Amended Safety Assessment of Acrylates Copolymers as Used in Cosmetics

Status:	Draft Final Amended Report for Panel Review
Release Date:	November 9, 2018
Panel Meeting Date:	December 3-4, 2018

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The 2018 Cosmetic Ingredient Review Expert Panel members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Ronald A. Hill, Ph.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; James G. Marks, Jr., M.D., Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The CIR Executive Director is Bart Heldreth, Ph.D. This safety assessment was prepared by Monice M. Fiume, Senior Director.

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Memorandum

To: CIR Expert Panel Members and Liaisons
From: Monice M. Fiume MMF
Senior Director, CIR
Date: November 9, 2018
Subject: Draft Final Amended Report of Acrylates Copolymers as Used in Cosmetics

At the September 2018 meeting, the Panel issued a Tentative Amended Report with the conclusion that the 126 ingredients named in this report are safe in cosmetics in the present practices of use and concentration described in the safety assessment when formulated to be non-irritating. The draft Final Amended Report (*acryco122018rep*) is submitted for your review at this meeting.

No new data have been received since the September Panel meeting. Comments provided by the Council prior to the September meeting (*acryco122018pcpc_1*), and on the Tentative Amended Report issued after that meeting (*acryco122018pcpc_2*), have mostly been addressed. One comment requires input from the Panel. In the comments received on the Tentative Amended Report, it is suggested that the paragraph regarding the risk assessment of Acrylates/C10-30 Alkyl Acrylates Crosspolymer in benzene should be deleted. Does the Panel agree with that comment, or, should this information remain in the report to support the statements in the Discussion regarding polymerization in benzene?

The following documents are also included with this report package:

acryco122018flow:	report flowchart
acryco122018hist:	report history
acryco122018prof:	data profile
acryco122018strat:	search strategy
acryco122018min:	transcripts for current review
acryco122018prev min:	transcript from the original deliberations of the previous safety assessments
acryco122018FDA:	2018 VCRP data

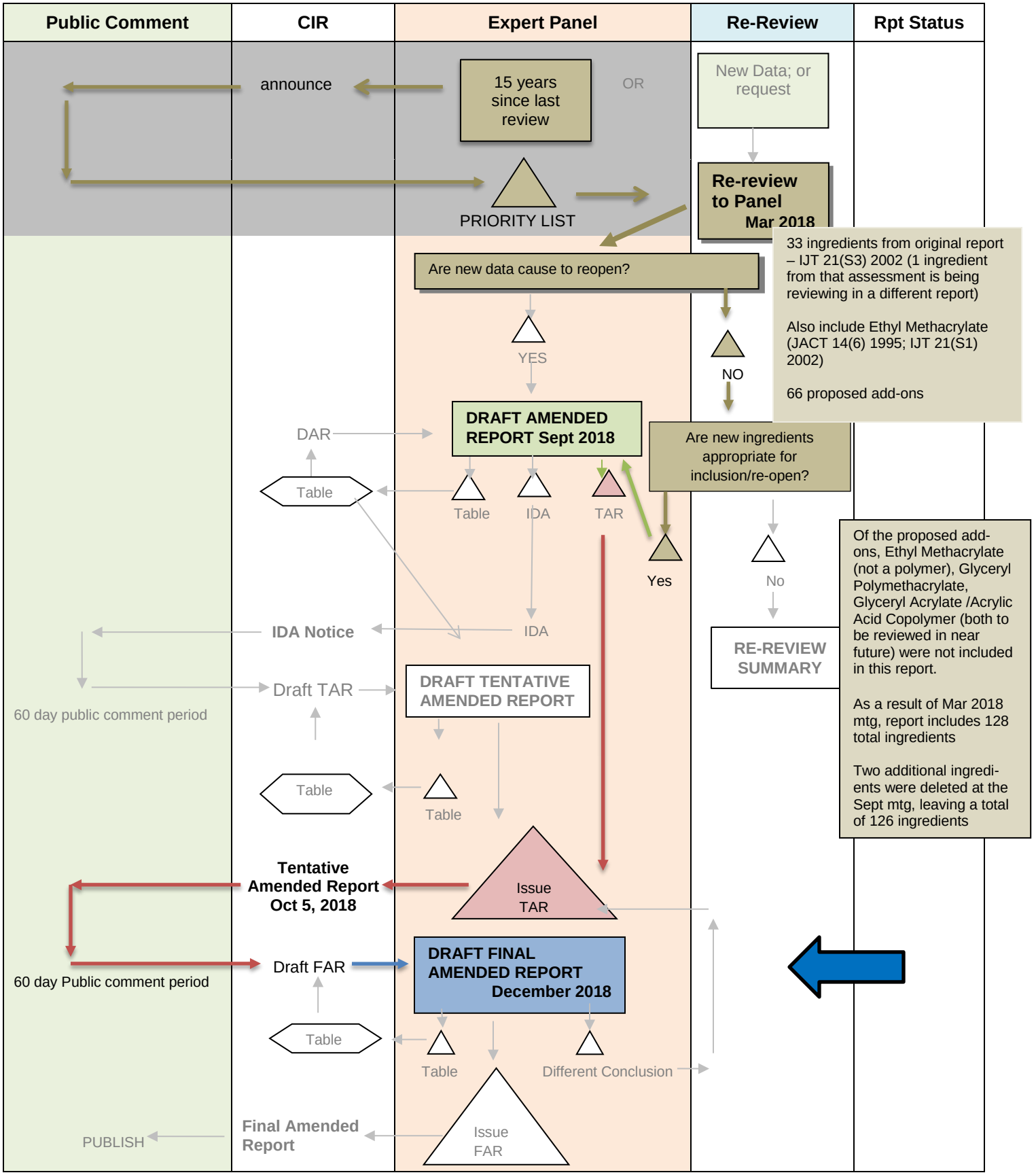
The reports on the previously-reviewed ingredients are available on the CIR website: https://www.cir-safety.org/ingredients.

The Panel should carefully review the Abstract, Discussion, and Conclusion of this safety assessment. If these are satisfactory, a Final Amended Report should be issued.

RE-REVIEW FLOW CHART

INGREDIENT/FAMILY Acrylates Copolymers

MEETING December 2018



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

CIR Report History: Acrylates Copolymers Re-Review

September 24-25, 2018: Draft Amended Report
The Panel reviewed the expanded RR document. A total of 128 ingredients were include in the DAR brought to Panel.

March 5-6, 2018: **Re-Review strategy presented to the Panel**
The Panel agreed to re-open the Final Report on the Safety Assessment of Acrylates Copolymer and 33 Related Cosmetic Ingredients (2002). The following was also decided:

- Panel determined that it was appropriate to exclude three ingredients that were part of the initial safety assessment [Acrylates/VP Copolymer, Vinyl Caprolactam/VP/Dimethylaminoethyl Methacrylate Copolymer, and VP/Dimethylaminoethylmethacrylate Copolymer] because they are part of a another ongoing safety assessment.
- The Panel determined that it is appropriate to include all the copolymers (including crosslinked copolymers (i.e., crosspolymers)) prepared from monomers that comprise, in part, acrylic acid and/or methacrylic acid; the methyl, ethyl, propyl, or butyl ester(s) of these acids; or the salts of one or both of these two acids
    - 70 previously unreviewed ingredients were added
- The following reports were added to the re-review:
    - Crosslinked Alkyl Acrylates (2017)
    - Report on Polymethyl Methacrylate (PMMA), Methyl Methacrylate Crosspolymer, and Methyl Methacrylate/Glycol Dimethacrylate Crosspolymer (2011)
    - Carbomers (1992; reaffirmed in 2003)

September 24-25, 2018: Draft Amended Report
The Panel deleted two ingredients (Styrene Acrylates Copolymer and Sodium Styrene/Acrylates Copolymer) from the report because they were recently reviewed in another document.

The Panel issued a Tentative Amended Report for public comment with the conclusion that the 126 ingredients named in the report are safe in cosmetics in the present practices of use and concentration described in the safety assessment when formulated to be non-irritating.

December 3-4, 2018: Draft Final Amended Report
No new data were received following the issuance of the Tentative Amended Report

Acrylates Copolymers RR – Dec 3-4, 2018 Panel Meeting – Writer, Monice Fiume																		
	Use	Method of Mfg	Impurities	Dermal Penetration	ADME	Animal Tox – Acute, Dermal	Animal Tox – Acute, Oral	Animal Tox, Acute, Inhalation	Animal Rptd Dose, Dermal	Animal Tox, Rptd Dose, Oral	Animal Tox – Rptd Dose, Inhalation	Repro/Dev Tox	Genotox	Carcinogen-icity	Dermal Irritation	Dermal Sensitization	Phototox	Ocular Irritation
Acrylates Copolymer	X	X, O	X, O		X	X, O	X, O	O		X	X, O	X	X, O	O	X, O	X, O		X, O
Acrylates Crosspolymer	X		O															O
Acrylates Crosspolymer-3	X																	
Acrylates Crosspolymer-4	X																	
Acrylates Crosspolymer-5																		
Acrylates/Ammonium Methacrylate Copolymer	X																	
Acrylates/Beheneth-25 Methacrylate Copolymer	X					X	X								X			X
Acrylates/Beheneth-25 Methacrylate/Steareth-30 Methacrylate Copolymer																		
Acrylates/C10-30 Alkyl Methacrylate Copolymer	X																	
Acrylates/C10-30Alkyl Acrylate Crosspolymer	X	O				O	O				O		O		O			O
Acrylates/C12-13 Alkyl Methacrylates/Methoxy-ethyl Acrylate Crosspolymer																		
Acrylates/C12-22 Alkyl Methacrylate Copolymer	X																	
Acrylates/C26-28 Olefin Copolymer																		
Acrylates/C5-8 Alkyl Acrylate Copolymer																		
Acrylates/Ceteareth-20 Methacrylate Crosspolymer																		
Acrylates/Ceteareth-20 Methacrylate Crosspolymer-2																		
Acrylates/Ceteth-20 Methacrylate Copolymer																		
Acrylates/Ethylhexyl Acrylate Copolymer	X																	
Acrylates/Ethylhexyl Acrylate Crosspolymer	X														O			
Acrylates/Ethylhexyl Acrylate/Glycidyl Methacrylate Crosspolymer																		
Acrylates/Hydroxyesters Acrylates Copolymer	X						X						X		X			X
Acrylates/Hydroxyethyl Acrylate/Lauryl Acrylate Copolymer																		
Acrylates/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer																		
Acrylates/Laureth-25 Methacrylate Copolymer																		
Acrylates/Lauryl Methacrylate Copolymer																		
Acrylates/Lauryl Methacrylate/Tridecyl Methacrylate Crosspolymer																		
Acrylates/Methoxy PEG-4 Methacrylate Copolymer																		
Acrylates/Methoxy PEG-15 Methacrylate Copolymer																		
Acrylates/Methoxy PEG-23 Methacrylate Copolymer	X																	

Acrylates Copolymers RR – Dec 3-4, 2018 Panel Meeting – Writer, Monice Fiume																		
	Use	Method of Mfg	Impurities	Dermal Penetration	ADME	Animal Tox – Acute, Dermal	Animal Tox – Acute, Oral	Animal Tox, Acute, Inhalation	Animal Rptd Dose, Dermal	Animal Tox, Rptd Dose, Oral	Animal Tox – Rptd Dose, Inhalation	Repro/Dev Tox	Genotox	Carcinogen-icity	Dermal Irritation	Dermal Sensitization	Phototox	Ocular Irritation
Acrylates/Methoxy PEG-90 Methacrylate Crosspolymer																		
Acrylates/Palmeth-25 Acrylate Copolymer	X																	
Acrylates/PEG-4 Dimethacrylate Crosspolymer																		
Acrylates/Steareth-20 Methacrylate Copolymer	X		X															
Acrylates/Steareth-20 Methacrylate Crosspolymer	X	X	O										O		O			
Acrylates/Steareth-30 Methacrylate Copolymer	X																	
Acrylates/Steareth-50 Acrylate Copolymer																		
Acrylates/Stearyl Methacrylate Copolymer	X																	
Acrylates/VA Copolymer	X	O	O			O	O						O		O			O
Acrylates/VA Crosspolymer	X																	
Acrylates/Vinyl Isodecanoate Crosspolymer	X	O	O				O								O			O
Acrylates/Vinyl Neodecanoate Crosspolymer	X	O	O			O	O	O					O		O			
Acrylic Acid/C12-22 Alkyl Acrylate Copolymer																		
Acrylic Acid/Stearyl Acrylate Copolymer	X																	
Allyl Methacrylate/Glycol Dimethacrylate Crosspolymer																		
Allyl Methacrylates Crosspolymer	X																	
Ammonium Acrylates Copolymer	X	O											O		O			O
Ammonium Acrylates/Ethylhexyl Acrylate Copolymer																		
Ammonium Acrylates/Methyl Styrene/Styrene Copolymer	X																	
Ammonium Polyacrylate	X																	
Ammonium Styrene/Acrylates Copolymer	X																	
Ammonium Styrene/Acrylates/Ethylhexyl Acrylate/Lauryl Acrylate Copolymer																		
Ammonium VA/Acrylates Copolymer																		
AMP-Acrylates Copolymer	X																	
Behenyl Methacrylate/t-Butyl Methacrylate Copolymer	X																	
Butyl Acrylate/Cyclohexyl Methacrylate Copolymer																		
Butyl Acrylate/Ethylhexyl Methacrylate Copolymer																		
Butyl Acrylate/Glycol Dimethacrylate Crosspolymer	X																	
Butyl Acrylate/Hydroxyethyl Methacrylate Copolymer																		
Butyl Methacrylate/Acryoyloxy PG Methacrylate Copolymer																		

Acrylates Copolymers RR – Dec 3-4, 2018 Panel Meeting – Writer, Monice Fiume																		
	Use	Method of Mfg	Impurities	Dermal Penetration	ADME	Animal Tox – Acute, Dermal	Animal Tox – Acute, Oral	Animal Tox, Acute, Inhalation	Animal Rptd Dose, Dermal	Animal Tox, Rptd Dose, Oral	Animal Tox – Rptd Dose, Inhalation	Repro/Dev Tox	Genotox	Carcinogen-icity	Dermal Irritation	Dermal Sensitization	Phototox	Ocular Irritation
C12-22 Alkyl Acrylate/Hydroxyethylacrylate Copolymer	X																	
C8-22 Alkyl Acrylates/Methacrylic Acid Crosspolymer	X																	
Calcium Potassium Carbomer																		
Carbomer	X	O				O	O	O		O					O	O	O	O
Cyclohexyl Methacrylate/Ethylhexyl Methacrylate Copolymer																		
Ethylene/Acrylic Acid Copolymer	X					O	O	0							O			O
Ethylene/Acrylic Acid/VA Copolymer																		
Ethylene/Calcium Acrylate Copolymer																		
Ethylene/Magnesium Acrylate Copolymer																		
Ethylene/Methacrylate Copolymer	X																	
Ethylene/Sodium Acrylate Copolymer	X																	
Ethylene/Zinc Acrylate Copolymer																		
Ethylhexyl Acrylate/Methoxy PEG-23 Methacrylate/Vinyl Acetate Copolymer																		
Ethylhexyl Acrylate/Methyl Methacrylate Copolymer	X																	
Glycol Dimethacrylate Crosspolymer																		
Glycol Dimethacrylate/Vinyl Alcohol Crosspolymer																		
Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer																		
Lauryl Acrylate Crosspolymer	X																	
Lauryl Acrylate/VA Copolymer																		
Lauryl Acrylate/VA Crosspolymer																		
Lauryl Methacrylate/Glycol Dimethacrylate Crosspolymer	X		O												O			
Lauryl Methacrylate/Sodium Methacrylate Crosspolymer	X																	
Methacrylic Acid/PEG-6 Methacrylate/PEG-6 Dimethacrylate Crosspolymer																		
Methacryloyl Ethyl Betaine/Acrylates Copolymer	X																	
Methoxy PEG-23 Methacrylate/Glyceryl Diisostearate Methacrylate Copolymer																		
Methyl Methacrylate Crosspolymer	X																	
Methyl Methacrylate/Glycol Dimethacrylate Crosspolymer	X																	

