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Safety Assessment of Alkyl PEG Ethers as Used in Cosmetics

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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.

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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] (CAS No. 68439-49-6)	C9-11 Pareth-4 (CAS No. 68439-46-3)	C12-14 Pareth 12 (CAS No. 68439-50-9)
Ceteareth-3[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 (CAS 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 (CAS No. 68002-97-1)	C12-15 Pareth 7 (CAS No. 68131-39-5)
Ceteareth-8[a] (CAS No. 68439-49-6)	C11-13 Pareth-6 (CAS No. 308060-94-8)	C12-15 Pareth 9 (CAS No. 68131-39-5)
Ceteareth-9[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 (CAS No. 68131-40-8)	C12-16 Pareth-5 (CAS No. 68551-12-2)
Ceteareth-13[a] (CAS No. 68439-49-6)	C11-15 Pareth-7 (CAS No. 68131-40-8)	C12-16 Pareth 7 (CAS No. 68551-12-2)
Ceteareth-14[a] (CAS No. 68439-49-6)	C11-15 Pareth-9 (CAS No. 68131-40-8)	C12-16 Pareth 9 (CAS No. 68551-12-2)
Ceteareth-15[a] (CAS No. 68439-49-6)	C11-15 Pareth-12 (CAS No. 68131-40-8)	C13-15 Pareth 21 (CAS No. 64425-86-1)
Ceteareth-16[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 (CAS 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 (CAS No. 246538-82-9)	C14-15 Pareth 12 (CAS 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 (CAS No. 68951-67-7)
Ceteareth 24[a] (CAS No. 68439-49-6)	C12-13 Pareth 1 (CAS No. 66455-14-9)	C20-22 Pareth 30
Ceteareth 25[a] (CAS No. 68439-49-6)	C12-13 Pareth 2 (CAS No. 66455-14-9)	C20-40 Pareth 3 (CAS No. 246538-83-0)
Ceteareth 27[a] (CAS No. 68439-49-6)	C12-13 Pareth 3 (CAS No. 66455-14-9)	C20-40 Pareth 10 (CAS No. 246538-83-0)
Ceteareth 28[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 (CAS 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 (CAS 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 (CAS 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] (CAS No. 68439-49-6)	C12-13 Pareth 10 (CAS No. 66455-14-9)	C30-50 Pareth 10 (CAS No. 246538-85-2)
Ceteareth 50[a] (CAS No. 68439-49-6)	C12-13 Pareth 15 (CAS No. 66455-14-9)	C30-50 Pareth 40 (CAS No. 246538-85-2)
Ceteareth 55[a] (CAS No. 68439-49-6)	C12-13 Pareth 23 (CAS No. 66455-14-9)	C40-60 Pareth 3 (CAS No. 246538-86-3)
Ceteareth 60[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 (CAS 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] (CAS No. 9004-98-2)	Coceth 5 (CAS No. 61791-13-7)
Oleth 5[a] (CAS No. 9004-98-2; 5353-27-5)	Oleth 82 (CAS No. 9004-98-2)	Coceth 6 (CAS No. 61791-13-7)
Oleth 6[a] (CAS No. 9004-98-2)	Oleth 100 (CAS No. 9004-98-2)	Coceth 7 (CAS No. 61791-13-7)
Oleth 7[a] (CAS No. 9004-98-2)	Oleth 106 (CAS No. 9004-98-2)	Coceth 8 (CAS No. 61791-13-7)
Oleth 8[a] (CAS No. 9004-98-2; 26996-03-2; 27040-03-5)	Cetoleth 2 (CAS No. 8065-81-4)	Coceth 10 (CAS No. 61791-13-7)
Oleth 9[a] (CAS No. 9004-98-2)	Cetoleth 4 (CAS No. 8065-81-4)	Coceth 20 (CAS No. 61791-13-7)
Oleth 10[a] (CAS 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 (CAS 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 (CAS No. 61791-28-4)
Oleth 20[a] (CAS No. 9004-98-2)	Cetoleth 18 (CAS No. 8065-81-4)	Talloweth 7 (CAS 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, $\geq$10%, thickening of the skin; formulation w/2.5%, minimal irritation; ceteth-10: 1 and 5%, erythema and edema, $\geq$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, $\geq$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 $\leq$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)), $\geq$21 g/kg (25% in corn oil or 40% in water); formulations with $\leq$ 2.75% steareth-2, >5 g/kg; steareth-10, 2.9 g/kg (unspecified concentration); steareth-20, $\sim$1.9 g/kg (unspecified concentration), $\sim$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, $\leq$60% and in formulation w/$\leq$2.75%, mildly irritating at most; steareth-10, 60%, mild irritant; steareth-20, 60%, mild irritant, in formulations w/$\leq$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/$\leq$4%, no toxic effects; dermal LD_{50}: >2.6 g/kg; formulation w/5%, 2 g/kg; Inhalation: 6-h exposure, 26 ppm (rats, mice, guinea pigs), slight irritation of mucous membranes, but no signs of systemic toxicity or mortality; 6 h exposure, 2220 mg/m^3, 100% mortality Short-term dermal: 20 day, 11.5%, 5x/day, exfoliative dermatitis, parakeratosis, hyperkeratosis (rabbits); 30 day, 30% in methyl alcohol and propylene glycol, dermal infiltrates of histocytes 3 mos dermal study: formulations w/20%, well-defined erythema, mild edema, no systemic toxicity (rabbits)	
	Dermal irritation/sensitization	Undiluted, minimally to slightly irritating; formulations w/2-4%, no to well-defined erythema and edema	
	Ocular irritation	Formulations w/$\leq$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, $\leq$6500 mg/m^3 (cynomolgus monkey); 6 wks, $\leq$ 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: $\leq$5.2 mL/kg, no maternal toxicity (rats)	
	Genotoxicity	Mutagenic effects: RK$^+$ 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)

