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Safety Assessment of Alkyl PEG/PPG Ethers as Used in Cosmetics

Status:	Draft Final Report for Panel Review
Release Date:	August 16, 2013
Panel Meeting Date:	September 9-10, 2013

The 2013 Cosmetic Ingredient Review Expert Panel members are: Chairman, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Ronald A. Hill, Ph.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; James G. Marks, Jr., M.D., Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The CIR Director is Lillian J. Gill, D.P.A. This safety assessment was prepared by Monice M. Fiume, Senior Scientific Analyst/Writer, and Bart A. Heldreth, Ph.D., Chemist.

1101 17th Street, NW, Suite 412 ♢ Washington, DC 20036-4702 ♢ ph 202.331.0651 ♢ fax 202.331.0088 ♢ cirinfo@cir-safety.org

Cosmetic Ingredient Review

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Memorandum

To: CIR Expert Panel Members and Liaisons
From: Monice M. Fiume MMF
Senior Scientific Analyst/Writer
Date: August 16, 2013
Subject: Safety Assessment of Alkyl PEG/PPG Ethers as Used in Cosmetics

Enclosed is the Draft Final Report on the Safety Assessment of Alkyl PEG/PPG Ethers as Used in Cosmetics. At the June meeting, the Panel determined that the 131 alkyl PEG/PPG ethers named in this review are all appropriate for inclusion in this safety assessment and that that these ingredients are safe in the present practices of use and concentration in cosmetics when formulated to be non-irritating.

The alkyl PEG/PPG ethers are the reaction products of an alkyl alcohol and one or more equivalents each of ethylene oxide and propylene oxide (forming repeats of PEG and PPG, respectively). These ingredients are similar to the alkyl PEG ether ingredients that have already been reviewed and found safe when formulated to be non-irritating by the Panel. The principle difference between these two groups of ingredients is inclusion of PPG repeat units that are used to fine-tune the surfactant properties of these ingredients. Inclusion of the PPGs did not raise any additional safety concerns for the Panel because the PPGs were reviewed recently by the CIR and found safe when formulated to be non-irritating.

Although there were few data available on the individual alkyl PEG/PPG ethers, the Panel relied on the existing data on the analogues to support the safety of this ingredient family. The Panel also noted the alkyl PEG/PPG ethers are larger molecules than alkyl PEG ethers and the PPGs, so they are less likely to penetrate the skin and enter the circulation, and, the maximum use concentration reported for the alkyl PEG/PPG ethers is lower than that reported in the safety assessments of the alkyl PEG ethers or the PPGs. Additional concerns, such as the possibility of the presence of the residual starting materials ethylene oxide and propylene oxide or the potential by-product 1,4-dioxane, and the possibility that these ingredients can be penetration enhancers, are addressed in the Discussion of the report.

Comments on the Tentative Report that were received from the Personal Care Products Council have been addressed. You will find a copy of these comments with this submission.

The CIR safety assessments on Alkyl PEG Ethers and on the PPGs are also included with this submission.

At this meeting it is expected the Panel will issue a Final Report.

1101 17th Street, NW Suite 412, Washington, DC 20036
(Main) 202-331-0651 (Fax) 202-331-0088
(Email) cirinfo@cir-safety.org (Website) www.cir-safety.org

Alkyl PEG – PPG Ethers

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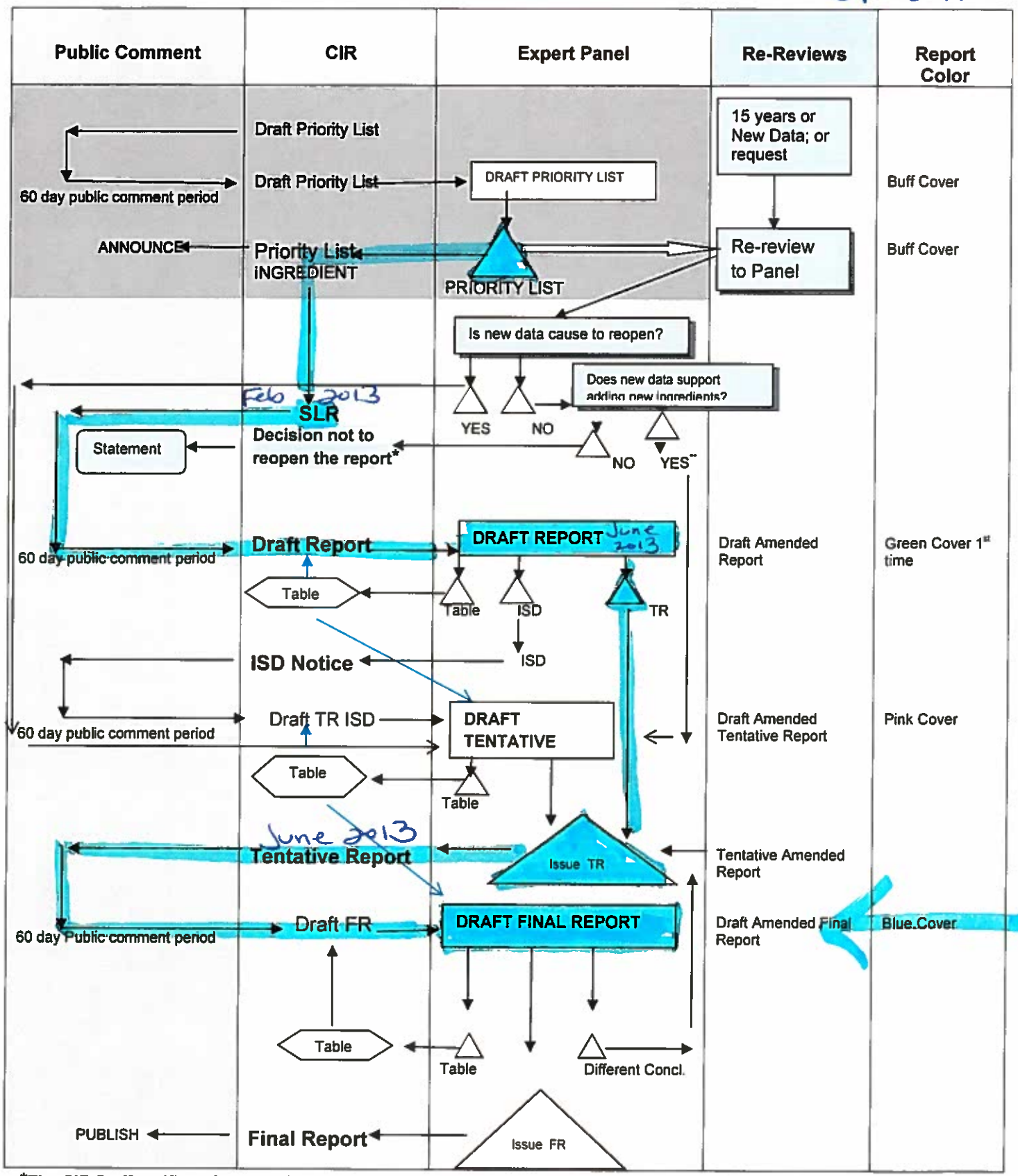
SAFETY ASSESSMENT FLOW CHART

Sept 2013



*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

Alkyl PEG/PPG Ethers Report History

February 11, 2013: Scientific Literature Review

The following unpublished data were received in response to the SLR:

1. Personal Care Products Council. 3-21-2013. Concentration of use by FDA Product Category: Alkyl PEG/PPG Ethers;
2. Personal Care Products Council. 1-31-2013. Propylene Glycol Isodeceth-4 and PPG-1-Isodeceth-4;
3. Personal Care Products Council. 5-2-2013. Concentration of use by FDA Product Category: PEG/PPG-14/2 Propylheptyl Ether;
4. Thomas J. Stephens & Associates Inc. 1994. Mattek Corporation Epiderm® skin model (EPI-100). Irritation potential of undiluted PPG-5-Ceteth-20;
5. Leberco Laboratories. 1973. PPG-5-Ceteth-20: Acute dermal irritation study in rabbits;
6. Bio-Toxicology Laboratories (BTL). 1973. Repeated insult patch test of PPG-5-Ceteth-20.

June 10-11, 2013: Draft Report for Panel Consideration

The Panel issued a Tentative Report with the conclusion that the 131 alkyl PEG/PPG ethers named in this safety assessment are safe in the present practices of use and concentration in cosmetics when formulated to be non-irritating.

Alkyl PEG/PPG Ethers Data Profile – Sept 2013 – Monice Fiume															
	Reported Use	**Method of Manufacture**	**Impurities**	**Toxicokinetics**	**Animal Tox – Acute, Dermal**	**Animal Tox – Acute, Oral**	**Animal Tox, Acute, Inhal**	**Animal Tox – Rptd Dose, Derm**	**Animal Tox, Rptd Dose, Oral**	**Animal Tox – Rptd Dose, Inhal**	**Repro/Dev Tox**	**Genotox**	**Carcinogenicity**	**Dermal Irr/Sens**	**Ocular Irritation**
Alkyl PEG/PPG Ethers (general)		**X**													
PEG-4-PPG-7 C13/C15 Alcohol															
PEG/PPG-3/6 Dimethyl Ether															
PEG/PPG-7/12 Dimethyl Ether															
PEG/PPG-9/2 Dimethyl Ether	**X**														
PEG/PPG-14/7 Dimethyl Ether	**X**														
PEG/PPG-17/4 Dimethyl Ether	**X**														
PEG/PPG-22/40 Dimethyl Ether															
PEG/PPG-27/14 Dimethyl Ether															
PEG/PPG-35/40 Dimethyl Ether	**X**														
PEG/PPG-36/41 Dimethyl Ether	**X**														
PEG/PPG-50/40 Dimethyl Ether	**X**														
PEG/PPG-52/32 Dimethyl Ether															
PEG/PPG-55/28 Dimethyl Ether	**X**														
PEG/PPG-4/2 Propylheptyl Ether															
PEG/PPG-6/2 Propylheptyl Ether															
PEG-7/PPG-2 Propylheptyl Ether															
PEG/PPG-8/2 Propylheptyl Ether															
PEG/PPG-10/2 Propylheptyl Ether															
PEG/PPG-14/2 Propylheptyl Ether															
PEG/PPG-40/2 Propylheptyl Ether															
PPG-2-Ceteareth-9	**X**														
PPG-4-Ceteareth-12															
PPG-10-Ceteareth-20															
PPG-1-Ceteth-1															
PPG-1-Ceteth-5															
PPG-1-Ceteth-10															
PPG-1-Ceteth-20															
PPG-2-Ceteth-1															
PPG-2-Ceteth-5															
PPG-2-Ceteth-10															
PPG-2-Ceteth-20															
PPG-4-Ceteth-1															
PPG-4-Ceteth-5															
PPG-4-Ceteth-10															
PPG-4-Ceteth-20	**X**														

Alkyl PEG/PPG Ethers Data Profile – Sept 2013 – Monice Fiume															
	Reported Use	**Method of Manufacture**	**Impurities**	**Toxicokinetics**	**Animal Tox – Acute, Dermal**	**Animal Tox – Acute, Oral**	**Animal Tox, Acute, Inhal**	**Animal Tox – Rptd Dose, Derm**	**Animal Tox, Rptd Dose, Oral**	**Animal Tox – Rptd Dose, Inhal**	**Repro/Dev Tox**	**Genotox**	**Carcinogenicity**	**Dermal Irr/Sens**	**Ocular Irritation**
PPG-5-Ceteth-20	X													X	
PPG-8-Ceteth-1	X														
PPG-8-Ceteth-2															
PPG-8-Ceteth-5															
PPG-8-Ceteth-10	X														
PPG-8-Ceteth-20	X														
PPG-2 C9-11 Pareth-5															
PPG-2 C9-11 Pareth-7															
PPG-2 C9-11 Pareth-8															
PPG-2 C9-11 Pareth-11															
PPG-2 C12-13 Pareth-8															
PPG-2 C12-15 Pareth-6															
PPG-4 C13-15 Pareth-15															
PPG-5 C9-15 Pareth-6															
PPG-6 C9-11 Pareth-5															
PPG-6 C12-15 Pareth-12															
PPG-6 C12-18 Pareth-11															
PPG-3 C12-14 Sec-Pareth-7															
PPG-4 C12-14 Sec-Pareth-5															
PPG-5 C12-14 Sec-Pareth-7															
PPG-5 C12-14 Sec-Pareth-9															
PPG-1-Deceth-4															
PPG-1-Deceth-5															
PPG-1-Deceth-6															
PPG-1-Deceth-7															
PPG-2-Deceth-3	X														
PPG-2-Deceth-5															
PPG-2-Deceth-7															
PPG-2-Deceth-8															
PPG-2-Deceth-10															
PPG-2-Deceth-12	X														
PPG-2-Deceth-15															
PPG-2-Deceth-20															
PPG-2-Deceth-30															
PPG-2-Deceth-40															
PPG-2-Deceth-50															
PPG-2-Deceth-60															

Alkyl PEG/PPG Ethers Data Profile – Sept 2013 – Monice Fiume															
	Reported Use	**Method of Manufacture**	**Impurities**	**Toxicokinetics**	**Animal Tox – Acute, Dermal**	**Animal Tox – Acute, Oral**	**Animal Tox, Acute, Inhal**	**Animal Tox – Rptd Dose, Derm**	**Animal Tox, Rptd Dose, Oral**	**Animal Tox – Rptd Dose, Inhal**	**Repro/Dev Tox**	**Genotox**	**Carcinogenicity**	**Dermal Irr/Sens**	**Ocular Irritation**
PPG-4-Deceth-4															
PPG-4-Deceth-6															
PPG-6-Deceth-4															
PPG-6-Deceth-9															
PPG-8-Deceth-6															
PPG-14-Deceth-6															
PPG-6-Decyltetradeceth-12															
PPG-6-Decyltetradeceth-20	**X**														
PPG-6-Decyltetradeceth-30	**X**														
PPG-13-Decyltetradeceth-24	**X**														
PPG-20-Decyltetradeceth-10	**X**														
PPG-9-Ethylhexeth-5															
PPG-1-Isodeceth-4															
PPG-1-Isodeceth-6															
PPG-1-Isodeceth-7															
PPG-1-Isodeceth-9															
PPG-2-Isodeceth-4															
PPG-2-Isodeceth-6															
PPG-2-Isodeceth-8															
PPG-2-Isodeceth-9															
PPG-2-Isodeceth-10															
PPG-2-Isodeceth-12	**X**														
PPG-2-Isodeceth-18															
PPG-2-Isodeceth-25															
PPG-3-Isodeceth-1															
PPG-4-Isodeceth-10															
PPG-3-Isosteareth-9	**X**														
PPG-2-Laureth-5															
PPG-2-Laureth-8															
PPG-2-Laureth-12															
PPG-3-Laureth-8															
PPG-3-Laureth-9															
PPG-3-Laureth-10															
PPG-3-Laureth-12															
PPG-4 Laureth-2															
PPG-4 Laureth-5															
PPG-4 Laureth-7															

Alkyl PEG/PPG Ethers Data Profile – Sept 2013 – Monice Fiume															
	Reported Use	**Method of Manufacture**	**Impurities**	**Toxicokinetics**	**Animal Tox – Acute, Dermal**	**Animal Tox – Acute, Oral**	**Animal Tox, Acute, Inhal**	**Animal Tox – Rptd Dose, Derm**	**Animal Tox, Rptd Dose, Oral**	**Animal Tox – Rptd Dose, Inhal**	**Repro/Dev Tox**	**Genotox**	**Carcinogenicity**	**Dermal Irr/Sens**	**Ocular Irritation**
PPG-4-Laureth-15															
PPG-5-Laureth-5	**X**														
PPG-6-Laureth-3															
PPG-25-Laureth-25	**X**		**X**												
PPG-3-Myreth-3															
PPG-3-Myreth-11															
PPG-2-PEG-11 Hydrogenated Lauryl Alcohol Ether															
PPG-3-PEG-6 Oleyl Ether															
PPG-9-Steareth-3															
PPG-23-Steareth-34															
PPG-30 Steareth-4															
PPG-34-Steareth-3	**X**														
PPG-38 Steareth-6															
PPG-1 Trideceth- 6	**X**														
PPG-1 Trideceth-13															
PPG-4 Trideceth-6															
PPG-6 Trideceth-8															
Propylene Glycol Capreth-4															
Propylene Glycol Isodeceth-4															
Propylene Glycol Isodeceth-12															
Propylene Glycol Laureth-6															
Propylene Glycol Oleth-5															

Appendix Data for the Alkyl PEG/PPG Esters Report – Data Profile - From the Safety Assessment on Alkyl PEG Ethers															
	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					

Appendix Data for the Alkyl PEG/PPG Esters Report – Data Profile - From the Safety Assessment on Alkyl PEG Ethers															
	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
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					
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															

Appendix Data for the Alkyl PEG/PPG Esters Report – Data Profile - From the Safety Assessment on Alkyl PEG Ethers															
	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
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					
Ceteth-3	X														

Appendix Data for the Alkyl PEG/PPG Esters Report – Data Profile - From the Safety Assessment on Alkyl PEG Ethers															
	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-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															

Appendix Data for the Alkyl PEG/PPG Esters Report – Data Profile - From the Safety Assessment on Alkyl PEG Ethers																
	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
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																
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																
Isosteareth-2	X															

Appendix Data for the Alkyl PEG/PPG Esters Report – Data Profile - From the Safety Assessment on Alkyl PEG Ethers															
	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
Isosteareth-3															
Isosteareth-5	X														
Isosteareth-8															
Isosteareth-10	X														
Isosteareth-12															
Isosteareth-15															
Isosteareth-16															
Isosteareth-20	X														
Isosteareth-22															
Isosteareth-25															
Isosteareth-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														
Laureth-21	X														
Laureth-23	X		X	X					X	X					X
Laureth-25	X														

Appendix Data for the Alkyl PEG/PPG Esters Report – Data Profile - From the Safety Assessment on Alkyl PEG Ethers															
	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-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														

Appendix Data for the Alkyl PEG/PPG Esters Report – Data Profile - From the Safety Assessment on Alkyl PEG Ethers															
	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
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
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														

Appendix Data for the Alkyl PEG/PPG Esters Report – Data Profile - From the Safety Assessment on Alkyl PEG Ethers															
	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
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															
Undeceth-9															
Undeceth-11	X														
Undeceth-40															
Undecyleneth-6															

Appendix Data for the Alkyl PEG/PPG Esters Report – Data Profile - From the Safety Assessment on Propylene Glycol, Tripropylene Glycol, and PPGs																
	Method of Manufacture	**Impurities**	**Toxicokinetics**	**Animal Tox – Acute, Dermal**	**Animal Tox – Acute, Oral**	**Animal Tox, Acute, Inhal**	**Animal Tox – Rptd Dose, Derm**	**Animal Tox, Rptd Dose, Oral**	**Animal Tox – Rptd Dose, Inhal**	**Repro/Dev Tox**	**Genotox**	**Carcinogenicity**	**Dermal Irr**	**Sensitization**	**Photoallergenicity**	**Ocular Irritation**
Propylene Glycol		X	X	X	X			X	X	X	X	X	X	X	X	X
Tripropylene Glycol	X										X					
PPGs (>3)		X		X	X		X	X					X			X

ALKYL PEG-PPG ETHERS – SEARCH STRATEGY

Get KMP results that give weekly updated search results

Searched SciFinder by CAS No. – set up KM alerts

154518-36-2
155683-77-5
166736-08-9
37251-67-5
37311-00-5
37311-01-6
37311-04-9
61419-46-3
64366-70-7
65150-81-4
68131-40-8
68154-97-2
68238-81-3
68439-51-0
68551-13-3
72484-69-6
9038-43-1
9087-53-0

- No relevant hits

Searched PPG or propylene glycol and each alcohol portion of the name in SciFinder

- No relevant hits

Used Bart's search strategies; refined by document type – set up KMP alerts:

- Substance search - 313 hits
- Alkoyxlated alcohol surfactant

Alkyl PEG/PPG Ethers – June 2013 – Full Panel

DR. BERGFELD: Okay, we're moving on to the next ingredient, which is Dr. Belsito's alkyl PEG/PPG ethers.

DR. BELSITO: Yeah, this is the alkyl PEG/PPG ethers. We felt that this was really similar to the alkyl PEG ethers that we had previously reviewed, except for the PPG repeat units. And we were prepared to go ahead with a safe as used conclusion when formulated to be non- irritating.

DR. MARKS: Our team seconds that motion.

DR. BERGFELD: All right. We have a motion that's been seconded. Any discussion?

DR. BELSITO: Yes. We don't have data on impurities on many, but from the -- again, from the alkyl PEG ethers report, we will use the same limitations, particularly in terms of dioxins. So, we will in the discussion limit what we are concerned about in terms of impurities.

These are surfactants and we know that at least from the alkyl PEG ethers some of them can increase penetration. We have no data on these materials, but that should be mentioned, the potential for penetration enhancement, given the nature of these chemicals.

We also thought that throughout the document we should add the summaries of the PEGs and the PPGs into the document, and use any needed information from those summaries in our discussion to support the safety.

DR. BERGFELD: Agreeable?

DR. MARKS: Yes.

DR. BERGFELD: Any other discussion? So, the motion has been made and seconded that this is safe, and we've had discussant points that will need to be addressed. All those in favor, indicate by raising your hand. Thank you.

(Motion approved by show of hands)

Belsito Team

DR. BELSITO: Okay, so, we may not be able to get through all of this, but at least we can get the opinion of Dan, Curt, and Paul about alkyl PEG/PPG ethers in terms of whether the grouping is okay and are there any that we don't like in that group and then maybe at that point, we'll need to break for lunch and then we can come back and actually look at the report.

So, the first issue is the grouping and this is PEG/PPG ethers. Dan --

DR. LIEBLER: Yes, I was just looking to make sure I was correct on this. I did not have any problem with the ingredients to be included.

DR. BELSITO: Paul, Curt?

DR. SNYDER: I'm trying to see which -- what page are we on with the lists of the --

DR. BELSITO: It starts on page 5 of 187.

DR. SNYDER: I only --

DR. BELSITO: Oh, that's the --

DR. SNYDER: Those are the tables.

DR. BELSITO: But that's a list of all the ingredients that --

DR. SNYDER: Correct.

DR. BELSITO: -- potentially are in here, right, Monice?

DR. SNYDER: Yes.

MS. FIUME: Yes.

DR. BELSITO: Yes.

DR. SNYDER: I only had a question about the laureths because the laureth report says that these are readily absorbed through the skin, a laureth, and is that a concern? That was one note that I had made. And then because we have one baby product that uses PPG-25-Laureth- 25.

DR. LIEBLER: So, I think there are two issues here. One is: Which ingredients belong in the report, should be considered together from sort of a functional and chemical perspective, and I think they all go together there. That's okay.

And then the issue will be little ones, dermal, penetration, and the usual discussions we get into over that versus big ones that aren't going to go anywhere that aren't going to penetrate the stratum corneum. So, I think you're still okay with inclusion of everything, Paul. Paul?

DR. SNYDER: Yes, yes.

DR. LIEBLER: And then the next issue would be properties as far as absorption and --

DR. BELSITO: Well, I think the next issue is that with the exception of PPG-25, Laureth-25, where we have some impurities is really a striking lack of impurities data for these and very little data on toxicology. I mean, I think from a skin standpoint, I'm sort of okay, but from other standpoints of absorption, reproductive effects, where are you guys coming in on these in this huge family of ingredients?

DR. SNYDER: I mean, I had tagged it with a 1,4-dioxane issue an impurity and I had tagged the laureth absorption. So, those were my sort of things that I needed to have alleviated a little bit in regards to datasets and do we have a dataset that allows us to have a read across in the method of manufacture and the impurities issue and then we can deal with the laureth issue in the context of -- because we do have a laureth report possibly.

DR. BELSITO: Yes, I mean, I had a comment here on the discussion page about restricting starting material impurities including dioxanes. And then in terms of, again, from my standpoint, safe as used when formulated to be nonirritating, but there was, again, a lot of data that from a toxicologic standpoint, I mean, I guess these look to me to be basically similar to ingredients we've looked at before, and in many cases being huge molecules which aren't going to do much when they get put on the skin. But, I mean, it's not my area of expertise and it's a huge family we've generated here.

DR. SNYDER: And along those lines, I had written that the PPG report, the PEG report had lots of good data. So, I felt the backbone of this was lots of good data behind it, but then it starts to drift in the chemistry of these particular groups.

MS. FIUME: Dr. Snyder, on PDF page 28, and I believe it was the alkyl PEG ethers report, there is a paragraph --

DR. SNYDER: What page of the PDF are you on, please?

DR. BELSITO: Twenty-eight.

MS. FIUME: Twenty-eight.

DR. SNYDER: Oh, I'm sorry, 28.

MS. FIUME: About halfway down the page where it talks about possible presence of 1.4 dioxane. In that language, it's acceptable and can also be brought into the discussion of this report because that was crafted for the alkyl PEG ethers report.

DR. SNYDER: Yes, that goes to the fact that if that's applicable and if the (inaudible) and the chemistry behind deriving these are similar, then I'm comfortable with that, but I just wanted to raise that as an issue.

(Pause)

DR. ANDERSEN: Yes, I think, Paul, it's anything that involves PEGs, I think you would want to flag it just as a heads-up, if for no other reason.

DR. SNYDER: Yes.

DR. BELSITO: Okay, so, I had said from a derm standpoint safe as used and Paul wants a little bit in the discussion about impurities and does anyone want to kick out or star any of these listed ingredients as being insufficient for reasons that I'm

not thinking of or is everyone comfortable with the safe as used? And, if so, how do we draft this discussion? When formulated to be non --

DR. SNYDER: Irritating, correct. I was largely okay with the group, provided that I was given some reassurance.

Specifically under the impurities on page 23, the second paragraph, it says it is not expected that there would be any significant amount of the residual starting material. So, I'm not certain that that's -- it's beyond my expertise. I'd rather see data to suggest that those starting materials are not present at significant levels because we do know that they are a contaminant.

DR. KLAASEN: Yes, I would second that. In fact, someplace in here, it said you can easily measure the 1.4 dioxane, but they didn't give us any numbers. I suspect it's probably not a major problem, but this dioxane is actually known to be a carcinogen, so, we should have some data, I think, on that.

Also, in general, I don't anticipate problems from this huge class. It is somewhat surprising that we don't have more data, but I think one could hopefully make some kind of a table -- I don't think was in this one -- about what documents have been written on various lake PEGs before and also the various fatty acids, et cetera. And that's the constituents of the molecules and trying to get that and make it a little clearer where that while we might not have these compounds per se, there's a lot of data of the original molecules from which they're made.

MS. FIUME: The data profile does address some of that. It has the information from alkyl PEG ethers report.

DR. KLAASEN: Okay, where's that at?

MS. FIUME: PDF page is probably starts around 13, 14, 15, and --

DR. ANDERSEN: Five, starts at five.

DR. KLAASEN: Yes.

MS. FIUME: Oh, it starts on page -- for the --

DR. ANDERSEN: Oh, for the --

MS. FIUME: I was looking for the constituent information.

DR. LIEBLER: If you could remind us of the color coding that you used, Monice. You've got some tan and you've got some blue and then white. Is that just to break up the groups?

MS. FIUME: It was to break up the groups.

DR. LIEBLER: Okay, okay. So, I think we've got all the constituent families that have been -- the constituent pieces of these ingredients that already reviewed.

DR. KLAASEN: Right.

DR. BELSITO: Yes.

DR. LIEBLER: And there really are no toxicology concerns, no safety concerns with these.

The only issue that might be raised is if you take these as a very large group, there are some gaps in the supporting toxicology, but that, I think, is really only a concern if you sort of set aside the fact that all the constituent pieces have been reviewed very thoroughly.

So, I don't have concern. I can imagine it being raised and need to think a little about how to address that.

DR. BELSITO: So, I guess, I mean, I think it's been pretty well addressed in the appendix, but I guess my question is I didn't understand how this was going to fit in with the final document because you have the summary for the alkyl PEG ethers, you have the summary for the --

SPEAKER: Propylene glycols.

DR. BELSITO: Propylene glycols, et cetera, and I understand the issue of not publishing things twice and these summaries are quite large because they were large families that we created, too, but is that appendix -- I mean, for instance, like in several derm journals now, this appendix would appear on the online version, but not in the print version.

DR. KLAASEN: Right.

DR. BELSITO: How is this appendix going to work?

MS. FIUME: I'm not sure because as soon as we worked with the journal, I was afraid to put all the information in because I knew at some point would have to come out and I've done it in those past documents and that's part of the reason those documents were provided and just the summaries were put in here.

If the discussion is built on the information in this appendix, my personal feeling is that I would like to see the appendix go with the report because it'll provide the support needed for the discussion. But I'm open to whatever suggestions you have.

DR. LIEBLER: I think, practically speaking, you couldn't possibly have this in a printed journal article, not in the 21st Century. So, you simply have to refer to the supplemental tables.

MS. FIUME: When you say you "refer to the supplemental tables," meaning create tables that have all of the data from the original reports and include it in here or create a link referring them to the published document itself and cite that the information that was used in those documents were used to provide the safety for this report and build the discussion from there?

DR. LIEBLER: I would just cite the original reports.

DR. ANDERSEN: Yes, I'm more in the direction of the summaries that Monice included at the end as appendixes are hugely robust. I'm not sure I'd repeat the discussions of all of those earlier documents, but the summaries are what you base the original decisions on.

SPEAKER: Yes.

DR. ANDERSEN: And those are pretty powerful. I would pull out the discussion parts that you want to repeat and use them in the actual safety assessment of the PEG, PPG ethers. So, you got language already that talks about concern and the possible presence of 1,4-dioxane and ethylene oxide as you should have with anything that starts with PEGs since PEGs are a part of this, The Panel stresses to the industry should continue to use the necessary procedures to remove 1,4-dioxane, ethylene oxide impurities before blending them into cosmetic formulations.

So, the heads-up again is perfectly appropriate and that wouldn't be redundant because, again, I don't think the discussion of the alkyl PEG ethers that's in this appendix is necessary, but that summary is just dynamite.

SPEAKER: Yes, I agree.

DR. ANDERSEN: It has that theme of we've looked at these constituents and they are not problematic.

DR. LIEBLER: I'd like to clarify my response about supplemental tables. When you asked me that question, I was still scrolling through the tables at the front of the report, the data summary tables, and there might in the future, and it might come from this panel or from the CIR, be a clever way to represent diverse chemical space in some HTML interact-able tool that would allow the people to see how the data maps across a complex chemical space. I don't know what that would look like, but I wouldn't put it past Bart and Ivan possibly to come up with, given enough coffee. (Laughter) So, but anyway, that's what I was looking at. So, scratch my comment about supplemental tables.

MS. FIUME: Did you see my face when you said that?

DR. LIEBLER: Yes.

MS. FIUME: To creating those tables.

DR. LIEBLER: No, no.

MS. FIUME: It could be another revenue source.

DR. LIEBLER: Yes.

MS. WEINTRAUB: I just wanted to point out sort of my notes from reading this, highlighted the data gaps, sort of what Dr. Liebler was referencing, and I think we've done this before and I feel like recently we've been reviewing a number of ingredients that have a lot of data gaps. So, I think it needs to be explained very clearly in the discussion why it wasn't a problem.

DR. LIEBLER: Yes.

MS. WEINTRAUB: And I know we have experience, especially recently, dealing with this.

DR. LIEBLER: What appeared to be data gaps on those tables, because they seem most obvious when you look at the tables at the beginning of the report --

MS. WEINTRAUB: Yes.

DR. LIEBLER: But if you actually think about the chemistry, they're not data gaps because there are so many ingredients there that map to just about the same point in chemical space, that in other words they are very similar, but they're one carbon difference from something else that has some data, but there are a whole lot of those that don't. So, it looks like a huge --

MS. WEINTRAUB: Right.

DR. LIEBLER: -- list of compounds that we have nothing for. We do have data for chemicals that are adjacent in chemical space and given that, given the fact that we've extensively reviewed all the constituents and that we've even dealt with the issue of the low molecular weight versions of the constituents and their safety, I really have no concerns.

The only thing I can think of is if somebody were to say okay, if you had a laureth with Laureth-2 or 3 so it's a relatively short polyethoxy and then maybe one PPG, that could still be absorbed, but then I think we have enough data from the PEG and PPG reports to fall back on to say that that doesn't really present a safety concern.

MS. WEINTRAUB: But also in the text itself, I believe it's on page 25 and 26, although, I guess it's page 3 of the report, but it seems like 25 and 26 in the PDF, where it says "toxicologic studies, reproductive and developmental toxicity."

DR. LIEBLER: Right.

MS. WEINTRAUB: There's a whole list of things where it said data wasn't found. No, I think it's just the textual --

DR. LIEBLER: Yes.

MS. WEINTRAUB: -- equivalent of what you were saying in the table. But it seems --

DR. BELSITO: Well, when Monice strikes up her summary on PPG and PEGs, there is going to be information in those areas.

MS. WEINTRAUB: Yes.

DR. BELSITO: Okay, so, what's been suggested, and I agree with Alan, is that the summaries that occurred in the appendix be broken up and brought into the various areas of the draft and then if there's anything important that we missed in the discussion, which was in the discussion that it should just be brought in, as well.

And I think the only other thing I would say is, and this will probably come in as we bring the discussion, we didn't bring in the issue of the potential for penetration enhancement, and while that is not here in this document, it is in I think the PPG or the PEG document.

MS. FIUME: It is in the alkyl PEG ethers document.

DR. BELSITO: Yes.

MS. FIUME: And also the summary of that document does discuss that these are expected to absorb in what was found and why that was not an issue.

DR. BELSITO: Right.

MS. FIUME: So, that will show up in the document, as well.

DR. BELSITO: Okay.

DR. SNYDER: I thought your memo, part of the report, the bottom paragraph, captured something that really set me -- when you said "if you agree that the only difference between the alkyl PEG ethers and the alkyl PEG- PPG ethers is the inclusion of the PPG repeat units, we need to capture that somehow in the introductory that the panel believes that there is no significant difference other than this repeat unit issue, and, therefore, all those data are relevant and there are lots of data. So, to me, that was a really good wording you had there, but I didn't quite see that captured in the body of the document.

DR. ANDERSEN: Well, she wasn't sure you were going to buy into it.

DR. LIEBLER: But to get back to Rachel's comment about these toxicokinetics not toxicological studies and not a repro, what we perhaps could say is published absorption distribution were not found, however, and then another sentence or two to briefly state that data on these analogous compounds, the PEGs and the PPGs were found in the respective reports. Because we do have data there and without those data, we wouldn't be comfortable with our conclusion.

MS. WEINTRAUB: I think that makes a lot of sense.

DR. LIEBLER: Yes, and it wouldn't look quite so bleak.

MS. WEINTRAUB: And it reflects the reality of what the panel reviewed to make this decision.

DR. LIEBLER: Right.

MS. WEINTRAUB: Yes.

DR. BELSITO: Okay, so, we're going to go safe as used, we're going to reorganize the report a little bit. We're going to make sure that anything in the discussion that's missed in the current discussion that was in the alkyl PEG ethers report and PPG and PEGs are brought into this report, although I think with the expectation of penetration enhancement, it's all pretty much there already. And that's it.

Any other comments?

(No response)

DR. BELSITO: Okay, wow, I thought we'd just agree on the family.

SPEAKER: Oh, wait, wait.

MS. FIUME: I have two questions to Dr. Belsito. It's safe as used when non-irritating?

DR. BELSITO: Non-irritating.

SPEAKER: Formulated to be non-irritating.

MS. FIUME: And then, Dr.Snyder, on page 22 of the PDF, the last sentence of the second paragraph does state about the PPG repeat units.

Do you want to emphasize more than that or is that going to be adequate?

DR. SNYDER: I just wanted that up front, in some place up front stating what body of data we used to make our assessment as a starting point because I think that was critical for this group.

DR. BELSITO: Great. Okay.

Marks Team

DR. MARKS: So the PEG, propylene glycol ethers, is next. And this is the first review of these alkyl PEG/PPG ethers. The alkyl PEG ether ingredients have been reviewed and have been found to be safe when formulated to be non-irritating. PPGs have also been review recently, found safe when formulated to be irritating. So now --

DR. SLAGA: To be non-irritating.

DR. MARKS: Non-irritating, yeah. Sorry, Tom. Thank you for correcting that for the transcript.

So both of these have been found to be safe when non-irritating. So now we're -- this combination of alkyl PEG plus PPG ethers. First review, Ron and Tom are okay to use the alkyl PEG ethers in the PPG and get a conclusion?

DR. SHANK: Safe, yes.

DR. MARKS: Non-irritating?

DR. SLAGA: Right.

DR. MARKS: Okay. So the insertion of the PPG shouldn't change the toxicologic effects of this. Okay.

Are all the ingredients, the 131 ingredients, I have page 5 and 6. We'll look there. Were they all fine? There wasn't anything that stood out that you would --

DR. SHANK: They're fine with me.

DR. SLAGA: They're fine with me, too.

DR. SHANK: But I'll leave it to our chemists.

DR. MARKS: Why do I have here -- yeah, Tom, I noted this under the impurities on page 23, the amount of residual starting materials. Is that any concern?

DR. HILL: Right. So if propylene oxide or ethylene oxide, or actually this isn't included in the starting materials, but the potential for forming dioxin. That's why that language is in there.

DR. MARKS: But that was covered in the other reports also.

DR. SHANK: Right.

DR. HILL: Well, I think, you know, there should be language in this report reflecting the same thing since there is, isn't there?

DR. MARKS: Right, exactly.

MS FIUME: I don't have the one for dioxane, but I will bring that in.

DR. HILL: And I -- I mean, I stretch my mind to try to think could there be any other similar molecules that would be of concern in these, and no in that case. It bothered me that we have, like, no data, impurities of manufacture any of these to speak of. I think there's one.

DR. MARKS: Okay.

DR. HILL: Yeah, PPG-25-laureth-25. We have some impurities there. That's it.

DR. MARKS: That's the only other comments? Skin tox looks good. So we would move forward with a tentative assessment as safe, and then part of the discussion certainly would be that starter material that we just discussed. Anything else?

DR. SLAGA: Nice report.

MS FIUME: I have a question.

DR. MARKS: It's a nice report. Did you hear that?

MS FIUME: Oh, thank you. I do have a question. I mean, it's slow coming up. In the Council comments, when they asked to bring in the 1-4 dioxane, they had also wanted -- and I don't remember this from the old reports, unless I'm just not remembering. Something about them being very volatile, so there would be very little expected. I don't think we've discussed the volatility in the old reports. Is that something that would be appropriate there?

DR. SHANK: Yes.

MS FIUME: Yes? Okay.

DR. HILL: Yes. I certainly remember discussing that issue on more than one of these. I don't know whether it got in the language of the other reports because I didn't go looking specifically for that. But the idea is that conscientious processing can remove those, and that people who are trying to do a good job formulating know that, and they're looking for that as a spec in the materials that they buy, et cetera, et cetera. So I think it's to try to give some sense of the ease with which they can be removed.

And then like some of the past situations where, okay, we have a polymer and it's a solid, and maybe they can't be so easily, that doesn't apply here.

MS FIUME: Yeah. I have the wording from the ethyl PEG ethers about -- of concern. "The Expert Panel with the possible presence of 1-4 dioxane, ethylene oxide, and a couple of others. And they'll stress the cosmetic industry should continue to use the necessary procedure to remove 1-4 dioxane and ethylene oxide impurities before blending them." I just never had anything about the volatility before.

DR. HILL: Where do we have it now?

MS FIUME: That is on PDF page 28.

DR. HILL: Okay, page 28.

MS FIUME: It's sort in the middle of the page.

DR. MARKS: "It's also of concern to the Expert Panel?"

MS FIUME: Yes.

DR. MARKS: If you look at --

DR. HILL: Yeah, I see it now. I've got it.

DR. MARKS: -- one, two, three, four, five paragraphs above the conclusion.

DR. HILL: But where is the statement of volatility?

MS FIUME: It was sent in the comments to me just before the panel meeting, so you will not have seen those --

DR. HILL: Okay.

MS FIUME: -- until the next time. But before I added it in --

DR. HILL: What are the comments? I'm sorry.

MS. FIUME: That's okay. My computer is very slow right now, so I'm just trying to find where I have --

MR. ANSELL: I don't believe we proposed specific language other than the impurities section should note volatility.

DR. HILL: Yeah. I mean, I think the only reason to note that is towards the ease to which -- the reasonable ease to which they're removable in manufacturing process, and also an indication of the odds that we expect much of them to be there are not high because they are so volatile. But I don't know without seeing what they wrote.

MS. FIUME: It was just they suggest because of the volatility, very little is expected. And that was just new language for me, so before I added it, I just wanted to make sure it was okay with the panel.

DR. HILL: I thought we used words like that somewhere -- not the PEGs or any of those, but somewhere along the line we did. But that might've been one of the solid polymers we were trying to argue that it's all okay.

MS. FIUME: Okay.

DR. MARKS: Any other comments?

DR. SLAGA: Not here.

DR. MARKS: So safe when formulated to be non- irritating.

Safety Assessment of Alkyl PEG/PPG Ethers as Used in Cosmetics

Status:	Draft Final Report for Panel Review
Release Date:	August 16, 2013
Panel Meeting Date:	September 9-10, 2013

The 2013 Cosmetic Ingredient Review Expert Panel members are: Chairman, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Ronald A. Hill, Ph.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; James G. Marks, Jr., M.D., Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The CIR Director is Lillian J. Gill, D.P.A. This safety assessment was prepared by Monice M. Fiume, Senior Scientific Analyst/Writer, and Bart A. Heldreth, Ph.D., Chemist.

1101 17th Street, NW, Suite 412 ◊ Washington, DC 20036-4702 ◊ ph 202.331.0651 ◊ fax 202.331.0088 ◊
cirinfo@cir-safety.org

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ABSTRACT

The CIR Expert Panel assessed the safety of 131 alkyl PEG/PPG ethers as used in cosmetics, concluding that these ingredients are safe in the present practices of use and concentration described in this safety assessment when formulated to be non-irritating. Most of the alkyl PEG/PPG ethers included in this review are reported to function in cosmetics as surfactants, skin conditioning agents, and/or emulsifying agents. The alkyl PEG/PPG ethers share very similar physiochemical properties with another group of ingredients that has been reviewed previously by the CIR Expert Panel and found safe when formulated to be non-irritating, i.e., the alkyl PEG ethers. The only difference between these two families is the inclusion of PPG repeat units, which are used to fine-tune the surfactant properties of this group. The Panel relied heavily on data on analogous ingredients, extracted from the alkyl PEG ethers and PPG reports, when making its determination of safety.

INTRODUCTION

This report assesses the safety of 131 alkyl PEG/PPG ethers (listed in Table 1) as used in cosmetics. Most of the alkyl PEG/PPG ethers included in this review are reported to function in cosmetics as surfactants, skin conditioning agents, and/or emulsifying agents.[1]

The alkyl PEG/PPG ethers are not expected to metabolize to individual components; therefore, incorporating information from existing Cosmetic Ingredient Review (CIR) safety assessments on the individual alcohols is not relevant in this safety assessment. However, knowing that the CIR Expert Panel found 369 alkyl PEG ethers (as well as future alkyl PEG ether cosmetic ingredients that vary from those 369 ethers only by the number of ethylene glycol repeat units), and polypropylene glycols (PPGs) ≥3 safe as used when formulated to be non-irritating[2,3] is relevant because these ingredients share very similar physiochemical profiles, with an internal mixture of various hydrophobicities/hydrophilicities, as expected in these sorts of alkoxyl-based, surfactant-like molecules.[4] The only difference between alkyl PEG ethers and alkyl PEG/PPG ethers is the inclusion of PPG repeat units which is simply used to fine-tune the surfactant properties of these ingredients.

At first glance, it appears there are very little data available on the alkyl PEG/PPG ether ingredients. However, data on analogous ingredients provide a good indication of the lack of toxicity of these ingredients. Accordingly, summary data from the alkyl PEG ether and PPG reports are included in this report as appropriate.

CHEMISTRY

Definition and Structure

Alkyl PEG/PPG ethers are the reaction products of an alkyl alcohol and one or more equivalents each of ethylene oxide and propylene oxide (forming repeats of polyethylene glycol (PEG) and polypropylene glycol (PPG), respectively).

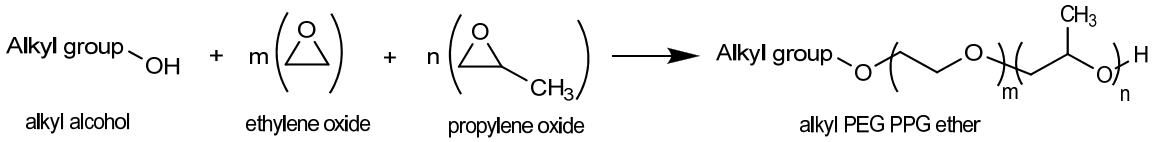


Figure 1. Alkyl PEG/PPG Ether synthesis

The definition of each ingredient, as given in the *International Cosmetic Ingredient Dictionary and Handbook*, is provided in Table 2.[1]

PPG-2-Laureth-5 represents one of the simplest ingredients in this review as the reaction product of lauryl alcohol, five equivalents of ethylene oxide, and two equivalents of propylene oxide.