Acrylates Copolymers RR – Dec 3-4, 2018 Panel Meeting – Writer, Monice Fiume																		
	Use	Method of Mfg	Impurities	Dermal Penetration	ADME	Animal Tox – Acute, Dermal	Animal Tox – Acute, Oral	Animal Tox, Acute, Inhalation	Animal Rptd Dose, Dermal	Animal Tox, Rptd Dose, Oral	Animal Tox – Rptd Dose, Inhalation	Repro/Dev Tox	Genotox	Carcinogen-icity	Dermal Irritation	Dermal Sensitization	Phototox	Ocular Irritation
Methyl Methacrylate/PEG/PPG-4/3 Methacrylate Crosspolymer	X																	
PEG/PPG-5/2 Methacrylate/Methacrylic Acid Crosspolymer																		
Poly C10-30 Alkyl Acrylate	X																	
Poly(Methoxy PEG-9 Methacrylate)																		
Polyacrylate-14	X																	
Polyacrylate-29																		
Polyacrylate-34																		
Polyacrylate-1 Crosspolymer	X		X															
Polyacrylic Acid	X	O	O				O											
Polybutyl Acrylate 9003-49-0																		
Polybutyl Methacrylate																		
Polyethylacrylate	X																	
Polyhydroxyethylmethacrylate																		
Polyisobutyl Methacrylate																		
Polymethyl Acrylate	X																	
Polymethyl Methacrylate	X	O	O				O								O			O
Polypropyl Methacrylate																		
Polystearyl Methacrylate																		
Potassium Acrylate Crosspolymer																		
Potassium Acrylates Copolymer	X																	
Potassium Acrylates/C10-30 Alkyl Acrylate Crosspolymer	X																	
Potassium Acrylates/Ethylhexyl Acrylate Copolymer																		
Potassium Aluminum Polyacrylate																		
Potassium Carbomer	X																	
Potassium Polyacrylate																		
Sodium Acrylate/Acrolein Copolymer																		
Sodium Acrylate/Vinyl Alcohol Copolymer	X																	
Sodium Acrylates Copolymer	X																	
Sodium Acrylates Crosspolymer-2	X		O				O						O					O
Sodium Acrylates/Beheneth-25 Methacrylate Crosspolymer																		
Sodium Acrylates/C10-30 Alkyl Acrylate Crosspolymer	X																	
Sodium Acrylates/Ethylhexyl Acrylate Copolymer																		

Acrylates Copolymers RR – Dec 3-4, 2018 Panel Meeting – Writer, Monice Fiume																		
	Use	Method of Mfg	Impurities	Dermal Penetration	ADME	Animal Tox – Acute, Dermal	Animal Tox – Acute, Oral	Animal Tox, Acute, Inhalation	Animal Rptd Dose, Dermal	Animal Tox, Rptd Dose, Oral	Animal Tox – Rptd Dose, Inhalation	Repro/Dev Tox	Genotox	Carcinogen-icity	Dermal Irritation	Dermal Sensitization	Phototox	Ocular Irritation
Sodium Acrylates/Vinyl Isodecanoate Crosspolymer	X																	
Sodium Carbomer	X																	
Sodium Polyacrylate	X	O	O									O	O		O			O
Sodium Polymethacrylate	X																	
Steareth-10 Allyl Ether/Acrylates Copolymer	X																	
Stearyl/Lauryl Methacrylate Crosspolymer																		
Styrene/Acrylate/Ammonium Methacrylate Copolymer	X																	
VA/Butyl Maleate/Isobornyl Acrylate Copolymer	X		X			X	X								X	X	X	X

***"X" indicates that new data were available in this category for the ingredient; "O" indicates that data from the original assessment were available**

***Ingredients in blue type were included in the original Safety Assessment of Acrylates Copolymer and 33 Related Cosmetic Ingredients[1]**
Ingredients in green type were reviewed in the Safety Assessment of Cross-Linked Alkyl Acrylates[2]
Ingredients in pink type were reviewed in the safety assessment of Polymethyl Methacrylate and other ingredients[3]
The ingredient in gray type was reviewed in the safety assessment of Carbomers[4]
The ingredients in black type have not yet been reviewed by CIR

Acrylates Copolymer – Re-Review

Ingredient	CAS #	InfoB	TOXNET	FDA	EU	ECHA	IUCLID	SIDS	ECETOC	HPVIS	NICNAS	NTIS	NTP	IARC	WHO	FAO	NIOSH	FEMA	Web
FROM ORIGINAL REPORT																			
Acrylates/Ammonium Methacrylate Copolymer	X	---																	
Acrylates Copolymer	159666-35-0 25035-69-2 25212-88-8 25685-29-4	CFR; nicnas		yes							yes								X
Acrylates/Hydroxyesters Acrylates Copolymer	25035-89-6	nicnas									yes								
Acrylates/Steareth-50 Acrylate Copolymer	X	---																	
Acrylates/Steareth-20 Methacrylate Copolymer	X	---																	X
Acrylates/VA Copolymer	X	CFR		yes															
Ammonium Acrylates Copolymer	X	---																	
Ammonium Polyacrylate	9003-03-6	CFR																	
Ammonium Styrene/ Acrylates Copolymer	63744-68-3	nicnas																	
Ammonium VA/ Acrylates Copolymer	X	---																	
AMP-Acrylates Copolymer	1203962-19-9	---																	
Ethylene/Acrylic Acid Copolymer	9010-77-9	CFR		yes															
Ethylene/Acrylic Acid/VA Copolymer	26713-18-8	---																	
Ethylene/Calcium Acrylate Copolymer	26445-96-5	CFR																	
Ethylene/Magnesium Acrylate Copolymer	27515-37-3	---																	
Ethylene/Methacrylate Copolymer	25103-74-6	---																	
Ethylene/Sodium Acrylate Copolymer	25749-98-8 25750-82-7	CFR		yes															
Ethylene/Zinc Acrylate Copolymer	28208-80-2 59650-68-9	---																	
Lauryl Acrylate/VA Copolymer	X	---																	
Methacryloyl Ethyl Betaine/Acrylates Copolymer	X	---																	
Polyacrylic Acid	9003-01-4	cfr; IARC		yes										yes					IARC
Potassium Aluminum Polyacrylate	X	---																	
Potassium Polyacrylate	25608-12-2	TRN		FedReg															

Ingredient	CAS #	InfoB	TOXNET	FDA	EU	ECHA	IUCLID	SIDS	ECETOC	HPVIS	NICNAS	NTIS	NTP	IARC	WHO	FAO	NIOSH	FEMA	Web
Potassium Polyacrylate																			
Sodium Acrylates/Acrolein Copolymer	X	---																	
Sodium Acrylates Copolymer	25549-84-2	---		CFR; FedReg															
Sodium Polyacrylate	25549-84-2 9003-04-7	Cfr; FR		yes															
Steareth-10 Allyl Ether/Acrylates Copolymer	109292-17-3	---																	
Styrene/Acrylates/ Ammonium Methacrylate Copolymer	X	---																	
VA/Butyl Maleate/Isobornyl Acrylate Copolymer	X	NICNAS									yes								
Vinyl Caprolactam/VP/ Dimethylaminoethyl Methacrylate Copolymer	X	---																	
VP/Dimethylaminoethyl-methacrylate Copolymer	30581-59-0	cfr		CFR															
PROPOSED ADD-ONS																			
Acrylates/Beheneth-25 Methacrylate Copolymer	X	nicnas									yes								X
Acrylates/Beheneth-25 Methacrylate/Steareth-30 Methacrylate Copolymer	888492-33-9	---																	
Acrylates/C5-8 Alkyl Acrylate Copolymer	X	---																	
Acrylates/C10-30 Alkyl Methacrylate Copolymer	X	---																	
Acrylates/C12-22 Alkyl Methacrylate Copolymer	X	nicnas									yes								
Acrylates/Ceteareth-20 Methacrylate Crosspolymer	X	---																	
Acrylates/Ceteareth-20 Methacrylate Crosspolymer-2	X	---																	
Acrylates/Ceteth-20 Methacrylate Copolymer	X	---																	
Acrylates/C26-28 Olefin Copolymer	X	---																	
Acrylates Crosspolymer-3	X	---																	
Acrylates Crosspolymer-4	X	---																	
Acrylates Crosspolymer-5	X	---																	

Ingredient	CAS #	InfoB	TOXNET	FDA	EU	ECHA	IUCLID	SIDS	ECETOC	HPVIS	NICNAS	NTIS	NTP	IARC	WHO	FAO	NIOSH	FEMA	Web
Acrylates/Ethylhexyl Acrylate Copolymer	X	---																	
Acrylates/Hydroxyethyl Acrylate/Lauryl Acrylate Copolymer	X	---																	
Acrylates/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer	X	---																	
Acrylates/Laureth-25 Methacrylate Copolymer	X	---																	
Acrylates/Lauryl Methacrylate Copolymer	X	---																	
Acrylates/Lauryl Methacrylate/Tridecyl Methacrylate Crosspolymer	X	---																	
Acrylates/Methoxy PEG-4 Methacrylate Copolymer	X	---																	
Acrylates/Methoxy PEG-15 Methacrylate Copolymer	X	---																	
Acrylates/Methoxy PEG-23 Methacrylate Copolymer	X	---																	
Acrylates/Methoxy PEG-90 Methacrylate Crosspolymer	957645-61-3	---																	
Acrylates/Palmeth-25 Acrylate Copolymer	X	nicnas									yes								
Acrylates/Steareth-30 Methacrylate Copolymer	75760-37-1	---																	
Acrylates/Stearyl Methacrylate Copolymer	X	---																	
Acrylates/VA Crosspolymer	X	---																	
Acrylic Acid/C12-22 Alkyl Acrylate Copolymer	X	---																	
Acrylic Acid/Stearyl Acrylate Copolymer	36120-03-3	---																	
Ammonium Acrylates/Ethylhexyl Acrylate Copolymer	X	---																	
Ammonium Acrylates/Methyl Styrene/Styrene Copolymer	X	---																	
Ammonium Styrene/ Acrylates/Ethylhexyl Acrylate/Lauryl Acrylate Copolymer	X	---																	

Ingredient	CAS #	InfoB	TOXNET	FDA	EU	ECHA	IUCLID	SIDS	ECETOC	HPVIS	NICNAS	NTIS	NTP	IARC	WHO	FAO	NIOSH	FEMA	Web
Behenyl Methacrylate/t-Butyl Methacrylate Copolymer	X	---																	
Butyl Acrylate/Cyclohexyl Methacrylate Copolymer	X	---																	
Butyl Acrylate/Ethylhexyl Methacrylate Copolymer	X	---																	
Butyl Acrylate/Hydroxy-ethyl Methacrylate Copolymer	X	---																	
Butyl Methacrylate/ Acryoyloxy PG Methacrylate Copolymer	1431551-12-0	---																	
C12-22 Alkyl Acrylate/Hydroxyethyl-acrylate Copolymer	X	---																	
Cyclohexyl Methacrylate/ Ethylhexyl Methacrylate Copolymer	82227-04-1	---																	
Ethylhexyl Acrylate/ Methoxy PEG-23 Meth-acrylate/Vinyl Acetate Copolymer	137455-77-7	---																	
Ethylhexyl Acrylate/ Methyl Methacrylate Copolymer	X	cfr		CFR															
Glycol Dimethacrylate Crosspolymer																			
Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer	X	---																	
Lauryl Acrylate Crosspolymer	X	---																	
Lauryl Acrylate/VA Crosspolymer	X	---																	
Methoxy PEG-23 Methacrylate/Glyceryl Diisostearate Meth-acrylate Copolymer	X	---																	
Methyl Methacrylate/ PEG/PPG-4/3 Meth-acrylate Crosspolymer	X	---																	
Polyacrylate-14																			
Polyacrylate-29																			
Polyacrylate-34																			
Polyacrylates- 1 Crosspolymer	X	nicnas									yes								
Polybutyl Acrylate	9003-49-0	cfr		CFR															
Polybutyl Methacrylate	9003-63-8	cfr		CFR															

Ingredient	CAS #	InfoB	TOXNET	FDA	EU	ECHA	IUCLID	SIDS	ECETOC	HPVIS	NICNAS	NTIS	NTP	IARC	WHO	FAO	NIOSH	FEMA	Web
Poly C10-30 Alkyl Acrylate	X	---																	
Polyethylacrylate	9003-32-1	cfr		CFR															
Polyhydroxyethyl-methacrylate	25249-16-5	---																	
Polyisobutyl Methacrylate	9011-15-8	---																	
Poly(Methoxy PEG-9 Methacrylate)	X	---																	
Polymethyl Acrylate	9003-21-8																		
Polypropyl Methacrylate	X	---																	
Polystearyl Methacrylate	X	---																	
Potassium Acrylate Crosspolymer	86416-97-9 (Na form)	---																	
Potassium Acrylates Copolymer	X	---																	
Potassium Acrylates/ Ethylhexyl Acrylate Copolymer	X	---																	
Sodium Acrylates/ Beheneth-25 Methacryl-ate Crosspolymer	X	---																	
Sodium Acrylates/ Ethylhexyl Acrylate Copolymer	X	---																	
Sodium Acrylate/Vinyl Alcohol Copolymer	27599-56-0 58374-38-2	---																	
Sodium Polymethacrylate	25086-62-8 54193-36-1	cfr																	
ADD-ONS – PREVIOUSLY REVIEWED INGREDIENTS																			
Crosslined Alkyl Acrylates (2012 on)																			
Acrylates/C10-30 Alkyl Acrylate Crosspolymer	X																		
Acrylates/C12-13 Alkyl Methacrylates/ Methoxyethyl Acrylate Crosspolymer	X																		
Acrylates Crosspolymer	26794-61-6; 74464-10-1																		
Acrylates/Ethylhexyl Acrylate Crosspolymer	X																		
Acrylates/Ethylhexyl Acrylate/Glycidyl Methacrylate Crosspolymer	X																		
Acrylates/PEG-4 Dimethacrylate Crosspolymer	X																		

