no data	
	genotoxicity	no data	
	carcinogenicity	no data	
	clinical assessment of safety	100%: not an irritant	
		3 retrospective studies w/dermatology patients: incidence of hypersensitivity ranged from 0.7-2.38%; removal of free fatty lanolin alcohols reduced incidence of hypersensitivity by 96%	
	important Discussion items	Discussion not included in report	
	Conclusion	safe for topical application	
Methyl Alcohol	ADME	in humans and animals, methyl alcohol is readily absorbed from the gastrointestinal and respiratory tract and through the skin; the mean rate of absorption through human skin was 0.192 $mg/cm^2/min$; the peak rate of absorption through human cadaver skin was reached with 30 min of exposure; only 2% of the dose was absorbed; the remainder was volatilized; the high water miscibility of methyl alcohol allowed distribution throughout all organs and tissues in direct relation to the body's water compartment; hepatic metabolism in humans accounted for 90-95% of the elimination of methyl alcohol, and the route of metabolism was methyl alcohol to formate to carbon dioxide and water.	16
	animal toxicology	only non-human primate species present a model of acute human methyl alcohol toxicity; lethal dose for rhesus monkey: 3 g/kg	
		oral LD_{50}: 5.6 g/kg (rat); 7.3-15.3 g/kg (mouse); dermal LD_{50}: 15.8 g/kg (rabbits); inhalation LC_{50}: 64 to >145 g/kg (rats), 33.6 g/kg (cats), 61.1 g/kg (mice)	
		short-term inhalation:4 wks, ≤6500 mg/m^3 (cynomolgus monkey); 6 wks, ≤ 10 g/kg no pulmonary changes (rats)	
		ocular toxicity to non-human primates after systemic exposure following administration by various routes is well documented	
	dermal irritation/sensitization	no data	
	ocular irritation	100%: necrosis of corneal epithelium in one study; moderate irritant *in vivo* and *in vitro*	
	repro/developmental toxicity	inhalation: maternal NOEL 10,000 ppm, teratogenic NOEL, 5000 ppm ; oral admin: ≤5.2 ml/kg, no maternal toxicity (rats)	
	genotoxicity	mutagenic effects: RK^+ mutatest; negative: Ames test, Syrian hamster embryo cell transformation assay, micronucleus test	
	carcinogenicity	no data	
	clinical assessment of safety	toxicity in humans is due to the metabolism of the alcohol to formate and formic acid; can cause severe metabolic acidosis, blindness, and death, and all routes of exposure were toxicologically equivalent	
		closed patch test: 0.7%: no irritation; 5%: slight irritation; 7 and 70%, positive reactions	

Table 2b. Summaries of information provided in previous reports (continued)

Ingredient	Parameter Evaluated	Outcome	Reference
	important Discussion items	because of toxicity, Panel did not state whether methyl alcohol is safe or unsafe as a solvent	
	Conclusion	safe as used to denature alcohol	
Myristyl Alcohol	animal toxicology	oral LD_{50} (rats): >8 g/kg; formulation w/0.8%, >5 g/kg; dermal LD_{50}: formulation w/0.8%, >2 g/kg	12
		inhalation: 3%, 1 h, ataxia and moderate nasal irritation in all animals 10 min after exposure, no mortality	
	dermal irritation/sensitization	formulation w/0.8%, non-irritating (rabbits)	
	ocular irritation	formulation w/0.8%: not irritating; formulation w/3%: mildly irritating (rinsed eyes), moderately irritating (unrinsed eyes)	
	repro/developmental toxicity	no data	
	genotoxicity	no data	
	carcinogenicity	no data	
	clinical assessment of safety	formulations w/0.1-0.25%, not irritants; formulations w/0.25-0.8%, not irritating in a 4-wk clinical study	
		formulations w/0.1-0.25%, not sensitizers	
		formulation w/0.1%, not a photosensitizer	
	important Discussion items	no relevant items identified	
	Conclusion	safe as used	
Octyl Dodecanol	animal toxicology	oral LD_{50} (rats): >5 g/kg, undiluted; formulation w/10.2%, >25 g/kg; dermal LD_{50}: >3 g/kg	10
	dermal irritation/sensitization	100%: irritation score of 0-1.13/4 (rabbits); 30%: irritation score 0/4 (rabbits); formulations w/4 and 10.2%, mild irritation, at most; technical grade: moderate to severe irritation (rabbits, guinea pigs, rats), no irritation (swine, humans)	
	ocular irritation	100%: irritation score of 1 or 4/110 (24 h)	
	repro/developmental toxicity	no data	
	genotoxicity	no data	
	carcinogenicity	no data	
	clinical assessment of safety	100%: mild irritation in 1/40 subjects; undiluted technical grade: no irritation; formulations w/3-10.2%: essentially non-irritating	
		screening patch tests for contact sensitization in large populations: incidence rate of 0.36% (6/1664) formulation w/10.2%: not phototoxic or photoallergenic	
	important Discussion items	no Discussion	
	Conclusion	safe as used	
Oleyl Alcohol	animal toxicology	oral LD_{50}: formulations w/8 or 20%, >10 g/kg	10
	dermal irritation/sensitization	100%: slightly to moderately irritating (rabbits): 25%: no to low irritation; 10%: non-irritating (rabbits); formulations w/8-20%, mild irritation, at most; formulation w/1.5%, irritating (rat and mice); technical grade: moderate to severe irritation (rabbits, guinea pigs, rats), no irritation (swine, humans)	
	ocular irritation	100%: essentially non- to minimally irritating; formulations w/1.5-20%, no or minimal transient irritation	
	repro/developmental toxicity	no data	
	genotoxicity	no data	
	carcinogenicity	no data	
	clinical assessment of safety	undiluted technical grade: no irritation; formulations w/2.5-20%, non-to mildly irritating	
		formulations w/2.5-12.7%, not sensitizers	
		screening patch tests for contact sensitization in large population: incidence rate of 0.6% (10/1664)	
		formulations w/2.5-8%, not photosensitizing	
		diluted hair dye product w/1.5%, not an ocular irritant	
	important Discussion items	Discussion not included in report	
	Conclusion	safe as used	

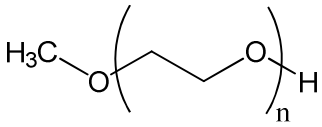
Table 2b. Summaries of information provided in previous reports (continued)

Ingredient	Parameter Evaluated	Outcome	Reference
Stearyl Alcohol	ADME	found naturally in various mammalian tissues; readily converted to stearic acid, another common constituent of mammalian tissues; results from several studies indicate that stearyl alcohol is poorly absorbed from the GI tract	10
	animal toxicology	oral LD_{50}: >8 g/kg;	
		3 mos dermal study: formulations w/8%,some dermal effects, , no systemic toxicity (rabbits)	
	dermal irritation/sensitization	100%: minimal to mild primary skin irritant (rabbits)	
		formulation w/24%: not a sensitizer	
	ocular irritation	100%: mildly irritating	
	repro/developmental toxicity	no data	
	genotoxicity	negative: Ames test	
	carcinogenicity	did not promote tumor formation in mice when tested with dimethylbenz[a]anthracene	
	clinical assessment of safety	100%: produced mild irritation in 1/80 subjects; formulations w/14-24% were non- to slightly irritating	
		formulations w/14-2%, not sensitizers	
		screening patch tests for contact sensitization in large population: incidence rate of 0.51% (19/3740)	
	important Discussion items	Discussion not included in report	
	Conclusion	safe as used	
Special Report on Ethylene Glycol and its Ethers	repro/developmental toxicity	it was found that metabolites of ethylene glycol monoalkyl ethers are repro. and developmental toxins; in general, however, the metabolites of concern are not expected to be formed in cosmetic formulations that contain polymers of ethylene glycol;. The toxicity of the metabolites is inversely proportional to the length of the alkyl chain; e.g., 2-butoxyethanol is not a reproductive toxicant	7

Table 3. Structures and Physical Properties
(unless otherwise noted, these values were calculated)[75]
"*" indicates those ingredients previously assessed by the CIR Expert Panel.

Methoxy PEG-n / PEG-n Methyl Ethers (a methyl group attached to a variable length PEG chain)

General Structure:

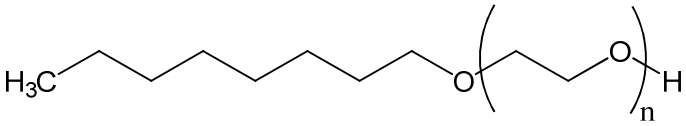


n = the average number of ethylene glycol units (e.g., PEG-7 Methyl Ether (or Methoxy PEG-7) is when n = 7)

INCI Name	Molecular Weight	M.P. / B.P.	$logK_{o/w}$
PEG-3 Methyl Ether (CAS No. **9004-74-4**; 112-35-6)	164.2	-44/249°C (exp)	-0.74
PEG-4 Methyl Ether (CAS No. **9004-74-4**)	208.25	62/291 °C	-1.73
PEG-6 Methyl Ether (CAS No. **9004-74-4**)	296.36	120/367 °C	-2.28
PEG-7 Methyl Ether (CAS No. **9004-74-4**)	340.41	149/404 °C	-2.55
Methoxy PEG-7 (CAS No. **9004-74-4**)	340.41	149/404 °C	-2.55
Methoxy PEG-10 (CAS No. **9004-74-4**)	472.57	215/510 °C	-3.38
Methoxy PEG-16 (CAS No. **9004-74-4**)	736.88	316/722°C	-5.02
Methoxy PEG-25 (CAS No. **9004-74-4**)	1132.36	350/1039 °C	-7.49
Methoxy PEG-40 (CAS No. **9004-74-4**)	1794.14	--/1568 °C	-11.61
Methoxy PEG-100 (CAS No. **9004-74-4**)	4437.40	--	--

Capreths (8 carbon chain with a variable PEG)

General Structure:

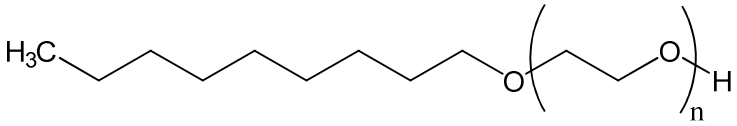


n = the average number of ethylene glycol units (e.g., Capreth-4 is when n = 4)

INCI Name	Molecular Weight	M.P. / B.P.	$logK_{o/w}$
Capryleth-4	306.44	127/380 °C	1.71
Capryleth-5	350.49	150/415 °C	1.43

Noneth-8 (9 carbon chain with an 8 unit PEG)

General Structure:



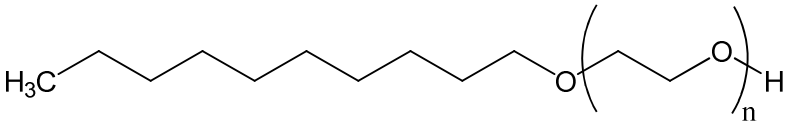
n = 9

INCI Name	Molecular Weight	M.P. / B.P.	$logK_{o/w}$
Noneth-8	496.67	225/532 °C	1.10

Table 3. Structures and Physical Properties (continued)

Deceths (10 carbon chain with a variable PEG)

General Structure:

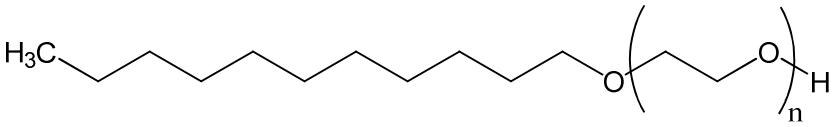


n = the average number of ethylene glycol units (e.g., Deceth-4 is when n = 4)

INCI Name	Molecular Weight	M.P. / B.P.	$logK_{o/w}$
Deceth-3 (CAS No. **26138-52-8**)	290.44	113/368 °C	2.96
Deceth-4 (CAS No. **26183-52-8;** 5703-94-6**)**	334.49	138/403 °C	2.69
Deceth-5 (CAS No. **26183-52-8**)	378.54	166/438 °C	2.42
Deceth-6 (CAS No. **26183-52-8**)	422.60	182/473 °C	2.14
Deceth-7 (CAS No. **26183-52-8**)	466.65	208/509 °C	1.87
Deceth-8 (CAS No. **26183-52-8**)	510.70	233/544 °C	1.59
Deceth-9 (CAS No. **26183-52-8**)	554.75	250/579 °C	1.32
Deceth-10 (CAS No. **26183-52-8**)	598.81	266/514 °C	1.04

Undeceths (11 carbon chain with a variable PEG)

General Structure:



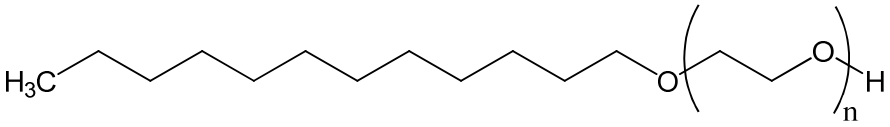
n = the average number of ethylene glycol units (e.g., Undeceth-3 is when n = 3)

INCI Name	Molecular Weight	M.P. / B.P.	$logK_{o/w}$
Undeceth-3 (CAS No. **34398-01-1**)	304.47	122/379 °C	3.46
Undeceth-5 (CAS No. **34398-01-1**)	392.57	174/450 °C	2.91
Undeceth-7 (CAS No. **34398-01-1**)	480.68	215/520 °C	2.36
Undeceth-8 (CAS No. **34398-01-1**)	524.73	239/556 °C	2.08
Undeceth-9 (CAS No. **34398-01-1**)	568.78	255/591 °C	1.81
Undeceth-11 (CAS No. **34398-01-1**)	656.89	288/661 °C	1.26
Undeceth-40 (CAS No. **34398-01-1**; 127036-24-2)	1931.34	350/1684 °C	-6.70

Table 3. Structures and Physical Properties (continued)

Laureths (12 carbon chain with a variable PEG)

General Structure:



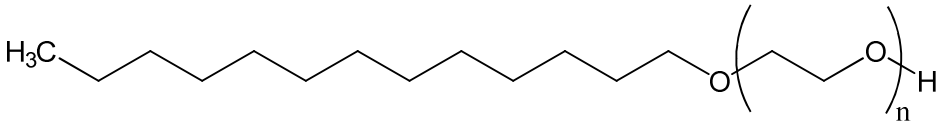
n = the average number of ethylene glycol units (e.g., Laureth-11 is when n = 11)

INCI Name	Molecular Weight	M.P. / B.P.	$logK_{o/w}$
Laureth-1 (CAS Nos. **9002-92-0**; 4536-30-5)	230.39	65/318 °C	4.50
Laureth-2 (CAS Nos. **9002-92-0**; 3055-93-4)	274.44	98/356 °C	4.22
Laureth-3 (CAS Nos. **9002-92-0**; 3055-94-5)	318.49	131/391 °C	3.95
Laureth-4* (CAS Nos. **9002-92-0**; 68439-50-9; 5274-68-0)	362.54	154/426 °C	3.67
Laureth-5 (CAS Nos. **9002-92-0**; 3055-95-6)	406.60	176/461 °C	3.40
Laureth-6 (CAS Nos. **9002-92-0;** 3055-96-7)	450.65	197/497 °C	3.12
Laureth-7 (CAS Nos. **9002-92-0**; 3055-97-8)	494.70	223/532 °C	2.85
Laureth-8 (CAS Nos. **9002-92-0**; 3055-98-8)	538.75	244/567 °C	2.57
Laureth-9 (CAS Nos. **9002-92-0**; 3055-99-0)	582.81	261/602 °C	2.30
Laureth-10 (CAS Nos. **9002-92-0; 68002-97-1**; 6540-99-4)	626.86	277/638 °C	2.03
Laureth-11 (CAS Nos. **9002-92-0; 68002-97-1**)	670.91	293/673 °C	1.75
Laureth-12 (CAS Nos. **9002-92-0; 68002-97-1**)	714.96	310/708 °C	1.48
Laureth-13 (CAS Nos. **9002-92-0; 68002-97-1**)	759.02	326/743 °C	1.20
Laureth-14 (CAS Nos. **9002-92-0; 68002-97-1**)	803.07	343/779 °C	0.93
Laureth-15 (CAS Nos. **9002-92-0; 68002-97-1**)	847.12	350/815 °C	0.65
Laureth-16 (CAS Nos. **9002-92-0; 68002-97-1**)	891.18	--/849 °C	0.38
Laureth-20 (CAS No. **9002-92-0**)	1067.39	--/990 °C	-0.72
Laureth-21 (CAS No. **9002-92-0**)	1111.44	--/1026 °C	-0.99
Laureth-23* (CAS No. **9002-92-0**)	1199.54	--/1096 °C	-1.54
Laureth-25 (CAS No. **9002-92-0**)	1287.65	--/1167 °C	-2.09
Laureth-30 (CAS No. **9002-92-0**)	1507.91	--/1343 °C	-3.46
Laureth-38 (CAS No. **9002-92-0**)	1860.33	--/1625 °C	-5.66
Laureth-40 (CAS No. **9002-92-0**)	1948.44	--/1696 °C	-6.21
Laureth-50	2388.96	--/2048 °C	-8.95

Table 3. Structures and Physical Properties (continued)

Trideceths (13 carbon chain with a variable PEG)

General Structure:

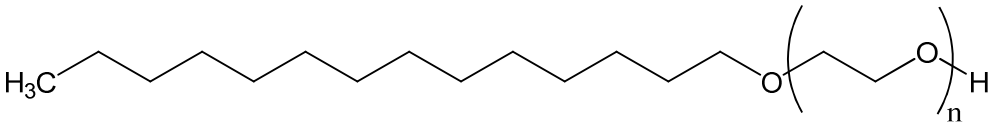


n = the average number of ethylene glycol units (e.g., Trideceth-3 is when n = 3)

INCI Name	Molecular Weight	M.P. / B.P.	$logK_{o/w}$
Trideceth-2 (CAS No. **24938-91-8**)	332.52	140/403 °C	4.44
Trideceth-3 (CAS No. **24938-91-8**; 4403-12-7)	376.57	162/438 °C	4.16
Trideceth-4	420.62	184/473 °C	3.89
Trideceth-5 (CAS No. **24938-91-8**)	464.48	205/508 °C	3.61
Trideceth-6 (CAS No. **24938-91-8**)	508.73	230/543 °C	3.34
Trideceth-7 (CAS No. **24938-91-8**)	552.78	249/579 °C	3.07
Trideceth-8 (CAS No. **24938-91-8**)	596.83	266/614 °C	2.79
Trideceth-9 (CAS No. **24938-91-8**; 69011-36-5)	640.89	282/649 °C	2.52
Trideceth-10 (CAS No. **24938-91-8**)	684.94	299/685 °C	2.24
Trideceth-11 (CAS No. **24938-91-8**)	728.99	315/720 °C	1.97
Trideceth-12 (CAS No. **24938-91-8**; 78330-21-9)	773.04	332/755 °C	1.69
Trideceth-15 (CAS No. **24938-91-8**)	905.20	350/861 °C	0.87
Trideceth-18 (CAS No. **24938-91-8**)	1037.36	--/967 °C	0.05
Trideceth-20 (CAS No. **24938-91-8**)	1125.46	--/1037 °C	-0.50
Trideceth-21 (CAS No. **24938-91-8**)	1169.52	--/1072 °C	-0.78
Trideceth-50 (CAS No. **24938-91-8**)	2447.04	--/2095 °C	-8.73

Myreths (14 carbon chain with a variable PEG)

General Structure:



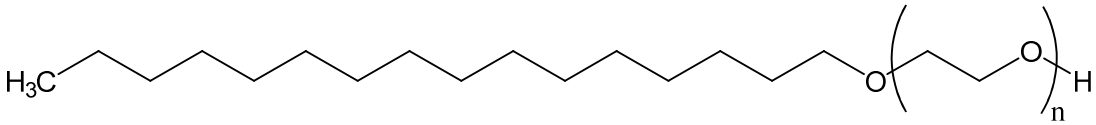
n = the average number of ethylene glycol units (e.g., Myreth-3 is when n = 3)

INCI Name	Molecular Weight	M.P. / B.P.	$logK_{o/w}$
Myreth-2 (CAS No. **27306-79-2)**	302.49	116/379 °C	5.20
Myreth-3 (CAS No. **27306-79-2;** 26826-30-2)	346.55	142/414 °C	4.93
Myreth-4 (CAS No. **27306-79-2**; 39034-24-7)	390.60	171/449 °C	4.65
Myreth-5 (CAS No. **27306-79-2**; 92669-010-7)	434.65	187/485 °C	4.38
Myreth-10 (CAS No. **27306-79-2**)	654.91	288/661 °C	3.01

Table 3. Structures and Physical Properties (continued)

Ceteths (16 carbon chain with a variable PEG)

General Structure:



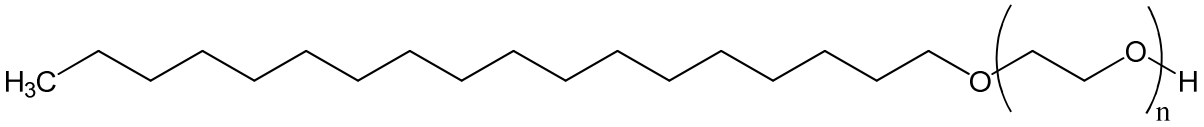
n = the average number of ethylene glycol units (e.g., Ceteth-3 is when n = 3)

INCI Name	Molecular Weight	M.P. / B.P.	$logK_{o/w}$
Ceteth-1* (CAS No. **9004-95-9**; 2136-71-2)	286.49	101/367 °C	6.46
Ceteth-2* (CAS No. **9004-95-9**; 5274-61-3)	330.54	134/402 °C	6.19
Ceteth-3* (CAS No. **9004-95-9**; 4484-59-7)	374.59	158/437 °C	5.91
Ceteth-4* (CAS No. **9004-95-9**; 5274-63-5)	418.64	187/473 °C	5.64
Ceteth-5* (CAS No. **9004-95-9**; 4478-97-1)	462.70	203/508 °C	5.36
Ceteth-6* (CAS No. **9004-95-9**; 5168-91-2)	506.75	228/543 °C	5.09
Ceteth-7 (CAS No. **9004-95-9**)	550.44	249/578 °C	4.81
Ceteth-10* (CAS No. **9004-95-9**; 14529-40-9)	682.96	299/684 °C	3.99
Ceteth-12* (CAS No. **9004-95-9**; 94159-75-8)	771.06	332/755 °C	3.44
Ceteth-13 (CAS No. **9004-95-9**)	815.12	348/790 °C	3.17
Ceteth-14* (CAS No. **9004-95-9**)	859.17	--/825 °C	2.89
Ceteth-15* (CAS No. **9004-95-9**)	903.22	--/860 °C	2.62
Ceteth-16* (CAS No. **9004-95-9**)	947.27	--/896 °C	2.34
Ceteth-17 (CAS No. **9004-95-9**)	991.33	--/931 °C	2.07
Ceteth-18 (CAS No. **9004-95-9**)	1035.39	--/966 °C	1.80
Ceteth-20* (CAS No. **9004-95-9**)	1123.48	--/1037 °C	1.25
Ceteth-23 (CAS No. **9004-95-9**)	1255.65	--/1142 °C	0.42
Ceteth-24* (CAS No. **9004-95-9**)	1299.69	--/1178 °C	0.15
Ceteth-25* (CAS No. **9004-95-9**)	1343.75	--/1213 °C	-0.13
Ceteth-30* (CAS No. **9004-95-9**)	1564.01	--/1389 °C	-1.50
Ceteth-40 (CAS No. **9004-95-9**)	2004.54	--/1742 °C	-4.24
Ceteth-45* (CAS No. **9004-95-9**)	2224.80	--/1918 °C	-5.61
Ceteth-150 (CAS No. **9004-95-9**)	6850.35	--/--	--

Table 3. Structures and Physical Properties (continued)

Steareths (18 carbon chain with a variable PEG)

General Structure:

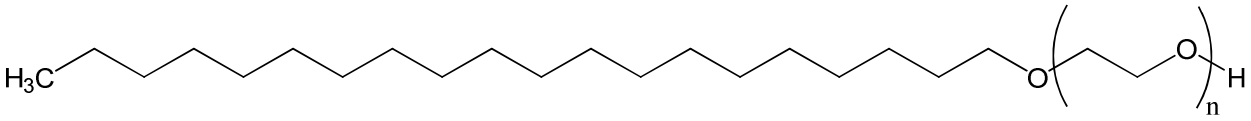


n = the average number of ethylene glycol units (e.g., Steareth-3 is when n = 3)

INCI Name	Molecular Weight	M.P. / B.P.	$logK_{o/w}$
Steareth-1 (CAS No. **9005-00-9**)	314.55	120/390 °C	7.44
Steareth-2* (CAS No. **9005-00-9**; 16057-43-5)	358.60	152/425 °C	7.17
Steareth-3 (CAS No. **9005-00-9**; 4439-32-1)	402.65	175/460 °C	6.89
Steareth-4* (CAS No. **9005-00-9**; 59970-10-4)	446.70	193/496 °C	6.62
Steareth-5 (CAS No. **9005-00-9**; 71093-13-5)	490.76	218/531 °C	6.34
Steareth-6 (CAS No. **9005-00-9**; 2420-29-3)	534.81	243/566 °C	6.07
Steareth-7 (CAS No. **9005-00-9**; 66146-84-7)	578.86	260/602 °C	5.80
Steareth-8 (CAS No. **9005-00-9**)	622.91	276/637 °C	5.52
Steareth-10* (CAS No. **9005-00-9**; 13149-86-5)	711.02	309/707 °C	4.97
Steareth-11* (CAS No. **9005-00-9**)	755.07	326/743 °C	4.70
Steareth-13* (CAS No. **9005-00-9**)	843.18	350/813 °C	4.15
Steareth-14 (CAS No. **9005-00-9**)	887.23	--/848 °C	3.87
Steareth-15* (CAS No. **9005-00-9**)	931.28	--/884 °C	3.60
Steareth-16 (CAS No. **9005-00-9**)	975.33	--/919 °C	3.33
Steareth-20* (CAS No. **9005-00-9**)	1151.54	--/1060 °C	2.23
Steareth-21 (CAS No. **9005-00-9**)	1195.60	--/1095 °C	1.95
Steareth-25 (CAS No. **9005-00-9**)	1371.81	--/1236 °C	0.86
Steareth-27 (CAS No. **9005-00-9**)	1459.91	--/1307 °C	0.71
Steareth-30 (CAS No. **9005-00-9**)	1592.07	--/1413 °C	-0.52
Steareth-40 (CAS No. **9005-00-9**)	2032.60	--/1765 °C	-3.26
Steareth-50 (CAS No. **9005-00-9**)	2473.12	--/2118 °C	-6.00
Steareth-80 (CAS No. **9005-00-9**)	3497.70	--/--	--
Steareth-100 (CAS No. **9005-00-9**)	4675.75	--/--	--
Steareth-200 (CAS No. **9005-00-9**)	9081.01	--/--	--

Arachideth-20 (20 carbon chain with a 20 unit PEG)

Structure:



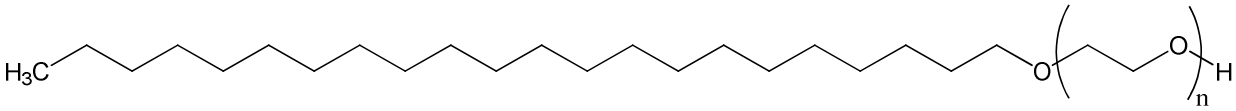
n = 20

INCI Name	Molecular Weight	M.P. / B.P.	$logK_{o/w}$
Arachideth-20	1179.60	--/1083 °C	3.21

Table 3. Structures and Physical Properties (continued)

Beheneths (22 carbon chain with a variable PEG)

General Structure:



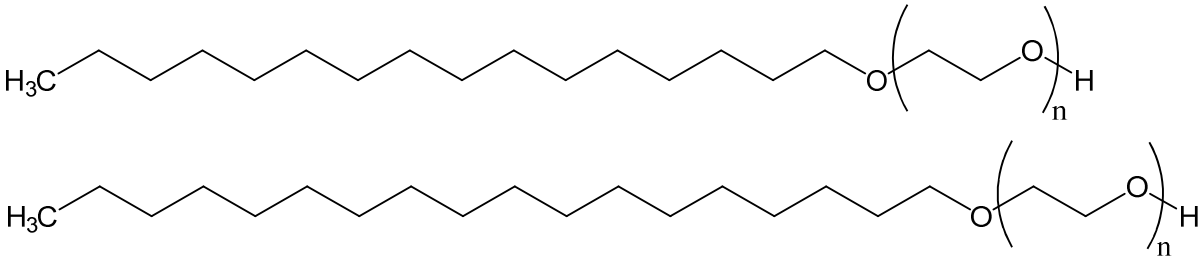
n = the average number of ethylene glycol units (e.g., Beheneth-2 is when n = 2)

INCI Name	Molecular Weight	M.P. / B.P.	$logK_{o/w}$
Beheneth-2	414.71	179/472 °C	9.13
Beheneth-5	546.85	249/577 °C	8.31
Beheneth-10	767.13	331/754 °C	6.94
Beheneth-15	987.39	--/930 °C	5.56
Beheneth-20	1207.65	--/1106 °C	4.19
Beheneth-25	1427.91	--/1283 °C	2.82
Beheneth-30	1648.18	--/1459 °C	1.45

Table 3. Structures and Physical Properties (continued)

Ceteareths (mixture of 16 and 18 carbon chains with a variable PEG)

General Structure:



n = the average number of ethylene glycol units (e.g., Ceteareth-3 is when n = 3)

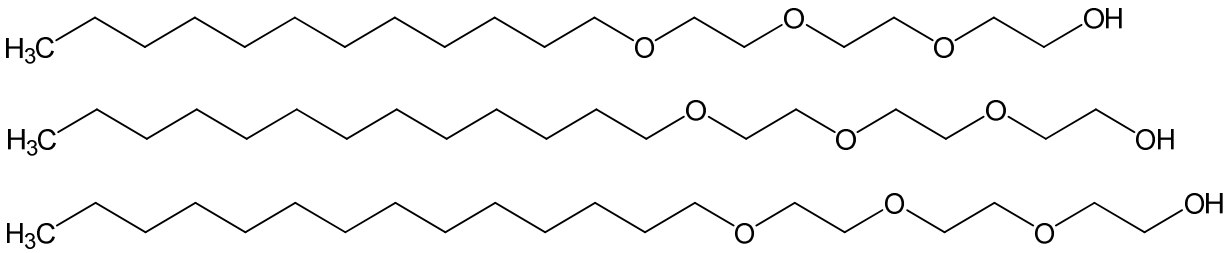
As these are mixtures of two molecules at unknown ratios, molecular weights and physical properties are not calculable.