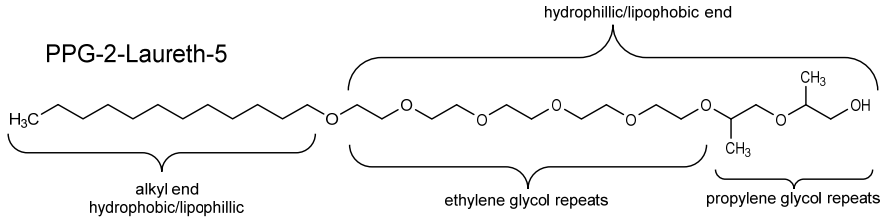


Figure 2. Alkyl PEG/PPG Ether structure – example: PPG-2-Laureth-5

Each of the alkyl PEG/PPG ethers is a surfactant-like molecule, with a chain structure that has a hydrophobic end and a hydrophilic end. Principally, these ingredients differ by variation of the alkyl chain length at the hydrophobic end and the number of alkoxide (PEG and PPG) repeat units at the poly-alkoxide, hydrophilic end. The structures in this report are drawn as block-type, alkoxide polymers only for simplicity's sake. The actual order of alkoxide repeats in each ingredient, and from each source of an ingredient, may be block, alternating, or random.

There are a number of nomenclature conventions to be aware of in this group. For example, PEG-4-PPG-7 C13/C15 alcohol is an ingredient wherein the alkyl chain is variably thirteen or fifteen carbons long ("C13/C15 alcohol") and the poly-alkoxide end consists of *an average* of four ethylene glycol repeats and seven propylene glycol repeats ("PEG-4-PPG-7"). PPG-2-laureth-5 is an ingredient (as shown in Figure 2) wherein the alkyl chain is derived from lauryl alcohol (i.e., is twelve carbons long; "laur") and the poly-alkoxide end consists of an average of five ethylene glycol repeats ("eth-5") and two propylene glycol repeats ("PPG-2"). As an example of a further variation on the naming convention, PEG/PPG-40/2 propylheptyl ether is an ingredient wherein the hydrophobic end is a seven carbon alkyl chain ("heptyl"), with a three carbon branch at the 2-position ("propyl"; this naming convention indicates a Guerbet alcohol, and thus substitution at the 2-position), and the poly-alkoxide end is comprised of *an average* of forty ethylene glycol repeats and two propylene glycol repeats ("PEG/PPG-40/2").

The dimethyl ethers are distinct in this group by being capped at both ends with methyl groups, instead of having one alkyl chain at one end. For example, PEG/PPG-3/6 dimethyl ether is an ingredient wherein one carbon is at each end of a poly-oxide chain, comprised of an average of three ethylene glycol repeats and six propylene glycol repeats.

Physical and Chemical Properties

Physical and chemical properties data on the alkyl PEG/PPG ethers are provided in Table 3.[5-26] Very few published data on specific properties were available, other than most of the alkyl PEG/PPG ethers are clear to slightly yellow liquids.

The alkyl PEG/PPG ethers, as alkoxylate polymers, are generally not defined as a single compound, but as a mixture of a homologous series with a medium-range molecular weight and a specific percentage by weight of the hydrophobic tail.[27] The degree of hydrophobicity and hydrophilicity are fine-tuned by the components that make up each ether. The hydrophobicity of the product can be controlled by the fatty alcohol used and the distribution of the propylene glycol block; alternatively, the hydrophilicity is controlled by varying the length and position of the ethylene glycol repeats

Method of Manufacture

The manufacture of alkyl PEG/PPG ethers consists of a number of variable steps.[28] The first step typically involves activating the alkyl alcohol (e.g., lauryl alcohol) with a metal hydroxide (e.g., potassium hydroxide), thereby generating an alkoxide (e.g., lauroxide; i.e. the initiator). This alkoxide is then reacted with ethylene oxide, propylene oxide, or a mixture of both (a mixture for random poly-alkoxides and consecutively for block poly-alkoxides; i.e., propagation). The propagation of the poly-alkoxide is then terminated with a Brønsted-Lowry type acid (e.g., hydrochloric acid), or in the case of the dimethyl ethers, a methyl halide (e.g., methyl iodide). This synthetic pathway (specifically, the addition of ethoxide) can potentially lead to the generation of some 1,4-dioxane; however, this byproduct can be monitored easily by gas chromatography and minimized via suitable process and purification accommodations.

Inclusion of propylene oxide into nonionic surfactants can be accomplished by 1) placement of a single block of propylene oxide between the alcohol and a block of ethylene oxide; 2) by placing a single block of propylene oxide after a single block of ethylene oxide; 3) by direct placement into the polyoxyethylene portion as a propylene oxide block or as an ethylene oxide-propylene oxide mix; or 4) by placing a single propylene oxide block in the middle of the ethylene oxide chain.[29] The propylene oxide placement affects the physical and surface active properties.

Impurities

No published impurities data were found, other than one source stating that PPG-25-laureth-25 contains ≤10 mg/L 1,4-dioxane.[30]

It is not expected that there would be any significant amount of the residual starting materials used in the manufacture of the alkyl PEG/PPG ethers (i.e., ethylene oxide and propylene oxide) or any significant amount of the residual by-product 1,4-dioxane found in these ingredients. Since these are volatile compounds, any levels present are expected to be low.

It is important that the formulators keep the levels of these starting materials and residual by-product low. The National Toxicology Program (NTP) *Report on Carcinogens, Twelfth Edition* states that ethylene oxide is known to be a human carcinogen based on sufficient evidence of carcinogenicity from studies in humans, including epidemiological studies and studies on mechanisms of carcinogenesis,[31] and that propylene oxide and 1,4-dioxane are reasonably anticipated to be human carcinogens based on sufficient evidence of carcinogenicity from studies in experimental animals[32,33] The International Agency for Research on Cancer (IARC) concluded there is limited evidence in humans and sufficient evidence in experimental animals for the carcinogenicity of ethylene oxide, with an overall evaluation that ethylene oxide is carcinogenic to humans.[34] For propylene oxide and 1,4-dioxane, the IARC concluded there is inadequate evidence in humans and there is

sufficient evidence in experimental animals for carcinogenicity, with an overall evaluation that propylene oxide is possibly carcinogenic to humans.[34,35]

USE

Cosmetic

The alkyl PEG/PPG ethers included in this review are reported to function in cosmetics mostly as surfactants, skin conditioning agents, and/or emulsifying agents.[1] The function(s) of each ingredient are provided in Table 2.

The FDA collects information from manufacturers on the use of individual ingredients in cosmetic formulations as a function of cosmetic product category in its Voluntary Cosmetic Registration Program (VCRP). VCRP data obtained from the FDA in 2013[36] and data received in response to a survey of the maximum reported use concentration by category conducted by the Personal Care Products Council (Council)[37,38] indicate that 26 of the 131 alkyl PEG/PPG ethers named in this safety assessment are currently used in cosmetic formulations; additionally, according to VCRP data, PPG-30-decyltetradeceth-10, an ingredient not named in the *International Cosmetic Ingredient Dictionary and Handbook*, has one reported use. PPG-5-ceteth-20 has the most reported uses, 445, followed by and PEG/PPG-36/41 dimethyl ether, 243 reported uses, and PPG-1-trideceth-6, 224 reported uses. All other in-use ingredients have less than 40 reported uses. (Table 4.)

According to the results of the concentration of use survey, PPG-5-ceteth-20 and PEG/PPG-14/7 dimethyl ether have the highest reported concentrations of use in leave-on formulations; PPG-5-ceteth-20 is used at up to 10% in "other" fragrance preparations and in tonics, dressings, and other hair grooming aids, and PEG/PPG-14/7 dimethyl ether is used at up to 7% in face and neck products and body and hand products. PPG-2-isodeceth-12 has the highest use concentration in rinse-off products; it is used at up to 10% in paste masks and mud packs. All other in-use alkyl PEG/PPG ethers are reported to be used in leave-on products at concentrations of 5% or below. (Table 4.) The 105 alkyl PEG/PPG ethers not reported to be in use are listed in Table 5.

In some cases, reports of uses were received in the VCRP, but no concentration of use data are available. For example, PPG-2-ceteareth-9 is reported to be used in 9 cosmetic formulations, but no use concentration data were reported. Additionally, for some ingredients, no reported uses were received in the VCRP, but a use concentration was provided in the industry survey. For example, PEG/PPG-55/28 dimethyl ether was not reported to be in use in the VCRP, but the industry survey indicated that it is used at up to 5% in shampoos and other non-coloring hair preparations and at 3% in face and neck formulations. It should be presumed in these cases that there is at least one use in every category for which a concentration is reported.

Some alkyl PEG/PPG ethers are reported to be used in products that are applied to baby skin (e.g., PPG-25-laureth-25 has one reported used in "other" baby products), to the eye area or mucous membranes (e.g., PEG/PPG-14/7 dimethyl ether is used in eye lotions at 5%), or that could possibly be ingested (e.g., PEG/PPG-36/41 dimethyl ether is used at 5% in lipsticks). Additionally, some of the alkyl esters are used in cosmetic sprays and could possibly be inhaled; the maximum reported use in spray formulation is 7% PEG/PPG-14/7 dimethyl ether in spray body and hand products. In practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters >10 μm, with propellant sprays yielding a greater fraction of droplets/particles <10 μm compared with pump sprays.[39,40] Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and thoracic regions of the respiratory tract and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.[41,42]

Some of the alkyl PEG/PPG ethers are used in spray deodorant products at low concentrations of use; the highest reported use concentration of this type was 0.19% PPG-8-ceteth-20.[37] There is some evidence indicating that deodorant spray products can release substantially larger fractions of particulates having aerodynamic equivalent diameters in the range considered to be respirable.[42] However, the information is not sufficient to determine whether significantly greater lung exposures result from the use of deodorant sprays, compared to other cosmetic sprays.

All of the alkyl PEG/PPG ethers included in this report are listed in the European Union inventory of cosmetic ingredients.[43]

Non-Cosmetic

In Europe, PPG-4-trideceth-6 can be used at 0.05 mg/kg in food contact materials; it is to be used only in polytetraflorothylene (PTFE) items sintered at high temperatures.[44] (PTFE is the non-stick coating used on cookware).[45]

The inclusion of PPG-5-ceteth-20 in the development of dermal[46] and nasal[47] drug delivery systems is being evaluated.[46] In both studies, systems composed of PPG-5-ceteth-20, oleic acid, and water were used to form thermodynamically-stable microemulsions that could phase into a liquid crystalline matrix.

Other examples of non-cosmetic industrial uses are provided in Table 6.[5,12,25]

TOXICOKINETICS

Published absorption, distribution, metabolism, and excretion data were not found. However, data on analogous compounds are available from the safety assessments of the alkyl PEG ethers and PPGs, and summaries of these data follow.

From the CIR safety assessment of Alkyl PEG Ethers: [2]

According to the original laureths report, in general, alkyl PEG ethers are readily absorbed through the skin of guinea pigs and rats and through the intestinal mucosa of rats, and they are quickly eliminated from the body through the urine, feces, and expired air. In rats, compounds analogous to laureth-9 are rapidly absorbed and excreted in the urine after oral, intraperitoneal, and 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 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, the 4-hour percutaneous absorption decreased from 22.9% for laureth-1 to 2.1% for laureth-10 solutions, 0.25% in ethanol. 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% for a 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.

From the CIR safety assessment of PPGs: [3]

In mammals, the major pathway of propylene glycol metabolism is to lactaldehyde and then lactate via hepatic alcohol and aldehyde dehydrogenases. When propylene glycol was administered intravenously to human subjects (patients), elimination from the body occurred in a dose-dependent manner. Animal studies using PPGs with avg mol wts of 425-2025 indicated that PPGs are readily absorbed from the gastrointestinal tract and excreted in the urine and feces.

Dermal penetration of propylene glycol from a ternary cosolvent solution through hairless mouse skin was 57% over a 24 h period. However, in a study in which propylene glycol was applied to the finger tip of a human subject, the results of thermal emission decay-Fourier transform infrared spectroscopy indicated that propylene glycol did not reach the dermis.

Penetration Enhancement

PPG-4-ceteth-20 did not enhance the penetration of tenoxicam, a non-steroidal anti-inflammatory drug, through guinea pig skin.[48] An in vitro study was performed in which the permeation through guinea pig skin of a 1.0% tenoxicam suspension containing 10% propylene glycol and 5.0% PPG-4-ceteth-20 was compared to that of tenoxicam without the surfactant. One gram of the test material was applied to the skin sample, and the receptor fluid was sampled every 3 h, for 48 h. The steady-state flux was $8.11 \pm 0.56 \times 10^{-5}$ $\mu g/s \cdot cm^2$ for tenoxicam without surfactant and $7.28 \pm 0.94 \times 10^{-5}$ $\mu g/s \cdot cm^2$ for tenoxicam with PPG-4-ceteth-20; penetration rates were not statistically significantly different.

From the CIR safety assessment of Alkyl PEG Ethers: [2]

Some alkyl PEG ethers, such as ceteareths and oleths, have been reported to enhance the penetration of certain compounds through the skin.

From the CIR safety assessment of PPGs: [3]

Propylene glycol can act as a penetration enhancer for some chemicals and under some conditions. Often, it works synergistically with other enhancers. The mechanism by which propylene glycol enhances penetration has not been definitively identified.

TOXICOLOGICAL STUDIES

No published single-dose or repeated-dose toxicity or ocular irritation studies were found. However, data on analogous compounds are available from the safety assessments of the alkyl PEG ethers and PPGs, and summaries of these data follow.

Single-Dose (Acute) Toxicity

From the CIR safety assessment of Alkyl PEG Ethers: [2]

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 indicated 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.

From the CIR safety assessment of PPGs: [3]

The oral LD_{50} of propylene glycol was >21 g/ kg for rats. The LD_{50} of PPG, mol wts 300-3900, ranged from 0.5-40 g/kg for rats, while the oral LD_{50} of PPGs, mol wts not given, ranged from 1.5-17 g/kg for guinea pigs . The dermal LD_{50} of propylene glycol was >11.2 g/kg for mice and was 13 g/kg for rats. The dermal LD_{50} of PPG, mol wts 425-2025, was >20 ml/kg for rabbits.

Repeated-Dose Toxicity

From the CIR safety assessment of Alkyl PEG Ethers: [2]

In 21-day, 90-day and 2-yr feeding studies, compounds analogous to laureth-9 had no-observable adverse effect levels (NOAELs) of 459-519, 50-785, and 50-162 mg/kg bw in rats. In a 13-day oral study with an unspecified deceth, doses of ≥25 g/kg resulted in death in rabbits. 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, while in a 91-day drinking water study, PEG-3 methyl ether had a NOAEL of 400 mg/kg/day for liver effects; testicular effects were observed, but were attributed to contamination with 2-methoxyethanol. In a 13-wk dietary study, 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. 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 a 2-wk dermal study, 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, while in a 13-wk study, moderate localized erythema was observed at all doses of 2.5% aq. C_{14-15} alkyl ethoxylate number $(AE)_7$ in rabbits. For PEG-3 methyl ether, some erythema and edema were observed with occlusive applications of 1000 mg/kg/day in a 12-day study 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 14- and 21-day studies, 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. 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.

From the CIR safety assessment of PPGs: [3]

All mice survived in a study in which mice were given 10% propylene glycol in drinking water for 14 days, and all rats and mongrel dogs survived oral dosing with up to 3.0 ml 100% propylene glycol, 3 times per day, for 3 days. In a subchronic study, a dose of ≤50,000 ppm propylene glycol given in the feed for 15 wks did not produce any lesions. PPG 750 did not cause any adverse effects when given at 0.1% for 10 days, but a concentration of 1% produced slight increases in liver and kidney weight. The highest no effect level of PPG 1200 fed to rats and dogs for 90 days was 0.3%. No adverse effects were seen in a 90-day study in which rats or dogs fed 501 or 810 mg/kg/day, respectively, PPG 2000. In a subchronic dermal study, 1 ml/kg PPG 2000 did not cause adverse effects in rabbits, but 5 and 10 ml/kg caused a slight depression in growth. Subchronic inhalation data reported some effects in rats due to propylene glycol exposure of 2.2 mg/l air for 6 h/day, 5 days/wk, for 13 wks, but these effects were inconsistent and without dose-response trends. No toxic effects were reported in chronic studies when rats or dogs were given feed containing 50 g/kg or 5 g/kg, respectively, propylene glycol.

Ocular Irritation

From the CIR safety assessment of Alkyl PEG Ethers: [2]

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.

From the CIR safety assessment of PPGs: [3]

Undiluted propylene glycol and PPG, mol wt 425-2025, were at most slight ocular irritants.

Mucosal Irritation

From the CIR safety assessment of Alkyl PEG Ethers: [2]

A single instillation of 1% Laureth-9 (vehicle not specified) into the nostrils of rats caused swelling after 4 h and severe damage to the nasal mucosa, with shedding of necrotic epithelium, after 2 days. Regeneration of the epithelium started by day 3. A single dose of undiluted laureth-9 and a repeated dose (5 days) of a 15% aq. solution was not an irritant to the vaginal mucosa of dogs.

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

No published reproductive and developmental toxicity studies were found. However, data on analogous compounds are available from the safety assessments of the alkyl PEG ethers and PPGs, and summaries of these data follow.

From the CIR safety assessment of Alkyl PEG Ethers: [2]

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 were 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.

From the CIR safety assessment of PPGs: [3]

Oral administration of propylene glycol did not have any adverse reproductive or developmental effects when evaluated in mice at concentrations of ≤5%, in rats at doses of ≤1600 mg/kg, in rabbits at doses of ≤1230 mg/kg, or in hamsters at doses of ≤1550 mg/kg. Embryonic development was reduced or inhibited completely in cultures of mouse zygotes exposed to 3.0 or 6.0 M propylene glycol, respectively. A study examining induction of cytogenetic aberrations in mice reported an increase in the frequency of premature centrosphere separation with 1300-5200 mg/kg propylene glycol. In zygotes from propylene glycol-dosed mice, hyperploidy was increased.

GENOTOXICITY

No published genotoxicity studies were found. However, data on analogous compounds are available from the safety assessments of the alkyl PEG ethers and PPGs, and summaries of these data follow.

From the CIR safety assessment of Alkyl PEG Ethers: [2]

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 an Ames test or clastogenic in in vitro or in vivo chromosomal aberration studies. PEG-3 methyl ether was not mutagenic or genotoxic 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.

From the CIR safety assessment of PPGs: [3]

Propylene glycol, ≤10,000 µg/plate, was not mutagenic in Ames tests with or without metabolic activation. Propylene glycol, tested at concentrations of 3.8-22.8 mg/ml, was a weak but potential inducer of sister chromatid exchanges (SCEs), causing a dose-dependent increase in SCEs in a Chinese hamster cell line. However in another SCE assay using human cultured fibro-

blasts and Chinese hamster cells with and without metabolic activation, propylene glycol was not mutagenic. Propylene glycol, 32 mg/ml, induced chromosomal aberrations in a Chinese hamster fibroblast line, but not in human embryonic cells. Propylene glycol was not mutagenic in mitotic recombination or basepair substitution assays, or in a micronucleus test or a hamster embryo cell transformation assay. (Concentration used not specified) Tripropylene glycol, ≤10,000 µg/plate, was not mutagenic in an Ames assay.

CARCINOGENICITY

No published carcinogenicity studies were found. However, data on analogous compounds are available from the safety assessments of the alkyl PEG ethers and PPGs, and summaries of these data follow.

From the CIR safety assessment of Alkyl PEG Ethers: [2]

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.

From the CIR safety assessment of PPGs: [3]

Undiluted propylene glycol was not carcinogenic in lifetime dermal study in mice, and it was not carcinogenic in a 2-yr chronic feed study in which rats were given ≤50,000 ppm propylene glycol in the diet.

IRRITATION AND SENSITIZATION

Non-Human

PPG-5-ceteth-20 was classified as a moderate to mild dermal irritant in an *in vitro* assay.[49] In an MTT (3-(4,5-dimethyl-thiazol-2-4)-2,5-diphenyltetrazolium bromide) cytotoxicity assay performed to predict dermal irritancy, PPG-5-ceteth-20 had an ET_{50} of 9.78 h; substances with an ET_{50} (i.e., time required to reduce tissue viability by 50%) in the range of 4-12 h have an expected irritancy of moderate to mild.

A single 24-h occlusive application of PPG-5-ceteth-20 was not a primary dermal irritant in rabbits.[50] Occlusive patches containing 0.5 ml undiluted PPG-5-ceteth-20 were applied for 24 h to both intact and abraded skin of three rabbits; the test sites were clipped free of hair. The patches were described as 2 x 2; units were not provided. The test sites were evaluated for reactions upon patch removal, and 48 h later. No erythema, eschar formation, or edema was observed at any of the test sites 24 or 72 h after application.

Non-human irritation and sensitization data on analogous compounds are also available from the safety assessments of the alkyl PEG ethers and PPGs, and summaries of these data follow.

From the CIR safety assessment of Alkyl PEG Ethers: [2]

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 a 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 in guinea pigs.

From the CIR safety assessment of PPGs: [3]

In one study using nude mice, 50% propylene glycol may have caused skin irritation, while in another study, 100% propylene glycol was minimally irritating to hairless mice. Undiluted propylene glycol was at most a mild dermal irritant in a Draize test using rabbits with intact and abraded skin. No reactions to undiluted propylene glycol were observed with guinea pigs, rabbits, or Gottingen swine. Using nude mice, hypertrophy, dermal inflammation, and proliferation were observed with 50% propylene glycol. These effects were not seen in hairless mice with undiluted propylene glycol. Propylene glycol (concentra-

tions not given) was negative in a number of sensitization/allergenicity assays using guinea pigs. In a study using guinea pigs, 0.5 ml propylene glycol was a weak sensitizer. PPG (concentration not stated), mol wt 425-2025, was not an irritant to rabbits.

Human

PPG-5-ceteth-20 was not a primary irritant, fatiguing agent, or sensitizer in a human repeated insult patch test (HRIPT).[51] Induction consisted of 10 occlusive patches containing 0.5 ml undiluted PPG-5-ceteth-20 applied to the inner aspect of the arm or forearm of 50 subjects. The first induction patch was applied for 48 h, and the remaining nine patches for 24 h; there was a 24-h rest period between patches. The test site was evaluated for reactions upon removal of each patch. A 48-h challenge patch was applied 10-14 days after the last induction patch. No reactions were observed in any of the subjects during induction or challenge.

Human irritation and sensitization data on analogous compounds are also available from the safety assessments of the alkyl PEG ethers and PPGs, and summaries of these data follow.

From the CIR safety assessment of Alkyl PEG Ethers: [2]

In a retrospective clinical study, 0.97% of patients had a weakly positive and 0.25% of 3186 patients had a strongly positive reaction to 0.5% laureth-9, and 1.77% had weakly and 0.34% of 6202 had strongly positive allergic contact reactions 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 $C_{14-15}AE_{6.5}$ was slightly irritating in 10 subjects when applied under an occlusive patch for 24 h. In a human repeat insult patch test (HRIPT) in 51 subjects 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% $C_{14-15}AE_7$ 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 in 20 subjects. These 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.

From the CIR safety assessment of PPGs: [3]

In some studies, propylene glycol induced skin irritation reactions in normal subjects and in patients, while in other studies, no irritation was reported in predictive tests. Reactions were observed at concentrations as low as 10% in a predictive test in 24 subjects and 2% in provocative tests, while in other studies, up to 100% propylene glycol was not reported to cause irritation. Use studies in 24-40 subjects of deodorants containing 35-73% propylene glycol did not report any potential for eliciting irritation or sensitization. Propylene glycol generally did not induce sensitization reactions when tested at 12-86%, although results were questionable in a 101 subject RIPT of a deodorant containing 73% propylene glycol. Additionally, in a modified Draize sensitization study with 203 subjects, propylene glycol (0.2 ml, concentration not stated) induced 19 cutaneous reactions at challenge. Propylene glycol did not produce a photoallergic response in a provocative photopatch test in 82 patients. Retrospective analysis of pools of patient patch test data indicated that ≤6.0% of patients tested had positive reactions to 30% aq. propylene glycol.

SUMMARY

Because the data from the alkyl PEG ethers report and PPG report are summary data from those reports, this summary only includes new data provided in this safety assessment.

This report is a safety assessment of 131 alkyl PEG/PPG ethers as used in cosmetics. Alkyl PEG/PPG ethers are the reaction products of an alkyl alcohol and one or more equivalents each of ethylene oxide and propylene oxide (forming repeats of PEG and PPG, respectively). Each of the alkyl PEG/PPG ethers has surfactant properties, with a chain structure that has a hydrophobic end and a hydrophilic end; the dimethyl ethers are distinct in this group by being capped at both ends with methyl groups, instead of having one alkyl chain at one end. The alkyl PEG/PPG ethers are typically manufactured by: 1) activating the alcohol by generating an alkoxide; 2) reacting the alkoxide with ethylene oxide, propylene oxide, or a mixture of both; and 3) terminating the propagation. The actual order of alkoxide repeats in each ingredient, and from each source of an ingredient, may be block, alternating, or random, and the propylene oxide placement affects the physical and surface-active properties. Based on this chemistry, the potentially carcinogenic compounds ethylene oxide and propylene oxide are potentially present at residual levels, along with the residual by-product 1,4-dioxane. In practice, these impurities are not present because of steps in the manufacturing process that remove them.

The alkyl PEG/PPG ethers are reported to function in cosmetics mostly as surfactants, skin conditioning agents, and/or emulsifying agents. VCRP data obtained from the FDA in 2013 and data received in response to a Council survey of maximum reported use concentration indicate that 26 of the alkyl PEG/PPG ethers named in this safety assessment are currently used in cosmetic formulations. PPG-5-ceteth-20 has the most reported uses, 445, and the highest reported concentration in leave-on products, 10%. Most of the in-use alkyl PEG/PPG ethers are used in less than 40 formulations and at concentrations of ≤5%.

In Europe, PPG-4-trideceth-6 can be used at 0.05 mg/kg in food contact materials; it is to be used only in PTFE items sintered at high temperatures. PPG-5-ceth-20 is being evaluated for inclusion in dermal and nasal drug delivery systems.

Often, surfactants can be penetration enhancers. However, PPG-4-ceteth-20 did not enhance the penetration of tenoxicam through guinea pig skin.

Undiluted PPG-5-ceteth-20 was predicted to be a mild to moderate dermal irritant based on the results of an MTT cytotoxicity assay, but it was not a primary irritant in rabbit skin, nor was it a primary irritant, fatiguing agent, or sensitizer in a 50 subject HRIPT.

DISCUSSION

Alkyl PEG/PPG ethers are the reaction products of an alkyl alcohol and one or more equivalents each of ethylene oxide and propylene oxide (forming repeats of PEG and PPG, respectively). The alkyl PEG/PPG ethers share very similar physiochemical properties with another family of ingredients that previously has been reviewed by the CIR Expert Panel and found safe when formulated to be non-irritating, i.e., the alkyl PEG ethers. The only difference between the alkyl PEG ethers and the alkyl PEG/PPG ethers is the inclusion of PPG repeat units, which are used to simply fine-tune the surfactant properties of these ingredients. The PPGs also have been found safe when formulated to be non-irritating by the CIR Expert Panel.

Although there are little data available on the individual alkyl PEG/PPG ethers, the Panel stated that existing data on analogous ingredients (from the alkyl PEG ethers and PPG safety assessments) support the safety of this ingredient family. These data provided the Panel with a good indication of a lack of toxicity of the alkyl PEG/PPG ethers. Additionally, the alkyl PEG/PPG ethers are larger molecules than alkyl PEG ethers and the PPGs, so they are less likely to penetrate the skin and enter the circulation. And, the maximum use concentration reported for the alkyl PEG/PPG ethers is lower than that reported in the safety assessments of the alkyl PEG ethers or the PPGs.

The Expert Panel was concerned about the possibility of the presence of residual starting materials used in the manufacture of the alkyl PEG/PPG ethers (i.e., ethylene oxide and propylene oxide) and of the residual by-product, 1,4-dioxane. These compounds are potentially carcinogenic. The Panel noted these are volatile compounds, and therefore levels of these compounds in cosmetics are expected to be below the level of toxicological concern. Although levels may be low, the Panel stressed that the cosmetics industry should continue to use the necessary procedures to remove these impurities from the ingredients before blending them into cosmetic formulations.

The Expert Panel recognized that some of the alkyl PEG/PPG ethers 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.

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

Finally, the Panel discussed the issue of incidental inhalation exposure of alkyl PEG/PPG ethers in products that could be inhaled. Because the alkyl PEG/PPG ethers are not expected to have chemical activity in biological systems, particles deposited in the nasopharyngeal or bronchial regions of the respiratory tract present no toxicological concerns. Coupled with the small actual exposure in the breathing zone, the expected particle size, and the concentrations at which the ingredients are used, the available information indicates that incidental inhalation would not be a significant route of exposure that might lead to local respiratory or systemic effects. A detailed discussion and summary of the Panel's approach to evaluating incidental inhalation exposures to ingredients in cosmetic products that may be aerosolized is available at http://www.cir-safety.org/cir-findings.

CONCLUSION

The CIR Expert Panel concluded that the following 131 alkyl PEG/PPG ethers are safe in the present practices of use and concentration in cosmetics described in this safety assessment when formulated to be non-irritating.

PEG-4-PPG-7 C13/C15 Alcohol*
PEG/PPG-3/6 Dimethyl Ether*
PEG/PPG-7/12 Dimethyl Ether*
PEG/PPG-9/2 Dimethyl Ether
PEG/PPG-14/7 Dimethyl Ether
PEG/PPG-17/4 Dimethyl Ether
PEG/PPG-22/40 Dimethyl Ether*
PEG/PPG-27/14 Dimethyl Ether*
PEG/PPG-35/40 Dimethyl Ether
PEG/PPG-36/41 Dimethyl Ether
PEG/PPG-50/40 Dimethyl Ether
PEG/PPG-52/32 Dimethyl Ether*
PEG/PPG-55/28 Dimethyl Ether
PEG/PPG-4/2 Propylheptyl Ether*
PEG/PPG-6/2 Propylheptyl Ether*
PEG-7/PPG-2 Propylheptyl Ether*
PEG/PPG-8/2 Propylheptyl Ether*
PEG/PPG-10/2 Propylheptyl Ether*
PEG/PPG-14/2 Propylheptyl Ether*
PEG/PPG-40/2 Propylheptyl Ether*
PPG-2-Ceteareth-9
PPG-4-Ceteareth-12*
PPG-10-Ceteareth-20*
PPG-1-Ceteth-1*
PPG-1-Ceteth-5*
PPG-1-Ceteth-10*
PPG-1-Ceteth-20*
PPG-2-Ceteth-1*
PPG-2-Ceteth-5*
PPG-2-Ceteth-10
PPG-2-Ceteth-20*
PPG-4-Ceteth-1*
PPG-4-Ceteth-5*
PPG-4-Ceteth-10*
PPG-4-Ceteth-20
PPG-5-Ceteth-20
PPG-8-Ceteth-1
PPG-8-Ceteth-2*
PPG-8-Ceteth-5*
PPG-8-Ceteth-10
PPG-8-Ceteth-20
PPG-2 C9-11 Pareth-5*
PPG-2 C9-11 Pareth-7*
PPG-2 C9-11 Pareth-8*
PPG-2 C9-11 Pareth-11*
PPG-2 C12-13 Pareth-8
PPG-2 C12-15 Pareth-6*
PPG-4 C13-15 Pareth-15*
PPG-5 C9-15 Pareth-6*
PPG-6 C9-11 Pareth-5*
PPG-6 C12-15 Pareth-12*
PPG-6 C12-18 Pareth-11*
PPG-3 C12-14 Sec-Pareth-7*
PPG-4 C12-14 Sec-Pareth-5*
PPG-5 C12-14 Sec-Pareth-7*
PPG-5 C12-14 Sec-Pareth-9*
PPG-1-Deceth-4*
PPG-1-Deceth-5*
PPG-1-Deceth-6*
PPG-1-Deceth-7*
PPG-2-Deceth-3
PPG-2-Deceth-5*
PPG-2-Deceth-7*
PPG-2-Deceth-8*
PPG-2-Deceth-10*
PPG-2-Deceth-12
PPG-2-Deceth-15*
PPG-2-Deceth-20*
PPG-2-Deceth-30*
PPG-2-Deceth-40*
PPG-2-Deceth-50*
PPG-2-Deceth-60*
PPG-4-Deceth-4*
PPG-4-Deceth-6*
PPG-6-Deceth-4*
PPG-6-Deceth-9*
PPG-8-Deceth-6*
PPG-14-Deceth-6*
PPG-6-Decyltetradeceth-12*
PPG-6-Decyltetradeceth-20
PPG-6-Decyltetradeceth-30
PPG-13-Decyltetradeceth-24
PPG-20-Decyltetradeceth-10
PPG-9-Ethylhexeth-5*
PPG-1-Isodeceth-4*
PPG-1-Isodeceth-6*
PPG-1-Isodeceth-7*
PPG-1-Isodeceth-9*
PPG-2-Isodeceth-4*
PPG-2-Isodeceth-6*
PPG-2-Isodeceth-8*
PPG-2-Isodeceth-9*
PPG-2-Isodeceth-10*
PPG-2-Isodeceth-12
PPG-2-Isodeceth-18*
PPG-2-Isodeceth-25*
PPG-3-Isodeceth-1*
PPG-4-Isodeceth-10*
PPG-3-Isostearath-9
PPG-2-Laureth-5*
PPG-2-Laureth-8*
PPG-2-Laureth-12*
PPG-3-Laureth-8*
PPG-3-Laureth-9*
PPG-3-Laureth-10*
PPG-3-Laureth-12*
PPG-4 Laureth-2*
PPG-4 Laureth-5*
PPG-4 Laureth-7*
PPG-4-Laureth-15*
PPG-5-Laureth-5
PPG-6-Laureth-3*
PPG-25-Laureth-25
PPG-3-Myreth-3*
PPG-3-Myreth-11*
PPG-2-PEG-11 Hydrogenated Lauryl Alcohol Ether*
PPG-3-PEG-6 Oleyl Ether*
PPG-9-Steareth-3*
PPG-23-Steareth-34*
PPG-30 Steareth-4*
PPG-34-Steareth-3
PPG-38 Steareth-6*
PPG-1 Trideceth- 6
PPG-1 Trideceth-13*
PPG-4 Trideceth-6*
PPG-6 Trideceth-8*
Propylene Glycol Capreth-4*
Propylene Glycol Isodeceth-4*
Propylene Glycol Isodeceth-12*
Propylene Glycol Laureth-6*
Propylene Glycol Oleth-5*

*Not reported to be in current use. 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.

TABLES

Table 1. Alkyl PEG/PPG Ethers included in this assessment

PEG-4-PPG-7 C13/C15 Alcohol	PPG-2 C9-11 Pareth-11	PPG-2-Isodeceth-4
PEG/PPG-3/6 Dimethyl Ether	PPG-2 C12-13 Pareth-8	PPG-2-Isodeceth-6
PEG/PPG-7/12 Dimethyl Ether	PPG-2 C12-15 Pareth-6	PPG-2-Isodeceth-8
PEG/PPG-9/2 Dimethyl Ether	PPG-4 C13-15 Pareth-15	PPG-2-Isodeceth-9
PEG/PPG-14/7 Dimethyl Ether	PPG-5 C9-15 Pareth-6	PPG-2-Isodeceth-10
PEG/PPG-17/4 Dimethyl Ether	PPG-6 C9-11 Pareth-5	PPG-2-Isodeceth-12
PEG/PPG-22/40 Dimethyl Ether	PPG-6 C12-15 Pareth-12	PPG-2-Isodeceth-18
PEG/PPG-27/14 Dimethyl Ether	PPG-6 C12-18 Pareth-11	PPG-2-Isodeceth-25
PEG/PPG-35/40 Dimethyl Ether	PPG-3 C12-14 Sec-Pareth-7	PPG-3-Isodeceth-1
PEG/PPG-36/41 Dimethyl Ether	PPG-4 C12-14 Sec-Pareth-5	PPG-4-Isodeceth-10
PEG/PPG-50/40 Dimethyl Ether	PPG-5 C12-14 Sec-Pareth-7	PPG-3-Isosteareth-9
PEG/PPG-52/32 Dimethyl Ether	PPG-5 C12-14 Sec-Pareth-9	PPG-2-Laureth-5
PEG/PPG-55/28 Dimethyl Ether	PPG-1-Deceth-4	PPG-2-Laureth-8
PEG/PPG-4/2 Propylheptyl Ether	PPG-1-Deceth-5	PPG-2-Laureth-12
PEG/PPG-6/2 Propylheptyl Ether	PPG-1-Deceth-6	PPG-3-Laureth-8
PEG-7/PPG-2 Propylheptyl Ether	PPG-1-Deceth-7	PPG-3-Laureth-9
PEG/PPG-8/2 Propylheptyl Ether	PPG-2-Deceth-3	PPG-3-Laureth-10
PEG/PPG-10/2 Propylheptyl Ether	PPG-2-Deceth-5	PPG-3-Laureth-12
PEG/PPG-14/2 Propylheptyl Ether	PPG-2-Deceth-7	PPG-4 Laureth-2
PEG/PPG-40/2 Propylheptyl Ether	PPG-2-Deceth-8	PPG-4 Laureth-5
PPG-2-Ceteareth-9	PPG-2-Deceth-10	PPG-4 Laureth-7
PPG-4-Ceteareth-12	PPG-2-Deceth-12	PPG-4-Laureth-15
PPG-10-Ceteareth-20	PPG-2-Deceth-15	PPG-5-Laureth-5
PPG-1-Ceteth-1	PPG-2-Deceth-20	PPG-6-Laureth-3
PPG-1-Ceteth-5	PPG-2-Deceth-30	PPG-25-Laureth-25
PPG-1-Ceteth-10	PPG-2-Deceth-40	PPG-3-Myreth-3
PPG-1-Ceteth-20	PPG-2-Deceth-50	PPG-3-Myreth-11
PPG-2-Ceteth-1	PPG-2-Deceth-60	PPG-2-PEG-11 Hydrogenated Lauryl Alcohol Ether
PPG-2-Ceteth-5	PPG-4-Deceth-4	PPG-3-PEG-6 Oleyl Ether
PPG-2-Ceteth-10	PPG-4-Deceth-6	PPG-9-Steareth-3
PPG-2-Ceteth-20	PPG-6-Deceth-4	PPG-23-Steareth-34
PPG-4-Ceteth-1	PPG-6-Deceth-9	PPG-30 Steareth-4
PPG-4-Ceteth-5	PPG-8-Deceth-6	PPG-34-Steareth-3
PPG-4-Ceteth-10	PPG-14-Deceth-6	PPG-38 Steareth-6
PPG-4-Ceteth-20	PPG-6-Decyltetradeceth-12	PPG-1 Trideceth- 6
PPG-5-Ceteth-20	PPG-6-Decyltetradeceth-20	PPG-1 Trideceth-13
PPG-8-Ceteth-1	PPG-6-Decyltetradeceth-30	PPG-4 Trideceth-6
PPG-8-Ceteth-2	PPG-13-Decyltetradeceth-24	PPG-6 Trideceth-8
PPG-8-Ceteth-5	PPG-20-Decyltetradeceth-10	Propylene Glycol Capreth-4
PPG-8-Ceteth-10	PPG-9-Ethylhexeth-5	Propylene Glycol Isodeceth-4
PPG-8-Ceteth-20	PPG-1-Isodeceth-4	Propylene Glycol Isodeceth-12
PPG-2 C9-11 Pareth-5	PPG-1-Isodeceth-6	Propylene Glycol Laureth-6
PPG-2 C9-11 Pareth-7	PPG-1-Isodeceth-7	Propylene Glycol Oleth-5
PPG-2 C9-11 Pareth-8	PPG-1-Isodeceth-9	

Table 2. Definitions, Structures, and, Functions

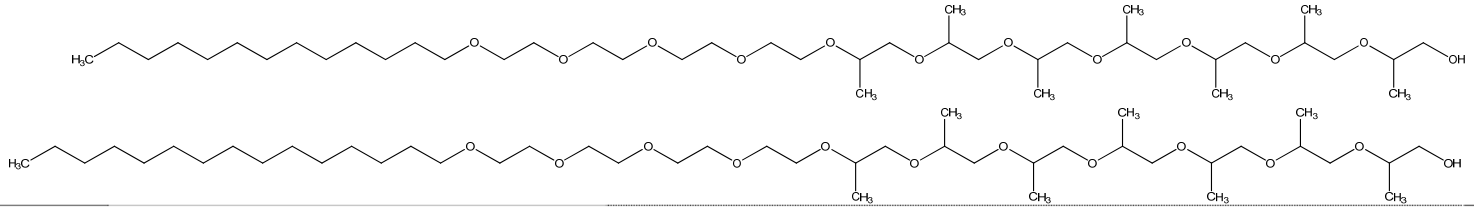
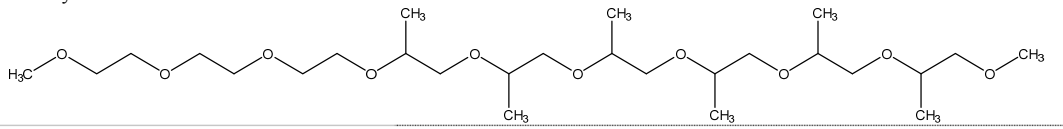
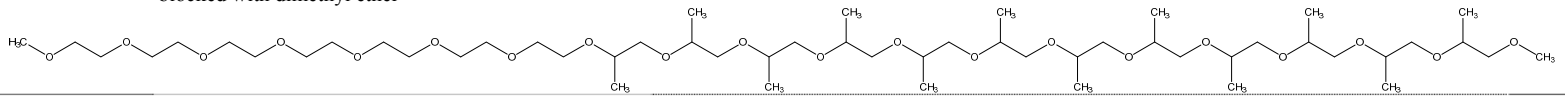
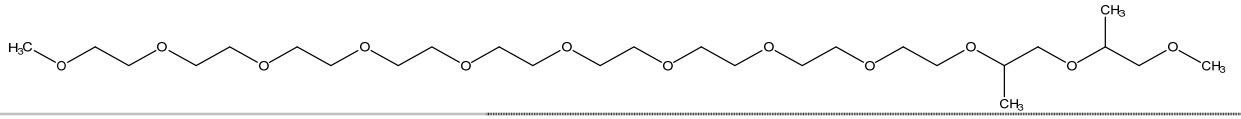
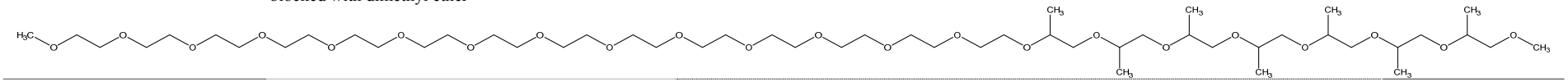
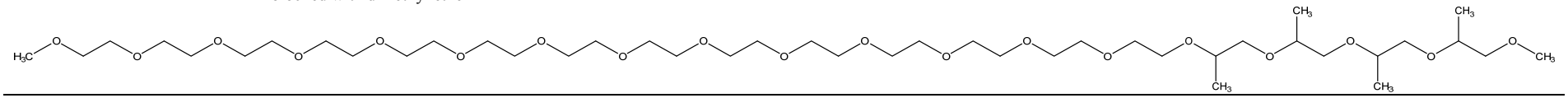
Ingredient (CAS No. if available)	Definition[1]	Structure[1] ;CIR staff*	Function
PEG-4-PPG-7 C13/C15 Alcohol	the polyoxypropylene, polyoxyethylene ether of a mixture of synthetic C13/C15 alcohols with an average propoxylation value of 7 and an average ethoxylation value of 4		surfactant – emulsifying agent
PEG/PPG-3/6 Dimethyl Ether (61419-46-3)	the copolymer produced by the interaction of 3 moles of ethylene oxide with 6 moles of propylene oxide end-blocked with methyl ether		skin conditioning agent - misc
PEG/PPG-7/12 Dimethyl Ether	copolymer produced by the interaction of 7 moles of ethylene oxide with 12 moles of propylene oxide end-blocked with dimethyl ether		skin conditioning agent - misc
PEG/PPG-9/2 Dimethyl Ether (61419-46-3)	the copolymer produced by the interaction of 9 moles of ethylene oxide with 2 moles of propylene oxide end-blocked with dimethyl ether		skin conditioning agent - misc
PEG/PPG-14/7 Dimethyl Ether (61419-46-3)	the copolymer produced by the interaction of 14 moles of ethylene oxide with 7 moles of propylene oxide end-blocked with dimethyl ether		skin conditioning agent - misc
PEG/PPG-17/4 Dimethyl Ether	the copolymer produced by the interaction of 17 moles of ethylene oxide with 4 moles of propylene oxide end-blocked with dimethyl ether		skin conditioning agent - misc