Ingredient	CAS #	InfoB	TOXNET	FDA	EU	ECHA	IUCLID	SIDS	ECETOC	HPVIS	NICNAS	NTIS	NTP	IARC	WHO	FAO	NIOSH	FEMA	Web
Acrylates/Steareth-20 Methacrylate Crosspolymer	X																		
Acrylates/Vinyl Isodecanoate Crosspolymer	X																		
Acrylates/Vinyl Neodecanoate Crosspolymer	X																		
Allyl Methacrylate/Glycol Dimethacrylate Crosspolymer	779327-42-3																		
Allyl Methacrylates Crosspolymer	182212-41-5																		
Butyl Acrylate/Glycol Dimethacrylate Crosspolymer	X																		
C8-22 Alkyl Acrylates/Methacrylic Acid Crosspolymer	X																		
Glycol Dimethacrylate/Vinyl Alcohol Crosspolymer	X																		
Lauryl Methacrylate/Glycol Dimethacrylate Crosspolymer	X																		
Lauryl Methacrylate/Sodium Methacrylate Crosspolymer	X																		
Methacrylic Acid/PEG-6 Methacrylate/PEG-6 Dimethacrylate Crosspolymer	X																		
PEG/PPG-5/2 Methacrylate/Methacrylic Acid Crosspolymer	X																		
Potassium Acrylates/C10-30 Alkyl Acrylate Crosspolymer	X																		
Sodium Acrylates Crosspolymer-2	X																		
Sodium Acrylates/C10-30 Alkyl Acrylate Crosspolymer	X																		
Sodium Acrylates/Vinyl Isodecanoate Crosspolymer	X																		

Ingredient	CAS #	InfoB	TOXNET	FDA	EU	ECHA	IUCLID	SIDS	ECETOC	HPVIS	NICNAS	NTIS	NTP	IARC	WHO	FAO	NIOSH	FEMA	Web
Stearyl/Lauryl Methacrylate Crosspolymer	X																		
PMMA ingredients																			
Methyl Methacrylate Crosspolymer	X																		
Methyl Methacrylate/Glycol Dimethacrylate Crosspolymer	25777-71-3																		
Polymethyl Methacrylate	9011-14-7																		
Carbomer																			
Carbomer	9003-01-4; 9007-16-3; 9007-17-4; 9062-04-8; 76050-42-5																		

Search Strategy

January 18, 2018

PubMed

Acrylates Copolymers that were Previously Reviewed

(((((((159666-35-0[EC/RN Number] OR 25035-69-2[EC/RN Number] OR 25212-88-8[EC/RN Number] OR 25685-29-4[EC/RN Number] OR 25035-89-6[EC/RN Number] OR 30581-59-0[EC/RN Number] OR 97-63-2[EC/RN Number])) OR (9003-03-6[EC/RN Number] OR 63744-68-3[EC/RN Number] OR 1203962-19-9[EC/RN Number] OR 9010-77-9[EC/RN Number] OR 26713-18-8[EC/RN Number] OR 26445-96-5[EC/RN Number] OR 27515-37-3[EC/RN Number] OR 25103-74-6[EC/RN Number] OR 25749-98-8[EC/RN Number] OR 25750-82-7[EC/RN Number] OR 28208-80-2[EC/RN Number] OR 59650-68-9[EC/RN Number])) OR (9003-01-4[EC/RN Number] OR 25608-12-2[EC/RN Number] OR 25549-84-2[EC/RN Number] OR 25549-84-2[EC/RN Number] OR 9003-04-7[EC/RN Number] OR 9010-92-8[EC/RN Number] OR 109292-17-3[EC/RN Number] OR 27306-39-4[EC/RN Number] OR 25034-86-0[EC/RN Number] OR 25085-34-1[EC/RN Number] OR 9010-92-8[EC/RN Number])))) OR (acrylates/ammonium methacrylate copolymer OR acrylates copolymer OR acrylates/hydroxy esters acrylates copolymer OR acrylates/steareth-50 acrylate copolymer OR acrylates/steareth-20 methacrylate copolymer OR acrylates/va copolymer OR ammonium acrylates copolymer OR ammonium polyacrylate OR ammonium styrene/acrylates copolymer OR ammonium va/acrylates copolymer OR amp-acrylates copolymer OR ethylene/acrylic acid copolymer OR ethylene/acrylic acid/va copolymer OR ethylene/calcium acrylate copolymer OR ethylene/magnesium acrylate copolymer OR ethylene/methacrylate copolymer OR ethylene/sodium acrylate copolymer OR ethylene/zinc acrylate copolymer OR lauryl acrylate/va copolymer OR methacryloyl ethyl betaine/acrylates copolymer OR polyacrylic acid OR potassium aluminum polyacrylate OR potassium polyacrylate OR sodium acrylates/acrolein copolymer OR sodium acrylates copolymer OR sodium polyacrylate OR sodium styrene/acrylates copolymer OR steareth-10 allyl ether/acrylates copolymer OR styrene/acrylates/ammonium methacrylate copolymer OR styrene/acrylates copolymer OR va/butyl maleate/isobornyl acrylate copolymer OR vinyl caprolactam/vp/dimethylaminoethyl methacrylate copolymer OR vp/dimethylaminoethyl methacrylate copolymer OR ethyl methacrylate)) AND ("1997"[PDAT] : "3000"[PDAT]) – **7717 hits**

Used limiting terms:

((((((((((159666-35-0[EC/RN Number] OR 25035-69-2[EC/RN Number] OR 25212-88-8[EC/RN Number] OR 25685-29-4[EC/RN Number] OR 25035-89-6[EC/RN Number] OR 30581-59-0[EC/RN Number] OR 97-63-2[EC/RN Number])) OR (9003-03-6[EC/RN Number] OR 63744-68-3[EC/RN Number] OR 1203962-19-9[EC/RN Number] OR 9010-77-

9[EC/RN Number] OR 26713-18-8[EC/RN Number] OR 26445-96-5[EC/RN Number] OR 27515-37-3[EC/RN Number] OR 25103-74-6[EC/RN Number] OR 25749-98-8[EC/RN Number] OR 25750-82-7[EC/RN Number] OR 28208-80-2[EC/RN Number] OR 59650-68-9[EC/RN Number])) OR (9003-01-4[EC/RN Number] OR 25608-12-2[EC/RN Number] OR 25549-84-2[EC/RN Number] OR 25549-84-2[EC/RN Number] OR 9003-04-7[EC/RN Number] OR 9010-92-8[EC/RN Number] OR 109292-17-3[EC/RN Number] OR 27306-39-4[EC/RN Number] OR 25034-86-0[EC/RN Number] OR 25085-34-1[EC/RN Number] OR 9010-92-8[EC/RN Number])))) OR (acrylates/ammonium methacrylate copolymer OR acrylates copolymer OR acrylates/hydroxyesters acrylates copolymer OR acrylates/steareth-50 acrylate copolymer OR acrylates/steareth-20 methacrylate copolymer OR acrylates/VA copolymer OR ammonium acrylates copolymer OR ammonium polyacrylate OR ammonium styrene/acrylates copolymer OR ammonium VA/acrylates copolymer OR AMP-acrylates copolymer OR ethylene/acrylic acid copolymer OR ethylene/acrylic acid/VA copolymer OR ethylene/calcium acrylate copolymer OR ethylene/magnesium acrylate copolymer OR ethylene/methacrylate copolymer OR ethylene/sodium acrylate copolymer OR ethylene/zinc acrylate copolymer OR lauryl acrylate/VA copolymer OR methacryloyl ethyl betaine/acrylates copolymer OR polyacrylic acid OR potassium aluminum polyacrylate OR potassium polyacrylate OR sodium acrylates/acrolein copolymer OR sodium acrylates copolymer OR sodium polyacrylate OR sodium styrene/acrylates copolymer OR steareth-10 allyl ether/acrylates copolymer OR styrene/acrylates/ammonium methacrylate copolymer OR styrene/acrylates copolymer OR VA/butyl maleate/isobornyl acrylate copolymer OR vinyl caprolactam/VP/dimethylaminoethyl methacrylate copolymer OR VP/dimethylaminoethyl methacrylate copolymer OR ethyl methacrylate))))))) AND ((toxic OR toxicity or toxicolog* OR mutagen* OR genotoxic* OR carcinogen* irritat* OR sensitiz* OR photosensiti* OR photoallerg* OR teratogen* OR reproducti* OR (dermal absorption) OR (tumor promotion))))) AND ("1997"[Date - Publication] : "3000"[Date - Publication]) – **139 hits**

Proposed Add-Ons

((888492-33-9[EC/RN Number] OR 957645-61-3[EC/RN Number] OR 75760-37-1[EC/RN Number] OR 36120-03-3[EC/RN Number] OR 1431551-12-0[EC/RN Number] OR 82227-04-1[EC/RN Number] OR 137455-77-7[EC/RN Number] OR 146126-21-8[EC/RN Number] OR 28474-30-8[EC/RN Number] OR 9003-49-0[EC/RN Number] OR 9003-63-8[EC/RN Number] OR 9003-32-1[EC/RN Number] OR 25249-16-5[EC/RN Number] OR 9011-15-8[EC/RN Number] OR 9003-21-8[EC/RN Number] OR 86416-97-9 [EC/RN Number] OR 27599-56-0[EC/RN Number] OR 58374-38-2[EC/RN Number] OR 25086-62-8 [EC/RN Number] OR 54193-36-1[EC/RN Number])) OR ((Acrylates AND Beheneth-25 AND Methacrylate AND Copolymer) OR (Acrylates AND Beheneth-25 Methacrylate AND Steareth-30 AND Methacrylate AND Copolymer) OR (Acrylates AND “C5-8” AND Alkyl AND Acrylate AND Copolymer) OR (Acrylates AND “C10-30” AND Alkyl AND Methacrylate AND Copolymer) OR (Acrylates AND (“C12-22”) AND Alkyl AND Methacrylate AND Copolymer) OR (Acrylates AND Ceteareth-20 AND Methacrylate AND Crosspolymer*) OR (Acrylates AND Ceteth-20 AND Methacrylate AND Copolymer) OR (Acrylates AND (“C26-28”) AND Olefin AND Copolymer) OR (Acrylates AND Crosspolymer*) OR (Acrylates AND Ethylhexyl AND Acrylate AND Copolymer) OR (Acrylates AND Hydroxyethyl AND Acrylate AND Lauryl AND Acrylate AND Copolymer) OR (Acrylates AND Hydroxyethyl AND Acrylate AND Methoxyethyl AND Acrylate AND Copolymer) OR (Acrylates AND Laureth-25 AND Methacrylate AND Copolymer) OR (Acrylates AND Lauryl AND Methacrylate AND Copolymer) OR (Acrylates AND Lauryl AND Methacrylate AND Tridecyl AND Methacrylate AND Crosspolymer) OR (Acrylates AND Methoxy AND PEG-4 AND Methacrylate AND Copolymer) OR (Acrylates AND Methoxy AND PEG-15 AND Methacrylate AND Copolymer) OR (Acrylates AND Methoxy AND PEG-23 AND Methacrylate AND Copolymer) OR (Acrylates AND Methoxy AND PEG-90 AND Methacrylate AND Crosspolymer) OR (Acrylates AND Palmeth-25 AND Acrylate AND Copolymer) OR (Acrylates AND Steareth-30 AND Methacrylate AND Copolymer) OR (Acrylates AND Stearyl AND Methacrylate AND Copolymer) OR (Acrylates AND (“VA” or vinyl acetate) AND Crosspolymer) OR (Acrylic Acid AND (“C12-22”) AND Alkyl AND Acrylate AND Copolymer) OR (Acrylic AND Acid AND Stearyl AND Acrylate AND Copolymer) OR (Ammonium AND Acrylates AND Ethylhexyl AND Acrylate AND Copolymer) OR (Ammonium AND Acrylates AND Methyl AND Styrene AND Styrene AND Copolymer) OR (Ammonium AND Styrene AND Acrylates AND Ethylhexyl AND Acrylate AND Lauryl AND Acrylate AND Copolymer) OR (Behenyl AND Methacrylate AND ((“t-“) OR tert) AND Butyl AND Methacrylate AND Copolymer) OR (Butyl AND Acrylate AND Cyclohexyl AND Methacrylate AND Copolymer) OR (Butyl AND Acrylate AND Ethylhexyl AND Methacrylate AND Copolymer) OR (Butyl AND Acrylate AND Hydroxyethyl AND Methacrylate AND Copolymer) OR (Butyl AND Methacrylate AND Acryoyloxy AND ((“PG”) OR (“propylene glycol”)) AND Methacrylate AND Copolymer) OR ((“C12-22”) AND Alkyl AND Acrylate AND Hydroxyethylacrylate AND Copolymer) OR (Cyclohexyl AND Methacrylate AND Ethylhexyl AND Methacrylate AND Copolymer) OR (Ethylhexyl AND Acrylate AND Methoxy AND PEG-23 AND Methacrylate AND Vinyl AND Acetate AND Copolymer) OR (Ethylhexyl AND Acrylate AND Methyl AND Methacrylate AND Copolymer) OR (Glyceryl AND Acrylate AND Acrylic AND Acid AND Copolymer) OR (Glyceryl AND Polymethacrylate) OR (Hydroxyethyl AND Acrylate AND Methoxyethyl AND Acrylate AND Copolymer) OR (Lauryl AND Acrylate AND Crosspolymer) OR (Lauryl AND Acrylate AND ((“VA”) OR (“vinyl acetate”)) AND Crosspolymer) OR (Methoxy AND PEG-23 AND Methacrylate AND Glyceryl AND Diisostearate AND Methacrylate AND Copolymer) OR (Methyl AND Methacrylate AND PEG AND (“PPG-4/3”) AND Methacrylate AND Crosspolymer) OR ((“Polyacrylates-1”) AND Crosspolymer) OR (Polybutyl AND Acrylate) OR (Polybutyl AND Methacrylate) OR (Poly AND (“C10-30”) AND Alkyl AND Acrylate) OR (Polyethylacrylate) OR (Polyhydroxyethylmethacrylate) OR (Polyisobutyl AND Methacrylate) OR (Poly AND Methoxy AND PEG-9 AND Methacrylate) OR (Polymethyl AND Acrylate) OR (Polypropyl AND Methacrylate) OR (Polystearyl AND Methacrylate) OR (Potassium AND Acrylate AND Crosspolymer) OR (Potassium AND Acrylates AND Copolymer) OR (Potassium AND Acrylates AND Ethylhexyl AND Acrylate AND Copolymer) OR (Sodium AND Acrylates AND Beheneth-25 AND Methacrylate AND Crosspolymer) OR (Sodium AND Acrylates AND Ethylhexyl AND Acrylate AND Copolymer) OR (Sodium AND Acrylate AND Vinyl AND Alcohol AND Copolymer) OR (Sodium AND Polymethacrylate)) – **2274 hits**