INCI Name	
Ceteareth-2* (CAS No. **68439-49-6**)	Molecular weight < 1000
Ceteareth-3* (CAS No. **68439-49-6**)	Molecular weight < 1000
Ceteareth-4* (CAS No. **68439-49-6**)	Molecular weight < 1000
Ceteareth-5* (CAS No. **68439-49-6**)	Molecular weight < 1000
Ceteareth-6* (CAS No. **68439-49-6**)	Molecular weight < 1000
Ceteareth-7* (CAS No. **68439-49-6**)	Molecular weight < 1000
Ceteareth-8* (CAS No. **68439-49-6**)	Molecular weight < 1000
Ceteareth-9* (CAS No. **68439-49-6**)	Molecular weight < 1000
Ceteareth-10* (CAS No. **68439-49-6**)	Molecular weight < 1000
Ceteareth-11* (CAS No. **68439-49-6**)	Molecular weight < 1000
Ceteareth-12* (CAS No. **68439-49-6**)	Molecular weight < 1000
Ceteareth-13* (CAS No. **68439-49-6**)	Molecular weight < 1000
Ceteareth-14* (CAS No. **68439-49-6**)	Molecular weight < 1000
Ceteareth-15* (CAS No. **68439-49-6**)	Molecular weight < 1000
Ceteareth-16* (CAS No. **68439-49-6**)	Molecular weight < 1000
Ceteareth-17* (CAS No. **68439-49-6**)	Molecular weight ~ 1000
Ceteareth-18* (CAS No. **68439-49-6**)	Molecular weight > 1000
Ceteareth-20* (CAS No. **68439-49-6**)	Molecular weight > 1000
Ceteareth-22* (CAS No. **68439-49-6**)	Molecular weight > 1000
Ceteareth-23* (CAS No. **68439-49-6**)	Molecular weight > 1000
Ceteareth-24* (CAS No. **68439-49-6**)	Molecular weight > 1000
Ceteareth-25* (CAS No. **68439-49-6**)	Molecular weight > 1000
Ceteareth-27* (CAS No. **68439-49-6**)	Molecular weight > 1000
Ceteareth-28* (CAS No. **68439-49-6**)	Molecular weight > 1000
Ceteareth-29* (CAS No. **68439-49-6**)	Molecular weight > 1000
Ceteareth-30* (CAS No. **68439-49-6**)	Molecular weight > 1000
Ceteareth-33* (CAS No. **68439-49-6**)	Molecular weight > 1000
Ceteareth-34* (CAS No. **68439-49-6**)	Molecular weight > 1000
Ceteareth-40* (CAS No. **68439-49-6**)	Molecular weight > 1000
Ceteareth-50* (CAS No. **68439-49-6**)	Molecular weight > 1000
Ceteareth-55* (CAS No. **68439-49-6**)	Molecular weight > 1000
Ceteareth-60* (CAS No. **68439-49-6**)	Molecular weight > 1000
Ceteareth-80* (CAS No. **68439-49-6**)	Molecular weight > 1000
Ceteareth-100* (CAS No. **68439-49-6)**	Molecular weight > 1000

Table 3. Structures and Physical Properties (continued)

Pareths (mixture of variable length carbons chains with a variable PEG)

Structure Example: C12-14 Pareth-3



As these are mixtures of more than one molecule at unknown ratios, molecular weights and physical properties are not calculable.

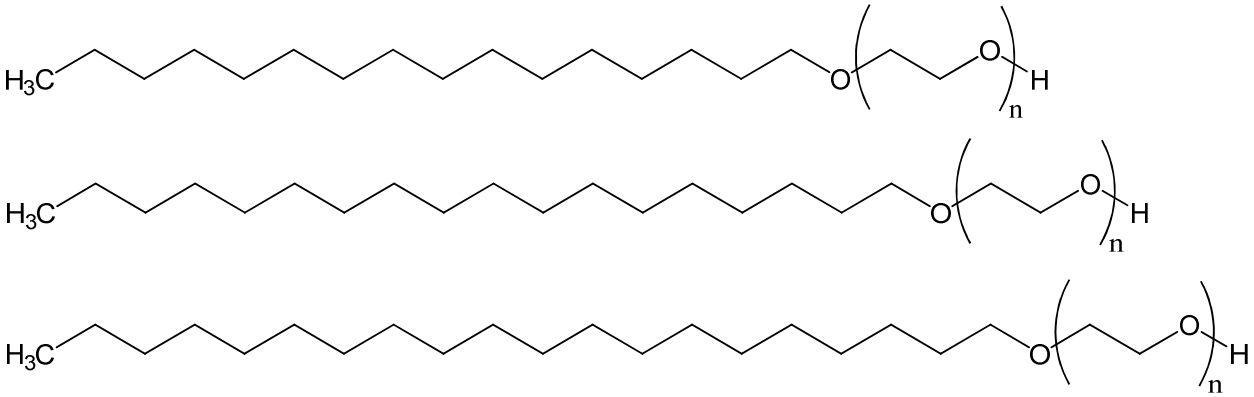
INCI Name	
C9-11 Pareth-3 (CAS No. **68439-46-3**)	Molecular weight < 1000
C9-11 Pareth-4 (CAS No. **68439-46-3**)	Molecular weight < 1000
C9-11-Pareth-6 (CAS No. **68439-46-3**)	Molecular weight < 1000
C9-11 Pareth-8 (CAS No. **68439-46-3**)	Molecular weight < 1000
C9-15 Pareth-8 (CAS No. **157627-88-8**)	Molecular weight < 1000
C10-16 Pareth-1 (CAS No. **68002-97-1**)	Molecular weight < 1000
C10-16 Pareth-2 (CAS No. **68002-97-1**)	Molecular weight < 1000
C11-13 Pareth-6 (CAS No. **308060-94-8**)	Molecular weight < 1000
C11-13 Pareth-9 (CAS No. **308060-94-8**)	Molecular weight < 1000
C11-13 Pareth-10 (CAS No. **308060-94-8**)	Molecular weight < 1000
C11-15 Pareth-3 (CAS No. **68131-40-8**)	Molecular weight < 1000
C11-15 Pareth-5 (CAS No. **68131-40-8**)	Molecular weight < 1000
C11-15 Pareth-7 (CAS No. **68131-40-8**)	Molecular weight < 1000
C11-15 Pareth-9 (CAS No. **68131-40-8**)	Molecular weight < 1000
C11-15 Pareth-12 (CAS No. **68131-40-8**)	Molecular weight < 1000
C11-15 Pareth-15 (CAS No. **68131-40-8**)	Molecular weight < 1000
C11-15 Pareth-20 (CAS No. **68131-40-8**)	Molecular weight > 1000
C11-15 Pareth-30 (CAS No. **68131-40-8**)	Molecular weight > 1000
C11-15 Pareth-40 (CAS No. **68131-40-8**)	Molecular weight > 1000
C11-21-Pareth-3 (CAS No. **246538-82-9**)	Molecular weight < 1000
C11-21-Pareth-10 (CAS No. **246538-82-9**)	Molecular weight < 1000
C12-13 Pareth-1 (CAS No. **66455-14-9**)	Molecular weight < 1000
C12-13 Pareth-2 (CAS No. **66455-14-9**)	Molecular weight < 1000
C12-13 Pareth-3 (CAS No. **66455-14-9**)	Molecular weight < 1000
C12-13 Pareth-4 (CAS No. **66455-14-9**)	Molecular weight < 1000
C12-13 Pareth-5 (CAS No**. 66455-14-9**)	Molecular weight < 1000
C12-13 Pareth-6 (CAS No. **66455-14-9**)	Molecular weight < 1000
C12-13 Pareth-7 (CAS No. **66455-14-9**)	Molecular weight < 1000
C12-13 Pareth-9 (CAS No. **66455-14-9**)	Molecular weight < 1000
C12-13 Pareth-10 (CAS No. **66455-14-9**)	Molecular weight < 1000
C12-13 Pareth-15 (CAS No. **66455-14-9**)	Molecular weight < 1000
C12-13 Pareth-23 (CAS No. **66455-14-9**)	Molecular weight > 1000
C12-14 Pareth-3 (CAS No. **68439-50-9**)	Molecular weight < 1000
C12-14 Pareth-5 (CAS No. **68439-50-9**)	Molecular weight < 1000
C12-14 Pareth-7 (CAS No. **68439-50-9**)	Molecular weight < 1000
C12-14 Pareth-9 (CAS No. **68439-50-9**)	Molecular weight < 1000
C12-14 Pareth-12 (CAS No. **68439-50-9**)	Molecular weight < 1000
C12-15 Pareth-2 (CAS No. **68131-39-5**)	Molecular weight < 1000
C12-15 Pareth-3 (CAS No. **68131-39-5**)	Molecular weight < 1000
C12-15 Pareth-4 (CAS No. **68131-39-5**)	Molecular weight < 1000
C12-15 Pareth-5 (CAS No. **68131-39-5**)	Molecular weight < 1000
C12-15 Pareth-7 (CAS No. **68131-39-5**)	Molecular weight < 1000
C12-15 Pareth-9 (CAS No. **68131-39-5**)	Molecular weight < 1000
C12-15 Pareth-10 (CAS No. **68131-39-5**)	Molecular weight < 1000

Table 3. Structures and Physical Properties (continued)

C12-15 Pareth-11 (CAS No. **68131-39-5**)	Molecular weight < 1000
C12-15 Pareth-12 (CAS No. **68131-39-5**)	Molecular weight < 1000
C12-16 Pareth-5 (CAS No. **68551-12-2**)	Molecular weight < 1000
C12-16 Pareth-7 (CAS No. **68551-12-2**)	Molecular weight < 1000
C12-16 Pareth-9 (CAS No. **68551-12-2**)	Molecular weight < 1000
C13-15 Pareth-21 (CAS No. **64425-86-1**)	Molecular weight > 1000
C14-15 Pareth-4 (CAS No. **68951-67-7**)	Molecular weight < 1000
C14-15 Pareth-7 (CAS No. **68951-67-7**)	Molecular weight < 1000
C14-15 Pareth-8 (CAS No. **68951-67-7**)	Molecular weight < 1000
C14-15 Pareth-11 (CAS No. **68951-67-7**)	Molecular weight < 1000
C14-15 Pareth-12 (CAS No. **68951-67-7**)	Molecular weight < 1000
C14-15 Pareth-13 (CAS No. **68951-67-7**)	Molecular weight < 1000
C20-22 Pareth-30	Molecular weight > 1000
C20-40 Pareth-3 (CAS No. **246538-83-0**)	Molecular weight < 1000
C20-40 Pareth-10 (CAS No. **246538-83-0**)	Molecular weight ~ 1000
C20-40 Pareth-24 (CAS No. **246538-83-0**)	Molecular weight > 1000
C20-40 Pareth-40 (CAS No. **246538-83-0**)	Molecular weight > 1000
C20-40 Pareth-95 (CAS No. **246538-83-0**)	Molecular weight > 1000
C22-24 Pareth-33 (CAS No. **246538-84-1**)	Molecular weight > 1000
C30-50 Pareth-3 (CAS No. **246538-85-2**)	Molecular weight < 1000
C30-50 Pareth-10 (CAS No. **246538-85-2**)	Molecular weight ~ 1000
C30-50 Pareth-40 (CAS No. **246538-85-2**)	Molecular weight > 1000
C40-60 Pareth-3 (CAS No. **246538-86-3)**	Molecular weight < 1000
C40-60 Pareth-10 (CAS No. **246538-86-3**)	Molecular weight > 1000

Hydrogenated Talloweths (mixture of 14, 16, and 18 carbon chains with a variable PEG)

General Structure:



n = the average number of ethylene glycol units (e.g., Hydrogenated Talloweth-12 is when n = 12)

As these are mixtures of more than one molecule at unknown ratios, molecular weights and physical properties are not calculable.

INCI Name

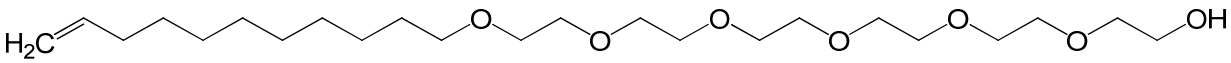
Hydrogenated Talloweth-12	Molecular weight < 1000
Hydrogenated Talloweth-25	Molecular weight > 1000

Table 3. Structures and Physical Properties (continued)

Partially Unsaturated Alkyl PEG Ethers

Undecyleneth-6 (Ω-1 unsaturated 11 carbon chain with a 6 unit PEG)

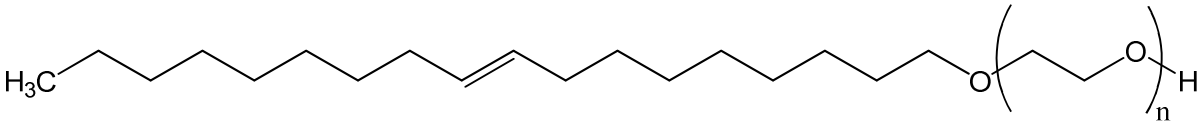
Structure:



INCI Name	Molecular Weight	M.P. / B.P.	$logK_{o/w}$
Undecyleneth-6	434.61	189/484 °C	2.50

Oleths (Ω-9 unsaturated 18 carbon chain with a variable PEG)

General Structure:



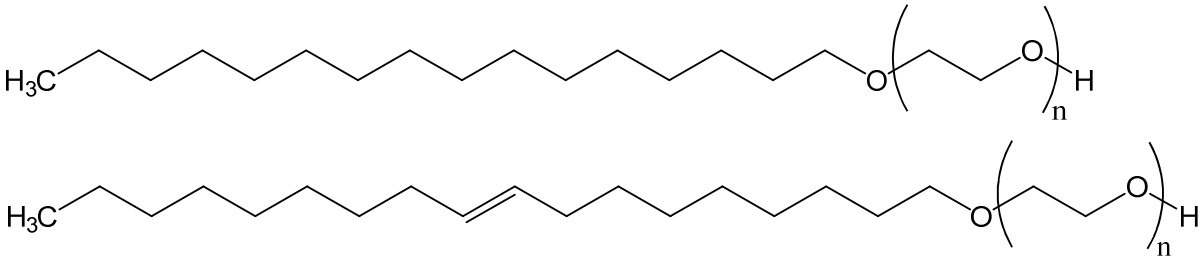
n = the average number of ethylene glycol units (e.g., Oleth-2 is when n = 2)

INCI Name	Molecular Weight	M.P. / B.P.	$logK_{o/w}$
Oleth-2* (CAS No. **9004-98-2**; 5274-65-7; 95287-03-9)	356.58	151/429 °C	6.95
Oleth-3* (CAS No. **9004-98-2**; 5274-66-8; 96459-08-4)	400.64	175/464 °C	6.68
Oleth-4* (CAS No. **9004-98-2**; 5353-26-4; 103622-85-1)	444.69	193/499 °C	6.40
Oleth-5* (CAS No. **9004-98-2**; 5353-27-5)	488.74	219/535 °C	6.13
Oleth-6* (CAS No. **9004-98-2**)	532.79	244/570 °C	5.86
Oleth-7* (CAS No. **9004-98-2**)	576.85	262/605 °C	5.58
Oleth-8* (CAS No. **9004-98-2**; 26996-03-2; 27040-03-5)	620.90	278/640 °C	5.31
Oleth-9* (CAS No. **9004-98-2**)	664.95	295/676 °C	5.03
Oleth-10* (CAS No. **9004-98-2**)	709.00	311/711 °C	4.76
Oleth-11* (CAS No. **9004-98-2**)	753.06	328/746 °C	4.48
Oleth-12* (CAS No. **9004-98-2**)	797.11	344/781 °C	4.21
Oleth-15* (CAS No. **9004-98-2**)	929.27	350/887 °C	3.39
Oleth-16* (CAS No. **9004-98-2; 25190-05-0**)	973.32	--/922 °C	3.11
Oleth-20* (CAS No. **9004-98-2**)	1149.53	--/1063 °C	2.01
Oleth-23* (CAS No. **9004-98-2**)	1281.69	--/1169 °C	1.19
Oleth-24 (CAS No. **9004-98-2**)	1325.74	--/1204 °C	0.92
Oleth-25* (CAS No. **9004-98**-2)	1369.79	--/1240 °C	0.64
Oleth-30* (CAS No. **9004-98-2**)	1590.05	--/1416 °C	-0.73
Oleth-35 (CAS No. **9004-98-2**)	1810.32	--/1592 °C	-2.10
Oleth-40* (CAS No. **9004-98-2**)	2030.58	--/1769 °C	-3.47
Oleth-44* (CAS No. **9004-98-2**)	2206.79	--/1910 °C	-4.57
Oleth-45 (CAS No. **9004-98-2**)	2250.84	--/1945 °C	-4.85
Oleth-50* (CAS No. **9004-98-2**)	2471.11	--/2121 °C	-6.22
Oleth-82 (CAS No. **9004-98-2**)	3880.79	--/--	--
Oleth-100 (CAS No. **9004-98-2**)	4673.73	--/--	--
Oleth-106 (CAS No. **9004-98-2**)	4938.05	--/--	--

Table 3. Structures and Physical Properties (continued)

Cetoleths (mixture of 16 carbon chain and Ω-9 unsaturated 18 carbon chains with a variable PEG)

General Structure:



n = the average number of ethylene glycol units (e.g., Ceteleth-6 is when n = 6)

As these are mixtures of two molecules at unknown ratios, molecular weights and physical properties are not calculable.

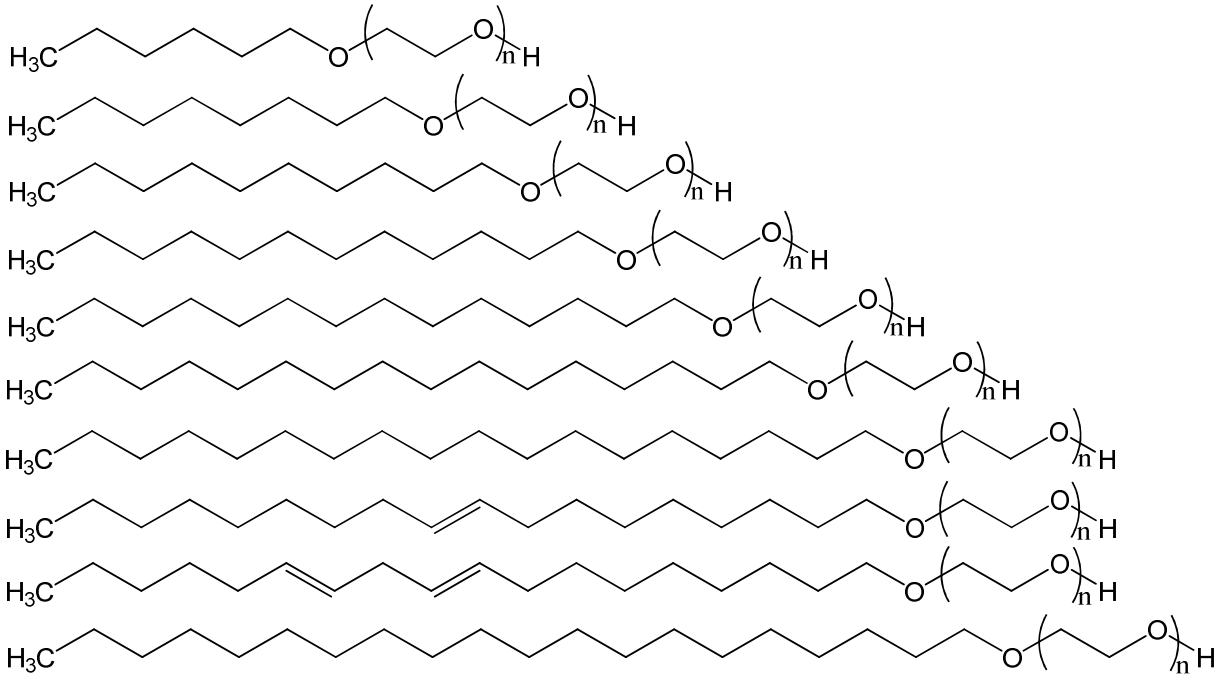
INCI Name

Cetoleth-2 (CAS No. **8065-81-4**)	Molecular weight < 1000
Cetoleth-4 (CAS No. **8065-81-4**)	Molecular weight < 1000
Cetoleth-5 (CAS No. **8065-81-4**)	Molecular weight < 1000
Cetoleth-6 (CAS No. **8065-81-4**)	Molecular weight < 1000
Cetoleth-10 (CAS No. **8065-81-4**)	Molecular weight < 1000
Cetoleth-11 (CAS No. **8065-81-4**)	Molecular weight < 1000
Cetoleth-15 (CAS No. **8065-81-4**)	Molecular weight < 1000
Cetoleth-18 (CAS No. **8065-81-4**)	Molecular weight > 1000
Cetoleth-20 (CAS No. **8065-81-4**)	Molecular weight > 1000
Cetoleth-22 (CAS No. **8065-81-4**)	Molecular weight > 1000
Cetoleth-24 (CAS No. **8065-81-4**)	Molecular weight > 1000
Cetoleth-25 (CAS No. **8065-81-4**)	Molecular weight > 1000
Cetoleth-30 (CAS No. **8065-81-4**)	Molecular weight > 1000

Table 3. Structures and Physical Properties (continued)

Coceths (mixture of 6, 8, 10, 12, 14, 18, Ω-9 unsaturated 18, Ω-6 unsaturated 18, and 20 carbon chains with a variable PEG)

General Structure:



n = the average number of ethylene glycol units (e.g., Coceth-3 is when n = 3)

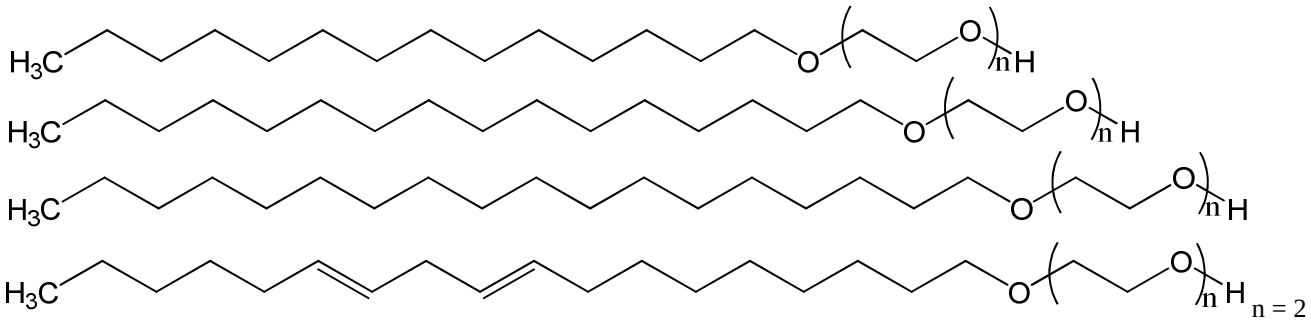
As these are mixtures of more than one molecule at unknown ratios, molecular weights and physical properties are not calculable.

INCI Name	
Coceth-3 (CAS No. **61791-13-7**)	Molecular weight < 1000
Coceth-5 (CAS No. **61791-13-7**)	Molecular weight < 1000
Coceth-6 (CAS No. **61791-13-7**)	Molecular weight < 1000
Coceth-7 (CAS No. **61791-13-7**)	Molecular weight < 1000
Coceth-8 (CAS No. **61791-13-7**)	Molecular weight < 1000
Coceth-10 (CAS No. **61791-13-7**)	Molecular weight < 1000
Coceth-20 (CAS No. **61791-13-7**)	Molecular weight > 1000
Coceth-25 (CAS No. **61791-13-7**)	Molecular weight > 1000

Table 3. Structures and Physical Properties (continued)

Palmeth-2 (mixture of 14, 16, 18, Ω-6 unsaturated 18, and Ω-6 unsaturated 18 carbon chains with a 2 unit PEG)

Structure:



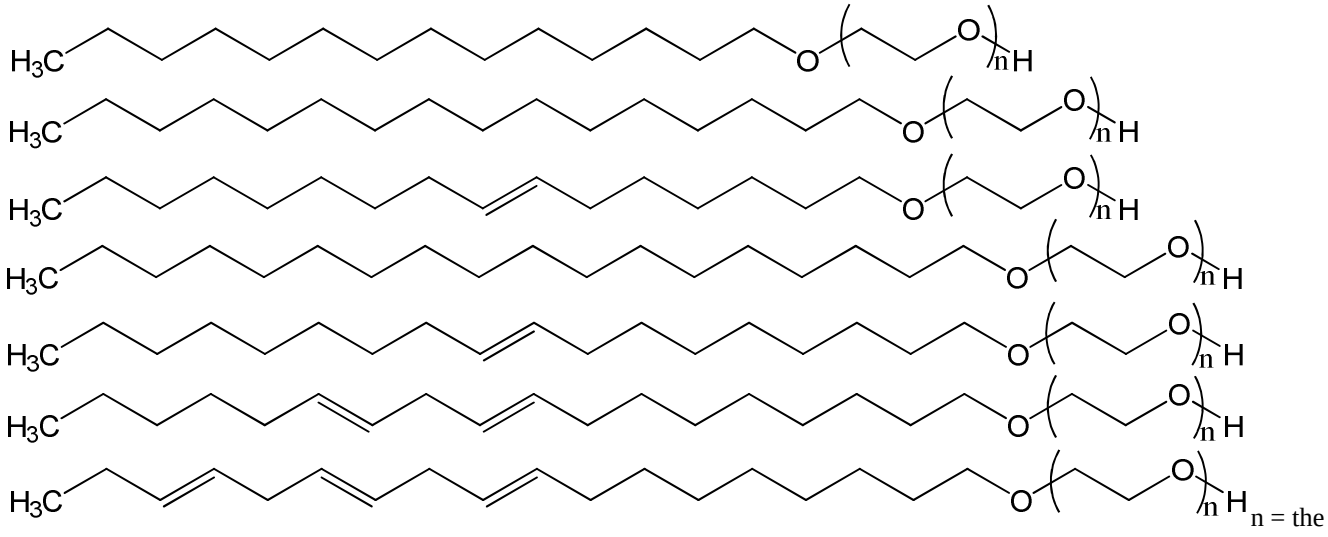
As palmeth-2 is a mixture of more than one molecule at unknown ratio, molecular weight and physical properties are not calculable.

INCI Name

Palmeth-2	Molecular weight < 1000

Talloweths (mixture of 14, 16, Ω-9 unsaturated 16, 18, Ω-9 unsaturated 18, Ω-6 unsaturated 18, and Ω-3 unsaturated 18 carbon chains with a variable PEG)

General Structure:



average number of ethylene glycol units (e.g., Talloweth-4 is when n = 4)

As these are mixtures of more than one molecule at unknown ratios, molecular weights and physical properties are not calculable.

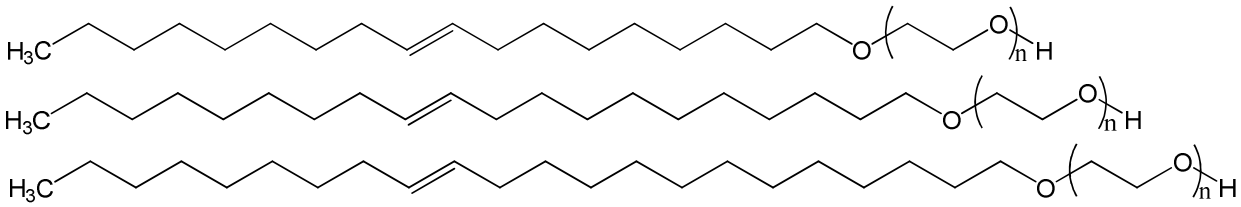
INCI Name

Talloweth-4 (CAS No. **61791-28-4**)	Molecular weight < 1000
Talloweth-5 (CAS No. **61791-28-4**)	Molecular weight < 1000
Talloweth-6 (CAS No. **61791-28-4**)	Molecular weight < 1000
Talloweth-7 (CAS No. **61791-28-4**)	Molecular weight < 1000
Talloweth-18 (CAS No. **61791-28-4**)	Molecular weight > 1000

Table 3. Structures and Physical Properties (continued)

PEG Jojoba Alcohols (mixture of Ω-9 unsaturated 18, Ω-9 unsaturated 20, and Ω-9 unsaturated 22 carbon chains with a variable PEG)

General Structure:



n = the average number of ethylene glycol units (e.g., PEG-15 Jojoba Alcohol is when n = 15)

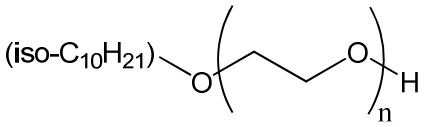
As these are mixtures of more than one molecule at unknown ratios, molecular weights and physical properties are not calculable.

INCI Name	
PEG-15 Jojoba Alcohol	Molecular weight < 1000
PEG-26 Jojoba Alcohol	Molecular weight > 1000
PEG-40 Jojoba Alcohol	Molecular weight > 1000

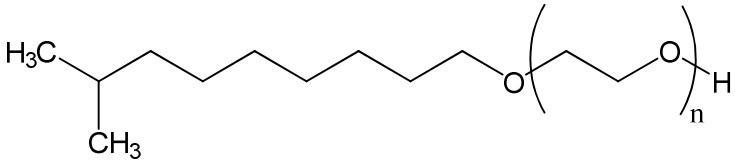
Branched Alkyl PEG Ethers

Isodeceths (mixture of various branched 10 carbon chains with a variable PEG)

General Structure:



n = the average number of ethylene glycol units (e.g., Isodeceth-4 is when n = 4); "iso" = a mixture of branched isomers, one example of which would be:



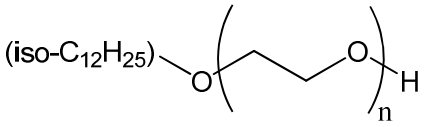
As these are mixtures of more than one isomer at unknown ratios, physical properties are not calculable.