Table 2. Definitions, Structures, and, Functions

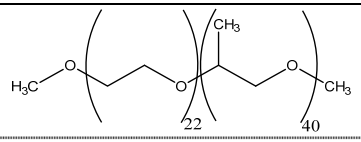
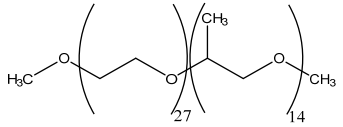
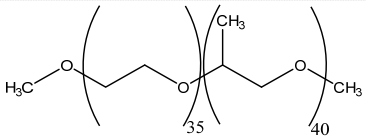
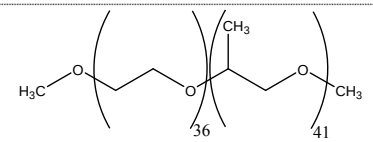
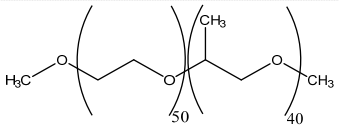
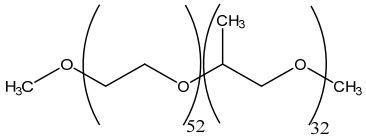
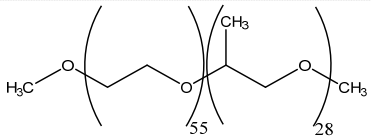
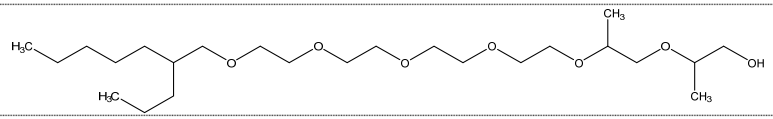
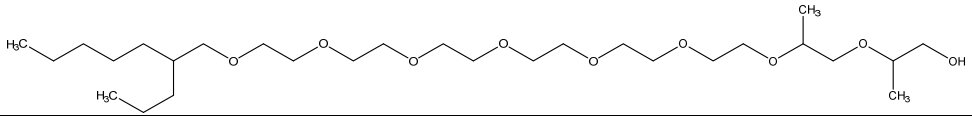
Ingredient (CAS No. if available)	Definition[1]	Structure[1 ;CIR staff*]	Function
PEG/PPG-22/40 Dimethyl Ether	a copolymer produced by the interaction of 22 moles of ethylene oxide with 40 moles of propylene oxide end-blocked with methyl ether		skin conditioning agent - misc
PEG/PPG-27/14 Dimethyl Ether	a copolymer produced by the interaction of 27 moles of ethylene oxide with 14 moles of propylene oxide end-blocked with methyl ether		skin conditioning agent - misc
PEG/PPG-35/40 Dimethyl Ether	the copolymer produced by interacting 35 moles of ethylene oxide with 40 moles of propylene oxide end-blocked with dimethyl ether		skin conditioning agent - misc
PEG/PPG-36/41 Dimethyl Ether	the copolymer produced by the interaction of 36 moles of ethylene oxide and 41 moles of propylene oxide end-blocked with methyl ether		skin conditioning agent - misc
PEG/PPG-50/40 Dimethyl Ether	the copolymer produced by the interaction of 50 moles of ethylene oxide with 40 moles of propylene oxide end-blocked with dimethyl ether		skin conditioning agent - misc
PEG/PPG-52/32 Dimethyl Ether	a copolymer produced by the interaction of 52 moles of ethylene oxide with 32 moles of propylene oxide end-blocked with methyl ether		skin conditioning agent - misc
PEG/PPG-55/28 Dimethyl Ether	a copolymer produced by the interaction of 55 moles of ethylene oxide with 28 moles of propylene oxide end-blocked with methyl ether		skin conditioning agent - misc
PEG/PPG-4/2 Propylheptyl Ether (166736-08-9)	the product formed by the reaction of 2-propylheptanol with an average of 4 moles of ethylene oxide and 2 moles of propylene oxide		surfactant – cleansing, dispersing, emulsifying, or solubilizing agent
PEG/PPG-6/2 Propylheptyl Ether (166736-08-9)	the product formed by the reaction of 2-propylheptanol with an average of 6 moles of ethylene oxide and 2 moles of propylene oxide		surfactant – cleansing, dispersing, emulsifying, or solubilizing agent

Table 2. Definitions, Structures, and, Functions

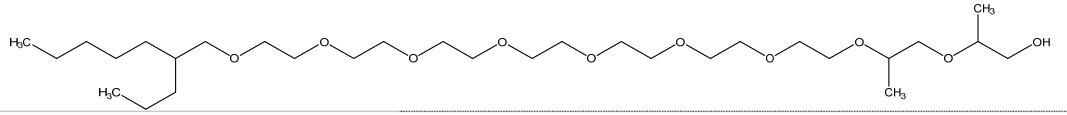
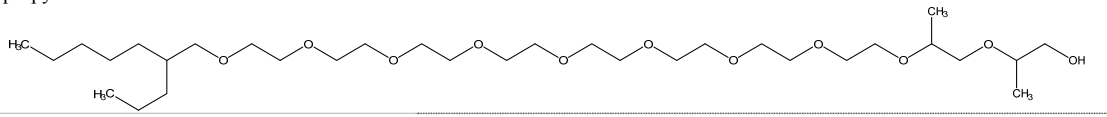
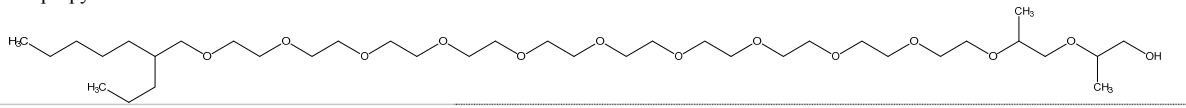
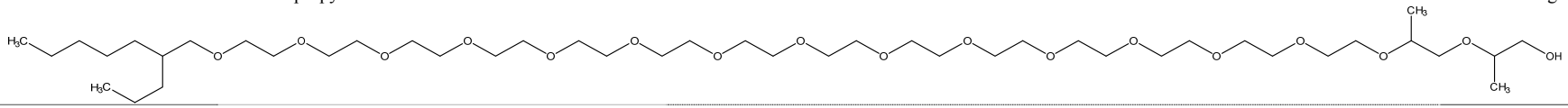
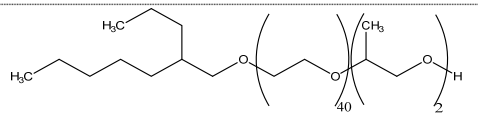
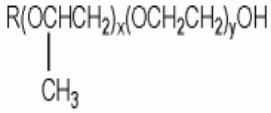
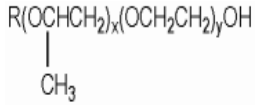
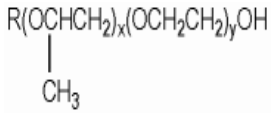
Ingredient (CAS No. if available)	Definition[1]	Structure[1] ;CIR staff*	Function
PEG-7/PPG-2 Propylheptyl Ether	the product formed by the reaction of 2-propylheptanol with an average of 7 moles of ethylene oxide and 2 moles of propylene oxide		surfactant – cleansing, dispersing, emulsifying, or solubilizing agent
PEG/PPG-8/2 Propylheptyl Ether (166736-08-9)	the product formed by the reaction of 2-propylheptanol with an average of 8 moles of ethylene oxide and 2 moles of propylene oxide		surfactant – cleansing, dispersing, emulsifying, or solubilizing agent
PEG/PPG-10/2 Propylheptyl Ether (166736-08-9)	the product formed by the reaction of 2-propylheptanol with an average of 10 moles of ethylene oxide and 2 moles of propylene oxide		surfactant – cleansing, dispersing, emulsifying, or solubilizing agent
PEG/PPG-14/2 Propylheptyl Ether (166736-08-9)	the product formed by the reaction of 2-propylheptanol with an average of 14 moles of ethylene oxide and 2 moles of propylene oxide		surfactant – cleansing, dispersing, emulsifying, or solubilizing agent
PEG/PPG-40/2 Propylheptyl Ether (166736-08-9)	the product formed by the reaction of 2-propylheptanol with an average of 40 moles of ethylene oxide and 2 moles of propylene oxide		surfactant – cleansing, dispersing, emulsifying, or solubilizing agent
PPG-2-Ceteareth-9	the polyoxypropylene, polyoxyethylene ether of Cetearyl Alcohol that conforms generally to the formula where R represents a blend of cetyl and stearyl radicals, x has an average value of 2 and y has an average value of 9		surfactant – emulsifying agent
PPG-4-Ceteareth-12	the polyoxypropylene, polyoxyethylene ether of Cetearyl Alcohol that conforms generally to the formula where R represents a blend of cetyl and stearyl radicals, x has an average value of 4 and y has an average value of 12		surfactant – emulsifying agent
PPG-10-Ceteareth-20	the polyoxypropylene, polyoxyethylene ether of Cetearyl Alcohol that conforms generally to the formulawhere R represents a blend of cetyl and stearyl radicals, x has an average value of 10 and y has an average value of 20		surfactant – emulsifying agent

Table 2. Definitions, Structures, and, Functions

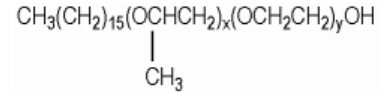
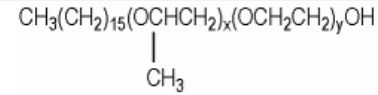
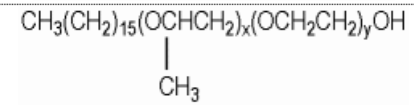
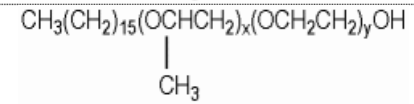
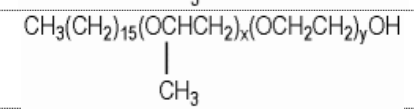
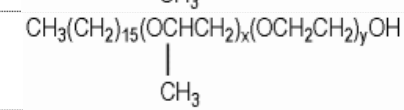
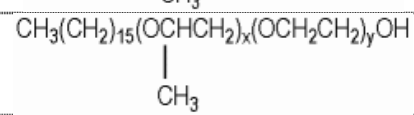
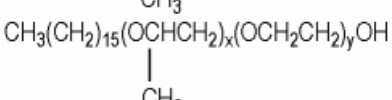
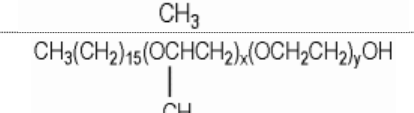
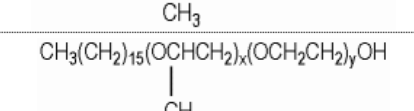
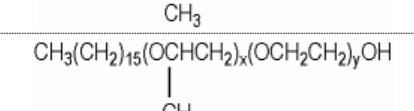
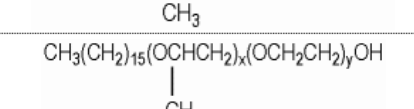
Ingredient (CAS No. if available)	Definition[1]	Structure[1] ;CIR staff*	Function
PPG-1-Ceteth-1 (37311-01-6; 9087-53-0)	the polyoxypropylene, polyoxyethylene ether of cetyl alcohol that conforms generally to the formula where x has an average value of 1 and y has an average value of 1		skin conditioning agent – emollient; surfactant – emulsifying agent
PPG-1-Ceteth-5 (37311-01-6; 9087-53-0)	the polyoxypropylene, polyoxyethylene ether of cetyl alcohol that conforms generally to the formula where x has an average value of 1 and y has an average value of 5		skin conditioning agent – emollient; surfactant – emulsifying agent
PPG-1-Ceteth-10 (37311-01-6; 9087-53-0)	the polyoxypropylene, polyoxyethylene ether of cetyl alcohol that conforms generally to the formula where x has an average value of 1 and y has an average value of 10		skin conditioning agent – emollient; surfactant – emulsifying agent
PPG-1-Ceteth-20 (37311-01-6; 9087-53-0)	the polyoxypropylene, polyoxyethylene ether of cetyl alcohol that conforms generally to the formulawhere x has an average value of 1 and y has an average value of 20		skin conditioning agent – emollient; surfactant – emulsifying and solubilizing agent
PPG-2-Ceteth-1 (37311-01-6; 9087-53-0)	the polyoxypropylene, polyoxyethylene ether of cetyl alcohol that conforms generally to the formula where x has an average value of 2 and y has an average value 1		skin conditioning agent – emollient; surfactant – emulsifying agent
PPG-2-Ceteth-5 (37311-01-6; 9087-53-0)	the polyoxypropylene, polyoxyethylene ether of cetyl alcohol that conforms generally to the formula where x has an average value of 2 and y has an average value of 5		skin conditioning agent – emollient; surfactant – emulsifying agent
PPG-2-Ceteth-10 (37311-01-6; 9087-53-0)	the polyoxypropylene, polyoxyethylene ether of cetyl alcohol that conforms generally to the formula where x has an average value of 2 and y has an average value of 10		skin conditioning agent – emollient; surfactant – emulsifying agent
PPG-2-Ceteth-20 (37311-01-6; 9087-53-0)	is the polyoxypropylene, polyoxyethylene ether of cetyl alcohol that conforms generally to the formula where x has an average value of 2 and y has an average value of 20		skin conditioning agent – emollient; surfactant – emulsifying and solubilizing agent
PPG-4-Ceteth-1 (37311-01-6; 9087-53-0)	the polyoxypropylene polyoxyethylene ether of cetyl alcohol that conforms generally to the formula where x has an average value of 4 and y has an average value of 1		skin conditioning agent – emollient; surfactant – emulsifying agent
PPG-4-Ceteth-5 (37311-01-6; 9087-53-0)	the polyoxypropylene, polyoxyethylene ether of cetyl alcohol that conforms generally to the formula where x has an average value of 4 and y has an average value of 5		skin conditioning agent – emollient; surfactant – emulsifying agent
PPG-4-Ceteth-10 (37311-01-6; 9087-53-0)	the polyoxypropylene, polyoxyethylene ether of cetyl alcohol that conforms generally to the formula where x has an average value of 4 and y has an average value of 10		surfactant – emulsifying agent
PPG-4-Ceteth-20 (37311-01-6; 9087-53-0)	the polyoxypropylene, polyoxyethylene ether of cetyl alcohol that conforms generally to the formula where x has an average value of 4 and y has an average value of 20		surfactant – emulsifying agent

Table 2. Definitions, Structures, and, Functions

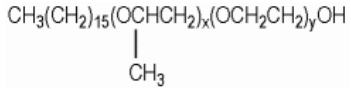
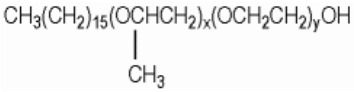
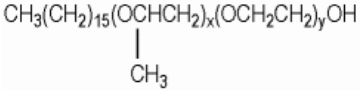
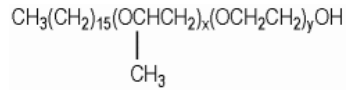
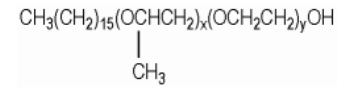
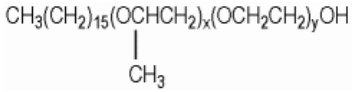
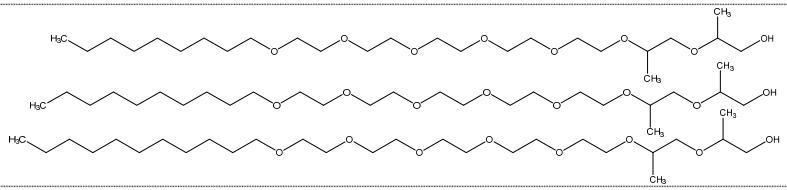
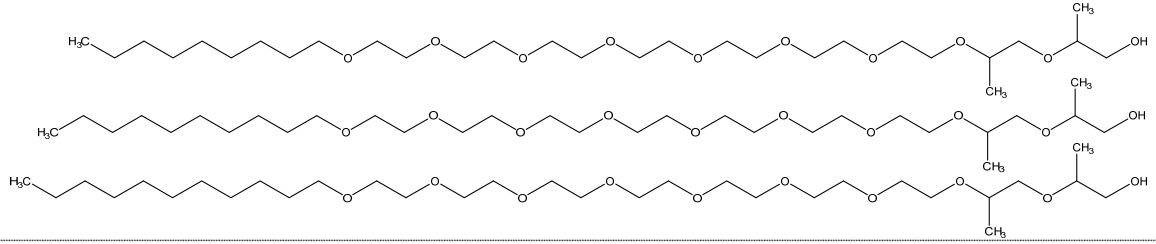
Ingredient (CAS No. if available)	Definition[1]	Structure[1] ;CIR staff*	Function
PPG-5-Ceteth-20 (37311-01-6; 9087-53-0)	the polyoxypropylene, polyoxyethylene ether of cetyl alcohol that conforms generally to the formula where x has an average value of 5 and y has an average value of 20		surfactant – emulsifying agent
PPG-8-Ceteth-1 (37311-01-6; 9087-53-0)	the polyoxypropylene, polyoxyethylene ether of cetyl alcohol that conforms generally to the formula where x has an average value of 8 and y has an average value of 1		skin conditioning agent – emollient; surfactant – emulsifying agent
PPG-8-Ceteth-2 (37311-01-6; 9087-53-0)	the polyoxypropylene, polyoxyethylene ether of cetyl alcohol that conforms generally to the formula where x has an average value of 8 and y has an average value of 2		skin conditioning agent – emollient; surfactant – emulsifying agent
PPG-8-Ceteth-5 (37311-01-6; 9087-53-0)	the polyoxypropylene, polyoxyethylene ether of cetyl alcohol that conforms generally to the formula where x has an average value of 8 and y has an average value of 5		skin conditioning agent – emollient; surfactant – emulsifying agent
PPG-8-Ceteth-10 (37311-01-6; 9087-53-0)	the polyoxypropylene, polyoxyethylene ether of cetyl alcohol that conforms generally to the formula where x has an average value of 8 and y has an average value of 10		skin conditioning agent – emollient; surfactant – emulsifying agent
PPG-8-Ceteth-20 (37311-01-6; 9087-53-0)	the polyoxypropylene, polyoxyethylene ether of cetyl alcohol that conforms generally to the formula where x has an average value of 8 and y has an average value of 20		surfactant – emulsifying agent
PPG-2 C9-11 Pareth-5	the polypropylene glycol ether of a mixture of synthetic C9-11 ethoxylated fatty alcohols containing an average of 5 moles of ethylene oxide and 2 moles of propylene oxide		surfactant – emulsifying agent
PPG-2 C9-11 Pareth-7	the polypropylene glycol ether of a mixture of synthetic C9-11 ethoxylated fatty alcohols containing an average of 7 moles of ethylene oxide and 2 moles of propylene oxide		surfactant – emulsifying agent

Table 2. Definitions, Structures, and, Functions

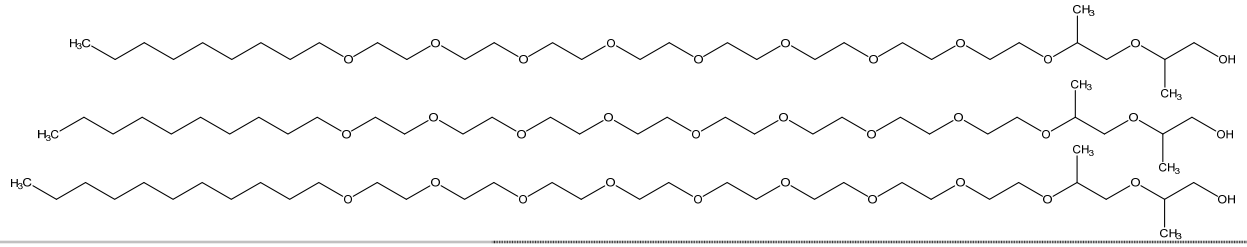
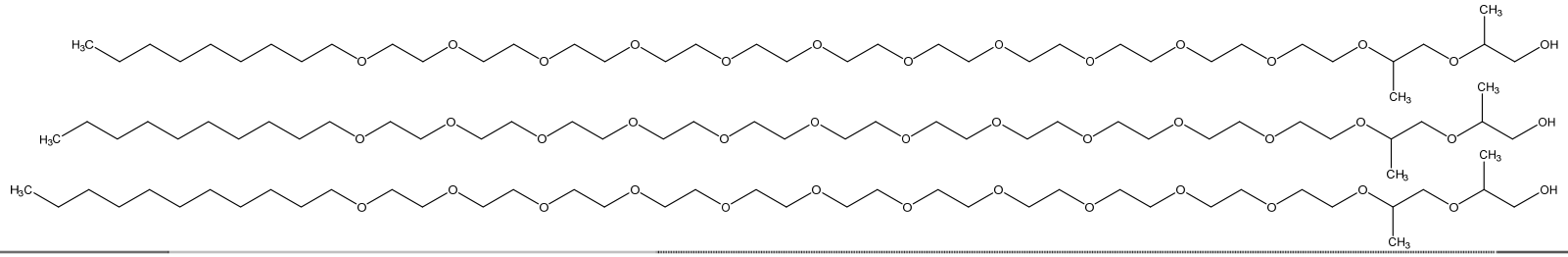
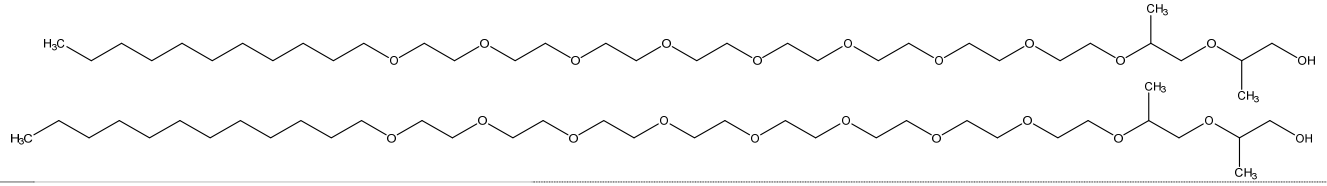
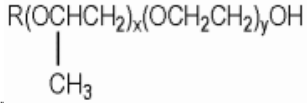
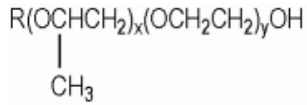
Ingredient (CAS No. if available)	Definition[1]	Structure[1] ;CIR staff*	Function
PPG-2 C9-11 Pareth-8	the polypropylene glycol ether of a mixture of synthetic C9-11 ethoxylated fatty alcohols containing an average of 8 moles of ethylene oxide and 2 moles of propylene oxide		surfactant – emulsifying and cleansing agent
PPG-2 C9-11 Pareth-11	the polypropylene glycol ether of a mixture of synthetic C9-11 ethoxylated fatty alcohols containing an average of 11 moles of ethylene oxide and 2 moles of propylene oxide		surfactant – emulsifying and cleansing agent
PPG-2 C12-13 Pareth-8	the polypropylene glycol ether of a mixture of synthetic C12-13 ethoxylated fatty alcohols containing an average of 8 moles of ethylene oxide and 2 moles of propylene oxide		surfactant – emulsifying agent
PPG-2 C12-15 Pareth-6	a polyoxyethylene, polyoxypropylene ether of a mixture of synthetic alcohols that conforms generally to the formula where R represents a C12-15 alcohol, x has an average value of 2 and y has an average value of 6		surfactant – emulsifying agent
PPG-4 C13-15 Pareth-15	the polyoxyethylene, polyoxypropylene ether of a mixture of synthetic alcohols that conforms generally to the formula where R represents an alcohol stem with 13-15 carbons in the alkyl chain, x has an average value of 4, and y has an average value of 15		surfactant – emulsifying agent

Table 2. Definitions, Structures, and, Functions

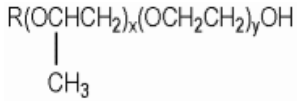
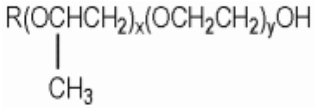
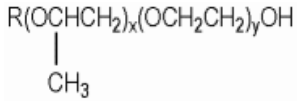
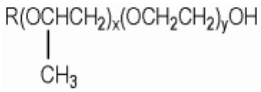
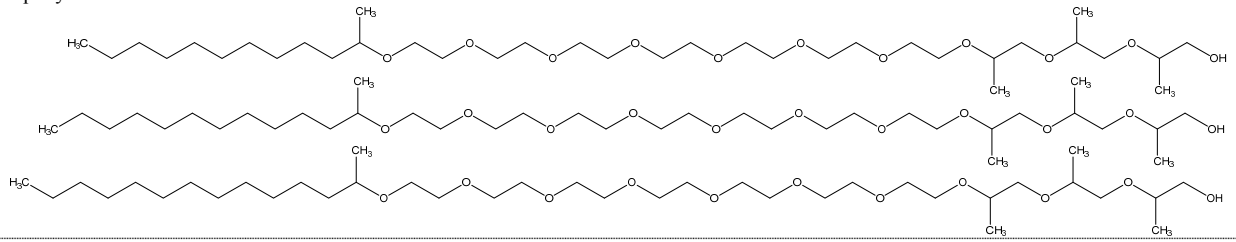
Ingredient (CAS No. if available)	Definition[1]	Structure[1] ;CIR staff*	Function
PPG-5 C9-15 Pareth-6	the polyoxyethylene, polyoxypropylene ether of a mixture of synthetic alcohols that conforms generally to the formula where R represents a fatty alcohol group with 9 to 15 carbons in the alkyl chain, x has an average value of 5 and y has an average value of 6		surfactant – emulsifying agent
PPG-6 C9-11 Pareth-5 (154518-36-2)	the polyoxypropylene, polyoxyethylene ether of a mixture of synthetic alcohols that conforms generally to the formula where R represents the C9-11 fatty alcohol group, x has an average value of 6 and y has an average value of 5		surfactant – emulsifying agent
PPG-6 C12-15 Pareth-12 (68551-13-3)[43]	the polyoxyethylene, polyoxypropylene ether of a mixture of synthetic alcohols that conforms generally to the formula where R represents an alkyl stem with 12-15 carbons, x has an average value of 6 and y has an average value of 12		surfactant – emulsifying agent
PPG-6 C12-18 Pareth-11	the polyoxyethylene, polyoxypropylene ether of a mixture of synthetic alcohols that conforms generally to the formula where R represents an alcohol stem with 12 to 18 carbons in the alkyl chain, x has an average value of 6 and y has an average value of 11		surfactant – emulsifying agent
PPG-3 C12-14 Sec-Pareth-7 (68131-40-8)[12]	the polyoxyethylene, polyoxypropylene ether of a mixture of synthetic secondary C12-14 alcohols with an average ethoxylation value of 7 and an average propoxylation value of 3		emulsion stabilizer; surfactant – emulsifying agent

Table 2. Definitions, Structures, and, Functions

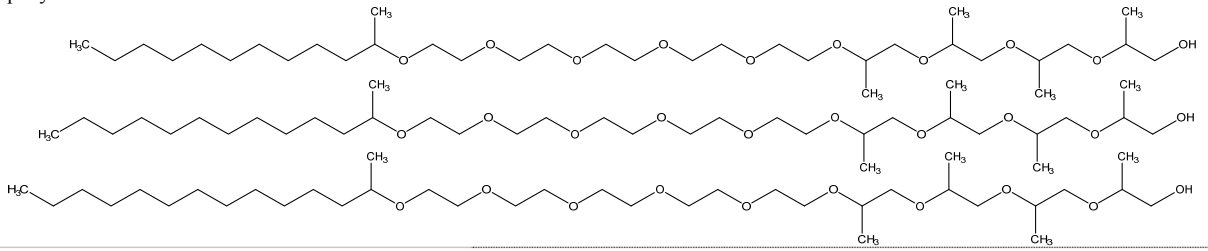
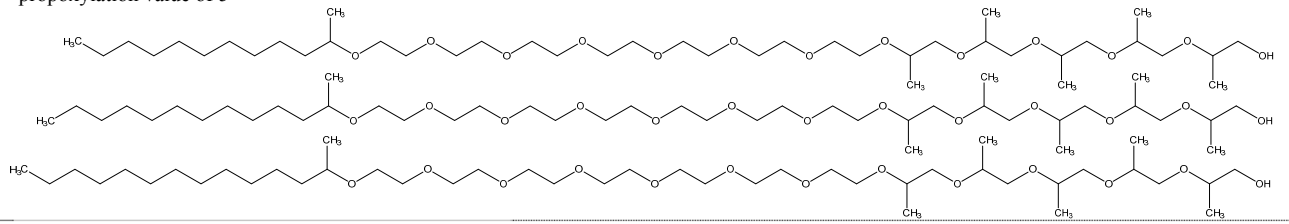
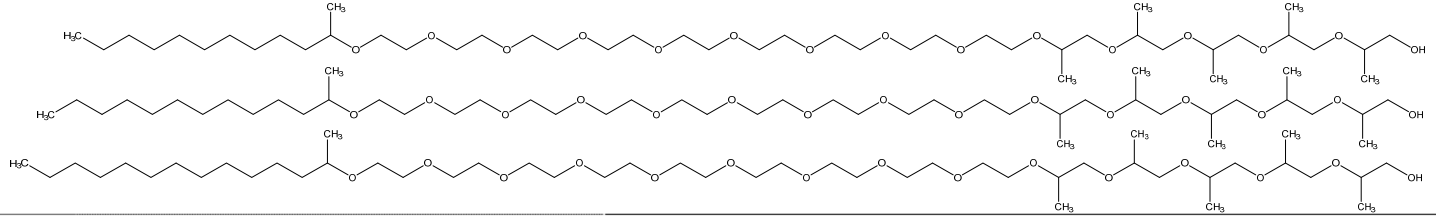
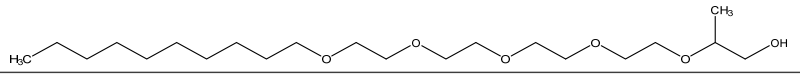
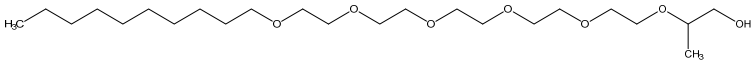
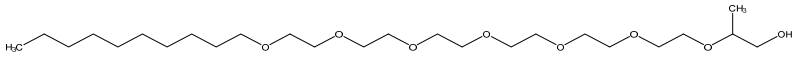
Ingredient (CAS No. if available)	Definition[1]	Structure[1 ;CIR staff*]	Function
PPG-4 C12-14 Sec-Pareth-5 (68131-40-8)[12]	the polyoxyethylene, polyoxypropylene ether of a mixture of synthetic secondary C12-14 alcohols with an average ethoxylation value of 5 and an average propoxylation value of 4		emulsion stabilizer; surfactant – emulsifying agent
PPG-5 C12-14 Sec-Pareth-7 (68131-40-8)[12]	the polyoxyethylene, polyoxypropylene ether of a mixture of synthetic secondary C12-14 alcohols with an average ethoxylation value of 7 and an average propoxylation value of 5		emulsion stabilizer; surfactant – emulsifying agent
PPG-5 C12-14 Sec-Pareth-9 (68131-40-8)[12]	the polyoxyethylene, polyoxypropylene ether of a mixture of synthetic secondary C12-14 alcohols with an average ethoxylation value of 9 and an average propoxylation value of 5		emulsion stabilizer; surfactant – emulsifying agent
PPG-1-Deceth-4	the polyoxyethylene, polyoxypropylene ether of decyl alcohol that conforms generally to the formula where x has an average value of 1 and y has an average value of 4		surfactant- cleansing and emulsifying agent
PPG-1-Deceth-5	the polyoxyethylene, polyoxypropylene ether of decyl alcohol that conforms generally to the formula where x has an average value of 1 and y has an average value of 5		surfactant- cleansing and emulsifying agent
PPG-1-Deceth-6	the polyoxyethylene, polyoxypropylene ether of decyl alcohol that conforms generally to the formula where x has an average value of 1 and y has an average value of 6		surfactant – emulsifying agent

Table 2. Definitions, Structures, and, Functions

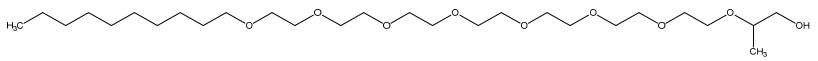
Ingredient (CAS No. if available)	Definition[1]	Structure[1] ;CIR staff*	Function
PPG-1-Deceth-7	the polyoxyethylene, polyoxypropylene ether of decyl alcohol that conforms generally to the formula where x has an average value of 1 and y has an average value of 7		surfactant- cleansing and emulsifying agent
PPG-2-Deceth-3 (37251-67-5)	the polyoxypropylene, polyoxyethylene ether of decyl alcohol that conforms generally to the formula where x has an average value of 2 and y has an average value of 3	$CH_3(CH_2)_8CH_2(OCHCH_2)_x(OCH_2CH_2)_yOH$ $\vert$ CH_3	surfactant – emulsifying agent
PPG-2-Deceth-5	the polyoxyethylene, polyoxypropylene ether of decyl alcohol that conforms generally to the formula where x has an average value 2 and y has an average value of 5	$CH_3(CH_2)_9(OCH_2CH_2)_y(OCHCH_2)_xOH$ $\vert$ CH_3	surfactant – emulsifying agent
PPG-2-Deceth-7 (37251-67-5)	the polyoxypropylene, polyoxyethylene ether of decyl alcohol that conforms generally to the formula where x has an average value of 2 and y has an average value of 7	$CH_3(CH_2)_8CH_2(OCHCH_2)_x(OCH_2CH_2)_yOH$ $\vert$ CH_3	surfactant – emulsifying agent
PPG-2-Deceth-8	the polyoxypropylene, polyoxyethylene ether of decyl alcohol that conforms generally to the formula where x has an average value of 2 and y has an average value of 8	$CH_3(CH_2)_8CH_2(OCHCH_2)_x(OCH_2CH_2)_yOH$ $\vert$ CH_3	surfactant – emulsifying agent
PPG-2-Deceth-10 (37251-67-5)	the polyoxypropylene, polyoxyethylene ether of decyl alcohol that conforms generally to the formula where x has an average value of 2 and y has an average value of 10	$CH_3(CH_2)_9(OCHCH_2)_x(OCH_2CH_2)_yOH$ $\vert$ CH_3	surfactant – emulsifying agent
PPG-2-Deceth-12 (37251-67-5)	the polyoxypropylene, polyoxyethylene ether of decyl alcohol that conforms generally to the formula where x has an average value of 2 and y has an average value of 12	$CH_3(CH_2)_8CH_2(OCHCH_2)_x(OCH_2CH_2)_yOH$ $\vert$ CH_3	surfactant – emulsifying agent
PPG-2-Deceth-15 (37251-67-5)	the polyoxypropylene, polyoxyethylene ether of decyl alcohol that conforms generally to the formula where x has an average value of 2 and y has an average value of 15	$CH_3(CH_2)_8CH_2(OCHCH_2)_x(OCH_2CH_2)_yOH$ $\vert$ CH_3	surfactant – emulsifying agent
PPG-2-Deceth-20 (37251-67-5)	the polyoxypropylene, polyoxyethylene ether of decyl alcohol that conforms generally to the formula where x has an average value of 2 and y has an average value of 20	$CH_3(CH_2)_8CH_2(OCHCH_2)_x(OCH_2CH_2)_yOH$ $\vert$ CH_3	surfactant – emulsifying agent
PPG-2-Deceth-30 (37251-67-5)	the polyoxyethylene, polyoxypropylene ether of decyl alcohol that conforms generally to the formula where x has an average value of 2 and y has an average value of 30	$CH_3(CH_2)_8CH_2(OCHCH_2)_x(OCH_2CH_2)_yOH$ $\vert$ CH_3	surfactant – emulsifying agent
PPG-2-Deceth-40	the polyoxyethylene, polyoxypropylene ether of decyl alcohol that conforms generally to the formula where x has an average value of 2 and y has an average value of 40	$CH_3(CH_2)_8CH_2(OCHCH_2)_x(OCH_2CH_2)_yOH$ $\vert$ CH_3	surfactant – emulsifying agent
PPG-2-Deceth-50	the polyoxyethylene, polyoxypropylene ether of decyl alcohol that conforms generally to the formula where x has an average value of 2 and y has an average value of 50	$CH_3(CH_2)_8CH_2(OCHCH_2)_x(OCH_2CH_2)_yOH$ $\vert$ CH_3	surfactant – emulsifying agent
PPG-2-Deceth-60	the polyoxyethylene, polyoxypropylene ether of decyl alcohol that conforms generally to the formula where x has an average value of 2 and y has an average value of 60	$CH_3(CH_2)_8CH_2(OCHCH_2)_x(OCH_2CH_2)_yOH$ $\vert$ CH_3	surfactant – emulsifying agent

Table 2. Definitions, Structures, and, Functions

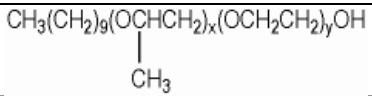
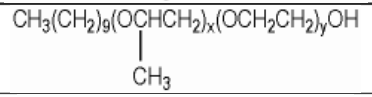
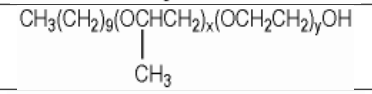
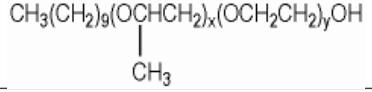
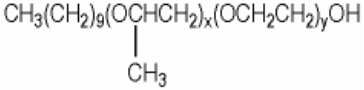
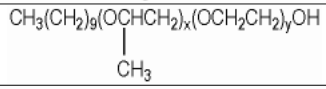
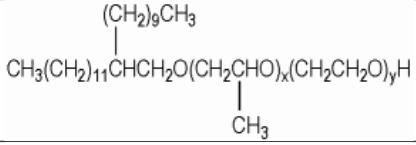
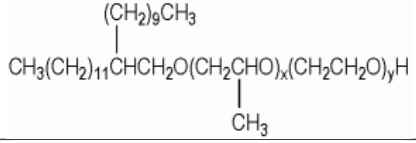
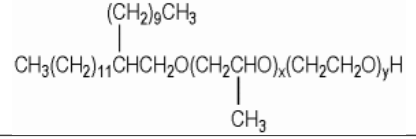
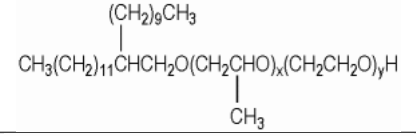
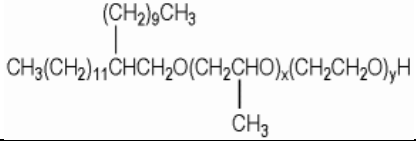
Ingredient (CAS No. if available)	Definition[1]	Structure[1] ;CIR staff*	Function
PPG-4-Deceth-4	the polyoxypropylene, polyoxyethylene ether of decyl alcohol that conforms generally to the formula where x has an average value of 4 and y has an average value of 4		surfactant – emulsifying agent
PPG-4-Deceth-6 (37251-67-5)	the polyoxypropylene, polyoxyethylene ether of decyl alcohol that conforms generally to the formula where x has an average value of 4 and y has an average value of 6		surfactant – emulsifying agent
PPG-6-Deceth-4 (68154-97-2)[43]	the polyoxypropylene, polyoxyethylene ether of decyl alcohol that conforms generally to the formula where x has an average value of 6 and y has an average value of 4		surfactant – emulsifying agent
PPG-6-Deceth-9 (68154-97-2)[43]	the polyoxypropylene, polyoxyethylene ether of decyl alcohol that conforms generally to the formula where x has an average value of 6 and y has an average value of 9		surfactant – emulsifying agent
PPG-8-Deceth-6 (68154-97-2)[43]	the polyoxypropylene, polyoxyethylene ether of decyl alcohol that conforms generally to the formula where x has an average value of 8 and y has an average value of 6		surfactant – emulsifying agent
PPG-14-Deceth-6	the polyoxypropylene, polyoxyethylene ether of decyl alcohol that conforms generally to the formula where x has an average value of 14 and y has an average value of 6		surfactant – emulsifying agent
PPG-6-Decyltetradeceth-12 (72484-69-6)[15]	the polyoxypropylene, polyoxyethylene ether of Decyltetradecanol that conforms generally to the formula where x has an average value of 6 and y has an average value of 12		surfactant – emulsifying agent
PPG-6-Decyltetradeceth-20 (72484-69-6)[16]	the polyoxypropylene, polyoxyethylene ether of Decyltetradecanol that conforms generally to the formula where x has an average value of 6 and y has an average value of 20		surfactant – emulsifying agent
PPG-6-Decyltetradeceth-30 (72484-69-6)[17]	the polyoxypropylene, polyoxyethylene ether of Decyltetradecanol that conforms generally to the formula where x has an average value of 6 and y has an average value of 30		surfactant – emulsifying agent
PPG-13-Decyltetradeceth-24	the polyoxypropylene, polyoxyethylene ether of Decyltetradecanol that conforms generally to the formula where x has an average value of 13 and y has an average value 24		surfactant – emulsifying agent
PPG-20-Decyltetradeceth-10	the polyoxypropylene, polyoxyethylene ether of Decyltetradecanol that conforms generally to the formula where x has an average value of 20 and y has an average value of 10		surfactant – emulsifying agent

Table 2. Definitions, Structures, and, Functions

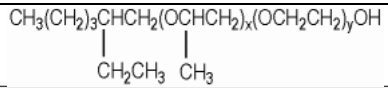
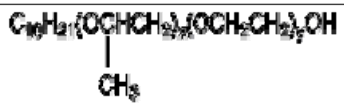
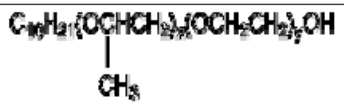
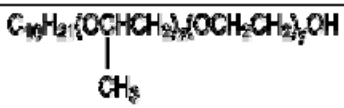
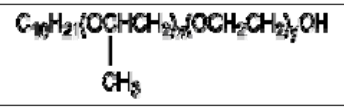
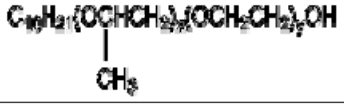
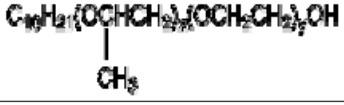
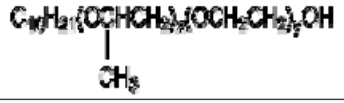
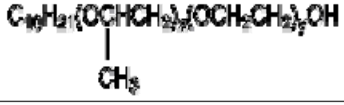
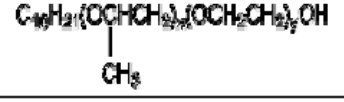
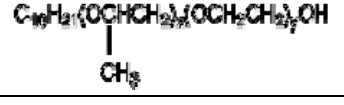
Ingredient (CAS No. if available)	Definition[1]	Structure[1] ;CIR staff*	Function
PPG-9-Ethylhexeth-5 (64366-70-7)	the polyoxypropylene, polyoxyethylene ether of octyl alcohol that conforms generally to the formula where x has an average value of 9 and y has an average value of 5		surfactant – emulsifying agent
PPG-1-Isodeceth-4	the polyoxyethylene, polyoxypropylene ether of isodecyl alcohol that conforms generally to the formula where x has an average value of 1 and y has an average value of 4 (a.k.a. Propylene Glycol Isodeceth-4)[52]		surfactant- cleansing and emulsifying agent
PPG-1-Isodeceth-6	is the polyoxyethylene, polyoxypropylene ether of isodecyl alcohol that conforms generally to the formula where x has an average value of 1 and y has an average value of 6		surfactant- cleansing and emulsifying agent
PPG-1-Isodeceth-7	the polyoxyethylene, polyoxypropylene ether of isodecyl alcohol that conforms generally to the formula where x has an average value of 1 and y has an average value of 7		surfactant- cleansing and emulsifying agent
PPG-1-Isodeceth-9	the polyoxyethylene, polyoxypropylene ether of isodecyl alcohol that conforms generally to the formula where x has an average value of 1 and y has an average value of 9		surfactant- cleansing and emulsifying agent
PPG-2-Isodeceth-4 (155683-77-5)[43]	the polyoxypropylene, polyoxyethylene glycol ether of isodecyl alcohol that conforms generally to the formula where x has an average value of 2 and y has an average value of 4		surfactant – emulsifying agent
PPG-2-Isodeceth-6 (155683-77-5)[43]	the polyoxyethylene, polyoxypropylene ether of isodecyl alcohol that conforms generally to the formula where x has an average value of 2 and y has an average value of 6		surfactant – emulsifying agent
PPG-2-Isodeceth-8 (155683-77-5)[43]	the polyoxyethylene, polyoxypropylene ether of isodecyl alcohol that conforms generally to the formula where x has an average value of 2 and y has an average value of 8		surfactant- cleansing and emulsifying agent
PPG-2-Isodeceth-9 (155683-77-5)[43]	the polyoxypropylene, polyoxyethylene ether of isodecyl alcohol that conforms generally to the formula where x has an average value of 2 and y has an average value of 9		surfactant – emulsifying agent
PPG-2-Isodeceth-10 (155683-77-5)[43]	the polyoxypropylene, polyoxyethylene ether of isodecyl alcohol that conforms generally to the formula:(structure)where x has an average value of 2 and y has an average value of 10		surfactant- cleansing and emulsifying agent
PPG-2-Isodeceth-12 (155683-77-5)[43]	the polyoxypropylene, polyoxyethylene ether of isodecyl alcohol that conforms generally to the formula where x has an average value of 2 and y has an average value of 12		surfactant – emulsifying agent
PPG-2-Isodeceth-18 (155683-77-5)[43]	the polyoxypropylene, polyoxyethylene ether of isodecyl alcohol that conforms generally to the formula where x has an average value of 2 and y has an average value of 18		surfactant- cleansing and emulsifying agent