Used Limiting Terms
((((888492-33-9[EC/RN Number] OR 957645-61-3[EC/RN Number] OR 75760-37-1[EC/RN Number] OR 36120-03-3[EC/RN Number] OR 1431551-12-0[EC/RN Number] OR 82227-04-1[EC/RN Number] OR 137455-77-7[EC/RN Number] OR 146126-21-8[EC/RN Number] OR 28474-30-8[EC/RN Number] OR 9003-49-0[EC/RN Number] OR 9003-63-8[EC/RN Number] OR 9003-32-1[EC/RN Number] OR 25249-16-5[EC/RN Number] OR 9011-15-8[EC/RN Number] OR 9003-21-8[EC/RN Number] OR 86416-97-9 [EC/RN Number] OR 27599-56-0[EC/RN Number] OR 58374-38-2[EC/RN Number] OR 25086-62-8 [EC/RN Number] OR 54193-36-1[EC/RN Number])) OR ((Acrylates AND Beheneth-25 AND Methacrylate AND Copolymer) OR (Acrylates AND Beheneth-25 Methacrylate AND Steareth-30 AND Methacrylate AND Copolymer) OR (Acrylates AND "C5-8" AND Alkyl AND Acrylate AND Copolymer) OR (Acrylates AND "C10-30" AND Alkyl AND Methacrylate AND Copolymer) OR (Acrylates AND ("C12-22") AND Alkyl AND Methacrylate AND Copolymer) OR (Acrylates AND Ceteareth-20 AND Methacrylate AND Crosspolymer*) OR (Acrylates AND Ceteth-20 AND Methacrylate AND Copolymer) OR (Acrylates AND ("C26-28") AND Olefin AND Copolymer) OR (Acrylates AND Crosspolymer*) OR (Acrylates AND Ethylhexyl AND Acrylate AND Copolymer) OR (Acrylates AND Hydroxyethyl AND Acrylate AND Lauryl AND Acrylate AND Copolymer) OR (Acrylates AND Hydroxyethyl AND Acrylate AND Methoxyethyl AND Acrylate AND Copolymer) OR (Acrylates AND Laureth-25 AND Methacrylate AND Copolymer) OR (Acrylates AND Lauryl AND Methacrylate AND Copolymer) OR (Acrylates AND Lauryl AND Methacrylate AND Tridecyl AND Methacrylate AND Crosspolymer) OR (Acrylates AND Methoxy AND PEG-4 AND Methacrylate AND Copolymer) OR (Acrylates AND Methoxy AND PEG-15 AND Methacrylate AND Copolymer) OR (Acrylates AND Methoxy AND PEG-23 AND Methacrylate AND Copolymer) OR (Acrylates AND Methoxy AND PEG-90 AND Methacrylate AND Crosspolymer) OR (Acrylates AND Palmeth-25 AND Acrylate AND Copolymer) OR (Acrylates AND Steareth-30 AND Methacrylate AND Copolymer) OR (Acrylates AND Stearyl AND Methacrylate AND Copolymer) OR (Acrylates AND ("VA" or vinyl acetate) AND Crosspolymer) OR (Acrylic Acid AND ("C12-22") AND Alkyl AND Acrylate AND Copolymer) OR (Acrylic AND Acid AND Stearyl AND Acrylate AND Copolymer) OR (Ammonium AND Acrylates AND Ethylhexyl AND Acrylate AND Copolymer) OR (Ammonium AND Acrylates AND Methyl AND Styrene AND Styrene AND Copolymer) OR (Ammonium AND Styrene AND Acrylates AND Ethylhexyl AND Acrylate AND Lauryl AND Acrylate AND Copolymer) OR (Behenyl AND Methacrylate AND (("t-") OR tert) AND Butyl AND Methacrylate AND Copolymer) OR (Butyl AND Acrylate AND Cyclohexyl AND Methacrylate AND Copolymer) OR (Butyl AND Acrylate AND Ethylhexyl AND Methacrylate AND Copolymer) OR (Butyl AND Acrylate AND Hydroxyethyl AND Methacrylate AND Copolymer) OR (Butyl AND Methacrylate AND Acryoyloxy AND (("PG") OR ("propylene glycol")) AND Methacrylate AND Copolymer) OR (("C12-22") AND Alkyl AND Acrylate AND Hydroxyethylacrylate AND Copolymer) OR (Cyclohexyl AND Methacrylate AND Ethylhexyl AND Methacrylate AND Copolymer) OR (Ethylhexyl AND Acrylate AND Methoxy AND PEG-23 AND Methacrylate AND Vinyl AND Acetate AND Copolymer) OR (Ethylhexyl AND Acrylate AND Methyl AND Methacrylate AND Copolymer) OR (Glyceryl AND Acrylate AND Acrylic AND Acid AND Copolymer) OR (Glyceryl AND Polymethacrylate) OR (Hydroxyethyl AND Acrylate AND Methoxyethyl AND Acrylate AND Copolymer) OR (Lauryl AND Acrylate AND Crosspolymer) OR (Lauryl AND Acrylate AND (("VA") OR ("vinyl acetate")) AND Crosspolymer) OR (Methoxy AND PEG-23 AND Methacrylate AND Glyceryl AND Diisostearate AND Methacrylate AND Copolymer) OR (Methyl AND Methacrylate AND PEG AND ("PPG-4/3") AND Methacrylate AND Crosspolymer) OR (("Polyacrylates-1") AND Crosspolymer) OR (Polybutyl AND Acrylate) OR (Polybutyl AND Methacrylate) OR (Poly AND ("C10-30") AND Alkyl AND Acrylate) OR (Polyethylacrylate) OR (Polyhydroxyethylmethacrylate) OR (Polyisobutyl AND Methacrylate) OR (Poly AND Methoxy AND PEG-9 AND Methacrylate) OR (Polymethyl AND Acrylate) OR (Polypropyl AND Methacrylate) OR (Polystearyl AND Methacrylate) OR (Potassium AND Acrylate AND Crosspolymer) OR (Potassium AND Acrylates AND Copolymer) OR (Potassium AND Acrylates AND Ethylhexyl AND Acrylate AND Copolymer) OR (Sodium AND Acrylates AND Beheneth-25 AND Methacrylate AND Crosspolymer) OR (Sodium AND Acrylates AND Ethylhexyl AND Acrylate AND Copolymer) OR (Sodium AND Acrylate AND Vinyl AND Alcohol AND Copolymer) OR (Sodium AND Polymethacrylate)))) AND (toxic OR toxicity or toxicolog* OR mutagen* OR genotoxic* OR carcinogen* irritat* OR sensitiz* OR photosensiti* OR photoallerg* OR teratogen* OR reproducti* OR (dermal absorption) OR (tumor AND promotion)) – **19 hits**

Glycol Dimethacrylate Crosspolymer – 0
((polyacrylate-14) OR (polyacrylate-29) OR (polyacrylate-34)) - o

Add-ons – Previously reviewed ingredients

May 21, 2018 – Previously Reviewed Add-Ons
Crosslinked Alkyl Acrylates
((((((((((((((((((((((((26794-61-6[EC/RN Number]) OR 74464-10-1[EC/RN Number]) OR 50657-38-0[EC/RN Number]) OR 779327-42-3[EC/RN Number]) OR 182212-41-5[EC/RN Number]) OR Acrylates/C10-30 Alkyl Acrylate Crosspolymer) OR Acrylates/C12-13 Alkyl Methacrylates/Methoxyethyl Acrylate Crosspolymer) OR Acrylates/Ethylhexyl Acrylate Crosspolymer) OR Acrylates/Ethylhexyl Acrylate/Glycidyl Methacrylate Crosspolymer) OR Acrylates/Steareth-20 Methacrylate Crosspolymer) OR Acrylates/Vinyl Isodecanoate Crosspolymer) OR Acrylates/Vinyl Neodecanoate Crosspolymer) OR Butyl Acrylate/Glycol Dimethacrylate Crosspolymer) OR C8-22 Alkyl Acrylates/Methacrylic Acid Crosspolymer) OR Glycol Dimethacrylate/Vinyl Alcohol Crosspolymer) OR Lauryl Methacrylate/Glycol Dimethacrylate Crosspolymer) OR Lauryl Methacrylate/Sodium

Methacrylate Crosspolymer) OR Methacrylic Acid/PEG-6 Methacrylate/PEG-6 Dimethacrylate Crosspolymer) OR PEG/PPG-5/2 Methacrylate/Methacrylic Acid Crosspolymer) OR Potassium Acrylates/C10-30 Alkyl Acrylate Crosspolymer) OR Sodium Acrylates Crosspolymer-2) OR Sodium Acrylates/C10-30 Alkyl Acrylate Crosspolymer) OR Sodium Acrylates/Vinyl Isodecanoate Crosspolymer) OR Stearyl/Lauryl Methacrylate Crosspolymer) AND (AND ("2010"[Date - Publication] : "3000"[Date - Publication]) – 4/713 hits

PMMA ingredients

((((((25777-71-3[EC/RN Number]) OR 9011-14-7[EC/RN Number]) OR Methyl Methacrylate Crosspolymer) OR Methyl Methacrylate/Glycol Dimethacrylate Crosspolymer)) AND ((toxic OR toxicity or toxicolog* OR mutagen* OR genotoxic* OR carcinogen* irritat* OR sensitiz* OR photosensiti* OR photoallerg* OR teratogen* OR reproducti* OR (dermal absorption) OR (tumor promotion)) AND ("2005"[Date - Publication] : "3000"[Date - Publication])) – 1/37 hits

Carbomer

(((((((9007-20-9[EC/RN Number]) OR 9003-01-4[EC/RN Number]) OR 9007-16-3[EC/RN Number]) OR 9007-17-4[EC/RN Number]) OR 9062-04-8[EC/RN Number]) OR carbomer(AND ((toxic OR toxicity or toxicolog* OR mutagen* OR genotoxic* OR carcinogen* irritat* OR sensitiz* OR photosensiti* OR photoallerg* OR teratogen* OR reproducti* OR (dermal absorption) OR (tumor promotion))) – 0/47

SCIFINDER – Feb 2, 2018

Ingredients Previously Reviewed

159666-35-0	25608-12-2	82227-04-1
25035-69-2	25549-84-2	137455-77-7
25212-88-8	25549-84-2	146126-21-8
25685-29-4	9003-04-7	28474-30-8
25035-89-6	9010-92-8	9003-49-0
63744-68-3	109292-17-3	9003-63-8
1203962-19-9	27306-39-4	9003-32-1
9010-77-9	25034-86-0	25249-16-5
26713-18-8	25085-34-1	9011-15-8
26445-96-5	9010-92-8	9003-21-8
27515-37-3	30581-59-0	86416-97-9
25103-74-6	97-63-2	27599-56-0
25749-98-8	888492-33-9	58374-38-2
25750-82-7	957645-61-3	25086-62-8
28208-80-2	75760-37-1	54193-36-1
59650-68-9	36120-03-3	
9003-01-4	1431551-12-0	

LINKS

Search Engines

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

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

Pertinent Websites

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

- FDA databases http://www.ecfr.gov/cgi-bin/ECFR?page=browse
- FDA search databases: http://www.fda.gov/ForIndustry/FDABasicsforIndustry/ucm234631.htm;,
- EAFUS: http://www.accessdata.fda.gov/scripts/fcn/fcnnavigation.cfm?rpt=eafuslisting&displayall=true
- GRAS listing: http://www.fda.gov/food/ingredientspackaginglabeling/gras/default.htm
- SCOGS database: http://www.fda.gov/food/ingredientspackaginglabeling/gras/scogs/ucm2006852.htm

- Indirect Food Additives: http://www.accessdata.fda.gov/scripts/fdcc/?set=IndirectAdditives
- Drug Approvals and Database: http://www.fda.gov/Drugs/InformationOnDrugs/default.htm
- http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/UCM135688.pdf
- FDA Orange Book: https://www.fda.gov/Drugs/InformationOnDrugs/ucm129662.htm
- OTC ingredient list: https://www.fda.gov/downloads/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cder/ucm135688.pdf
- (inactive ingredients approved for drugs: http://www.accessdata.fda.gov/scripts/cder/iig/

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

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

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

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

Botanical Websites, if applicable

- Dr. Duke's - https://phytochem.nal.usda.gov/phytochem/search
- Taxonomy database - http://www.ncbi.nlm.nih.gov/taxonomy
- GRIN (U.S. National Plant Germplasm System) - https://npgsweb.ars-grin.gov/gringlobal/taxon/taxonomysimple.aspx
- Sigma Aldrich plant profiler- http://www.sigmaaldrich.com/life-science/nutrition-research/learning-center/plant-profiler.html
- American Herbal Products Association Botanical Safety Handbook (database) - http://www.ahpa.org/Resources/BotanicalSafetyHandbook.aspx
- European Medicines Agency Herbal Medicines - http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/landing/herbal_search.jsp
- National Agricultural Library NAL Catalog (AGRICOLA) https://agricola.nal.usda.gov/
- The Seasoning and Spice Association List of Culinary Herbs and Spices
- http://www.seasoningandspice.org.uk/ssa/background_culinary-herbs-spices.aspx

Fragrance Websites, if applicable

- IFRA (International Fragrance Association) – http://www.ifraorg.org/
- Research Institute for Fragrance Materials (RIFM)

ACRYLATES COPOLYMERS – RE-REVIEW

Full Panel – September 25, 2018

DR. MARKS: Back to the copolymers. Don, I'll trade you one brown algae and a paraben for the copolymers. At any rate, yes. In the March meeting, the panel looked at the final report and safety assessment of acrylates copolymers and 33 related other cosmetic ingredients, which were published in 2002. This is a re-review. It was opened to add a number of other copolymers; and the concern of course, again, with these, are what are the monomers and sensitivity from them.

We had a robust discussion about this yesterday and had several potential outcomes. One was the close without moving forward, so essentially close and the reopening. The other was an insufficient data versus safe when formulated to avoid irritation. Our team felt we should move to close the report, don't reopen. This was not a no-brainer. And in the past, we've used that sort of somewhat of a litmus test as rather to open and add. If we add an ingredient and they weren't a no-brainer, then we wouldn't reopen.

There were a number of reports with safe conclusions that had different caveats, such as avoid irritation, avoid polymerization of benzene, avoid skin contact for nail ingredients. We felt that trying to put all that together, in a conclusion, that it wasn't a no-brainer with its add-ons; so, we would like to just leave the original report from 2002 as a re-review and not open it to add these other ingredients. So, that's a motion. Close without moving forward.

DR. BERGFELD: A second, or a comment?

DR. BELSITO: First, regarding the benzene materials, we had previously found those polymerized in benzene to be insufficient. And I'll let Monice comment, but it's our understanding that when something is insufficient it's not being reopened and included in this report.

MS. FIUME: That's correct. There's one crosslinked alkyl acrylates that was polymerized in benzene. And in the introduction, it does state that we're not reviewing that ingredient when polymerized in benzene. But it is included for all other solvents, because it was found insufficient when polymerized in benzene.