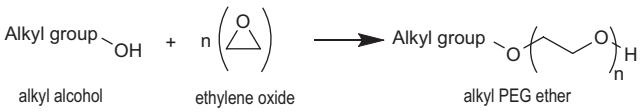
Table 2B. (continued)

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]

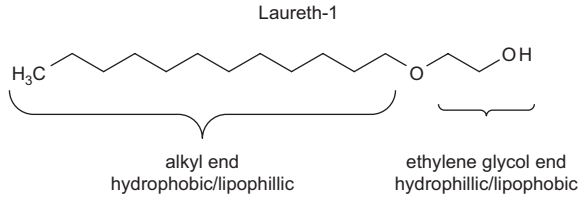
Chemistry

Definition and Structure

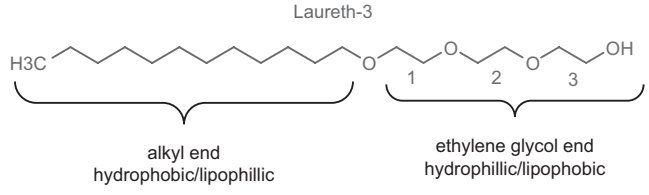
Alkyl PEG ethers. An alkyl PEG ether is the reaction product of an alkyl alcohol and 1 or more equivalents of ethylene oxide.[17]



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).

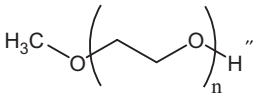
The European Commission's Scientific Committee on Consumer Products (SCCP) opinion on polidocanol (laureth 9) stated that these ingredients describe a class of alcohol ethoxylates with an average alkyl chain of 12 to 14 carbon atoms and an ethylene oxide chain of 9 ethylene oxide units.[19] To describe 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:

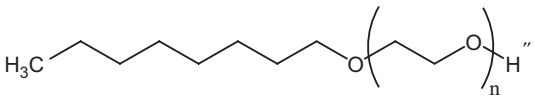


n = the average number of ethylene glycol units (eg, PEG-7 Methyl Ether (or Methoxy PEG-7) is when n = 7)

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:

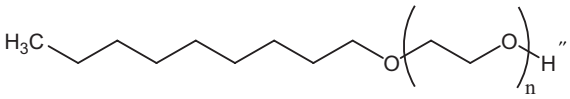


n = the average number of ethylene glycol units (eg, Capreth-4 is when n = 4)

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:

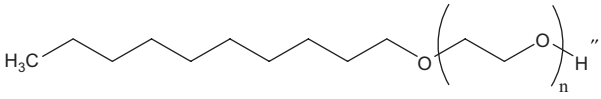


n = 9

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:



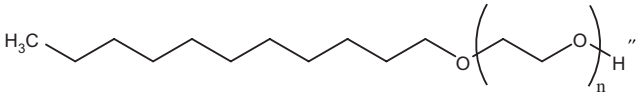
n = the average number of ethylene glycol units (eg, Deceth-4 is when n = 4)

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;** 5703-94-6**)**	334.49	138/403 °C	2.69
Deceth-5 (CAS No. **26183-52-8**)	378.54	166/438 °C	2.42
Deceth-6 (CAS No. **26183-52-8**)	422.60	182/473 °C	2.14
Deceth-7 (CAS No. **26183-52-8**)	466.65	208/509 °C	1.87
Deceth-8 (CAS No. **26183-52-8**)	510.70	233/544 °C	1.59
Deceth-9 (CAS No. **26183-52-8**)	554.75	250/579 °C	1.32

(continued)

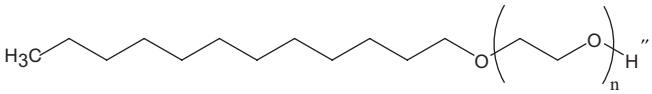
Table 3. (continued)

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:			



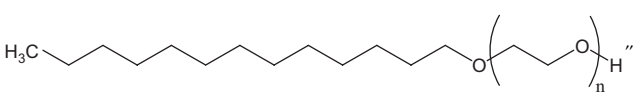
n = the average number of ethylene glycol units (eg, Undeceth-3 is when n = 3)

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)

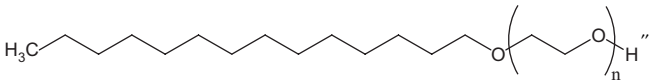
Table 3. (continued)

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:

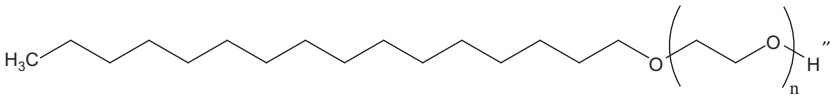


n = the average number of ethylene glycol units (eg, Myreth 3 is when n = 3)

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:



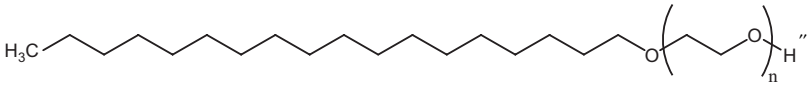
n = the average number of ethylene glycol units (eg, Ceteth 3 is when n = 3)

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)

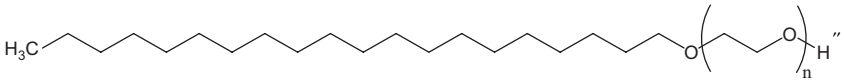
Table 3. (continued)

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:			



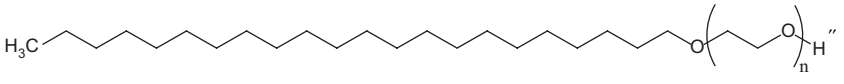
n = the average number of ethylene glycol units (eg, Steareth-3 is when n = 3)