Table 2. Definitions, Structures, and, Functions

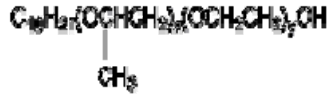
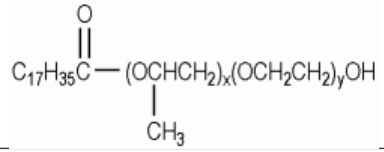
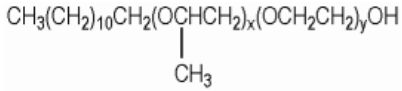
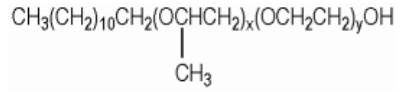
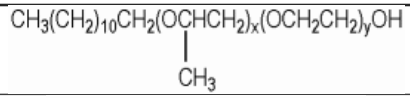
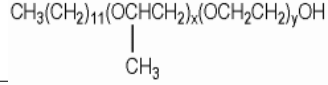
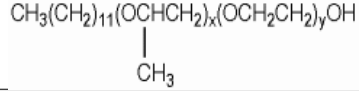
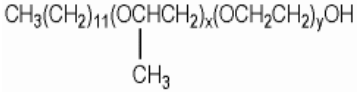
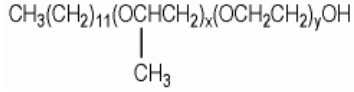
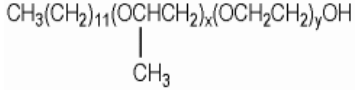
Ingredient (CAS No. if available)	Definition[1]	Structure[1] ;CIR staff*	Function
PPG-2-Isodeceth-25 (155683-77-5)[43]	the polyoxypropylene, polyoxyethylene ether of isodecyl alcohol that conforms generally to the formula where x has an average value of 2 and y has an average value of 25		surfactant- cleansing and emulsifying agent
PPG-3-Isodeceth-1 (155683-77-5)[43]	the polyoxypropylene, polyoxyethylene ether of isodecyl alcohol that conforms generally to the formula where x has an average value of 3 and y has an average value of 1		skin conditioning agent - emollient
PPG-4-Isodeceth-10	the polyoxypropylene, polyoxyethylene ether of isodecyl alcohol that conforms generally to the formula where x has an average value of 4 and y has an average value of 10		surfactant- cleansing and emulsifying agent
PPG-3-Isosteareth-9	the polyoxypropylene, polyoxyethylene ether of Isostearyl Alcohol that conforms generally to the formula where x has an average value of 3 and y has an average value of 9		surfactant- emulsifying agent
PPG-2-Laureth-5	the polyoxypropylene, polyoxyethylene ether of Lauryl Alcohol that conforms generally to the formula where x has an average value of 2 and y has an average value of 5		skin conditioning agent – emollient; surfactant-emulsifying agent
PPG-2-Laureth-8	the polyoxypropylene, polyoxyethylene ether of Lauryl Alcohol (q.v.) that conforms generally to the formula where x has an average value of 2 and y has an average value of 8		skin conditioning agent – emollient; surfactant-emulsifying agent
PPG-2-Laureth-12	the polyoxypropylene, polyoxyethylene ether of Lauryl Alcohol that conforms generally to the formula where x has an average value of 2 and y has an average value of 12		surfactant- emulsifying agent
PPG-3-Laureth-8	the polyoxypropylene, polyoxyethylene ether of Lauryl Alcohol that conforms generally to the formula where x has an average value of 3 and y has an average value of 8		surfactant- emulsifying agent
PPG-3-Laureth-9	the polyoxypropylene, polyoxyethylene ether of Lauryl Alcohol that conforms generally to the formula where x has an average value of 3 and y has an average value of 9		surfactant- emulsifying agent
PPG-3-Laureth-10	the polyoxypropylene, polyoxyethylene derivative of Lauryl Alcohol that conforms generally to the formula where x has an average value of 3 and y has an average value of 10		surfactant- emulsifying agent
PPG-3-Laureth-12	the polyoxypropylene, polyoxyethylene derivative of Lauryl Alcohol that conforms generally to the formula where x has an average value of 3 and y has an average value of 12		surfactant- emulsifying agent
PPG-4 Laureth-2 (68439-51-0)[43]	the polyoxypropylene, polyoxyethylene ether of Lauryl Alcohol that conforms to the formula where x has an average value of 4 and y has an average of value of 2		skin conditioning agent – emollient; surfactant-emulsifying agent

Table 2. Definitions, Structures, and, Functions

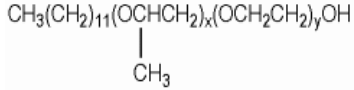
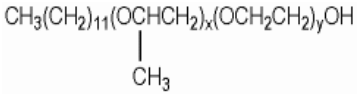
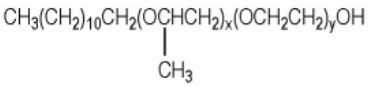
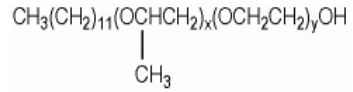
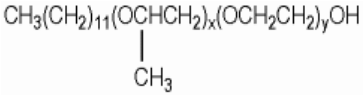
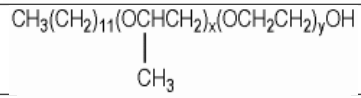
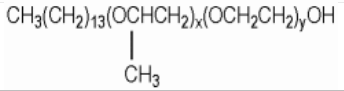
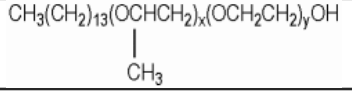
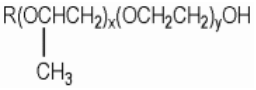
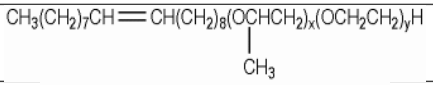
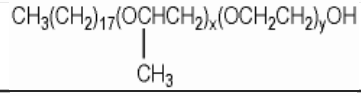
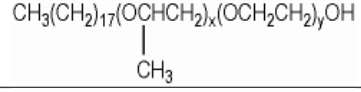
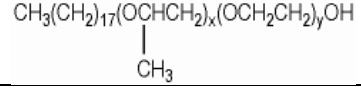
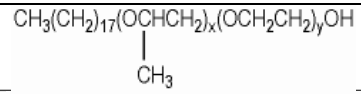
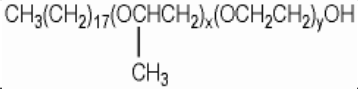
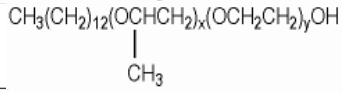
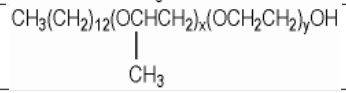
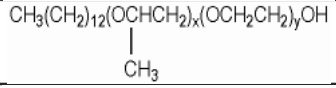
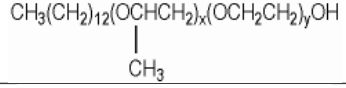
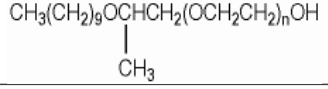
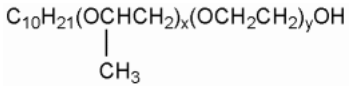
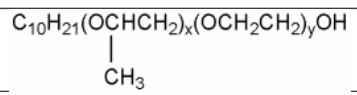
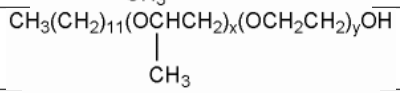
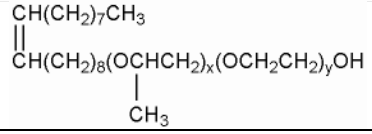
Ingredient (CAS No. if available)	Definition[1]	Structure[1] ;CIR staff*	Function
PPG-4 Laureth-5 (68439-51-0)[43]	the polyoxypropylene, polyoxyethylene ether of Lauryl Alcohol that conforms generally to the formula where x has an average of 4 and y has an average value of 5		skin conditioning agent – emollient; surfactant-emulsifying agent
PPG-4 Laureth-7	the polyoxypropylene, polyoxyethylene ether of Lauryl Alcohol that conforms generally to the formula where x has an average value of 4 and y has an average value of 7		skin conditioning agent – emollient; surfactant-emulsifying agent
PPG-4-Laureth-15	the polyoxyethylene, polyoxypropylene ether of Lauryl Alcohol that conforms generally to the formula where x has an average value of 4 and y has an average value of 15		skin conditioning agent – emollient; surfactant-emulsifying agent
PPG-5-Laureth-5	the polyoxyethylene, polyoxypropylene ether of lauryl alcohol that conforms generally to the formula where x has an average value of 5 and y has an average value of 5		skin conditioning agent – emollient; surfactant-emulsifying agent
PPG-6-Laureth-3	the polyoxypropylene, polyoxyethylene ether of lauryl alcohol that conforms generally to the formula where x has an average value of 6 and y has an average value of 3		skin conditioning agent – emollient; surfactant-emulsifying agent
PPG-25-Laureth-25 (37311-00-5; 68238-81-3[43])	the polyoxypropylene, polyoxyethylene ether of Lauryl Alcohol that conforms generally to the formula where x has an average value of 25 and y has an average value of 25		surfactant- emulsifying agent
PPG-3-Myreth-3 (37311-04-9)	the polyoxypropylene, polyoxyethylene ether of myristyl alcohol that conforms generally to the formula where x has an average value of 3 and y has an average value of 3		skin conditioning agent – emollient; surfactant-emulsifying agent
PPG-3-Myreth-11 (37311-04-9)	the polyoxypropylene, polyoxyethylene ether of myristyl alcohol that conforms generally to the formula where x has an average value of 3 and y has an average value of 11		surfactant- emulsifying agent
PPG-2-PEG-11 Hydrogenated Lauryl Alcohol Ether	a polyoxypropylene, polyoxyethylene ether of hydrogenated lauryl alcohol that conforms generally to the formula where x has an average value of 2, y has an average value of 11, and R represents the alkyl groups derived from hydrogenated lauryl alcohol		surfactant- emulsifying agent
PPG-3-PEG-6 Oleyl Ether	the polyoxypropylene, polyoxyethylene derivative of oleyl alcohol that conforms to the formula where x has an average value of 3 and y has an average value of 6		surfactant- emulsifying agent
PPG-9-Steareth-3 (9038-43-1)	the polyoxypropylene, polyoxyethylene ether of stearyl alcohol that conforms generally to the formula where x has an average value of 9 and y has an average value of 3		skin conditioning agent – emollient
PPG-23-Steareth-34 (9038-43-1)	the polyoxypropylene, polyoxyethylene ether of stearyl alcohol that conforms generally to the formula where x has an average value of 23 and y has an average value of 34		skin conditioning agent – emollient; surfactant-emulsifying agent
PPG-30 Steareth-4	the polyoxypropylene, polyoxyethylene ether of stearyl alcohol that conforms generally to the formula where x has an average value of 30 and y has an average value of 4		skin conditioning agent – emollient; surfactant-emulsifying agent

Table 2. Definitions, Structures, and, Functions

Ingredient (CAS No. if available)	Definition[1]	Structure[1 ;CIR staff*]	Function
PPG-34-Steareth-3	the polyoxypropylene, polyoxyethylene ether of stearyl alcohol that conforms generally to the formula where x has an average value of 34 and y has an average value of 3		skin conditioning agent – emollient; surfactant-emulsifying agent
PPG-38 Steareth-6	the polyoxypropylene, polyoxyethylene ether of stearyl alcohol that conforms generally to the formula where x has an average value of 38 and y has an average value of 6		skin conditioning agent – emollient; surfactant-emulsifying agent
PPG-1 Trideceth- 6	the polyoxypropylene, polyoxyethylene ether of tridecyl alcohol that conforms generally to the formula where x has an average value of 1 and y has an average value of 6		skin conditioning agent – emollient; surfactant-emulsifying agent
PPG-1 Trideceth-13	the polyoxypropylene, polyoxyethylene ether of tridecyl alcohol that conforms generally to the formula where x has an average value of 1 and y has an average value of 13		skin conditioning agent – emollient; surfactant-emulsifying agent
PPG-4 Trideceth-6 (65150-81-4)[43]	the polyoxypropylene, polyoxyethylene ether of tridecyl alcohol that conforms generally to the formula where x has an average value of 4 and y has an average value of 6		skin conditioning agent – emollient; surfactant-emulsifying agent
PPG-6 Trideceth-8	the polyoxypropylene, polyoxyethylene ether of tridecyl alcohol that conforms generally to the formula where x has an average value of 6 and y has an average value of 8		skin conditioning agent – emollient; surfactant-emulsifying agent
Propylene Glycol Capreth-4	the propylene glycol ether of a polyethylene glycol derivative of capryl alcohol that conforms generally to the formula where n has an average value of 4		surfactant- emulsifying agent
Propylene Glycol Isodeceth-4	the propylene glycol ether of ethoxylated isodecyl alcohol that conforms generally to the formula where x has an average value of 1 and y has an average value of 4 (a.k.a. PPG-1-Isodeceth-4)[52]		surfactant- emulsifying agent
Propylene Glycol Isodeceth-12	the propylene glycol ether of ethoxylated isodecyl alcohol that conforms generally to the formula where x has an average value of 1 and y has an average value of 12		surfactant- emulsifying agent
Propylene Glycol Laureth-6	the propylene glycol ether of Laureth-6 that conforms generally to the formula where x has an average value of 1 and y has an average value of 6		surfactant- emulsifying agent
Propylene Glycol Oleth-5	the propylene glycol ether of Oleth-5 that conforms generally to the formula where x has an average value of 1 and y has an average value of 5		surfactant- emulsifying agent

*when available, the structure depicted in the *International Cosmetic Ingredient Dictionary and Handbook* were used; when there was no structure available, CIR staff drew the structure

Table 3. Physical and Chemical Properties

Property	Description	Reference
	PPG-5 C9-15 Pareth-6	
physical state and appearance	colorless to yellowish liquid	25
active content	100%	25
solubility	soluble in water	25
stability	stable in acid and alkali	25
	PPG-3 C12-14 Sec-Pareth-7	
odor	odorless	12
specific gravity	0.969 (20/20°C)	12
stability	stable to both acid and alkali; do not react with water or air under normal conditions	12
	PPG-4 C12-14 Sec-Pareth-5	
odor	odorless	12
specific gravity	0.956 (20/20°C)	12
stability	stable to both acid and alkali; do not react with water or air under normal conditions	12
	PPG-5 C12-14 Sec-Pareth-7	
odor	odorless	12
specific gravity	0.975 (20/20°C)	12
stability	stable to both acid and alkali; do not react with water or air under normal conditions	12
	PPG-5 C12-14 Sec-Pareth-9	
odor	odorless	12
specific gravity	0.979 (20/20°C)	12
stability	stable to both acid and alkali; do not react with water or air under normal conditions	12
	PPG-2 C12-15 Pareth-6	
physical state	liquid	14
active content	100% by wt	14
	PPG-4-Ceteth-1	
physical state and appearance	colorless to pale yellow liquid	7
	PPG-4-Ceteth-10	
physical state and appearance	colorless liquid	19
	colorless to pale yellow petrolatum-like substance	8
	PPG-4-Ceteth-20	
physical state and appearance	white solid	20
	colorless to pale yellow waxy substance	9
	PPG-5-Ceteth-20	
physical state	liquid	11
	clear to slightly hazy liquid	21
boiling point	310.9°C (760 mm Hg)	6
solubility	soluble in water and isopropanol	11
	dispersible in mineral oil	
	PPG-8-Ceteth-1	
physical state and appearance	colorless liquid	22
	PPG-8-Ceteth-20	
physical state and appearance	yellow solid	23
	PPG-2-Deceth-3	
physical state and appearance	slightly yellow oil	13
	PPG-2-Deceth-5	
physical state and appearance	slightly yellow oil	13
	PPG-2-Deceth-7	
physical state and appearance	slightly yellow turbid oil	13
	PPG-2-Deceth-8	
physical state and appearance	clear liquid	5
active content	90% (water content; 10%)	5
density	1020 kg/m^3 (20°C)	5
solubility	soluble in water, ethanol, propylene glycol, and 2-propanol	5
	dispersible in low aromatic solvent, white spirit, and xylene	
	PPG-2-Deceth-10	
physical state and appearance	slightly yellow soft paste	13
	PPG-2-Deceth-12	
physical state and appearance	slightly yellow soft paste	13
	PPG-2-Deceth-15	
physical state and appearance	slightly yellow soft wax	13
	PPG-2-Deceth-20	
physical state and appearance	slightly yellow soft wax	13
	PPG-2-Deceth-30	
physical state and appearance	slightly yellow soft wax	13
	PPG-6-Deceth-4	
physical state	liquid	14
active content	100% by wt	14
	PPG-6-Deceth-9	
physical state	liquid	14
active content	100% by wt	14

Table 3. Physical and Chemical Properties

Property	Description	Reference
	PPG-8-Deceth-6	
physical state	liquid	14
active content	100% by wt	14
	PPG-6 Decyltetradeceth-12	
physical state and appearance	yellow solid	15
	PPG-6-Decyltetradeceth-20	
physical state and appearance	yellow solid	16
	PPG-6-Decyltetradeceth-30	
physical state and appearance	yellow solid	17
	PPG-9-Ethylhexeth-5	
physical state and appearance	colorless to yellow liquid with a mild odor	10
boiling point	decomposes prior to boiling	10
	PPG-3-Isodeceth-1	
physical state	liquid	18
	PPG-4-Laureth-2	
physical state	liquid	14
active content	100%	14
	PPG-4-Laureth-5	
physical state	liquid	14
active content	100%	14
	PPG-25-Laureth-25	
physical state and appearance	colorless or pale yellow liquid	24
	colorless or straw-colored clear liquid	30
solubility	soluble in water	24
density	1.046±2%	30
pH	6.8±0.4	30
	PPG-1 Trideceth-13	
physical state and appearance	colorless liquid	26
active content	95%	26
solubility	soluble in water	26
	Propylene Glycol Oleth-5	
physical state	liquid	14
active content	100%	14

Table 4. Frequency and concentration of use according to duration and type of exposure

	# of Uses[36]	*Max Conc of Use (%)*[37]	*# of Uses*[36]	*Max Conc of Use (%)*[37]	*# of Uses*[36]	*Max Conc of Use (%)*[37]
	PEG/PPG-9/2 Dimethyl Ether		**PEG/PPG-14/7 Dimethyl Ether**		**PEG/PPG-17/4 Dimethyl Ether**	
Totals*	**NR**	**0.01-2**	**35**	**0.00011-7**	**11**	**0.1-5**
Duration of Use						
Leave-On	*NR*	*0.01-2*	*34*	*0.00011-7*	*11*	*0.1-5*
Rinse-Off	*NR*	*0.03-0.97*	*1*	*0.01-3*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type						
Eye Area	NR	0.01	NR	0.01-5	NR	3
Incidental Ingestion	NR	NR	NR	1	NR	NR
Incidental Inhalation-Spray	NR	0.05	1[a]	0.12-7	NR	NR
Incidental Inhalation-Powder	NR	NR	NR	0.01	NR	NR
Dermal Contact	NR	0.01-1	35	0.01-7	11	0.1-5
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	0.03-2	NR	0.12-3	NR	NR
Hair-Coloring	NR	NR	NR	0.5	NR	NR
Nail	NR	NR	NR	0.00011-1	NR	NR
Mucous Membrane	NR	NR	NR	1	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR

Table 4. Frequency and concentration of use according to duration and type of exposure

	# of Uses[36]	*Max Conc of Use (%)*[37]	*# of Uses*[36]	*Max Conc of Use (%)*[37]	*# of Uses*[36]	*Max Conc of Use (%)*[37]
	PEG/PPG-35/40 Dimethyl Ether		**PEG/PPG-36/41 Dimethyl Ether**		**PEG/PPG-50/40 Dimethyl Ether**	
Totals*	**NR**	**1-3**	**243**	**0.1-5**	**2**	**0.05-2**
Duration of Use						
Leave-On	*NR*	*1-3*	*243*	*0.1-5*	*NR*	*0.05*
Rinse Off	*NR*	*3*	*NR*	*0.1-1*	*2*	*0.4-2*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type						
Eye Area	NR	NR	91	0.1-1	NR	0.4
Incidental Ingestion	NR	NR	27	5	NR	NR
Incidental Inhalation-Spray	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Powder	NR	NR	6	0.1	NR	NR
Dermal Contact	NR	1-3	215	0.1-1	2	0.5-2
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	1	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	27	5	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR
	PEG/PPG-55/28 Dimethyl Ether		**PPG-2-Ceteareth-9**		**PPG-2-Ceteth-10**	
Totals*	**NR**	**0.05-5**	**9**	**NR**	**1**	**NR**
Duration of Use						
Leave-On	*NR*	*0.5-5*	*5*	*NR*	*1*	*NR*
Rinse-Off	*NR*	*0.05-5*	*4*	*NR*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type						
Eye Area	NR	NR	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Powder	NR	NR	NR	NR	NR	NR
Dermal Contact	NR	0.5-3	8	NR	1	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	0.05-5	1	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR
	PPG-4-Ceteth-20		**PPG-5-Ceteth-20**		**PPG-8-Ceteth-1**	
Totals	**2**	**NR**	**445**	**0.05-10**	**NR**	**0.01**
Duration of Use						
Leave-On	*2*	*NR*	*217*	*0.05-10*	*NR*	*0.01*
Rinse Off	*NR*	*NR*	*202*	*0.5-9*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*26*	*1.5*	*NR*	*NR*
Exposure Type						
Eye Area	NR	NR	5	0.05-0.81	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	NR	NR	28 [a,b]	0.14-5; 1.5-10[b]	NR	NR
Incidental Inhalation-Powder	NR	NR	NR	NR	NR	NR
Dermal Contact	2	NR	195	0.05-9	NR	0.01
Deodorant (underarm)	NR	NR	4 [b]	3-5	NR	NR
Hair - Non-Coloring	NR	NR	240	0.14-10	NR	NR
Hair-Coloring	NR	NR	8	2-3.1	NR	NR
Nail	NR	NR	2	0.1-1.5	NR	NR
Mucous Membrane	NR	NR	73	1.5-9	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR

Table 4. Frequency and concentration of use according to duration and type of exposure

	# of Uses[36]	*Max Conc of Use (%)*[37]	*# of Uses*[36]	*Max Conc of Use (%)*[37]	*# of Uses*[36]	*Max Conc of Use (%)*[37]
	PPG-8-Ceteth-10		**PPG-8-Ceteth-20**		**PPG-2-Deceth-3**	
Totals*	**NR**	**0.036**	**10**	**0.072-2**	**NR**	**0.4**
Duration of Use						
Leave-On	*NR*	*NR*	*9*	*0.1-1.1*	*NR*	*0.4*
Rinse-Off	*NR*	*0.036*	*1*	*0.072-2*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*0.075*	*NR*	*NR*
Exposure Type						
Eye Area	NR	NR	NR	0.3	NR	0.4
Incidental Ingestion	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	NR	NR	NR	0.19; 0.7[a]	NR	NR
Incidental Inhalation-Powder	NR	NR	NR	1.1	NR	NR
Dermal Contact	NR	NR	10	0.075-2	NR	NR
Deodorant (underarm)	NR	NR	NR	spray: 0.19 not spray: 1	NR	NR
Hair - Non-Coloring	NR	0.036	NR	0.075-1	NR	NR
Hair-Coloring	NR	NR	NR	0.05	NR	NR
Nail	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	0.075	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR
	PPG-2-Deceth-12		**PPG-6-Decyltetradeceth-20**		**PPG-6-Decyltetradeceth-30**	
Totals*	**1**	**0.24-3**	**2**	**NR**	**18**	**0.25-2**
Duration of Use						
Leave-On	*NR*	*0.24-3*	*2*	*NR*	*15*	*0.25-2*
Rinse-Off	*1*	*NR*	*NR*	*NR*	*3*	*0.3-0.5*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type						
Eye Area	NR	0.24	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	NR	NR	NR	NR	1[a]	NR
Incidental Inhalation-Powder	NR	NR	NR	NR	NR	NR
Dermal Contact	NR	NR	2	NR	18	0.25-2
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	3	NR	NR	NR	NR
Hair-Coloring	1	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR
	PPG-13-Decyltetradeceth-24		**PPG-20-Decyltetradeceth-10**		**PPG-30-Decyltetradeceth-10[#]**	
Totals	**37**	**0.03**	**2**	**0.1-2**	**1**	**NR**
Duration of Use						
Leave-On	*34*	*0.03-2*	*2*	*0.1-2*	*NR*	*NR*
Rinse Off	*3*	*0.3-1*	*NR*	*1*	*1*	*NR*
Diluted for (Bath) Use	*NR*	*2*	*NR*	*NR*	*NR*	*NR*
Exposure Type						
Eye Area	NR	0.1-0.3	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	2	NR	NR
Incidental Inhalation-Spray	1[a]	0.075-0.9; 2[b]	NR	0.1-0.3	NR	NR
Incidental Inhalation-Powder	NR	0.03	NR	NR	NR	NR
Dermal Contact	37	0.03-2	1	0.1-2	1	NR
Deodorant (underarm)	NR	spray: 0.17 not spray: 0.057	NR	spray: 0.18 not spray: 0.4	NR	NR
Hair - Non-Coloring	NR	0.3-0.9	1	0.3-1	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	2	NR	2	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR

Table 4. Frequency and concentration of use according to duration and type of exposure

	# of Uses[36]	*Max Conc of Use (%)*[37]	*# of Uses*[36]	*Max Conc of Use (%)*[37]	*# of Uses*[36]	*Max Conc of Use (%)*[37]
	PPG-2-Isodeceth-12		**PPG-3-Isostereth-9**		**PPG-5-Laureth-5**	
Totals	**4**	**0.5-10**	**3**	**NR**	**8**	**0.033**
Duration of Use						
Leave-On	*2*	*0.5-1.5*	*3*	*NR*	*5*	*0.033*
Rinse Off	*2*	*10*	*NR*	*NR*	*3*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type						
Eye Area	NR	NR	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	NR	NR	2[b]	NR	NR	NR
Incidental Inhalation-Powder	NR	NR	NR	NR	NR	NR
Dermal Contact	2	0.5-10	3	NR	7	0.033
Deodorant (underarm)	NR	NR	NR	NR	2[b]	NR
Hair - Non-Coloring	2	1.5	NR	NR	1	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR
	PPG-25-Laureth-25		**PPG-34-Steareth-3**		**PPG-1-Trideceth-6**	
Totals	**31**	**0.4-2**	**NR**	**1.9**	**224**	**0.024-0.4**
Duration of Use						
Leave-On	*27*	*0.4-2*	*NR*	*NR*	*127*	*0.05-0.4*
Rinse Off	*4*	*NR*	*NR*	*1.9*	*97*	*0.024-0.3*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type						
Eye Area	2	0.72-1.5	NR	NR	1	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	NR	NR	NR	NR	1[a]	0.05
Incidental Inhalation-Powder	NR	NR	NR	NR	NR	NR
Dermal Contact	29	0.4-2	NR	NR	38	0.2-0.27
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	2	NR	NR	1.9	168	0.05-0.4
Hair-Coloring	NR	NR	NR	NR	11	0.024-0.25
Nail	NR	NR	NR	NR	5	NR
Mucous Membrane	1	NR	NR	NR	NR	NR
Baby Products	1	NR	NR	NR	NR	NR

*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.
included in the VCRP, but not listed in the *International Cosmetic Ingredient Dictionary and Handbook*
[a] Includes suntan products, in that it is not known whether or not the reported product is a spray.
[b] Includes products for which it is not known whether or not the product is a spray.
NR – none reported

Table 5. No reported use [36-38]

PEG-4-PPG-7 C13/C15 Alcohol	PPG-6 C9-11 Pareth-5	PPG-2-Isodeceth-8
PEG/PPG-3/6 Dimethyl Ether	PPG-6 C12-15 Pareth-12	PPG-2-Isodeceth-9
PEG/PPG-7/12 Dimethyl Ether	PPG-6 C12-18 Pareth-11	PPG-2-Isodeceth-10
PEG/PPG-22/40 Dimethyl Ether	PPG-3 C12-14 Sec-Pareth-7	PPG-2-Isodeceth-18
PEG/PPG-27/14 Dimethyl Ether	PPG-4 C12-14 Sec-Pareth-5	PPG-2-Isodeceth-25
PEG/PPG-52/32 Dimethyl Ether	PPG-5 C12-14 Sec-Pareth-7	PPG-3-Isodeceth-1
PEG/PPG-4/2 Propylheptyl Ether	PPG-5 C12-14 Sec-Pareth-9	PPG-4-Isodeceth-10
PEG/PPG-6/2 Propylheptyl Ether	PPG-1-Deceth-4	PPG-2-Laureth-5
PEG-7/PPG-2 Propylheptyl Ether	PPG-1-Deceth-5	PPG-2-Laureth-8
PEG/PPG-8/2 Propylheptyl Ether	PPG-1-Deceth-6	PPG-2-Laureth-12
PEG/PPG-10/2 Propylheptyl Ether	PPG-1-Deceth-7	PPG-3-Laureth-8
PEG/PPG-14/2 Propylheptyl Ether	PPG-2-Deceth-5	PPG-3-Laureth-9
PEG/PPG-40/2 Propylheptyl Ether	PPG-2-Deceth-7	PPG-3-Laureth-10
PPG-4-Ceteareth-12	PPG-2-Deceth-8	PPG-3-Laureth-12
PPG-10-Ceteareth-20	PPG-2-Deceth-10	PPG-4 Laureth-2
PPG-1-Ceteth-1	PPG-2-Deceth-15	PPG-4 Laureth-5
PPG-1-Ceteth-5	PPG-2-Deceth-20	PPG-4 Laureth-7
PPG-1-Ceteth-10	PPG-2-Deceth-30	PPG-4-Laureth-15
PPG-1-Ceteth-20	PPG-2-Deceth-40	PPG-6-Laureth-3
PPG-2-Ceteth-1	PPG-2-Deceth-50	PPG-3-Myreth-3
PPG-2-Ceteth-5	PPG-2-Deceth-60	PPG-3-Myreth-11
PPG-2-Ceteth-20	PPG-4-Deceth-4	PPG-2-PEG-11 Hydrogenated Lauryl Alcohol Ether
PPG-4-Ceteth-1	PPG-4-Deceth-6	PPG-3-PEG-6 Oleyl Ether
PPG-4-Ceteth-5	PPG-6-Deceth-4	PPG-9-Steareth-3
PPG-4-Ceteth-10	PPG-6-Deceth-9	PPG-23-Steareth-34
PPG-8-Ceteth-2	PPG-8-Deceth-6	PPG-30 Steareth-4
PPG-8-Ceteth-5	PPG-14-Deceth-6	PPG-38 Steareth-6
PPG-2 C9-11 Pareth-5	PPG-6-Decyltetradeceth-12	PPG-1 Trideceth-13
PPG-2 C9-11 Pareth-7	PPG-9-Ethylhexeth-5	PPG-4 Trideceth-6
PPG-2 C9-11 Pareth-8	PPG-1-Isodeceth-4	PPG-6 Trideceth-8
PPG-2 C9-11 Pareth-11	PPG-1-Isodeceth-6	Propylene Glycol Capreth-4
PPG-2 C12-13 Pareth-8	PPG-1-Isodeceth-7	Propylene Glycol Isodeceth-4
PPG-2 C12-15 Pareth-6	PPG-1-Isodeceth-9	Propylene Glycol Isodeceth-12
PPG-4 C13-15 Pareth-15	PPG-2-Isodeceth-4	Propylene Glycol Laureth-6
PPG-5 C9-15 Pareth-6	PPG-2-Isodeceth-6	Propylene Glycol Oleth-5

Table 6. Examples of non-cosmetic uses

Ingredient	Use	Reference
PPG-5 C9-15 Pareth-6	industrial washer and cleansing agents	[25]
PPG C12-14 sec-Pareths	nonionic surfactants in the paper and pulp, metal, textile, plastics and paint, pesticide, and leather and fur industries	[12]
PPG-2-Deceth-8	all-purpose cleaner and emulsifier in the paints and coatings	[5]

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PEG/PPG-14/7 DIMETHYL ETHER	11E - Shaving Cream	1	
PEG/PPG-14/7 DIMETHYL ETHER	12C - Face and Neck (exc shave)	17	
PEG/PPG-14/7 DIMETHYL ETHER	12D - Body and Hand (exc shave)	5	
PEG/PPG-14/7 DIMETHYL ETHER	12F - Moisturizing	6	
PEG/PPG-14/7 DIMETHYL ETHER	12G - Night	3	
PEG/PPG-14/7 DIMETHYL ETHER	12I - Skin Fresheners	1	
PEG/PPG-14/7 DIMETHYL ETHER	12J - Other Skin Care Preps	1	
PEG/PPG-14/7 DIMETHYL ETHER	13B - Indoor Tanning Preparations	1	
PEG/PPG-17/4 DIMETHYL ETHER	12C - Face and Neck (exc shave)		6
PEG/PPG-17/4 DIMETHYL ETHER	12F - Moisturizing		3
PEG/PPG-17/4 DIMETHYL ETHER	12G - Night		2
PEG/PPG-36/41 DIMETHYL ETHER	03A - Eyebrow Pencil	1	
PEG/PPG-36/41 DIMETHYL ETHER	03B - Eyeliner	4	
PEG/PPG-36/41 DIMETHYL ETHER	03C - Eye Shadow	85	
PEG/PPG-36/41 DIMETHYL ETHER	03F - Mascara	1	
PEG/PPG-36/41 DIMETHYL ETHER	07A - Blushers (all types)	18	
PEG/PPG-36/41 DIMETHYL ETHER	07B - Face Powders	6	
PEG/PPG-36/41 DIMETHYL ETHER	07C - Foundations	1	
PEG/PPG-36/41 DIMETHYL ETHER	07E - Lipstick	27	
PEG/PPG-36/41 DIMETHYL ETHER	07G - Rouges	86	
PEG/PPG-36/41 DIMETHYL ETHER	07I - Other Makeup Preparations	14	
PEG/PPG-50/40 DIMETHYL ETHER	12A - Cleansing	2	
PPG-2-CETEARETH-9	05F - Shampoos (non-coloring)	1	
PPG-2-CETEARETH-9	12A - Cleansing	3	
PPG-2-CETEARETH-9	12C - Face and Neck (exc shave)	4	
PPG-2-CETEARETH-9	12J - Other Skin Care Preps	1	
PPG-2-CETETH-10	12C - Face and Neck (exc shave)	1	
PPG-4-CETETH-20	12C - Face and Neck (exc shave)	2	
PPG-5-CETETH-20	02A - Bath Oils, Tablets, and Salts	8	
PPG-5-CETETH-20	02B - Bubble Baths	14	
PPG-5-CETETH-20	02D - Other Bath Preparations	4	
PPG-5-CETETH-20	03B - Eyeliner	1	
PPG-5-CETETH-20	03E - Eye Makeup Remover	2	
PPG-5-CETETH-20	03G - Other Eye Makeup Preparations	2	
PPG-5-CETETH-20	04A - Cologne and Toilet waters	8	
PPG-5-CETETH-20	04E - Other Fragrance Preparation	3	
PPG-5-CETETH-20	05A - Hair Conditioner	25	
PPG-5-CETETH-20	05B - Hair Spray (aerosol fixatives)	14	
PPG-5-CETETH-20	05F - Shampoos (non-coloring)	95	
PPG-5-CETETH-20	05G - Tonics, Dressings, and Other Hair Groomir	56	
PPG-5-CETETH-20	05I - Other Hair Preparations	50	
PPG-5-CETETH-20	06A - Hair Dyes and Colors (all types requiring ca	2	
PPG-5-CETETH-20	06C - Hair Rinses (coloring)	1	
PPG-5-CETETH-20	06D - Hair Shampoos (coloring)	3	
PPG-5-CETETH-20	06H - Other Hair Coloring Preparation	2	
PPG-5-CETETH-20	07C - Foundations	2	
PPG-5-CETETH-20	07D - Leg and Body Paints	1	
PPG-5-CETETH-20	07F - Makeup Bases	3	
PPG-5-CETETH-20	07I - Other Makeup Preparations	1	

PPG-5-CETETH-20	08B - Cuticle Softeners	1
PPG-5-CETETH-20	08C - Nail Creams and Lotions	1
PPG-5-CETETH-20	10A - Bath Soaps and Detergents	37
PPG-5-CETETH-20	10B - Deodorants (underarm)	4
PPG-5-CETETH-20	10E - Other Personal Cleanliness Products	10
PPG-5-CETETH-20	11A - Aftershave Lotion	5
PPG-5-CETETH-20	11E - Shaving Cream	1
PPG-5-CETETH-20	12A - Cleansing	23
PPG-5-CETETH-20	12C - Face and Neck (exc shave)	7
PPG-5-CETETH-20	12D - Body and Hand (exc shave)	21
PPG-5-CETETH-20	12F - Moisturizing	15
PPG-5-CETETH-20	12G - Night	2
PPG-5-CETETH-20	12H - Paste Masks (mud packs)	1
PPG-5-CETETH-20	12I - Skin Fresheners	6
PPG-5-CETETH-20	12J - Other Skin Care Preps	11
PPG-5-CETETH-20	13B - Indoor Tanning Preparations	3
PPG-8-CETETH-20	12A - Cleansing	1
PPG-8-CETETH-20	12C - Face and Neck (exc shave)	2
PPG-8-CETETH-20	12D - Body and Hand (exc shave)	1
PPG-8-CETETH-20	12F - Moisturizing	6
PPG-2-DECETH-12	06H - Other Hair Coloring Preparation	1
PPG-6-DECYLTETRADECETH-20	12F - Moisturizing	1
PPG-6-DECYLTETRADECETH-20	12J - Other Skin Care Preps	1
PPG-6 DECYLTETRADECETH-30	12A - Cleansing	3
PPG-6 DECYLTETRADECETH-30	12C - Face and Neck (exc shave)	2
PPG-6 DECYLTETRADECETH-30	12D - Body and Hand (exc shave)	1
PPG-6 DECYLTETRADECETH-30	12F - Moisturizing	6
PPG-6 DECYLTETRADECETH-30	12J - Other Skin Care Preps	2
PPG-6 DECYLTETRADECETH-30	13B - Indoor Tanning Preparations	2
PPG-6-DECYLTETRADECETH-30	12J - Other Skin Care Preps	2
PPG-13-DECYLTETRADECETH-24	12A - Cleansing	3
PPG-13-DECYLTETRADECETH-24	12C - Face and Neck (exc shave)	23
PPG-13-DECYLTETRADECETH-24	12F - Moisturizing	4
PPG-13-DECYLTETRADECETH-24	12I - Skin Fresheners	4
PPG-13-DECYLTETRADECETH-24	12J - Other Skin Care Preps	2
PPG-13-DECYLTETRADECETH-24	13A - Suntan Gels, Creams, and Liquids	1
PPG-20 DECYLTETRADECETH-10	05G - Tonics, Dressings, and Other Hair Groomir	1
PPG-20 DECYLTETRADECETH-10	11A - Aftershave Lotion	1
PPG-2-ISODECETH-12	05G - Tonics, Dressings, and Other Hair Groomir	1
PPG-2-ISODECETH-12	05I - Other Hair Preparations	1
PPG-2-ISODECETH-12	12A - Cleansing	1
PPG-2-ISODECETH-12	12H - Paste Masks (mud packs)	1
PPG-3-ISOSTEARETH-9	04A - Cologne and Toilet waters	2
PPG-3-ISOSTEARETH-9	11A - Aftershave Lotion	1
PPG-5-LAURETH-5	05F - Shampoos (non-coloring)	1

PPG-5-LAURETH-5	07F - Makeup Bases	1
PPG-5-LAURETH-5	10B - Deodorants (underarm)	2
PPG-5-LAURETH-5	12A - Cleansing	1
PPG-5-LAURETH-5	12F - Moisturizing	1
PPG-5-LAURETH-5	12H - Paste Masks (mud packs)	1
PPG-5-LAURETH-5	12J - Other Skin Care Preps	1
PPG-25-LAURETH-25	01C - Other Baby Products	1
PPG-25-LAURETH-25	03B - Eyeliner	1
PPG-25-LAURETH-25	03C - Eye Shadow	1
PPG-25-LAURETH-25	05A - Hair Conditioner	2
PPG-25-LAURETH-25	10E - Other Personal Cleanliness Products	1
PPG-25-LAURETH-25	12A - Cleansing	1
PPG-25-LAURETH-25	12C - Face and Neck (exc shave)	6
PPG-25-LAURETH-25	12D - Body and Hand (exc shave)	5
PPG-25-LAURETH-25	12F - Moisturizing	10
PPG-25-LAURETH-25	12J - Other Skin Care Preps	3
PPG-1 TRIDECETH-6	03D - Eye Lotion	1
PPG-1 TRIDECETH-6	05A - Hair Conditioner	81
PPG-1 TRIDECETH-6	05C - Hair Straighteners	1
PPG-1 TRIDECETH-6	05E - Rinses (non-coloring)	2
PPG-1 TRIDECETH-6	05G - Tonics, Dressings, and Other Hair Groomir	49
PPG-1 TRIDECETH-6	05I - Other Hair Preparations	35
PPG-1 TRIDECETH-6	06A - Hair Dyes and Colors (all types requiring cá	1
PPG-1 TRIDECETH-6	06H - Other Hair Coloring Preparation	10
PPG-1 TRIDECETH-6	07I - Other Makeup Preparations	1
PPG-1 TRIDECETH-6	08B - Cuticle Softeners	1
PPG-1 TRIDECETH-6	08E - Nail Polish and Enamel	1
PPG-1 TRIDECETH-6	08G - Other Manicuring Preparations	3
PPG-1 TRIDECETH-6	12A - Cleansing	2
PPG-1 TRIDECETH-6	12C - Face and Neck (exc shave)	3
PPG-1 TRIDECETH-6	12D - Body and Hand (exc shave)	3
PPG-1 TRIDECETH-6	12F - Moisturizing	27
PPG-1 TRIDECETH-6	12J - Other Skin Care Preps	2
PPG-1 TRIDECETH-6	13B - Indoor Tanning Preparations	1

International Journal of Toxicology
31(Supplement 2) 169S-244S

DOI: 10.1177/1091581812444141
http://ijt.sagepub.com
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Safety Assessment of Alkyl PEG Ethers as Used in Cosmetics

Monice M. Fiume[1], Bart Heldreth[2], Wilma F. Bergfeld[3], Donald V. Belsito[3], Ronald A. Hill[3], Curtis D. Klaassen[3], Daniel Liebler[3], James G. Marks, Jr[3], Ronald C. Shank[3], Thomas J. Slaga[3], Paul W. Snyder[3], and F. Alan Andersen[4]

Abstract

The CIR Expert Panel assessed the safety of Alkyl PEG Ethers as used in cosmetics. These ingredients primarily function in cosmetics as surfactants, and some have additional functions as skin-conditioning agents, fragrance ingredients, and emulsion stabilizers. The Panel reviewed available relevant animal and clinical data, as well as information from previous CIR reports; when data were not available for individual ingredients, the Panel extrapolated from the existing data to support safety. The Panel concluded that the Alkyl PEG ethers are safe as used when formulated to be nonirritating, 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.

Keywords

alkyl peg ethers, safety, cosmetics

Introduction

This report assesses the safety of 369 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.

In 1983, the Cosmetic Ingredient Review (CIR) Expert Panel concluded that 2 alkyl PEG ethers, laureth 4 and laureth 23, were safe as cosmetic ingredients in the present practices of use and concentration.[1] In rereviewing that finding, a determination was made to include the broader group of alkyl PEG ethers.

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 in function. Therefore, the entire family of alkyl PEG ethers is included in this rereview, and the entire list 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.

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.

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] 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.