INCI Name	Molecular Weight
Isodeceth-4	334.49
Isodeceth-5	378.54
Isodeceth-6	422.60

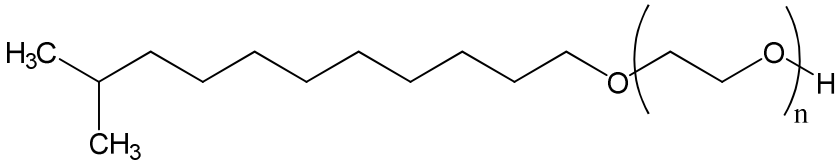
Table 3. Structures and Physical Properties (continued)

Isolaureths (mixture of various branched 12 carbon chains with a variable PEG)

General Structure:



n = the average number of ethylene glycol units (e.g., Isolaureth-10 is when n = 10); "iso" = a mixture of branched isomers, one example of which would be:

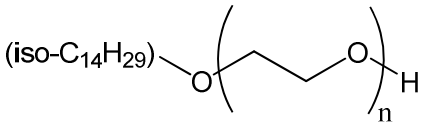


As these are mixtures of more than one isomer at unknown ratios, physical properties are not calculable.

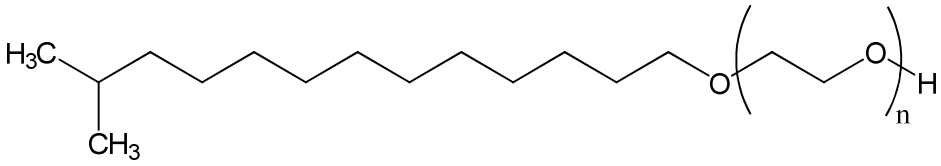
INCI Name	Molecular Weight
Isolaureth-3 (CAS No. **39365-90-7**)	318.49
Isolaureth-6 (CAS No. **39365-90-7**)	450.65
Isolaureth-10 (CAS No. **39365-90-7**)	626.86

Isomyreths (mixture of various branched 14 carbon chains with a variable PEG)

General Structure:



n = the average number of ethylene glycol units (e.g., Isomyreth-9 is when n = 9); "iso" = a mixture of branched isomers, one example of which would be:



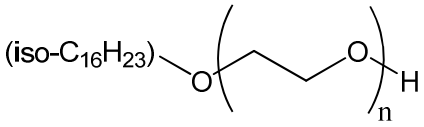
As these are mixtures of more than one isomer at unknown ratios, physical properties are not calculable.

INCI Name	Molecular Weight
Isomyreth-3	346.55
Isomyreth-9	610.86

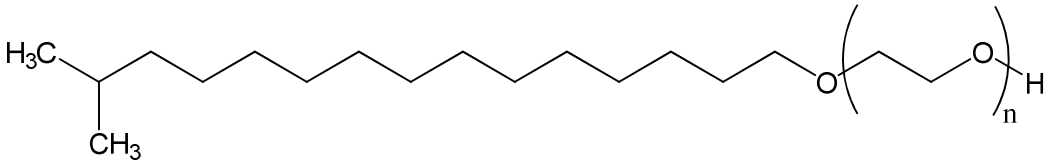
Table 3. Structures and Physical Properties (continued)

Isoceteths (mixture of various branched 16 carbon chains with a variable PEG)

General Structure:



n = the average number of ethylene glycol units (e.g., Isoceteth-5 is when n = 5); "iso" = a mixture of branched isomers, one example of which would be:



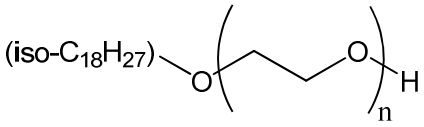
As these are mixtures of more than one isomer at unknown ratios, physical properties are not calculable.

INCI Name	Molecular Weight
Isoceteth-5 (CAS No. **69364-63-2**)	462.70
Isoceteth-7 (CAS No. **69364-63-2**)	550.81
Isoceteth-10 (CAS No. **69364-63-2**)	682.97
Isoceteth-12 (CAS No. **69364-63-2**)	771.07
Isoceteth-15 (CAS No. **69364-63-2**)	903.23
Isoceteth-20 (CAS No. **69364-63-2**)	1123.49
Isoceteth-25 (CAS No. **69364-63-2**)	1343.75
Isoceteth-30 (CAS No. **69364-63-2**)	1564.02

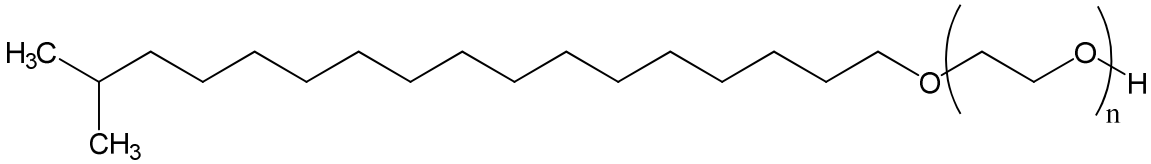
Table 3. Structures and Physical Properties (continued)

Isosteareths (mixture of various branched 18 carbon chains with a variable PEG)

General Structure:



n = the average number of ethylene glycol units (e.g., Isosteareth-6 is when n = 6); "iso" = a mixture of branched isomers, one example of which would be:



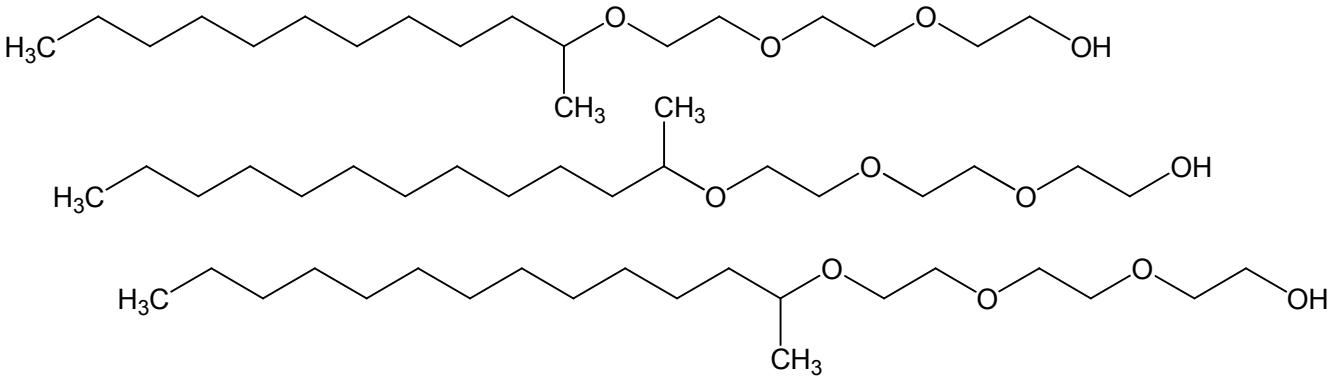
As these are mixtures of more than one isomer at unknown ratios, physical properties are not calculable.

INCI Name	Molecular Weight
Isosteareth-2 (CAS No. **52292-17-8**)	358.60
Isosteareth-3 (CAS No. **52292-17-8**)	402.65
Isosteareth-5 (CAS No. **52292-17-8**)	490.76
Isosteareth-8 (CAS No. **52292-17-8**)	622.91
Isosteareth-10 (CAS No. **52292-17-8**)	711.02
Isosteareth-12 (CAS No. **52292-17-8**)	799.12
Isosteareth-15 (CAS No. **52292-17-8**)	931.28
Isosteareth-16 (CAS No. **52292-17-8**)	975.33
Isosteareth-20 (CAS No. **52292-17-8**)	1151.54
Isosteareth-22 (CAS No. **52292-17-8**)	1239.65
Isosteareth-25 (CAS No. **52292-17-8**)	1371.81
Isosteareth-50 (CAS No. **52292-17-8**)	2473.12

Table 3. Structures and Physical Properties (continued)

***sec*-Pareths** (mixture of variable length α-branched carbons chains with a variable PEG)

Structure Example: C12-14 *sec*-Pareth-3

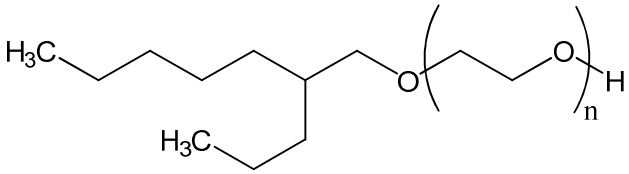


As these are mixtures of more than one molecule at unknown ratios, molecular weights and physical properties are not calculable.

INCI Name	
C11-15 Sec-Pareth-12 (CAS No. **68131-40-8**)	Molecular weight < 1000
C12-14 Sec-Pareth-3 (CAS No. **84133-50-6**)	Molecular weight < 1000
C12-14 Sec-Pareth-5 (CAS No. **84133-50-6**)	Molecular weight < 1000
C12-14 Sec-Pareth-7 (CAS No. **84133-50-6**)	Molecular weight < 1000
C12-14 Sec-Pareth-8 (CAS No. **84133-50-6**)	Molecular weight < 1000
C12-14 Sec-Pareth-9 (CAS No. **84133-50-6**)	Molecular weight < 1000
C12-14 Sec-Pareth-12 (CAS No. **84133-50-6**)	Molecular weight < 1000
C12-14 Sec-Pareth-15 (CAS No. **84133-50-6**)	Molecular weight < 1000
C12-14 Sec-Pareth-20 (CAS No. **84133-50-6**)	Molecular weight ~ 1000
C12-14 Sec-Pareth-30 (CAS No. **84133-50-6**)	Molecular weight > 1000
C12-14 Sec-Pareth-40 (CAS No. **84133-50-6**)	Molecular weight > 1000
C12-14 Sec-Pareth-50 (CAS No. **84133-50-6**)	Molecular weight > 1000

PEG Propylheptyl Ethers (3 carbon chain β-substituted 7 carbon chain with a variable PEG)

General Structure:



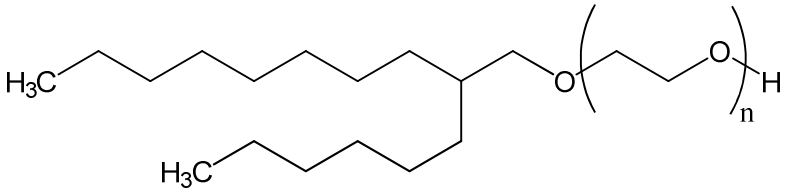
n = the average number of ethylene glycol units (e.g., PEG-7 Propylheptyl Ether is when n = 7)

INCI Name	Molecular Weight	M.P. / B.P.	$logK_{o/w}$
PEG-7 Propylheptyl Ether	466.65	201/502°C	1.79
PEG-8 Propylheptyl Ether	510.70	227/537°C	1.52

Table 3. Structures and Physical Properties (continued)

Hexyldeceths (6 carbon chain beta-substituted (β-substituted) ten carbon chain with a variable PEG)

General Structure:

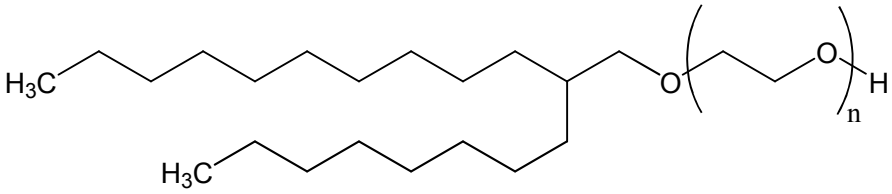


n = the average number of ethylene glycol units (e.g., Hexyldeceth-2 is when n = 2)

INCI Name	Molecular Weight	M.P. / B.P.	$logK_{o/w}$
Hexyldeceth-2 (CAS No. **52609-19-5**)	330.55	125/395 °C	6.11
Hexyldeceth-20 (CAS No. **52609-19-5**)	1123.49	--/1030 °C	1.17

Octyldodeceths (8 carbon chain β-substituted 12 carbon chain with a variable PEG)

General Structure:



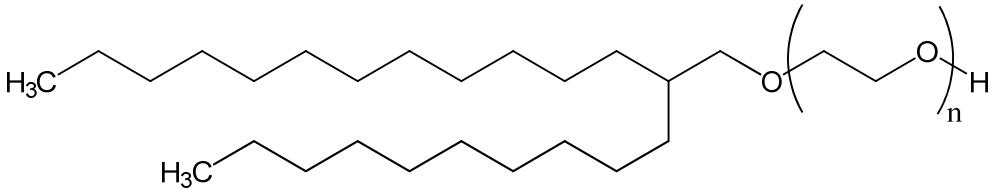
n = the average number of ethylene glycol units (e.g., Octyldodeceth-2 is when n = 2)

INCI Name	Molecular Weight	M.P. / B.P.	$logK_{o/w}$
Octyldodeceth-2 (CAS No. **32128-65-7**)	386.65	161/441°C	8.08
Octyldodeceth-5 (CAS No. **32128-65-7**)	518.81	227/547 °C	7.25
Octyldodeceth-10 (CAS No. **32128-65-7**)	739.07	317/723 °C	5.88
Octyldodeceth-16 (CAS No. **32128-65-7**)	1003.39	--/935 °C	4.23
Octyldodeceth-20 (CAS No. **32128-65-7**)	1179.60	--/1076 °C	3.14
Octyldodeceth-25 (CAS No. **32128-65-7**)	1399.86	--/1252 °C	1.77
Octyldodeceth-30 (CAS No. **32128-65-7**)	1620.12	--/1429 °C	0.39

Table 3. Structures and Physical Properties (continued)

Decyltetradeceths (10 carbon chain β-substituted 14 carbon chain with a variable PEG)

General Structure:



n = the average number of ethylene glycol units (e.g., Decyltetradeceth-15 is when n = 15)

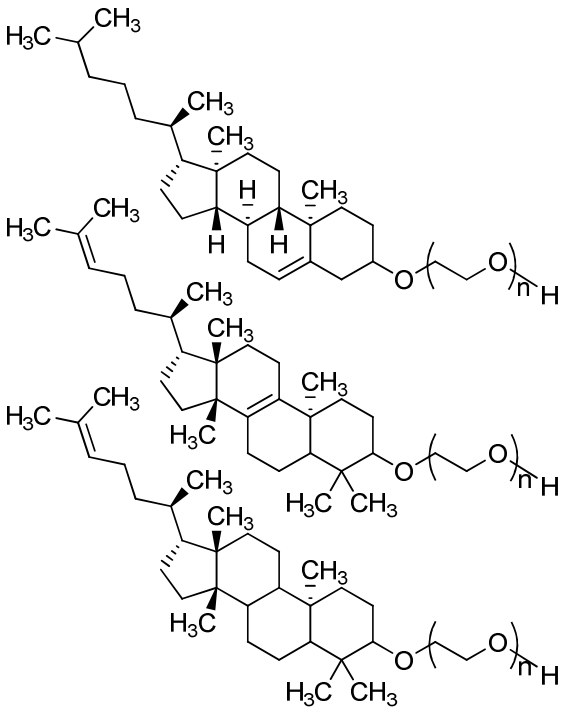
INCI Name	Molecular Weight	M.P. / B.P.	$logK_{o/w}$
Decyltetradeceth-5	574.92	256/594	9.22
Decyltetradeceth-10	795.18	339/770	7.85
Decyltetradeceth-15	1015.44	--/946	6.47
Decyltetradeceth-20	1235.70	--/1123	5.10
Decyltetradeceth-25	1455.97	--/1299	3.73
Decyltetradeceth-30	1676.23	--/1475	2.36

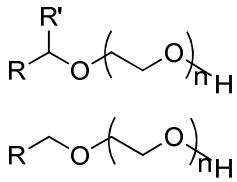
Table 3. Structures and Physical Properties (continued)

Sterol Containing PEG Ethers

Laneths (mixture of various length saturated and partially unsaturated, straight and branched alkyl chains; cholesterol; lanosterol; and dihydrolanosterol with a variable PEG)

General Structure:





R & R' = saturated or partially unsaturated alkyl chains of various lengths

n = the average number of ethylene glycol units (e.g., Laneth-25 is when n = 25)

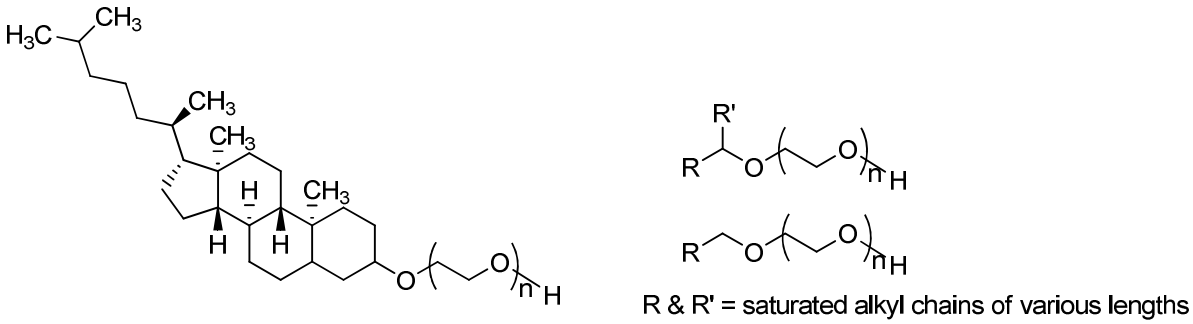
As these are mixtures of more than one molecule at unknown ratios, molecular weights and physical properties are not calculable.

INCI Name	
Laneth-5* (CAS No. **61791-20-6**)	Molecular weight < 1000
Laneth-10 (CAS No. **61791-20-6**)	Molecular weight < 1000
Laneth-15 (CAS No. **61791-20-6**)	Molecular weight > 1000
Laneth-16* (CAS No. **61791-20-6**)	Molecular weight > 1000
Laneth-20 (CAS No. **61791-20-6**)	Molecular weight > 1000
Laneth-25* (CAS No. **61791-20-6**)	Molecular weight > 1000
Laneth-40 (CAS No. **61791-20-6**)	Molecular weight > 1000
Laneth-50 (CAS No. **61791-20-6**)	Molecular weight > 1000
Laneth-60 (CAS No. **61791-20-6**)	Molecular weight > 1000
Laneth-75 (CAS No. **61791-20-6**)	Molecular weight > 1000

Table 3. Structures and Physical Properties (continued)

Hydrogenated Laneths (mixture of various length saturated alkyl chains and dihydrocholesterol with a variable PEG)

General Structure:



n = the average number of ethylene glycol units (e.g., Hydrogenated Laneth-5 is when n = 5)

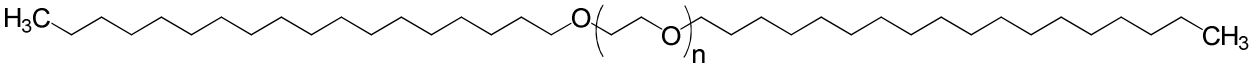
As these are mixtures of more than one molecule at unknown ratios, molecular weights and physical properties are not calculable.

INCI Name	
Hydrogenated Laneth-5	Molecular weight < 1000
Hydrogenated Laneth-20	Molecular weight > 1000
Hydrogenated Laneth-25	Molecular weight > 1000

Dialkyl PEG Ethers

Hydrogenated Dimer Dilinoleths and PEG-4 Distearyl Ether (variable PEG capped at each end with a saturated 18 carbon chain)

General Structure:

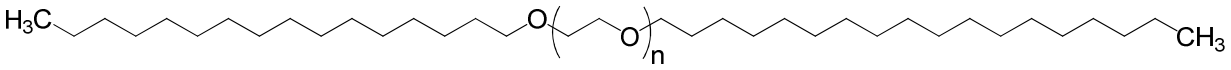


n = the average number of ethylene glycol units (e.g., Hydrogenated Dimer Dilinoeth-60 is when n = 60; PEG-4 Distearyl Ether is when n = 4)

INCI Name	Molecular Weight	M.P. / B.P.	$logK_{o/w}$
PEG-4 Distearyl Ether	699.18	294/673 °C	15.67
Hydrogenated Dimer Dilinoleth-20	1404.02	--/1237 °C	11.28
Hydrogenated Dimer Dilinoleth-30	1844.55	--/1599 °C	8.53
Hydrogenated Dimer Dilinoleth-40	2285.07	--/1943 °C	5.79
Hydrogenated Dimer Dilinoleth-60	3166.13	--/--	--
Hydrogenated Dimer Dilinoleth-80	4047.18	--/--	--

Table 3. Structures and Physical Properties (continued)

PEG Cetyl Stearyl Diether and Steareth-60 Cetyl Ether (variable PEG capped at one end with a saturated 18 carbon chain and at the other end with a saturated 16 carbon chain)
Structure:

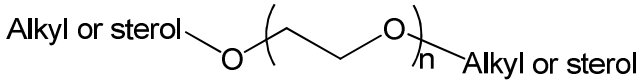


n = the average number of ethylene glycol units (e.g., Steareth-60 Cetyl Ether is when n = 60)

As the number of ethylene glycol units present in PEG-Cetyl Stearyl Diether is unknown, molecular weight and physical properties are not calculable.

INCI Name	Molecular Weight	M.P. / B.P.	$logK_{o/w}$
PEG-Cetyl Stearyl Diether	--	--/--	--
Steareth-60 Cetyl Ether (CAS No. **9005-00-9**)	3138.07	--/--	--

PEG-4 Ditallow Ether (a 4 unit PEG independently capped at each end with one of a 14, 18, 18, Ω-9 unsaturated 18, Ω-6 unsaturated 18, or Ω-3 unsaturated 18 carbon chain) and ***PEG-16 Cetyl/Oleyl/Stearyl/Lanolin Alcohol Ether*** (a 16 unit PEG independently capped at each end with a variable length saturated or partially unsaturated alkyl chain, cholesterol, lanosterol or dihydrolanosterol)
General Structure:



n = the average number of ethylene glycol units (e.g., PEG-16 Cetyl/Oleyl/Stearyl/Lanolin Alcohol Ether is when n = 16)

As these are mixtures of more than one molecule at unknown ratios, molecular weights and physical properties are not calculable.

INCI Name	
PEG-4 Ditallow Ether	Molecular weight < 1000
PEG-16 Cetyl/Oleyl/Stearyl/Lanolin Alcohol Ether	--

"*" indicates those ingredients previously assessed by the CIR Expert Panel.

Table 4a. Current and historical frequency and concentration of use according to duration and type of exposure - previously reviewed ingredients

	# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)	
	1981[1]	2010[25]	1981[1]	2010[27]	1981[1].	2010[25]	1981[1]	2010[27]	1996[3]	2010[25]	1996[3]	2010[27]	1996[3]	2010[25]	1996[3]	2010[27]
	Laureth-4				**Laureth-23**				**Ceteth-1**				**Ceteth-2**			
Totals[b]	**202**	**441**	**≤25**	**0.0002-21**	**218**	**404**	**≤5**	**0.0002-8**	**NR**	**NR**	**NR**	**0.2-3**	**33**	**214**	**5[c]**	**0.2-4**
Duration of Use																
Leave-On	*134*	*236*	*≤10*	*0.002-21*	*52*	*197*	*≤5*	*0.003-3*	*NR*	*NR*	*NR*	*0.3-2*	*8*	*17*	*NR*	*0.5-4*
Rinse Off	*68*	*205*	*≤25*	*0.0002-12*	*166*	*207*	*≤5*	*0.0002-8*	*NR*	*NR*	*NR*	*0.2-3*	*25*	*197*	*5*	*0.2-3*
Exposure Type																
Eye Area	86	40	0.1-5	0.007-4	2	12	1-5	0.003-0.09	NR	NR	NR	0.4	NR	3	NR	NR
Possible Ingestion	NR	NR	NR	0.02-0.2	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Inhalation	2	7	≤0.1	NR	2	1	≤5	3	NR	NR	NR	NR	NR	NR	NR	NR
Dermal Contact	151	264	≤10	0.0002-21	60	147	≤5	0.0002-7	NR	NR	NR	0.2-2	8	11	NR	0.5-3
Deodorant (underarm)	15	9	0.1-10	0.8	10	15	0.1-5	0.4-2	NR	NR	NR	NR	NR	NR	NR	0.8-3
Hair - Non-Coloring	28	145	≤10	0.01-4	147	145	≤5	0.008-8	NR	NR	NR	0.2-3	23	22	5	0.2-4
Hair-Coloring	21	30	0.1-25	0.04-6	6	107	≤5	0.04-2	NR	NR	NR	0.7	NR	180	NR	0.5
Nail	2	NR	1-5	2-7	5	1	≤1	2	NR	NR	NR	NR	2	1	NR	NR
Mucous Membrane	7	70	0.1-10	0.0002-2	9	10	≤5	0.0002-2	NR	NR	NR	0.2	2	NR	NR	NR
Bath Products	8	15	0.1-10	8-12	3	2	0.1-1	NR	NR	NR	NR	NR	NR	NR	NR	NR
Baby Products	NR	15	NR	NR	1	2	0.1-1	NR	NR	NR	NR	NR	NR	NR	NR	NR

	# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)	
	1996[3]	2010[25]	1996[3]	2010[27]	1996[3]	2010[25]	1996[3]	2010[27]	1996[3]	2010[25]	1996[3]	2010[27]	1996[3]	2010[25]	1996[3]	2010[27]
	Ceteth-3				**Ceteth-5**				**Ceteth-6**				**Ceteth-10**			
Totals	**NR**	**NR**	**NR**	**0.2**	**2**	**NR**	**NR**	**NR**	**NR**	**NR**	**NR**	**0.006-0.06**	**16**	**36**	**0.15[c]**	**0.02-5**
Duration of Use																
Leave-On	*NR*	*NR*	*NR*	*NR*	*2*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*0.006*	*12*	*26*	*0.15*	*0.02-3*
Rinse Off	*NR*	*NR*	*NR*	*0.2*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*0.06*	*4*	*10*	*NR*	*0.6-5*
Exposure Type																
Eye Area	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	3	NR	0.1
Possible Ingestion	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Inhalation	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	1	1	0.15	NR
Dermal Contact	NR	NR	NR	NR	2	NR	NR	NR	NR	NR	NR	NR	11	26	NR	0.1-1
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	1	NR	NR
Hair - Non-Coloring	NR	NR	NR	0.2	NR	NR	NR	NR	NR	NR	NR	0.006-0.06	5	10	NR	3-5
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	0.02-0.08
Mucous Membrane	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Bath Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR

Table 4a. Current and historical frequency and concentration of use according to duration and type of exposure - previously reviewed ingredients (2010) - continued

	# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)	
	1996[3]	2010[25]	1996[3]	2010[27]	1996[3]	2010[25]	1996[3]	2010[27]	1996[3]	2010[25]	1996[3]	2010[27]	1996[3]	2010[25]	1996[3]	2010[27]
	Ceteth-12				**Ceteth-14**				**Ceteth-15**				**Ceteth-16**			
Totals	**3**	**NR**	**NR**	**0.02**	**2**	**NR**	**NR**	**NR**	**NR**	**7**	**NR**	**2**	**18**	**9**	**5[c]**	**0.06-1**
Duration of Use																
Leave-On	*2*	*NR*	*NR*	*0.02*	*NR*	*NR*	*NR*	*NR*	*NR*	*1*	*NR*	*NR*	*13*	*7*	*NR*	*0.06*
Rinse Off	*1*	*NR*	*NR*	*NR*	*2*	*NR*	*NR*	*NR*	*NR*	*6*	*NR*	*2*	*5*	*2*	*5*	*0.5-1*
Exposure Type																
Eye Area	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Possible Ingestion	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Inhalation	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Dermal Contact	1	NR	NR	0.02	2	NR	NR	NR	NR	1	NR	NR	11	7	NR	0.06
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	2	NR	NR	0.06
Hair - Non-Coloring	NR	NR	NR	NR	NR	NR	NR	NR	NR	2	NR	2	7	2	5	NR
Hair-Coloring	2	NR	NR	NR	NR	NR	NR	NR	NR	3	NR	NR	NR	NR	NR	0.5-1
Nail	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	1	NR	NR	NR	NR	NR	NR	NR	2	NR	NR	NR
Bath Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	1	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR

	# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)	
	1996[3]	2010[25]	1996[3]	2010[27]	1996[3]	2010[25]	1996[3]	2010[27]	1996[3]	2010[25]	1996[3]	2010[27]	1996[3]	2010[25]	1996[3]	2010[27]
	Ceteth-20				**Ceteth-24**				**Ceteth-25**				**Ceteth-29****			
Totals	**114**	**220**	**25[c]**	**0.04-4**	**67**	**169**	**NR**	**0.0009-2**	**1**	**1**	**NR**	**0.6-3**	**NR**	**NR**	**<1[c]**	**NR**
Duration of Use																
Leave-On	*43*	*145*	*25*	*0.2-3*	*42*	*117*	*NR*	*0.05-2*	*NR*	*1*	*NR*	*0.6-3*	*NR*	*NR*	*NR*	*NR*
Rinse Off	*8*	*75*	*NR*	*0.04-4*	*25*	*52*	*NR*	*0.0009-0.5*	*1*	*NR*	*NR*	*1-2*	*NR*	*NR*	*<1*	*NR*
Exposure Type																
Eye Area	NR	30	NR	0.3-0.9	3	3	NR	0.05-0.2	NR	NR	NR	NR	NR	NR	NR	NR
Possible Ingestion	NR	NR	NR	NR	1	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Inhalation	1	1	NR	2	5	NR	NR	0.2	NR	NR	NR	NR	NR	NR	NR	NR
Dermal Contact	54	190	NR	0.04-4	46	117	NR	0.0009-2	1	1	NR	1-3	NR	NR	NR	NR
Deodorant (underarm)	1	2	NR	0.82	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	46	28	NR	0.2-2	1	11	NR	0.05-0.5	NR	NR	NR	0.6	NR	NR	<1	NR
Hair-Coloring	9	NR	NR	NR	20	41	NR	NR	NR	NR	NR	1	NR	NR	NR	NR
Nail	NR	1	NR	0.8	NR	NR	NR	0.09	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	2	26	NR	0.04-4	NR	1	NR	0.0009	NR	NR	NR	NR	NR	NR	NR	NR
Bath Products	NR	NR	NR	NR	2	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Baby Products	1	NR	NR	NR	1	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR