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**; 16057-43-5)	358.60	152/425 °C	7.17
Steareth 3 (CAS No. **9005-00-9**; 4439-32-1)	402.65	175/460 °C	6.89
Steareth 4[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)

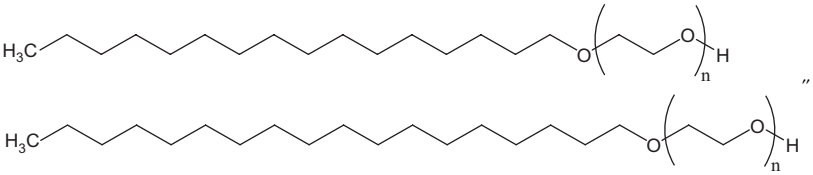
Table 3. (continued)

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.

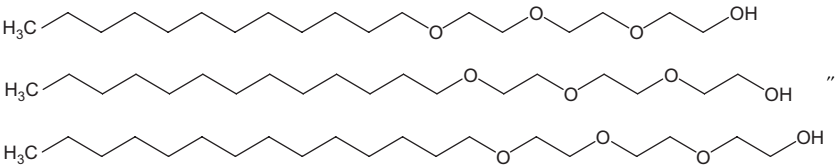
INCI Name	
Ceteareth 2[a] (CAS No. **68439-49-6**)	Molecular weight < 1000
Ceteareth 3[a] (CAS No. **68439-49-6**)	Molecular weight < 1000
Ceteareth 4[a] (CAS No. **68439-49-6**)	Molecular weight < 1000
Ceteareth 5[a] (CAS No. **68439-49-6**)	Molecular weight < 1000
Ceteareth 6[a] (CAS No. **68439-49-6**)	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.

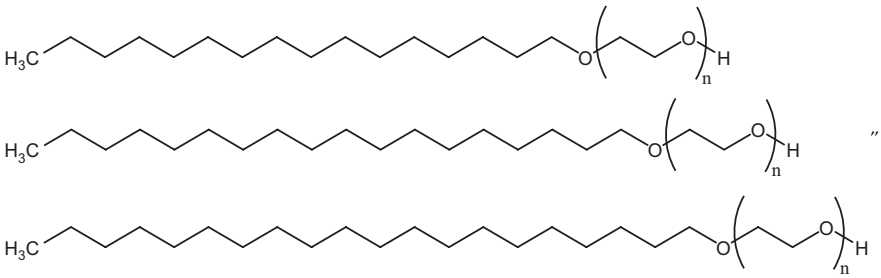
INCI Name	
C9-11 Pareth 3 (CAS No. **68439-46-3**)	Molecular weight < 1000
C9-11 Pareth 4 (CAS No. **68439-46-3**)	Molecular weight < 1000
C9-11-Pareth 6 (CAS No. **68439-46-3**)	Molecular weight < 1000
C9-11 Pareth 8 (CAS No. **68439-46-3**)	Molecular weight < 1000
C9-15 Pareth 8 (CAS No. **157627-88-8**)	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 (CAS No. **68551-12-2**)	Molecular weight < 1000
C13-15 Pareth 21 (CAS No. **64425-86-1**)	Molecular weight > 1000
C14-15 Pareth 4 (CAS No. **68951-67-7**)	Molecular weight < 1000
C14-15 Pareth 7 (CAS No. **68951-67-7**)	Molecular weight < 1000
C14-15 Pareth 8 (CAS No. **68951-67-7**)	Molecular weight < 1000
C14-15 Pareth 11 (CAS No. **68951-67-7**)	Molecular weight < 1000
C14-15 Pareth 12 (CAS No. **68951-67-7**)	Molecular weight < 1000
C14-15 Pareth 13 (CAS No. **68951-67-7**)	Molecular weight < 1000
C20-22 Pareth 30	Molecular weight > 1000
C20-40 Pareth 3 (CAS No. **246538-83-0**)	Molecular weight < 1000
C20-40 Pareth 10 (CAS No. **246538-83-0**)	Molecular weight ~ 1000
C20-40 Pareth 24 (CAS No. **246538-83-0**)	Molecular weight > 1000
C20-40 Pareth 40 (CAS No. **246538-83-0**)	Molecular weight > 1000
C20-40 Pareth 95 (CAS No. **246538-83-0**)	Molecular weight > 1000
C22-24 Pareth 33 (CAS No. **246538-84-1**)	Molecular weight > 1000
C30-50 Pareth 3 (CAS No. **246538-85-2**)	Molecular weight < 1000
C30-50 Pareth 10 (CAS No. **246538-85-2**)	Molecular weight ~ 1000
C30-50 Pareth 40 (CAS No. **246538-85-2**)	Molecular weight > 1000
C40-60 Pareth 3 (CAS No. **246538-86-3)**	Molecular weight < 1000
C40-60 Pareth 10 (CAS No. **246538-86-3**)	Molecular weight > 1000

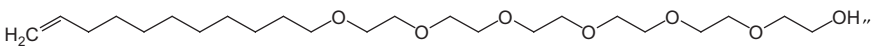
Hydrogenated Talloweths (mixture of 14, 16, and 18 carbon chains with a variable PEG)
General Structure:



n = the average number of ethylene glycol units (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.