[1]Senior Scientific Analyst/Writer
[2]Chemist, Cosmetic Ingredient Review, NW, Washington, DC, USA
[3]The 2011 Cosmetic Ingredient Review Expert Panel members
[4]CIR Director, Cosmetic Ingredient Review, NW, Washington, DC, USA

Corresponding Author:
F. Alan Andersen, Cosmetic Ingredient Review, 1101 17th Street, NW, Suite 412, Washington, DC 20036, USA
Email: cirinfo@cir-safety.org

Table 1. Alkyl PEG Ethers Group

Alkyl PEG ethers		
Laureth 4[a] (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[a] (CAS No. 9002-92-0)	Ceteth-14[a] (CAS No. 9004-95-9)	Steareth 25 (CAS No. 9005-00-9)
Laureth 1 (CAS Nos. 9002-92-0; 4536-30-5)	Ceteth 15[a] (CAS No. 9004-95-9)	Steareth 27 (CAS No. 9005-00-9)
Laureth 2 (CAS Nos. 9002-92-0; 3055-93-4)	Ceteth 16[a] (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[a] (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[a] (CAS No. 9004-95-9)	Steareth 200 (CAS No. 9005-00-9)
Laureth 9 (CAS Nos. 9002-92-0; 3055-99-0)	Ceteth 25[a] (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[a] (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[a] (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[b]	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[a] (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[a] (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[a] (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[a] (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[a] (CAS No. 9004-95-9; 4484-59-7)	Steareth 10[a] (CAS No. 9005-00-9; 13149-86-5)	Methoxy PEG-7 (CAS No. 9004-74-4)
Ceteth 4[a] (CAS No. 9004-95-9; 5274-63-5)	Steareth 11[a] (CAS No. 9005-00-9)	Methoxy PEG-10 (CAS No. 9004-74-4)
Ceteth 5[a] (CAS No. 9004-95-9; 4478-97-1)	Steareth 13[a] (CAS No. 9005-00-9)	Methoxy PEG-16 (CAS No. 9004-74-4)
Ceteth 6[a] (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[a] (CAS No. 9005-00-9)	Methoxy PEG-40 (CAS No. 9004-74-4)
Ceteth 10[a] (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[a] (CAS No. 9004-95-9; 94159-75-8)	Steareth 20[a] (CAS No. 9005-00-9)	

(continued)

Table 1. (continued)

Alkyl PEG ether mixtures

Ceteareth-2[a] (CA5 No. 68439-49-6)	C9-11 Pareth-4 (CA5 No. 68439-46-3)	C12-14 Pareth 12 (CAS No. 68439-50-9)
Ceteareth-3[a] (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[a] (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[a] (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[a] (CAS No. 68439-49-6)	C10-16 Pareth-1 (CA5 No. 68002-97-1)	C12-15 Pareth 5 (CAS No. 68131-39-5)
Ceteareth-7[a] (CAS No. 68439-49-6)	C10-16 Pareth-2 (CA5 No. 68002-97-1)	C12-15 Pareth 7 (CAS No. 68131-39-5)
Ceteareth-8[a] (CA5 No. 68439-49-6)	C11-13 Pareth-6 (CAS No. 308060-94-8)	C12-15 Pareth 9 (CAS No. 68131-39-5)
Ceteareth-9[a] (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[a] (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[a] (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[a] (CAS No. 68439-49-6)	C11-15 Pareth-5 (CA5 No. 68131-40-8)	C12-16 Pareth-5 (CA5 No. 68551-12-2)
Ceteareth-13[a] (CAS No. 68439-49-6)	C11-15 Pareth-7 (CA5 No. 68131-40-8)	C12-16 Pareth 7 (CA5 No. 68551-12-2)
Ceteareth-14[a] (CA5 No. 68439-49-6)	C11-15 Pareth-9 (CA5 No. 68131-40-8)	C12-16 Pareth 9 (CA5 No. 68551-12-2)
Ceteareth-15[a] (CA5 No. 68439-49-6)	C11-15 Pareth-12 (CA5 No. 68131-40-8)	C13-15 Pareth 21 (CAS No. 64425-86-1)
Ceteareth-16[a] (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[a] (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[a] (CAS No. 68439-49-6)	C11-15 Pareth-30 (CA5 No. 68131-40-8)	C14-15 Pareth 8 (CAS No. 68951-67-7)
Ceteareth-20[a] (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[a] (CAS No. 68439-49-6)	C11-21-Pareth-3 (CA5 No. 246538-82-9)	C14-15 Pareth 12 (CA5 No. 68951-67-7)
Ceteareth 23[a] (CAS No. 68439-49-6)	C11-21-Pareth 10 (CAS No. 246538-82-9)	C14-15 Pareth 13 (CA5 No. 68951-67-7)
Ceteareth 24[a] (CA5 No. 68439-49-6)	C12-13 Pareth 1 (CAS No. 66455-14-9)	C20-22 Pareth 30
Ceteareth 25[a] (CA5 No. 68439-49-6)	C12-13 Pareth 2 (CAS No. 66455-14-9)	C20-40 Pareth 3 (CAS No. 246538-83-0)
Ceteareth 27[a] (CAS No. 68439-49-6)	C12-13 Pareth 3 (CAS No. 66455-14-9)	C20-40 Pareth 10 (CA5 No. 246538-83-0)
Ceteareth 28[a] (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[a] (CAS No. 68439-49-6)	C12-13 Pareth 5 (CA5 No. 66455-14-9)	C20-40 Pareth 40 (CAS No. 246538-83-0)
Ceteareth 30[a] (CAS No. 68439-49-6)	C12-13 Pareth 6 (CA5 No. 66455-14-9)	C20-40 Pareth 95 (CAS No. 246538-83-0)
Ceteareth 33[a] (CAS No. 68439-49-6)	C12-13 Pareth 7 (CA5 No. 66455-14-9)	C22-24 Pareth 33 (CAS No. 246538-84-1)
Ceteareth 34[a] (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[a] (CA5 No. 68439-49-6)	C12-13 Pareth 10 (CAS No. 66455-14-9)	C30-50 Pareth 10 (CA5 No. 246538-85-2)
Ceteareth 50[a] (CA5 No. 68439-49-6)	C12-13 Pareth 15 (CAS No. 66455-14-9)	C30-50 Pareth 40 (CA5 No. 246538-85-2)
Ceteareth 55[a] (CAS No. 68439-49-6)	C12-13 Pareth 23 (CAS No. 66455-14-9)	C40-60 Pareth 3 (CA5 No. 246538-86-3)
Ceteareth 60[a] (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[a] (CAS No. 68439-49-6)	C12-14 Pareth 5 (CAS No. 68439-50-9)	Hydrogenated Talloweth 12
Ceteareth 100[a] (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 (CA5 No. 68439-50-9)	

Partially unsaturated alkyl PEG ethers

Undecyleneth 6	Oleth 40[a] (CAS No. 9004-98-2)	
Oleth 2[a] (CAS No. 9004-98-2; 5274-65-7; 95287-03-9)	Oleth 44[a] (CAS No. 9004-98-2)	Cetoleth-30 (CAS No. 8065-81-4)
Oleth 3[a] (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[a] (CAS No. 9004-98-2; 5353-26-4; 103622-85-1)	Oleth 50[a] (CA5 No. 9004-98-2)	Coceth 5 (CAS No. 61791-13-7)
Oleth 5[a] (CAS No. 9004-98-2; 5353-27-5)	Oleth 82 (CA5 No. 9004-98-2)	Coceth 6 (CA5 No. 61791-13-7)
Oleth 6[a] (CA5 No. 9004-98-2)	Oleth 100 (CA5 No. 9004-98-2)	Coceth 7 (CAS No. 61791-13-7)
Oleth 7[a] (CA5 No. 9004-98-2)	Oleth 106 (CA5 No. 9004-98-2)	Coceth 8 (CA5 No. 61791-13-7)
Oleth 8[a] (CA5 No. 9004-98-2; 26996-03-2; 27040-03-5)	Cetoleth 2 (CA5 No. 8065-81-4)	Coceth 10 (CAS No. 61791-13-7)
Oleth 9[a] (CAS No. 9004-98-2)	Cetoleth 4 (CA5 No. 8065-81-4)	Coceth 20 (CA5 No. 61791-13-7)
Oleth 10[a] (CA5 No. 9004-98-2)	Cetoleth 5 (CAS No. 8065-81-4)	Coceth 25 (CAS No. 61791-13-7)
Oleth 11[a] (CAS No. 9004-98-2)	Cetoleth 6 (CA5 No. 8065-81-4)	Palmeth 2
Oleth 12[a] (CAS No. 9004-98-2)	Cetoleth 10 (CAS No. 8065-81-4)	Talloweth 4 (CAS No. 61791-28-4)
Oleth 15[a] (CAS No. 9004-98-2)	Cetoleth 11 (CAS No. 8065-81-4)	Talloweth 5 (CAS No. 61791-28-4)
Oleth 16[a] (CAS No. 9004-98-2; 25190-05-0)	Cetoleth 15 (CAS No. 8065-81-4)	Talloweth 6 (CA5 No. 61791-28-4)
Oleth 20[a] (CAS No. 9004-98-2)	Cetoleth 18 (CAS No. 8065-81-4)	Talloweth 7 (CA5 No. 61791-28-4)
Oleth 23[a] (CAS No. 9004-98-2)	Cetoleth 20 (CAS No. 8065-81-4)	Talloweth 18 (CAS No. 61791-28-4)

(continued)

Table 1. (continued)

Partially unsaturated alkyl PEG ethers		
Oleth 24 (CAS No. 9004-98-2)	Cetoleth 22 (CAS No. 8065-81-4)	PEG-15 Jojoba Alcohol
Oleth 25[a] (CAS No. 9004-98-2)	Cetoleth 24 (CAS No. 8065-81-4)	PEG-26 Jojoba Alcohol
Oleth 30[a] (CAS No. 9004-98-2)	Cetoleth 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
Sterol-containing PEG ethers		
Laneth 5[a] (CAS No. 61791-20-6)	Laneth 25[a] (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[a] (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		

[a] Ingredient has been reviewed previously.
[b] 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

(continued)

Table 2A. (continued)

Ingredient	Conclusion	Reference
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 $\geq$ 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; eg, 2-butoxyethanol is not a reproductive toxicant	7

Table 2B. Summaries of Information Provided in Previous Reports

Ingredient	Parameter Evaluated	Outcome	Reference
Previously Reviewed 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 nonirritating to 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	

(continued)

Table 2B. (continued)

Ingredient	Parameter Evaluated	Outcome	Reference
	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, 3.59 g/kg	
		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	Primary irritation index (PII) (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%, nonirritating; 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	
	Important discussion items	Discussion not included in report	
	Conclusion	Safe for topical application	
Laureths	Chemicals that may be present	Special grades of laureth-4 may 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	

(continued)

Table 2B. (continued)

Ingredient	Parameter Evaluated	Outcome	Reference
	Animal toxicology	Acute oral: undiluted laureth-4, practically nontoxic (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 nonirritating (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 participants	
	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 Months dermal: formulation containing 4% steareth-20 (rabbits), no systemic toxicity, some dermal irritation	
	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	

(continued)

Table 2B. (continued)

Ingredient	Parameter Evaluated	Outcome	Reference
	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; eg PEG-8 is rapidly absorbed by the gastrointestinal (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, $\leq$5.6 g/kg/day, no systemic toxicity (rats) inhalation: PEG-75, $\leq$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, -160 M and -180 M and any PEG $\geq$ 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	
	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	

(continued)

Table 2B. (continued)

Ingredient	Parameter Evaluated	Outcome	Reference
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 nonirritating	
	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	
	Repro/developmental toxicity	Sc 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	

(continued)

Table 2B. (continued)

Ingredient	Parameter Evaluated	Outcome	Reference
		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) 15- and 30-Day dermal studies: 12.5%, some erythema and edema, very slight incrassination of the epidermal germinative zone	13
	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%, nonirritating in vitro	
	Repro/developmental toxicity	No data	
	Genotoxicity	Negative, $\leq$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	

(continued)

Table 2B. (continued)

Ingredient	Parameter Evaluated	Outcome	Reference
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 nonhuman 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 nonhuman 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	
	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 Inhalation: 3%, 1 h, ataxia and moderate nasal irritation in all animals 10 min after exposure, no mortality	12

(continued)

Table 2B. (continued)

Ingredient	Parameter Evaluated	Outcome	Reference
	Dermal irritation/sensitization	Formulation w/0.8%, nonirritating (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 participants; undiluted technical grade: no irritation; formulations w/3%-10.2%: essentially nonirritating 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%: nonirritating (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	
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 Months 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	

(continued)

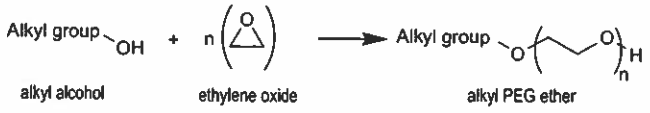
Table 2B. (continued)

Ingredient	Parameter Evaluated	Outcome	Reference
	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 participants; 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; eg, 2-butoxyethanol is not a reproductive toxicant	7

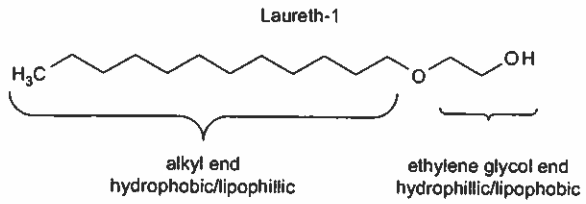
Chemistry

Definition and Structure

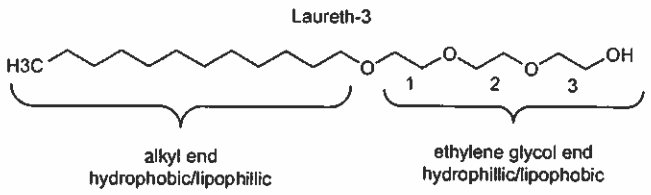
Alkyl PEG ethers. An alkyl PEG ether is the reaction product of an alkyl alcohol and 1 or more equivalents of ethylene oxide.[17]



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 (ie, 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 2 ethylene glycol units:



Each of the methoxy PEGs and PEG methyl ethers (2 International Nomenclature Cosmetic Ingredient [INCI] naming conventions that both mean a methyl group attached to a variable length PEG chain); capryleths (8 carbon chains with a variable PEG); noneths (9 carbon chains with a variable PEG); deceths (10 carbon chains with a variable PEG); undeceths (11 carbon chains with a variable PEG); laureths (12 carbon chains with a variable PEG); trideceths (13 carbon chains with a variable PEG); myreths (14 carbon chains with a variable PEG); ceteths (16 carbon chains with a variable PEG); steareths (18 carbon chains with a variable PEG); arachideth 20 (20 carbon chains with a 20-unit PEG chain); and beheneths (22 carbon chains with a variable PEG) follow this simple structural motif, as shown above for laureth 3 (and in more detail in Table 3).

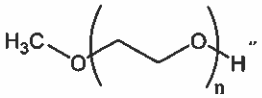
The European Commission's Scientific Committee on Consumer Products (SCCP) opinion on polidocanol (laureth 9) stated that these ingredients describe a class of alcohol ethoxylates with an average alkyl chain of 12 to 14 carbon atoms and an ethylene oxide chain of 9 ethylene oxide units.[19] To describe these alcohol ethoxylates, both the alkyl chain length and the number of ethylene oxide units are given, for example $C_{12\text{-}14}$ $AE_{6\text{-}12}$. This terminology will be used to describe laureth analogs for which safety test data were available.

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.

Table 3. Structures and Physical Properties (unless otherwise noted, these values were calculated)[18]

Methoxy PEG-n / PEG-n Methyl Ethers (a methyl group attached to a variable length PEG chain)

General Structure:

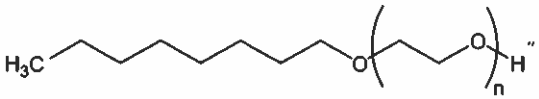


n = the average number of ethylene glycol units (eg, PEG-7 Methyl Ether (or Methoxy PEG-7) is when n = 7)

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 chains with a variable PEG)

General Structure:

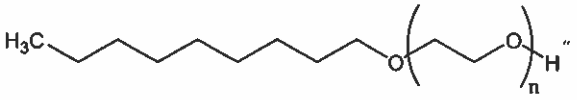


n = the average number of ethylene glycol units (eg, Capreth-4 is when n = 4)

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 chains with an 8-unit PEG)

General Structure:

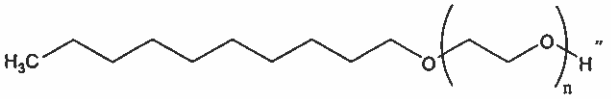


n = 9

INCI Name	Molecular Weight	M.P. / B.P.	$logK_{o/w}$
Noneth-8	496.67	225/532 °C	1.10

Deceths (10 carbon chains with a variable PEG)

General Structure:



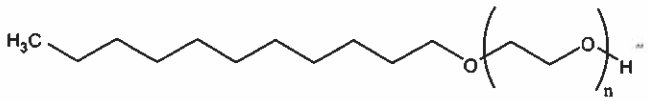
n = the average number of ethylene glycol units (eg, Deceth-4 is when n = 4)

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**; S703-94-6)	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

(continued)

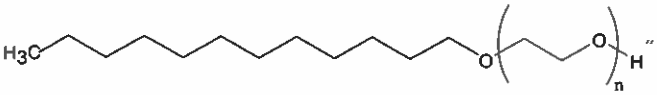
Table 3. (continued)

Methoxy PEG-n / PEG-n Methyl Ethers (a methyl group attached to a variable length PEG chain)			
Deceth-10 (CAS No. **26183-52-8**)	598.81	266/514 °C	1.04
Undeceths (11 carbon chains with a variable PEG)			
General Structure:			



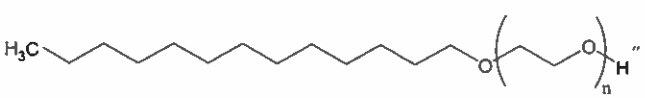
n = the average number of ethylene glycol units (eg, Undeceth-3 is when n = 3)

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
Laureths (12 carbon chains with a variable PEG)			
General Structure:			



n = the average number of ethylene glycol units (eg, 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[a] (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[a] (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
Trideceths (13 carbon chains with a variable PEG)			
General Structure:			



n = the average number of ethylene glycol units (eg, Trideceth-3 is when n = 3)

(continued)

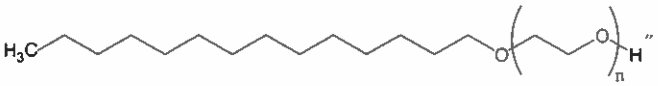
Table 3. (continued)

Methoxy PEG-n / PEG-n Methyl Ethers (a methyl group attached to a variable length PEG chain)

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 chains with a variable PEG)

General Structure:

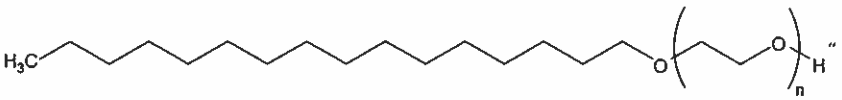


n = the average number of ethylene glycol units (eg, Myreth 3 is when n = 3)

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

Ceteths (16 carbon chains with a variable PEG)

General Structure:



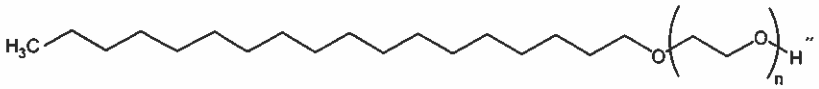
n = the average number of ethylene glycol units (eg, Ceteth 3 is when n = 3)

INCI Name	Molecular Weight	M.P. / B.P.	$logK_{o/w}$
Ceteth 1[a] (CAS No. **9004-95-9**; 2136-71-2)	286.49	101/367 °C	6.46
Ceteth 2[z] (CAS No. **9004-95-9**; 5274-61-3)	330.54	134/402 °C	6.19
Ceteth 3[a] (CAS No. **9004-95-9**; 4484-59-7)	374.59	158/437 °C	5.91
Ceteth 4[a] (CAS No. **9004-95-9**; 5274-63-5)	418.64	187/473 °C	5.64
Ceteth 5[a] (CAS No. **9004-95-9**; 4478-97-1)	462.70	203/508 °C	5.36
Ceteth 6[a] (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[a] (CAS No. **9004-95-9**; 14529-40-9)	682.96	299/684 °C	3.99
Ceteth 12[a] (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[a] (CAS No. **9004-95-9**)	859.17	–/825 °C	2.89
Ceteth 15[a] (CAS No. **9004-95-9**)	903.22	–/860 °C	2.62
Ceteth 16[a] (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[a] (CAS No. **9004-95-9**)	1123.48	–/1037 °C	1.25

(continued)

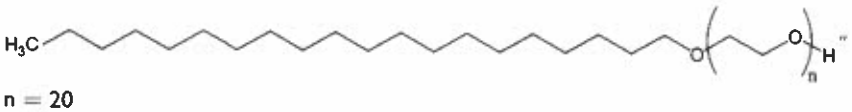
Table 3. (continued)

Methoxy PEG-n / PEG-n Methyl Ethers (a methyl group attached to a variable length PEG chain)			
Ceteth 23 (CAS No. **9004-95-9**)	1255.65	–/1142 °C	0.42
Ceteth 24[a] (CAS No. **9004-95-9**)	1299.69	–/1178 °C	0.15
Ceteth 25[a] (CAS No. **9004-95-9**)	1343.75	–/1213 °C	-0.13
Ceteth 30[a] (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[a] (CAS No. **9004-95-9**)	2224.80	–/1918 °C	-5.61
Ceteth 150 (CAS No. **9004-95-9**)	6850.35	–/–	–
Steareths (18 carbon chains with a variable PEG)			
General Structure:			



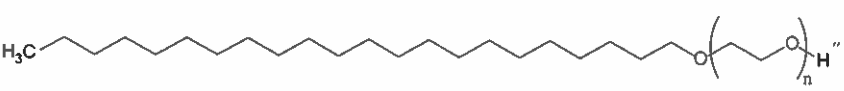
n = the average number of ethylene glycol units (eg, Steareth-3 is when n = 3)

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[a] (CAS No. **9005-00-9**; 1605 7-43-5)	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[a] (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[a] (CAS No. **9005-00-9**; 13149-86-5)	711.02	309/707 °C	4.97
Steareth 11[a] (CAS No. **9005-00-9**)	755.07	326/743 °C	4.70
Steareth 13[a] (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[a] (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[a] (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 chains 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
Beheneths (22 carbon chains with a variable PEG)			
General Structure:			



n = the average number of ethylene glycol units (eg, Beheneth-2 is when n = 2)

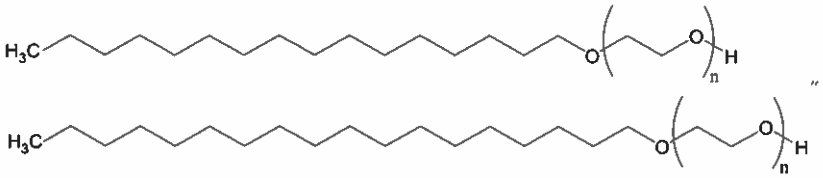
(continued)

Table 3. (continued)

Methoxy PEG-n / PEG-n Methyl Ethers (a methyl group attached to a variable length PEG chain)

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

Ceteareths (mixture of 16 and 18 carbon chains with a variable PEG)
General Structure:



n = the average number of ethylene glycol units (eg, Ceteareth 3 is when n = 3)
As these are mixtures of two molecules at unknown ratios, molecular weights, and physical properties are not calculable.

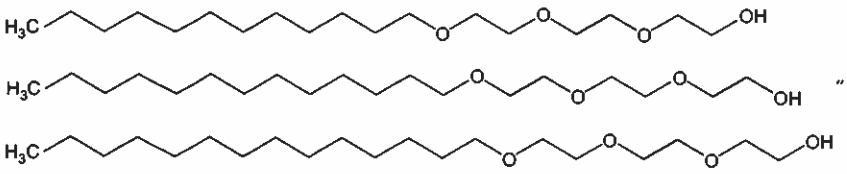
INCI Name	
Ceteareth 2[a] (CAS No. **68439-49-6**)	Molecular weight < 1000
Ceteareth 3[a] (CAS No. **68439-49-6**)	Molecular weight < 1000
Ceteareth 4[a] (CAS No. **68439-49-6**)	Molecular weight < 1000
Ceteareth 5[a] (CAS No. **68439-49-6**)	Molecular weight < 1000
Ceteareth 6[a] (CAS No. **68439-49-6**)	Molecular weight < 1000
Ceteareth 7[a] (CAS No. **68439-49-6**)	Molecular weight < 1000
Ceteareth 8[a] (CAS No. **68439-49-6**)	Molecular weight < 1000
Ceteareth 9[a] (CAS No. **68439-49-6**)	Molecular weight < 1000
Ceteareth 10[a] (CAS No. **68439-49-6**)	Molecular weight < 1000
Ceteareth 11[a] (CAS No. **68439-49-6**)	Molecular weight < 1000
Ceteareth 12[a] (CAS No. **68439-49-6**)	Molecular weight < 1000
Ceteareth 13[a] (CAS No. **68439-49-6**)	Molecular weight < 1000
Ceteareth 14[a] (CAS No. **68439-49-6**)	Molecular weight < 1000
Ceteareth 15[a] (CAS No. **68439-49-6**)	Molecular weight < 1000
Ceteareth 16[a] (CAS No. **68439-49-6**)	Molecular weight < 1000
Ceteareth 17[a] (CAS No. **68439-49-6**)	Molecular weight ~ 1000
Ceteareth 18[a] (CAS No. **68439-49-6**)	Molecular weight > 1000
Ceteareth 20[a] (CAS No. **68439-49-6**)	Molecular weight > 1000
Ceteareth 22[a] (CAS No. **68439-49-6**)	Molecular weight > 1000
Ceteareth 23[a] (CAS No. **68439-49-6**)	Molecular weight > 1000
Ceteareth 24[a] (CAS No. **68439-49-6**)	Molecular weight > 1000
Ceteareth 25[a] (CAS No. **68439-49-6**)	Molecular weight > 1000
Ceteareth 27[a] (CAS No. **68439-49-6**)	Molecular weight > 1000
Ceteareth 28[a] (CAS No. **68439-49-6**)	Molecular weight > 1000
Ceteareth 29[a] (CAS No. **68439-49-6**)	Molecular weight > 1000
Ceteareth 30[a] (CAS No. **68439-49-6**)	Molecular weight > 1000
Ceteareth 33[a] (CAS No. **68439-49-6**)	Molecular weight > 1000
Ceteareth 34[a] (CAS No. **68439-49-6**)	Molecular weight > 1000
Ceteareth 40[a] (CAS No. **68439-49-6**)	Molecular weight > 1000
Ceteareth 50[a] (CAS No. **68439-49-6**)	Molecular weight > 1000
Ceteareth 55[a] (CAS No. **68439-49-6**)	Molecular weight > 1000
Ceteareth 60[a] (CAS No. **68439-49-6**)	Molecular weight > 1000
Ceteareth 80[a] (CAS No. **68439-49-6**)	Molecular weight > 1000
Ceteareth 100[a] (CAS No. **68439-49-6**)	Molecular weight > 1000

(continued)

Table 3. (continued)

Methoxy PEG-n / PEG-n Methyl Ethers (a methyl group attached to a variable length PEG chain)

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.

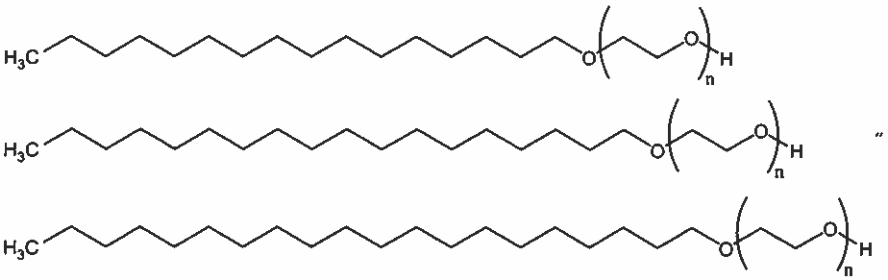
INCI Name	
C9-11 Pareth 3 (CAS No. **68439-46-3**)	Molecular weight < 1000
C9-11 Pareth 4 (CAS No. **68439-46-3**)	Molecular weight < 1000
C9-11-Pareth 6 (CAS No. **68439-46-3**)	Molecular weight < 1000
C9-11 Pareth 8 (CAS No. **68439-46-3**)	Molecular weight < 1000
C9-15 Pareth 8 (CAS No. **157627-88-8**)	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
C12-15 Pareth 11 (CAS No. **68131-39-5**)	Molecular weight < 1000
C12-15 Pareth 12 (CAS No. **68131-39-5**)	Molecular weight < 1000

(continued)

Table 3. (continued)

Methoxy PEG-n / PEG-n Methyl Ethers (a methyl group attached to a variable length PEG chain)	
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 (CA5 No. **68551-12-2**)	Molecular weight < 1000
C13-15 Pareth 21 (CAS No. **64425-86-1**)	Molecular weight > 1000
C14-15 Pareth 4 (CA5 No. **68951-67-7**)	Molecular weight < 1000
C14-15 Pareth 7 (CA5 No. **68951-67-7**)	Molecular weight < 1000
C14-15 Pareth 8 (CA5 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 (CA5 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 (CA5 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

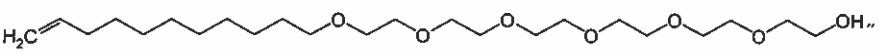
Hydrogenated Talloweths (mixture of 14, 16, and 18 carbon chains with a variable PEG)
General Structure:



n = the average number of ethylene glycol units (eg, 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.

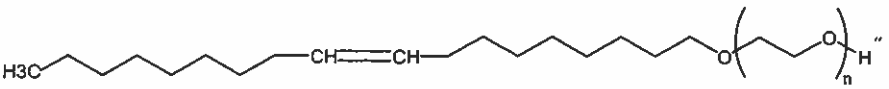
INCI Name	
Hydrogenated Talloweth 12	Molecular weight < 1000
Hydrogenated Talloweth 25	Molecular weight > 1000

Partially Unsaturated Alkyl PEG Ethers
Undecyleneth-6 (Ω-1 unsaturated 11 carbon chains with a 6-unit PEG)
Structure:



INCI Name	Molecular Weight	MP/BP	$logK_{o/w}$
Undecyleneth 6	434.61	189/484 °C	2.50

Oleths (Ω-9 unsaturated 18 carbon chains with a variable PEG)
General Structure:



n = the average number of ethylene glycol units (eg, Oleth 2 is when n = 2)

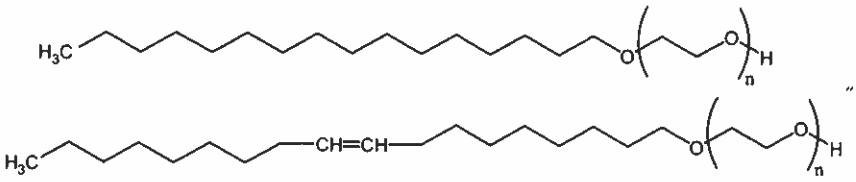
(continued)

Table 3. (continued)

Methoxy PEG-n / PEG-n Methyl Ethers (a methyl group attached to a variable length PEG chain)

INCI Name	Molecular Weight	MP/BP	$logK_{o/w}$
Oleth 2[a] (CAS No. **9004-98-2**; 5274-65-7; 95287-03-9)	356.58	151/429 °C	6.95
Oleth 3[a] (CAS No. **9004-98-2**; 5274-66-8; 96459-08-4)	400.64	175/464 °C	6.68
Oleth 4[a] (CAS No. **9004-98-2**; 5353-26-4; 103622-85-1)	444.69	193/499 °C	6.40
Oleth 5[a] (CAS No. **9004-98-2**; 5353-27-5)	488.74	219/535 °C	6.13
Oleth 6[a] (CAS No. **9004-98-2**)	532.79	244/570 °C	5.86
Oleth 7[a] (CAS No. **9004-98-2**)	576.85	262/605 °C	5.58
Oleth 8[a] (CAS No. **9004-98-2**; 26996-03-2; 27040-03-5)	620.90	278/640 °C	5.31
Oleth 9[a] (CAS No. **9004-98-2**)	664.95	295/676 °C	5.03
Oleth 10[a] (CAS No. **9004-98-2**)	709.00	311/711 °C	4.76
Oleth 11[a] (CAS No. **9004-98-2**)	753.06	328/746 °C	4.48
Oleth 12[a] (CAS No. **9004-98-2**)	797.11	344/781 °C	4.21
Oleth 15[a] (CAS No. **9004-98-2**)	929.27	350/887 °C	3.39
Oleth 16[a] (CAS No. **9004-98-2**; **25190-05**-0)	973.32	–/922 °C	3.11
Oleth 20[a] (CAS No. **9004-98-2**)	1149.53	–/1063 °C	2.01
Oleth 23[a] (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[a] (CAS No. **9004-98-2**)	1369.79	–/1240 °C	0.64
Oleth 30[a] (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[a] (CAS No. **9004-98-2**)	2030.58	–/1769 °C	-3.47
Oleth 44[a] (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[a] (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	–/–	–

Ceteoleths (mixture of 16 carbon chains and Ω-9 unsaturated 18 carbon chains with a variable PEG)
General Structure:



n = the average number of ethylene glycol units (eg, Ceteoleth 6 is when n = 6)
As these are mixtures of 2 molecules at unknown ratios, molecular weights, and physical properties are not calculable.

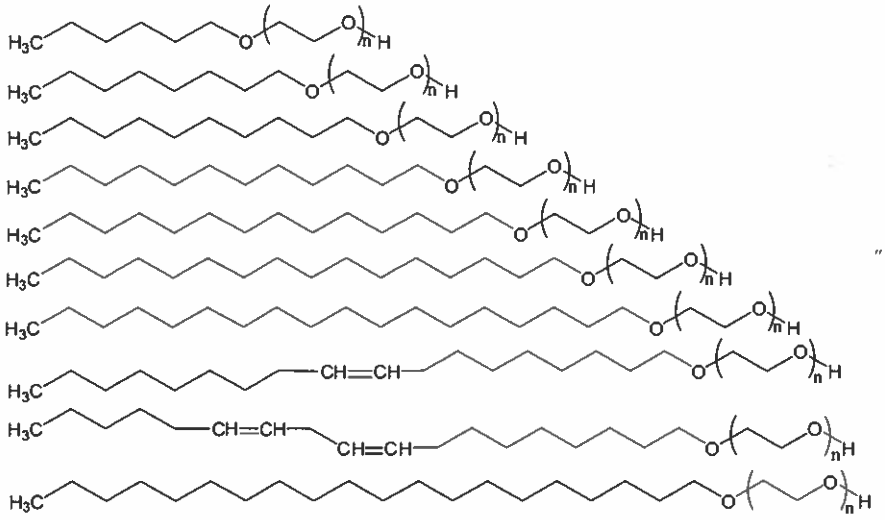
INCI Name	
Ceteth 2 (CAS No. **8065-81-4**)	Molecular weight < 1000
Ceteth 4 (CAS No. **8065-81-4**)	Molecular weight < 1000
Ceteth 5 (CAS No. **8065-81-4**)	Molecular weight < 1000
Ceteth 6 (CA5 No. **8065-81-4**)	Molecular weight < 1000
Ceteth 10 (CAS No. **8065-81-4**)	Molecular weight < 1000
Ceteth 11 (CAS No. **8065-81-4**)	Molecular weight < 1000
Ceteth 15 (CAS No. **8065-81-4**)	Molecular weight < 1000
Ceteth 18 (CAS No. **8065-81-4**)	Molecular weight > 1000
Ceteth 20 (CAS No. **8065-81-4**)	Molecular weight > 1000
Ceteth 22 (CAS No. **8065-81-4**)	Molecular weight > 1000
Ceteth 24 (CAS No. **8065-81-4**)	Molecular weight > 1000
Ceteth 25 (CAS No. **8065-81-4**)	Molecular weight > 1000
Ceteth 30 (CAS No. **8065-81-4**)	Molecular weight > 1000

(continued)

Table 3. (continued)

Methoxy PEG-n / PEG-n Methyl Ethers (a methyl group attached to a variable length PEG chain)

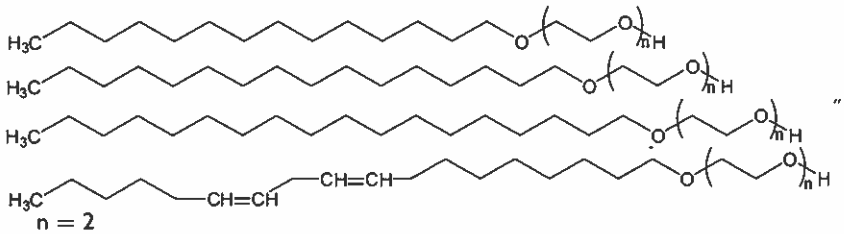
Caceths (mixture of 6, 8, 10, 12, 14, 18, Ω 9 unsaturated 18, Ω-6 unsaturated 18, and 20 carbon chains with a variable PEG)
General Structure:



n = the average number of ethylene glycol units (eg, 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

Palmeth 2 (mixture of 14, 16, 18, Ω-6 unsaturated 18, and Ω-6 unsaturated 18 carbon chains with a 2-unit PEG)
Structure:



n = 2
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

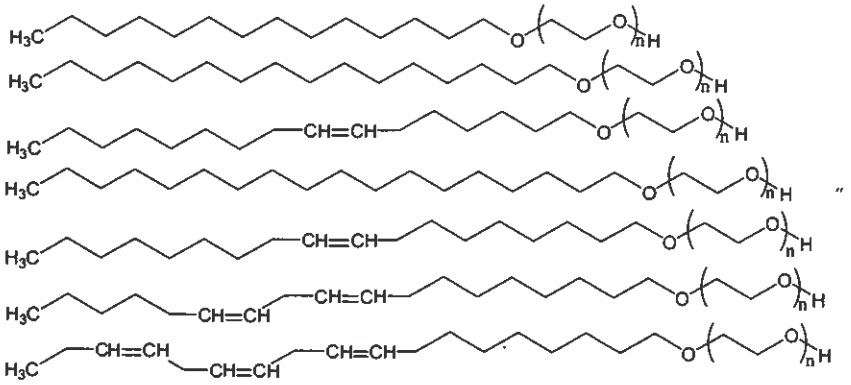
Tallaweths (mixture of 14, 16, Ω-9 unsaturated 16, 18, Ω-9 unsaturated 18, Ω-6 unsaturated 18, and Ω-3 unsaturated 18 carbon chains with a variable PEG)

(continued)

Table 3. (continued)

Methoxy PEG-n / PEG-n Methyl Ethers (a methyl group attached to a variable length PEG chain)

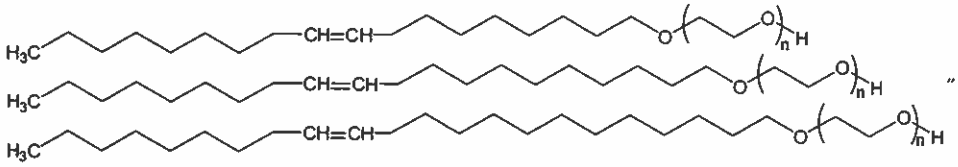
General Structure:



n = the average number of ethylene glycol units (eg, 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

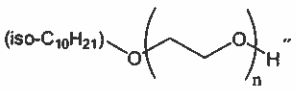
PEG Jojoba Alcohols (mixture of Ω-9 unsaturated 18, Ω-9 unsaturated 20, and Ω-9 unsaturated 22 carbon chains with a variable PEG)
General Structure:



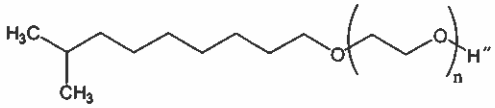
n = the average number of ethylene glycol units (eg, PEG-15 Jojoba Alcohol is when n = 15)
As these are mixtures of more than one molecule at unknown ratios, molecular weights and physical properties are not calculable.

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 (eg, 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.

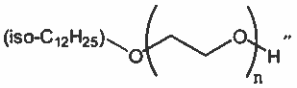
(continued)

Table 3. (continued)

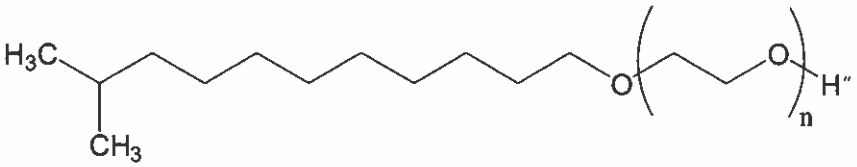
Methoxy PEG-n / PEG-n Methyl Ethers (a methyl group attached to a variable length PEG chain)

INCI Name	Molecular Weight
Isodeceth 4	334.49
Isodeceth 5	378.54
Isodeceth 6	422.60

Isolaureths (mixture of various branched 12 carbon chains with a variable PEG)
General Structure:



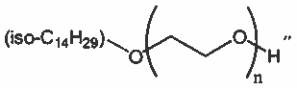
n = the average number of ethylene glycol units (eg, Isolaureth 10 is when n = 10); "iso" = a mixture of branched isomers, one example of which would be:



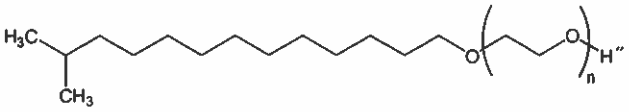
As these are mixtures of more than one isomer at unknown ratios, physical properties are not calculable.

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:



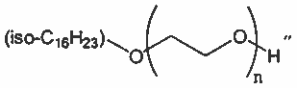
n = the average number of ethylene glycol units (eg, Isomyreth 9 is when n = 9); "iso" = a mixture of branched isomers, one example of which would be:



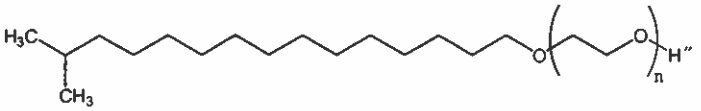
As these are mixtures of more than one isomer at unknown ratios, physical properties are not calculable.

INCI Name	Molecular Weight
Isomyreth 3	346.55
Isomyreth 9	610.86

Isoceteths (mixture of various branched 16 carbon chains with a variable PEG)
General Structure:



n = the average number of ethylene glycol units (eg, 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.

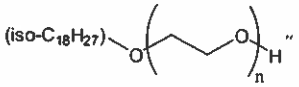
(continued)

Table 3. (continued)

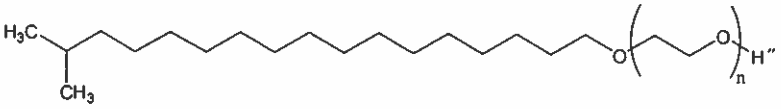
Methoxy PEG-n / PEG-n Methyl Ethers (a methyl group attached to a variable length PEG chain)

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

Isosteareths (mixture of various branched 18 carbon chains with a variable PEG)
General Structure:



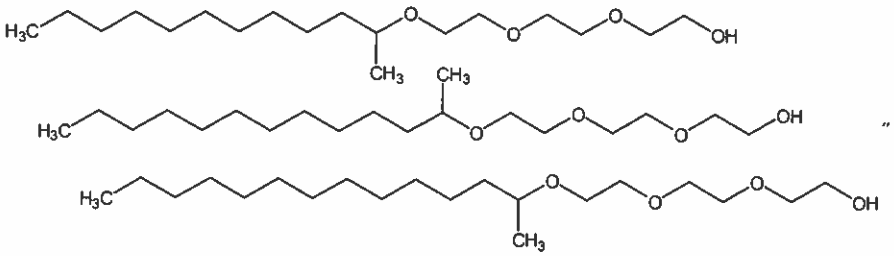
n = the average number of ethylene glycol units (eg, Isosteareth 6 is when n = 6); "iso" = a mixture of branched isomers, one example of which would be:



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

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

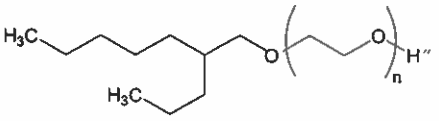
(continued)

Table 3. (continued)

Methoxy PEG-n / PEG-n Methyl Ethers (a methyl group attached to a variable length PEG chain)

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

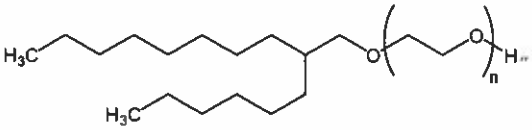
PEG Propylheptyl Ethers (3 carbon chains β-substituted 7 carbon chains with a variable PEG)
General Structure:



n = the average number of ethylene glycol units (eg, 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

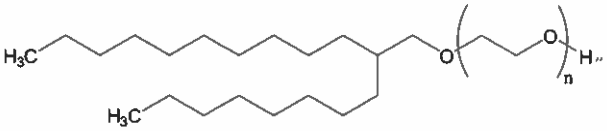
Hexyldeceths (6 carbon chains beta-substituted (β-substituted) 10 carbon chains with a variable PEG)
General Structure:



n = the average number of ethylene glycol units (eg, 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

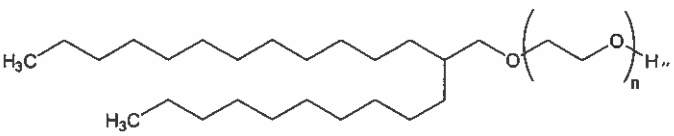
Octyldodeceths (8 carbon chains β-substituted 12 carbon chains with a variable PEG)
General Structure:



n = the average number of ethylene glycol units (eg, 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

Decyltetradeceths (10 carbon chain β-substituted 14 carbon chains with a variable PEG)
General Structure:



n = the average number of ethylene glycol units (eg, Decyltetradeceth 15 is when n = 15)

(continued)

Table 3. (continued)

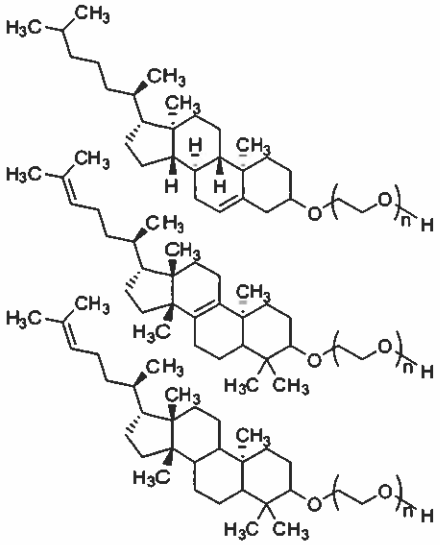
Methoxy PEG-n / PEG-n Methyl Ethers (a methyl group attached to a variable length PEG chain)

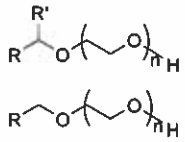
INCI Name	Molecular Weight	M.P. / B.P.	$logK_{o/w}$
Decyltetradeceth 5	574.92	256/594	9.22
Decyltetradeceth 10	795.18	339/770	7.85
Decyltetradeceth 15	1015.44	–/946	6.47
Decyltetradeceth 20	1235.70	–/1123	5.10
Decyltetradeceth 25	1455.97	–/1299	3.73
Decyltetradeceth 30	1676.23	–/1475	2.36

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

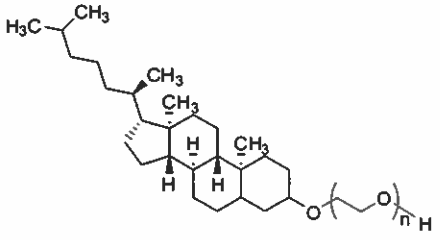
n = the average number of ethylene glycol units (eg, Laneth 25 is when n = 25)

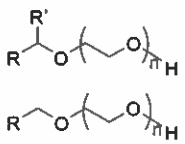
As these are mixtures of more than one molecule at unknown ratios, molecular weights and physical properties are not calculable.