Table 4a. Current and historical frequency and concentration of use according to duration and type of exposure - previously reviewed ingredients (2010) - continued

	# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)	
	1996[3]	2010[25]	1996[3]	2010[27]	1986[6]	2010[25]	1986[6]	2010[27]	1986[6]	2010[25]	1986[6]	2010[27]	1986[6]	2010[25]	1986[6]	2010[27]
	Ceteth-30				**Steareth-2**				**Steareth-4**				**Steareth-6**			
Totals	**2**	**1**	**NR**	**NR**	**107[d]**	**593**	**≤10[d]**	**0.008-10**	**NR**	**41**	**NR**	**0.02-3**	**NR**	**NR**	**NR**	**3**
Duration of Use																
Leave-On	*NR*	*NR*	*NR*	*NR*	*NR*	*527*	*NR*	*0.1-5*	*NR*	*2*	*NR*	*0.02-1*	*NR*	*NR*	*NR*	*3*
Rinse Off	*2*	*1*	*NR*	*NR*	*NR*	*66*	*NR*	*0.008-10*	*NR*	*39*	*NR*	*0.1-3*	*NR*	*NR*	*NR*	*NR*
Exposure Type																
Eye Area	NR	NR	NR	NR	NR	59	NR	0.2-3	NR	NR	NR	0.02	NR	NR	NR	NR
Possible Ingestion	NR	NR	NR	NR	NR	2	NR	1-2	NR	NR	NR	NR	NR	NR	NR	NR
Inhalation	NR	NR	NR	NR	NR	8	NR	0.8	NR	NR	NR	1	NR	NR	NR	NR
Dermal Contact	NR	NR	NR	NR	NR	545	NR	0.008-5	NR	38	NR	0.02-2	NR	NR	NR	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	58	NR	0.5-3	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	2	NR	NR	NR	NR	32	NR	1-10	NR	3	NR	0.1-3	NR	NR	NR	3
Hair-Coloring	NR	1	NR	NR	NR	1	NR	0.8-3	NR	NR	NR	0.5	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	2	NR	5	NR	NR	NR	0.06	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	NR	19	NR	0.008-3	NR	25	NR	0.1-2	NR	NR	NR	NR
Bath Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	9	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	2	NR	4	NR	NR	NR	NR	NR	NR	NR	NR

	# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)	
	1986[6]	2010[25]	1986[6]	2010[27]	1986[6]	2010[25]	1986[6]	2010[27]	1986[6]	2010[25]	1986[6]	2010[27]	1986[6]	2010[25]	1986[6]	2010[27]
	Steareth-7				**Steareth-10**				**Steareth-15**				**Steareth-20**			
Totals	**NR**	**10**	**NR**	**NR**	**Nr [e]**	**49**	**NR [e]**	**0.5-4**	**NR [e]**	**2**	**NR [e]**	**NR**	**NR [e]**	**433**	**NR [e]**	**0.006-20**
Duration of Use																
Leave-On	*NR*	*5*	*NR*	*NR*	*NR*	*46*	*NR*	*0.5-4*	*NR*	*2*	*NR*	*NR*	*NR*	*377*	*NR*	*0.006-20*
Rinse Off	*NR*	*5*	*NR*	*NR*	*NR*	*3*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*56*	*NR*	*0.007-3*
Exposure Type																
Eye Area	NR	NR	NR	NR	NR	6	NR	0.5-2	NR	NR	NR	NR	NR	59	NR	0.02-4
Possible Ingestion	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Inhalation	NR	NR	NR	NR	NR	1	NR	NR	NR	1	NR	NR	NR	2	NR	NR
Dermal Contact	NR	9	NR	NR	NR	48	NR	0.5-4	NR	2	NR	NR	NR	380	NR	0.006-8
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR	NR	1	NR	NR	NR	49	NR	0.6-2
Hair - Non-Coloring	NR	1	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	46	NR	0.01-20
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	3
Nail	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	1	NR	0.7-2
Mucous Membrane	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	11	NR	0.007-2
Bath Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	1	NR	NR
Baby Products	NR	1	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR

Table 4a. Current and historical frequency and concentration of use according to duration and type of exposure - previously reviewed ingredients (2010) - continued

	# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)	
	1996[2]	2010[25]	1996[2]	2010[27]	1996[2]	2010[25]	1996[2]	2010[27]	1996[2]	2010[25]	1996[2]	2010[27]	1996[2]	2010[25]	1996[2]	2010[27]
	Ceteareth-2				**Ceteareth-3**				**Ceteareth-4**				**Ceteareth-5**			
Totals	**NR**	**NR**	**NR**	**2**	**1**	**10**	**5[c]**	**2**	**NR**	**1**	**NR**	**NR**	**20**	**24**	**10[c]**	**NR**
Duration of Use					**1**											
Leave-On	*NR*	*NR*	*NR*	*NR*	*1*	*8*	*NR*	*2*	*NR*	*1*	*NR*	*NR*	*14*	*7*	*NR*	*NR*
Rinse Off	*NR*	*NR*	*NR*	*2*	*NR*	*2*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*6*	*17*	*NR*	*NR*
Exposure Type																
Eye Area	NR	NR	NR	NR	NR	1	NR	NR	NR	NR	NR	NR	1	NR	NR	NR
Possible Ingestion	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Inhalation	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Dermal Contact	NR	NR	NR	NR	1	9	NR	NR	NR	NR	NR	NR	12	5	NR	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	2	NR	NR	NR	NR	NR	1	NR	NR	7	3	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	1	16	NR	NR
Nail	NR	NR	NR	NR	NR	1	NR	2	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Bath Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR

	# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)	
	1996[2]	2010[25]	1996[2]	2010[27]	1996[2]	2010[25]	1996[2]	2010[27]	1996[2]	2010[25]	1996[2]	2010[27]	1996[2]	2010[25]	1996[2]	2010[27]
	Ceteareth-6				**Ceteareth-7**				**Ceteareth-10**				**Ceteareth-12**			
Totals	**9**	**36**	**25[c]**	**0.008-5**	**NR**	**NR**	**NR**	**0.2**	**29**	**2**	**5[c]**	**0.003-11**	**57**	**127**	**50[c]**	**0.02-4**
Duration of Use																
Leave-On	*3*	*26*	*NR*	*0.008-0.8*	*NR*	*NR*	*NR*	*NR*	*3*	*1*	*NR*	*0.003-11*	*43*	*93*	*NR*	*0.02-2*
Rinse Off	*6*	*10*	*NR*	*2*	*NR*	*NR*	*NR*	*0.2*	*26*	*1*	*NR*	*0.5-2*	*14*	*34*	*NR*	*0.1-4*
Exposure Type																
Eye Area	1	1	NR	NR	NR	NR	NR	NR	NR	NR	NR	0.02-8	NR	4	NR	0.02-0.1
Possible Ingestion	2	2	NR	NR	NR	NR	NR	NR	NR	NR	NR	11	NR	NR	NR	NR
Inhalation	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	1	1	NR	0.3
Dermal Contact	8	34	NR	0.008-2	NR	NR	NR	NR	2	2	NR	0.003-11	55	114	NR	0.02-4
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	3	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	NR	NR	NR	0.2	NR	NR	NR	NR	2	13	NR	0.3-1
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR	26	NR	NR	0.5-2	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR	1	NR	NR	NR	NR	NR	NR	2
Mucous Membrane	NR	1	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	4	NR	NR
Bath Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Baby Products	NR	14	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	1	NR	NR

Table 4a. Current and historical frequency and concentration of use according to duration and type of exposure - previously reviewed ingredients (2010) - continued

	# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)	
	1996[2]	2010[25]	1996[2]	2010[27]	1996[2]	2010[25]	1996[2]	2010[27]	1996[2]	2010[25]	1996[2]	2010[27]	1996[2]	2010[25]	1996[2]	2010[27]
	Ceteareth-15				**Ceteareth-16**				**Ceteareth-17**				**Ceteareth-20**			
Totals	**11**	**6**	**10**	**0.2-10**	**NR**	**1**	**NR**	**NR**	**NR**	**NR**	**5[c]**	**NR**	**452**	**955**	**10[c]**	**0.008-11**
Duration of Use																
Leave-On	*2*	*5*	*3.5*	*0.2-10*	*NR*	*1*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*156*	*630*	*NR*	*0.02-11*
Rinse Off	*9*	*1*	*10*	*1-2*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*296*	*326*	*NR*	*0.008-10*
Exposure Type																
Eye Area	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	5	19	NR	0.02-3
Possible Ingestion	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Inhalation	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	1	5	NR	0.8
Dermal Contact	2	5	1.35	1-4	NR	1	NR	NR	NR	NR	NR	NR	203	673	NR	0.02-4
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	16	NR	0.5
Hair - Non-Coloring	1	1	10	0.2-10	NR	NR	NR	NR	NR	NR	NR	NR	136	166	NR	0.008-11
Hair-Coloring	8	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	112	113	NR	0.3-10
Nail	NR	NR	3.5	4	NR	NR	NR	NR	NR	NR	NR	NR	NR	1	NR	3-5
Mucous Membrane	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	2	6	NR	0.2-3
Bath Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	1	2	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	1	2	NR	NR

	# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)	
	1996[2]	2010[25]	1996[2]	2010[27]	1996[2]	2010[25]	1996[2]	2010[27]	1996[2]	2010[25]	1996[2]	2010[27]	1996[2]	2010[25]	1996[2]	2010[27]
	Ceteareth-22				**Ceteareth-23**				**Ceteareth-25**				**Ceteareth-30**			
Totals	**NR**	**NR**	**NR**	**1**	**NR**	**3**	**NR**	**NR**	**33**	**308**	**NR**	**0.03-16**	**26**	**42**	**NR**	**0.09-0.3**
Duration of Use																
Leave-On	*NR*	*NR*	*NR*	*1*	*NR*	*NR*	*NR*	*NR*	*1*	*73*	*NR*	*0.1-16*	*11*	*14*	*NR*	*0.09-0.3*
Rinse Off	*NR*	*NR*	*NR*	*NR*	*NR*	*3*	*NR*	*NR*	*32*	*234*	*NR*	*0.03-2*	*15*	*28*	*NR*	*NR*
Exposure Type																
Eye Area	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	1	1	NR	NR
Possible Ingestion	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Inhalation	NR	NR	NR	NR	NR	NR	NR	NR	NR	2	NR	NR	NR	NR	NR	NR
Dermal Contact	NR	NR	NR	1	NR	NR	NR	NR	1	39	NR	0.1-16	13	15	NR	0.09-0.3
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	0.5	1	1	NR	0.3
Hair - Non-Coloring	NR	NR	NR	NR	NR	NR	NR	NR	2	59	NR	0.03-8	5	1	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	3	NR	NR	30	210	NR	0.3-2	8	26	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR	NR	1	NR	14-16	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	NR	NR	NR	NR	NR	1	NR	NR	NR	NR	NR	NR
Bath Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	1	NR	0.1	NR	NR	NR	NR

Table 4a. Current and historical frequency and concentration of use according to duration and type of exposure - previously reviewed ingredients (2010) - continued

	# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)	
	1996[2]	2010[25]	1996[2]	2010[27]	1996[2]	2010[25]	1996[2]	2010[27]	1996[2]	2010[25]	1996[2]	2010[27]	1996[2]	2010[25]	1996[2]	2010[27]
	Ceteareth-33				**Ceteareth-50**				**Ceteareth-60**				**Ceteareth-100**			
Totals	**5**	**82**	**NR**	**0.2-9**	**NR**	**44**	**NR**	**3-6**	**NR**	**5**	**NR**	**NR**	**37**	**37**	**NR**	**NR**
Duration of Use																
Leave-On	*1*	*46*	*NR*	*0.2-8*	*NR*	*NR*	*NR*	*4*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Rinse Off	*4*	*36*	*NR*	*0.8-9*	*NR*	*44*	*NR*	*3-6*	*NR*	*5*	*NR*	*NR*	*37*	*37*	*NR*	*NR*
Exposure Type																
Eye Area	NR	1	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Possible Ingestion	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Inhalation	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Dermal Contact	1	49	NR	0.2-8	NR	NR	NR	4	NR	NR	NR	NR	NR	NR	NR	NR
Deodorant (underarm)	NR	NR	NR	1-5	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	4	26	NR	0.8-9	NR	NR	NR	NR	NR	2	NR	NR	NR	NR	NR	NR
Hair-Coloring	NR	7	NR	2	NR	44	NR	3-6	NR	3	NR	NR	37	37	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Bath Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR

	# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)	
	1996[4]	2010[25]	1996[4]	2010[27]	1996[4]	2010[25]	1996[4]	2010[27]	1996[4]	2010[25]	1996[4]	2010[27]	1996[4]	2010[25]	1996[4]	2010[27]
	Oleth-2				**Oleth-3**				**Oleth-4**				**Oleth-5**			
Totals	**14**	**177**	**≤25[c]**	**0.1-18**	**11**	**34**	**NR**	**0.3-10**	**NR**	**NR**	**NR**	**1-4**	**26**	**174**	**NR**	**0.06-10**
Duration of Use																
Leave-On	*5*	*25*	*≤25*	*0.1-10*	*6*	*23*	*NR*	*0.3-4*	*NR*	*NR*	*NR*	*NR*	*16*	*38*	*NR*	*0.3-10*
Rinse Off	*9*	*152*	*NR*	*0.2-18*	*5*	*11*	*NR*	*7-10*	*NR*	*NR*	*NR*	*1-4*	*10*	*136*	*NR*	*0.06-10*
Exposure Type																
Eye Area	NR	NR	NR	NR	NR	NR	NR	0.4	NR	NR	NR	NR	NR	NR	NR	0.3
Possible Ingestion	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Inhalation	NR	NR	NR	0.1-5	1	1	NR	NR	NR	NR	NR	NR	3	NR	NR	NR
Dermal Contact	6	17	NR	0.3-6	6	8	NR	0.3-7	NR	NR	NR	NR	17	14	NR	0.3-10
Deodorant (underarm)	NR	2	NR	0.4	NR	NR	NR	1	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	8	14	≤25	0.1-10	5	20	NR	4	NR	NR	NR	1	9	36	NR	0.06-10
Hair-Coloring	NR	146	NR	0.2-18	NR	6	NR	10	NR	NR	NR	4	NR	126	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	3-4
Mucous Membrane	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Bath Products	3	2	NR	6	NR	NR	NR	7	NR	NR	NR	NR	1	2	NR	10
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR

Table 4a. Current and historical frequency and concentration of use according to duration and type of exposure - previously reviewed ingredients (2010) - continued

	# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)	
	1996[4]	2010[25]	1996[4]	2010[27]	1996[4]	2010[25]	1996[4]	2010[27]	1996[4]	2010[25]	1996[4]	2010[27]	1996[4]	2010[25]	1996[4]	2010[27]
	Oleth-8				**Oleth-9**				**Oleth-10**				**Oleth-12**			
Totals	**8**	**NR**	**NR**	**1-2**	**2**	**NR**	**NR**	**NR**	**97**	**370**	**25[c]**	**0.2-14**	**NR**	**1**	**NR**	**1-2**
Duration of Use																
Leave-On	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*48*	*57*	*NR*	*0.2-14*	*NR*	*1*	*NR*	*1-2*
Rinse Off	*8*	*NR*	*NR*	*1-2*	*2*	*NR*	*NR*	*NR*	*49*	*313*	*NR*	*0.2-5*	*NR*	*NR*	*NR*	*NR*
Exposure Type																
Eye Area	NR	NR	NR	NR	NR	NR	NR	NR	3	2	NR	0.5	NR	NR	NR	1
Possible Ingestion	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	0.2	NR	NR	NR	NR
Inhalation	NR	NR	NR	NR	NR	NR	NR	NR	7	5	NR	4-6	NR	NR	NR	NR
Dermal Contact	NR	NR	NR	NR	2	NR	NR	NR	64	44	25	0.2-6	NR	1	NR	1-2
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	0.5	NR	NR	NR	NR
Hair - Non-Coloring	8	NR	NR	1-2	NR	NR	NR	NR	12	115	25	0.3-14	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR	21	213	NR	0.2-5	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	NR	NR	NR	NR	1	6	NR	0.5-3	NR	NR	NR	NR
Bath Products	NR	NR	NR	NR	2	NR	NR	NR	1	1	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR

	# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)	
	1996[4]	2010[25]	1996[4]	2010[27]	1996[4]	2010[25]	1996[4]	2010[27]	1996[4]	2010[25]	1996[4]	2010[27]	1996[4]	2010[25]	1996[4]	2010[27]
	Oleth-15				**Oleth-16**				**Oleth-20**				**Oleth-25**			
Totals	**3**	**NR**	**NR**	**0.4-0.7**	**13**	**9**	**5[c]**	**0.03-0.8**	**321**	**246**	**25[c]**	**0.01-17**	**3**	**3**	**NR**	**0.2**
Duration of Use																
Leave-On	*3*	*NR*	*NR*	*0.4*	*9*	*7*	*NR*	*0.03-0.5*	*205*	*146*	*25*	*0.1-17*	*3*	*3*	*NR*	*NR*
Rinse Off	*NR*	*NR*	*NR*	*0.7*	*4*	*2*	*NR*	*0.8*	*116*	*100*	*NR*	*0.01-6*	*NR*	*NR*	*NR*	*0.2*
Exposure Type																
Eye Area	2	NR	NR	NR	NR	NR	NR	NR	2	6	NR	2	NR	NR	NR	NR
Possible Ingestion	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	0.2	NR	NR	NR	NR
Inhalation	NR	NR	NR	NR	NR	NR	NR	0.06	5	3	25	NR	NR	NR	NR	NR
Dermal Contact	3	NR	NR	0.4-0.7	5	7	NR	0.03-0.06	91	104	25	0.1-4	3	3	NR	NR
Deodorant (underarm)	1	NR	NR	NR	NR	NR	NR	0.06	1	12	NR	0.9-3	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	8	2	NR	NR	225	139	NR	0.01-17	NR	NR	NR	0.2
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	0.8	4	3	NR	1	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR	1	NR	NR	4	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	NR	NR	NR	NR	4	22	NR	4	NR	NR	NR	NR
Bath Products	NR	NR	NR	NR	1	NR	NR	NR	3	2	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	0.03	4	NR	NR	NR	NR	NR	NR	NR

Table 4a. Current and historical frequency and concentration of use according to duration and type of exposure - previously reviewed ingredients (2010) - continued

	# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)	
	1996[4]	2010[25]	1996[4]	2010[27]	1996[4]	2010[25]	1996[4]	2010[27]	1976[5]	2010[25]	1976[5]	2010[27]	1976[5]	2010[25]	1976[5]	2010[27]
	Oleth-30				Oleth-50				Laneth-5				Laneth-16			
Totals	**200**	**213**	**NR**	**3-8**	**NR**	**NR**	**NR**	**0.3-4**	**46**	**44**	**0.1-10**	**0.8**	**40**	**17**	**≤5**	**0.08-2**
Duration of Use																
Leave-On	*18*	*1*	*NR*	*NR*	*NR*	*NR*	*NR*	*1*	*12*	*2*	*0.1-10*	*NR*	*22*	*14*	*≤5*	*0.08*
Rinse Off	*182*	*212*	*NR*	*3-8*	*NR*	*NR*	*NR*	*0.3-4*	*34*	*42*	*0.1-5*	*0.8*	*18*	*3*	*≤5*	*0.7-2*
Exposure Type																
Eye Area	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	1	NR	NR
Possible Ingestion	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Inhalation	17	NR	NR	NR	NR	NR	NR	NR	1	NR	1-5	NR	6	NR	≤5	NR
Dermal Contact	1	1	NR	8	NR	NR	NR	1-4	13	3	0.1-10	NR	26	14	≤5	0.08
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	2	NR	0.1-5	0.08
Hair - Non-Coloring	NR	NR	NR	NR	NR	NR	NR	0.5-2	2	NR	1-5	NR	12	2	≤5	NR
Hair-Coloring	199	212	NR	3	NR	NR	NR	0.3	31	41	0.1-5	0.8	1	NR	1-5	0.7-2
Nail	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	NR	NR	NR	NR	NR	1	NR	NR	2	NR	0.1-5	NR
Bath Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	3	NR	0.1-5	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR

	# of Uses		Conc. of Use (%)	
	1976[5]	2010[25]	1976[5]	2010[27]
	Laneth-25			
Totals	**9**	**3**	**0.1-10**	**NR**
Duration of Use				
Leave-On	*6*	*3*	*0.1-10*	*NR*
Rinse Off	*3*	*NR*	*0.1-5*	*NR*
Exposure Type				
Eye Area	NR	NR	NR	NR
Possible Ingestion	NR	NR	NR	NR
Inhalation	5	NR	1-5	NR
Dermal Contact	7	3	0.1-10	NR
Deodorant (underarm)	NR	NR	NR	NR
Hair - Non-Coloring	2	NR	0.1-5	NR
Hair-Coloring	NR	NR	NR	NR
Nail	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR
Bath Products	1	NR	1-5	NR
Baby Products	NR	NR	NR	NR

[b]Note - 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.

[c]only the maximum concentration was specified in the original report

[d]information on use per category not specified in the original report

[e]use indicated in original report, but included in combination with other ingredients and not given individually

[f]this ingredient was reported to be used in the orginial report, but now has noreported use

**this ingredient had concentration of use information listed in the original report, but it was not then and is not now listed in the International Cosmetic Ingredient Dictionary and Handbook

NR - not reported to be used

Table 4b. Frequency and concentration of use according to duration and type of exposure - newly reviewed ingredients

	# of Uses[25]	Conc of Use (%)[26]	# of Uses[25]	Conc of Use (%)[26]	# of Uses[25]	Conc of Use (%)[26]	# of Uses[25]	Conc of Use (%)[26]	# of Uses[25]	Conc of Use (%)[26]	# of Uses[25]	Conc of Use (%)[26]
	Laureth-1		**Laureth-2**		**Laureth-3**		**Laureth-5**		**Laureth-6**		**Laureth-7**	
Totals[a]	**1**	**7-15**	**176**	**0.005-9**	**97**	**0.0004-20**	**NR**	**0.0002**	**2**	**6-8**	**932**	**0.001-4**
Duration of Use												
Leave-On	*NR*	*NR*	*9*	*0.005-7*	*33*	*0.02-0.8*	*NR*	*0.0002*	*NR*	*NR*	*853*	*0.001-4*
Rinse Off	*1*	*7-15*	*167*	*0.2-9*	*64*	*0.0004-20*	*NR*	*NR*	*2*	*6-8*	*79*	*0.2-2*
Exposure Type												
Eye Area	NR	NR	NR	0.2	NR	NR	NR	NR	NR	NR	70	0.02-0.4
Possible Ingestion	NR	NR	NR	0.005	NR	NR	NR	NR	NR	NR	NR	0.05-00.4
Inhalation	NR	NR	NR	0.8	NR	NR	NR	NR	NR	NR	5	NR
Dermal Contact	NR	7	76	0.005-7	55	0.0004-0.8	NR	NR	NR	6-8	828	0.01-4
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	1	NR
Hair - Non-Coloring	NR	12	43	0.6-5	14	0.5-1	NR	0.0002	1	NR	91	0.047-2
Hair-Coloring	1	15	57	0.2-9	28	2-20	NR	NR	1	NR	8	0.2-0.3
Nail	NR	NR	NR	NR	1	NR	NR	NR	NR	NR	4	0.02-0.1
Mucous Membrane	NR	NR	41	0.5-0.9	4	0.02	NR	NR	NR	6-8	4	0.02-0.2
Bath Products	NR	NR	7	NR	19	NR	NR	NR	NR	NR	5	NR
Baby Products	NR	NR	2	NR	NR	NR	NR	NR	NR	NR	7	NR

	Laureth-8		**Laureth-9**		**Laureth-10**		**Laureth-11**		**Laureth-12**		**Laureth-14**	
Totals	**NR**	**0.05-8**	**110**	**0.0003-2**	**71**	**0.05-8**	**17**	**2-5**	**241**	**0.02-6**	**1**	**NR**
Duration of Use												
Leave-On	*NR*	*0.05-0.2*	*23*	*0.0003-1*	*5*	*0.4-0.5*	*6*	*2*	*10*	*0.02-2*	*NR*	*NR*
Rinse Off	*NR*	*6-8*	*87*	*0.006-2*	*66*	*0.05-8*	*11*	*5*	*231*	*0.3-6*	*1*	*NR*
Exposure Type												
Eye Area	NR	0.08	NR	1	NR	NR	NR	NR	2	0.05-0.06	NR	NR
Possible Ingestion	NR	NR	NR	NR	NR	NR	NR	NR	1	NR	NR	NR
Inhalation	NR	NR	1	0.3	1	NR	NR	NR	NR	NR	NR	NR
Dermal Contact	NR	0.05-8	6	0.3-1	43	0.05-8	NR	2	29	0.02-6	1	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	100	0.0003-2	27	0.09-5	17	5	10	0.3-3	NR	NR
Hair-Coloring	NR	NR	4	NR	1	NR	NR	NR	202	1-5	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	6-8	2	NR	14	0.05-8	NR	NR	18	6	1	NR
Bath Products	NR	NR	2	NR	10	NR	NR	NR	1	NR	NR	NR
Baby Products	NR	NR	NR	NR	2	NR	NR	N0	NR	NR	NR	NR

Table 4b. Frequency and concentration of use according to duration and type of exposure - newly reviewed ingredients (continued)

	# of Uses[25]	Conc of Use (%)[26]	# of Uses[25]	Conc of Use (%)[26]	# of Uses[25]	Conc of Use (%)[26]	# of Uses[25]	Conc of Use (%)[26]	# of Uses[25]	Conc of Use (%)[26]	# of Uses[25]	Conc of Use (%)[26]
	Laureth-16		**Laureth-20**		**Laureth-21**		**Laureth-25**		**Laureth-30**		**Beheneth-10**	
Totals	**12**	**3**	**6**	**0.0008-5**	**14**	**0.003-0.6**	**4**	**0.03-3**	**3**	**0.02-0.3**	**13**	**0.5-5**
Duration of Use												
Leave-On	*NR*	*NR*	*6*	*0.0008-0.06*	*14*	*0.003-0.6*	*NR*	*3*	*3*	*0.02-0.3*	*8*	*0.5-4*
Rinse Off	*12*	*3*	*NR*	*5*	*NR*	*NR*	*4*	*0.03-0.2*	*NR*	*0.07*	*5*	*5*
Exposure Type												
Eye Area	NR	NR	4	0.02-0.06	13	0.003-0.6	NR	3	2	03.02-0.3	NR	5
Possible Ingestion	NR	NR	NR	NR	NR	0.03	NR	NR	NR	NR	NR	NR
Inhalation	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Dermal Contact	NR	NR	2	0.0008-0.05	4	0.003-0.6	NR	3	1	0.07-0.3	11	0.5-5
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	1
Hair - Non-Coloring	12	3	NR	5	NR	NR	4	0.03-0.2	NR	NR	2	4
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR	NR	0.07	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	2	NR
Bath Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR

	Beheneth-20		**Beheneth-25**		**Beheneth-30**		**Deceth-3**		**Deceth-5**		**Deceth-7**	
Totals	**9**	**0.7-2**	**17**	**1-3**	**6**	**0.2-3**	**235**	**NR**	**74**	**NR**	**6**	**1**
Duration of Use												
Leave-On	*9*	*0.7-2*	*17*	*1-3*	*6*	*0.3-3*	*NR*	*NR*	*NR*	*NR*	*3*	*1*
Rinse Off	*NR*	*NR*	*NR*	*1*	*NR*	*0.2*	*235*	*NR*	*74*	*NR*	*3*	*1*
Exposure Type												
Eye Area	3	0.7	2	3	3	1-3	NR	NR	NR	NR	NR	NR
Possible Ingestion	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Inhalation	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	2	NR
Dermal Contact	9	0.7-2	17	1-3	4	0.3-3	NR	NR	NR	NR	3	1
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	1	NR	NR	NR	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	235	NR	74	NR	NR	NR
Nail	NR	NR	NR	NR	1	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	NR	0.2	NR	NR	NR	NR	NR	1
Bath Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	3	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR

Table 4b. Frequency and concentration of use according to duration and type of exposure - newly reviewed ingredients (continued)

	# of Uses[25]	*Conc of Use (%)*[26]	*# of Uses*[25]	*Conc of Use (%)*[26]	*# of Uses*[25]	*Conc of Use (%)*[26]	*# of Uses*[25]	*Conc of Use (%)*[26]	*# of Uses*[25]	*Conc of Use (%)*[26]	*# of Uses*[25]	*Conc of Use (%)*[26]
	Deceth-8		**Deceth-9**		**Myreth-3**		**Myreth-4**		**Myreth-10**		**Steareth-16**	
Totals	**5**	**NR**	**NR**	**18-23**	**NR**	**3**	**NR**	**0.02-0.4**	**2**	**NR**	**9**	**0.2-1**
Duration of Use												
Leave-On	*3*	*NR*	*NR*	*18*	*NR*	*3*	*NR*	*0.02-0.4*	*2*	*NR*	*7*	*0.2*
Rinse Off	*2*	*NR*	*NR*	*23*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*2*	*0.4-1*
Exposure Type												
Eye Area	NR	NR	NR	18	NR	NR	NR	NR	NR	NR	NR	NR
Possible Ingestion	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Inhalation	NR	NR	NR	NR	NR	NR	NR	0.02-0.4	NR	NR	NR	0.2
Dermal Contact	5	NR	NR	NR	NR	3	NR	NR	2	NR	7	0.2
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	2	NR
Hair-Coloring	NR	NR	NR	23	NR	NR	NR	NR	NR	NR	NR	0.4-1
Nail	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Bath Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR

	Steareth-21		**Steareth-25**		**Steareth-30**		**Steareth-33****		**Steareth-50**		**Steareth-100**	
Totals	**891**	**0.01-7**	**6**	**0.3-2**	**7**	**0.5**	**1**	**NR**	**NR**	**4**	**51**	**0.02-6**
Duration of Use												
Leave-On	*379*	*0.01-7*	*6*	*0.3-2*	*2*	*NR*	*NR*	*NR*	*NR*	*4*	*43*	*0.3-6*
Rinse Off	*512*	*0.04-5*	*NR*	*NR*	*5*	*0.5*	*1*	*NR*	*NR*	*NR*	*8*	*0.02-0.5*
Exposure Type												
Eye Area	43	0.4-2	NR	NR	NR	NR	NR	NR	NR	NR	1	0.3-1
Possible Ingestion	1	0.5-1	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Inhalation	3	2	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Dermal Contact	399	0.04-4	6	0.3-2	6	NR	1	NR	NR	4	47	0.02-6
Deodorant (underarm)	19	0.8-2	NR	NR	NR	NR	NR	NR	NR	NR	17	2-6
Hair - Non-Coloring	104	<1-7	NR	NR	1	0.5	NR	NR	NR	NR	3	2
Hair-Coloring	388	0.5--5	NR	NR	NR	NR	NR	NR	NR	NR	1	0.3
Nail	1	0.01-1	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	6	0.04-2	NR	NR	NR	NR	NR	NR	NR	NR	NR	0.5
Bath Products	3	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	0.02
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR

Table 4b. Frequency and concentration of use according to duration and type of exposure - newly reviewed ingredients (continued)

	# of Uses[25]	Conc of Use (%)[26]	# of Uses[25]	Conc of Use (%)[26]	# of Uses[25]	Conc of Use (%)[26]	# of Uses[25]	Conc of Use (%)[26]	# of Uses[25]	Conc of Use (%)[26]	# of Uses[25]	Conc of Use (%)[26]
	Steareth-200		**Trideceth-3**		**Trideceth-5**		**Trideceth-6**		**Trideceth-7**		**Tricedeceth-8**	
Totals	**NR**	**1**	**19**	**4**	**12**	**0.2-0.9**	**189**	**0.008-6**	**2**	**NR**	**NR**	**0.1**
Duration of Use												
Leave-On	*NR*	*NR*	*5*	*NR*	*NR*	*0.9*	*88*	*0.008-0.5*	*2*	*NR*	*NR*	*0.1*
Rinse Off	*NR*	*1*	*14*	*4*	*12*	*0.2-0.9*	*90*	*0.1-6*	*NR*	*NR*	*NR*	*NR*
Exposure Type												
Eye Area	NR	NR	NR	NR	NR	NR	1	NR	NR	NR	NR	NR
Possible Ingestion	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Inhalation	NR	NR	NR	NR	NR	NR	2	0.06	NR	NR	NR	NR
Dermal Contact	NR	1	11	4	NR	NR	93	0.06-5	2	NR	NR	0.1
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	8	NR	11	NR	82	0.1-6	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	1	0.2-0.9	14	5	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	0.008-0.08	NR	NR	NR	NR
Mucous Membrane	NR	NR	10	4	NR	NR	2	NR	NR	NR	NR	NR
Bath Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	0.5	NR	NR	NR	NR

	Trideceth-9		**Trideceth-10**		**Trideceth-12**		**Undeceth-3**		**Undecdeth-5**		**Undeceth-11**	
Totals	**135**	**0.00001-13**	**36**	**0.06-3**	**601**	**0.005-2**	**79**	**37**	**23**	**0.02-0.2**	**23**	**0.04**
Duration of Use												
Leave-On	*79*	*0.002-8*	*17*	*0.06-0.5*	*195*	*0.006-0.5*	*NR*	*NR*	*7*	*0.02-0.2*	*7*	*0.04*
Rinse Off	*56*	*0.00001-13*	*19*	*0.1-3*	*406*	*0.005-2*	*79*	*37*	*16*	*NR*	*16*	*NR*
Exposure Type												
Eye Area	2	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Possible Ingestion	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Inhalation	5	4	NR	NR	1	0.02-0.08	NR	NR	NR	NR	NR	NR
Dermal Contact	92	0.0003-13	8	0.006-3	4	0.005-0.5	NR	NR	1	NR	1	NR
Deodorant (underarm)	1	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	43	0.00001-1	28	0.1-0.5	506	0.006-2	NR	NR	21	0.02-0.2	21	0.04
Hair-Coloring	NR	NR	NR	NR	91	0.06-0.3	79	37	1	NR	1	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	17	NR	NR	NR	NR	NR	NR	NR	1	NR	1	NR
Bath Products	2	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Baby Products	1	NR	NR	NR	NR	0.2	NR	NR	NR	NR	NR	NR

Table 4b. Frequency and concentration of use according to duration and type of exposure - newly reviewed ingredients (continued)

	# of Uses[25]	Conc of Use (%)[26]	# of Uses[25]	Conc of Use (%)[26]	# of Uses[25]	Conc of Use (%)[26]	# of Uses[25]	Conc of Use (%)[26]	# of Uses[25]	Conc of Use (%)[26]	# of Uses[25]	Conc of Use (%)[26]
	Methoxy PEG-16		**C9-11 Pareth-6**		**C9-11 Pareth-8**		**C11-15 Pareth-3**		**C11-15 Pareth-5**		**C11-15 Pareth-7**	
Totals	**NR**	**0.4**	**NR**	**5**	**NR**	**0.3**	**11**	**16**	**1**	**NR**	**187**	**0.00008-1**
Duration of Use												
Leave-On	*NR*	*NR*	*NR*	*NR*	*NR*	*0.3*	*NR*	*NR*	*1*	*NR*	*69*	*0.008-1*
Rinse Off	*NR*	*0.4*	*NR*	*5*	*NR*	*NR*	*11*	*16*	*NR*	*NR*	*118*	*0.00008-1*
Exposure Type												
Eye Area	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	1	0.03
Possible Ingestion	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	0.3
Inhalation	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	2	0.008-0.07
Dermal Contact	NR	0.4	NR	NR	NR	NR	NR	NR	1	NR	NR	0.02-0.3
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	NR	0.3	NR	NR	NR	NR	182	0.00008-1
Hair-Coloring	NR	NR	NR	NR	NR	NR	11	16	NR	NR	4	1
Nail	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Bath Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR

	C11-15 Pareth-9		C11-15 Pareth-40		C12-13 Pareth-3		C12-13 Pareth-7		C12-13 Pareth-23		C12-14 Pareth-3	
Totals	**137**	**0.1-6**	**1**	**NR**	**73**	**0.009-32**	**NR**	**0.09**	**46**	**0.02-0.2**	**NR**	**0.5**
Duration of Use												
Leave-On	*7*	*0.1-6*	*1*	*NR*	*35*	*0.009-25*	*NR*	*NR*	*25*	*0.04-0.2*	*NR*	*0.5*
Rinse Off	*130*	*NR*	*NR*	*NR*	*38*	*0.2-32*	*NR*	*0.09*	*21*	*0.02-0.06*	*NR*	*NR*
Exposure Type												
Eye Area	NR	NR	NR	NR	NR	0.04	NR	NR	NR	0.06	NR	NR
Possible Ingestion	NR	NR	NR	NR	1	NR	NR	NR	1	NR	NR	NR
Inhalation	1	6	NR	NR	NR	0.1	NR	NR	NR	NR	NR	NR
Dermal Contact	1	6	NR	NR	53	0.009-32	NR	NR	26	0.04-0.2	NR	0.5
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	7	0.1	1	NR	20	0.02-0.1	NR	0.09	20	0.02-0.06	NR	NR
Hair-Coloring	129	NR	NR	NR	NR	0.1	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	2	8	NR	NR	2	NR	NR	NR
Bath Products	NR	NR	NR	NR	16	9-32	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR	2	NR	NR	NR

Table 4b. Frequency and concentration of use according to duration and type of exposure - newly reviewed ingredients (continued)

	# of Uses[25]	Conc of Use (%)[26]	# of Uses[25]	Conc of Use (%)[26]	# of Uses[25]	Conc of Use (%)[26]	# of Uses[25]	Conc of Use (%)[26]	# of Uses[25]	Conc of Use (%)[26]	# of Uses[25]	Conc of Use (%)[26]
	C12-14 Pareth-12		**C12-15 Pareth-3**		**C12-15 Pareth-7**		**C12-15 Pareth-9**		**C12-15 Pareth-12**		**C12-16 Pareth-7**	
Totals	**41**	**0.02-3**	**231**	**0.001-25**	**7**	**0.5-0.7**	**NR**	**0.00003-0.06**	**NR**	**0.5-22**	**NR**	**0.02-0.1**
Duration of Use												
Leave-On	*33*	*0.08-3*	*NR*	*0.001-3*	*7*	*0.5*	*NR*	*0.003*	*NR*	*0.6-2*	*NR*	*0.04*
Rinse Off	*8*	*0.02-0.04*	*231*	*0.0001-25*	*NR*	*0.7*	*NR*	*0.00003-0.06*	*NR*	*0.5-22*	*NR*	*0.02-0.1*
Exposure Type												
Eye Area	NR	2	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Possible Ingestion	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Inhalation	NR	NR	NR	3	NR	NR	NR	0.003	NR	NR	NR	NR
Dermal Contact	31	0.08-3	NR	0.0001-3	7	0.5-0.7	NR	0.006	NR	0.6-22	NR	NR
Deodorant (underarm)	NR	NR	NR	0.0001	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	10	0.02-0.08	2	0.0001-0.05	NR	NR	NR	0.00003-0.06	NR	0.5-2	NR	0.02-0.1
Hair-Coloring	NR	NR	229	25	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	0.2	NR	NR	NR	NR	NR	2	NR	NR
Mucous Membrane	NR	NR	NR	NR	NR	NR	NR	NR	NR	22	NR	NR
Bath Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	2	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR

	C12-16 Pareth-9		C20-40 Pareth-3		C20-40 Pareth-10		C20-40 Pareth-40		C20-40 Pareth-95		Oleth-82	
Totals	**78**	**0.003-0.02**	**NR**	**2**	**16**	**0.05-13**	**1**	**2**	**1**	**1-7**	**2**	**NR**
Duration of Use												
Leave-On	*11*	*NR*	*NR*	*NR*	*14*	*0.05-0.9*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Rinse Off	*67*	*0.003-0.02*	*NR*	*2*	*2*	*13*	*1*	*2*	*1*	*1-7*	*2*	*NR*
Exposure Type												
Eye Area	NR	NR	NR	NR	NR	0.7	NR	NR	NR	NR	NR	NR
Possible Ingestion	NR	NR	NR	NR	5	0.9	NR	NR	NR	NR	NR	NR
Inhalation	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Dermal Contact	NR	NR	NR	2	16	0.05-13	1	2	1	1-7	NR	NR
Deodorant (underarm)	NR	NR	NR	NR	8	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	78	0.003-0.02	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	2	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	NR	NR	NR	NR	NR	7	NR	NR
Bath Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR

Table 4b. Frequency and concentration of use according to duration and type of exposure - newly reviewed ingredients (continued)

	# of Uses[25]	Conc of Use (%)[26]	# of Uses[25]	Conc of Use (%)[26]	# of Uses[25]	Conc of Use (%)[26]	# of Uses[25]	Conc of Use (%)[26]	# of Uses[25]	Conc of Use (%)[26]	# of Uses[25]	Conc of Use (%)[26]
	Oleth-106		**Ceteth-25**		**Coceth-7**		**Coceth-8**		**Coceth-10**		**Talloweth-4**	
Totals	**NR**	**5**	**1**	**NR**	**7**	**0.2**	**10**	**NR**	**NR**	**0.04-0.2**	**NR**	**0.02**
Duration of Use												
Leave-On	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*0.2*	*NR*	*0.02*
Rinse Off	*NR*	*5*	*1*	*NR*	*7*	*0.2*	*10*	*NR*	*NR*	*0.04*	*NR*	*NR*
Exposure Type												
Eye Area	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Possible Ingestion	NR	NR	NR	NR	3	NR	NR	NR	NR	NR	NR	NR
Inhalation	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Dermal Contact	NR	NR	1	NR	6	0.2	10	NR	NR	0.04-0.2	NR	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	1	NR	NR	NR	NR	NR	NR	NR
Hair-Coloring	NR	5	NR	NR	NR	0.2	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	0.02
Mucous Membrane	NR	NR	NR	NR	3	NR	10	NR	NR	NR	NR	NR
Bath Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR

	Talloweth-5		**Talloweth-6**		**Isodeceth-6**		**Isolaureth-6**		**Isoceteth-10**		**Isoceteth-20**	
Totals	**NR**	**0.002**	**NR**	**0.002**	**NR**	**0.6**	**22**	**0.0001**	**10**	**0.002-4**	**106**	**0.2-21**
Duration of Use												
Leave-On	*NR*	*NR*	*NR*	*NR*	*NR*	*0.6*	*4*	*NR*	*10*	*0.003-0.5*	*84*	*0.2-21*
Rinse Off	*NR*	*0.002*	*NR*	*0.002*	*NR*	*NR*	*17*	*0.0001*	*NR*	*0.002-0.5*	*22*	*0.3-2*
Exposure Type												
Eye Area	NR	NR	NR	NR	NR	NR	NR	NR	1	0.006	6	0.4-0.5
Possible Ingestion	NR	NR	NR	NR	NR	NR	NR	NR	NR	0.009	NR	NR
Inhalation	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	2
Dermal Contact	NR	0.002	NR	NR	NR	0.6	NR	NR	10	0.003-0.1	32	0.2-4
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	1	NR
Hair - Non-Coloring	NR	NR	NR	0.002	NR	NR	13	0.0001	NR	0.002-4	68	0.2-21
Hair-Coloring	NR	NR	NR	NR	NR	NR	9	NR	NR	NR	NR	0.4
Nail	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	0.002	NR	NR	NR	NR	NR	NR	NR	NR	1	0.5
Bath Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	0.5
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR

Table 4b. Frequency and concentration of use according to duration and type of exposure - newly reviewed ingredients (continued)

	# of Uses[25]	Conc of Use (%)[26]	# of Uses[25]	Conc of Use (%)[26]	# of Uses[25]	Conc of Use (%)[26]	# of Uses[25]	Conc of Use (%)[26]	# of Uses[25]	Conc of Use (%)[26]	# of Uses[25]	Conc of Use (%)[26]
	Isoceteth-25		**Isosteareth-2**		**Isosteareth-5**		**Isosteareth-10**		**Isosteareth-20**		**C12-14 Sec-Pareth-5**	
Totals	**1**	**0.002-0.1**	**2**	**1**	**NR**	**0.006**	**8**	**1**	**14**	**0.5-6**	**5**	**0.06-0.09**
Duration of Use												
Leave-On	*1*	*0.002-0.1*	*1*	*NR*	*NR*	*0.006*	*5*	*1*	*12*	*1-6*	*1*	*0.06*
Rinse Off	*NR*	*0.004*	*1*	*1*	*NR*	*NR*	*3*	*NR*	*2*	*0.5-2*	*4*	*0.09*
Exposure Type												
Eye Area	NR	NR	NR	NR	NR	NR	NR	NR	NR	0.8	NR	NR
Possible Ingestion	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Inhalation	NR	NR	1	NR	NR	NR	NR	NR	2	NR	NR	NR
Dermal Contact	1	0.1	NR	NR	NR	0.006	3	1	3	0.5-5	NR	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	1	1	3	1-5	NR	NR
Hair - Non-Coloring	NR	0.002-0.004	2	1	NR	NR	5	NR	11	2-6	5	0.06-0.09
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Bath Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR

	C12-14 Sec-Pareth-7		**PEG-7 Propylheptyl Ether**		**PEG-8 Propylheptyl Ether**		**Octyldodeceth-16**		**Octyldodeceth-20**		**Octyldodeceth-25**	
Totals	**5**	**0.03-0.05**	**12**	**NR**	**NR**	**0.005-0.05**	**1**	**0.1-2**	**17**	**0.1-18**	**10**	**0.1-17**
Duration of Use												
Leave-On	*2*	*0.03*	*NR*	*NR*	*NR*	*0.005-0.05*	*1*	*0.1-2*	*16*	*0.2-18*	*4*	*0.5-1*
Rinse Off	*3*	*0.05*	*12*	*NR*	*NR*	*NR*	*NR*	*0.5-1*	*1*	*0.1-2*	*6*	*0.1-17*
Exposure Type												
Eye Area	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	2	0.1
Possible Ingestion	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Inhalation	NR	NR	NR	NR	NR	0.005-0.05	NR	2	NR	4	NR	NR
Dermal Contact	NR	NR	NR	NR	NR	NR	1	0.1-2	15	0.2-18	10	0.1-17
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	1	NR	NR	NR	NR
Hair - Non-Coloring	5	0.03-0.05	12	NR	NR	NR	NR	1	2	0.1-1	NR	0.5
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	1	NR	NR	NR	0.5
Nail	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	NR	NR	NR	0.5	NR	2	NR	10
Bath Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR

Table 4b. Frequency and concentration of use according to duration and type of exposure - newly reviewed ingredients (continued)

	# of Uses[25]	Conc of Use (%)[26]	# of Uses[25]	Conc of Use (%)[26]	# of Uses[25]	Conc of Use (%)[26]	# of Uses[25]	Conc of Use (%)[26]
	Laneth-15		**Laneth-20**		**Laneth-40**		**PEG-4 Distearyl Ether**	
Totals	**44**	**0.1-30**	**4**	**0.5-0.7**	**NR**	**1-30**	**2**	**NR**
Duration of Use								
Leave-On	*9*	*0.1-3*	*3*	*0.5*	*NR*	*NR*	*NR*	*NR*
Rinse Off	*35*	*0.5-30*	*1*	*0.7*	*NR*	*1-30*	*2*	*NR*
Exposure Type								
Eye Area	NR	NR	NR	NR	NR	NR	NR	NR
Possible Ingestion	NR	NR	NR	NR	NR	NR	NR	NR
Inhalation	NR	NR	NR	NR	NR	NR	NR	NR
Dermal Contact	1	0.3	3	NR	NR	NR	NR	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	43	0.1-30	1	0.5-0.7	NR	1-30	2	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	NR	NR	NR	NR
Bath Products	NR	NR	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

NR - not reported

[a]Note - Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types my not equal the sum of total uses.

**this ingredient had frequency of use information available from FDA, but it is not then and is not now listed in the International Cosmetic Ingredient Dictionary and Handbook

Table 4c. Ingredients With No Reported Current Use

Arachideth-20
Beheneth-2
Beheneth-5
Beheneth-15
C9-11 Pareth-3
C9-11 Pareth-4
C9-15 Pareth-8
C10-16 Pareth-1
C10-16 Pareth-2
C11-13 Pareth-6
C11-13 Pareth-9
C11-13 Pareth-10
C11-15 Pareth-12
C11-15 Pareth-15
C11-15 Pareth-20
C11-15 Pareth-30
C11-21-Pareth-3
C11-21-Pareth-10
C12-13 Pareth-1
C12-13 Pareth-2
C12-13 Pareth-4
C12-13 Pareth-5
C12-13 Pareth-6
C12-13 Pareth-9
C12-13 Pareth-10
C12-13 Pareth-15
C12-14 Pareth-5
C12-14 Pareth-7
C12-14 Pareth-9
C12-15 Pareth-2
C12-15 Pareth-4
C12-15 Pareth-5
C12-15 Pareth-10
C12-15 Pareth-11
C12-16 Pareth-5
C13-15 Pareth-21
C14-15 Pareth-4
C14-15 Pareth-7
C14-15 Pareth-8
C14-15 Pareth-11
C14-15 Pareth-12
C14-15 Pareth-13
C20-22 Pareth-30
C20-40 Pareth-24
C22-24 Pareth-33
C30-50 Pareth-3
C30-50 Pareth-10
C30-50 Pareth-40
C40-60 Pareth-3
C40-60 Pareth-10
C11-15 Sec-Pareth-12
C12-14 Sec-Pareth-3
C12-14 Sec-Pareth-8
C12-14 Sec-Pareth-9
C12-14 Sec-Pareth-12
C12-14 Sec-Pareth-15
C12-14 Sec-Pareth-20
C12-14 Sec-Pareth-30
C12-14 Sec-Pareth-40
C12-14 Sec-Pareth-50
Capryleth-4
Capryleth-5
Ceteareth-4
Ceteareth-8
Ceteareth-9
Ceteareth-11
Ceteareth-13
Ceteareth-14
Ceteareth-16
Ceteareth-18
Ceteareth-23
Ceteareth-24
Ceteareth-27
Ceteareth-28
Ceteareth-29
Ceteareth-34
Ceteareth-40
Ceteareth-55
Ceteareth-60
Ceteareth-80
Ceteareth-100
Ceteth-4
Ceteth-5
Ceteth-7
Ceteth-13
Ceteth-14
Ceteth-17
Ceteth-18
Ceteth-23
Ceteth-30
Ceteth-40
Ceteth-45
Ceteth-150
Cetoleth-2
Cetoleth-4
Cetoleth-5
Cetoleth-6
Cetoleth-10
Cetoleth-11
Cetoleth-15
Cetoleth-18
Cetoleth-20
Cetoleth-22
Cetoleth-24
Cetoleth-30
Coceth-20
Coceth-25
Coceth-3
Coceth-5
Coceth-6
Deceth-4
Deceth-6
Deceth-10
Decyltetradeceth-10
Decyltetradeceth-15
Decyltetradeceth-20
Decyltetradeceth-25
Decyltetradeceth-30
Decyltetradeceth-5
Hexyldeceth-2
Hexyldeceth-20
Hydrogenated Dimer Dilinoleth-20
Hydrogenated Dimer Dilinoleth-30
Hydrogenated Dimer Dilinoleth-40
Hydrogenated Dimer Dilinoleth-60
Hydrogenated Dimer Dilinoleth-80
Hydrogenated Laneth-5
Hydrogenated Laneth-20
Hydrogenated Laneth-25
Hydrogenated Talloweth-12
Hydrogenated Talloweth-25
Isoceteth-5
Isoceteth-7
Isoceteth-12
Isoceteth-15
Isoceteth-30
Isodeceth-4
Isodeceth-5
Isolaureth-10
Isolaureth-3
Isomyreth-3
Isomyreth-9
Isostearet h-3
Isostearet h-8
Isostearet h-12
Isostearet h-15
Isostearet h-16
Isostearet h-22
Isostearet h-25
Isostearet h-50
Laneth-10
Laureth-13
Laureth-15
Laneth-50
Laneth-60
Laneth-75
Laureth-38
Laureth-40
Laureth-50
Methoxy PEG-7
Methoxy PEG-10
Methoxy PEG-25
Methoxy PEG-40
Methoxy PEG-100
Myreth-2
Myreth-5
Noneth-8
Octyldodeceth-2
Octyldodeceth-5
Octyldodeceth-10
Octyldodeceth-30
Oleth-6
Oleth-7
Oleth-9
Oleth-11
Oleth-23
Oleth-24
Oleth-35
Oleth-40
Oleth-44
Oleth-45
Oleth-100
Palmeth-2
PEG-16 Cetyl/Oleyl/Stearyl/Lanolin Alcohol Ether
PEG-Cetyl Stearyl Diether
PEG-4 Ditallow Ether
PEG-15 Jojoba Alcohol
PEG-26 Jojoba Alcohol
PEG-40 Jojoba Alcohol
PEG-3 Methyl Ether
PEG-4 Methyl Ether
PEG-6 Methyl Ether
PEG-7 Methyl Ether
Steareth-1
Steareth-3
Steareth-5
Steareth-7
Steareth-8
Steareth-11
Steareth-13
Steareth-14
Steareth-15
Steareth-27
Steareth-40
Steareth-80
Steareth-60 Cetyl Ether
Talloweth-18
Talloweth-7
Trideceth-2
Trideceth-4
Trideceth-11
Trideceth-15
Trideceth-18
Trideceth-20
Trideceth-21
Trideceth-50
Undeceth-40
Undeceth-7
Undeceth-8
Undeceth-9
Undecyleneth-6

Table 5. Acute toxicity studies

Ingredient	Animals	No./Group	Dose	LD_{50}	Reference
			ORAL		
Laureths					
Laureth-9	albino Swiss Webster mice	10 M		3300 mg/kg (24 h); 3050 mg/kg (7day)	43
compounds analogous to Laureth-9					
$C_{12-13}AE_{6.5}$	albino rats	5M/5F	25% aq solution, neat, 612-5000 mg/kg	2120 mg/kg	33
$C_{12-13}AE_{6.5}$	Fischer 344 rats	5 M/F	50% in corn oil, 900-2500 mg/kg	2500 mg/kg M); 1637 mg/kg (F)	33
$C_{12-15}AE_{7}$	Fischer 344 rats	5M/5F	undiluted, 700-5000 mg/kg	1642 mg/kg	33
$C_{12-15}AE_{11}$	rat	5M/5F	50% in corn oil, 1000-2000 mg/kg	>2000 mg/kg (M); 1000-2000 mg/kg (F)	33
$C_{12-14}AE_{6}$	rat	5M/5F	neat, 5010-10,000 mg/kg	4900 mg/kg	33
$C_{12-13}AE_{6.5}$	beagle			1650 mg/kg	33
$C_{14-15}AE_{7}$	monkey		neat	6700 mg/kg	33
Ceteths					
	ddY mice	10	undiluted	2880 mg/kg (M); 2602 mg/kg (F)	44
PEG Methyl Ethers					
PEG-3 Methyl Ether	Wistar rats			12.6 g/kg	20
PEG-3 Methyl ether	Carworth-Wistar rats	5	diluted with either water, corn oil, or agar	11.3 ml/kg (11.8 g/kg)	20
PEG-3 Methyl Ether	Carworth Farms-Nelson rats	males	4, 8, or 16 ml/kg	11.3 g/kg; all animals dosed with 16 ml/kg died in 1 day	20
PEG-7 Methyl Ethers	rats			>16 ml/kg	21
C9-11 Pareths					
C9-11 Pareth-3	rats			2700-10,000 mg/kg	46
C9-11 Pareth-5	rats			2900 mg/kg	46
C9-11 Pareth-6	rats			1200-4100 mg/kg	46
C9-11 Pareth-6	Fischer 344 rats	5M/5F	320-3260 mg/kg	1378 mg/kg	45
C9-11 Pareth-8	rats			1000-2700 mg/kg	46
C12-13 Pareths					
	Wistar albino rats	4M/4F	5 or 10 g/kg	10,000 mg/kg	**47**
C12-13 Pareth-2	Wistar albino rats	4M/4F	10 g/kg	>10,000 mg/kg	**48**
C12-13 Pareth-3	rats			7600 mg/kg	**46**
C12-13 Pareth-7	rats			4600 mg/kg	**46**
C12-15 Pareths					
C12-15 Pareth-3	rats			2300 mg/kg	**46**
C12-15 Pareth-7	rats			1700-2700 mg/kg	**46**
C12-15 Pareth-9	rats			1600-5600 mg/kg	**46**
C12-15 Pareth-12	rats			1800 mg/kg	**46**
C14-15 Pareths					
C14-15 Pareth-7	rats			2300-2700 mg/kg	46
C14-15 Pareth-11	rats			1000 mg/kg	46
C14-15 Pareth-13	rats			1000 mg/kg	46
			DERMAL		
Laureths					
Laureth-4	rabbits			0.93 ml/kg (males); 1.78 ml/kg (females); pulmonary lesions were observed with 3 days of a single dermal application	49
Laureth-4	rats			potential for neurotoxicity observed within 48 h after dosing (details not provided)	49
Analogs of Laureth-9 described in the SCCP opinion paper					
$C_{12-14}AE_{6}$	rabbits		neat	>2000 mg/kg	33
$C_{12-14}AE_{9}$	rabbits		neat	>2000 mg/kg	33

Table 5. Acute toxicity studies

Ingredient	Animals	No./Group	Dose	LD_{50}	Reference
$C_{12-15}AE_7$	rats	5M/5F	neat	>2000 mg/kg	33
$C_{13-15}AE_7$	rats	6M/6F	40% in corn oil; dosage volume to skin, 2.3 ml/kg	>920 mg/kg	33
PEG Methyl Ethers					
PEG-3 Methyl Ether	New Zealand White rabbits	2 or 5 M	2.5 (n=2), 5 (n=4), or 10 ml/kg (n=2); 24 h occlusive application	7.1 ml/kg (7.4 g/kg)	20
PEG-7 Methyl Ether	rabbits			>16 ml/kg	21
C9-11 Pareths					
C9-11 Pareth-3	rabbits			>5000 mg/kg	46
C9-11 Pareth-3	rats			>2000 mg/kg	46
C9-11 Pareth-5	rats			>2000 mg/kg	46
C9-11 Pareth-6	rabbits			>2000-5000 mg/kg	46
C9-11 Pareth-6	NZW rabbits	4M/4F	2.0 g/kg (occ.)	>2000 mg/kg; mild to moderate irritation observed at patch removal	45
C9-11 Pareth-8	rats			4000 mg/kg	46
C12-13 Pareths					
	Wistar albino rats	4M/4F	2.0 g/kg (occ.)	>2000 m/kg	47
C12-13 Pareth-2	Wistar albino rats	4M/4F	1, 2, or 4 g/kg (occ.)	> 2000 mg/kg; ~4000 mg/kg	48
C12-13 Pareth-3	rabbits			3300 mg/kg	46
C12-13 Pareth-7	rabbits			2000 mg/kg	46
C12-15 Pareths					
C12-15 Pareth-3	rabbits			3000 mg/kg	46
C12-15 Pareth-7	rabbits			2300-5000 mg/kg	46
C12-15 Pareth-9	rabbits			2500-3400 mg/kg	46
C12-15 Pareth-12	rabbits			2500 mg/kg	46
C14-15 Pareths					
C14-15 Pareth-7	rabbits			<5000 mg/kg	46
^{46}C14-15 Pareth-7	rats			>5000 mg/kg	46
C14-15 Pareth-11	rabbits			5000 mg/kg	46
C14-15 Pareth-13	rabbits			5000 mg/kg	46
			INHALATION		
Methyl Ethers					
PEG-3 Methyl Ether	Wistar rats		1 h exposure to 200 mg/l	no LC_{50} established; no mortality or toxicity observed	20
PEG-3 Methyl Ether	rats	6F	8 hr exposure to concentrated vapor	no LC_{50} established; no mortality	20
			PARENTERAL		
Laureths					
Laureth-9	albino Swiss Webster mice	10M		100 mg/kg (i.v.)	43
Laureth-9	Sprague-Dawley rats	12M	1%, intratracheally	Moderate pulmonary lesions were observed in the bronchi, bronchioles and alveoli after 1, 3, and 7 days	50