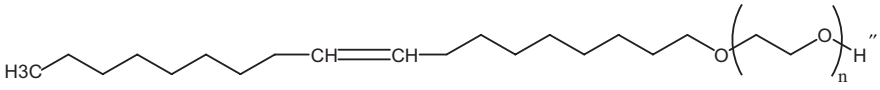
INCI Name	
Hydrogenated Talloweth 12	Molecular weight < 1000
Hydrogenated Talloweth 25	Molecular weight > 1000

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)

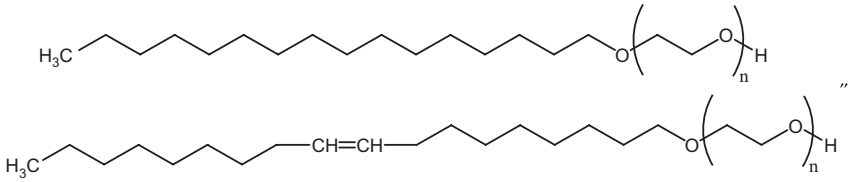
(continued)

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	–/–	–

Ceteleths (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, Ceteleth 6 is when n = 6)
As these are mixtures of 2 molecules at unknown ratios, molecular weights, and physical properties are not calculable.

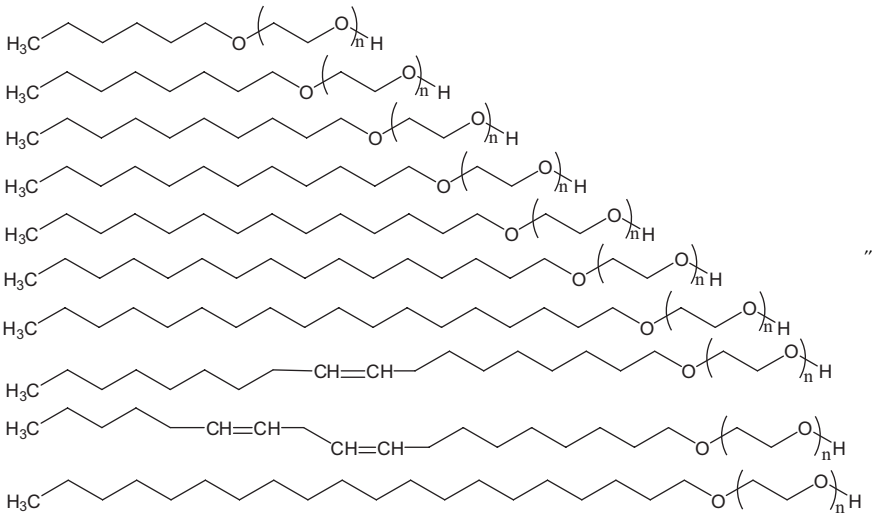
INCI Name	
Ceteleth 2 (CAS No. **8065-81-4**)	Molecular weight < 1000
Ceteleth 4 (CAS No. **8065-81-4**)	Molecular weight < 1000
Ceteleth 5 (CAS No. **8065-81-4**)	Molecular weight < 1000
Ceteleth 6 (CAS No. **8065-81-4**)	Molecular weight < 1000
Ceteleth 10 (CAS No. **8065-81-4**)	Molecular weight 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

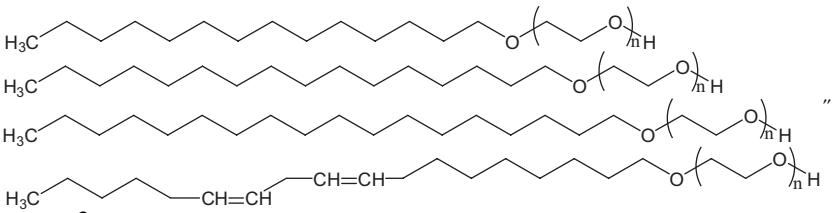
Coceths (mixture of 6, 8, 10, 12, 14, 18, Ω 9 unsaturated 18, Ω-6 unsaturated 18, and 20 carbon chains with a variable PEG)
General Structure:



n = the average number of ethylene glycol units (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

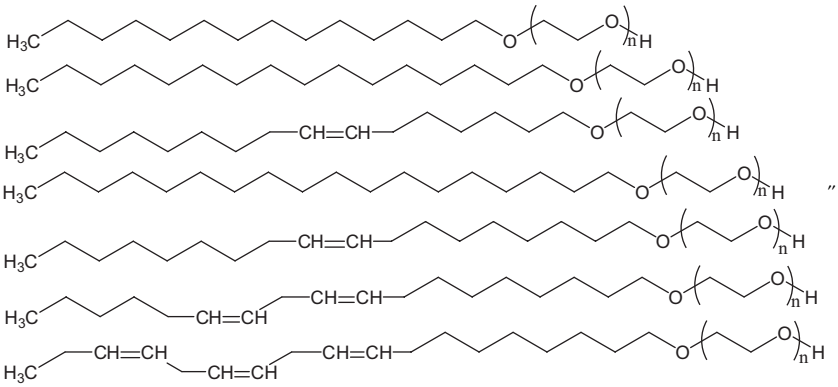
Talloweths (mixture of 14, 16, Ω-9 unsaturated 16, 18, Ω-9 unsaturated 18, Ω-6 unsaturated 18, and Ω-3 unsaturated 18 carbon chains with a variable PEG)

(continued)

Table 3. (continued)

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

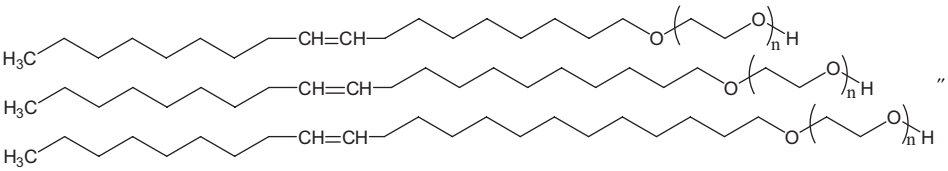
General Structure:



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

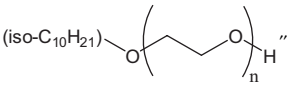
PEG Jojoba Alcohols (mixture of Ω-9 unsaturated 18, Ω-9 unsaturated 20, and Ω-9 unsaturated 22 carbon chains with a variable PEG)
General Structure:



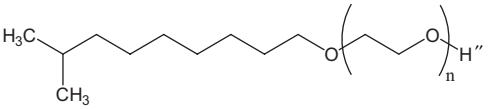
n = the average number of ethylene glycol units (eg, PEG-15 Jojoba Alcohol is when n = 15)
As these are mixtures of more than one molecule at unknown ratios, molecular weights and physical properties are not calculable.