INCI Name	
Laneth 5[a] (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[a] (CAS No. **61791-20-6**)	Molecular weight > 1000
Laneth 20 (CAS No. **61791-20-6**)	Molecular weight > 1000
Laneth 25[a] (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

Hydrogenated Laneths (mixture of various length saturated alkyl chains and dihydrocholesterol with a variable PEG)

General Structure:





R & R' = saturated alkyl chains of various lengths

(continued)

Table 3. (continued)

Methoxy PEG-n / PEG-n Methyl Ethers (a methyl group attached to a variable length PEG chain)

n = the average number of ethylene glycol units (eg, 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

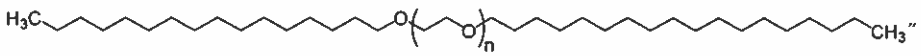
Dialkyl PEG Ethers

Hydrogenated Dimer Dilinaleths and PEG-4 Distearyl Ether (variable PEG capped at each end with a saturated 18 carbon chains)
General Structure:

n = the average number of ethylene glycol units (eg, Hydrogenated Dimer Dilinoeth-60 is when n = 60; PEG-4 Distearyl Ether is when n = 4)

INCI Name	Molecular Weight	MP/BP	$logK_{o/w}$
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 60	3166.13	–/–	–
Hydrogenated Dimer Dilinoleth 80	4047.18	–/–	–

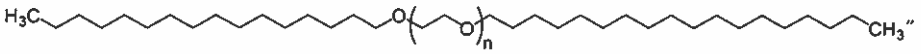
PEG Cetyl Stearyl Diether and Steareth 60 Cetyl Ether (variable PEG capped at one end with a saturated 18 carbon chains and at the other end with a saturated 16 carbon chains)
Structure:



n = the average number of ethylene glycol units (eg, 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	MP/BP	$logK_{o/w}$

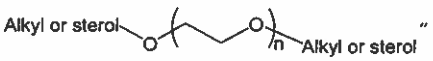
Structure:



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	–/–	–

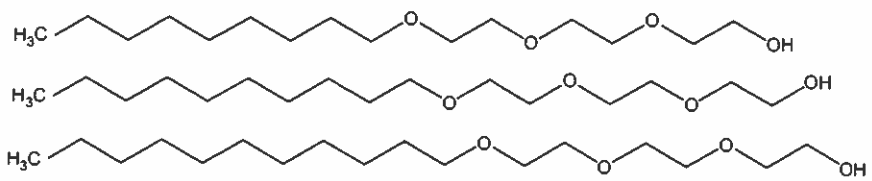
PEG-4 Ditallow Ether (a 4-unit PEG independently capped at each end with one of a 14, 18, 18, Ω-9 unsaturated 18, Ω-6 unsaturated 18, or Ω-3 unsaturated 18 carbon chains) and ***PEG-16 Cetyl/Oleyl/Stearyl/Lanolin Alcohol Ether*** (a 16-unit PEG independently capped at each end with a variable length saturated or partially unsaturated alkyl chain, cholesterol, lanosterol or dihydrolanosterol)
General Structure:



n = the average number of ethylene glycol units (eg, 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.

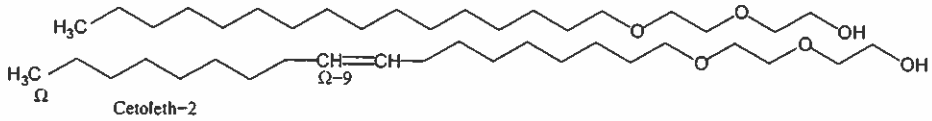
INCI Name	
PEG-4 Ditallow Ether	Molecular weight < 1000
PEG-16 Cetyl/Oleyl/Stearyl/Lanolin Alcohol Ether	–

[a] Indicates those ingredients previously assessed by the CIR Expert Panel.



C9-11Pareth-3

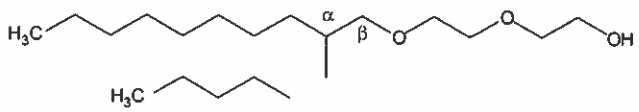
Partially unsaturated alkyl PEG ethers. Also included in this review are partially unsaturated straight chain ingredients. These include undecyleneth 6 (omega 1 [Ω-1] unsaturated 11 carbon chains with a 6-unit PEG); oleths (Ω-9 unsaturated 18 carbon chains with a variable PEG); cetoleths (mixture of 16 carbon chains 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

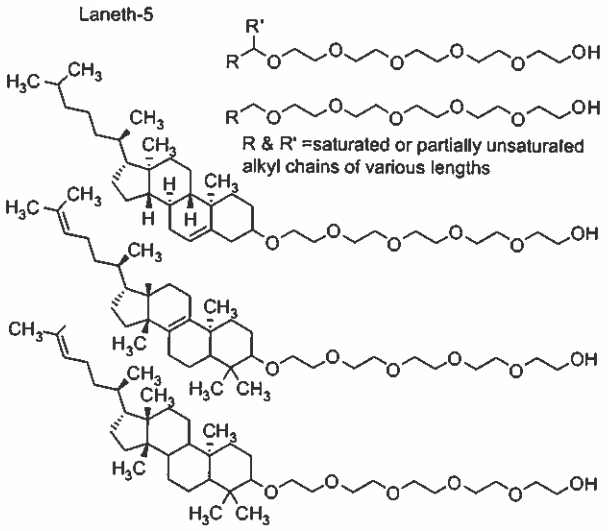
Although the above Ω-9 unsaturated chain is drawn with stereochemical ambiguity at the double bond, the *cis* isomer is actually more likely if the parent alcohol was obtained from natural sources.

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); isostearеths (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 chains beta-substituted [β-substituted] 7 carbon chains with a variable PEG); hexyldeceths (6 carbon chains β-substituted 10 carbon chains with a variable PEG); octyldodeceths (8 carbon chains β-substituted 12 carbon chains with a variable PEG); and decyltetradeceths (10 carbon chains β-substituted 14 carbon chains with a variable PEG). For example, hexyldeceth 2 is as shown:



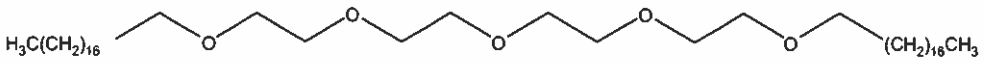
Hexyldeceth-2

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 (2 INCI naming conventions that both mean a variable PEG capped at each end with a saturated 18 carbon chains); PEG cetyl stearyl diether and steareth 60 cetyl ether (2 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 chains); 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.

Ultraviolet Absorption

While no ultraviolet (UV) absorption data were available, the ingredients included in this review would not be expected to have any meaningful UV absorption. None of these ingredients contain metals or halogens. 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 (eg, stearyl alcohol is used to synthesize steareths) with an alkali earth metal (eg, potassium hydroxide) or alkoxide (eg, sodium methoxide). The reaction continues to propagate (ie, 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 (eg, hydrochloric acid). Dioxane (1,4-diethylene dioxide; 1,4-dioxane) is commonly formed as a by-product. Finally, a finishing step is commonly employed via the addition of 1 or more oxidizing agents (eg, hydrogen peroxide) or antioxidants/stabilizers (eg, butylated hydroxytoluene [BHT] or α-tocopherol [vitamin E]).

Some of the ingredients in this report are derived from tallow. The CIR accepts the Food and Drug Administration (FDA) determination (21 CFR 700.27(a)), that prohibited cattle materials do not include tallow derivatives.

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.[20] PEG-3 methyl ether has a purity of approximately 90% to 96% triethylene glycol monomethyl ether by volume; major impurities and/or unreacted starting material include tetraethylene glycol monomethyl ether, diethylene glycol, methoxydiglycol, and triethylene glycol.[21] Production samples of PEG-7 methyl ether typically contain a combined concentration of 0.02% to 0.05% of ethylene glycol and 0.1% of water.[22] In past assessments, CIR has acknowledged the possible presence of 2 contaminants of concern: 1,4-dioxane and unreacted ethylene oxide (a gas), which are possible oxidation products in alkyl PEG ethers.[2-4]

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 (ie, 3000 ppm or 0.3%).[23,24] However, these are not typical storage conditions.

In 4 newly opened samples of laureth 5, the formaldehyde content ranged from 0.4 to 6 μg/g, while the peroxide content ranged from 0 to 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 years, but surfactants are normally stored at room temperature; they generally become semisolid 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 months 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 months and was handled, that is stirred for 1 hour 4×/d, 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 as surfactants in cosmetics.[25] 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, aqueous. and nonaqueous, 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.

In 2010, according to data supplied to the FDA as part of the Voluntary Cosmetic Registration Program (VCRP), laureth 4 was used in 441 formulations and laureth 23 was used in 404 formulations.[26] 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.[27,28] 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 eyeliners, and ceteareth 10, which is used at 11% in lipsticks.

The frequencies and concentrations of use are summarized in Tables 4A and B. 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[26] or the Council survey.[27] 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 the 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 $\leq$10 μm are respirable. Particles with a d_a from 0.1 to 10 μm settle in the upper respiratory tract and particles with a d_a <0.1 μm settle in the lower respiratory tract.[29,30]

Particle diameters of 60 to 80 μm and $\geq$80 μm have been reported for anhydrous hair sprays and pump hair sprays, respectively.[31] In practice, aerosols should have at least 99% of their particle diameters in the 10 to 110 μm range and the mean particle diameter in a typical aerosol spray has been reported as ~38 μm.[32] 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 the use of PEG-containing medications is now well understood in the burn treatment community, and the caveat regarding the use of cosmetic products containing PEGs on damaged skin was removed for PEGs and PEG-containing ingredients.[15]

All of the ingredients included in this review are listed in the European Union (EU) inventory of cosmetic ingredients.[33] The SCCP opinion paper exists for laureth 9 and was initiated due to concern that laureth 9 has an anesthetic effect.[19] While not restricted according to the EU, the SCCP concluded that laureth 9 does not pose a risk when used at $\leq$3% in leave on products and $\leq$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 that is, by the average alkyl chain length (C) and by the average alcohol ethoxylate number (AE), for example $C_{12\text{-}15}AE_7$.

Noncosmetic

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] 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.[36]

Toxicokinetics

Oral Administration

Laureths

Nonhuman. Female Colworth Wistar rats (number not given) were used to determine the pharmacokinetics of compounds analogous to laureth 9.[19] [^{14}C]-labeled $C_{12}AE_3$, $C_{12}AE_6$, and

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[26]	1981[1]	2010[28]	1981[1]	2010[26]	1981[1]	2010[28]	1996[3]	2010[26]	1996[3]	2010[28]	1996[3]	2010[26]	1996[3]	2010[28]
	Laureth 4				Laureth 23				Ceteth 1				Ceteth 2			
Totals[a]	202	441	≤ 25	0.0002-21	218	404	≤ 5	0.0002-8	NR	NR	NR	0.2-3	33	214	5c	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—NonColoring	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
	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	0.15c	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—Noncoloring	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

(continued)

Table 4A. (continued)

	# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)	
	1981[1]	2010[26]	1981[1]	2010[28]	1981[1]	2010[26]	1981[1]	2010[28]	1996[3]	2010[26]	1996[3]	2010[28]	1996[3]	2010[26]	1996[3]	2010[28]
	Ceteth 12				Ceteth 14				Ceteth 15				Ceteth 16			
Totals	3	NR	NR	0.02	2	NR	NR	NR	NR	7	NR	2	18	9	5c	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—Noncoloring	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
	Ceteth 20				Ceteth 24				Ceteth 25				Ceteth 29b			
Totals	114	220	25c	0.04-4	67	169	NR	0.0009-2	1	1	NR	0.6-3	NR	NR	<1c	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—Noncoloring	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

(continued)

Table 4A. (continued)

	# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)	
	1981[1]	2010[26]	1981[1]	2010[28]	1981[1]	2010[26]	1981[1]	2010[28]	1996[3]	2010[26]	1996[3]	2010[28]	1996[3]	2010[26]	1996[3]	2010[28]
	Ceteth 30				Steareth 2				Steareth 4				Steareth 6			
Totals	2	1	NR	NR	107d	593	≤ 10d	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—Noncoloring	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
	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—Noncoloring	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

(continued)

Table 4A. (continued)

	# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)	
	1981[1]	2010[26]	1981[1]	2010[28]	1981[1]	2010[26]	1981[1]	2010[28]	1996[3]	2010[26]	1996[3]	2010[28]	1996[3]	2010[26]	1996[3]	2010[28]
	Ceteareth 2				Ceteareth 3				Ceteareth 4				Ceteareth 5			
Totals	NR	NR	NR	2	1	10	5c	2	NR	1	NR	NR	20	24	10c	NR
Duration of Use																
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—Noncoloring	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
	Ceteareth 6				Ceteareth 7				Ceteareth 10				Ceteareth 12			
Totals	9	36	25c	0.008-5	NR	NR	NR	0.2	29	2	5c	0.003-11	57	127	50c	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—Noncoloring	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

(continued)

Table 4A. (continued)

	# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)	
	1981[1]	2010[26]	1981[1]	2010[28]	1981[1]	2010[26]	1981[1]	2010[28]	1996[3]	2010[26]	1996[3]	2010[28]	1996[3]	2010[26]	1996[3]	2010[28]
	Ceteareth 15				Ceteareth 16				Ceteareth 17				Ceteareth 20			
Totals	11	6	10	0.2-10	NR	1	NR	NR	NR	NR	5c	NR	452	955	10c	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—Noncoloring	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
	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—Noncoloring	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

(continued)

Table 4A. (continued)

	# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)	
	1981[1]	2010[26]	1981[1]	2010[28]	1981[1]	2010[26]	1981[1]	2010[28]	1996[3]	2010[26]	1996[3]	2010[28]	1996[3]	2010[26]	1996[3]	2010[28]
	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—Noncoloring	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
	Oleth 2				Oleth 3				Oleth 4				Oleth 5			
Totals	14	177	≤ 25c	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—Noncoloring	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

(continued)

Table 4A. (continued)

	# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)	
	1981[1]	2010[26]	1981[1]	2010[28]	1981[1]	2010[26]	1981[1]	2010[28]	1996[3]	2010[26]	1996[3]	2010[28]	1996[3]	2010[26]	1996[3]	2010[28]
	Oleth 8				Oleth 9				Oleth 10				Oleth 12			
Totals	8	NR	NR	1-2	2	NR	NR	NR	97	370	25c	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—Noncoloring	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
	Oleth 15				Oleth 16				Oleth 20				Oleth 25			
Totals	3	NR	NR	0.4-0.7	13	9	5c	0.03-0.8	321	246	25c	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—Noncoloring	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

(continued)

Table 4A. (continued)

	# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)		# of Uses		Conc. of Use (%)	
	1981[1]	2010[26]	1981[1]	2010[28]	1981[1]	2010[26]	1981[1]	2010[28]	1996[3]	2010[26]	1996[3]	2010[28]	1996[3]	2010[26]	1996[3]	2010[28]
	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—Noncoloring	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

(continued)

Table 4A. (continued)

	# 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—Noncoloring	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

Abbreviation: NR, not reported to be used.

a 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.

b 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.

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.

Table 4B. Frequency and Concentration of Use According to Duration and type of Exposure—Newly Reviewed Ingredients

	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]
	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—Noncoloring	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—Noncoloring	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

(continued)

Table 4B. (continued)

	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]
	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—Noncoloring	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—Noncoloring	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

(continued)

Table 4B. (continued)

	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]
	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—Noncoloring	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[b]		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—Noncoloring	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

(continued)

Table 4B. (continued)

	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]
	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—Noncoloring	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—Noncoloring	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

(continued)

Table 4B. (continued)

	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]
	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—Noncoloring	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—Noncoloring	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

(continued)

Table 4B. (continued)

	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]
	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—Noncoloring	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	0.003-0.3	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	0.003-0.3[29]	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—Noncoloring	78	0.003-0.3	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

(continued)

Table 4B. (continued)

	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]
	Oleth 106		Ceteleth 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—Noncoloring	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—Noncoloring	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

(continued)

Table 4B. (continued)

	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]
	Isoceteth 25		Isostereth 2		Isostereth 5		Isostereth 10		Isostereth 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—Noncoloring	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—Noncoloring	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

(continued)

Table 4B. (continued)

	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]	# of Uses[26]	Conc of Use (%)[27]
	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—Noncoloring	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				

Abbreviations: NR, not reported; FDA, US Food and Drug Administration.

[a] 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.

[b] 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	C12-14 Sec-Pareth 30	Decyltetradeceth 10	Noneth 8
Beheneth 2	C12-14 Sec-Pareth 40	Decyltetradeceth 15	Octyldodeceth 2
Beheneth 5	C12-14 Sec-Pareth 50	Decyltetradeceth 20	Octyldodeceth 5
Beheneth 15	Capryleth 4	Decyltetradeceth 25	Octyldodeceth 10
C9-11 Pareth 3	Capryleth 5	Decyltetradeceth 30	Octyldodeceth 30
C9-11 Pareth 4	Ceteareth 4	Hexyldeceth 2	Oleth 6
C9-15 Pareth 8	Ceteareth 8	Hexyldeceth 20	Oleth 7
C10-16 Pareth 1	Ceteareth 9	Hydrogenated Dimer Dilinoleth 20	Oleth 9
C10-16 Pareth 2	Ceteareth 11	Hydrogenated Dimer Dilinoleth 30	Oleth 11
C11-13 Pareth 6	Ceteareth 13	Hydrogenated Dimer Dilinoleth 40	Oleth 23
C11-13 Pareth 9	Ceteareth 14	Hydrogenated Dimer Dilinoleth 60	Oleth 24
C11-13 Pareth 10	Ceteareth 16	Hydrogenated Dimer Dilinoleth 80	Oleth 35
C11-15 Pareth 12	Ceteareth 18	Hydrogenated Laneth 5	Oleth 40
C11-15 Pareth 15	Ceteareth 23	Hydrogenated Laneth 20	Oleth 44
C11-15 Pareth 20	Ceteareth 24	Hydrogenated Laneth 25	Oleth 45
C11-15 Pareth 30	Ceteareth 27	Hydrogenated Talloweth 12	Oleth 100
C11-21-Pareth 3	Ceteareth 28	Hydrogenated Talloweth 25	Palmeth 2
C11-21-Pareth 10	Ceteareth 29	Isoceteth 5	PEG-16 Cetyl/Oleyl/Stearyl/ Lanolin Alcohol Ether
C12-13 Pareth 1	Ceteareth 34	Isoceteth 7	PEG-Cetyl Stearyl Diether
C12-13 Pareth 2	Ceteareth 40	Isoceteth 12	PEG-4 Ditallow Ether
C12-13 Pareth 4	Ceteareth 55	Isoceteth 15	PEG-15 Jojoba Alcohol
C12-13 Pareth 5	Ceteareth 60	Isoceteth 30	PEG-26 Jojoba Alcohol
C12-13 Pareth 6	Ceteareth 80	Isodeceth 4	PEG-40 Jojoba Alcohol
C12-13 Pareth 9	Ceteareth 100	Isodeceth 5	PEG-3 Methyl Ether
C12-13 Pareth 10	Ceteth 4	Isolaureth 3	PEG-4 Methyl Ether
C12-13 Pareth 15	Ceteth 5	Isolaureth 10	PEG-6 Methyl Ether
C12-14 Pareth 5	Ceteth 7	Isomyreth 3	PEG-7 Methyl Ether
C12-14 Pareth 7	Ceteth 13	Isomyreth 9	Steareth 1
C12-14 Pareth 9	Ceteth 14	Isostearet 3	Steareth 3
C12-15 Pareth 2	Ceteth 17	Isostearet 8	Steareth 5
C12-15 Pareth 4	Ceteth 18	Isostearet 12	Steareth 7
C12-15 Pareth 5	Ceteth 23	Isostearet 15	Steareth 8
C12-15 Pareth 10	Ceteth 30	Isostearet 16	Steareth 11
C12-15 Pareth 11	Ceteth 40	Isostearet 22	Steareth 13
C12-16 Pareth 5	Ceteth 45	Isostearet 25	Steareth 14
C13-15 Pareth 21	Ceteth 150	Isostearet 50	Steareth 15
C14-15 Pareth 4	Cetoleth 2	Laneth 10	Steareth 27
C14-15 Pareth 7	Cetoleth 4	Laneth 50	Steareth 40
C14-15 Pareth 8	Cetoleth 5	Laneth 60	Steareth 80
C14-15 Pareth 11	Cetoleth 6	Laneth 75	Steareth 60 Cetyl Ether
C14-15 Pareth 12	Cetoleth 10	Laureth 13	Talloweth 7
C14-15 Pareth 13	Cetoleth 11	Laureth 15	Talloweth 18
C20-22 Pareth 30	Cetoleth 15	Laureth 38	Trideceth 2
C20-40 Pareth 24	Cetoleth 18	Laureth 40	Trideceth 4
C22-24 Pareth 33	Cetoleth 20	Laureth 50	Trideceth 11
C30-50 Pareth 3	Cetoleth 22	Methoxy PEG-7	Trideceth 15
C30-50 Pareth 10	Cetoleth 24	Methoxy PEG-10	Trideceth 18
C30-50 Pareth 40	Cetoleth 30	Methoxy PEG-25	Trideceth 20
C40-60 Pareth 3	Coceth 3	Methoxy PEG-40	Trideceth 21
C40-60 Pareth 10	Coceth 5	Methoxy PEG-100	Trideceth 50
C11-15 Sec-Pareth 12	Coceth 6	Myreth 2	Undeceth 7
C12-14 Sec-Pareth 3	Coceth 20	Myreth 5	Undeceth 8
C12-14 Sec-Pareth 8	Coceth 25		Undeceth 9
C12-14 Sec-Pareth 9	Deceth 4		Undeceth 40
C12-14 Sec-Pareth 12	Deceth 6		Undecyleneth 6
C12-14 Sec-Pareth 15	Deceth 10		
C12-14 Sec-Pareth 20	Decyltetradeceth 5		

$C_{12}AE_{10}$ were each administered orally by gavage, intraperitoneal (ip) injection, and subcutaneous (sc) injection, and the rats were then placed in metabolism cages for 4 days for collection of feces, urine, and expired air (radioactive label position not specified). Radioactivity was primarily recovered in the urine. With oral administration of $C_{12}AE_3$, $C_{12}AE_6$, and $C_{12}AE_{10}$, 78.3%, 76.3%, and 49.8%, respectively, was recovered in the urine; 6.9%, 11.8%, and 17.4%, respectively, was recovered in the feces; 6.5%, 8.1%, and 12.4%, respectively, was recovered in expired air; and 2.5%, 1.8%, and 4.5%, respectively, was recovered in the carcass. Total recovery was 94.3%, 98.2%, and 84.2%, respectively. With ip administration of $C_{12}AE_3$, $C_{12}AE_6$, and $C_{12}AE_{10}$, 84.5%, 85.1%, and 61.5%, respectively, was recovered in the urine; 6.2%, 9.1%, and 18.2%, respectively, was recovered in the feces; 6.7%, 4.1%, and 14.2%, respectively, was recovered in expired air; and 1.8%, 0.8%, and 3.2%, respectively, was recovered in the carcass. Total recovery was 95.3%, 99.4%, and 97.1%, respectively. With sc administration of $C_{12}AE_3$, $C_{12}AE_6$, and $C_{12}AE_{10}$, 87.5%, 83.5%, and 61.2%, respectively, was recovered in the urine; 4.4%, 10.2%, and 19.9%, respectively, was recovered in the feces, 4.3%, 4.6%, and 11.7%, respectively, was recovered in expired air, and 3.7%, 2.9%, and 4.9%, respectively, was recovered in the carcass. Total recovery was 99.8%, 101.2%, and 97.7%, respectively. 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, 2 distinct polar metabolites were detected in the urine (but not characterized), with no parent compound.

In another arm of this study, [^{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 participants.[19] The participants 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 hours 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% to 89% of the radioactivity was recovered within 144 hours 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.[37] 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.[19] [^{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-minute wash with 1% w/v $C_{12}AE_3$ and 1% w/v $C_{12}AE_6$, 4 to 5 $\mu g/cm^2$ penetrated, while in a similar study using $C_{12}AE_{10}$, only 0.85 $\mu g/cm^2$ penetrated rat skin. For all 3 test compounds, penetration was proportional to longer durations of contact and multiple applications. The highest penetration rate, 8.4 $\mu g/cm^2$, was observed after 20 minutes 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 hours. By 72 hours, 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 participants.[19] 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 participants for 8 hours. The test site was protected by a nonocclusive metal shield. After repeated washing, the area was tape stripped 10 times. Blood samples, urine, feces, and expired air were collected at various intervals. The majority of the radioactive solution, that is 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 $\mu g/g$ at 8, 12, and 24 hours, respectively, were found in the blood of 1 participant. The total radioactivity recovered was 82.4% for one participant and 94.7% for the other.

The percutaneous absorption of laureth 9 through damaged skin was evaluated using 22 patients with atopic dermatitis.[37] 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 hours after showering. Percutaneous penetration was quantified by measuring laureth 9 blood concentrations and urinary excretion rates. Blood concentrations were 0.015 to 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.[38] 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 hour) was 34 ± 7.7 $\mu g/cm^2$ per h, indicating that PEG-3 methyl ether would not readily penetrate the skin. The diffusion barrier function of the skin was slightly diminished after 12 hours 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).[39] 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 hours after dosing but was apparent after 24 and 48 hours.

Oleths. Oleths have been reported to increase the permeability of isolated stratum corneum in in vitro studies.[40] (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.[40]

Toxicologogical studies

Single Dose (Acute) Toxicity

Acute toxicity studies are summarized in Table 5. The lowest reported LD_{50} value was >1 g/kg for oral exposure. No mortality was reported in 2 inhalation studies.

Oral

Laureths. The acute oral toxicity of laureth 9 was evaluated using groups of 10 male albino Swiss Webster mice.[42] The oral LD_{50} values after 24 hours and 7 days were 3300 and 3050 mg/kg, respectively. In rats, the oral LD_{50} ranged from 1642 to 4900 mg/kg per bw using analogs of laureth 9, applied neat.[19] For a 50% solution of the analogs in corn oil, the oral LD_{50} ranged from greater than the highest dose tested (2000 mg/kg) to 2500 mg/kg bw for male rats and from 1000 to 2000 mg/kg/bw for female rats. The oral LD_{50} of laureth 9 in Beagle dogs 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.[43] The oral LD_{50} was 2880 mg/kg for males and 2602 mg/kg for females.

PEG methyl ethers. PEG-3 methyl ether has an LD_{50} of ≥11 300 mg/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.[44] The groups of animals were dosed by gavage with 320 to 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 to 2900 mg/kg, are provided in Table 5.[45]

C12-13 Pareths. The acute oral toxicity of a C12-13 pareth (avg chain length not specified) was determined.[46] Groups of 4 male and 4 female Wistar albino rats were dosed by gavage with 5000 or 10 000 mg/kg of the test material. One female of the 5000 mg/kg group and 2 males and 3 females of the 10 000 mg/kg group died by day 11. The oral LD_{50} was approximately 10 000 mg/kg.

The acute oral toxicity of C12-13 pareth 2 was also determined.[47] Four male and 4 female rats were dosed by gavage with 10 000 mg/kg. One female died on day 4; the LD_{50} was greater than the highest dose tested. The oral LD_{50} values of various C12-13 pareths for rats, which range from 4600 to 7600 mg/kg, are provided in Table 5.[45]

C12-15 pareths. The oral LD_{50} values of various C12-15 pareths for rats, which range from 1600 to 5600 mg/kg, are provided in Table 5.[45]

C14-15 pareths. The oral LD_{50} values of various C14-15 pareths for rats, which range from 1000 to 2700 mg/kg, are provided in Table 5.[45]

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.[48] (Details not specified.) Pulmonary lesions were found within 3 days of a single dermal application. In rats, the potential for

Table 5. Acute Toxicity Studies

Ingredient	Animals	No./Group	Dose	LD_{50} (LC_{50} for inhalation studies)	Reference
			ORAL		
Laureths					
Laureth 9	Albino Swiss Webster mice	10 M		3300 mg/kg (24 h); 3050 mg/kg (7 day)	42
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	19
$C_{12-13}AE_{6.5}$	Fischer 344 rats	5 M/F	50% in corn oil, 900-2500 mg/kg	2500 mg/kg M); 1637 mg/kg (F)	19
$C_{12-15}AE_{7}$	Fischer 344 rats	5M/5F	undiluted, 700-5000 mg/kg	1642 mg/kg	19
$C_{12-15}AE_{11}$	Rat	5M/5F	50% in corn oil, 1000-2000 mg/kg	males: greater than highest dose tested; females: 1000-2000 mg/kg	19
$C_{12-14}AE_{6}$	Rat	5M/5F	neat, 5010-10 000 mg/kg	4900 mg/kg	19
$C_{12-13}AE_{6.5}$	Beagle			1650 mg/kg	19
$C_{14-15}AE_{7}$	Monkey		neat	6700 mg/kg	19
Ceteths					
	ddY mice	10	undiluted	2880 mg/kg (M); 2602 mg/kg (F)	43
PEG Methyl Ethers					
PEG-3 Methyl Ether	Wistar rats			12 600 mg/kg	21
PEG-3 Methyl ether	Carworth-Wistar rats	5	diluted with either water, corn oil, or agar	11.3 mL/kg (11 800 mg/kg)	21
PEG-3 Methyl Ether	Carworth Farms-Nelson rats	males	4, 8, or 16 mL/kg	11,300 mg/kg; all animals dosed with 16 mL/kg died in 1 day	21
PEG-7 Methyl Ethers	Rats			>16 mL/kg	22
C9-11 Pareths					
C9-11 Pareth 3	Rats			2700-10 000 mg/kg	45
C9-11 Pareth 5	Rats			2900 mg/kg	45
C9-11 Pareth 6	Rats			1200-4100 mg/kg	45
C9-11 Pareth 6	Fischer 344 rats	5M/5F	320-3260 mg/kg	1378 mg/kg	44
C9-11 Pareth 8	Rats			1000-2700 mg/kg	45
C12-13 Pareths					
	Wistar albino rats	4M/4F	5000 or 10 000 mg/kg	10 000 mg/kg	46
C12-13 Pareth 2	Wistar albino rats	4M/4F	10 000 mg/kg	greater than highest dose tested	47
C12-13 Pareth 3	Rats			7600 mg/kg	45
C12-13 Pareth 7	Rats			4600 mg/kg	45
C12-15 Pareths					
C12-15 Pareth 3	Rats			2300 mg/kg	45
C12-15 Pareth 7	Rats			1700-2700 mg/kg	45
C12-15 Pareth 9	Rats			1600-5600 mg/kg	45
C12-15 Pareth 12	Rats			1800 mg/kg	45
C14-15 Pareths					
C14-15 Pareth 7	Rats			2300-2700 mg/kg	45
C14-15 Pareth 11	Rats			1000 mg/kg	45
C14-15 Pareth 13	Rats			1000 mg/kg	45
			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	48
Laureth 4	Rats			potential for neurotoxicity observed within 48 h after dosing (details not provided)	48

(continued)

Table 5. (continued)

Ingredient	Animals	No./Group	Dose	LD_{50} (LC_{50} for inhalation studies)	Reference
Analogs of Laureth 9 described in the SCCP opinion paper					
$C_{12-14}AE_6$	Rabbits		neat	>2000 mg/kg	19
$C_{12-14}AE_9$	Rabbits		neat	>2000 mg/kg	19
$C_{12-15}AE_7$	Rats	5M/5F	neat	>2000 mg/kg	19
$C_{13-15}AE_7$	Rats	6M/6F	40% in corn oil; dosage volume to skin, 2.3 mL/kg	>920 mg/kg	19
PEG Methyl Ethers					
PEG-3 Methyl Ether	NZW 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 (7400 mg/kg)	21
PEG-7 Methyl Ether	Rabbits			>16 mL/kg	22
C9-11 Pareths					
C9-11 Pareth 3	Rabbits			>5000 mg/kg	45
C9-11 Pareth 3	Rats			>2000 mg/kg	45
C9-11 Pareth 5	Rats			>2000 mg/kg	45
C9-11 Pareth 6	Rabbits			>2000-5000 mg/kg	45
C9-11 Pareth 6	NZW rabbits	4M/4F	2000 mg/kg (occ.)	>2000 mg/kg; mild to moderate irritation observed at patch removal	44
C9-11 Pareth 8	Rats			4000 mg/kg	45
C12-13 Pareths					
	Wistar albino rats	4M/4F	2000 mg/kg (occ.)	>2000 m/kg	46
C12-13 Pareth 2	Wistar albino rats	4M/4F	1000, 2000, or 4000 mg/kg (occ.)	> 2000 mg/kg; ~4000 mg/kg	47
C12-13 Pareth 3	Rabbits			3300 mg/kg	45
C12-13 Pareth 7	Rabbits			2000 mg/kg	45
C12-15 Pareths					
C12-15 Pareth 3	Rabbits			3000 mg/kg	45
C12-15 Pareth 7	Rabbits			2300-5000 mg/kg	45
C12-15 Pareth 9	Rabbits			2500-3400 mg/kg	45
C12-15 Pareth 12	Rabbits			2500 mg/kg	45
C14-15 Pareths					
C14-15 Pareth 7	Rabbits			<5000 mg/kg	45
^{45}C14-15 Pareth 7	Rats			>5000 mg/kg	45
C14-15 Pareth 11	Rabbits			5000 mg/kg	45
C14-15 Pareth 13	Rabbits			5000 mg/kg	45
			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	21
PEG-3 Methyl Ether	Rats	6F	8 hr exposure to concentrated vapor	no LC_{50} established; no mortality	21
			PARENTERAL		
Laureths					
Laureth 9	Albino Swiss Webster mice	10M		100 mg/kg (i.v.)	42
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	48

neurotoxicity was observed within 48 hours 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.[19] 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 was 7.1 mL/kg (7400 mg/kg) in New Zealand White (NZW) 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 NZW rabbits.[44] A dose of 2000 mg/kg was applied under a 4 inches × 4 inches occlusive patch to the shaved back of the animals. Mild-to-moderate irritation was observed at patch removal, and mild and moderate edema was still observed after 14 days. The dermal LD_{50} was greater than the highest dose tested. The dermal LD_{50} values of various C9-11 pareths, which range from 2000 to 5000 mg/kg for rabbits and 2000 to 4000 mg/kg for rats, are provided in Table 5.[45]

C12-13 pareths. The acute dermal toxicity of a C12-13 pareth was determined.[46] Undiluted test material, 2000 mg/kg, was applied under occlusion to shaved dorsal skin of 4 male and 4 female Wistar albino rats. The dermal LD_{50} was greater than the dose tested.

The acute dermal toxicity of C12-13 pareth 2 was determined as described above.[47] The test article, 1000, 2000, or 4000 mg/kg, was applied for 24 hours 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 >2000 mg/kg and was approximately 4000 mg/kg.

The dermal LD_{50} values of various C12-13 pareths, which range from 2000 to 3300 mg/kg for rabbits, are provided in Table 5.[45]

C12-15 pareths. The dermal LD_{50} values of various C12-15 pareths, which range from 2300 to 5000 mg/kg for rabbits, are provided in Table 5.[45]

C14-15 pareths. The dermal LD_{50} values of various C14-15 pareths, which range from 2500 to 5000 mg/kg for rabbits and is >5000 mg/kg for rats, are provided in Table 5.[45]

Inhalation

PEG methyl ethers. In 2 separate studies, rats were either exposed to 200 mg/L PEG-3 methyl ether for 1 hour or exposed to concentrated vapor for 8 hours.[20] All animals survived both studies, and the LC_{50} value was not established in either study.

Other

Laureths. The acute intravenous (iv) toxicity of laureth 9 was evaluated using groups of 10 male albino Swiss Webster mice.[42] The iv LD_{50}, after 24 hours 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.[41] 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.[19] Groups of 6 Colworth Wistar rats, 3 per gender, were fed 0.023% to 1.5% $C_{12\text{-}14}AE_7$, $C_{12\text{-}15}AE_7$, and $C_{12\text{-}15}AE_{11}$ in the diet for 21 days. A group of 6 male and 6 female rats were 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 $C_{12\text{-}14}AE_7$, 459 mg/kg bw $C_{12\text{-}15}AE_7$, and 519 mg/kg bw $C_{12\text{-}15}AE_{11}$.

Groups of Colworth Wistar rats, number per group not specified, were fed 0.03% to 1.0% active material $C_{12\text{-}15}AE_7$ and $C_{12\text{-}14}AE_7$ 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, hepatocyte 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 per bw/d $C_{12\text{-}15}AE_7$ and 110 mg/kg per bw/d $C_{12\text{-}14}AE_7$.

$C_{14\text{-}15}AE_7$ was fed to groups of 6 male and 6 female Wistar rats at concentrations of 300 to 10 000 ppm of active ingredient for 90 days. The control group was comprised 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 $C_{14\text{-}15}AE_7$.

In another 90-day study, $C_{14\text{-}15}AE_7$ 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% $C_{14\text{-}15}AE_7$, corresponding to 700 mg/kg bw for males and 785 mg/kg bw for females.

In a 2-year study, rats, number per group not specified, were fed 0.1%, 0.5%, and 1% $C_{12\text{-}13}AE_{6.5}$ and $C_{14\text{-}15}AE_7$ in the diet. Reduced feed consumption, resulting in decreased body weight gains, was observed in the females fed 0.5% and 1% and in the males fed 1%. 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 per bw/d.

$C_{14\text{-}15}AE_7$ was fed to rats, number per group not specified, at concentrations of 0%, 0.1%, 0.5%, and 1% in the diet for 2 years. Body weights were decreased for females of the 0.5% and 1% groups and for males of the 1% group. Increases in 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 months but not at 2 years. The NOAEL was 0.5%, corresponding to 190 and 162 mg/kg per bw/d 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.[42] 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 postdose 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 per d PEG-3 methyl ether 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 per d 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 per d PEG-3 methyl ether 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 to body 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. Based on liver effects, the researchers assigned a NOAEL of 400 mg/kg per d and a lowest observable adverse effect level (LOAEL) of 1200 mg/kg per d PEG-3 methyl ether. Based on testicular effects, the researchers assigned a NOAEL of 1200 mg/kg per d and LOAEL of 4000 mg/kg per d. However, the Environmental Protection Agency (EPA) reviewed the information and determined that the LOAEL for testicular effects in this study was between 400 and 1200 mg/kg per 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.[49] 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 hematological 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, or 1000 mg/kg per d of an unspecified oleth.[50] One male and 1 female died after 2 doses of 1000 mg/kg, at which point the high dose was reduced to 750 mg/kg per d. Two additional

high-dose males died after the third or fourth dose, and 2 additional females in moribund condition were killed after 7 doses. A mid-dose male was killed after 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.[48] Doses of 495, 990, or 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 week 1 and for 4 days during week 2. The test sites were occlusively wrapped for at least 6 hours, 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. No other treatment-related clinical signs of toxicity were observed.

A dose of 2 mL/kg bw of 2.5% aqueous $C_{14\text{-}15}AE_7$, a compound analogous to laureth 9, was applied 5 days a week, 6 h/d for 13 weeks to groups of 3 male and 3 female rabbits.[19] 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 animals.

PEG methyl ethers. Groups of 5 rats/gender were dosed dermally with 0, 1000, 2500, or 4000 mg/kg per d PEG-3 methyl ether, 6 h/d.[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 per d 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.[20,38] A dose of 1000 mg/kg per d was applied neatly to the shaved skin (size of test area not specified) on the back of each animal, 6 h/d, 5 d/week for 3 weeks, under an occlusive covering; the animals were restrained during dosing. Six hours 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 hours 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 was evaluated by applying doses of 0, 400, 1200, or 4000 mg/kg bw to a shaved site on the backs of 10 Sprague-Dawley rats/gender/group for 6 h/d, 5 d/week, for 13 days.[20] The test material was uniformly spread on a 12 cm^2 area under a semiocclusive covering. Additional groups of 5 rats/gender per dose were used for interim evaluations. There were no indications of systemic toxicity, and the researchers did not consider testicular effects in 1 high-dose and 1 mid-dose male to be test article related. (Dermal effects were not described.) The researchers assigned a NOAEL of 4000 mg/kg per bw/d PEG-3 methyl ether. However, the EPA reviewed that data and, based on testicular effects in 2 males, assigned a 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/week. 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 d/week.

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 were 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 of 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 hours, the test site was wiped. Five applications were made during week 1, and 4 were made during week 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 were 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 d/week, 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 aqueous C9-11 pareth 6, 3 d/week for 13 weeks.[44] 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 parameters 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.[51] The applications were made 5 times/week for 13 weeks, followed by a 4-week 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 hours 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-week interim sacrifice, moderate epidermal hyperplasia, hyperkeratosis, and inflammatory infiltrates were observed microscopically, and after 13 weeks, slight-to-moderate hyperplasia was reported. After the 4-week recovery period, there were no specific microscopic findings. There were no toxicologically significant findings.

Dermal Irritation

Dermal irritation studies using animals are summarized in Table 6. Depending on the alkyl PEG ether studied, results range from nonirritating to severely irritating.

Animal Studies

Laureths. Laureth 9 was applied undiluted or as a 15% or 20% aqueous solution under occlusion to the intact and abraded skin of rabbits (number, strain, and gender not specified).[42] The test sites were scored 24 and 72 hours after application. A slight irritant effect was observed on intact and abraded skin 24 hours, but not 72 hours, 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 hours' readings.

The dermal irritation potential of a number of test substances analogous to laureth 9 was determined.[19] $C_{14\text{-}15}AE_7$, 0.5 mL at 10%, 25%, or 100%, was not irritating when applied to rabbits under a semiocclusive patch for 4 hours; the primary irritation index (PII) was 1.7. Following a 4-hour 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-hour 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.[42] The formulation was applied using occlusive patches to intact and abraded skin of 4 rabbits, and the sites were scored 24 and 72 hours after application. The aerosol formulation containing 20% laureth 9 was a mild irritant.

A mixture containing 1/10 g of laureth (chain length unspecified; composition percentage not stated) was applied to the shaved dorsal skin of 6 male albino rabbits.[53] The test site was occluded for 24 hours, 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 necrosis of the skin for 2 of the test animals.

PEG methyl ethers. PEG-3 methyl ether was applied to intact and abraded skin of 5 NZW rabbits at a dose of 2 g/kg, and the site was covered for 24 hours.[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.)

Undiluted PEG-3 methyl ether, 0.1 mL, was applied uncovered to the skin of 5 rabbits for 24 hours.[20] PEG-3 methyl ether caused minimal irritation, with an irritation score of 2/10 at 24 hours.

C9-11 pareths. The primary dermal irritation potential of undiluted C9-11 pareth 6 was evaluated in a Draize test using

Table 6. Dermal Irritation and Sensitization

Ingredient	Concentration[a]	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	42
	1S, 20% aqueous			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	42
Laureth (unspecified)	Unspecified	6 Male albino rabbits	0.10 g applied under occlusion	Strong irritant with necrosis occurring in 2 animals.	53
Compounds analogous to Laureth 9					
$C_{14-15}AE_7$	10 or 25% m/v aqueous; undiluted	Rabbits	0.5 ml, semi-occluded, 4 h	PII = 1.7/8; not irritating	19
$C_{12-14}AE_{10}$	Undiluted	Rabbits	occlusive application, 4 h	PII = 4.1/8; moderate irritant	19
$C_{13}AE_6$	Undiluted	Rabbits	occlusive application, 4 h	PII = 5.1/8; moderate irritant	19
$C_{13}AE_{6.5}$	Undiluted	Rabbits`	occlusive application, 4 h	PII = 5.5/8; severe irritant	19
$C_{12-14}AE_6$	Undiluted	Rabbits	occlusive application, 4 h	PII = 6.3/8; severe irritant	19
$C_{14-15}AE_7$	Undiluted	Rabbits	occlusive application, 24 h	PII = 6.42/8; severe irritant; slight to moderate erythema and moderate to severe edema	19
PEG Methyl Ethers					
PEG-3 Methyl Ether	Neat	5 NZW 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	44
C9-11 pareth 3	Undiluted	6 Albino rabbits	Draize test	Severely irritating	45
C9-11 pareth 5	Undiluted	6 Albino rabbits	Draize test	Severely irritating	45
	0.1, 1, 10%	6 Albino rabbits	Draize test	0.1%—nonirritating; 1% - minimally irritating; 10%—slightly irritating	
C9-11pareth 6	Undiluted	6 Albino rabbits	Draize test	Severely irritating	45
	0.1, 1%	Rabbits	Draize test	0.1%—Nonirritating; 1%—slightly irritating	45
C9-11 pareth 8	Undiluted	6 Albino rabbits	Draize test	Severely irritating	45
	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	46
C12-13 pareth 2	Undiluted	3 Male NZW rabbits	Draize test	Moderately irritating with no necrosis observed	47
C12-13 pareth 3	Undiluted	6 Albino rabbits	Draize test	Severely irritating	45
C12-13 pareth 7	Undiluted	6 Albino rabbits	Draize test	Mildly to severely irritating	45
C12-13 pareth 7	0.1%, 1%, and 10%	6 Albino rabbits	Draize test	0.1%—Nonirritating; 1%—mildly irritating; 10%—moderately irritating	
C12-15 Pareths					
C12-15 pareth 3	Undiluted	6 Albino rabbits	Draize test	Moderately to extremely irritating	45
C12-15 pareth 7	Undiluted	6 Albino rabbits	Draize test	Moderately irritating	45
	0.1%, 1%, 10%	6 Albino rabbits	Draize test	0.1, 1%—mildly irritating; 10%—moderately irritating	

(continued)

Table 6. (continued)

Ingredient	Concentration[a]	Animals	Procedure	Results	Reference
C12-15 pareth 9	Undiluted	6 Albino rabbits	Draize test	Severely irritating	45
	0.1%, 1%	6 Albino rabbits	Draize test	Nonirritating	
C12-15 pareth 12	50%	6 Albino rabbits	Draize test	Minimally irritating	45
C14-15 Pareths					
C14-15 pareth 7	Undiluted	6 Albino rabbits	Draize test	Severely irritating	45
	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	45
	0.1%, 1%, and 10%	6 Albino rabbits	Draize test	0.1%—nonirritating; 1% - slightly irritating; 10%—moderately to severely irritating	
C14-15 pareth 13	Undiluted	6 Albino rabbits	Draize test	Moderately irritating	45
C14-15 pareth 18	Undiluted	6 Albino rabbits	Draize test	Mildly irritating	45
	0.1%, 1%, and 10%	6 Albino rabbits	Draize test	0.1% nonirritating; 1%—minimally irritating; 10%—slightly irritating	
			DERMAL SENSITIZATION		
Laureths					
Laureth 5	Induction: 10% aqueous laureth 5, challenge: 0%-5% aqueous 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.	24
Laureth 9	0.02% Aqueous 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	42
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	42
Compounds analogous to Laureth 9					
$C_{12-15}AE_7$	Intraderm. induction: 0.05% aqueous; top. induction: 20% aqueous; top. challenge: 15% aqueous	20 Test and 10 control guinea pigs	Magnusson-Kligman sensitization study	Not sensitizing	19
$C_{14-15}AE_7$	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	19
$C_{12-14}AE_6$	Induction: undiluted; challenge: 50% in de-ionized water	20 Test and 10 control guinea pigs	Buehler method	Not sensitizing	19
$C_{12-14}AE_9$	Induction: undiluted; challenge: 50% in de-ionized water	21 Test and 10 control guinea pigs	Buehler method	not sensitizing	19
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	42
C9-11 pareths					
C9-11 pareth 6	1% Aqueous	4 Groups of 5 male and 5 female Dunkin-Hartley albino guinea pigs	Buehler method	No sensitization reactions	44

(continued)

Table 8. (Continued)

Ingredient	Concentration[a]	Animals	Procedure	Results	Reference
C9-11 pareth 3	Not specified	Guinea pigs (number, gender, strain not specified)	Not specified	Not sensitizing	45
C9-11 pareth 5	Not specified	Guinea pigs (number, gender, strain not spec)	Not specified	Not sensitizing	45
C9-11 pareth 6	Not specified	Guinea pigs (number, gender, strain not specified)	Not specified	Not sensitizing	45
C9-11 pareth 8	Not specified	Guinea pigs (number, gender, strain not specified)	Not specified	Not sensitizing	45
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	46
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	47
C12-13 pareth 3	Not specified	Guinea pigs (number, gender, strain not specified)	Not specified	Not sensitizing	45
C12-13 pareth 7	Not specified	Guinea pigs (number, gender, strain not specified)	Not specified	Nonsensitizing to low sensitizing	45
C12-15 Pareths					
C12-15 pareth 3	Not specified	Guinea pigs (number, gender, strain not specified)	Not specified	Not sensitizing	45
C12-15 pareth 7	Not specified	Guinea pigs (number, gender, strain not specified)	Not specified	Not sensitizing	45
C12-15 pareth 9	Not specified	Guinea pigs (number, gender, strain not specified)	Not specified	Not sensitizing	45
C14-15 pareths					
C14-15 pareth 7	Not specified	Guinea pigs (number, gender, strain not specified)	Not specified	Not sensitizing	45
C14-15 pareth 11	Not specified	Guinea pigs (number, gender, strain not specified)	Not specified	Not sensitizing	45
C14-15 pareth 13	Not specified	Guinea pigs (number, gender, strain not specified)	Not specified	Not sensitizing	45
C14-15 pareth 18	Not specified	Guinea pigs (number, gender, strain not specified)	Not specified	Not sensitizing	45

[a] The vehicle is identified when known.