DR. MARKS: So, is that going to be in the conclusion, if we were to move forward? Because that's one of the caveats.

DR. HILL: Carbomers have benzene.

MS. FIUME: And carbomers wasn't addressed as clearly. When the re-review was done, it did state they acknowledged the industry of removing benzene from carbomer. If I remember correctly, the problem with the crosslinked alkyl acrylates was that it was unclear whether or not it could be produced and be below the levels that are acceptable, based on good manufacturing -- GMP.

The discussion could address benzene as a solvent. You can limit it. You can say, it can't be polymerized in benzene; that's the panel's prerogative. But for that one ingredient, it's not part of this review.

DR. BELSITO: That was one issue. So, we knocked out any ingredient that was polymerized in benzene; and thought that Monice did a very good job in the introduction of pointing that out, it could be brought back together in the discussion.

We went safe as used when formulated to be nonirritating. And there were actually two ingredients that could be removed from the report, because they were already reviewed and in another report.

DR. MARKS: So, just because they were in another report, they'd be removed? Because this new report would have a lot of ingredients which were in former reports.

DR. BELSITO: But they were only recently reviewed, correct?

MS. FIUME: I believe it was 2014. It was the styrene and vinyl type ingredients.

DR. BELSITO: Yes.

DR. LIEBLER: We realize it could go either way; and we felt, therefore, there wasn't a compelling reason to bring them over if they'd just been done.

DR. BELSITO: Right. It was also felt that they could equally belong in either report, the styrene report or this report. So, there was no reason to take them out from a recent report where they were equally relevant.

DR. MARKS: So, we've handled the benzene, handled the irritation from the original 2002, final report. How did you deal with avoid skin contact for nail ingredients? Was that in the conclusion, or is that in the discussion? Because I think we could go forward. Ron Shank, what do you feel in terms of close versus issuing a tentative amended report?

DR. BELSITO: I think that you could do it either way. I would ask for some guidance from Bart and Monice. You could say that, you know, these acrylates products that are safe as used in nail products should be used to minimized contact with skin, as

we've always done. Or, safe as used, they're used as nail products; and in the discussion simply say, acrylates that are designed to be used as nail enamels should be applied in such a way to minimize contact with skin.

DR. SLAGA: We have what we need in discussion?

DR. MARKS: Yes, I'm fine with that. Ron Shank?

DR. SHANK: Are you assuming that all of these 128 add-ons are molecules that are so large that they would not penetrate the stratum corneum?

DR. BELSITO: Dan, you can address that.

DR. LIEBLER: Yeah, I didn't feel that we were assuming it; I thought the data provided to us supported that. But yes, they're all large molecules.

DR. SHANK: For all 128?

DR. LIEBLER: Yes.

DR. HILL: I was concerned that the last set of data we had, we had some that had low molecular weight fractions. And I applaud the industry for supplying that in the 10, 11, 12, 13, 14 percent range. And so, then if you're using it in an eyeshadow, for example, at 20 percent concentration, which some of them are in leave-ons, you could have a significant amount of these low molecular weight species. So, for me, after getting that information, I thought we really need sensitization studies as a sentinel for any other possible thing that can happen, from reactive things like acrylates at concentration of use, for every single one of them. And that's how I felt about it.

DR. LIEBLER: Yes, I mean, we normally think of low molecular weight, and absorption, and other toxicities, other than sensitization.

DR. HILL: But sensitization, for me, serves as a sentinel if you've got things that are known to be reactive in there. Because if we see sensitization at concentration of use -- which I don't guess that this is a big problem out there in the world right now clinically, but then quite a few of these are not in use, I didn't do a tally. I mean, we always have the caveat that if another one will be used, that is not in current use, you go with the concentration of use, so that could be 20 percent. Do we really know enough?

DR. SLAGA: It should be in the discussion.

DR. HILL: So, we can discuss this thoroughly, and that might be fine; but for me, as a sentinel for other possible things, I really want to see sensitization and concentration of use for every single one of them.

DR. MARKS: Okay, I will withdraw my motion, and endorse the Belsito team motion. So, either, Don, you can move or I will move, whichever you want. So, I withdraw my former motion and propose another motion, that we issue a tentative amended report, with a conclusion safe when formulated to avoid irritation.

DR. BELSITO: Second.

DR. BERGFELD: Seconded. So, it's been moved and seconded. Any other comments? We've taken Ron Hill's comments to light and we'll be including those in the discussion in some way. Anything else? Seeing nothing else, I'll call for the vote then. All those in favor? Unani -- oh, it's not unanimous. Against?

DR. HILL: I'm against for exactly the reasons I stated.

DR. BERGFELD: Okay, one against, majority rules. Okay, we're moving on then. Thank you. Now, we're going to the fatty amides, Dr. Belsito, Alkoxylated Fatty Amides.

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DR. BELSITO: Right. So, we're good. Then acrylates copolymer. What a bear. It's almost as bad as brown algae.

We had at one point, when we were reviewing one of these groups, eliminating any that were polymerized in benzene.

MS. FIUME: You didn't eliminate them. In the crosslinked alkyl acrylates, there was one ingredient that could be polymerized in benzene or other solvents. It's eliminated from the re-review because when it was polymerized in benzene the data were insufficient, and we don't re-review something that is insufficient.

For that ingredient, if it's not polymerized in benzene, it's in this document. But if it's polymerized in benzene, it's been excluded from the re-review because it was previously insufficient.

DR. BELSITO: But is that made clear any place?

MS. FIUME: Is that what?

DR. BELSITO: I don't think it's made clear in the document.

MS. FIUME: I thought I had listed it in the intro. I can make it --

DR. BELSITO: In the intro what I read is, in 2000 published…….except when polymerized in benzene. Acrylate may be polymerized in benzene. The available data were insufficient to make a determination of safety. Okay, yes you did, I guess I just didn't pick it up.

DR. LIEBLER: Yeah. Pretty clear.

DR. BELSITO: But then on the crosslinked alkyl acrylates, you have, ethyl acetate plus cyclohexane, water, n-hexane and benzene named as solvents. So, the solvents don't matter? This is the top of page 97, PDF.

MS. FIUME: I can remove it. That was brought in from the old report and I didn't remove the benzene part. I just brought it in as is.

DR. BELSITO: Okay.

DR. LIEBLER: Will this stay in our final version, this text? Or do you need to worry about it?

MS. FIUME: It's in it until it gets published. Every time you review it, we keep the italicized text. But when it goes to the Journal, they don't want to republish existing information, so it all comes out.

DR. LIEBLER: Right, so that will -- my point is it will go away, so I don't think you need to do anything about it. I mean, you could, but it doesn't matter.

MS. FIUME: Okay. I'll just put it in brackets or something so that we know.

DR. BELSITO: So, the same thing with the levels of acrylates being as high as 1,500 parts per million, that will go away too. This is the middle of the page, Composition and Impurities, the first paragraph.

DR. LIEBLER: With the upper limit?

DR. BELSITO: Upper limit of 1,500.

DR. LIEBLER: Right, that will all go away?

MS. FIUME: Right, all the italicized text.

DR. BELSITO: The same thing with the benzene and the carbomer?

MS. FIUME: That will go away from the text, but I don't know if it was ever addressed in that carbomers report, specifically. So, the discussion would probably need to address benzene levels in carbomers because I don't think it was addressed in the original report. That's from about 1982. It was the first time it was reviewed and there was actually no discussion in the report.

DR. BELSITO: It says, however, when the safety of carbomers was reassessed in 2003, the Panel acknowledged the industry practice of removing benzene from carbomer.

MS. FIUME: Yes, sorry about that.

DR. BELSITO: The highest leave-on is 50 percent, except for nails where it's up to 98.6. We're assuming no benzene. Then there is that amine restriction on AMP-acrylates of 5 percent in the EU, which I guess would have to go into our discussion. Safe as used -- do we need to say, when formulated to be nonirritating?

DR. LIEBLER: Is there enough irritation to require -- I didn't have it in mine, but --

DR. KLAASSEN: It's non to mildly irritating.

DR. BELSITO: And it's used up to 50 percent. Dermal irritation, not stated slightly irritating, not stated non-irritating, 25 percent non-irritating, 5 grams slurry in alcohol, slight erythema observed in 20 percent.

DR. LIEBLER: I leave it to you to make that call.

DR. BELSITO: It's used fairly high; 50 percent is the highest leave on. And there are a couple studies that are iffy, so I mean, just to cover your tail, I'd say --

DR. LIEBLER: Fine.

DR. BELSITO: Do we need -- so, in the discussion we need to limit residual monomer, right?

DR. LIEBLER: Right.

DR. BELSITO: Do we want to, again, point out precluding any that are polymerized with benzene?

MS. FIUME: We can. There have been different ways that we have handled benzene. Yeah, it was in the crosslinked alkyl acrylates discussion where it was talked about and then found insufficient. I don't remember -- I think the problem with that

ingredient was that it was unknown how much benzene was residual; and we didn't want to do risk assessment either on that -- you can.

DR. BELSITO: Which is good manufacturing practices to keep residual monomers at a low level to preclude benzene, low levels of other soft solvents. Nail use not a concern despite the fact we don't have data that goes up to 96.5 percent. Do we need a justification for grouping all of these together? Just throwing that out.

DR. LIEBLER: For the groupings that we've used?

DR. ANSELL: Well, we don't want to reopen this (inaudible) into this grouping.

DR. BELSITO: No, I understand, but just for the general public. Just something I threw out there.

DR. KLAASSEN: I don't think we can justify it.

MS. FIUME: There is the start of a justification in the second paragraph in the introduction. "The Panel determined that it was appropriate to include all the copolymers, including cross-linked copolymers" -- which are the cross polymers -- "prepared from monomers that comprise, in part, acrylic acid and/or methacrylic acid, the methyl, ethyl, propyl, or butyl esters of these acids, or the salts of one or both of these acids. Based on this rationale, the 128 ingredients described below are included in the re-review."

DR. BELSITO: I don't think we need to review that in the discussion. Safe as used when formulated to be nonirritating.

MS. FIUME: I do have a question. The Council did question -- two of the ingredients that are currently listed, sodium styrene acrylates copolymer and styrene acrylates copolymer, where in the styrene is vinyl polymers report, from a few years ago. Do you want them removed from this report? They were originally part of the original acrylates copolymer review; they were in the 2014 report.

DR. BELSITO: I don't know, I'm not a chemist. Where do they belong?

DR. LIEBLER: Like you could argue, they can be in either report. I don't think the issue is really chemistry at all. It's more of a question of, what is the practice or the thinking of CIR in terms of the ease of access to the data in the reports. What's the way our audience will get to the data for the ingredient they are interested in?

MS. FIUME: The data is in that original report. I would need to pull data from that report into here to keep them. But there are other styrene ingredients that have not been reviewed, that are listed in this report, so the information would probably need to come in no matter what.

DR. LIEBLER: I mean, if they exist in the report and it's easy for somebody who is interested to find them in that report, then there is no need to bring them into this report.

MS. FIUME: Okay.

DR. LIEBLER: Unless it's not easy for them to find the information and then we pull it into this report because this is where they might look. I guess the question is, for somebody who would want access to data, where would they want to look, what's the easiest path for them?

MS. FIUME: I'm guessing they would search by ingredient, so they can find the actual document.

DR. BELSITO: Right.

DR. LIEBLER: The ingredient takes you to the report?

MS. FIUME: It takes you to the report.

DR. LIEBLER: So, it doesn't really matter. I would say, don't go to the extra trouble of lifting them out of the other report and putting them here.

MS. FIUME: Okay, so just delete those two from this one?

DR. LIEBLER: Yes.

MS. FIUME: Okay.

DR. BELSITO: Which two are we deleting? But we're keeping any data in to support the other styrenes?

MS. FIUME: I haven't pulled the data in yet, apparently, so I would need to still pull it in. It's the sodium styrene acrylates copolymer and styrene acrylates copolymer. But as I said, there are several styrene-containing copolymers that were not reviewed in that 2014 report.

DR. BELSITO: It's the sodium acrylates copolymer?

MS. FIUME: No, the styrene acrylates copolymer and the sodium styrene acrylates copolymer. On Table 1 it's the last third and sixth ingredient.

DR. BELSITO: Paul's only comment was, "Monomer content, molecular weight range issues." I don't know what he means by that.

DR. LIEBLER: Molecular range issues, there is not an issue. In other words, there are none of these that are small enough to be absorbed significantly, so that goes away. And the monomer content is just a discussion item.

DR. BELSITO: We do in discussion?

DR. LIEBLER: Yeah. I thought you could use text from the above prior reports for the discussion, crib them together. Key points are high molecular weight precludes absorption and systemic tox; data support lack of sensitization. And just remember to minimize the residual monomers.

MS. FIUME: Systemic tox?

DR. LIEBLER: Yes.

MS. FIUME: What was the rest of the sentence?

DR. LIEBLER: High molecular weight precludes absorption and systemic tox.

MS. FIUME: Oh, and systemic?

DR. LIEBLER: Yes.

Marks Team – September 24, 2018

DR. MARKS: Okay team, are you ready? I know you've been waiting for me; my computer booting up here. The first group of ingredients are the draft amended report on the acrylates copolymers. And in the March meeting, a final report on the safety assessment of acrylate copolymer and 33 related cosmetic ingredients were published in 2002. We reopened that report from 2002, in this past March meeting, and added a number of copolymers.

Tom and Ron, do you like the 128 ingredients? A lot of ingredients because we had a lot of add-ons. And what comments? The 2002 report was safe when formulated to avoid irritation of the ingredients in that report. And we had concerns about monomers, the acrylic acid, methacrylic acid, et cetera.

And in a discussion, a report, these polymers are low and below that would induce sensitization. And then we also had some polymers that were used on nails and we advised that they should avoid the contact when they're used as nail ingredients. And also, we should avoid polymerization in benzene in some of these.

It's a lot of ingredients with some variations in the conclusion from previously. Ron, Ron and Tom, what do you think? We should be moving on to a tentative amended report. Question is, what is the conclusion and are the 128 ingredients that are proposed okay?

DR. SHANK: If all the 128 proposed ingredients are so large that they wouldn't cross the stratum corneum, then I would say okay. Otherwise, there are so many unknowns, I would recommend not including any of them initially. And this is a re-review summary.

DR. EISENMANN: My comment on what's suggested is not include the styrene-containing ingredients, because there's a styrene copolymer report that you've already done. And if those styrene ingredients are left in the report, then some more information from the styrene report needs to be brought in. Because we did submit some unpublished data on the styrene acrylates copolymers that's not in this report yet.

If that report hasn't been published yet, my feeling is you don't really need to bring in those because you've -- I think it was a 2014 review of styrene-containing ingredients.

DR. HILL: I would counter that by saying that if that information is good to go, we should port it over; because I feel like the acrylates would drive any toxicology or safety issues, much more so than a styrene; polymerized styrene, but that's just my take on it.

DR. MARKS: Ron, do we then need the molecular weight of all these polymers to answer your question?

DR. SHANK: Yes. What's the advantage to adding these to old reports and then issuing it all over again?