Table 6. Dermal irritation and sensitization

Ingredient	Concentration*	Animals	Procedure	Results	Reference
			Dermal Irritation		
Laureths					
laureth-9	undiluted	rabbits (number, gender strain not specified)	Draize test	slight irritation at intact sites and moderate irritation at abraded sites at 24 and 72 h	43
	15, 20% aq.			slight irritant effect on intact and abraded skin at 24 h	
laureth-9	20% in a contraceptive aerosol formulation	4 rabbits (gender and strain not specified)	Draize test	mild irritant	43
laureth (unspecified)	unspecified	6 male albino rabbits	0.10 g applied under occlusion	Strong irritant with necrosis occurring in 2 animals.	55
compounds analogous to Laureth-9					
$C_{14\text{-}15}AE_7$	10 or 25% m/v aq.; undiluted	rabbits	0.5 ml, semi-occluded, 4 h	PII = 1.7/8; not irritating	33
$C_{12\text{-}14}AE_{10}$	undiluted	rabbits	occlusive application, 4 h	PII = 4.1/8; moderate irritant	33
$C_{13}AE_6$	undiluted	rabbits	occlusive application, 4 h	PII = 5.1/8; moderate irritant	33
$C_{13}AE_{6.5}$	undiluted	rabbits`	occlusive application, 4 h	PII = 5.5/8; severe irritant	33
$C_{12\text{-}14}AE_6$	undiluted	rabbits	occlusive application, 4 h	PII = 6.3/8; severe irritant	33
$C_{14\text{-}15}AE_7$	undiluted	rabbits	occlusive application, 24 h	PII = 6.42/8; severe irritant; slight to moderate erythema and moderate to severe edema	33
PEG Methyl Ethers					
PEG-3 Methyl Ether	neat	5 New Zealand white rabbits	2.0 g/kg applied under occlusion; intact and abraded skin	intact skin: erythema in 4 rabbits; no edema abraded skin: erythema in 1 rabbit edema in 1 rabbit	20
PEG-3 Methyl Ether	undiluted	5 rabbits	0.01 ml applied uncovered for 24 h	irritation grade 2/10 (minimal irritation)	20
C9-11 Pareths					
C9-11 pareth-6	not specified	3 male and 3 female NZW rabbits	Draize test; 1" sq. of gauze used for application	moderately irritating	45
C9-11 pareth-3	undiluted	6 albino rabbits	Draize test	severely irritating	46
C9-11 pareth-5	undiluted	6 albino rabbits	Draize test	severely irritating	46
	0.1, 1, 10%	6 albino rabbits	Draize test	0.1% - non-irritating; 1% - minimally irritating; 10% - slightly irritating	
C9-11pareth-6	undiluted	6 albino rabbits	Draize test	severely irritating	46
	0.1, 1%	rabbits	Draize test	0.1% - non-irritating; 1% -slightly irritating	46
C9-11 pareth-8	undiluted	6 albino rabbits	Draize test	severely irritating	46

Table 6. Dermal irritation and sensitization

Ingredient	Concentration*	Animals	Procedure	Results	Reference
	0.1, 1, 10%	6 albino rabbits	Draize test	0.1% -minimally irritating; 1% - mildly irritating; 10% - moderately irritating	
C12-13 Pareths					
C12-13 pareth (unspecified)	undiluted	3 male NZW rabbits	Draize test	moderately irritating with necrosis and cracking of skin	47
C12-13 pareth-2	undiluted	3 male NZW rabbits	Draize test	moderately irritating with no necrosis observed	48
C12-13 pareth-3	undiluted	6 albino rabbits	Draize test	severely irritating	46
C12-13 pareth-7	undiluted	6 albino rabbits	Draize test	mildly to severely irritating	46
C12-13 pareth-7	0,1, 1, and 10%	6 albino rabbits	Draize test	0.1% - non-irritating; 1% - mildly irritating; 10% - moderately irritating	
C12-15 Pareths					
C12-15 pareth-3	undiluted	6 albino rabbits	Draize test	moderately to extremely irritating	46
C12-15 pareth-7	undiluted	6 albino rabbits	Draize test	moderately irritating	46
	0.1, 1, 10%	6 albino rabbits	Draize test	0.1, 1% - mildly irritating; 10% - moderately irritating	
C12-15 pareth-9	undiluted	6 albino rabbits	Draize test	severely irritating	46
	0.1, 1%	6 albino rabbits	Draize test	non-irritating	
C12-15 pareth-12	50%	6 albino rabbits	Draize test	minimally irritating	46
C14-15 Pareths					
C14-15 pareth-7	undiluted	6 albino rabbits	Draize test	severely irritating	46
	0.1, 1, and 10%	6 albino rabbits	Draize test	0.1% - minimally irritating; 1% - mildly irritating; 10% - moderately irritating	
C14-15 pareth-11	undiluted	6 albino rabbits	Draize test	moderately to severely irritating	46
	0.1, 1, and 10%	6 albino rabbits	Draize test	0.1% - non-irritating; 1% - slightly irritating; 10% - moderately to severely irritating	
C14-15 pareth-13	undiluted	6 albino rabbits	Draize test	moderately irritating	46
C14-15 pareth-18	undiluted	6 albino rabbits	Draize test	mildly irritating	46
	0.1, 1, and 10%	6 albino rabbits	Draize test	0.1% non-irritating; 1% - minimally irritating; 10% - slightly irritating	
Dermal Sensitization					
Laureths					
laureth-5	Induction: 10% aq. laureth-5, challenge: 0-5% aq. laureth-5	15 Dunkin-Hartley guinea pigs	Modified cumulative contact enhancement test	no sensitization reactions observed; confluent erythema observed at 96 h in 1 test and 1 control animal at the 5% challenge and at 48 and 72 h in 1-2 test and control animals at the 1% challenge.	23
laureth-9	0.02% aq. solution	Groups of 7 male guinea pigs	Intracutaneous test; injections 3w/wk for 10 injections; challenge was a single injection 2 wks later	no direct or delayed sensitization reactions	43

Table 6. Dermal irritation and sensitization

Ingredient	Concentration*	Animals	Procedure	Results	Reference
laureth-9	0.1% solution of an aerosol contraceptive formulation containing 20% laureth-9	Groups of 7 male guinea pigs	Intracutaneous test; injections 3x/wk for 10xs; challenge: single injection 2 wks later	no direct or delayed sensitization reactions	43
compounds analogous to Laureth-9					
$C_{12-15}AE_7$	intraderm. induction: 0.05% aq.; top. induction: 20% aq.; top. challenge: 15% aq.	20 test and 10 control guinea pigs	Magnusson-Kligman sensitization study	not sensitizing	33
$C_{14-15}AE_7$	intraderm. induction: 0.2% in corn oil.; top. induction: undiluted.; top. challenge: 60% in corn oil	20 test and 10 control guinea pigs	Magnusson-Kligman sensitization study	not sensitizing	33
$C_{12-14}AE_6$	induction: undiluted; challenge: 50% in deionized water	20 test and 10 control guinea pigs	Buehler method	not sensitizing	33
$C_{12-14}AE_9$	induction: undiluted; challenge: 50% in deionized water	21 test and 10 control guinea pigs	Buehler method	not sensitizing	33
laureth-9	0.1% solution of an aerosol contraceptive formulation containing 20% laureth-9	Groups of 7 male guinea pigs	Intracutaneous test; injections 3x/wk for 10 totals; challenge was a single injection 2 wks later	no direct or delayed sensitization reactions	43
C9-11 Pareths					
C9-11 pareth-6	1% aq.	4 groups of 5 male and 5 female Dunkin-Hartley albino guinea pigs	Buehler method	no sensitization reactions	45
C9-11 pareth-3	not specified	guinea pigs (number, gender, strain not specified)	not specified	not sensitizing	46
C9-11 pareth-5	not specified	guinea pigs (number, gender, strain not spec)	not specified	not sensitizing	46
C9-11 pareth-6	not specified	guinea pigs (number, gender, strain not specified)	not specified	not sensitizing	46
C9-11 pareth-8	not specified	guinea pigs (number, gender, strain not specified)	not specified	not sensitizing	46
C12-13 Pareths					
C12-13 pareth (unspecified)	intradermal induction: 0.5% , topical induction: 50%, challenge: 25% ; in corn oil	10 male and 10 female guinea pigs (strain not provided)	Magnusson-Kligman maximization study	Trace erythema was observed for 1 female test animal at each reading; test material was considered a very weak sensitizer	47
C12-13 pareth-2	intradermal induction: 0.10%; topical induction: undiluted; challenge: 50%; in corn oil	10 male and 10 female guinea pigs (strain not provided)	Magnusson-Kligman maximization study	not sensitizing	48

Table 6. Dermal irritation and sensitization

Ingredient	Concentration*	Animals	Procedure	Results	Reference
C12-13 pareth-3	not specified	guinea pigs (number, gender, strain not specified)	not specified	not sensitizing	46
C12-13 pareth-7	not specified	guinea pigs (number, gender, strain not specified)	not specified	non-sensitizing to low sensitizing	46
C12-15 Pareths					
C12-15 pareth-3	not specified	guinea pigs (number, gender, strain not specified)	not specified	not sensitizing	46
C12-15 pareth-7	not specified	guinea pigs (number, gender, strain not specified)	not specified	not sensitizing	46
C12-15 pareth-9	not specified	guinea pigs (number, gender, strain not specified)	not specified	not sensitizing	46
C14-15 Pareths					
C14-15 pareth-7	not specified	guinea pigs (number, gender, strain not specified)	not specified	not sensitizing	46
C14-15 pareth-11	not specified	guinea pigs (number, gender, strain not specified)	not specified	not sensitizing	46
C14-15 pareth-13	not specified	guinea pigs (number, gender, strain not specified)	not specified	not sensitizing	46
C14-15 pareth-18	not specified	guinea pigs (number, gender, strain not specified)	not specified	not sensitizing	46

*the vehicle is identified when known

Table 7. Ocular irritation

Ingredient	Concentration*	Animals	Procedure	Results	Reference
Laureths					
laureth-9	5% aq.	rabbits (number, gender strain unspecified)		not irritating; had a slight anesthetic effect on the eye	39
compounds analogous to Laureth-9					
$C_{12-14}AE_6$	undiluted	3 rabbits	Draize test	EII = 27.1/110; moderately irritating	33
$C_{13}AE_{5-6.5}$	undiluted	3 rabbits	Draize test	EII = 44/110; severely irritating	33
$C_{13}AE_6$	undiluted	3 rabbits	Draize test	EII = 44/110; severely irritating	33
$C_{12-14}AE_{10}$	undiluted	3 rabbits	Draize test	EII = 37/110; moderately to severely irritating	33
$C_{11-15}AE_{11}$	undiluted		Draize test	EII = 39/110; moderately to severely irritating	33
$C_{12-14}AE_7$	undiluted	9 rabbits	0.1 ml applied; eyes of 3 rabbits rinsed	$MAS_{unrinsed}$ = 18; MAS_{rinsed} = 12	33
$C_{14-15}AE_{11}$	undiluted	9 rabbits	0.1 ml applied; eyes of 3 rabbits rinsed	$MAS_{unrinsed}$ = 30.7; MAS_{rinsed} = 32	33
$C_{12-13}AE_{6.5}$	100%; 0.1, 1, 10% aq.	2 rabbits	0.2 ml placed in the conjunctival sac	100% - severely irritating; 10% - moderately irritating; 1 and 0.1% - non-irritating	33
$C_{12-15}AE_7$	undiluted and 0.5% aq.	3 rabbits	0.1 ml	$EII_{undiluted}$ = 27.8/110, moderately irritating; $EII_{0.5\%}$ = 0.2/110, not irritating	33
$C_{13-15}AE_{11}$	undiluted and 0.5% aq.	3 rabbits	0.1 ml	$EII_{undiluted}$ = 40.1/110, severely irritating; 0.5% - only minor signs of irritation	33
PEG Methyl Ethers					
PEG-3 Methyl Ether	various, unspecified	rabbits	various, unspecified	grade 1/10, slightly irritating	20
C9-11 Pareths					
C9-11 pareth-3	undiluted, unrinsed	albino rabbits (number and gender unspecified)	Draize test	severely irritating	46
	undiluted, rinsed			mildly irritating	
C9-11 pareth-5	undiluted, unrinsed	albino rabbits (number and gender unspecified)	Draize test	severely irritating	46
	0.1, 1, 10%			0.1 and 1% - non-irritating; 10% - moderately irritating	
C9-11 pareth-6	undiluted, unrinsed	albino rabbits (number and gender unspecified)	Draize test	severely irritating	46
	undiluted, rinsed			moderately to severely irritating	
	0.1, 1%			non-irritating	
C9-11 pareth-8	undiluted, unrinsed	albino rabbits (number and gender unspecified)	Draize test	severely irritating	46
	0.1, 1, 10%			0.1% - non-irritating; 1% - slightly irritating; 10% -severely irritating	
C12-13 Pareths					
C12-13 pareth-3	undiluted, unrinsed	albino rabbits (number and gender unspecified)	Draize test	moderately to extremely irritating	46
C12-13 pareth-7	undiluted, unrinsed	albino rabbits (number and gender unspecified)	Draize test	severely irritating	46

Table 7. Ocular irritation

Ingredient	Concentration*	Animals	Procedure	Results	Reference
C12-13 pareth-7	undiluted, rinsed	albino rabbits (number and gender unspecified)		minimally irritating	46
	0,1, 1, and 10%	albino rabbits (number and gender unspecified)		0.1 and 1% - non-irritating; 10% - moderately irritating	
C12-13 pareth (unspecified)	undiluted, unrinsed	3 NZW rabbits (gender unspecified)	0.2 ml placed in the conjunctival sac	mildly irritating	47
C12-13 pareth-2	undiluted, unrinsed	3 NZW rabbits (gender unspecified)	0.2 ml placed in the conjunctival sac	non-irritating	48
C12-15 Pareths					
C12-15 pareth-3	undiluted, unrinsed	albino rabbits (number and gender unspecified)	Draize test	severely irritating	46
C12-15 pareth-7	undiluted, unrinsed	albino rabbits (number and gender unspecified)	Draize test	moderately irritating	46
	undiluted, rinsed			mildly to moderately irritating	
	0.1, 1, 10%			0.1% - non-irritating; 1% - minimally irritating; 10% -mildly irritating	
C12-15 pareth-9	undiluted, unrinsed	albino rabbits (number and gender unspecified)	Draize test	severely to extremely irritating	46
	0.1, 1%			non-irritating	
C12-15 pareth-12	undiluted, unrinsed	albino rabbits (number and gender unspecified)	Draize test	severely irritating	46
C14-15 Pareths					
C14-15 pareth-7	undiluted, unrinsed	albino rabbits (number and gender unspecified)	Draize test	moderately to severely irritating	46
	undiluted, rinsed			mildly irritating	
	0.1, 1, and 10%			0.1 and 1% - non-irritating; 10% - mildly irritating	
C14-15 pareth-11	undiluted, unrinsed	albino rabbits (number and gender unspecified)	Draize test	severely irritating	46
	0.1, 1, and 10%			0.1% - non-irritating; 1% - slightly to mildly irritating; 10% - severely irritating	
C14-15 pareth-13	undiluted, unrinsed	albino rabbits (number and gender unspecified)	Draize test	severely irritating	46
C14-15 pareth-18	undiluted, unrinsed	albino rabbits (number and gender unspecified)	Draize test	minimally to mildly irritating	46
	0.1, 1, and 10%			0.1 and 1% - non-irritating; 10% - practically non- irritating	
Oleths					
oleth-20	5%	rabbits (number, gender strain unspecified)	Draize test	mild, transient conjunctival redness and chemosis	76

*the vehicle is identified when known

Table 8. Case reports

	Subject	Presentation	Follow-Up Testing/Discussion	Reference
			Laureths	
laureth-4	14 yr old female	eczematous lesions redeveloped after use of a commercial acne ointment	in patch-testing with the individual components of the ointment, the patient had strong reactions to 0.1 and 1% laureth-4 in ethanol; a control group of 20 patients did not react	73
laureth-4	79 yr old female	patient had a venous ulceration	10 patients with strong positive reactions to lanolin alcohol were patch tested with laureth-4 in ethanol; 1 patient had strong reactions to 0.1 and 1% and a weak reaction to 0.01%	73
laureth-7	21 yr old female	pruritic follicular papules on face; rash resolved after discontinuation of new cosmetics	patch testing with 1% laureth-7 caused papules at 72 h and follicular papules at 96 h; no irritation response in 6 normal subjects; a 7-day use test with 1% produced follicular papules in 7 days	72
laureth-9	52 yr old female	developed typical contact dermatitis after using an ointment containing laureth-9	Patch testing with 3% laurethh-9 was positive	71
laureth-9	16 patients	patients had chronic dermatitis	all 16 initially had positive patch test reactions to laureth-9; in repeat testing, only 2 of 6 patients had a positive reaction	68
laureth-9	32 yr old female	occurrence of eczema after using a new moisturizer lotion several times per day	in patch testing with the "Italian standard series" and her own product, reaction was only seen to the product; upon patch testing with product components, positive reactions were observed with laureth-9 (and polyquternium-7)	69
laureth-2; laureth-9	48 yr old female	patient had a significant reaction after using a hair dye, she then used a dry scalp shampoo and had an eczematous eruption over the scalp, down the neck, to the abdomen	patch testing found that in addition to p-phenylenediamine (PPD) and 4-aminophenol (hair dye ingredients), the subject reacted to 3% laureth-9 (a component of the shampoo) and to laureth-2	70
laureth-9	50-yr old female	following treatment with a microfoam of laureth-, the patient developed confluent erythematous and edematous papules where the product was applied, swelling and papules then spread	the patient and 5 controls were skin prick tested with 2% laureth-9 ; the patient and 2 controls had papular eruptions; the patient was later patch tested with 2% aq or 2% in petrolatum laureth-9; a pruritic eruption was reported 24 h after testing	36
laureth-12	47-yr old female	history of recurrent facial swelling and scalp irritation following hair dye use	patch testing with hair dye constituents reported positive reactions to laureth-12 (and t-butylhydroquinone); patch testing was negative for PPD	67
			Oleths	
oleth-5	30-yr old male	patient had an urticarial rash linked to use of a finishing hair wax	following patch testing with the hair wax ingredients, positive visicubullous reactions were seen with oleth-5 (and oleth-3-phosphate); patch testing was negative in 20 controls; the patient had a delayed hypersensitivity reaction	66
			PEG Methyl Ethers	
PEG-7 methyl ether	74-yr old female	developed eczema after use of gel for actinic keratoses	patch testing with the individual components, including PEG-7 methyl ether, gave negative results on the back; in patch testing on the upper arm with the components, strong positive reactions to 5 and 10% in pet were seen after 4 days; in controls, patch test results were negative at 24 h	74
PEG-7 methyl ether	60-yr old female	developed vesicular eczema after use of gel for actinic keratoses	patch testing with the individual components of the gel gave positive reactions to 1and 5% aq. PEG-7 methyl ether	77

REFERENCES

1. Elder, RL (ed). Final report on the safety assessment of Laureths -4 and -23. *J Am Coll Toxicol*. 1983;2:(7):1-15.
2. Andersen, FA (ed). Final report on the safety assessment of Ceteareth-2, -3, -4, -5, -6, -7, -8, -9, -10, -11, -12, -13, -14, -15, -16, -17, -18, -19, -20, -22, -23, -24, -25, -27, -28, -29, -30, -33, -34, -40, -50, -55, -60, -80, and -100. *Int J Toxicol*. 1999;18:(Suppl 3):41-49.
3. Andersen, FA (ed). Final report on the safety assessment of Ceteth-1, -2, -3, -4, -5, -6, -10, -12, -14, -15, -16, 20, -24, -25, -30, and -45. *Int J Toxicol*. 1999;18:(Suppl 2):1-8.
4. Andersen, FA (ed). Final report on the safety assessment of Oleth-2, -3, -4, -5, -6, -7, -8, -9, -10, -11, -12, -15, -16, -20, -23, -25, -30, -40, -44, and -50. *Int J Toxicol*. 1999;18:(Suppl 2):17-24.
5. Elder, RL (ed). Final report on the safety assessment of Laneth-10 Acetate group. *J Am Coll Toxicol*. 1982;1:(4):1-23.
6. Elder, RL (ed). Final report on the safety assessment of Steareth-2, -4, -6, -7, -10, -11, -13, -15, and -20. *J Am Coll Toxicol*. 1988;7:(6):881-910.
7. Andersen, FA (ed). Special report; Reproductive and developmental toxicity of ethylene glycol and its ethers. *Int J Toxicol*. 1999;18:(Suppl 2):53-67.
8. Andersen, FA (ed). Final report onthe safety assessment of Methyl Alcohol. *Int J Toxicol*. 2001;20:(1):57-85.
9. Elder, RL (ed). Final report of the safety assessment for Acetylated Lanolin Alcohol and related compounds. *J Environ Pathol Toxicol*. 1980;4:(4):63-92.
10. Elder, RL (ed). Final report on the safety assessment of Stearyl Alcohol, Oleyl Alcohol, and Octyl Dodecanol. *J Am Coll Toxicol*. 1985;4:(5):1-29.
11. Elder, RL (ed). Final report on the safety assessment of Cholesterol. *J Am Coll Toxicol*. 1986;5:(5):491-516.
12. Elder, RL (ed). Final report o the safety assessment of Cetearyl Alcohol, Cetyl Alcohol, Isostearyl Alcohol, Myristyl Alcohol, and Behenyl Alcohol. *J Am Coll Toxicol*. 1988;7:(3):359-413.
13. Becker LC, Andersen, FA, and Cosmetic Ingredient Review Expert Panel. Final report of the safety assessment of Simmondsia Chinensis (Jojoba) Seed Oil, Simmondsia Chinensis (Jojoba) Seed Wax, Hydrogenated Jojoba Oil, Hydrolyzed Jojoba Esters, Isomerized Jojoba Oil, Jojoba Esters, Simmondsia Chinensis (Jojoba) Butter, Jojoba Alcohol, and Synthetic Jojoba Oil. 2008.
14. Diamante, CD, Andersen, FA, and Cosmetic Ingredient Review Expert Panel. Amended safety assessment of Cocos Nucifera (Coconut) Oil, Coconut Acid, Hydrogenated Coconut Acid, Hydrogenated Coconut Oil, Ammonium Cocomonoglyceride Sulfate, Butylene Glycol Cocoate, Caprylic/Capric/Coco Glycerides, Cocoglycerides, Coconut Alcohol, Coconut Oil Decyl Esters, Decyl Cocoate, Ethylhexyl Cocoate, Hydrogenated Coco-Glycerides, Isodecyl Cocoate, Lauryl Cocoate, Magnesium Cocoate, Methyl Cocoate, Octyldodecyl Cocoate, Pentaerythrityl Cocoate, Potassium Cocoate, Potassium Hydrogenated Cocoate, Sodium Cocoate, Sodium Cocomonoglyceride Sulfate, Sodium Hydrogenated Cocoate, and Tridecyl Cocoate. 2008.
15. Andersen, FA and Cosmetic Ingredient Review Expert Panel. Final amended safety assessement 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. 6-29-2010.
16. Andersen, FA (ed). Final report on the safety assessment of Methyl Alcohol. *Int J Toxicol*. 2001;20:(1):57-85.
17. Hinton C (ed.). The Chemistry and Manufacture of Cosmetics. 2002.
18. US EPA. EPI Suite (for Windows). 2009. Washington DC: Environmental Protection Agency.
19. Personal Care Products Council. Comments on the draft report on the ethoxylated alcohols for the June 28-29, 2010 CIR Expert Panel meeting. Correspondence submitted by the Council (4 pp). 6-21-2010.
20. Organisation of Economic Co-operation and Development.SIDS Intial Assessment Report for SIAM 4. 2-(2-(2-Methoxyethoxy)-ethanol. CAS NO. 112-35-6. (PEG-3 Methyl Ether). 2005. http://www.chem.unep.ch/irptc/sids/OECDSIDS/112356.pdf. Accessed 10-26-2010.
21. Hermansky, S. J. and Leung, H. W. Cutaneous toxicity studies with methoxy polyethylene glycol-350 (MPEG-350) in rats and rabbits. *Food Chem Toxicol*. 1997;35:1031-1039.
22. Bergh, M., Magnusson, K., Nilsson, J. L. G., and Karlberg, A.-T. Formation of formaldehyde and peroxides by air oxidation of high purity polyoxyethylene surfactants. *Contact Derm*. 1998;39:14-20.
23. Bergh M, Shao LP, HAgelthron G, Gavert E, Nilsson LG, and Karlberg A-T. Contact allergens from surfactants. *J Pharm Sci*. 1998;87:(3):276-282.
24. Personal Care Products Council. 2010. Monograph proofs of ethoxylated alchohols dated 3/15/2010. (Unpublished data - 78 pp).
25. Food and Drug Administration (FDA). Frequency of use of cosmetic ingredients. *FDA Database*. 2010. Washington, DC: FDA.
26. Personal Care Products Council. Concentration of use of alkyl PEG ethers included in the March 2010 concentration of use survey, i.e., those not previously reviewed by CIR. 2010.

27. Personal Care Products Council. Updated concentration of use - ethoxylated alcohols, May 2010 concentration of use survey. 8-11-2010.
28. James AC, Stahlhofen W, Rudolf G, and et al. Deposition of inhaled particles. *Annals of the ICRP*. 1994;24:(1-3):321-2.
29. Oberdorster G, Oberdorster E, and Oberdosrster J. An Emerging Discipline Evolving from Studies of Ultrafine Particles. *Environ Health Perspect*. 2005;113:(7):823-829.
30. Bower D. Unpublished information on hair spray particle sizes provided at the September 9, 1999 CIR Expert Panel meeting. 1999.
31. Johnson MA. Influence of particle size. *Spray Technology and Marketing*. 2004;(November):24-27.
32. European Commission.European Commission Health and Consumers Cosmetics - Cosing - Database. 2010. http://ec.europa.eu/consumers/cosmetics/cosing/.
33. Scientific Committee on Consumer Products.Opinion on polidocanol (laureth-9). 10-2-2007. http://ec.europa.eu/health/ph_risk/committees/04_sccp/docs/sccp_o_113.pdf. Accessed 5-13-2010.
34. Miller RR. Metabolism and disposition of glycol ethers. *Drug Metabolism Reviews*. 1987;18:(1):1-22.
35. Food and Drug Administration (FDA).List of Indirect Additives Used in Food Contact Substances. 5-10-2010. http://www.accessdata.fda.gov/scripts/fcn/fcnNavigation.cfm?rpt=iaListing&displayAll=true. Accessed 5-14-0010.
36. Henriquez-Santana, A., Fernandez-Guarino, M., González deOlano, D., Gonzalez-Cervera, J., Huertas-Barbudo, B., and Aldanondo, I. Urticaria induced by Etoxisclerol (polidocanol). *J Eur Acad Dermatol Venereol*. 2008;22:261-262.
37. Food and Drug Administration (FDA).FDA Important Alert 66-49: Detention Without Physical Examination Of All Polidocanol Finished Dosage Form Products And Active Pharmaceutical Ingredients (APIs) From All Sources Under All Brand Names Including Aetoxisclerol, Aethoxysklerol, And Sclerovein. 10-2-2009. http://www.accessdata.fda.gov/cms_ia/importalert_195.html. Accessed 5-23-2010.
38. Hoberman, A. M., Krasavage, W. J., Christian, M. S., and Stack, C. R. Developmental toxicity studies of triethylene glycol monomethyl ether administered orally to rats and rabbits. *J Am Coll Toxicol*. 1996;15:(5):349-370.
39. Fruijitier-Pölloth, C. Safety assessment on polyethylene glycols (PEGs) and their derivatives as used in cosmetic products. *Toxicol*. 2005;214:1-38.
40. Leber, A. P., Scott, R. C., Hodge, M. C. E., Johnson, D., and Krasavage, W. J. Triethylene glycol ethers: Evaluations of in vitro absorption through human epidermis, 21-day dermal toxicity in rabbits, and a developmental toxicity screen in rats. *J Am Coll Toxicol*. 1990;9:(5):507-515.
41. Zhou, M. and Donovan, M. D. Recovery of the nasal mucosa following laureth 9 induced damage. *Int.J.Pharm.* 1996;130:93-102.
42. Fruijtier-Polloth, Claudia. Safety Assessment on Polyethylene Glycols (PEGs) and Their Derivatives as Used in Cosmetic Products. *Toxicology*. 2005;214:1-38.
43. Berberian, D. A., Gorman, W. G., Drobeck, H. P., Coulston, F., and Slighter, R. G., Jr. The toxicology and biological properties of laureth 9 (a polyoxyethylene lauryl ether), a new spermicidal agent. *Toxicol Appl Pharmacol.* 1965;7:206-214.
44. Hasegawa, R., Nakaji, Y., Kurokawa, Y., and Tobe, M. Acute toxicity tests on 113 environmental chemicals. *Sci Rep Res Inst Tohoku Univ, -C*. 1989;36:(1-4):10-16.
45. Gingell, R. and Lu, C. C. Acute, subchronic, and reproductive toxicity of a linear alcohol ethoxylate surfactant in the rat. *J Am Coll Toxicol*. 1991;10:(4):477-486.
46. Shell Chemical Company. Human safety of neodol products. 1981.
47. Shell Oil Company. Initial submission. Toxicology of detergents: Acute mammalian toxicity, skin and eye irritancy and skin sensitizing potential of Dobanol 25-3 (Final report). W-attaqch & lttr 011792. 1-20-1978.
48. Shell Oil Company. Initial submission. Toxicology of detergent intermediates: Acute mammalian toxicity, skin and eye irritancy, and skin sensitizing potential of Dobanol 23-2 (Final report). W-ltte 111291. 10-1-1979.
49. Bushy Run Research Center. Tergitol nonionic surfactant 24-L-60N: Nine-day cutaneous dose toxicity study with neurotoxicity evaluation in albino rats. 1-29-1990.
50. Suzuki, M., Machida, M., Adachi, K., Otabe, K., Sugimoto, T., Hayashi, M., and Awazu, S. Histopathological study of the effects of a single intratracheal instillation of surface active agents on lung in rats. *J Toxicol Sci*. 2000;25:(1):49-55.
51. International Research and Development Corporation. Pilot teratology study in rabbits. 6-20-1980.
52. Sittingbourne Research Centre. A subchronic (90-day) feeding study on dobanol 45-7 (C14-15 Pareth-7) in rats. 8-27-1982.
53. Exponent. Letter from James Messina to the EPA regarding a dose selection study for an OECD definitive study. Re: alkyl alkoxylate, CAS # 9004-98-2 (oleths). 1-18-2008.
54. Procter & Gamble Company. Initial submission: 91-day percutaneous toxicity study in rabbits on E-9305.02 and E-0122.01 with cover letter dated 081292. 9-1-1981.