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.

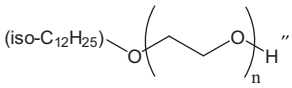
(continued)

Table 3. (continued)

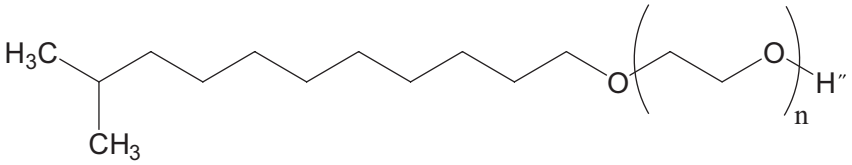
Methoxy PEG-n / PEG-n Methyl Ethers (a methyl group attached to a variable length PEG chain)

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:



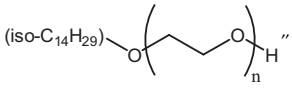
n = the average number of ethylene glycol units (eg, Isolaureth 10 is when n = 10); "iso" = a mixture of branched isomers, one example of which would be:



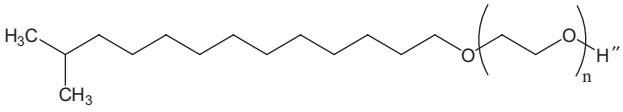
As these are mixtures of more than one isomer at unknown ratios, physical properties are not calculable.

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:



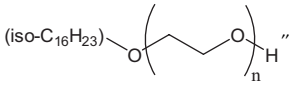
n = the average number of ethylene glycol units (eg, Isomyreth 9 is when n = 9); "iso" = a mixture of branched isomers, one example of which would be:



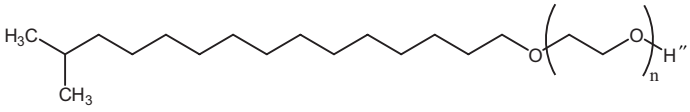
As these are mixtures of more than one isomer at unknown ratios, physical properties are not calculable.

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.

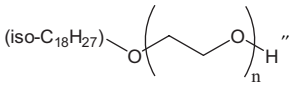
(continued)

Table 3. (continued)

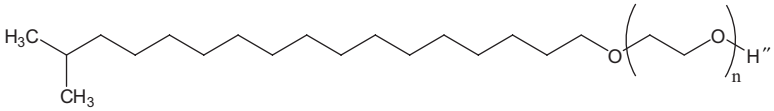
Methoxy PEG-n / PEG-n Methyl Ethers (a methyl group attached to a variable length PEG chain)

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:



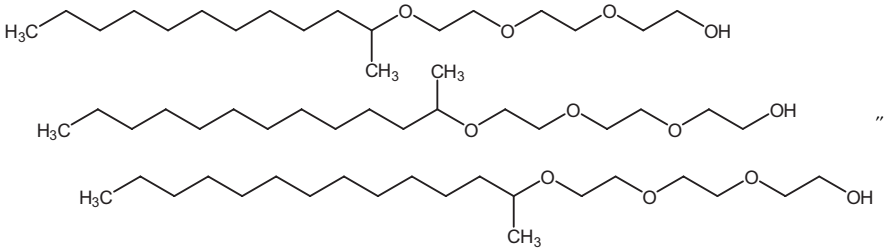
n = the average number of ethylene glycol units (eg, Isosteareth 6 is when n = 6); "iso" = a mixture of branched isomers, one example of which would be:



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

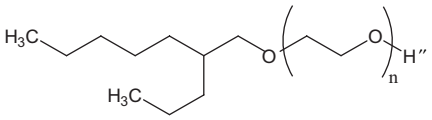
(continued)

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

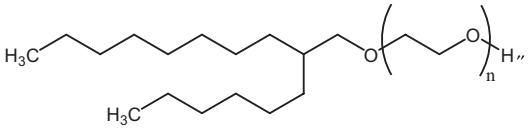
PEG Propylheptyl Ethers (3 carbon chains β-substituted 7 carbon chains with a variable PEG)
General Structure:



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

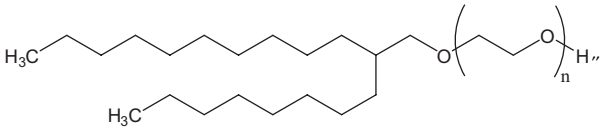
Hexyldeceths (6 carbon chains beta-substituted (β-substituted) 10 carbon chains with a variable PEG)
General Structure:



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

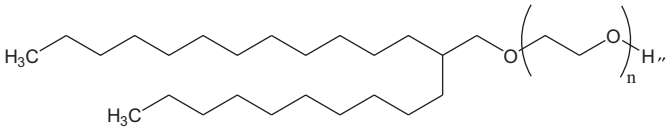
Octyldodeceths (8 carbon chains β-substituted 12 carbon chains with a variable PEG)
General Structure:



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)