DR. MARKS: I thought the proposal was adding a lot of new ingredients. And as we've done in the past, the purpose would be to add a number of new ingredients and then combine the reports into one report.

DR. SHANK: These aren't all no-brainer compounds to put together. There's a lot of unknowns about these compounds. We're going to use old reports to justify these new ones and say they're all safe.

DR. HILL: No.

DR. SHANK: And I don't think that's a correct way to go.

DR. HILL: Yeah, so I'm not thinking that we will use all the old ingredients to justify the new ones. I wrote down that we need molecular weight distribution characterization for every single one of them. And we need low molecular weight fractions, especially details below molecular weight 1000.

I wrote down that there's a nice presentation format indicative of the type of information, that's needed and helpful, on page 196 of the report. Where we have an average molecular weight, and that less than 1 weight percent is molecular weight less than 1000. Because then that tells us what are the chances that we'd have anything for sensitization.

We know there's residual monomers of this type here. We would be reading across, I think, and assuming that those are typical across the group. And that assumption is somewhat of a leap, but maybe not unreasonable. Once we have all the molecular weights, and we get some idea about that, and we have physical descriptions, then we can know, yes, this one is like that one. We're going to explicitly say in the discussion we're making the assumption that the monomer levels will be comparable to these others that are like that and be done with it. But I certainly can appreciate your take on it.

Of these, some of them had to come up for re-review. Like carbomers, right, we were due -- I thought there was at least one of them that was due. And I don't remember beyond that if that was the only one or not. Because if I remember, we had a 2017 report, a 2011 report; but I thought the carbomers -- I wrote them down somewhere -- were older.

MS. FIUME: The carbomers report was old. The others were 2011 and 2017.

DR. HILL: Okay. All right. There were four total though, weren't there?

MS. FIUME: It was the original one that's in question, the acrylates copolymers. Then there was the 2017 report on crosslinked alkyl acrylates, the polymethyl methacrylate report, And then the carbomers report.

DR. HILL: Yes. The acrylates copolymer was 2002. That's also past the 15-year mark as well, right?

MS. FIUME: Well, that is the report that is being brought forward for the re-review.

DR. MARKS: It's being reopened.

DR. HILL: There's that one and then three more, two of which are more recent.

MS. FIUME: Yes.

DR. HILL: Okay. And I think the discussion last time was that really these all do fit together. But then really the question is, do you go back and keep the carbomers separate and review that? It's really now named as one ingredient, if I understand correctly.

MS. FIUME: It is one ingredient now.

DR. HILL: But there were differences that were noted definitely in some of the carbomers and the characterizations we had, notably, in terms of residual benzene. And I suspect they may not be using benzene anymore, or they're being really rigorous about what the EU has done in terms of drawing the line. And that would translate to us I'm pretty sure. In the carbomers, I think it was explicitly pointed out, discussed and so -- anyway.

DR. MARKS: We have don't reopen, reopen, get the molecular weights. So, that would be an insufficient data announcement at this point. And we want to see the molecular weight ranges. We'd like to know what the lowest molecular weight is so that we can address the issue of sensitization to the monomers. Tom, your input?

DR. SLAGA: No. I agree. Would go with that and I had some problem with too many conclusions --

DR. MARKS: Pardon?

DR. SLAGA: Oh, I'm sorry. I just said there's several different conclusions if you brought them all together --

DR. MARKS: Exactly.

DR. SLAGA: -- you would have to change some things. I have problems with that; it would be better not to have them.

DR. MARKS: The copolymer and 33-related cosmetic ingredients, it was formulate to avoid irritation. And then it refers back to the ethyl methacrylate. Don't touch the skin when you're putting on the nail. Then we have the crosslinked alkyl acrylates. That's the one in which, don't use benzene.

And then there's another report in that the number of monomers would be below the sensitization. So yeah, we have to somehow bring all those -- yeah, I know. Ron Shank, you're -- the easier course is say, don't reopen.

DR. SHANK: I thought Ron Shank's was the easiest.

DR. MARKS: And these extra ones that want to be added on, do them separately. And you're right, we used to use the no-brainer rule as to when we reopen and add ingredients.

DR. SHANK: If you have older reports that have different conclusions with different caveats, I don't see the advantage of trying to put them all together. They've already been published. And then try to add a whole bunch more, where we have very little information, and say this is a new report.

DR. SLAGA: You'd have to have two separate conclusions.

DR. MARKS: Mm-hmm.

DR. SHANK: I think this can be handled as just a summary.

DR. SLAGA: I agree.

DR. HILL: Well, I didn't look at it in the light of determining whether the one that's reopened is to be amended. All the information we need is there. I'm not sure that it is, is what I'm saying. If I don't have molecular weight averages and some sense of distribution, and low molecular weight on all of those, then for me that's insufficient. And that all occurred before I was on the panel. And even the one that came out in 2011, that was from when I just started and some of that's a little shaky from where I sit.

DR. MARKS: Tomorrow I'll move -- it sounds like we've come to the conclusion, team, close this report. Don't reopen. And the reasons are previous -- I would say the primary reason, it's not a no-brainer.

DR. SHANK: Well, we're trying to combine reports that have different conclusions with different caveats. And then adding over 100 more. And I don't see the advantage to that.

MS. FIUME: Can I ask a question? All of the previous reports were actually safe as used, except for one of the crosslinked alkyl acrylates, which was insufficient only when polymerized in benzene. But the other reports were safe as used, correct? Except for maybe safe when formulated to be nonirritating. But basically, they were all safe conclusions.

And we've done it in the past, when we've done re-reviews. That if it makes sense to combine ingredients, even though they've been recently reviewed; so that in the future when we go to re-review if the large group fits together, that we have combined them in the past.

DR. SHANK: I think they fit together if they're also large, that they don't cross the stratum corneum. Without that assurance, then I don't think we know they all fit together.

MS. FIUME: So rather than not reopen, we've done it before, where we've take the next step, ask for data -- because at any time you can reverse the decision to reopen. But if we got the data to show that they fit together, we could go forward if the information show that. And if not, then stop the re-review, rather than stop it at this point.

Because there are some acrylate copolymers that are new ingredients that weren't in the original review. And that original review did have probably a grouping that may or may not have been put together at this point. But they are those 34 ingredients that were originally reviewed.

So even if the larger group didn't fit, there are acrylate copolymers that might be worthwhile to at least include in this re-review, even if you didn't include the entire group at the next point. If you get the information and decide they don't all fit, rather than close the re-review at this point.

DR. HILL: For me, I just think we're not strictly following the no-brainer rule anymore. Because if we were, we would have a lot of groups that aren't groups, at this point, over the last five years. But we sometimes are grouping things administratively when it also makes sense, in principle, from a chemical point of view.

And in this particular case, there seems to be a high probability, in my mind at least, that all of these are going to be molecular weight where the polymers themselves are well above any kind of threshold, plus the physical chemical characteristics that go with them to be able to cross the stratum corneum.

And then the concern lands on the residual monomers. The concern lands on any low molecular weight tail that would be molecular weight below 1000, which can in fact penetrate into the skin. And those all would be in common.

And then any of these that don't have that information, as far as I'm concerned, split conclusion, they're insufficient, you don't read across to them. And then they're on the list, they've been reviewed. And if somebody wants to support it, they can come forward with data, we can reopen, et cetera, et cetera, et cetera.

That's my take on this. It's a monster group. I know where you're coming from.

DR. EISENMANN: Very few of the new ones have any use at all. I don't think you're going to get any data on those. So, you know, it's kind of wasting time, I think.

DR. HILL: So, not reopening from that point of view makes sense?

MS. FIUME: But in the past we haven't used lack of use as a reason to not include an ingredient.

DR. HILL: Plus, I always think that's no reported uses, no uses that come up in the survey.

DR. EISENMANN: Correct. But frequently, it's also no suppliers; so, there's no one to ask for the information.

DR. HILL: Well, we could footnote no current suppliers. I don't have any way, I know, to personally search that. I've asked, but I don't get that answer. Maybe there isn't any exhausted way, but you all have as good a way as anybody in the world I believe.

DR. EISENMANN: All I do is look to see who's reporting to us. I can't say who -- you know, there might be somebody out in the world that's making these; but for polymers it tends to be one company to make this ingredient, rather than some other stuff.

DR. HILL: Agree. Agree.

DR. MARKS: Can we handle, Ron Shank, per your concerns and also, Ron Hill, and all of ours -- I mean, the issue is the monomers. Can we have a conclusion, or in a discussion, that the monomer levels are so low that they would not be sensitizing; and perhaps address it that way since -- Carol, addressing your concern, that if they aren't in use we aren't going to get molecular weight ranges. So, we'll be right back to the same place we were right now, is we're dealing with what we know are large polymers. But the concerns are obviously the component of those polymers or the monomers that could penetrate the stratum corneum and cause really a sensitization.

Is there any other toxicologic concern other than sensitization with these ingredients? I mean, benzene was addressed again, can refer back to that and --

DR. HILL: Acrylates, if they penetrate into the skin under conditions of the use, yeah. I mean, those are known carcinogens.

DR. MARKS: Carcinogens, if they penetrate. But is that again the monomer?

DR. HILL: Well, no -- well, yes, it is in that particular case. And we do have percentages as high as 1 percent, 1.5 percent, 1.2 percent. The real issue is -- because I think in most cases the suppliers would assert that yeah they're there, but they don't get released under conditions of use.

And so, that's, I think, an issue that's still pending that I've talked about more than once over the years; which is it's in a cream and we put it in leave-on in the hair and hit it with a hot blow dryer, or is there any significance to that release. And I haven't seen any studies come forth to really address that rigorously; or if there are, we haven't been capturing them. I'm not trying to raise gremlins where we don't need to.

DR. MARKS: Right.

DR. HILL: But I think to just completely write it off -- so there is some writing in the 2017 report, where I think at least finally got a good solid discussion on this. There's still, in my mind, a few loose ends where we need to have some science done. And it ought to be crowd source because there must be more than one supplier of some of these polymers. But then, I don't know. But some of the major ones, I think, they have the horsepower to consider doing it should they choose.

DR. MARKS: I think we're down to -- it's been a good discussion. We're down to choice between a tentative amended report, versus insufficient data announcement, versus don't reopen. And we've heard -- what do you think about handling -- we can ask for more -- the molecular weight ranges, but we know we aren't going to get that for all these 128.

What do you think about having a conclusion, something formulated at -- monomer level is below sensitization. Something to that effect. Oh, Ron, you're smiling. And we can go back to don't reopen. I'm just kind of sorting through what we will move tomorrow. What I'll move. And then we'll obviously see what the Belsito team has -- their take on it. Wilma?

DR. BERGFELD: Yeah, I just want to say, you've move away from the increased use and increased concentrations. So, they're being used. If you don't reopen, in some ways you work against safety, because you're letting those things exist without reviewing them. Those ingredients.

DR. HILL: And I will say this about the sensitization. Where I think there could be a reactive involved in anything more extreme like precancerous affect, I think sensitization is a great sentinel. Because if you see that, you know there might be an issue. If you really never see that, there isn't probably an issue. That's not 1000 percent rule, but I think it's a pretty good sentinel in general for that sort of thing.

DR. MARKS: And we're going to get back to this monomer issue with pyrrolidone. Again, there's acrylates in that. In there, there was one reference where in the discussion it was stated that if you had between 100 to 200, as I recollect, you would not sensitize -- molecular weight -- you would not sensitize. I'm trying to remember how -- we'll get to that.

Which of those proposals tomorrow, team, do you like? Move forward with a tentative amended report with a conclusion to formulate to minimize monomers? And we can have a robust discussion about what we mean by that. That's one idea.

The other is insufficient data announcement. We want to get as much as we can with a molecular weight range and monomer levels. We'd want that anyway, no matter moving forward. But we could formally do it as an insufficient data announcement.

And then lastly, the idea of not reopening at all because this isn't a no-brainer. And I guess those extra add-ons could be perhaps another report. I don't know. It's kind of kicking the can down the road, but that's okay. Which do you prefer, team? I think that's the options. Is there another option? We can't ignore it, that's not an option.

DR. SHANK: No. I would then go with the insufficient data requesting molecular weights on all these new, what is it 128, ingredients. And assurance that the monomer levels are below -- I'll go along with sensitization. There's more to toxicity than sensitization.

DR. MARKS: Right. That's why I asked that question.

DR. SLAGA: I thought it was irritation too.

DR. MARKS: Yeah. Irritation was in one of the conclusions. Actually, in the 33, as I recollect; it was formulate to be nonirritating.

DR. SHANK: If it's just irritation, you can say when formulated to be nonirritating.

DR. MARKS: Yeah. But what we really want to know is, what's the amount of monomers and is there a potential for sensitization. I think that's the hard -- and then presumably using sensitization as a bellwether for perhaps other toxic effects from the monomers.

DR. BERGFELD: Jim?

DR. MARKS: Yes?

DR. BERGFELD: Are you going to address the response that was from the SCC Committee? The memorandum from Alexandra on March 5th. Where it talks about deleting some of the ingredients that were put into this 128? And for a variety for reasons.

DR. MARKS: That's where I, right in the beginning, when I asked are the ingredients okay. Wilma, I have the memo.

DR. BERGFELD: Well, we talked about the styrene already, and I guess you left that one in. We talked about the monomers. But there are -- on the second page, there is a glycerol polymethyl acrylate which doesn't belong in the report for this group. Acrylate copolymers with four or more monomers, I guess, don't belong there either.

DR. MARKS: Which page are you on, Wilma?

DR. BERGFELD: This is on the memorandum that we got of March 5th from Alexandra, from the Scientific Committee of the PCPC. CIR Scientific Committee.

DR. MARKS: Is that in the PDF? What page on the PDF?

DR. HILL: Three hundred.

DR. MARKS: Three hundred?

DR. HILL: Yeah.

DR. MARKS: Thank you.

MS. FIUME: They were addressed last time. That's the March one?

DR. BERGFELD: March 5th, yeah.

MS. FIUME: That was addressed at the last meeting.

DR. BERGFELD: Oh, okay. So those are all out?

MS. FIUME: Yes. The question was the styrene for this meeting. And there are two ingredients that are in that styrene report. The other styrene ingredients are not included in that report, unless I've missed them. It would be the sodium styrene acrylate copolymers and styrene acrylates copolymers were reviewed recently in the report on styrene and vinyl type styrene copolymers as used in cosmetics. But there are additional styrene type polymers in this report that have not been reviewed previously.

DR. HILL: And that last thing you said was going to be my comment. That's part of the reason I argued we should bring them over into here if we are, in fact, keeping this open.

MS. FIUME: I'm sorry, Dr. Hill, keep the two that were just reviewed and bring in the data?

DR. HILL: Yeah. That's what I think we should do. Because again, it's not that styrene monomer has no toxicology, but I still think the acrylates are more likely to drive anything that would be of safety concern in this one. But then Ron Shank may want to comment on that.

DR. MARKS: Okay. Wilma, did we answer your questions?

DR. BERGFELD: Yeah. I just thought it should be addressed. Thank you.