55. DuPont. Letter from Dr. A.M.Kaplan to the EPA describing a 1971 skin irritation study of a formulations containing a laureth (9002-92-0). 11-23-2009.
56. Marzulli FN and Ruggles DI. Rabbit eye irritation: collaborative study. *J Assoc Off Anal Chem.* 2010;56:905-914.
57. Chemical Manufacturers Association (Bates, H.K.). Developmental neurotoxicity evaluation of triethylene glycol monomethyl ether (CAS 112-35-6) administered by gavage to timed-mated CD rats on gestional day 6 though postnatal day 21. 1992.
58. Zeiger, E., Anderson, B., Haworth, S., Lawlor, T., Mortelmans, K., and Speck, W. Salmonella mutagenicity tests: III. Results from the testing of 255 chemicals. *Environ Mutagen.* 1987;9:(Suppl 9):1-110.
59. Matthews, E. J., Spalding, J. W., and Tennant, R. W. Transformation of BALB/c-3T3 cells: V. Transformation responses of 168 chemicals compared with mutagenicity in Salmonella and carcinogenicity in rodent bioassays. *Environ Health Perspect.* 1993;101:(Suppl 2):347-482.
60. Loveday, K. S., Anderson, B. E., Resnick, M. A., and Zeiger, E. Chromosome aberration and sister chromatid exchange tests in Chinese hamster ovary cells in vitro. V: Results with 46 chemicals. *Environ Mol Mutagen.* 1990;16:272-303.
61. Myhr, B. C. and Caspary, W. J. Chemical mutagenesis at the thymidine kinase locus in L5178Y mouse lymphoma cells: Results for 31 coded compounds in the National Toxicology Program. *Environ Mol Mutagen.* 1991;18:51-83.
62. Shelby, M. D., Erexson, G. L., Hook, G. J., and Tice, R. R. Evaluation of a three-exposure mouse bone marrow micronucleus protocol: Results with 49 chemicals. *Environ Mol Mutagen.* 1993;21:160-179.
63. Goossens, A., Beck, M. H., Haneke, E., Mcfadden, J. P., Nolting, S., Durupt, G., and Ries, G. Adverse cutaneous reactions to cosmetic allergens. *Contact Derm.* 1999;40:112-113.
64. Uter, W., Geier, J., and Fuchs, T. Contact allergy to polidocanol, 1992 to 1999. *J Allergy Clin Immunol.* 2000;106:(6):1203-1204.
65. Bárány E, Lindberg M, and Lodén M. Unexpected skin barrier influence from nonionic emulsifiers. *Int J Pharm.* 2000;195:189-195.
66. Abdullah, A., Walker, S., Tan, C. Y., and Foulds, I. S. Sensitization of oleth-3-phosphate and oleth-5 in a hair wax. *Contact Derm.* 1997;37:188.
67. Field, S., Hazelwood, E., Bourke, B., and Bourke, J. F. Allergic contact dermatitis from tertiary-butylhydroquinone and Laureth 12 in a hair dye. *Contact Derm.* 2007;56:116-117.
68. Frosch, P. J. and Schulze-Dirks, A. Contact allergy caused by polidocanol (thesit). *Hautarzt.* 1989;40:(3):146-149.
69. Gallo, R., Basso, M., Voltolini, S., and Guarrera, M. Allergic contact dermatitis from laureth-9 and polyquaternium-7 in a skin-care product. *Contact Derm.* 2001;45:356-357.
70. Grills, C. E. and Cooper, S. M. Polidocanol: a potential contact allergen in shampoo. *Contact Derm.* 2007;56:178.
71. Huber-Riffeser, G. Allergic contact dermatitis to polidocanol (Thesit). *Contact Derm.* 1978;4:(4):245.
72. Kimura, M. and Kawada, A. Follicular contact dermatitis due to polyoxyethylene laurylether. *J Am Acad Dermatol.* 2000;42:(5 Pt 2):879-880.
73. Svensson, A. Allergic contact dermatitis to laureth-4. *Contact Derm.* 1988;18:(2):113-114.
74. Taibjee, S. M., Prais, L., and Foulds, I. S. Allergic contact dermatitis from polyethylene glycol monomethyl ether 350 in Solaraze gel. *Contact Derm.* 2003;49:170-171.
75. US EPA. EPI Suite (for Windows). 2009. (4.0):Washington DC: Environmental Protection Agency.
76. Marzulli FN and Ruggles DI. Rabbit eye irritation: collaborative study. *J Assoc Off Anal Chem.* 1973;56:905-914.
77. Kleyn, C. E., Bharati, A., and King, C. M. Contact dermatitis from 3 different allergens in Solaraze gel. *Contact Derm.* 2004;51:215-216.

DATA

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: F. Alan Andersen, Ph.D.
Director - COSMETIC INGREDIENT REVIEW (CIR)

FROM: John Bailey, Ph.D.
Industry Liaison to the CIR Expert Panel

DATE: August 11, 2010

SUBJECT: Updated Concentration of Use Ethoxylated Alcohols, May 2010 Concentration of Use Survey

1101 17th Street, N.W., Suite 300 | Washington, D.C. 20036-4702 | 202.331.1770 | 202.331.1969 (fax) | www.personalcarecouncil.org

Concentration of Use by FDA Product Category
Ceteareth-2, Ceteareth-3, Ceteareth-4, Ceteareth-5, Ceteareth-6, Ceteareth-7, Ceteareth-8, Ceteareth-9, Ceteareth-10, Ceteareth-11, Ceteareth-12, Ceteareth-13, Ceteareth-14, Ceteareth-15, Ceteareth-16, Ceteareth-17, Ceteareth-18, Ceteareth-20, Ceteareth-22, Ceteareth-23, Ceteareth-24, Ceteareth-25, Ceteareth-27, Ceteareth-28, Ceteareth-29, Ceteareth-30, Ceteareth-33, Ceteareth-34, Ceteareth-40, Ceteareth-50, Ceteareth-55, Ceteareth-60, Ceteareth-80, Ceteareth-100, Ceteth-1, Ceteth-2, Ceteth-3, Ceteth-4, Ceteth-5, Ceteth-6, Ceteth-7, Ceteth-10, Ceteth-12, Ceteth-13, Ceteth-14, Ceteth-15, Ceteth-16, Ceteth-17, Ceteth-18, Ceteth-20, Ceteth-23, Ceteth-24, Ceteth-25, Ceteth-30, Ceteth-40, Ceteth-45, Ceteth-150, Hydrogenated Laneth-5, Hydrogenated Laneth-20, Hydrogenated Laneth-25, Laneth-5, Laneth-10, Laneth-15, Laneth-16, Laneth-20, Laneth-25, Laneth-40, Laneth-50, Laneth-60, Laneth-75, Laureth-1, Laureth-2, Laureth-3, Laureth-4, Laureth-5, Laureth-6, Laureth-7, Laureth-8, Laureth-9, Laureth-10, Laureth-11, Laureth-12, Laureth-13, Laureth-14, Laureth-15, Laureth-16, Laureth-20, Laureth-21, Laureth-23, Laureth-25, Laureth-30, Laureth-38, Laureth-40, Laureth-50, Oleth-2, Oleth-3, Oleth-4, Oleth-5, Oleth-6, Oleth-7, Oleth-8, Oleth-9, Oleth-10, Oleth-11, Oleth-12, Oleth-15, Oleth-16, Oleth-20, Oleth-23, Oleth-24, Oleth-25, Oleth-30, Oleth-35, Oleth-40, Oleth-44, Oleth-45, Oleth-50, Oleth-82, Oleth-100, Oleth-106, Steareth-1, Steareth-2, Steareth-3, Steareth-4, Steareth-5, Steareth-6, Steareth-7, Steareth-8, Steareth-10, Steareth-11, Steareth-13, Steareth-14, Steareth-15, Steareth-16, Steareth-20, Steareth-21, Steareth-25, Steareth-27, Steareth-30, Steareth-40, Steareth-50, Steareth-80, Steareth-100, Steareth-200, Steareth-60 Cetyl Ether and PEG-16 Cetyl/Oleyl/Stearyl/Lanolin Alcohol Ether*

Ingredient	Product Category	Concentration of Use
Ceteareth-2	Rinses (noncoloring)	2%
Ceteareth-3	Other manicuring preparations	2%
Ceteareth-6	Depilatories	2%
Ceteareth-6	Body and hand creams, lotions and powders	0.8%
Ceteareth-6	Moisturizing creams, lotions and powders	0.008%
Ceteareth-7	Shampoos (noncoloring)	0.2%
Ceteareth-10	Eye shadow	8%
Ceteareth-10	Eye lotion	0.02%
Ceteareth-10	Hair dyes and colors (all types requiring caution statement and patch test)	0.5%
Ceteareth-10	Hair rinses (coloring)	2%
Ceteareth-10	Face powders	0.003%

Ceteareth-10	Foundations	1%
Ceteareth-10	Lipstick	11%
Ceteareth-10	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	2%
Ceteareth-10	Face and neck creams, lotions and powders	0.05%
Ceteareth-10	Night creams, lotions and powders	0.02%
Ceteareth-12	Eye lotion	0.02%
Ceteareth-12	Eye makeup remover	0.1%
Ceteareth-12	Hair conditioners	0.3%
Ceteareth-12	Shampoos (noncoloring)	0.5%
Ceteareth-12	Tonics, dressings and other hair grooming aids	1%
Ceteareth-12	Other manicuring preparations	2%
Ceteareth-12	Other shaving preparations	4%
Ceteareth-12	Face and neck creams, lotions and powders	0.3-1%
Ceteareth-12	Body and hand creams, lotions and powders	0.02-0.5%
Ceteareth-12	Body and hand sprays	0.3%
Ceteareth-12	Skin fresheners	0.3%
Ceteareth-12	Other skin care preparations	2%
Ceteareth-12	Indoor tanning preparations	0.3-0.4%
Ceteareth-15	Shampoos (noncoloring)	2%
Ceteareth-15	Tonics, dressings and other hair grooming aids	0.2-10%
Ceteareth-15	Cuticle softeners	4%
Ceteareth-15	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	1%
Ceteareth-15	Indoor tanning preparations	3%
Ceteareth-20	Eyeliner	3%
Ceteareth-20	Eye shadow	0.02-1%
Ceteareth-20	Eye lotion	0.2-0.7%
Ceteareth-20	Mascara	0.05-0.3%
Ceteareth-20	Hair conditioners	0.008-9%
Ceteareth-20	Hair straighteners	0.9-3%

Ceteareth-20	Tonics, dressings and other hair grooming aids	0.2-11%
Ceteareth-20	Other hair preparations (noncoloring)	2%
Ceteareth-20	Hair dyes and colors (all types requiring caution statement and patch test)	0.3-10%
Ceteareth-20	Hair bleaches	0.5%
Ceteareth-20	Other hair coloring preparations	2%
Ceteareth-20	Blushers (all types)	0.05%
Ceteareth-20	Foundations	0.3-0.8%
Ceteareth-20	Makeup bases	0.5-0.9%
Ceteareth-20	Other makeup preparations	0.3%
Ceteareth-20	Other manicuring preparations	3-5%
Ceteareth-20	Bath soaps and detergents	0.7%
Ceteareth-20	Deodorants (underarm)	0.5%
Ceteareth-20	Other personal cleanliness products	0.2-3%
Ceteareth-20	Aftershave lotions	0.4-2%
Ceteareth-20	Other shaving preparations	0.2%
Ceteareth-20	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.2-4%
Ceteareth-20	Depilatories	1-2%
Ceteareth-20	Face and neck creams, lotions and powders	0.05-2%
Ceteareth-20	Body and hand creams, lotions and powders	0.7-3%
Ceteareth-20	Body and hand sprays	0.8%
Ceteareth-20	Moisturizing creams, lotions and powders	0.9-2%
Ceteareth-20	Night creams, lotions and powders	0.9%
Ceteareth-20	Paste masks (mud packs)	0.7-3%
Ceteareth-20	Skin fresheners	0.3-0.5%
Ceteareth-20	Other skin care preparations	1-3%
Ceteareth-20	Suntan gels, creams and liquids	0.3-3%
Ceteareth-20	Indoor tanning preparations	1-3%
Ceteareth-22	Body and hand creams, lotions and powders	1%
Ceteareth-25	Baby lotions, oils, powders and creams	0.1%

Ceteareth-25	Hair conditioners	0.8%
Ceteareth-25	Permanent waves	0.3%
Ceteareth-25	Shampoos (noncoloring)	0.03%
Ceteareth-25	Tonics, dressings and other hair grooming aids	0.1-8%
Ceteareth-25	Other hair preparations (noncoloring)	2%
Ceteareth-25	Hair dyes and colors (all types requiring caution statement and patch test)	0.3-2%
Ceteareth-25	Other manicuring preparations	14-16%
Ceteareth-25	Deodorants (underarm)	0.5%
Ceteareth-25	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.1%
Ceteareth-25	Depilatories	1-2%
Ceteareth-25	Face and neck creams, lotions and powders	0.4-0.5%
Ceteareth-25	Body and hand creams, lotions and powders	0.3-2%
Ceteareth-25	Night creams, lotions and powders	0.3%
Ceteareth-30	Deodorants (underarm)	0.3%
Ceteareth-30	Face and neck creams, lotions and powders	0.09%
Ceteareth-33	Hair conditioners	0.8-9%
Ceteareth-33	Tonics, dressings and other hair grooming aids	2%
Ceteareth-33	Hair dyes and colors (all types requiring caution statement and patch test)	2%
Ceteareth-33	Deodorants (underarm)	1-5%
Ceteareth-33	Face and neck creams, lotions and powders	3%
Ceteareth-33	Body and hand creams, lotions and powders	0.2-3%
Ceteareth-33	Moisturizing creams, lotions and powders	2%
Ceteareth-33	Night creams, lotions and powders	5%
Ceteareth-33	Other skin care preparations	1-8%
Ceteareth-50	Hair dyes and colors (all types requiring caution statement and patch test)	3-6%
Ceteareth-50	Foundations	4%
Ceteth-1	Eyeliner	0.4%

Ceteth-1	Hair conditioners	0.2%
Ceteth-1	Permanent waves	0.5%
Ceteth-1	Rinses (noncoloring)	0.2%
Ceteth-1	Shampoos (noncoloring)	3%
Ceteth-1	Tonics, dressings and other hair grooming aids	2%
Ceteth-1	Hair dyes and colors (all types requiring caution statement and patch test)	0.7%
Ceteth-1	Bath soaps and detergents	0.2%
Ceteth-1	Face and neck creams, lotions and powders	2%
Ceteth-1	Other skin care preparations	0.3%
Ceteth-2	Hair conditioners	0.6%
Ceteth-2	Hair straighteners	1%
Ceteth-2	Permanent waves	0.2-3%
Ceteth-2	Tonics, dressings and other hair grooming aids	0.9-4%
Ceteth-2	Hair dyes and colors (all types requiring caution statement and patch test)	0.5%
Ceteth-2	Deodorants (underarm)	0.8-3%
Ceteth-2	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	3%
Ceteth-2	Face and neck creams, lotions and powders	0.5-1%
Ceteth-2	Paste masks (mud packs)	1%
Ceteth-2	Other skin care preparations	3%
Ceteth-2	Suntan gels, creams and liquids	0.6%
Ceteth-3	Rinses (noncoloring)	0.2%
Ceteth-6	Shampoos (noncoloring)	0.06%
Ceteth-6	Tonics, dressings and other hair grooming aids	0.006%
Ceteth-10	Eye lotion	0.1%
Ceteth-10	Hair conditioners	5%
Ceteth-10	Tonics, dressings and other hair grooming aids	3%
Ceteth-10	Foundations	0.2-1%
Ceteth-10	Other manicuring preparations	0.02-0.08%

Ceteth-10	Depilatories	0.6%
Ceteth-10	Face and neck creams, lotions and powders	0.1-0.2%
Ceteth-12	Face and neck creams, lotions and powders	0.02%
Ceteth-15	Shampoos (noncoloring)	2%
Ceteth-16	Hair bleaches	1%
Ceteth-16	Other hair coloring preparations	0.5%
Ceteth-16	Deodorants (underarm)	0.06%
Ceteth-20	Eye lotion	0.4-0.9%
Ceteth-20	Mascara	0.3%
Ceteth-20	Hair conditioners	0.6-1%
Ceteth-20	Hair straighteners	2%
Ceteth-20	Permanent waves	0.2%
Ceteth-20	Shampoos (noncoloring)	2%
Ceteth-20	Other hair preparations (noncoloring)	0.2%
Ceteth-20	Other manicuring preparations	0.8%
Ceteth-20	Bath soaps and detergents	0.04-4%
Ceteth-20	Deodorants (underarm)	0.82%
Ceteth-20	Other shaving preparations	2%
Ceteth-20	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	1-3%
Ceteth-20	Face and neck creams, lotions and powders	0.4-3%
Ceteth-20	Body and hand creams, lotions and powders	2-3%
Ceteth-20	Body and hand sprays	0.8%
Ceteth-20	Moisturizing creams, lotions and powders	0.08-3%
Ceteth-20	Moisturizing sprays	2%
Ceteth-20	Night creams, lotions and powders	0.5%
Ceteth-20	Other skin care preparations	0.4-2%
Ceteth-20	Indoor tanning preparations	0.2%
Ceteth-24	Eye shadow	0.2%
Ceteth-24	Eye lotion	0.05-0.2%

Ceteth-24	Perfumes	0.2%
Ceteth-24	Other fragrance preparations	0.2%
Ceteth-24	Hair conditioners	0.2%
Ceteth-24	Permanent waves	0.5%
Ceteth-24	Shampoos (noncoloring)	0.05%
Ceteth-24	Tonics, dressings and other hair grooming aids	0.5%
Ceteth-24	Foundations	0.2-0.8%
Ceteth-24	Other makeup preparations	0.3%
Ceteth-24	Cuticle softeners	0.09%
Ceteth-24	Bath soaps and detergents	0.0009%
Ceteth-24	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.09-0.3%
Ceteth-24	Face and neck creams, lotions and powders	0.05-2%
Ceteth-24	Body and hand creams, lotions and powders	0.09-0.7%
Ceteth-24	Moisturizing creams, lotions and powders	0.7%
Ceteth-24	Night creams, lotions and powders	0.2%
Ceteth-24	Paste masks (mud packs)	0.2%
Ceteth-24	Skin fresheners	0.05-0.09%
Ceteth-24	Other skin care preparations	0.07%
Ceteth-24	Suntan gels, creams and liquids	0.5%
Ceteth-24	Indoor tanning preparations	0.2%
Ceteth-25	Tonics, dressings and other hair grooming aids	0.6%
Ceteth-25	Hair bleaches	1%
Ceteth-25	Face and neck creams, lotions and powders	1%
Ceteth-25	Body and hand creams, lotions and powders	1%
Ceteth-25	Moisturizing creams, lotions and powders	3%
Ceteth-25	Paste masks (mud packs)	2%
Laneth-5	Hair dyes and colors (all types requiring caution statement and patch test)	0.8%
Laneth-15	Hair conditioners	10-30%
Laneth-15	Hair straighteners	0.5-3%

Laneth-15	Tonics, dressings and other hair grooming aids	0.1-3%
Laneth-15	Other skin care preparations	0.3%
Laneth-16	Hair bleaches	2%
Laneth-16	Other hair coloring preparations	0.7%
Laneth-16	Deodorants (underarm)	0.08%
Laneth-20	Hair straighteners	0.7%
Laneth-20	Tonics, dressings and other hair grooming aids	0.5%
Laneth-40	Hair conditioners	10-30%
Laneth-40	Hair straighteners	1-3%
Laureth-1	Shampoos (noncoloring)	12%
Laureth-1	Hair dyes and colors (all types requiring caution statement and patch test)	15%
Laureth-1	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	7%
Laureth-2	Eye shadow	0.2%
Laureth-2	Other fragrance preparations	0.8%
Laureth-2	Hair conditioners	0.6-5%
Laureth-2	Shampoos (noncoloring)	0.6-0.9%
Laureth-2	Hair dyes and colors (all types requiring caution statement and patch test)	4-9%
Laureth-2	Other hair coloring preparations	0.2%
Laureth-2	Lipstick	0.005%
Laureth-2	Bath soaps and detergents	0.9%
Laureth-2	Other personal cleanliness products	0.5%
Laureth-2	Aftershave lotions	0.02%
Laureth-2	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.3-2%
Laureth-2	Depilatories	7%
Laureth-2	Face and neck creams, lotions and powders	7%
Laureth-2	Night creams, lotions and powders	0.2%
Laureth-2	Paste masks (mud packs)	0.2%

Laureth-2	Skin fresheners	0.2%
Laureth-2	Other skin care preparations	0.5%
Laureth-3	Hair conditioners	<1%
Laureth-3	Shampoos (noncoloring)	0.5-1%
Laureth-3	Tonics, dressings and other hair grooming aids	0.8%
Laureth-3	Hair dyes and colors (all types requiring caution statement and patch test)	3-20%
Laureth-3	Hair bleaches	2-10%
Laureth-3	Other personal cleanliness products	0.02%
Laureth-3	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.0004%
Laureth-3	Face and neck creams, lotions and powders	0.05%
Laureth-3	Body and hand creams, lotions and powders	0.8%
Laureth-3	Moisturizing creams, lotions and powders	0.02%
Laureth-4	Bath oils, tablets and salts	10%
Laureth-4	Bubble baths	8-12%
Laureth-4	Eyebrow pencil	0.007%
Laureth-4	Eyeliner	2-4%
Laureth-4	Eye shadow	0.02%
Laureth-4	Eye lotion	0.05-0.2%
Laureth-4	Mascara	0.02-0.3%
Laureth-4	Other eye makeup preparations	0.03%
Laureth-4	Hair conditioners	0.01-4%
Laureth-4	Rinses (noncoloring)	0.2%
Laureth-4	Shampoos (noncoloring)	0.4-2%
Laureth-4	Tonics, dressings and other hair grooming aids	0.05-3%
Laureth-4	Hair dyes and colors (all types requiring caution statement and patch test)	0.05-6%
Laureth-4	Other hair coloring preparations	0.04-0.3%
Laureth-4	Blushers (all types)	0.06-0.8%
Laureth-4	Face powders	0.004-1%

Laureth-4	Foundations	0.002-0.5%
Laureth-4	Lipstick	0.02-0.2%
Laureth-4	Other makeup preparations	0.1%
Laureth-4	Cuticle softeners	7%
Laureth-4	Other manicuring preparations	2-6%
Laureth-4	Bath soaps and detergents	0.0002-2%
Laureth-4	Deodorants (underarm)	0.8%
Laureth-4	Other personal cleanliness products	0.3-2%
Laureth-4	Skin cleansing (cold creams, cleansing lotions, liquids and pads	4-21%
Laureth-4	Face and neck creams, lotions and powders	0.09-1%
Laureth-4	Body and hand creams, lotions and powders	0.02-20%
Laureth-4	Other skin care preparations	4-5%
Laureth-4	Suntan gels, creams and liquids	0.2%
Laureth-4	Indoor tanning preparations	3%
Laureth-4	Other suntan preparations	0.1%
Laureth-5	Tonics, dressings and other hair grooming aids	0.0002%
Laureth-6	Other personal cleanliness products	6-8%
Laureth-7	Eyeliner	0.02-0.06%
Laureth-7	Eye shadow	0.07-0.2%
Laureth-7	Eye lotion	0.04-0.4%
Laureth-7	Mascara	0.06%
Laureth-7	Other eye makeup preparations	0.3%
Laureth-7	Powders (dusting and talcum)	0.07%
Laureth-7	Hair conditioners	0.04-2%
Laureth-7	Shampoos (noncoloring)	<1%
Laureth-7	Tonics, dressings and other hair grooming aids	0.2-0.4%
Laureth-7	Other hair preparations (noncoloring)	0.9%
Laureth-7	Hair dyes and colors (all types requiring caution statement and patch testing)	0.3%
Laureth-7	Hair tints	0.2%

Laureth-7	Blushers (all types)	0.2%
Laureth-7	Face powders	0.001-0.2%
Laureth-7	Foundations	0.1-0.5%
Laureth-7	Lipstick	0.05-0.4%
Laureth-7	Makeup bases	0.05-0.4%
Laureth-7	Rouges	0.2%
Laureth-7	Other makeup preparations	0.02-0.3%
Laureth-7	Cuticle softeners	0.02-0.1%
Laureth-7	Other manicuring preparations	0.3%
Laureth-7	Other personal cleanliness products	0.020.2%
Laureth-7	Aftershave lotions	0.05-0.2%
Laureth-7	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.09-0.4%
Laureth-7	Face and neck creams, lotions and powders	0.04-4%
Laureth-7	Body and hand creams, lotions and powders	0.004-0.4%
Laureth-7	Moisturizing creams, lotions and powders	0.2-0.3%
Laureth-7	Night creams, lotions and powders	0.08-0.4%
Laureth-7	Skin fresheners	0.3%
Laureth-7	Other skin care preparations	0.02-0.3%
Laureth-7	Suntan gels, creams and liquids	0.5%
Laureth-7	Indoor tanning preparations	0.2-0.4%
Laureth-8	Eye lotion	0.08%
Laureth-8	Other personal cleanliness products	6-8%
Laureth-8	Aftershave lotions	0.2%
Laureth-8	Face and neck creams, lotions and powders	0.08%
Laureth-8	Body and hand creams, lotions and powders	0.08%
Laureth-8	Other skin care preparations	0.05%
Laureth-9	Eye makeup remover	1%
Laureth-9	Hair conditioners	0.09-0.3%
Laureth-9	Hair sprays (aerosol fixatives)	0.3%

Laureth-9	Permanent waves	0.06%
Laureth-9	Shampoos (noncoloring)	0.006-2%
Laureth-9	Tonics, dressings and other hair grooming aids	0.0003%
Laureth-9	Face and neck creams, lotions and powders	0.3%
Laureth-9	Body and hand creams, lotions and powders	0.4%
Laureth-9	Moisturizing creams, lotions and powders	1%
Laureth-10	Hair conditioners	5%
Laureth-10	Shampoos (noncoloring)	0.09-1%
Laureth-10	Other personal cleanliness products	0.05-8%
Laureth-10	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	1-5%
Laureth-10	Face and neck creams, lotions and powders	0.4%
Laureth-10	Body and hand creams, lotions and powders	0.5%
Laureth-11	Hair conditioners	5%
Laureth-11	Face and neck creams, lotions and powders	2%
Laureth-12	Eye shadow	0.05%
Laureth-12	Eye lotion	0.06%
Laureth-12	Hair conditioners	0.3-1%
Laureth-12	Shampoos (noncoloring)	3%
Laureth-12	Tonics, dressings and other hair grooming aids	2%
Laureth-12	Hair dyes and colors (all types requiring caution statement and patch test)	5%
Laureth-12	Hair tints	1%
Laureth-12	Blushers (all types)	0.1%
Laureth-12	Foundations	0.04-0.3%
Laureth-12	Bath soaps and detergents	6%
Laureth-12	Face and neck creams, lotions and powders	0.03-1%
Laureth-12	Body and hand creams, lotions and powders	0.02-1%
Laureth-12	Moisturizing creams, lotions and powders	0.3%
Laureth-12	Night creams, lotions and powders	0.2%
Laureth-12	Other skin care preparation	0.05%