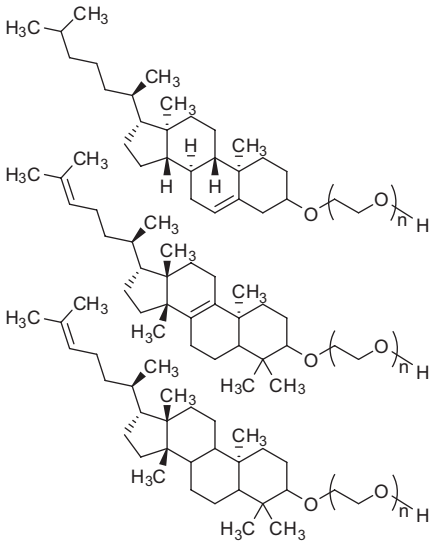
Methoxy PEG-n / PEG-n Methyl Ethers (a methyl group attached to a variable length PEG chain)

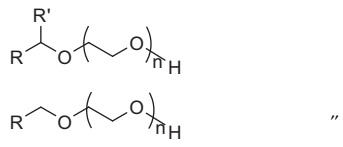
INCI Name	Molecular Weight	M.P. / B.P.	$logK_{o/w}$
Decyltetradeceth 5	574.92	256/594	9.22
Decyltetradeceth 10	795.18	339/770	7.85
Decyltetradeceth 15	1015.44	–/946	6.47
Decyltetradeceth 20	1235.70	–/1123	5.10
Decyltetradeceth 25	1455.97	–/1299	3.73
Decyltetradeceth 30	1676.23	–/1475	2.36

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

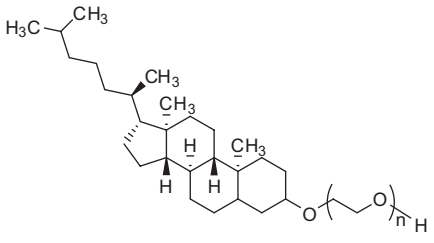
n = the average number of ethylene glycol units (eg, Laneth 25 is when n = 25)

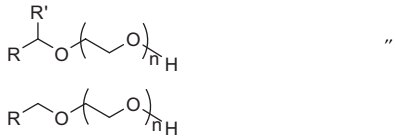
As these are mixtures of more than one molecule at unknown ratios, molecular weights and physical properties are not calculable.

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)

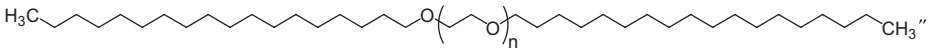
Methoxy PEG-n / PEG-n Methyl Ethers (a methyl group attached to a variable length PEG chain)

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

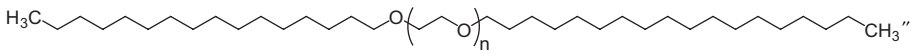
Hydrogenated Dimer Dilinoleths and PEG-4 Distearyl Ether (variable PEG capped at each end with a saturated 18 carbon chains)
General Structure:



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	–/–	–

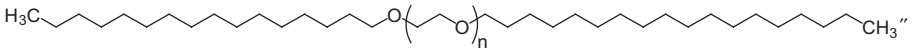
PEG Cetyl Stearyl Diether and Steareth 60 Cetyl Ether (variable PEG capped at one end with a saturated 18 carbon chains and at the other end with a saturated 16 carbon chains)
Structure:



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	$logK_{o/w}$

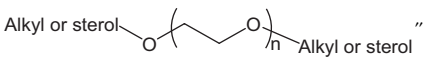
Structure:



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	–/–	–

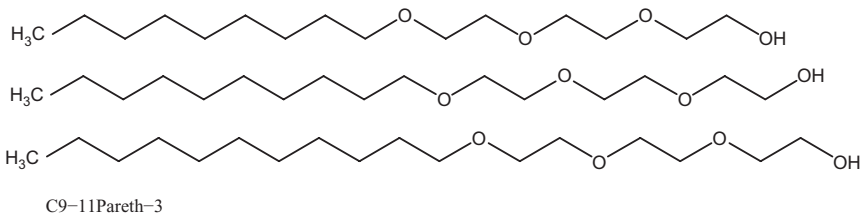
PEG-4 Ditallow Ether (a 4-unit PEG independently capped at each end with one of a 14, 18, 18, Ω-9 unsaturated 18, Ω-6 unsaturated 18, or Ω-3 unsaturated 18 carbon chains) and ***PEG-16 Cetyl/Oleyl/Stearyl/Lanolin Alcohol Ether*** (a 16-unit PEG independently capped at each end with a variable length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



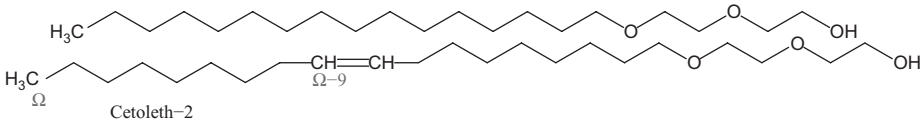
n = the average number of ethylene glycol units (eg, PEG-16 Cetyl/Oleyl/Stearyl/Lanolin Alcohol Ether is when n = 16)
As these are mixtures of more than one molecule at unknown ratios, molecular weights and physical properties are not calculable.

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.