DR. MARKS: Good.

DR. HILL: I think we did discuss it some last time, because that memo came out before the meeting.

DR. BERGFELD: Yeah.

DR. MARKS: Okay. If I get the sense of the team, an insufficient data announcement will be the motion tomorrow. And what we would like to see, the molecular weight ranges and monomer levels of the new ingredients, so it can be formulated to minimize the monomers. Or just get the ranges at this point? Is that correct, am I interpreting what you said, Ron Shank?

DR. SHANK: Yes. Well, then this really isn't a re-review. Because we don't re-review and then ask for -- we'll be including new things and then we say it's insufficient because we don't know very much about the new things. And so that doesn't sound like a re-review kind of report. It would be a totally new report, I guess.

DR. SLAGA: A no-brainer.

DR. MARKS: Yes. I think that's what Ron Hill was saying earlier, we've gotten away from the no-brainers. Because it seems like the ones we've reopened, more recently, we have asked for more data before we've come to a conclusion. We're back to should we reopen or not. Ron Shank, I know the way you feel.

DR. SHANK: What would staff like to --

MS. FIUME: It would still be considered a re-review, because the initiation for the report was the 2002 report on the acrylates copolymers. When we consider a re-review, the first look is are there no-brainer ingredients? Secondly, are there data to cause it to reopen? And then if we've grouped them, once it's been decided that, yes, these ingredients fit together, it is okay to ask for information. Because there are questions that you need answered to go ahead and finalize the conclusion. So, we have done this in the past.

DR. HILL: Here's an example of one of those. In the carbomers report we have details of the manufacturing process of proprietary information. I assert that that's essentially always true. But then for safety assessment it would make a big difference -- in this particular instance, I was focused on the word catalyst when I was reading. If it's really a catalyst, such as a zeolite, okay it's filtered off, no problem. If it's a free radical initiator, then really at least some information about can it be retained as an impurity in the final product; and if so, does that have any consequence.

I realize we review ingredients and not what's supplied by a particular vendor. But we do use the information that's regarded as, here's what we received, we're proceeding with the assumption that this is typical and basing everything off that. But we have nothing in that particular case.

I feel like we got less than what would be available in a spec sheet. But then this report was from way back in 2003 when it finally came out, so it's old stuff. And I don't know what the customs were at that time. And then there are a few other things, but that was just one mentioned while we're discussing the particular issue of reopen/don't reopen.

DR. MARKS: Okay. Team, where do you want to go? Tentative amended report? Insufficient data announcement? Don't reopen? I think there's our three choices. And I kind of got the sense that we're going to do an insufficient data announcement and go ahead and proceed forward. And the insufficient data gives us the molecular weight ranges and monomer levels for the new ingredients. Does that sound -- Tom, what do you think?

DR. SLAGA: I mean, Ron's point about it doesn't sound good to open something, then add something and then ask for more data. I mean, I know we probably have done that in the past. But I guess, I would lean towards do not open.

DR. MARKS: Not open. Not open, Ron Shank?

DR. SHANK: Yes.

DR. MARKS: Yes.

DR. HILL: I'm age before beauty, I can defer to my senior colleagues who've been at this a long time. But my preference would be an insufficient data analysis just to bring things up to current science in some cases.

DR. MARKS: Well, what I'm going to do tomorrow is say that our team favored not reopening. But we also discussed issuing an insufficient data announcement. I may ask Ron and Ron, both of you to comment on that. I'll try and summarize that basically with don't reopen because this is not a no-brainer. There's a lot of new ingredients and we want new information; and we don't think that's exactly how a re-review should be done. And then we'll see where we head.

I get the sense we're a little bit fluid. If the Belsito team has good reasons for proceeding forward, we'll probably concur with that. We won't be rigid on the do not open -- or reopen. Actually, at this point we actually have a -- technically I guess, Monice, we have opened it, we're just going to close it.

MS. FIUME: Yes. You would close it.

DR. MARKS: Okay.

DR. HILL: The other administrative question I would have is these other things that I think are pending needs. They're not a ton, but there are a few. Should I just wait and see where we land? Because we usually don't read too lengthy a list on the Tuesday.

DR. MARKS: Yeah. I think let's wait.

DR. HILL: That works for me.

DR. MARKS: Okay. Let me make a few notes here, excuse me, team. Okay I think I've captured that. Team, tomorrow don't hesitate -- after I move that we close this report without moving forward, and I'll mention the insufficient data announcement, but we'll make that motion. Don't hesitate to chime in, so to speak. Okay. Any other comments about this? These ingredients? Okay so tomorrow I'll move we'll close without moving forward.

Full Panel – March 6, 2018

DR. BELSITO: This is another situation where in 2002, we looked at the acrylates copolymer and 33 related cosmetic ingredients. It's time to relook at it. In the process of doing so, we found on PDF page 7, a whole list of potential acrylates that could be added.

We looked at this list and we thought that most could be added. We were told the glyceryl polymethacrylate and glyceryl acrylate/acrylic acid copolymer had already been included in the styrene report. We were -- is that correct?

MS. FIUME: Yeah.

DR. BELSITO: We eliminated -- why did we eliminated glyceryl poly and glyceryl acrylates?

MS. FIUME: High frequency of use and it should be coming up soon.

DR. BELSITO: Oh. High frequency of use and will be coming up on its own. Then some of these were included in the styrene report and could be eliminated. We wanted that checked to make sure that we weren't double dipping. Also, looking at other acrylates that could have potentially been put into the styrene report, but were not, they could be added into this report.

Then the question became, because we had looked at so many other acrylates in the past, some of which will be coming up in the near future for review, others that we reviewed in 2017, could have materials added to them. We thought that we, in combining all of this, could bring in the acrylates copolymers report that we're adding. We could bring in the crosslink acrylates as used in cosmetics that we had reviewed in 2017.

And that we could bring in the polymethylmethacrylate/methyl methacrylate cross polymer, et cetera, that was reviewed in 2011. And that we could bring in the carbomer report; and that's now just a single carbomer rather than other numbers that was reviewed in 1982, the last full review. However, we did want to bring in ethyl methacrylate.

So, essentially, bringing in all of the acrylic copolymers, but not the monomers. And taking a look at this, making sure that we're not including any ingredients that were included in the styrene report. But again, excluding the glyceryl because, based upon volume of use, it will be reviewed on its own.

DR. BERGFELD: Comments, Dr. Marks?

DR. MARKS: We agree. We would second the reopening to add ingredients. I'm not quite sure why we would want to separate out one or two if they fit in this group chemically, so that all of them would be together. Like the ethyl methacrylate and the glyceryl, you mentioned, because of high frequency of use. If it's included in here, wouldn't that safety assessment take care of it?

DR. BELSITO: We didn't want to look at the monomers.

DR. LIEBLER: Yeah. The ethyl methacrylate is a monomer, so it's totally different.

DR. MARKS: Okay. I got you.

DR. BERGFELD: Ron Hill?

DR. HILL: I thought we might potentially want to keep some of the data, but not the ingredient itself, on the ethyl methacrylate, depending on if we can remove it when we decide it's not relevant. But I thought we could keep data from that.

I'm comfortable separating out the glyceryl ones as suggested. I'm comfortable if we were to have left them in, but I'm comfortable with leaving them out as they suggested.

I would just like to see if we could consider, even if we keep it in the other report -- and I know this would be an exceptional thing -- to put those five acrylates from the fluorinated polymer report, at least the data for them, in whatever we put together for this one. I think it's going to take them some time to assemble this particular one anyway, and then we can decide where they belong.

But the kinds of data we would be soliciting for read across, for the acrylates, we might be able to read across to those five and get them cleared with a little bit of further information about the fluorine chemistry, whereas that won't be the case in the other report.

DR. BERGFELD: I think that can be done without comment and dealt with later.

DR. HILL: Okay.

DR. BERGFELD: Any other comments? Paul? Curt?

DR. HILL: How about in terms of need, then, are we getting to that?

DR. BERGFELD: Yes. In just a moment. So, we're going to call to question?

DR. BELSITO: No need to look at needs until we see a report.

DR. HILL: Right. I know. Okay. All right. So, we don't have -- this is just guidance, right?

DR. BELSITO: We're just deciding to reopen this and add these ingredients.

DR. HILL: Right. Okay. Cool.

DR. BERGFELD: Bart reminds me that this is just a strategy to an approach. So, any comments now would be well received, if there are any others. Seeing none, the meeting is now concluded. And I just wanted to --

Belsito Team – March 5, 2018

DR. BELSITO: Okay, so acrylates copolymers, that's where we're going next. And the major question is, what are we doing with this document? What are we adding in, what are we not adding in? I'll pass that over to Dan.

DR. LIEBLER: I'm commenting on the memo on PDF Page 2. I agree that we should add the cross-linked alkyl acrylates and the polymethyl methacrylate, methyl methacrylate crosspolymer, methyl methacrylate/glycol dimethacrylate crosspolymer. The first two bullet, I agree.

And then the last bullet, the ones entitled carbomers, I keep this separate. They are a variable mix of the same precursors, which give the family a clear identity. Either they all go into the current re-review, or they stay together as a separate report, which I favor.

MS. FIUME: Okay so all of those now go under the name carbomer?

DR. LIEBLER: Right.

MS. FIUME: So, it's one ingredient? It's now one ingredient?

DR. LIEBLER: I see.

MS. FIUME: And it would be up for re-review next year? Oh, no, this year.

DR. BELSITO: Right. The crosslinked alkyl acrylates are actually the group that we're asked to review?

DR. LIEBLER: Right.

DR. BELSITO: So that's in there regardless. You're saying the polymethyl methacrylate go in.

MS. FIUME: I'm sorry, actually, the group that we're reviewing is the acrylates copolymers.

DR. BELSITO: So, the crosslinked --

MS. FIUME: They were reviewed in -- it was published in 2017. But some of the ingredients that were listed as the possible addons have cross polymers.

DR. BELSITO: Okay. Dan, you're saying we're adding the crosslinked alkyl acrylates?

DR. LIEBLER: Yes.

DR. BELSITO: The polymethyl methacrylate group?

DR. LIEBLER: Right.

DR. LIEBLER: But the carbomers you don't think we should add in?

DR. LIEBLER: Yeah. Now, even though it's now simply known as one ingredient, or carbomer, it's just a mixture of all this stuff.

MS. FIUME: Yeah. Carbomer, they're all technical --

DR. SNYDER: That's already in a published report. That's already in the report, right? Isn't it?

MS. FIUME: It was published way back in '82. When it was reaffirmed in 2003, it was as the ingredient carbomer. And under the technical name there is various carbomers, various numbers after it. But it's one ingredient.

DR. LIEBLER: Okay. I think we can include them.

DR. BELSITO: So, Dan, you're saying add the carbomers.

DR. LIEBLER: Add the carbomer. Yeah, I didn't read that part carefully enough; that this is simply known as one ingredient, which is a mixture of all of these similar components. Since it's one ingredient, it makes more sense to just put it in with this.

MS. FIUME: Do you want to see what the monograph looks like? Does that help you at all?

DR. LIEBLER: At the moment, no. Maybe later, yes.

DR. BELSITO: Monice, if I just heard you, we just did the acrylates copolymers --

MS. FIUME: Crosslinked alkyl acrylates just got -- it was done back in about 2011. It just got published.

DR. BELSITO: Okay. So, the one we did last year in 2017, the acrylates copolymer we're not adding into this? Is that correct?

DR. SNYDER: No. That's the alkyl acrylates in 2017.

MS. FIUME: Now you see why you have this strategy. A group of 34 total acrylates copolymers was published in 2002.

DR. BELSITO: Right.

MS. FIUME: In 2017, we published the monograph on the crosslinked alkyl acrylates. But as part of the list of potential addons, there are cross polymers listed as well. I didn't know if you wanted those ingredients brought in, that information brought in; I didn't know how it needed to play --

DR. BELSITO: The 2017 information?

MS. FIUME: Yes.

DR. LIEBLER: The first bullet.

DR. BELSITO: Okay.

DR. LIEBLER: And so, I think yes. And just to be clear there are copolymers and cross polymers or crosslinked polymers and they're different. Chemically, they're a bit different; they contain many of the same things. And they're similar enough for our purposes -- in their uses and the considerations of safety for endpoints, they're similar enough that they certainly belong together in a review.

DR. BELSITO: Okay.

DR. LIEBLER: But copolymer, and crosspolymer or crosslinked polymers are distinct, and that's why they have different names.

DR. BELSITO: Okay. But the document that we're actually being asked to look at for review is the acrylates copolymers, and 33 related, that we did in 2002. That's what's bringing this all up, right?

MS. FIUME: Right.

DR. BELSITO: Okay.

MS. FIUME: And that list of ingredients is on PDF Page 4.

DR. BELSITO: Okay.

MS. FIUME: It names the ingredients that were in that document.

DR. BELSITO: So that's the actual one we need to review?

MS. FIUME: Yes.

DR. BELSITO: Okay. So, we're obviously reviewing that to bring in additional acrylates copolymers, which brings in additional crosslinked alkyl acrylates copolymers, so we're opening up the 2017 report. And while we're doing that we're

going to have the polymethyl methacrylate group and the carbomer group. That's where we've come so far. Okay. What about ethyl methacrylate, which we did in 2002?

DR. LIEBLER: Is that the --

DR. BELSITO: That's the nail.

DR. LIEBLER: That's the monomer.

DR. BELSITO: Right.

DR. LIEBLER: Nope.

DR. BELSITO: Do not add it?

DR. LIEBLER: Nope.

DR. BELSITO: And the crosslinked alkyl acrylates we are adding in?

DR. LIEBLER: Correct.

DR. BELSITO: And the polymethyl methacrylate we are adding in?

DR. LIEBLER: Correct.

DR. SNYDER: Crosspolymers, yes.

DR. BELSITO: Right. And then the carbomer we're adding.

DR. LIEBLER: Yes.

DR. BELSITO: So basically, everything that Monice mentioned in this, we're adding in except for the ethyl methacrylate monomer. Is that correct?

DR. SNYDER: Correct. At this point we're reopening --

DR. BELSITO: Right.

DR. SNYDER: -- with the potential to add these depending on what the data say.

DR. BELSITO: Okay. And do we want to delete acrylate/VP (VA) copolymers since it was included in the vinylpyrrolidone Polymers 2018 report?

So, we reviewed that with the acrylates copolymer, the document under consideration that is bringing in the add-ons in 2002. But then it looks like we just reviewed it with another group called vinylpyrrolidone polymers.

MS. FIUME: Right.

DR. LIEBLER: I mean, I don't object to having it in, but I don't know if that doubling up the review, having the same ingredient in two different reviews.

DR. BELSITO: Is that double dipping?

DR. LIEBLER: Yeah. I'd like to hear what you and Bart have to say about that.

MS. FIUME: We're recommending deleting it. We've done this before where something's been reviewed and then brought into another -- reviewed as part of another family. We've gone ahead and deleted them from the group. So, we can delete this.

DR. BELSITO: Yes. I'd be fine. I said yes. Anyone else have a comment there?