3 male and 3 female NZW rabbits at a dose of 2 g/kg.[44] The test substance was applied to a 1-inch square of gauze, and the gauze was applied to the shaved backs of the animals under an occlusive patch for 24 hours. The test site was scored at patch removal after 24 and 72 hours. 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.[45] All of these ingredients were severely irritating. Some dilutions (vehicle not specified) were also tested. C9-11 pareth 5 was nonirritating at 0.1%, minimally irritating at 1%, and slightly irritating at 10%. C9-11 Pareth 6 was nonirritating 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.[46] A single occlusive patch of undiluted test material was applied to intact and abraded skin for 24 hours, and the test sites were graded at 24 hours, 72 hours, 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 hours, 72 hours, 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.[47] 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.[45] 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 nonirritating 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.[45] 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 nonirritating 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.[45] 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 nonirritating at 0.1%, slightly irritating at 1%, and moderately to severely irritating at 10%. C14-15 pareth 18 was nonirritating at 0.1%, minimally irritating at 1%, and slightly irritating at 10%.

Dermal Sensitization

Animal sensitization studies are summarized in Table 6. Alkyl PEG ethers are not significant sensitizers in these animal studies.

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.[23] At induction, occlusive applications of 200 mg of 10% aqueous 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% aqueous laureth 5 was applied to the shaved left flank for 24 hours using Finn chambers. The test sites were evaluated 48, 72, or 96 hours after application. Laureth 5 did not produce a sensitization reaction. However, confluent erythema was seen in 1 test and 2 control animals at 48 hours and in 2 test animals and 1 control animal at 72 hours and 1 test and 1 control animal with the 1% induction and at 96 hours in 1 test and 1 control animal with the 5% challenge.

Groups of 7 male guinea pigs were dosed intracutaneously with a 0.02% aqueous solution of laureth 9 or a 0.1% solution of an aerosol contraceptive formulation containing 20% laureth 9, to determine the sensitization potential.[42] The injections were made 3 times/week for a total of 10 applications. The first injection volume was 0.05 mL, and the subsequent injections were 0.1 mL. A control group was injected with distilled water. Two weeks 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.[19] In Magnusson-Kligman guinea pig maximization tests in which intradermal induction used concentrations of 0.05% to 0.2%, dermal induction used concentrations of 20% to 100%, and challenge was with concentrations of 15% to 60%, the compounds were nonsensitizing. In Buehler studies using guinea pigs, the products were applied undiluted during induction and at 50% aqueous at challenge. Again, no sensitization was observed.

C9-11 pareths. The sensitization potential of a 1% aqueous solution of C9-11 pareth 6 was evaluated using the Buehler

method.[44] 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 d/week, 6 h/d, for 3 consecutive weeks. The rest period duration was not stated. Signs of sensitization were scored 24 and 48 hours 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 studies of guinea pigs (details not given).[45]

C12-13 pareths. The dermal sensitization potential of a C12-13 pareth (chain length not specified) was evaluated with a Magnusson-Kligman maximization study.[46] 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 hours 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.[47] 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 (details not given).[45]

C12-15 pareths. C12-15 pareth 3, C12-15 pareth 7, and C12-15 pareth 9 were not sensitizers in guinea pig studies (details not given).[45]

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 (details not given).[45]

Human Irritation/Sensitization Studies

Laureths. In a retrospective European study of allergic contact response, only 1 of 475 patients had an allergic contact reaction to laureth 4.[54] From 1992 to 1999, 3186 patients were patch tested with 0.5% laureth 9.[55] Based on a 72-hour reading, 0.94% had questionable (erythematous), 0.88% had slightly irritating, 0.97% had weakly positive, and 0.25% had strongly positive reactions. For 6202 patients that were patch tested with 3% laureth 9, 1.79% of the participants had questionable, 0.48% had irritating, 1.77% had weakly positive, and 0.34% had strongly positive reactions. 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.[19] In a 3-patch application test using 10 participants, undiluted or 25% aqueous $C_{14-15}AE_7$ was applied under occlusive patches for 4 hours on 3 alternate days. Slight to negligible irritation was observed. In a 24-hour occlusive patch test with 8 participants, a 10% aqueous solution of $C_{12-13}AE_{6.5}$ was slightly irritating.

A human repeat insult patch test (HRIPT) was completed with 51 participants to determine the sensitization potential of aerosol cream preparations containing 10%, 15%, and 20% laureth 9.[42] During induction, occlusive patches were applied for 24 hours to the anterolateral surface of the upper arm, 3 times/week for 3 weeks. Challenge patches were applied 16 days after removal of the last induction patch, and those patches were left in place for 24 hours.

During induction, reactions were observed for all 3 preparations with patches 3 to 9. Most of the reactions were mild (1+). A 2+ reaction was recorded for some participants 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 participants 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 participants had reactions that were indicative of sensitization.

The HRIPTs were performed with test substances that were analogous to laureth 9.[19] In an HRIPT performed using 108 participants, 24-hour induction patches with 0.3 mL of 5%, 10%, or 25% aqueous $C_{12-15}AE_7$ and $C_{12-15}AE_9$ were applied 3 times/week for 9 weeks. A 24-hour challenge patch was applied after a 2-week nontreatment period. During induction, patches with 25% of the test materials caused very slight primary skin irritation, with slight erythema seen in 6 of 108 participants induced with 25% $C_{12-15}AE_7$ and in 15 of 108 participants induced with 25% $C_{12-15}AE_9$. At induction with 5%, very slight erythema was seen in 1 and 5 participants 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% aqueous $C_{12-13}AE_{6.5}$ and $C_{12-15}AE_{12}$ were applied to 12 participants per test material. With both induction concentrations of $C_{12-15}AE_6$, 1 participant 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% aqueous solution, were evaluated in another HRIPT with 12 participants following the same protocol. Very slight primary skin irritation was observed with $C_{12-13}AE_{6.5}$, with very slight erythema observed for 1 participant 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 participants wore patches containing 2.5% aqueous $C_{14-15}AE_7$ (144 participants) or $C_{12-13}AE_{6.5}$ (165 participants) for up to 3 weeks, with challenge

following a 17-day nontreatment period. Skin hyperactivity was observed in 1 participant exposed to $C_{12\text{-}13}AE_{6.5}$.

Steareths. Steareth 2, steareth 10, and steareth 21 were evaluated on normal and damaged skin.[56] The test compounds were applied at a concentration of 5% w/v in a water/mineral oil (50:50) mixture, with a vehicle control; 50 µL of each test compound and the control were applied to normal skin of the volar forearm of 20 participants for 48 hours. For damaged skin, the skin was irritated using sodium lauryl sulfate prior to application of the test material. At 24 hours 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 3 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 was evaluated using groups of 20 participants.[20] The test material, 0.03 mL, was applied to the gauze center of a 3/8 inches × 1½ inches bandage and placed on the skin for 24 hours. One hour after removal, the procedure was repeated for 3 consecutive days. At 24 hours,10 participants had an erythema score of 1/4 and 3 participants had a score of 2/4. By 72 hours, 7 participants had an erythema score of 1, and 13 participants has an erythema score of 2. No edema was observed. The average total irritation score by 72 hours was 1.65, and the test material was slightly irritating.

C12-13 pareths. In an HRIPT (number of participants not given), C12-13 pareth 7, tested at concentrations of 1%, 5%,and 15%, produced very slight irritation and was not a sensitizer.[45]

C12-15 pareths. In an HRIPT (number of participants not given), 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.[45] C12-15 pareth 12 was very slightly irritating (5%) or nonirritating (15%). None of the C12-15 pareths were sensitizers in human participants.

Case Reports

Case reports have appeared sporadically over the past 30 years.[57–66] The majority of the reports are skin reactions to laureths, especially laureth 9. Reactions included, but were not limited to, eczema, contact dermatitis, and a pruritic rash.

Ocular Irritation

Rabbit ocular irritation studies of alkyl PEG ethers are summarized in Table 7. Laureths and laureth analogs were slight-to-moderate ocular irritants;[19,37] PEG methyl ether was a slight ocular irritant;[20] In studies using albino rabbits, C9-11 pareths, C12-13 pareths, C12-15 pareths, and C14-15 pareths were nonirritating at low concentrations, with irritation increasing with concentration, and with severe ocular irritation if the albino rabbit eye was not rinsed;[45] C12-13 pareths were nonirritating to mildly irritating in studies using NZW rabbits;[46,47] and Oleth 20 at 5% produced only mild, transient conjuctival redness, and chemosis.[68]

Mucosal Irritation

Laureths. Sprague-Dawley rats (number not given)[39] were exposed to 25 mL of 1% laureth 9 placed into the left nostril of each test animal, while saline was instilled into the nostril of the negative controls. Four hours 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 and 10.

Undiluted laureth 9 was instilled (5 mL) 1 time into the vagina of 2 dogs.[42] No irritation was observed in the cervical or vaginal mucosa of either dog on day 0 or 3. Laureth 9 at 15% aqueous (5 mL) instilled once daily for 5 days (number of dogs not specified). Again, no mucosal irritation was observed.

Reproductive and Developmental Toxicity

Dermal

C9-11 pareths. A 2-generation reproductive study was performed using Fischer 344 rats to examine whether C9-11 pareth 6 had any effect on reproductive parameters.[44] 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 aqueous 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 per 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

Table 7. Ocular Irritation

Ingredient	Concentration[a]	Animals	Procedure	Results	Reference
Laureths					
Laureth 9	5% Aqueous	Rabbits (number, gender strain unspecified)		Not irritating; had a slight anesthetic effect on the eye	35
compounds analogous to Laureth 9					
$C_{12-14}AE_6$	Undiluted	3 Rabbits	Draize test	EII = 27.1/110; moderately irritating	19
$C_{13}AE_{5-6.5}$	Undiluted	3 Rabbits	Draize test	EII = 44/110; severely irritating	19
$C_{13}AE_6$	Undiluted	3 Rabbits	Draize test	EII = 44/110; severely irritating	19
$C_{12-14}AE_{10}$	Undiluted	3 Rabbits	Draize test	EII = 37/110; moderately to severely irritating	19
$C_{11-15}AE_{11}$	Undiluted		Draize test	EII = 39/110; moderately to severely irritating	19
$C_{12-14}AE_7$	Undiluted	9 Rabbits	0.1 ml applied; eyes of 3 rabbits rinsed	$MAS_{unrinsed} = 18$; $MAS_{rinsed} = 12$	19
$C_{14-15}AE_{11}$	Undiluted	9 Rabbits	0.1 ml applied; eyes of 3 rabbits rinsed	$MAS_{unrinsed} = 30.7$; $MAS_{rinsed} = 32$	19
$C_{12-13}AE_{6.5}$	100%; 0.1, 1, 10% Aqueous	2 Rabbits	0.2 ml placed in the conjunctival sac	100%—severely irritating; 10%—moderately irritating; 1% and 0.1%—nonirritating	19
$C_{12-15}AE_7$	Undiluted and 0.5% aqueous	3 Rabbits	0.1 ml	$EII_{undiluted} = 27.8/110$, moderately irritating; $EII_{0.5\%} = 0.2/110$, not irritating	19
$C_{13-15}AE_{11}$	Undiluted and 0.5% aqueous	3 Rabbits	0.1 ml	$EII_{undiluted} = 40.1/110$, severely irritating; 0.5% - only minor signs of irritation	19
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	45
	Undiluted, rinsed			mildly irritating	
C9-11 pareth-5	Undiluted, unrinsed	Albino rabbits (number and gender unspecified)	Draize test	severely irritating	45
	0.1, 1, 10%			0.1% and 1%—nonirritating; 10%—moderately irritating	
C9-11 pareth 6	Undiluted, unrinsed	Albino rabbits (number and gender unspecified)	Draize test	severely irritating	45
	Undiluted, rinsed			moderately to severely irritating	
	0.1, 1%			nonirritating	
C9-11 pareth 8	Undiluted, unrinsed	Albino rabbits (number and gender unspecified)	Draize test	severely irritating	45
	0.1, 1, 10%			0.1%—nonirritating; 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	45
C12-13 pareth 7	Undiluted, unrinsed	Albino rabbits (number and gender unspecified)	Draize test	severely irritating	45

(continued)

Table 7. (continued)

Ingredient	Concentration[a]	Animals	Procedure	Results	Reference
C12-13 pareth 7	Undiluted, rinsed	Albino rabbits (number and gender unspecified)		minimally irritating	45
	0.1%, 1%, and 10%	Albino rabbits (number and gender unspecified)		0.1% and 1%—nonirritating; 10%—moderately irritating	
C12-13 pareth (unspecified)	Undiluted, unrinsed	3 NZW rabbits (gender unspecified)	0.2 ml placed in the conjunctival sac	Mildly irritating	45
C12-13 pareth 2	Undiluted, unrinsed	3 NZW rabbits (gender unspecified)	0.2 ml placed in the conjunctival sac	nonirritating	47
C12-15 Pareths					
C12-15 pareth 3	Undiluted, unrinsed	albino rabbits (number and gender unspecified)	Draize test	Severely irritating	45
C12-15 pareth 7	Undiluted, unrinsed	Albino rabbits (number and gender unspecified)	Draize test	Moderately irritating	45
	Undiluted, rinsed			Mildly to moderately irritating	
	0.1%, 1%, 10%			0.1%—nonirritating; 1%—minimally irritating; 10%—mildly irritating	
C12-15 pareth 9	Undiluted, unrinsed	Albino rabbits (number and gender unspecified)	Draize test	Severely to extremely irritating	45
	0.1%, 1%			Nonirritating	
C12-15 pareth 12	Undiluted, unrinsed	Albino rabbits (number and gender unspecified)	Draize test	Severely irritating	45
C14-15 Pareths					
C14-15 pareth 7	Undiluted, unrinsed	Albino rabbits (number and gender unspecified)	Draize test	Moderately to severely irritating	45
	Undiluted, rinsed			Mildly irritating	
	0.1%, 1%, and 10%			0.1% and 1%—nonirritating; 10%—Mildly irritating	
C14-15 pareth 11	Undiluted, unrinsed	Albino rabbits (number and gender unspecified)	Draize test	Severely irritating	45
	0.1%, 1%, and 10%			0.1%—nonirritating; 1%—slightly to mildly irritating; 10%—severely irritating	
C14-15 pareth 13	Undiluted, unrinsed	Albino rabbits (number and gender unspecified)	Draize test	Severely irritating	45
C14-15 pareth 18	Undiluted, unrinsed	Albino rabbits (number and gender unspecified)	Draize test	Minimally to mildly irritating	45
	0.1%, 1%, and 10%			0.1% and 1%—nonirritating; 10%—practically nonirritating	
Oleths					
Oleth 20	5%	Rabbits (number, gender strain unspecified)	Draize test	mild, transient conjunctival redness and chemosis	67

[a] The vehicle is identified when known.

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.[19] 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 to 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 were the evidence of maternal toxicity. No effects on reproductive parameters were noted. During the study, 9 control animals and 31 test animals died. Based on maternal toxicity, the NOAEL was >50 mg/kg per bw/d.

Groups of 25 male and 25 female CD rats were used to evaluate the reproductive toxicity of $C_{14\text{-}15}AE_7$ in a 2-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 per bw/d). In 3 test groups, males and females were given treated feed throughout the study; in another 3 groups, females only were dosed, and dosing was performed on days 6 to 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 $C_{14\text{-}15}AE_7$ was >0.5% (equivalent to 250 mg/kg per bw/d).

In addition, effects on the F_C generation, that is 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 per bw/d.

The reproductive toxicity of $C_{12}AE_6$ was evaluated in a similar study, and the 5 rats were fed 0, 25, 50, or 250 mg/kg per bw/d 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 mg/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 per bw/d, and the NOAELs for maternal and developmental toxicity were 50 mg/kg per bw/d $C_{12}AE_6$ 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 at a volume of 10 mL/kg on days 7 to 16 of gestation.[38] 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 postnatal day (PND) 21.[69] 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 an increase in kidney weights at the highest dose. Birth weights of females in the mid-dose group and males and females in the high-dose group were significantly increased compared to controls. However, postnatal weight gains were decreased at various times. No effects on motor activity were observed.

The developmental toxicity of PEG-3 methyl ether was evaluated using rats and rabbits.[36] 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 to 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 nongravid, 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 decreased in the high-dose group, and feed consumption was statistically decreased in the 2500 mg/kg group on days 12 to 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 $\geq$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 per d PEG-3 methyl ether. The NOAEL for maternal toxicity in the rat was 1250 mg/kg per d.

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 to 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 to 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 1 doe of the 1000 rng/kg groups died on day 18 of gestation.

Maternal weight gains were decreased for the high-dose group during dosing, but a rebound effect occurred during the posttreatment 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 postdosing, 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 2 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 per d PEG-3 methyl ether, respectively. The NOAEL for maternal toxicity was 500 mg/kg per d, and the presumed NOAEL for developmental toxicity was 1500 mg/kg per d.

Groups of 64 gravid female Sprague-Dawley rats were dosed orally, by gavage, with 0, 300, 1650, or 3000 mg/kg per d PEG-3 methyl ether on days 6 to 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 1 female pup from each litter were killed on 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. Kidney weights of maternal rats were statistically significantly increased in the high-dose group 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.[70] In a standard transformation assay with BALB/c-3T3 cells, laureth (tested at 0.00132-0.0417 and 0.00625-0.0250 mmol/L) was inactive.[71] 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).[72] 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; 1 test without metabolic activation produced questionable results, and 1 with metabolic activation had inconclusive results.[73] In a mouse bone marrow micronucleus assay, laureth was not genotoxic when tested at doses of 31.25 to 125 mg/kg.[74]

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.[19] 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 aqueous PEG-3 methyl ether was evaluated in an Ames test using 4 strains of *Salmonella 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 3 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 to 110 mg/plate were tested using 5 strains of *S 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.[44] 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.[19] Groups of 65 rats/gender were fed a diet containing 0%, 0.1%, 0.5%, and 1% $C_{14-15}AE_7$ for 2 years. At 1 year, 14 to 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 years. Feed consumption, and correspondingly, body weight gain, was decreased 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.

Summary

Laureth 4 and laureth 23 have previously been reviewed by the 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 1 or more equivalents of ethylene oxide. In preparing a rereview document, it was noted that a large number of ingredients included in the *International Cosmetic Ingredient Dictionary and Handbook* belong to this family and could 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. Data from these 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 (eg, laureth 4 has an average number of ethylene oxide repeat units equal to 4 but may include some laureth 5, laureth 3 etc). There are some ingredients in this report with known average distributions of alkyl chain length and degree of unsaturation (eg, 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.

None of the alkyl PEG ethers included in this review would be expected to have any biologically significant UV 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 by-product, 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) may be present. 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.

Of the 369 ingredients included in this report, 148 are in use. 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 eyeliners, and ceteareth 10, which is used at 11% in lipsticks. All of the alkyl PEG ethers named in this report are listed in the EU inventory of cosmetic ingredients.

According to the original laureths report, in general, alkyl PEG ethers are readily absorbed through the skin of guinea pigs and rats and through the intestinal mucosa of rats, and they are quickly eliminated from the body through the urine, feces, and expired air. In rats, compounds analogous to laureth 9 are rapidly absorbed and excreted in the urine after oral, ip, and sc 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 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, the 4-hour percutaneous absorption decreased from 22.9% for laureth 1 to 2.1% for laureth 10 solutions, 0.25% in ethanol. 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 participants, the majority of the dose could be wiped away from the test site after 8 hours; less than 2% was found in the urine. With atopic patients, the calculated dermal absorption rate for laureth 9 was 0.0017% for a 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 to 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 to 1.78 mL/kg for rabbits, and the researchers indicated 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 hour and to concentrated vapors for 8 hours.

In 21-day, 90-day, and 2-year feeding studies, compounds analogous to laureth 9 had dietary NOAELs of 459 to 519, 50 to 785, and 50 to 162 mg/kg bw in rats. In a 13-day oral study with an unspecified deceth, doses of $\geq$25 g/kg resulted in death in rabbits. In a 14-day drinking water study, PEG-3 methyl ether was mildly to moderately toxic at 4 g/kg and severely toxic at $\geq$8 g/kg, while in a 91-day drinking water study, PEG-3 methyl ether had a NOAEL of 400 mg/kg per d for liver effects; testicular effects were observed but were attributed to contamination with 2-methoxyethanol. In a 13-week dietary study, a dose of $\leq$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. For an unspecified oleth administered orally to rats, doses of $\geq$750 mg/kg resulted in either death or significant signs of toxicity, and 1 of 6 animals given 3000 mg/kg per d for 17 days was killed in moribund condition. However, at necropsy, the organs and tissues appeared normal.

In a 2-week dermal study, dosing with 495 to 1980 mg/kg per d undiluted laureth 4 under occlusion did not result in erythema or edema, and no toxicologically significant results were reported, while in a 13-week study, moderate localized erythema was observed at all doses levels of 2.5% aqueous $C_{14-15}AE_7$ in rabbits. For PEG-3 methyl ether, some erythema and edema were observed with occlusive applications of 1000 mg/kg per d in a 12-day study using rats; however, 1 study using rats reported a NOAEL of 4000 mg/kg per d. Similar results were observed with PEG-7 methyl ether in 14- and 21-day studies, in which $\leq$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. The dermal responses observed in a 13-week studies involving application of $\leq$25% aqueous 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.

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 hours. The dermal irritation potentials of several compounds that were analogous to laureth 9 were determined. Under semiocclusive conditions with a 4-hour application, $C_{14-15}AE_7$, 0.5 mL at 10%, 25%, or 100%, were not irritating to rabbit skin. Following a 4-hour 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-hour 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. Nonocclusive 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 nonirritating 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% aqueous 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% to 1.0% solutions were nonirritating 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% to 1%, these ingredients were nonirritating to mildly irritating; while at 10%, they were moderately to severely irritating in some cases and practically nonirritating 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% aqueous solution, laureth 9 was not an irritant to the vaginal mucosa of dogs.

In a 2-generation reproductive study, dermal administration of ≤25% C9-11 pareth 6 did not have a toxicologically significant effect on dams or offspring. In 2-generation oral reproductive studies with dietary administration of compounds analogous to laureth 9, the NOAEL for reproductive toxicity was >250 mg/kg per bw/d, and the NOAELs for maternal and developmental toxicity was 50 mg/kg per bw/d. 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 to 15 of gestation, the maternal and developmental NOELs for rats were 625 mg/kg per d, and the NOAEL for maternal toxicity was 1250 mg/kg per d. For rabbits given ≤1500 mg/kg PEG-3 methyl ether on days 6 to 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 per d PEG-3 methyl ether, respectively. The NOAEL for maternal toxicity was 500 mg/kg per d, and the presumed NOAEL for developmental toxicity was 1500 mg/kg per d. 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 CHO 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 genotoxic 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 years.

In a retrospective clinical study, 0.97% of patients had a weakly positive and 0.25% of patients had a strongly positive reaction to 0.5% laureth 9, and 1.77% and 0.34% had weakly and strongly positive allergic contact reactions, respectively, to 3% laureth 9. Undiluted and 25% aqueous $C_{14-15}AE_7$ produced negligible to slight irritation in an occlusive 3-patch application test, and a 10% aqueous solution of $C_{12-13}AE_{6.5}$ was slightly irritating when applied under an occlusive patch for 24 hours. In an HRIPT of formulations containing laureth 9, 12% of participants 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% to 25%, were not sensitizers. In HRIPTs to determine the sensitization potential of 1% to 15% C12-13 pareth 7 and 5% to 25% C12-15 pareth 7, slight or mild irritation was observed, but the ingredients were not sensitizers to human participants. The clinical effect of steareth 2, 10, and 21 was evaluated on normal and damaged skin. The stearethes 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

Alkyl PEG ethers, including the previously reviewed ingredients, laureth 4 and laureth 23, are very similar to one another—structurally, functionally, and toxicologically. While these ingredients comprise a large group, fundamentally, all simple alkyl PEG ethers are the reaction products of alkyl alcohols and 1 or more equivalents of ethylene oxide.

The Expert Panel noted gaps in the available safety data for some of the alkyl PEG ethers in this safety assessment. The available data on many of the ingredients are sufficient, however, and similar structural activity relationships, biologic functions, and cosmetic product usage, suggest that the available data may be extrapolated to support the safety of the entire group. For example, a concern was expressed regarding the extent of dermal absorption for certain long-chain, branched alkyl PEG ethers because of a lack of information on dermal absorption and metabolism. The consensus of the Panel 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. Additionally, the Panel has previously reviewed a number of the alkyl PEG ethers as individual groups, that is ceteareths, ceteths, laneths, oleths, and stearethes; and in this report, the Panel has relied to a great extent on data from these past reports.

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.

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 to 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 ≤10 μm are respirable. In the absences of inhalation toxicity data, the Panel determined that alkyl PEG ethers can be used safely in aerosol products, 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. Because 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 CIR Expert Panel considered the dangers inherent in using animal-derived ingredients, namely the transmission of infectious agents. While tallow may be used in the manufacture of some ingredients in this safety assessment and is clearly animal derived, the Expert Panel notes that tallow is highly processed and tallow derivatives even more so. The Panel agrees with determinations by the US FDA that tallow derivatives are not risk materials for transmission of infectious agents.

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 nonirritating.

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 nonirritating. Were ingredients in this group not in current use (as indicated by *) 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*

Authors' Note

Unpublished sources cited in this report are available from the Director, Cosmetic Ingredient Review, 1101 17th St, Suite 412, Washington, DC 20036, USA.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: The articles in this supplement were sponsored by the Cosmetic Ingredient Review. The Cosmetic Ingredient Review is financially supported by the Personal Care Products Council.

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International Journal of Toxicology
31(Supplement 2) 245S-260S

DOI: 10.1177/1091581812461381
http://ijt.sagepub.com
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Safety Assessment of Propylene Glycol, Tripropylene Glycol, and PPGs as Used in Cosmetics

Monice M. Fiume[1], Wilma F. Bergfeld[2], Donald V. Belsito[2], Ronald A. Hill[2], Curtis D. Klaassen[2], Daniel Liebler[2], James G. Marks Jr[2], Ronald C. Shank[2], Thomas J. Slaga[2], Paul W. Snyder[2], and F. Alan Andersen[3]

Abstract

Propylene glycol is an aliphatic alcohol that functions as a skin conditioning agent, viscosity decreasing agent, solvent, and fragrance ingredient in cosmetics. Tripropylene glycol functions as a humectant, antioxidant, and emulsion stabilizer. Polypropylene glycols (PPGs), including PPG-3, PPG-7, PPG-9, PPG-12, PPG-13, PPG-15, PPG-16, PPG-17, PPG-20, PPG-26, PPG-30, PPG-33, PPG-34, PPG-51, PPG-52, and PPG-69, function primarily as skin conditioning agents, with some solvent use. The majority of the safety and toxicity information presented is for propylene glycol (PG). Propylene glycol is generally nontoxic and is noncarcinogenic. Clinical studies demonstrated an absence of dermal sensitization at use concentrations, although concerns about irritation remained. The CIR Expert Panel determined that the available information support the safety of tripropylene glycol as well as all the PPGs. The Expert Panel concluded that PG, tripropylene glycol, and PPGs $\geq$3 are safe as used in cosmetic formulations when formulated to be nonirritating.

Keywords

propylene glycol, tripropylene glycol, PPGs

Introduction

A safety assessment of propylene glycol (PG) and polypropylene glycols (PPGs) was published in 1994.[1] On the basis of the available data, the Cosmetic Ingredient Review (CIR) Expert Panel concluded that these ingredients were safe for use in cosmetic products at concentrations up to 50.0%. In that assessment, the specific PPG chain lengths were not identified, however, concentration of use data were reported for PPG-9, PPG-26, and PPG 425. Currently, the *International Cosmetic Ingredient Dictionary and Handbook* names PPG-3, PPG-7, PPG-9, PPG-12, PPG-13, PPG-15, PPG-16, PPG-17, PPG-20, PPG-26, PPG-30, PPG-33, PPG-34, PPG-51, PPG-52, and PPG-69. Because new studies published after the 1994 assessment are available, that address the safety of PG and PPGs, the Expert Panel considered these data in support of the safety of these specific PPGs currently listed in the *International Cosmetic Ingredient Dictionary* as well as all chain lengths that may be added in the future.

This report is an update of the 1994 safety assessment and, as such, it contains information that was published after the 1994 assessment was issued.

Dipropylene glycol is not included in this report since it was previously reviewed in a separate report. In 1985, the Expert Panel determined that dipropylene glycol was safe as used in cosmetics.[1] That conclusion was confirmed in 2006.[2]

Tripropylene glycol, which has not been reviewed, is included in this report. Tripropylene glycol is different from PPG-3. The PPG-n designations all acknowledge that these ingredients are produced in a polymerization reaction that can lead to some different chain length compounds, since the process in not end blocked. Tripropylene glycol is an ingredient that contains only the "3" chain length.

Chemistry

Definition and Structure

Propylene glycol (CAS No. 57-55-6) is an aliphatic alcohol that conforms generally to the formula in Figure 1.[3] Tripropylene

[1] Cosmetic Ingredient Review Scientific Analyst/Writer
[2] Cosmetic Ingredient Review Expert Panel Member
[3] Director, Cosmetic Ingredient Review

Corresponding Author:
F. Alan Andersen, Cosmetic Ingredient Review, 1101 17th Street, NW, Suite 412, Washington, DC 20036, USA
Email: cirinfo@cir-safety.org

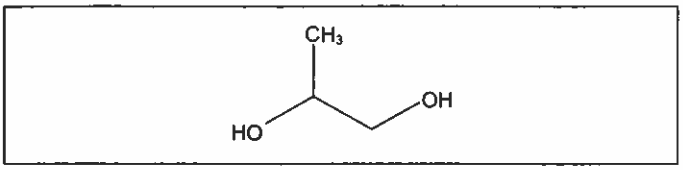

Figure 1. Propylene glycol.

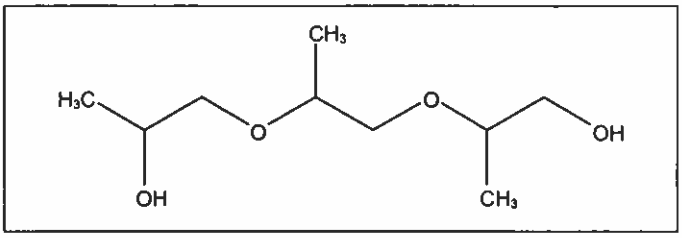

Figure 2. Tripropylene glycol.

glycol (CAS No. 24800-44-0) is an organic compound that conforms to the formula in Figure 2.[3] Synonyms for PG and tripropylene glycol are listed in Table 1.

The PPGs (generic CAS No. 25322-69-4) are polymers of propylene oxide that conform generally to the formula in Figure 3.[3] According to the *International Cosmetic Ingredient Dictionary and Handbook*, international nomenclature cosmetic ingredient (INCI) names for the PPGs refer to the average "n" value corresponding to the propylene oxide chain length of the polymer; that is, PPG-3 would have an average chain length of 3. (Synonyms for PPGs are also listed in Table 1.)

As stated above, the INCI names for cosmetic PPGs refer to the chain length. However, different naming conventions are used in identifying PPGs and the potential for confusion exists. When the official INCI name for each ingredient is used, the name is given as PPG, dash, and then the average number of units, for example, PPG-3. However, the PPGs can also be identified using the average molecular weight as part of the name; this is indicated as PPG, space, average molecular weight, for example, PPG 200. Table 2 gives the INCI name, molecular weight name where available, and calculated molecular weight of the PPGs.

Physical and Chemical Properties

The physical and chemical properties of PG, tripropylene glycol, and the PPGs are summarized in Table 3.

Method of Manufacture

Tripropylene glycol (as well as dipropylene glycol) is formed by sequential addition of propylene oxide to PG.[4] The products are formed simultaneously and separated by distillation.

Impurities

In the original safety assessment on PG, Dow Chemical Co recommended that US Pharmacopoeia (USP)-grade PG be used in cosmetics.[5] According to recent information, the USP has set safety limits of diethylene glycol and ethylene glycol content at a maximum of 0.1%.[6] The USP grade PG manufactured by Dow contains diethylene glycol and ethylene glycol at concentrations that are nondetectable (quantification limit of 0.008% wt/wt). Dow also has stated that they meet or exceed all requirements currently found in the European Pharmacopoeia, Japanese Pharmacopoeia, and Food Chemicals Codex. Two companies submitted information regarding the concentration of propylene oxide in PPGs used to make finished products.[7] Both companies report a maximum of 10 ppm propylene oxide.

Use

Cosmetic

Propylene glycol is used in cosmetic formulations as a skin conditioning agent (humectant or miscellaneous), viscosity decreasing agent, solvent, or fragrance ingredient.[3] The PPGs function primarily as skin conditioning agents, with some functioning as solvents. Tripropylene glycol functions as a humectant, antioxidant, or emulsion stabilizer.

At the time of the original safety assessment, according to information supplied to the Food and Drug Administration (FDA) by industry as part of the Voluntary Cosmetic Registration Program (VCRP), PG was used in 5676 cosmetic formulations at concentrations ranging from 0% to >50%.[5] Both PPG-9 and PPG-26 were used in 6 and 10 cosmetic formulations, respectively, at concentrations of 0.1% to 5%, and PPG 425 (thought to be synonymous with PPG-9) was used in 1 cosmetic formulation at a concentration range of 1% to 5%.

The frequency and concentration of use of PG has increased. Recent VCRP data indicate that PG is used in 9094 cosmetic formulations (out of 34 391 total formulations reported).[8] Polypropylene glycol (chain length not specified) is reported to have 45 uses. Polypropylene glycol-9 is reported to be used in 84 cosmetic formulations, and PPG-12 is used in 3, PPG-15 in 1, PPG-17 in 3, PPG-26 in 2, and PPG-30 in 5 cosmetic formulations. Tripropylene glycol is used in 8 formulations. A survey of current use concentrations conducted by the Personal Care Products Council (the Council) reported that PG is used at concentrations of 0.0008% to 99%.[9] Propylene glycol, which is used in 313 of the 580 deodorant products reported to the VCRP,[8] is used at concentrations of 3% to 73%; this is the greatest leave-on concentration used.[9] The highest concentration of use of PG is 99%, but that use is in products that will be diluted, for example bath oils, tablets, or salts. Additionally, the Council survey results reported that PPG-9 is used at 0.05% to 22%, PPG-12 at 1%, PPG-17 at 1% to 2%, PPG-26 at 0.2%, and PPG-34 at 20%. Tripropylene glycol is used at concentrations up to 22%; the 22% is in an underarm deodorant. Table 4 presents current product formulation data for PG, tripropylene glycol, and the PPGs.

Propylene glycol is used in hair sprays, and its effects on the lungs that may be induced by aerosolized products containing

Table 1. Synonyms

Chemical Name	Synonyms/Other Technical Names
Propylene glycol 5	1,2-dihydroxypropane; 2-hydroxypropanol; methyl glycol; methylene glycol; methylethyl glycol; methylethylene glycol; monopropyl glycol; monopropylene glycol; propane-1,2-diol; 1,2-propanediol; propane-1,2-glycol; α-propylene glycol; 1,2-propylene glycol; propyleneglycolum (EP); trimethyl glycol
Tripropylene glycol	2-(2-(2-hydroxypropoxy)propoxy)propan-1-ol3
PPG-n (n =average chain length)	polyoxypropylene (n)3; polypropylene glycol (n)3

Abbreviations: PPG, polypropylene glycol.

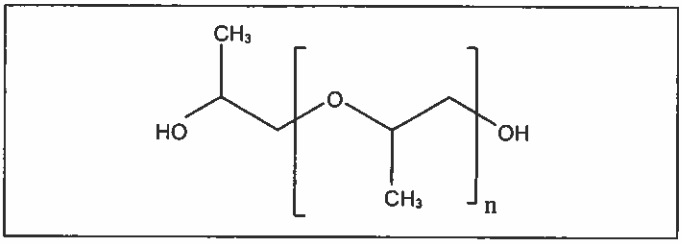

Figure 3. Polypropylene glycol.

n indicates average propylene oxide chain length and is reflected in the name, for example, PPG-12 would have n = 11

this ingredient may be 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 $\leq$10 μm are respirable. Particles with a d_a from 0.1 to 10 μm settle in the upper respiratory tract and particles with a $d_a < 0.1$ μm settle in the lower respiratory tract.[10,11] Particle diameters of 60 to 80 μm and $\geq$80 μm have been reported for anhydrous hair sprays and pump hairsprays, respectively.[12] In practice, aerosols should have at least 99% of their particle diameters in the 10 to 110 μm range and the mean particle diameter in a typical aerosol spray has been reported as ~38 μm.[13] Therefore, most aerosol particles are deposited in the nasopharyngeal region and are not respirable.

Tripropylene glycol, PG, and PPGs are not included in the list of ingredients that are prohibited for use in the European Union[14] or on the list of ingredients restricted or prohibited for use in Japan.[15]

Noncosmetic

Propylene glycol is generally recognized as safe (GRAS) as a direct food additive when used in accordance with good manufacturing practices, and it is approved as a direct and indirect food additive.[16] According to the Joint FAO/WHO Expert Committee on Food Additives (JECFA), the acceptable daily intake (ADI) of PG is 25 mg/kg/bw/d.[17] In Japan, the Ministry of Health, Labour, and Welfare (MHLW) specified that according to the food sanitation law, PG has no potential to cause harm to human health.[18]

Table 2. PPG INCI Names, Molecular Weight Names, and Calculated Molecular Weights[a]

PPG INCI name (PPG-n; n =avg number of moles of propylene oxide)	Molecular Weight Name as Indicated by the Trade Name Listed in the Dictionary	Calculated Molecular Weight (n × 58) + 18
PPG-3	PPG 200	192
PPG-7		424
PPG-9	PPG 400 or PPG 425	540
PPG-12		714
PPG-13		772
PPG-15		888
PPG-16	PPG 950	946
PPG-17	PPG 1000	1004
PPG-20	PPG 1200	1178
PPG-26	PPG 2000	1526
PPG-30	PPG 4000	1758
PPG-33		1932
PPG-34		1990
PPG-51		2976
PPG-52	PPG 3000	3034
PPG-69		4020

Abbreviations: PPG, polypropylene glycol; INCI, international nomenclacure cosmetic ingredient.

In original report, but not specifically listed in table:
PPG 225
PPG 300
PPG 750
PPG 1025
PPG 2025
PPG 3900

Propylene glycol is used as an inactive ingredient in a number of FDA-approved drug products. It has been approved at concentrations up to 98.09% in topical drugs and 92% in oral solutions.[19] There is inadequate evidence to establish PG as GRAS and effective in OTC pediculicide drug products.

Propylene glycol has many uses in pharmaceuticals, food, and manufacturing.[20] It is used in organic synthesis, especially for PPG and polyester resins.[21]

Polypropylene glycol is approved as a secondary direct food and additive and as an indirect food additive.[16] Polypropylene glycol has many industrial uses.[21]

Tripropylene glycol also has many uses in pharmaceuticals, food, and manufacturing. It is used as an intermediate in resins, plasticizers, pharmaceuticals, insecticides, and the production of ethers and esters.[22]

Table 3. Chemical and Physical Properties

Characteristic	Description
Propylene glycol[S]	
Color and form	Colorless viscous stable hygroscopic liquid
Odor	Practically odorless
Molecular weight	76.09[20]
Solubility	Miscible in water, acetone, and chloroform; soluble in ether; miscible with water, alcohol, and many organic solvents
Melting point	−59°C; −60°C
Boiling point	187.3°C; 188.2°C
Freezing point	−59°C
Density/specific gravity	1.036 @ 25°C /4°C; 1.0381 @ 20°C/20°C
Disassociation constant (pKa)	14.8 @ 25°C
Octanol/water partition coefficient	log K_{ow} = -0.92
Index of refraction	1.4323 @ 20°C; 1.4293 @ 27°C
Tripropylene glycol	
Color and form	Colorless liquid[22,S6]; slightly viscous[22]
Odor	Odorless[22,S6]
Molecular weight	192.26[22]
Solubility	Soluble in water, methanol, and ether; miscible with alcohol[22]; miscible in water[S6]
Melting point	<−30°C[22,S6]
Boiling point	271°C[22,S7]
Density/specific gravity	1.019 @ 20°C/20°C[22]
Octanol/water partition coefficient	log P_{ow} = −0.5[S6,S7]
Index of refraction	1.4449 @ 20°C/D[22]
reactivity	Combustible[21]
Polypropylene glycols	
Color and form	Clear, colorless or practically colorless, viscous liquid[S8]
Molecular weight	Dependent on chain length
Solubility	Lower mol wt polymers are soluble in water[S]; soluble in such organic solvents as aliphatic ketones and alcohols but is insoluble in ether and most aliphatic hydrocarbons (mol wts not defined)[S8]
pH	Between 6 and 9[59]
Density	1.002-1.007[60]
Reactivity	Nonvolatile; combustible[S]

Toxicokinetics

Absorption

Propylene glycol. The dermal penetration of [^{14}C]PG through excised female hairless mouse skin from the temary cosolvent containing 10 mol% oleic acid and 6 mol% dimethyl isosorbide in 84% PG was determined.[23] Over a 24-hour period, the cumulative penetration of PG was 57.1% of the applied amount.

The dermal absorption of PG was determined in the outermost layers of skin using thermal emission decay–Fourier transform infrared (TED-FTIR) spectroscopy.[24] Propylene glycol was applied to the fingertip of one human participant for 30 minutes using PG-soaked cotton wool. The site was wiped and allowed to dry for 1 minute. The thickness of the surface layer of stratum corneum probed was 0.71 µm. Measurements were performed every 25 minutes over a 3-hour period, with 1 measurement taking 15 minutes. The concentration of PG remaining at the surface of the stratum corneum decreased over time. At 12 and 32 minutes, the maximum concentration of PG was found at a depth of <1 µm, while at 107 and 157 minutes, the maximum concentration of PG was found at a depth of 3 to 4 µm. At a depth of 6 µm, the greatest concentration of PG, 0.2%, was seen at 32 minutes. The authors suggested that PG molecules diffuse into stratum corneum only to a depth of 6 to 7 µm, approximately. The researchers also suggested that PG molecules do not reach the dermis.

Dermal Penetration Enhancement

Propylene glycol. Propylene glycol has been described as a penetration enhancer, and penetration enhancers act by various mechanisms to perturb diffusional pathways through the skin. Proposed mechanisms of penetration enhancement by PG include alteration of barrier function by its effects on a keratin structure or a PG-induced increase in the solution capacity within the stratum corneum.[23] Examples of the effect of PG on penetration are summarized in Table 5.