Laureth-16	Shampoos (noncoloring)	3%
Laureth-20	Eyebrow pencil	0.05%
Laureth-20	Mascara	0.03-0.06%
Laureth-20	Other eye makeup preparations	0.02%
Laureth-20	Shampoos (noncoloring)	5%
Laureth-20	Face and neck creams, lotions and powders	0.0008%
Laureth-20	Other skin care preparations	0.03%
Laureth-21	Eyeliner	0.6%
Laureth-21	Eye shadow	0.006-0.2%
Laureth-21	Mascara	0.03-0.07%
Laureth-21	Blushers (all types)	0.003%
Laureth-21	Lipstick	0.03%
Laureth-23	Eye lotion	0.09%
Laureth-23	Mascara	0.003%
Laureth-23	Colognes and toilet waters	3%
Laureth-23	Hair conditioners	0.02-2%
Laureth-23	Permanent waves	2-4%
Laureth-23	Rinses (noncoloring)	0.4%
Laureth-23	Shampoos (noncoloring)	0.05-0.4%
Laureth-23	Tonics, dressings and other hair grooming aids	0.008-2%
Laureth-23	Other hair preparations (noncoloring)	8%
Laureth-23	Other hair coloring preparations	0.04-0.5%
Laureth-23	Cuticle softeners	2%
Laureth-23	Bath soaps and detergents	0.0002%
Laureth-23	Deodorants (underarm)	0.4-2%
Laureth-23	Other personal cleanliness products	0.07-2%
Laureth-23	Beard softeners	3%
Laureth-23	Shaving cream (aerosol, brushless and lather)	2-7%
Laureth-23	Other shaving preparations	0.1%
Laureth-23	Skin cleansing (cold creams, cleansing lotions, liquids	0.04-1%

	and pads)	
Laureth-23	Face and neck creams, lotions and powders	0.4-1%
Laureth-23	Body and hand creams, lotions and powders	0.4-2%
Laureth-23	Other skin care preparations	2%
Laureth-23	Suntan gels, creams and liquids	0.2%
Laureth-25	Eyeliner	3%
Laureth-25	Hair conditioners	0.09%
Laureth-25	Permanent waves	0.03%
Laureth-25	Shampoos (noncoloring)	0.04-0.2%
Laureth-30	Eyeliner	0.3%
Laureth-30	Mascara	0.02-0.3%
Laureth-30	Hair tints	0.07%
Laureth-30	Face and neck creams, lotions and powders	0.07%
Oleth-2	Bath oils, tablets and salts	6%
Oleth-2	Other fragrance preparations	5%
Oleth-2	Hair conditioners	0.5-4%
Oleth-2	Hair sprays (aerosol fixatives)	0.1%
Oleth-2	Tonics, dressings and other hair grooming aids	3-10%
Oleth-2	Hair dyes and colors (all types requiring caution statement and patch test)	0.2-18%
Oleth-2	Hair tints	1%
Oleth-2	Deodorants (underarm)	0.4%
Oleth-2	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.3-3%
Oleth-2	Face and neck creams, lotions and powders	0.8%
Oleth-2	Body and hand creams, lotions and powders	1%
Oleth-3	Bath oils, tablets and salts	7%
Oleth-3	Eye lotion	0.4%
Oleth-3	Tonics, dressings and other hair grooming aids	4%
Oleth-3	Hair dyes and colors (all types requiring caution statement and patch test)	10%

Oleth-3	Deodorants (underarn)	1%
Oleth-3	Face and neck creams, lotions and powders	0.4%
Oleth-3	Body and hand creams, lotions and powders	1%
Oleth-3	Suntan gels, creams and liquids	0.3%
Oleth-4	Permanent waves	1%
Oleth-4	Hair dyes and colors (all types requiring caution statement and patch test)	4%
Oleth-5	Bath oils, tablets and salts	10%
Oleth-5	Eye lotion	0.3%
Oleth-5	Hair conditioners	0.5-3%
Oleth-5	Hair straighteners	1%
Oleth-5	Permanent waves	5%
Oleth-5	Rinses (noncoloring)	0.06%
Oleth-5	Shampoos (noncoloring)	0.06%
Oleth-5	Tonics, dressings and other hair grooming aids	5-10%
Oleth-5	Nail creams and lotions	4%
Oleth-5	Other manicuring preparations	3%
Oleth-5	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	1%
Oleth-5	Face and neck creams, lotions and powders	0.7%
Oleth-5	Body and hand creams, lotions and powders	3%
Oleth-5	Moisturizing creams, lotions and powders	1%
Oleth-5	Skin fresheners	0.3%
Oleth-8	Hair conditioners	2%
Oleth-8	Permanent waves	1%
Oleth-10	Eye lotion	0.5%
Oleth-10	Perfumes	6%
Oleth-10	Other fragrance preparations	4%
Oleth-10	Hair conditioners	0.3-1%
Oleth-10	Shampoos (noncoloring)	1%
Oleth-10	Tonics, dressings and other hair grooming aids	0.3-11%

Oleth-10	Other hair preparations (noncoloring)	14%
Oleth-10	Hair dyes and colors (all types requiring caution statement and patch test)	0.2-5%
Oleth-10	Mouthwashes and breath fresheners (liquids and sprays)	0.2%
Oleth-10	Bath soaps and detergents	1%
Oleth-10	Deodorants (underarm)	0.5%
Oleth-10	Other personal cleanliness products	0.5-3%
Oleth-10	Other shaving preparations	1%
Oleth-10	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.3-4%
Oleth-10	Face and neck creams, lotions and powders	0.2-0.8%
Oleth-10	Body and hand creams, lotions and powders	0.2-8%
Oleth-10	Moisturizing creams, lotions and powders	0.6%
Oleth-10	Paste masks (mud packs)	0.2-0.4%
Oleth-10	Other skin care preparations	0.5%
Oleth-10	Suntan gels, creams and liquids	0.3%
Oleth-12	Eyeliner	1%
Oleth-12	Body and hand creams, lotions and powders	2%
Oleth-15	Face and neck creams, lotions and powders	0.4%
Oleth-15	Paste masks (mud packs)	0.7%
Oleth-16	Baby lotions, oils, powders and creams	0.03%
Oleth-16	Colognes and toilet waters	0.06%
Oleth-16	Hair bleaches	0.8%
Oleth-16	Other hair coloring preparations	0.5%
Oleth-16	Deodorants (underarm)	0.06%
Oleth-20	Eyeliner	2%
Oleth-20	Hair conditioners	0.2-2%
Oleth-20	Permanent waves	1%
Oleth-20	Rinses (noncoloring)	3%
Oleth-20	Shampoos (noncoloring)	0.01-3%

Oleth-20	Tonics, dressings and other hair grooming aids	0.3-17%
Oleth-20	Other hair preparations (noncoloring)	6%
Oleth-20	Hair dyes and colors (all types requiring caution statement and patch test)	1%
Oleth-20	Hair bleaches	1%
Oleth-20	Foundations	0.3%
Oleth-20	Cuticle softeners	4%
Oleth-20	Nail polish and enamel	4%
Oleth-20	Mouthwashes and breath fresheners (liquids and sprays)	0.2%
Oleth-20	Deodorants (underarm)	0.9-3%
Oleth-20	Other personal cleanliness products	4%
Oleth-20	Aftershave lotions	0.4%
Oleth-20	Shaving cream (aerosol, brushless and lather)	4%
Oleth-20	Other shaving preparations	0.5%
Oleth-20	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.7-3%
Oleth-20	Face and neck creams, lotions and powders	0.1-2%
Oleth-20	Body and hand creams, lotions and powders	0.2-0.9%
Oleth-20	Moisturizing creams, lotions and powders	0.4%
Oleth-20	Paste masks (mud packs)	0.1-0.7%
Oleth-20	Skin fresheners	1%
Oleth-20	Other skin care preparations	0.9-3%
Oleth-25	Permanent waves	0.2%
Oleth-30	Hair dyes and colors (all types requiring caution statement and patch test)	3%
Oleth-30	Shaving cream (aerosol, brushless and lather)	8%
Oleth-50	Hair conditioners	0.7%
Oleth-50	Permanent waves	2%
Oleth-50	Rinses (noncoloring)	0.5%
Oleth-50	Hair dyes and colors (all types requiring caution statement and patch test)	0.3%

Oleth-50	Depilatories	4%
Oleth-50	Face and neck creams, lotions and powders	1%
Oleth-106	Hair dyes and colors (all types requiring caution statement and patch test)	5%
Steareth-2	Other baby products	4%
Steareth-2	Eyeliner	1%
Steareth-2	Eye shadow	0.2-2%
Steareth-2	Eye lotion	0.8-3%
Steareth-2	Eye makeup remover	2%
Steareth-2	Mascara	0.2-2%
Steareth-2	Hair conditioners	1-10%
Steareth-2	Tonics, dressings and other hair grooming aids	1-5%
Steareth-2	Hair dyes and colors (all types requiring caution statement and patch test)	3%
Steareth-2	Hair rinses (coloring)	0.8%
Steareth-2	Blushers (all types)	0.2-0.7%
Steareth-2	Face powders	0.4%
Steareth-2	Foundations	0.2-3%
Steareth-2	Lipstick	1-2%
Steareth-2	Makeup bases	0.1-2%
Steareth-2	Other makeup preparations	1%
Steareth-2	Nail creams and lotions	5%
Steareth-2	Bath soaps and detergents	0.008%
Steareth-2	Deodorants (underarm)	0.5-3%
Steareth-2	Other personal cleanliness products	1-3%
Steareth-2	Aftershave lotions	1%
Steareth-2	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.3-2%
Steareth-2	Depilatories	2%
Steareth-2	Face and neck creams, lotions and powders	0.4-5%
Steareth-2	Body and hand creams, lotions and powders	0.3-3%

Steareth-2	Body and hand sprays	0.8%
Steareth-2	Moisturizing creams, lotions and powders	1-3%
Steareth-2	Night creams, lotions and powders	0.8-3%
Steareth-2	Paste masks (mud packs)	0.5%
Steareth-2	Skin fresheners	0.5%
Steareth-2	Other skin care preparations	0.6-3%
Steareth-2	Suntan gels, creams and liquids	2-3%
Steareth-2	Indoor tanning preparations	0.3-1%
Steareth-4	Eyeliner	0.02%
Steareth-4	Hair conditioners	1%
Steareth-4	Hair sprays (aerosol fixatives)	1%
Steareth-4	Permanent waves	3%
Steareth-4	Rinses (noncoloring)	1%
Steareth-4	Shampoos (noncoloring)	0.1-1%
Steareth-4	Tonics, dressings and other hair grooming aids	1%
Steareth-4	Hair dyes and colors (all types requiring caution statement and patch testing)	0.5%
Steareth-4	Other manicuring preparations	0.06%
Steareth-4	Bath soaps and detergents	0.1%
Steareth-4	Other personal cleanliness products	0.3-2%
Steareth-4	Other skin care preparations	0.06-0.2%
Steareth-6	Tonics, dressings and other hair grooming aids	3%
Steareth-10	Eye lotion	0.5-2%
Steareth-10	Other eye makeup preparations	2%
Steareth-10	Foundations	4%
Steareth-10	Face and neck creams, lotions and powders	0.9-3%
Steareth-10	Body and hand creams, lotions and powders	1-2%
Steareth-16	Colognes and toilet waters	0.2%
Steareth-16	Hair bleaches	1%
Steareth-16	Other hair coloring preparations	0.4%

Steareth-20	Eyeliner	0.3%
Steareth-20	Eye lotion	0.08-2%
Steareth-20	Eye makeup remover	0.8%
Steareth-20	Mascara	2-4%
Steareth-20	Other eye makeup preparations	0.02%
Steareth-20	Hair conditioners	1%
Steareth-20	Tonics, dressings and other hair grooming aids	0.01-20%
Steareth-20	Other hair preparations (noncoloring)	0.2%
Steareth-20	Hair dyes and colors (all types requiring caution statement and patch test)	3%
Steareth-20	Blushers (all types)	0.1-8%
Steareth-20	Foundations	0.03-2%
Steareth-20	Other makeup preparations	0.02-0.03%
Steareth-20	Nail creams and lotions	0.7%
Steareth-20	Other manicuring preparations	2%
Steareth-20	Bath soaps and detergents	0.007-2%
Steareth-20	Deodorants (underarm)	0.6-2%
Steareth-20	Other personal cleanliness products	2%
Steareth-20	Aftershave lotions	2%
Steareth-20	Shaving cream (aerosol, brushless and lather)	0.05%
Steareth-20	Shaving soaps (cakes, sticks, etc)	0.01%
Steareth-20	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.01-1%
Steareth-20	Depilatories	3%
Steareth-20	Face and neck creams, lotions and powders	0.08-3%
Steareth-20	Body and hand creams, lotions and powders	0.9-3%
Steareth-20	Moisturizing creams, lotions and powders	0.6%
Steareth-20	Night creams, lotions and powders	0.03-0.09%
Steareth-20	Paste masks (mud packs)	0.08%
Steareth-20	Other skin care preparations	0.006-0.03%
Steareth-20	Suntan gels, creams and liquids	0.3%

Steareth-20	Indoor tanning preparations	0.2%
Steareth-21	Eyeliner	1%
Steareth-21	Eye shadow	0.4-0.6%
Steareth-21	Eye lotion	0.8-2%
Steareth-21	Other eye makeup preparations	2%
Steareth-21	Hair conditioners	<1-3%
Steareth-21	Tonics, dressings and other hair grooming aids	2-7%
Steareth-21	Other hair preparations (noncoloring)	2%
Steareth-21	Hair dyes and colors (all types requiring caution statement and patch test)	2-5%
Steareth-21	Hair tints	2%
Steareth-21	Hair rinses (coloring)	0.5%
Steareth-21	Blushers (all types)	0.4-0.6%
Steareth-21	Face powders	2%
Steareth-21	Foundations	0.05-3%
Steareth-21	Leg and body paints	0.7%
Steareth-21	Lipstick	0.5-1%
Steareth-21	Other makeup preparations	0.4-2%
Steareth-21	Cuticle softeners	1%
Steareth-21	Other manicuring preparations	0.01%
Steareth-21	Bath soaps and detergents	0.04%
Steareth-21	Deodorants (underarm)	0.8-2%
Steareth-21	Other personal cleanliness products	2%
Steareth-21	Aftershave lotions	0.7-3%
Steareth-21	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.5-3%
Steareth-21	Face and neck creams, lotions and powders	0.9-4%
Steareth-21	Body and hand creams, lotions and powders	0.9-3%
Steareth-21	Foot powders and sprays	2%
Steareth-21	Moisturizing creams, lotions and powders	2%
Steareth-21	Night creams, lotions and powders	0.8-2%

Steareth-21	Paste masks (mud packs)	2%
Steareth-21	Other skin care preparations	3%
Steareth-21	Suntan gels, creams and liquids	3%
Steareth-25	Body and hand creams, lotions and powders	2%
Steareth-25	Moisturizing creams, lotions and powders	0.3%
Stearaeth-30	Other hair preparations (noncoloring)	0.5%
Steareth-50	Face and neck creams, lotions and powders	4%
Steareth-100	Bath oils, tablets and salts	0.02%
Steareth-100	Eye lotion	0.3-1%
Steareth-100	Tonics, dressings and other hair grooming aids	2%
Steareth-100	Hair dyes and colors (all types requiring caution statement and patch test)	0.3%
Steareth-100	Other makeup preparations	3%
Steareth-100	Bath soaps and detergents	0.5%
Steareth-100	Deodorants (underarm)	2-6%
Steareth-100	Shaving cream (aerosol, brushless and lather)	0.5%
Steareth-100	Face and neck creams, lotions and powders	0.4-1%
Steareth-100	Body and hand creams, lotions and powders	1-3%
Steareth-100	Moisturizing creams, lotions and powders	0.5%
Steareth-100	Other skin care preparations	2-3%
Steareth-200	Shaving cream (aerosol, brushless and lather)	1%

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

Information collected in 2010
Table prepared July 9, 2010
Updated August 11, 2010

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: F. Alan Andersen, Ph.D.
Director - COSMETIC INGREDIENT REVIEW (CIR)

FROM: John Bailey, Ph.D.
Industry Liaison to the CIR Expert Panel

DATE: June 21, 2010

SUBJECT: Comments on the Draft Report on the Ethoxylated Alcohols for the June 28-29, 2010 CIR Expert Panel Meeting

Memo - In the future, it would be helpful if memos were dated with the date they were written.

Please consider removing PEG-3 Methyl Ether, PEG-4 Methyl Ether, PEG-7 Methyl Ether, Methoxy PEG-7, Methoxy PEG-10, Methoxy PEG-16, Methoxy PEG-25, Methoxy PEG-40 and Methoxy PEG-100 from this report. As these ingredients are all defined as having an average number of ethylene oxide units they have the potential of containing Methoxyethanol and Methoxydiglycol (both in the Dictionary). Both Methoxyethanol and Methoxydiglycol are not permitted for use in cosmetics in Europe, and both are developmental toxicants. As indicated on p.6, the functions reported for the methyl ingredients (solvents, humectants) are different than the functions reported for the majority of the other ingredients included in this report.

If the methyl group ingredients are removed from the report, the CIR Expert Panel should be asked if a statement that extends the report conclusion to other Alkyl PEG Ethers (in the same families as in this report) added to the Dictionary in the future should be added to this report (similar to what has been done in the PPG report).

p.1 - In the last paragraph of the Introduction, it is not clear what is meant by "chain length". The CAS numbers appear to be specific for alkyl group chain length, but not the number of units of ethylene oxide.

p.5 - In the first sentence of this page, please indicate that the number of moles of ethylene oxide in each ingredient is an average number.

p.6 - In the last paragraph, please change "do not function as surfactants" to "are not reported to function as surfactants".

p.7, 29 - The actual maximum use concentration of C12-13 Pareth-3 in a dermal leave-on preparation (perfume) was 25% not 23% as indicated in the report. When all of the concentration of use information is available, it would be helpful to include a list of ingredients for which no uses were reported in either the FDA VCRP information or the Council concentration of use survey.

p.8 - If there was a vehicle in the methyl alcohol dermal penetration study, it should be stated.

p.8 - As the size of these ingredients varies greatly, it would be helpful to state which alkyl PEG ethers were found to be readily absorbed through the skin of guinea pigs and rats and through the

intestinal mucosa of rats.

p.3 - If the PEG Methyl ethers are left in the report, the purity of the compound used in studies of triethylene glycol monomethyl ether (PEG-3 Methyl Ether) (references 32, 38) needs to be stated.

p.3 - In the dermal penetration study of PEG-3 Methyl Ether, what does the value 34 ± 7.7 $\mu g/cm^2/hr$ represent? The material that entered the receptor fluid? Or does it also include the material in the skin?

p.9 - Please provide the names of the drugs for which the penetration was enhanced by Laureth-9. What concentration of Laureth-9 damaged the nasal mucosa?

p.9 - Please provide the names of the compounds for which the penetration was increased by Oleth ingredients.

p.11 - Are g/kg the correct units for the 6-week inhalation study of methyl alcohol in rats?

p.14 - In the 14-day dermal rat study, what compound was studied (reference 22)? In the second sentence it says "PEG-7".

p.14 - The 90-day dermal study of PEG-7 Methyl Ether should be moved to the Subchronic Exposure section.

p.15 - If available, please provide the purity of the PEG-3 Methyl Ether (called triethylene glycol monomethyl ether in the study title) used in the 13 week dermal toxicity study (reference 51).

p.17 - What concentration of stearyl alcohol was not comedogenic to rabbit ears?

p.20 - Please provide the species used in the studies of ocular irritation of behenyl alcohol and formulations containing oleyl alcohol.

p.21 - How did the investigators (reference 54) determine that Laureth-9 had an anesthetic effect on the cornea of rabbit eyes?

p.21 - What solvent was used to dilute C12-13 Pareth-3 in the ocular irritation study (reference 43).

p.22 -The information under the heading on ethylene glycol is not about ethylene glycol at all. It is about metabolites of small ethylene glycol monoalkyl ethers, such as methoxyethanol. If this information is left in the report, it needs to be included in a separate section and made more specific as to which ethylene glycol monoalkyl ethers are reproductive and developmental toxicants. Methoxyethanol and Ethoxyethanol (CIR unsafe) are reproductive and developmental toxicants. Butoxyethanol (CIR safe with qualifications) is not a reproductive and developmental toxicant. Information about the lack of reproductive and developmental toxicity of ethylene glycol can be found in the NTP report on ethylene glycol at http://cerhr.niehs.nih.gov/chemicals/egpg/ethylene/eg.html that was completed in 2004.

p.22 - It is not correct to state that ethylene glycol is a reproductive toxicant. See the NTP Center for the Evaluation of Risks to Human Reproduction (CERHR) report on ethylene glycol at http://cerhr.niehs.nih.gov/chemicals/egpg/ethylene/eg.html that was completed in 2004 (summary is on p.120-124). The ethylene glycol report includes the following conclusions. "The Expert Panel judges the likelihood of adverse developmental toxicity in the humans from such levels of exposure to be of negligible concern. The Panel concludes that the lack of reproductive toxicity in experimental animal studies indicates there is negligible concern for reproductive effects in humans."

p.22 - The general statement that "monoalkyl ethers of ethylene glycol are reproductive toxins and teratogenic agents" under the Ceteareths, Ceteths, and Oleths subheading needs to be made

more specific as longer chain, e.g., butoxyethanol, are not reproductive and developmental toxicants.

p.22 - In the cholesterol subsection, please give the time during gestation when subcutaneous administration of cholesterol to gravid dams results in palate anomalies (if given after the palate is developed, these anomalies will not be observed).

p.23 - Did Leber et al. (1990) (reference 38), Chemical Manufacturers Association (reference 56) or Hoberman et al. (1996) provide any indication of the purity of the triethylene glycol monomethyl ether (PEG-3 Methyl Ether) tested?

p.24 - What concentrations or doses of PEGs were tested in the genotoxicity assays? What concentration of cholesterol "was not active in a mammalian cell DNA synthesis inhibition test for mutagenic carcinogens."

p.25 - What doses of PEG-8 and what species were used in the PEG-8 carcinogenicity studies? What doses/concentrations of cholesterol were used in studies examining its carcinogenicity potential?

p.26 - What concentrations of PEG-6 and PEG-8 were associated with hypersensitivity? It should be mentioned that the dermal penetration study of PEG-4 with and without tape stripping was an *in vitro* study.

p.27 - The information about oleyl alcohol needs to be deleted from the octyl dodecanol subsection. This information is already included in the oleyl alcohol subsection.

p.28 - If available, please include the number of subjects and solvents used in the HRIPTs of C12-13 Pareth-7 and C12-15 Pareth-7.

p.28 - It is not clear what is meant by "Laureth-1 is the simplest"? Is it the only ingredient in the report with an average of only 1 ethylene oxide group?

p.29 - Correct "Foe example.." to "For example..."

p.29 - The statement: "In general, alkyl PEG ethers are readily absorbed through the skin of guinea pigs and rats...." is an over generalization. Only some of these compounds readily penetrate the skin.

p.30 - Please indicate if 10,000 ppm C14-15 Pareth-7 is a dietary or drinking water concentration.

p.30 - What was the duration of the dermal study of C9-11 Pareth-6?

p.30 - What duration and what species was tested in the dermal study of Laureth-9 (second complete paragraph on this page)?

p.30 - The ingredients to which "Dilutions of these ingredients..." refers is not clear. What was the solvent in these dilutions?

p.30 - What concentrations were used in the sensitization studies?

p.30 - In the last paragraph, what compound at a dose of 3000 mg/kg resulted in increased length of gestation and increased maternal kidney weights?

p.31 - What kind of effects did the case studies of the laureths report?

Table 2 - Please update the conclusion for the Ceteareths with the new conclusion from the PEG report.

Table 3 - As metabolites of larger ethylene glycol monoalkyl ethers are not reproductive and developmental toxicants, please be more specific in the conclusion for the special report on ethylene glycol ethers.

CIR Panel Book Page 77-100 - Is the information on these pages considered to be Table 4? Although it is presented on p.4 of the report, it would be helpful to repeat the reference for the physical

and chemical properties in the Table, and based on the reference (EPI Suite), it would be helpful to indicate that the values were calculated (if this is correct). The definitions for these ingredients in the Dictionary say when n is an average of the number in the name, rather than when n = the number as indicated in Table 4.

Table 7 - The information in the row for PEG-7 Methyl Ether is not complete, as only the "Animals" column contains information.

Table 8 - If available, please include the vehicle with which the compounds were diluted. Under C12-13, what is meant by "(cunspec.)"?

Table 10 - Searching the internet indicates amerchol L 101 is a trade name for lanolin alcohol. Please check this table as it includes numerous typographical errors.

Table 11 - The heading of the last entry should not be ethylene glycol. Ethylene glycol is not a reproductive or developmental toxicant (see discussion under p. 22). Metabolites of some smaller ethylene glycol monoalkyl ethers , e.g., methoxyethanol and ethoxyethanol are reproductive toxicants.

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: F. Alan Andersen, Ph.D.
Director - COSMETIC INGREDIENT REVIEW (CIR)

FROM: John Bailey, Ph.D. 9/17/10
Industry Liaison to the CIR Expert Panel

DATE: September 17, 2010

SUBJECT: Comments on the Tentative Amended Report on Alkyl PEG Ethers as Used in Cosmetics

It would be helpful to include the abstract in the tentative report so the public has the opportunity to read the abstract and provide comments.

p.5 - As BHA, BHT, citric acid and α-tocopherol are specifically added to the ingredients, they should not be discussed in the Impurities section.

p.6 - Since PEG Methyl Ethers and Methoxy PEGs are two names for the same types of ingredients is it really necessary to have two headings?

p.6 - The CIR Expert Panel has concluded that Formaldehyde is safe in cosmetic products up to 0.2%, and that BHA and BHT are safe as used in cosmetic products. Therefore, the following sentence is not correct. "The Panel has stated that cosmetic preparations should not contain these impurities, nor should they contain peroxides, formaldehyde, BHT, or BHA." The information about impurities for all of the ingredients should not be under the Methoxy PEGs heading. The opinions of the CIR Expert Panel should be presented in the Discussion section of the report.

p.7 - Either in a table or in the text, it would be helpful to state which ingredients had no uses reported to either the VCRP or the Council concentration of use surveys.

p.8, 32 - PEG-Cetyl Stearyl Diether is included in the EU Cosmetic Inventory as Polyoxyethylene Cetyl Stearyl Diether. Both the INCI name and the Cosing name are designated as Japan names.

p.9 - As the Dictionary defines PEG-3 Methyl Ether containing an average of 3 moles of ethylene glycol, it would be helpful to be more specific when stating the purity of PEG-3 Methyl Ether. Was this material 98.7% triethylene glycol monomethyl ether (TGME)? Was the material studied in the dermal penetration study of PEG-3 Methyl Ether 99.9% TGME?

p.9 - Please present the dermal penetration study of PEG-3 Methyl Ether in the Percutaneous Absorption section.

p.10 - Please provide a reference for the human percutaneous absorption study. What was measured in the blood and urine, e.g., did the compound have a some type of label?

p.12 - In the description of Methyl Alcohol, does ocular toxicity refer to blindness that can result from systemic exposure to Methyl Alcohol? Or is this referring to a direct effect on the eyes?

p.15 - Please provide the concentration of TGME used in the dermal toxicity study of PEG-3 Methyl Ether.

p.17 - Please provided the vehicle used in the 13-week dermal study of the Laureth compound.

p.17 - Please provide the concentration of TGME used in the 13-week dermal toxicity study of PEG-3 Methyl Ether.

p.18 - Either provide the number of animals used in the Chronic Oral Exposure section, or indicate that additional details regarding these studies are presented in the Carcinogenicity section.

p.18-9 - The Dermal Irritation heading should be changed to Dermal Irritation and Sensitization or the information about the sensitization potential of the previously reviewed ingredients should be removed from this section.

p.20-21, 23, 24, 31 - If available please provide the vehicle used for all the studies in which the ingredients were diluted, e.g., references 44, 45, 56, 40.

p.24 - When describing the Cholesterol developmental effects, it would be helpful to note that palate anomalies are observed when the dams are treated while the palate is being formed.

p.16 - Please provide the concentration of TGME used in the developmental toxicity (references 38, 58 and 36) of PEG-3 Methyl Ether.

p.28 - Please define MNNG, DMA, MNU and DMBA.

p.29 - What is meant by "essentially non- to non-irritating"?

p.32 - As discussed above, it is not correct to state that BHT and BHA are possible impurities. These ingredients are intentionally added to some ingredients as antioxidants. Both BHT and BHA have been reviewed by the CIR Expert Panel and found safe as used in cosmetic products.

p.33 - In the Summary, please provide the mg/kg/day doses rather than the dietary concentrations for the short-term oral study of the Laureth compound.

p.34 - At what dose was localized erythema observed in the 13-week study of the Laureth compound?

p.34 - What was the route of exposure used in the PEG-3 Methyl Ether study?

p.35 - The meaning of the following sentence is not clear. "Compounds analogous to laureth-9 were not mutagenic in a Ames test of clastogenic in *in vitro* or *in vivo* chromosomal aberration study."

p.36 - As stated above, it is not consistent with previous CIR Expert Panel conclusions to state that Formaldehyde, BHT and BHA should not be present in alkyl PEG ether ingredients.

p.36 - The paragraph concerning potential transmission of BSE and viruses in inconsistent with current FDA policy. The Federal Register: September 7, 2005 (Volume 70, Number 172) states:

> "The exemption of tallow derivatives from the definition of ``prohibited cattle materials" does not depend on the source tallow for the derivatives. For the reasons discussed in the preamble to the interim final rule, tallow derivatives present a negligible risk of transmitting the agent that causes BSE regardless of the source tallow. Therefore, all tallow derivatives are exempt from the ban on the use of prohibited cattle materials in human food and cosmetics."

The paragraph is also inconsistent with international guidelines. The 2010 Terrestrial Animal Health Code of the World Organization for Animal Health (OiE) at http://www.oie.int/eng/normes/mcode/en_chapitre_1.11.5.htm lists "tallow with maximum level of insoluble impurities of 0.15% in weight and derivatives made from this tallow" under the heading "Safe Commodities" that "should not require any BSE

related conditions, regardless of the BSE risk status of the cattle population of the exporting country, zone or compartment".

Based on this code, it would be appropriate to state that tallow derivatives which may be used to make some of the ingredients included in this report must be made from tallow containing a maximum level of insoluble impurities of 0.15% in weight.

The paragraph as currently written implies that some of these ingredients may be derived from humans, which is not correct. Please do not include "human" or "Human Immunodeficiency Virus (HIV)" when discussing these ingredients.

Table 4 - Please provide the meaning of "*" at either the beginning or end of the table.

Table 7, Table 8 - For those studies in which diluted material was studied, it would be helpful if the vehicle was included.

Table 10 - What is the purpose of this table? If it is strictly a tool for the CIR Expert Panel, no changes are necessary. If it is intended for publication, some discussion items need to be edited. For example "inhalation boiler plate" needs to be changed.