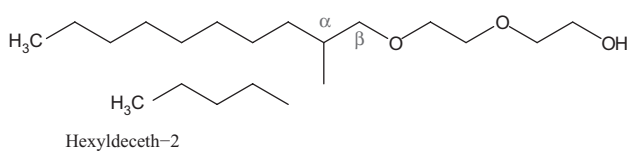


Partially unsaturated alkyl PEG ethers. Also included in this review are partially unsaturated straight chain ingredients. These include undecyleneth 6 (omega 1 [Ω-1] unsaturated 11 carbon chains with a 6-unit PEG); oleths (Ω-9 unsaturated 18 carbon chains with a variable PEG); cetoleths (mixture of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

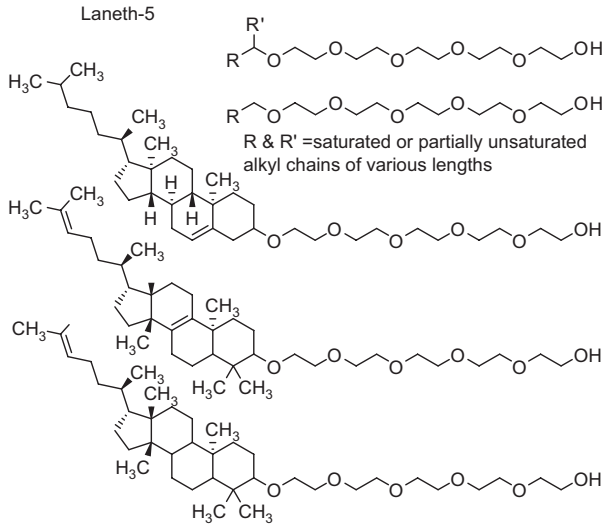


Although the above Ω-9 unsaturated chain is drawn with stereochemical ambiguity at the double bond, the *cis* isomer is actually more likely if the parent alcohol was obtained from natural sources.

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); isostearethss (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:

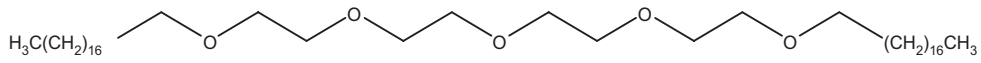


Sterol-containing PEG ethers. Another grouping of ingredients within this review contains PEG ethers of sterols. These ingredients consist of the laneths (mixture of various length saturated and partially unsaturated alkyl chains, cholesterol, lanosterol, and dihydrolanosterol with a variable PEG) and 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 $\sim$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		Cetoleth 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		Isosteareth 2		Isosteareth 5		Isosteareth 10		Isosteareth 20		C12-14 Sec-Pareth 5	
Totals	1	0.002-0.1	2	1	NR	0.006	8	1	14	0.5-6	5	0.06-0.09
Duration of Use												
Leave On	1	0.002-0.1	1	NR	NR	0.006	5	1	12	1-6	1	0.06
Rinse Off	NR	0.004	1	1	NR	NR	3	NR	2	0.5-2	4	0.09
Exposure Type												
Eye Area	NR	NR	NR	NR	NR	NR	NR	NR	NR	0.8	NR	NR
Possible Ingestion	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Inhalation	NR	NR	1	NR	NR	NR	NR	NR	2	NR	NR	NR
Dermal Contact	1	0.1	NR	NR	NR	0.006	3	1	3	0.5-5	NR	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	1	1	3	1-5	NR	NR
Hair—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
Beheneth 2
Beheneth 5
Beheneth 15
C9-11 Pareth 3
C9-11 Pareth 4
C9-15 Pareth 8
C10-16 Pareth 1
C10-16 Pareth 2
C11-13 Pareth 6
C11-13 Pareth 9
C11-13 Pareth 10
C11-15 Pareth 12
C11-15 Pareth 15
C11-15 Pareth 20
C11-15 Pareth 30
C11-21-Pareth 3
C11-21-Pareth 10
C12-13 Pareth 1
C12-13 Pareth 2
C12-13 Pareth 4
C12-13 Pareth 5
C12-13 Pareth 6
C12-13 Pareth 9
C12-13 Pareth 10
C12-13 Pareth 15
C12-14 Pareth 5
C12-14 Pareth 7
C12-14 Pareth 9
C12-15 Pareth 2
C12-15 Pareth 4
C12-15 Pareth 5
C12-15 Pareth 10
C12-15 Pareth 11
C12-16 Pareth 5
C13-15 Pareth 21
C14-15 Pareth 4
C14-15 Pareth 7
C14-15 Pareth 8
C14-15 Pareth 11
C14-15 Pareth 12
C14-15 Pareth 13
C20-22 Pareth 30
C20-40 Pareth 24
C22-24 Pareth 33
C30-50 Pareth 3
C30-50 Pareth 10
C30-50 Pareth 40
C40-60 Pareth 3
C40-60 Pareth 10
C11-15 Sec-Pareth 12
C12-14 Sec-Pareth 3
C12-14 Sec-Pareth 8
C12-14 Sec-Pareth 9
C12-14 Sec-Pareth 12
C12-14 Sec-Pareth 15
C12-14 Sec-Pareth 20
C12-14 Sec-Pareth 30
C12-14 Sec-Pareth 40
C12-14 Sec-Pareth 50
Capryleth 4
Capryleth 5
Ceteareth 4
Ceteareth 8
Ceteareth 9
Ceteareth 11
Ceteareth 13
Ceteareth 14
Ceteareth 16
Ceteareth 18
Ceteareth 23
Ceteareth 24
Ceteareth 27
Ceteareth 28
Ceteareth 29
Ceteareth 34
Ceteareth 40
Ceteareth 55
Ceteareth 60
Ceteareth 80
Ceteareth 100
Ceteth 4
Ceteth 5
Ceteth 7
Ceteth 13
Ceteth 14
Ceteth 17
Ceteth 18
Ceteth 23
Ceteth 30
Ceteth 40
Ceteth 45
Ceteth 150
Cetoleth 2
Cetoleth 4
Cetoleth 5
Cetoleth 6
Cetoleth 10
Cetoleth 11
Cetoleth 15
Cetoleth 18
Cetoleth 20
Cetoleth 22
Cetoleth 24
Cetoleth 30
Coceth 3
Coceth 5
Coceth 6
Coceth 20
Coceth 25
Deceth 4
Deceth 6
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 12
Isoceteth 15
Isoceteth 30
Isodeceth 4
Isodeceth 5
Isolaureth 3
Isolaureth 10
Isomyreth 3
Isomyreth 9
Isostearet h 3
Isostearet h 8
Isostearet h 12
Isostearet h 15
Isostearet h 16
Isostearet h 22
Isostearet h 25
Isostearet h 50
Laneth 10
Laneth 50
Laneth 60
Laneth 75
Laureth 13
Laureth 15
Laureth 38
Laureth 40
Laureth 50
Methoxy PEG-7
Methoxy PEG-10
Methoxy PEG-25
Methoxy PEG-40
Methoxy PEG-100
Myreth 2
Myreth 5
Noneth 8
Octyldodeceth 2
Octyldodeceth 5
Octyldodeceth 10
Octyldodeceth 30
Oleth 6
Oleth 7
Oleth 9
Oleth 11
Oleth 23
Oleth 24
Oleth 35
Oleth 40
Oleth 44
Oleth 45
Oleth 100
Palmeth 2
PEG-16 Cetyl/Oleyl/Stearyl/Lanolin Alcohol Ether
PEG-Cetyl Stearyl Diether
PEG-4 Ditallow Ether
PEG-15 Jojoba Alcohol
PEG-26 Jojoba Alcohol
PEG-40 Jojoba Alcohol
PEG-3 Methyl Ether
PEG-4 Methyl Ether
PEG-6 Methyl Ether
PEG-7 Methyl Ether
Steareth 1
Steareth 3
Steareth 5
Steareth 7
Steareth 8
Steareth 11
Steareth 13
Steareth 14
Steareth 15
Steareth 27
Steareth 40
Steareth 80
Steareth 60 Cetyl Ether
Talloweth 7
Talloweth 18
Trideceth 2
Trideceth 4
Trideceth 11
Trideceth 15
Trideceth 18
Trideceth 20
Trideceth 21
Trideceth 50
Undeceth 7
Undeceth 8
Undeceth 9
Undeceth 40
Undecyleneth 6