Toxicology

Cytotoxicity

Propylene glycol. The cytotoxicity of PG was determined in assays that measured inhibition of human foreskin fibroblasts and keratinocytes, inhibition of collagen contraction by

Table 4. Frequency and Concentration of Use

Product Category	Freq of Use 2009[8,a]	Conc of Use (%) 2009[9]
Propylene glycol		
Baby products		
Shampoos	6 (56)	0.005-0.4
Lotions/oils/powders/creams	18 (137)	0.02
Others	26 (143)	0.001-0.003[b]
Bath preparations		
Oils, tablets, and salts	23 (314)	1-99
Bubble baths	24 (169)	1-5
Capsules	1 (4)	Not reported
Others	64 (234)	Not reported
Eye makeup preparations		
Eyebrow pencils	3 (144)	2-14
Eyeliners	94 (754)	0.2-16
Eye shadows	40 (1215)	0.03-18
Lotions	66 (254)	0.02-47
Makeup removers	21 (128)	0.03-2
Mascaras	130 (499)	0.3-16
Others	115 (365)	7[c]
Fragrance preparations		
Colognes and toilet waters	304 (1377)	0.3-6
Perfumes	117 (666)	0.03-5
Powders	3 (221)	0.005-1
Others	120 (566)	0.2-70
Noncoloring hair preparations		
Conditioners	446 (1226)	0.08-42
Sprays (aerosol fixatives)	60 (312)	0.003-4
Straighteners	129 (178)	4-25
Permanent waves	7 (69)	0.3-10
Rinses (noncoloring)	9 (33)	0.5-10
Shampoos	494 (1361)	0.06-5
Tonics, dressings, etc	468 (1205)	0.3-40
Wave sets	11 (51)	Not reported
Others	318 (807)	0.3-38
Hair coloring preparations		
Hair dyes and colors	1361 (2393)	5-15
Hair tints	20 (21)	10
Hair rinses	NR	1
Hair shampoos	16 (40)	Not reported
Hair color sprays (aerosol)	7 (7)	Not reported
Hair lighteners	5 (21)	Not reported
Hair bleaches	13 (149)	Not reported
Others	23 (168)	6-16
Makeup preparations		
Blushers	17 (434)	0.2-67
Face powders	15 (661)	0.009-0.2
Foundations	134 (589)	4-57
Leg and body paints	4 (29)	0.03-0.4
Lipsticks	39 (1883)	0.1-8
Makeup bases	42 (117)	0.1-21
Makeup fixatives	3 (45)	Not reported
Others	75 (485)	2-19
Manicuring preparations		
Basecoats and undercoats	3 (79)	Not reported
Cuticle softeners	11 (27)	4
Nail creams and lotions	6 (14)	0.02-12
Nail polish and enamel	8 (333)	0.008-0.9
Nail polish and enamel removers	2 (24)	0.0008-6
Others	15 (138)	Not reported
Oral hygiene products		
Dentrifrices	4 (59)	0.02-10
Mouthwashes and breath fresheners	9 (74)	0.04-5
Others	4 (86)	Not reported
Personal cleanliness products		
Bath soaps and detergents	502 (1665)	0.01-25
Underarm deodorants	313 (580)	3-73
Douches	4 (14)	1
Feminine deodorants	9 (19)	Not reported
Others	272 (792)	2-10[d]
Shaving preparations		
Aftershave lotions	174	0.02-8
Preshave lotions	1 (22)	Not reported
Shaving creams	37 (122)	4-40
Shaving soaps	3 (10)	Not reported
Others	59 (134)	Not reported
Skin care preparations		
Cleansers	398 (1446)	0.5-39
Depilatories	14 (42)	0.006-13
Face and neck	558 (1583)	5-30
Body and hand	648 (1744)	0.009-68
Face and neck sprays	No category	6
Body and hand sprays	No category	1-10
Foot powders and sprays	11 (47)	0.03
Moisturizing products	846 (2508)	0.2-41
Night preparations	121 (353)	0.004-20
Paste masks (mud packs)	136 (441)	0.1-11
Skin fresheners	84 (259)	0.002-7
Others	415 (1308)	2-20[e]
Suntan preparations		
Suntan gels/creams/liquids	43 (107)	0.01-5
Indoor tanning preparations	86 (240)	1-33
Others	19 (62)	10
Total for propylene glycol	9747 (34,391)	0.0008-99
Tripropylene glycol		
Fragrance preparations		
Perfumes	1 (666)	Not reported
Personal cleanliness products		
Underarm deodorants	7 (580)	21-22
Skin care preparations		
Moisturizing creams/lotions/powders	Not reported	0.00004
Total for tripropylene glycol	8	0.00004-22
Polypropylene glycol		
Fragrance preparations		
Colognes and toilet waters	30 (1377)	Not reported
Perfumes	4 (666)	Not reported
Hair coloring preparations		
Hair dyes and colors (requiring caution stmt)	6 (2393)	Not reported
Hair bleaches	1 (149)	Not reported
Makeup preparations (not eye)		
Blushers (all types)	1 (434)	Not reported

(continued)

(continued)

Table 4. (continued)

Product Category	Freq of Use 2009[8,a]	Conc of Use (%) 2009[9]
Personal cleanliness preparations		
Others	1 (792)	Not reported
Shaving preparations		
Aftershave lotions	1 (367)	Not reported
Skin care preparations		
Cleansers	1 (1446)	Not reported
Face and neck preparations (excl. shaving)	1 (1583)	Not reported
Suntan preparations		
Indoor tanners	1 (240)	Not reported
Total for polypropylene glycol	47	Not reported
PPG-9		
Bath preparation		
Others	3 (234)	Not reported
Eye makeup preparations		
Eye lotions	Not reported	11
Noncoloring hair preparations		
Shampoos (noncoloring)	74 (1361)	0.5
Personal cleanliness products		
Bath soaps and detergents	Not reported	22
Others	33 (792)	Not reported
Skin care preparations		
Cleansers	Not reported	0.05-0.4
Depilatories	Not reported	4
Face and neck creams, lotions, and powders	Not reported	15
Skin fresheners	Not reported	4
Total for PPG-9	110	0.05-22
PPG-12		
Noncoloring hair preparations		
Hair conditioners	2 (1226)	Not reported
Tonics, dressings, other hair grooming aids	1 (1205)	Not reported
Skin care preparations		
Face and neck creams, lotions, and powders	Not reported	1
Total for PPG-12	3	1
PPG-15		
Eye makeup preparations		
Eyeliners	1 (754)	Not reported
Total for PPG-15	1	Not reported
PPG-17		
Skin care preparations		
Face and neck (excl. shaving)	3 (1583)	1
Moisturizing creams, lotions, and powders	Not reported	1
Suntan preparations		
Suntan gels, creams, and liquids	Not reported	2
Total for PPG-17	3	1-2
PPG-26		
Fragrance preparations		
Perfumes	1 (666)	Not reported
Skin care preparations		
Face and neck creams, lotions, and powders	Not reported	0.2
Paste masks (mud packs)	Not reported	0.2
Others	1 (1308)	Not reported
Total for PPG-26	2	0.2
PPG-30		
Noncoloring hair preparations		
Tonics, dressings, other hair grooming aids	1 (1205)	Not reported
Skin care preparations		
Cleansers	3 (1446)	Not reported
Face and neck (excl. shaving)	1 (1583)	Not reported
Totals for PPG-30	5	Not reported
PPG-34		
Skin care preparations		
Paste masks (mud packs)	Not reported	20
Total for PPG-34	Not reported	20

[a] Total number in category given in parentheses.
[b] 0.003% in a rinse-off product.
[c] 7% in a brow and lash gel.
[d] 2% in a shower gel; 6% in a foot scrub.
[e] 6% in a vaginal area moisturizer/lubricant.

fibroblasts, and changes in cell morphology of fibroblasts and keratinocytes.[25] Fibroblast and keratinocyte proliferation was inhibited within 3 days after administration of PG; no significant changes in cell proliferation occurred with a 6-day administration. Propylene glycol was a moderately potent inhibitor, with an IC_{50} (concentration causing 50% proliferation inhibition) of 280 mmol/L for fibroblasts and 85 mmol/L for keratinocytes. The effect of PG on collagen contraction by fibroblasts was concentration dependent throughout the entire study. The concentration causing 50% contraction inhibition was 180 mmol/L.

The effect of PG on changes in cell morphology also was examined.[25] A gradual detachment of cells from the culture accompanied by changes in cell shape occurred in confluent keratinocyte cultures when the concentration of PG was increased above 5%. After 24 hours, replacing medium containing 5% PG with PG-free medium resulted in almost complete recovery within 48 hours. However, this recovery did not occur with 7% PG. Similar results were observed with fibroblasts, and the concentration inducing irreversible cell damage in both fibroblast and keratinocytes cultures was 660 mmol/L PG.

Single-Dose Toxicity

Oral

Polypropylene glycols. The acute toxicity of PPG 425 was evaluated using 2 groups of 3 rats (strain and gender not specified).[26] The rats were given a single oral dose of 250 or 1000 mg/kg PPG 425 by gavage and observed for 14 days. Animals of the low-dose groups had convulsions and loss of coordination, whereas animals of the high-dose group had

Table 5. Penetration Enhancement by PG

Test Chemical	Barrier	Methods	Results
Dihydroergotamine (DHE) mesylate	Excised male New Zealand white rabbit skin	-In vitro diffusion using Franz diffusion cells; several vehicles were used to examine their effect on the penetration of 16.0 mg/mL DHE; the penetration of various concentrations of DHE in PG was also examined	-the avg amount of DHE that penetrated from a water base during 24 h was 0.3 μg, with a max. rate of absorption of 0.02 μg/h during the 9- to 12- hour period; with a PG-vehicle, the avg amount of DHE that penetrated was 7.25 μg, with a max rate of absorption of 0.3 μg/h during the 12- to 24-hour time period; for comparison, the amount absorbed with PEG-400 and liquid paraffin vehicles was 3.05 and 4.14 μg DHE over 24 hours; -the avg amount of DHE that penetrated with 8, 16, 30, and 50 mg/mL DHE in PG was 3.78, 7.25, 14.47, and 38.98 μg over 24 hours[61]
Betamethasone 17-valerate (BMV); hydrocortisone 17-butyrate HCB); hydrocortisone (HC) (topical glucocorticoids [GCs])	Excised human abdominal skin	-The multilayer membrane system (MMS) was used to evaluate the penetration of the GC/PG gel formulations; time intervals for the penetration studies were 200 min and 24 h; -the relationship between the physicochemical properties of the drugs in binary PG/water mixtures and the rate and extent of their penetration was studied; -in vitro penetration through skin was determined	-with BMV gels, PG acted as a cosolvent as penetration was thermodynamically controlled; 10%-80% PG was evaluated—BMV penetration was almost unaffected with 10%-40% PG, was slightly increased with 40%-60% PG, and was decreased with >60% PG; the greatest amount of BMV in whole skin was found with 40% PG; -penetration of HCB with 10%-80% PG was evaluated, and the greatest penetration was with 20% PG; -with HC, the rate and penetration increased with increasing PG contents from 5% to 80% in suspension-type gel formulation; the enhancement effect of PG masked the thermodynamically-controlled behavior of HC; increased penetration of HC with increasing PG concentration was detected in the stratum corneum and the viable epidermis, but the amount permeating into the dermis was independent of PG content[62]
Pyrene butyric acid (PBA)	Excised female human breast skin	-Dermal penetration through skin was determined using glass diffusion cells; -the MMS was used for liberation studies; -the effect of fatty acids was also evaluated	-high PBA release rates from PG were seen in the MMS; -PBA and PG appear to penetrate simultaneously into the stratum corneum; at 1000 minutes, the ratio is increased indicating an accumulation or deposition of PBA due to more rapid PG-transfer into the epidermis; -PG penetrated better with the addition of fatty acids; mode of enhancement is non-specific[37]
Aspirin	Excised porcine ear epidermis	-in vitro studies using Franz cells, FTRI, and TEWL were used to determine penetration enhancement by PG, ethanol, and combinations of the 2	in all of the studies, the percutaneous absorption of aspirin was increased greatest with 80% ethanol/20% PG; these results were very similar to ethanol alone; PG alone did not significantly increase absorption of aspirin[63]
Diclofenac sodium (DFS)	Excised male Wistar rat skin	-DF5 gels were dissolved in water, a 20%-60% PG/water mixture, or 30%-40% PG/3%-5% isopropyl myristate (IPM)/water (pH 7.2)	-PG acted as a cosolvent, not a penetration enhancer; -PG/IPM synergistically enhanced drug flux; maximum enhancement ratios were with 40% PG[64]

convulsions. One high-dose animal died on day 1. All low-dose animals and the remaining 2 high-dose animals survived until study termination.

Parenteral

Propylene glycol. An acute study was performed in which female ICR mice were dosed intraperitoneally (ip) with 2600, 5200, or 10 400 mg/kg PG.[27] All except the high-dose mice survived 6 days after dosing. (The number of high-dose mice that died was not given.) Signs of toxicity, such as lethargy and ruffled hair coats, were not observed in the 2600 and 5200 groups.

Repeated-Dose Toxicity

Oral

Propylene glycol. Groups of 6 inbred male Wistar rats were dosed orally by gavage, daily, with 294.23 mg PG/100 g body wt (as 1 mL 28.4%/100 g) for 10 (group 1), 20 (group 2), or 30 days (group 3), and the effects on a number of intestinal parameters were determined.[28] Control groups received an equal volume of saline for 10, 20, or 30 days. After termination of dosing, animals were fasted overnight and then killed. All animals survived until study termination. Body weight gains were statistically significantly decreased for animals in group 1 and increased for animals in groups 2 and 3. A number of enzyme activities were enhanced; statistically significant increases were seen in sucrase activity in groups 1 and 2 and lactase and γ-glutamyl transpeptidase activity in group 3. Absorptive function was assessed by measuring nutrient uptake. Statistically significant increases of D-glucose and calcium uptake were seen in all groups and of glycine, L-asparate, and L-lysine uptake was seen in groups 1 and 2. Scanning electron microscopy revealed that PG did not affect the intestinal mucosal surface.

Nineteen male Han:Wistar rats were given drinking water containing 40 g/L PG for 2 weeks; a control group of 16 rats was given tap water.[29] The animals were placed in metabolism cages during the last 24 hours of dosing and urine was collected. Propylene glycol administration did not have any effect on urinary excretion of oxalic or alkoxyacetic acid, nor did it affect pH or urinary metabolites. Propylene glycol did not cause any renal effects.

Groups of 8 male and 8 female CD-1 mice were given 0.5%, 1.0%, 2.5%, 5.0%, and 10.0% PG in the drinking water for 14 days.[30] Negative controls were given untreated drinking water. Body weight gains of test animals were similar to or greater than controls. No animals died during the study.

Inhalation

Male and female Sprague-Dawley rats (number per group not given) were exposed to 0.16, 1.0, or 2.2 mg PG/L air for 6 hours/d, 5 days/week, for 13 weeks in a nose-only inhalation study.[31] There was no difference in body weights for any of the male dose groups, while mid- and high-dose females had significantly decreased body weights starting on days 64 and 50 of the study, respectively. Feed consumption was decreased for the females starting on days 50 and 43, respectively. Relevant differences occurred in some hematological parameters, serum enzyme activities, and lung, spleen, liver, and kidney weights; however these differences were inconsistent and without dose–response trends. The mid- and high-dose animals had increased goblet cells and increased mucin within these cells.

Ocular Irritation

Propylene glycol. The ocular irritation potential of PG was determined using groups of 6 male and female New Zealand white albino rabbits.[32] First, a single application of 1 drop of PG was instilled into the conjunctival sac of the left eye of each rabbit, and the eye was not rinsed. In the second part of the study, 1 drop of PG was instilled into the conjunctival sac of the left eye every 24 hours for 3 consecutive days. At both times, the contralateral eye was untreated and served as the control. The eyes were examined on days 1, 2, 3, and 7. With the single application, slight-to-moderate conjunctival hyperemia was observed on day 1 and resolved by day 2. The highest total score was 19 of 550, well below the category of marginal irritant (score of 65). Multiple instillations resulted in similar observations, with slight hyperemia lasting up to day 3 in 2 rabbits. The highest total score following multiple installations was 38 of 550, again below the category of marginal irritant.

Dermal Irritation/Sensitization

Propylene glycol. The dermal irritation potential of 100% PG was evaluated with male hairless SKH1 hr/hr mice.[33] Propylene glycol was instilled in polyvinyl chloride cups (vol 0.3 cm^3) on the dorsal side of 3 mice. The test substance remained in contact with the skin for 24 hours. At the end of the 24 hours, the animals were killed and a sample of the exposed skin was examined microscopically. Propylene glycol was minimally irritating, with a total score of 7 (maximum score =77).

Reproductive and Developmental Toxicity

Propylene glycol. The reproductive and developmental effects of PG were evaluated using mice, rats, rabbits, and hamsters.[34] Groups of 25 or 28 female albino CD-1 outbred mice were mated and 22, 22, 22, 20, and 23 gravid mice were dosed by oral intubation with 0.0, 16.0, 74.3, 345.0, and 1600.0 mg/kg aq PG on days 6 to 15 of gestation. Groups of 25 to 28 female albino Wistar rats were mated and 22, 23, 22, 20, and 24 were dosed as above, respectively. Positive control groups of 23 mice and 21 rats were given 150.0 or 250.0 mg/kg aspirin, respectively. Body weights were recorded at various intervals and general observations were made daily. Caesarian sections were performed on days 17 and 20 for all mice and rats, respectively. All fetuses were examined macroscopically for visceral or skeletal defects. Administration of PG did not affect

maternal or fetal survival in mice or rats, and there were no statistically significant differences in fetal anomalies between test and negative control groups in mice or rats.

Groups of 11, 11, 12, 14, and 13 gravid female Dutch-belted rabbits were dosed by oral intubation with 0, 12.3, 57.1, 267.0, or 1230.0 mg/kg aq PG on days 6 to 18 of gestation, respectively. A positive control group of 10 gravid rabbits was given 2.5 mg/kg 6-aminonicotinamide. Body weights were recorded at various intervals and general observations were made daily. Caesarian sections were performed on day 29. All fetuses were examined macroscopically and kept for 24 hours to evaluate survival. The pups were then examined viscerally and for skeletal defects. Administration of PG did not affect maternal or fetal survival, and there were no statistically significant differences in fetal anomalies between test and negative control group.

Groups of 24-27 female golden hamsters were mated and 21, 24, 25, 22, and 22 gravid hamsters were dosed by oral intubation with 0.0, 15.5, 72.0, 334.5, and 1550.0 mg/kg aq PG on days 6 to 10 of gestation, respectively. Positive controls were given 250.0 mg/kg aspirin. Body weights were recorded at various intervals and general observations were made daily. Caesarian sections were performed on day 14. All fetuses were examined macroscopically and for visceral or skeletal defects. Administration of PG did not affect matemal or fetal survival, and there were no statistically significant differences in fetal anomalies between test and negative control groups.

Propylene glycol was used as a vehicle in a reproductive and behavioral development study.[35] It was administered to 15 gravid Sprague-Dawley rats orally by gavage on days 7 to 18 of gestation at a volume of 2 mL/kg. Propylene glycol did not have any effects on reproductive or behavioral development parameters.

Female ICR mice were used to determine whether PG induced cytogenetic aberrations in mouse metaphase II (MII) oocytes that predispose zygotes to aneuploidy.[27] Groups of mice were first given an ip injection of 7.5 IU eCG to augment follicular maturation followed 48 hours later with 5 IU human chorionic gonadotropin (hCG) to induce ovulation. After 3 hours, mice were dosed ip with 1300, 2600, or 5200 mg/kg PG in distilled water. A control group was given distilled water only. For the MII portion of the study, ovulated oocytes were collected from 20 test animals/group and 30 control animals and processed for cytogenetic analysis 16 hours after administration of PG. The number of oocytes collected from test animals was nonstatistically significantly increased compared to controls. A statistically significant change in hyperploidy, hypoploidy, or single chromatids was not observed. An increase in the frequency of PCS at each dose was statistically significant, and the incidence of premature anaphase was statistically significantly greater in the 5200 mg/kg dose group as compared to controls. Neither metaphase I nor diploid oocytes were found.

For the zygote portion of the study, the female mice were paired with undosed males immediately after being given hCG; the females were dosed ip with 1300, 2600, or 5200 mg/kg PG 3 hours after hCG administration. The males were removed 16 hours after dosing with PG. Mated females were given colchine 22 hours after dosing with PG; zygotes were collected 18 hours later. There were 30, 40, 49, and 66 mice in the control, 1300, 2600, and 5200 mg/kg groups, respectively. The increase in hyperploidy was statistically significant in all test groups compared to controls. A statistically significant change was not seen for polyploidy or hypoploidy, and zygotes containing PCS, premature anaphase, or single chromatids were not found. The authors noted that there was no statistically significant difference in the proportion of zygotes collected for each group compared to oocytes. However, the number of zygotes analyzed compared to the number placed on slides was significantly decreased in the test groups; a relatively large portion of these zygotes had clumped chromosomes.

Genotoxicity

Tripropylene glycol. In a preincubation study with tripropylene glycol using *Salmonella typhimurium* strains TA1535, TA100, TA97, and TA98, the results were negative using concentrations of 0 to 10 000 µg/plate with and without metabolic activation.[36]

Clinical Assessment of Safety

Propylene glycol. Propylene glycol dermal penetration was reportedly enhanced by the addition of fatty acids, such as oleic acid.[37] Transepidermal water loss (TEWL) and attenuated total reflectance (ATR)-FTIR were used to evaluate participants exposed to PG and/or oleic acid.[38] The TEWL was determined using 10 participants (number of males and females not specified) with application of occlusive chambers containing nothing, 300 µL PG, or 300 µL 0.16 mol/L oleic acid in PG, for 3 or 24 hours. The fourth site was not treated and not occluded. The TEWL measurements were started 3 hours after chamber removal to reduce volatile solvents on the skin surface in order to avoid interference with the Evaporimeter. The site treated with oleic acid/PG increased water loss for a longer period in comparison to the PG only or empty sites. The 3- and 24-hour applications of PG resulted in an enhanced water loss ratio of 1.1. With oleic acid/PG, these values were 2.0 and 2.1, respectively.

For the ATR-FTIR portion, an occlusion system containing PG or oleic acid/PG was applied to the forearm of each participant; a third site was untreated. The chambers were removed after 3 hours, and ATR-FTIR spectra were recorded. Upon removal at the site where oleic acid/PG was applied, the absorbance at the wavelength measuring free acid indicated the presence of extra free acid, while the absorbance at the wavelength characteristic of esterified ester lipids was similar to untreated and PG-treated sites. The absorbance ratio for these 2 wavelengths leveled off to that of the untreated site 3 hours after removal of the chambers, indicating migration of oleic acid into lower cell layers or lateral spreading within the stratum corneum. The researchers also examined ATR-FTIR

Table 6. Clinical Dermal Irritation/Sensitization Studies With Propylene Glycol—Predictive

Dose	Participants	Procedure	Results
Irritation			
69.15% in a deodorant	20	24-h SIOPT	PII—0.25; significantly less irritating than the reference control[40]
68.06 in a deodorant	20	SIOPT	PII—0.13[41]
PG	12	occlusive chambers for 3 or 24 h; LDV	irritation index—1.1 (3 h); 1.2 (24 h) —slight erythema[42]
0.16 mol/L oleic acid/PG	12	occlusive chambers for 3 or 24 h; LDV	irritation index—2.1 (3 h); 3.9 (24 h) —clearly visible erythema[42]
35% in a deodorant	26 M	30-day use study	no potential for eliciting irritation or sensitization[43]
65.2% in a deodorant	40 F	30-day use study	no potential for eliciting irritation or sensitization[44]
73% in a deodorant	24 M	30-day use study	no potential for eliciting irritation or sensitization[65]
65.8% in a deodorant	26 M	4-week use study	no potential for eliciting irritation or sensitization[46]
Sensitization			
69.15%	18 M; 7F	maximization test	no sensitization reactions[47]
73% in a deodorant	30 M; 71F	RIPT	scores of + to 2 observed throughout the study; 4 participants discontinued during induction due to a repeat moderate reaction[48]
86% in a deodorant	99	RIPT	one + score observed throughout the study; no sensitization[49]

when the oleic acid/PG site was tape stripped 5 times, removing 50% of the thickness of the stratum corneum, 2 hours after removal of the application chambers. The results indicated oleic acid accumulates in a deeper layer after the tape stripping.

Dermal Irritation/Sensitization

Propylene glycol. Intradermal injection of 0.02 mL undiluted PG produced a wheal-and-flare reaction within minutes, while the same volume applied epidermally did not produce any reaction.[39] These authors reported that, occasionally, subjective or sensory irritation sometimes occurred in volunteers after application of various concentrations of PG. Some researchers have proposed classifying skin reactions to PG into 4 groups: (1) irritant contact dermatitis; (2) allergic contact dermatitis; (3) nonimmunologic contact urticaria; and (4) subjective or sensory irritation.

Predictive Testing—Irritation

The results of the clinical dermal predictive irritation and sensitization studies on PG described in this section are summarized in Table 6.

Propylene glycol. A 24-hour single insult occlusive patch test (SIOPT) was performed on an undiluted deodorant formulation containing 69.15% PG using 20 participants (gender not specified).[40] A clear stick deodorant was used as a reference control. The test sites were scored on a scale of 0 to 4. With the test formulation, 4 participants had a score of ± (minimal faint uniform or spotty erythema) and 3 participants had a score of 1 (pink-red erythema visibly uniform in the entire contact area.) The primary irritation index (PII) for the deodorant containing 69.15% PG was 0.25. This product was significantly less irritating than the reference control, which had a PII of 0.93 and 17 of 20 participants with scores between ± and 3.

In another SIOPT, a deodorant formulation containing 68.06% PG was tested undiluted using 20 participants (gender not specified)[41] A deodorant currently in use was used as a reference control. Three participants had a score of ± and 1 had a score of 1 to the test formulation. The PII for the test formulation was 0.13, which was not significantly different than the PII of 0.15 for the reference control.

The irritation index for PG and 0.16 mol/L oleic acid/PG was determined using 12 participants (number per gender not specified) by applying occlusive chambers containing these 2 test substance to the volar forearm for 3 or 24 hours.[42] An empty chamber was applied to a third site, and the fourth site was an untreated control. Laser Doppler velocimetry (LDV) was used to measure blood flow upon removal. After 3 and 24 hours, the irritation index for PG was 1.1 (6 participants) and 1.2 (10 participants), respectively, indicating a 1-fold increase in blood flow to the test site. The irritation index for oleic acid/PG was 2.1 (6 participants) and 3.9 (10 participants) after 3 and 24 hours, respectively. Visually, the 24-hour application of PG produced only slight erythema, while the 24-hour application of oleic acid/PG produced clearly visible irritation.

Thirty-day use studies were completed with 26 male, 40 female, and 24 male participants to evaluate the potential for deodorant sticks containing 35%,[43] 65.2%,[44] and 73% PG,[45] respectively, to induce dermal irritation and/or sensitization. The participants were instructed to apply the product to the underarm once daily for 30 days. None of the participants had any irritation or sensitization reactions, and the researchers concluded that the deodorant sticks containing 35%, 65.2%, or 73% PG did not demonstrate a potential for eliciting dermal irritation or sensitization. In a 4-week use study completed with 26 male participants following the same procedure, a deodorant stick containing 65.8% PG also did not demonstrate a potential for eliciting dermal irritation or sensitization.[46]

Predictive Testing—Sensitization

Propylene glycol. A maximization test was completed with 25 participants, 18 male and 7 female, to determine the sensitization potential of a deodorant containing 69.15% PG.[47] During the induction phase, an occlusive patch containing 0.1 mL of 0.25% aq sodium lauryl sulfate (SLS) was applied for 24 hours to the outer arm, volar forearm, or the back of each participant. That patch was removed and an occlusive patch containing 0.1 mL of the test substance was applied to the same site for 48 to 72 hours, after which time the patch was removed and the site examined. If there was no irritation, the sequence was repeated with the SLS and test article patches for a total of 5 induction exposures. If irritation occurred at any time, the SLS patch was excluded. After a 10-day nontreatment period, a challenge was performed in which a previously unexposed site opposite the test site was first pretreated with an occlusive patch containing 0.1 mL of 5% aq SLS for 1 hour. Then an occlusive patch containing the test substance was applied for 48 hours, and the site was scored 1 hour and 24 hours after removal. All the scores were 0 for all participants following challenge. No sensitization reactions were seen to a deodorant containing 69.15% PG.

An RIPT was completed with 101 participants, 30 male and 71 female, to determine the sensitization potential of a stick deodorant formulation containing 73% PG.[48] During the induction phase, semiocclusive patches containing 0.2 g of the test material were applied to the upper back of each participant for 24 hours, 3 times per week, for a total of 9 applications. The first patch was scored (scale of 0-4) immediately after removal, while all others were scored prior to application of the next patch 24 to 48 hours later. During the induction phase, a score of 2 (moderate reaction) resulted in moving the patch to an adjacent site, while a second score of 2 or scores of 3 to 4 (marked severe) resulted in discontinuation of dosing. The challenge was performed approximately 2 weeks after the final induction patch using the same procedure but at an adjacent previously untested site. Challenge sites were scored 24 and 72 hours after application. Scores of + (barely perceptible or spotty erythema) to 2, with some dryness, were observed throughout the study. Four participants discontinued dosing during the induction phase because of a second moderate reaction. While the authors stated that a stick deodorant formulation containing 73% PG "did not indicate a clinically significant potential for dermal irritation or allergic contact sensitization," the Expert Panel questioned that conclusion since repeated reactions were observed.

Another RIPT was completed with 99 participants to determine the sensitization potential of a stick antiperspirant formulation containing 86% PG.[49] (Initially, 113 participants were enrolled in the study; withdrawal was not due to adverse effects.) Occlusive patches containing 0.2 g of the test formulation were applied to the infrascapular region of the back 9 times during induction and once during challenge. One "+" reaction was observed during the entire study. There was no evidence of sensitization with an antiperspirant containing 86% PG.

Provocative Testing—Sensitization

Propylene glycol. Thirty-six patients with chronic venous insufficiency (CVI) were patch tested with 5% PG in petrolatum by application to the back for 2 days.[50] Twelve patients were male; 2, 5, and 5, had first-, second-, and third-degree CVI, respectively. Twenty-four patients were female; 5 and 19 had second- and third-degree CVI, respectively. (Procedural details not provided.) The results were read after 2 and 3 days; doubtful reactions were read after 4 days. The sensitization rate as a percentage of all patients was 8.3%. The sensitization rate of patients with second- and third-degree CVI tested with PG was 10% and 8.3%, respectively. Significant differences were found between males and females; 12.5% of females were sensitized while 0% of males were sensitized.

During the period 2000 to 2004, 308 patients, 111 males and 197 females, with contact dermatitis were patch-tested using the European standard series and some additional chemicals, including PG.[51] Patches were applied to the upper back using Finn chambers that were held in place with Scanpor tape. The patches were removed after 2 days, and the sites were evaluated after 30 minutes and 4 days. Propylene glycol, 5% in petrolatum, did not cause any positive reactions.

Photoallergenicity

Propylene glycol. Over a 2-year period, 30 males and 52 females with photoallergic contact dermatitis were photopatch tested with a standard series of sunscreens as well as some additional chemicals, including PG.[52] (Dose not given.) The allergens were applied in duplicate on the back and covered with opaque tape. After 24 hours, the tape was removed, the test sites evaluated, and one set of test sites was irradiated with an UVA dose of 5 J/cm^2 (using a Daavlin UVA cabinet), giving an irradiance of 10.4 mW/cm^2; this provided a 320 to 400 nm spectrum. The test sites, which were not covered after irradiation, were evaluated 24 and 72 hours later. While some positive reactions were observed to other test agents, PG did not produce a photoallergenic or contact allergy response.

Enhancement of Irritation Effects

Propylene glycol. The effect of the addition of PG to an isopropanol vehicle on the irritant reaction of benzoic acid was determined in a nonocclusive test using 15 participants, 7 males and 8 females.[53] Benzoic acid in isopropanol was tested at concentrations of 31, 62, 125, and 250 mmol/L without PG as well as with the addition of 1%, 2%, 5%, 10%, and 25% PG. The vehicles were also tested. Visual appearance, laser Doppler flowmetry, and skin color (using a Minolta chromameter) were measured at 20, 40, and 60 minutes after application. Propylene glycol enhanced the strength of the reactions to 125 and 250 mmol/L benzoic acid but not to 31 or 62 mmol/L benzoic acid. (This was observed using all 3 measurement methods.) Enhancement was observed with the addition of 1% PG, and maximal enhancement was attained with 5%. No reaction to application of the vehicles was observed.

Retrospective Analyses

The North America Contact Dermatitis Group (NACDG) performed a number of retrospective analyses on various dermatological conditions, determining that ≤6.0% of patients tested had positive reactions to 30% aq PG. These studies are summarized in Table 7.

Case Reports

A few case reports have been described concerning PG and hand dermatitis or atopic dermatitis. Patch test results generally had a positive reaction to PG in these case studies. Improvement was seen with the avoidance of PG-containing products.[54,55]

Summary

Both PG and PPGs were reviewed by the CIR Expert Panel in 1994, and it was concluded that these ingredients were safe for use in cosmetic products at concentrations up to 50.0%. This rereview was opened to amend the conclusion (the concentration of use of PG is >50%), consider new data, and to add new ingredients so that all of the PPGs identified in the *International Cosmetic Ingredient Dictionary and Handbook*, that is, PPG-3, PPG-7, PPG-9, PPG-12, PPG-13, PPG-15, PPG-16, PPG-17, PPG-20, PPG-26, PPG-30, PPG-33, PPG-34, PPG-51, PPG-52, and PPG-69, as well as tripropylene glycol, are included.

Propylene glycol is an aliphatic alcohol that is manufactured as a reaction product of propylene oxide and water. Tripropylene glycol is manufactured by sequential addition of propylene oxide to PG and is only of 3 chain length. Polypropylene glycols are manufactured by the addition of propylene oxide to dipropylene glycol and have average chain lengths of their "n" value; for example, PPG-3 would have an average chain length of 3. The USP grade PG (used in cosmetics) manufactured by Dow contains diethylene glycol and ethylene glycol at concentrations that are nondetectable (quantification limit of 0.008% wt/wt). Two companies reported that the concentration of propylene oxide in PPGs used to make finished products is ≤10 ppm propylene oxide.

In 1984, PG was reported to the FDA as being used in 5676 cosmetic formulations at concentrations of 0% to >50%. As of 2009, the use of PG has increased significantly, and PG was reported to FDA as being used in 9747 cosmetic formulations. Concentration of use has also increased, with bath oil/tablet/salt preparations containing up to 99% PG and leave-on formulations, including deodorants, containing up to 73% PG. The PPGs are not as widely used as PG, and the maximum reported concentration is 22%. Tripropylene glycol is used in 8 formulations, 7 of which are deodorants, at up to 22%.

Dermal penetration of PG from a ternary cosolvent solution through hairless mouse skin was 57% over a 24-hour period. Using TED-FTIR spectroscopy, it appeared that PG molecules did not reach the dermis in human skin.

Propylene glycol can act as a penetration enhancer for some chemicals and under some conditions. Often, it works synergistically with other enhancers. The mechanism by which PG enhances penetration has not been definitively identified.

Few toxic effects were seen in dosing with PG or PPGs. In an acute oral toxicity study, 3 of 3 rats dosed with 250 mg/kg and 2 of 3 rat dosed with 1000 mg/kg PPG 425 survived. All mice survived in a repeated-dose oral toxicity study in which mice were given 10% PG in drinking water for 14 days. Repeated-dose inhalation data reported some effects in rats due to PG exposure of 2.2 mg/L air for 6 hours/d, 5 days/week, for 13 weeks, but these effects were inconsistent and without dose–response trends.

Undiluted PG was less than marginally irritating to rabbit eyes In a dermal irritation study in mice, undiluted PG was minimally irritating.

Oral administration of PG did not have any adverse reproductive or developmental effects when evaluated in mice and rats at doses of ≤1600 mg/kg, rabbits at doses of ≤1230 mg/kg, or hamsters at doses of ≤1550 mg/kg. A study examining induction of cytogenetic aberrations in mice reported an increase in the frequency of premature centrosphere separation with 1300 to 5200 mg/kg PG. In zygotes from PG-dosed mice, hyperploidy was increased.

Tripropylene glycol, ≤10 000 µg/plate, was not mutagenic in an Ames assay.

Combined exposure to PG and oleic acid synergistically enhanced the dermal penetration of both compounds. Addition of PG to an isopropanol vehicle enhanced the irritant reactions of benzoic acid; maximal enhancement was seen with 5% PG.

The dermal irritation potentials of deodorant formulations containing 68.06% or 69.15% PG were evaluated in an SIOPT and compared to a reference in-use control formulation; the formulations containing PG were no more irritating or even less irritating than the reference control. Use studies of deodorant formulations containing 35% to 73% PG did not report any potential for eliciting irritation or sensitization. Deodorant formulations containing 69.15% or 86% PG did

Table 7. Retrospective Analyses With Propylene Glycol

No. of Patients	Years Studied	% PG	Methods	Findings
Not given	1984-1996	10 aq.	data were collected from NACDG-reported studies; the SPIN for each allergen was calculated as the proportion of the population allergic by the weighted clinician-assessed likelihood of relevance of the reaction	the SPIN rank for PG has changed over time: 23 in 1984-1985; 40 in 1992-1994; 41 in 1994-1996[66]
45 138 patients (16 210 males; 28 928 females)	1992-2002	20 aq.	Analysis of a large pool of IVDK patch-test data, examining possible relevance of patient characteristics	- 1044 patients (2.3%), 412 males and 632 females, had positive reactions; 895, 129, and 20 patients had 1+, 2+, and 3+ reactions, respectively; of the 895 1+ reactions, 114 were to PG only; - 1041 doubtful, 43 follicular, and 271 irritant reactions were observed; - there were little difference between patients with positive and negative reactions to PG; the greatest difference was the high portion (27.2% vs. 13.1%) of patients with leg dermatitis – this was the only sig. risk factor; - the most common concomitant reactions were with fragrance mix, balsam of Peru, lanolin alcohol, amerchol L-101, and nickel sulfate[67]
23 359 patients	1996-2006	30 aq.	retrospective cross-sectional analysis of NACDG patch-test data to evaluate the patient characteristics, clinical relevance (definite – positive reaction to a PG-containing item; probable—PG was present in the skin contactants; possible—skin contact with PG-containing material was likely), source of exposure, and occupational relationship	- 810 patients (3.5%) had reactions to PG; 12.8% of the reactions were definitely relevant, 88.3% were currently relative (definite, probable or possible relevance), 4.2% were occupation related; -135 patients were positive to only PG; in these patients, the face was the most commonly-affected area (25.9%), a scattered or generalized pattern was next (23.7%); - the most common concomitant reactions were with balsam of Peru, fragrance mix, formaldehyde, nickel sulfate, and bacitracin[68]
1494 patients w/SGD (patient pop. 10 061)	2001-2004	30 aq.	retrospective analysis of cross-sectional NACDG data using only patients with SGD as the sole site affected	89 patients (6.0%) had positive reactions to PG; 94% of the reactions were currently relative, with 30.3, 20.2, and 42.7% being of definite, probable, and possible relevance[69]
10 061 patients	2001-2004	30 aq.	retrospective analysis of cross-sectional NACDG data to determine reactions to foods	109 patients (1.1%), 37 males and 72 females, had 122 reactions to foods; of those 122 reactions, 5 were to PG[70]

Abbreviations: IVDK, Information Network of Departments of Dermatology; NACDG, North America Contact Dermatitis Group; SGD, scattered generalized distribution; SPIN, significance-prevalence index number

not induce sensitization reactions; however, questionable results were obtained in an RIPT of a deodorant containing 73% PG.

In a provocative study in which the sensitization potential of PG was evaluated in patients with contact dermatitis, 5% PG in petrolatum did not cause any positive reactions in a patch test. Retrospective analysis of pools of patient patch test data, mostly NACDG data, indicated that, 6.0% or less of patients tested had positive reactions to 30% aq PG. Additionally, PG (concentration not specified) did not produce a photoallergic response in a provocative photopatch test.

Discussion

The CIR Expert Panel reopened the 1994 safety assessment of PG and PPGs to address the safety of current high-use-concentrations of PG as well as to add all the PPGs currently listed in the *International Cosmetic Ingredient Dictionary and Handbook*. This report is intended to also address the safety of similar PPGs that may be used as cosmetic ingredients in the future.

Since tripropylene glycol is similar to PG and the PPGs, its safety can be supported by the existing data and, therefore, the Panel included tripropylene glycol in this safety assessment.

Propylene oxide is used in the manufacture of PPGs but should not appear in cosmetic formulations because of safety concerns. The Panel expects that PPGs contain $\leq$10 ppm propylene oxide, ensuring the safety of formulations in which PPGs are used.

Both PG and PPGs were not considered to be acute or chronic toxicants in oral or dermal studies, were not genotoxic or carcinogenic, and were not reproductive or developmental toxicants, supporting that their use in cosmetics would be safe in regard to these end points.

At the time of the original safety assessment, a concentration limit of 50% PG and PPGs was established based on the results of existing irritation and sensitization studies. The potential for skin irritation was especially of concern under occlusive conditions, and this potential could be concentration dependent. An RIPT performed using a stick antiperspirant containing 86% PG produced no evidence of sensitization. Additionally, use studies of deodorant sticks containing 35% to 73% PG did not demonstrate a potential for eliciting dermal irritation or sensitization. Therefore, the Panel determined that PG would not present a sensitization risk at the concentrations currently in use.

The Expert Panel did note that PG may act as a penetration enhancer. Some cosmetic ingredients have been regarded as safe based on the fact that they do not penetrate the skin. If PG enhances penetration of such ingredients, then they should not exist together in formulation.

Additionally, PG is used in aerosols. 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 to 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 absence of significant inhalation toxicity data, the Panel determined that PG can be used safely in hair sprays because the product particle size is not respirable.

The CIR Expert Panel, as noted earlier, considers that the available data for PPG-3 through PPG-69 would extend to any PPG-n to be used in cosmetics in the future. There are no concerns regarding residual monomers in PPGs. If the "n" in PPG-n is 32, for example, ample evidence suggests that its toxicity would be no different from PPG-30 or PPG-33. If the "n" is 120, the ingredient would be sufficiently large so that no dermal penetration would be possible.

Conclusion

The CIR Expert Panel concluded that PG, tripropylene glycol, PPG-3, -7, -9, -12, -13, -15, -16, -17, 20, -26, -30, -33, -34, -51, -52, -69, and any PPG $\geq$3 are safe as cosmetic ingredients in the present practices of use and concentration as described in this safety assessment when formulated to be nonirritating. 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 the group.

Authors' Note

Unpublished sources cited in this report are available from the Director, Cosmetic Ingredient Review, 1101 17th St, Suite 412, Washington, DC 20036, USA.

Declaration of Conflicting Interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: The articles in this supplement were sponsored by the Cosmetic Ingredient Review. The Cosmetic Ingredient Review is financially supported by the Personal Care Products Council.

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Erratum

International Journal of Toxicology
31(Supplement 2) 2615

DOI: 10.1177/1091581812464367
http://ijt.sagepub.com

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The second author should have been listed as Bart Heldreth.

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: F. Alan Andersen, Ph.D.
Director - COSMETIC INGREDIENT REVIEW (CIR)

FROM: Halyna Breslawec, Ph.D.
Industry Liaison to the CIR Expert Panel

DATE: June 5, 2013

SUBJECT: Comments on the Draft Report on the Alkyl PEG/PPG Ether Ingredients Prepared for the June 10-11, 2013 CIR Expert Panel Meeting

p.2 - If the RoC listings of ethylene and propylene oxides are going to be included in the Impurities section, why is the RoC listing of 1,4-dioxane omitted? The impurities section should note that ethylene oxide, propylene oxide and 1,4-dioxane are volatile and therefore, levels in ingredients are expected to be low.

p.3 - In the Use section, please note that the 5% use concentration for PEG/PPG-55/28 was reported for shampoos and other hair care products.

p.3, 4 - Rather than stating that PPG-3-Trideceth-6 can be used in food, it should be stated that it can be used in food contact materials.

1101 17th Street, N.W., Suite 300 | Washington, D.C. 20036-4702 | 202.331.1770 | 202.331.1969 (fax) | www.personalcarecouncil.org

Personal Care Products Council
Committed to Safety, Quality & Innovation

1101 17th Street, N.W., Suite 300
Washington, D.C. 20036-4702

Memorandum

TO: Lillian Gill, Ph.D.
Director - COSMETIC INGREDIENT REVIEW (CIR)

FROM: Halyna Breslawec, Ph.D.
Industry Liaison to the CIR Expert Panel

DATE: July 22, 2013

SUBJECT: Comments on the Tentative Report on the Alkyl PEG/PPG Ether Ingredients

p.4 - As dermal penetration decreases with increasing molecular weight, it would be helpful to indicate the approximate molecular weight range of the alkyl PEG ethers that were "readily absorbed through the skin of guinea pigs and rats".

p.4 - The last paragraph in the summary of the PPG dermal penetration data does not make sense. If 57% of the Propylene Glycol penetrated hairless mouse skin, it is hard to understand why none of it reached the dermis. Is the spectroscopy study a different study? Was it completed in a different species?

p.6 - What solvent was used in the rat nasal mucosa irritation study of Laureth-9? What was the duration of exposure in this study?

p.7 - How many carcinogenicity studies of Propylene Glycol have been completed? The sentence, "Propylene glycol was not carcinogenic in other oral, dermal, and subcutaneous studies." suggests that many studies are available. Were all these studies completed in rodents?

p.7 - Please delete the word "expected" in the following phrase: "...to predict expected dermal irritancy."

p.8 - Please give some indication of the number of subjects in the human studies of the alkyl PEG ethers and the PPG ingredients.

p.5, Table 2 - In the definition of PEG/PPG-8/2 Propylheptyl Ether "propylene ox" needs to be corrected.

p.14, Table 2 - In the definition of PPG-2-Laureth-8, "and y has an average value of 5" needs to be changed to "and y has an average value of 8". The structure for PPG-2-Laureth-12 in the Table is not the same as shown in the Dictionary. In the Dictionary the ethylene group has an x and the propylene group has y. Therefore, in Table 2, either the structure needs to be corrected to be the same as in the Dictionary, or the definition needs to be corrected. To correspond to the structure shown in Table 2, the definition should state: "that conforms to the formula where x has an average value of 2 and y has an average value of 12."

p.17, Table 2 - Please correct "when there was not structure available"

p.20, Table 4 - Under PPG-5-Ceteth-20, in the Incidental Inhalation-Spray row, please correct 41.5-10 (it should be 1.5-10).