$C_{12}AE_{10}$ 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 μg/cm^2 penetrated, while in a similar study using $C_{12}AE_{10}$, only 0.85 μg/cm^2 penetrated rat skin. For all 3 test compounds, penetration was proportional to longer durations of contact and multiple applications. The highest penetration rate, 8.4 μg/cm^2, was observed after 20 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 μg/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 $\geq$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
	15, 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					
$C_{12\text{-}15}AE_7$	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
$C_{14\text{-}15}AE_7$	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
$C_{12\text{-}14}AE_6$	Induction: undiluted; challenge: 50% in de-ionized water	20 Test and 10 control guinea pigs	Buehler method	Not sensitizing	19
$C_{12\text{-}14}AE_9$	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 6. (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 $C_{14\text{-}15}AE_7$ 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 $C_{12\text{-}13}AE_{6.5}$ 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 $C_{12\text{-}15}AE_7$ and $C_{12\text{-}15}AE_9$ 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% $C_{12\text{-}15}AE_7$ and in 15 of 108 participants induced with 25% $C_{12\text{-}15}AE_9$. At induction with 5%, very slight erythema was seen in 1 and 5 participants for $C_{12\text{-}15}AE_7$ and $C_{12\text{-}15}AE_9$, 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 $C_{12\text{-}13}AE_{6.5}$ and $C_{12\text{-}15}AE_{12}$ were applied to 12 participants per test material. With both induction concentrations of $C_{12\text{-}15}AE_6$, 1 participant developed mild erythema. Erythema was not observed with $C_{12\text{-}15}AE_6$. Upon challenge, there was no evidence of sensitization with either test substance.

$C_{12\text{-}15}AE_{6.5}$ and $C_{12\text{-}15}AE_9$, 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 $C_{12\text{-}13}AE_{6.5}$, with very slight erythema observed for 1 participant at 4 different readings. $C_{12\text{-}15}AE_9$ 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 $C_{14\text{-}15}AE_7$ (144 participants) or $C_{12\text{-}13}AE_{6.5}$ (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					
$C_{12\text{-}14}AE_6$	Undiluted	3 Rabbits	Draize test	EII = 27.1/110; moderately irritating	19
$C_{13}AE_{5\text{-}6.5}$	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
$C_{12\text{-}14}AE_{10}$	Undiluted	3 Rabbits	Draize test	EII = 37/110; moderately to severely irritating	19
$C_{11\text{-}15}AE_{11}$	Undiluted		Draize test	EII = 39/110; moderately to severely irritating	19
$C_{12\text{-}14}AE_7$	Undiluted	9 Rabbits	0.1 ml applied; eyes of 3 rabbits rinsed	$MAS_{unrinsed} = 18$; $MAS_{rinsed} = 12$	19
$C_{14\text{-}15}AE_{11}$	Undiluted	9 Rabbits	0.1 ml applied; eyes of 3 rabbits rinsed	$MAS_{unrinsed} = 30.7$; $MAS_{rinsed} = 32$	19
$C_{12\text{-}13}AE_{6.5}$	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
$C_{12\text{-}15}AE_7$	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
$C_{13\text{-}15}AE_{11}$	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 mg/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 $\leq$5000 μg/plate or clastogenic in a chromosomal aberration assay using CHO cells at concentrations of $\leq$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 $\leq$5000 μg/plate with and without metabolic activation, in an HGPRT forward mutation assay in CHO cells at concentrations of $\leq$5000 μg/plate with and without metabolic activation, and in an in vivo mouse micronucleus test at concentrations of $\leq$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 $C_{14\text{-}15}AE_7$ produced negligible to slight irritation in an occlusive 3-patch application test, and a 10% aqueous solution of $C_{12\text{-}13}AE_{6.5}$ 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

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