DR. LIEBLER: No.

DR. BELSITO: And then, Dan, the potential add-ons that are listed on PDF Page 7. Huge list.

DR. LIEBLER: Wow. Add them all except the last line ethyl methacrylate.

DR. BELSITO: Where is this?

DR. SNYDER: Previously reviewed, but similar.

DR. BELSITO: Oh.

DR. LIEBLER: On PDF 7. Where it says previously reviewed.

DR. BELSITO: Oh, we already said we weren't going to do them, right?

DR. LIEBLER: Right. Well, it's listed too. You asked about this page so what's what I said. Anyway, everything on the page except ethyl methacrylate belongs in the report.

DR. SNYDER: Man, some of these -- ethylhexyl acrylate/methoxy PEG-23 methacrylate/vinyl.

DR. KLAASSEN: -- the difference between monomers and polymers.

DR. LIEBLER: And of course, not the vinylpyrrolidone, but you've got that already.

DR. BELSITO: Okay. And then, Monice, I didn't understand crosslink substance that occurred below that; diallyl maleate. What was that in reference too?

MS. FIUME: In the crosslink --

DR. BELSITO: Do we want to add those?

MS. FIUME: No. It was just identifying what the crosslinked substances are. We did that in the crosslink alkyl acrylates report. It's just trying to show you what's new versus what you've already looked at, because I didn't know if it mattered. It's just identifying -- in case there was any problematic substances.

DR. BELSITO: These are the crosslinkers that we've already reviewed in the prior report?

MS. FIUME: Well, they were the crosslinked substances, yeah, in the previous report.

DR. BELSITO: And would there be any new crosslink substances that would be brought in as a result of everything else we're adding now? It would probably be nice to have a little table on that as well when we look at this. Do you think, Dan?

DR. LIEBLER: Well, the crosslink substances aren't cosmetic ingredients, right?

MS. FIUME: Right. Well, some of them are, not all of them.

DR. LIEBLER: If any of them are, then I think they would need to be considered separately because they're not the polymers. They're small molecules that crosslink polymers, which is how they're used in this context. And they wouldn't be suitable to include in this report for the same reason ethyl methacrylate is not suitable to include because they're small.

MS. FIUME: I wasn't proposing them for inclusion --

DR. LIEBLER: Right.

MS. FIUME: -- in the original report --

DR. BELSITO: But do we want tox data for them since they could be contaminants? Is that what --

DR. SNYDER: Yeah. Impurities.

MS. FIUME: They were identified in case there were any concerns. Usually, I believe, they're not residual, but they look --

DR. LIEBLER: I don't think we needed extra tox data on these up front. I think we do need to know impurities -- method of manufacturer, composition impurities.

DR. SNYDER: It's going to be key to the report.

DR. LIEBLER: Right.

DR. BELSITO: Okay. So, we don't need those at this point? We'll need impurity data and then decide where to go from that?

DR. SNYDER: Right.

MS. FIUME: So now that we've done that, I believe this morning there was a document from --

DR. BELSITO: Bart, yeah.

MS. FIUME: -- the council, talking about the strategy. I don't know if that affects anything.

DR. ANSELL: No. I don't think it raises any --

MS. FIUME: Any question? We're okay?

DR. ANSELL: Yeah. Any new issues. We wanted to address the monomer. There's questions of the vinyl pyrrolidone polymers and the one ester, which had been included.

MS. FIUME: Because as usual, these are the re-review with add-ons, there's always the option later on to remove --

DR. BELSITO: To take them out.

DR. SNYDER: Yeah, we're just opening and considering them as add-ons at this point, yes.

MS. FIUME: So, the next time you see, you'll see a draft document with everything that was identified today.

DR. BELSITO: Do we want to address this issue of the styrene that they're specifically bringing up? I mean, that had to do with the one we kicked out. Are there other that have -- ammonium acrylate, methyl, styrene and styrene copolymer? But these weren't reviewed in the prior report. Is that correct?

MS. FIUME: Sodium styrene/acrylates copolymer was reviewed. Styrene acrylates copolymer was reviewed. And styrene acrylates/ammonium methacrylate copolymer was reviewed in the original report.

DR. BELSITO: In this original report?

MS. FIUME: Yeah. In the acrylates copolymers, yes.

DR. BELSITO: Okay. But are there any that we reviewed in that -- so which ones are we kicking out, that was put into the pyrrolidone report?

MS. FIUME: Acrylates VP copolymer.

DR. BELSITO: Okay. Have we looked at styrenes? Were any of these included in the styrene group? Have any of these, that the council is raising, been previously reviewed? Or even if they have not, is there a family where they would better be suited for? You see what I'm saying?

MS. FIUME: Yeah.

DR. ANSELL: There were two styrene-based ones. Ammonium acrylates/methyl styrene/styrene copolymers and ammonium styrene/acrylates/ethylhexyl/ lauryl acrylate could have fit within the safety assessment of styrene and mono type styrene copolymers.

DR. LIEBLER: So, there is a styrene report?

DR. SNYDER: Styrene copolymer. Yeah.

DR. LIEBLER: And it has been done recently, or?

DR. ANSELL: 2014.

DR. LIEBLER: Oh, 2014. Okay. Short memory. And these ingredients are in that report?

MS. FIUME: I'm trying to get to it right now.

DR. LIEBLER: So, if they were in that report, we don't need to include them in this report for the same reason as the vinylpyrrolidone. And if they weren't in that report, we can include them in this report.

DR. ANSELL: Right. I think Monice can resolve this, but our comment was really that they belong there, not that they were there.

DR. LIEBLER: Yeah. If they weren't there --

DR. BELSITO: Then they're going to dangle out there for another 14 years before the styrene report comes up for re-review. And I thought you were interested in getting things cleared. If we can clear them in this report, can't we correct that mistake when it comes up again in 2029, when none of us will be on this panel and someone else can grapple with that argument?

DR. ANSELL: Of course, defer.

DR. BELSITO: I think we should go through these individually.

MS. FIUME: I'm not seeing any overlap right now with what was reviewed in the styrene report, but we'll make sure that we're not reviewing them twice.

DR. LIEBLER: Okay. I mean, they are acrylate containing polymers, so in that sense they can certainly fit in this group. I mean, many of the other ingredients here have other monomer components that could lead them to be classified in other ways. But they all are acrylates.

We're all acrylates here.

DR. BELSITO: Okay. Continuing with this letter from council, we've already decided not to put in the methacrylate ester monomers.

Then there's, glyceryl polymethacrylate does not appear to belong in this report. And it's not clear if glyceryl acrylate/acrylic acid copolymer belongs. Perhaps a separate report added to the 2019 priority list should be created for these two ingredients, plus glyceryl polyacrylate.

And then goes on to mention that glyceryl monoester/glyceryl polyacrylate was included in the original glyceryl monoester report but was not considered appropriate for the glyceryl monoester report at the time of the re-review so it's been orphaned.

DR. LIEBLER: Those two are listed here in that list on page 7.

DR. BELSITO: Right. But council's recommending we not include them and we review two ingredients separately. Why is that Jay, do you know?

DR. ANSELL: It's not quite that declarative. If not, then it should be done. But I think, you know, if you want to put it in here, we don't necessarily object.

DR. BELSITO: Dan?

DR. LIEBLER: Keep it in.

DR. BELSITO: Keep it in.

DR. SNYDER: At this point consider it, right.

DR. LIEBLER: Because otherwise, there's not a solution. I mean, they're orphaned and it's not certain that the glyceryl will be another report for sure.

DR. LORETZ: Yah. the frequency of use was 337, so it was thought that it would come up naturally. The question was, did it really belong here, or would it be better separate.

DR. BELSITO: So, it's going to come up based on volume of use regardless?

DR. LIEBLER: Oh, so it will come up? It won't just stay orphaned indefinitely?

DR. BELSITO: Right.

DR. LIEBLER: Okay, then we can leave them out.

DR. BELSITO: Potential add-ons, add everything in except glyceryl. What are the two? Glyceryl polymethacrylate?

MS. FIUME: And glyceryl acrylate/acrylic acid copolymer.

DR. BELSITO: Okay. And then the next point; acrylate copolymers with four or more monomers or ingredients that would have long names are generally considered polyacrylate X. Have the polyacrylate X ingredients, for example, polyacrylate-14, yadda, yadda, yadda.

Been reviewed to determine if it's appropriate to include any of these ingredients in the acrylate copolymer report. Some of the polyacrylate X ingredients containing styrene were included in the styrene copolymer report and should not be included in this re-review.

If I'm reading this correctly, there are two issues. Are there additional ingredients that were in the styrene copolymer report that we said we're going to review in this one? And are there polyacrylates that we haven't included that should be included in this one?

MS. FIUME: We're going to double check on the styrenes to make sure that we're not --

DR. BELSITO: Double dipping.

MS. FIUME: -- double dipping. And I want to say I think a number of polyacrylates have been reviewed but let me double check. That might be included in that report. Polyacrylate-2 was in the styrene report.

DR. BELSITO: And what about 5, 12, 15 -- I guess, just check to make sure there are no polyacrylates dangling out there that could potentially be added to this report.

MS. FIUME: That's 5, 12, 15, 16, 18, 21 and 30, they were all in the styrene report.

DR. BELSITO: Okay. And are there others in the INCI dictionary?

MS. FIUME: We'll double check. I think Bart may have looked, but we'll make sure we have them all.

DR. LIEBLER: I mean, we're presented with these big heterogeneous lists of ingredients, that you could make an argument to include or not include any of them. So, we either follow that logic and include them, or we pull things out if there's going to be another report, or if there is another report, but they really belong.

DR. SNYDER: But it seems to be there is somewhat of a subgrouping for the method of manufacture that would suggest that there's -- we don't need method of manufacture for every individual one, but there could be some subgroupings that we're --

DR. LIEBLER: True. We're not going to have data on everything. I'm sure we'll have enough data --

DR. BELSITO: You don't think so?

DR. LIEBLER: I'm finished talking.

DR. KLAASSEN: Maybe we could make the family a little larger and have it all carbon-containing chemicals.

DR. BELSITO: Okay. As there are already many ingredients in this report with potential additions, the ingredients from the acrylates crosspolymer are new acrylate crosspolymers, polymethyl methacrylate and carbomers should not be added to this report. I think we've already said we want to add them and then we can always throw them out. Okay.

So, that we've address council. Okay. Anything else on the acrylates? Who's going to have the --

MS. FIUME: Tomorrow?

DR. BELSITO: No. Not tomorrow. But who's going to have the wonder of writing this up if we don't throw things out?

MS. FIUME: We'll see though. We do have new staff, so you know.

DR. SNYDER: You're reporting, Don.

DR. SNYDER: Delegate, delegate, delegate.

MS. FIUME: Exactly.

DR. KLAASSEN: Might be a top one for beginners.

MS. FIUME: You know, sometimes you just have to be thrown right into the fire. Only way to learn.

Marks Team – March 5, 2018

DR. MARKS: Anything else? If not, let's move on and this will be the last one before lunch I think. It's 11:41. I think we should move on, not ready quite yet for lunch. Is that okay, Ron and Tom?

We have the acrylates copolymers.

DR. HELDRETH: I'll cover it.

DR. MARKS: Okay. Great. We have a memo from Monice, dated February 23 of this year. Strategy for acrylates copolymer and related ingredients re-review. In 2002, the CIR published a final report on the acrylates copolymers and 33 related cosmetic ingredients and concluded that they were safe in cosmetics when formulated to avoid irritation. It's been 15 years and it's time for a re-review, so that's why we're looking at these ingredients again.

Then there was a proposal to have possibly 65 add-ons that have not been looked at by the CIR. Then also ethyl methacrylate. Accordingly, there are some questions in this memo. The CIR is requesting the panel's guidance on inclusion of these 65 ingredients, this re-review. You see under the bullet points, the crosslinked alkyl acrylates published in 2017. The polymethyl methacrylate, et cetera, published in 2011. Then carbomers, which were published in '82 and '03. It's a whole huge group which, if we reopen it, we could potentially include.

DR. BERGFELD: Did you include the acrylates that we considered under the fluoropolymers?

DR. MARKS: Yes. We're going to get -- I mentioned that to Ron before we took a break. Would those go? So, I think the first question is, do we want to reopen it and have an amended tentative report with these new ingredients, these added ingredients?

DR. SLAGA: Reopen and add?

DR. MARKS: Reopen and add, reopen and add, okay.

DR. BERGFELD: I agree.

DR. MARKS: Go ahead, Carol.

DR. EISENMANN: It's not turning on right now. But ethyl methacrylate, I don't think will belong in this report; it is the one I especially don't think it belongs. Because you already have a monomer report, and maybe it goes in that monomer report. It just has very few uses, and it is used in a similar manner to the monomers that are in that report.

So, in that report it's -- although I know it's ready, it's the timing for reopening and looking at it again, the issue. I think we're okay with waiting until you look at it with the monomers report.

The other one I was a little -- glyceryl polymethacrylate. I don't know if that belongs. There is a glyceryl polyacrylate that has kind of been orphaned. You originally reviewed with the monoesters; and then when you re-reviewed the glyceryl monoesters, it got left off appropriately.

I don't know if you either want to do a report with those two ingredients or put them both in this report. That one was kind of -- it depends on if you think that glyceryl polymethacrylate is appropriate. I think that's the most important comments we have.

The other comments are generally -- you've already created some bins of polymers and do you leave those bins the way they are, or do you keep -- like you have a group of styrene copolymers. So, maybe the styrene ones don't belong in here, they go in with the styrene. Or there is going to be soon a VP copolymer report, so all of those would take precedence. You have a cross polymer report; maybe all the cross polymers go in there.

There is also a group of ingredients, polyacrylates with a number. And these are named that way because they would have really long numbers -- really long names, I should say. They have four or more monomers. I think those still have to be

reviewed to see if some of them are appropriate for this report. I think probably there are a few that are appropriate for this report.

DR. HELDRETH: We had similar issues trying to think about, what's the bin going to be here. And part of the problem is the original report that had 33 ingredients to it, it also contained some styrene ones and a polyvinylpyrrolidone one. One additional option may be that we go ahead and start this re-review and break it into pieces and have actual multiple re-reviews going on with the bins that you chose.

Maybe we pull the styrene ones out of here and start a re-review of it, but separately as a styrenes.

DR. EISENMANN: Well, I don't think you need to do it yet. You can do it when -- the time period when the styrene -- because I don't think there's any of these ingredients that really -- other than the glyceryl polymethacrylate. That has a fairly high use level.

Other than that, I don't think the other ingredients warrant pushing them forward. They can come up when the next time -- when the monomers come up, when the styrene polymers come up, when the cross polymers come up. I don't think there's any rush to review any of the other ones, but the glyceryl polymethacrylate has 300 and some uses, which I think would put it into the 2019 priority list if you decide to take it out of this one.

DR. MARKS: Tom, Ron, how do you want to approach it?

DR. HILL: I'm still -- with the exception of the -- was it the ethyl methacrylate? And I don't know what to do about the one that has the PVP, which has been suggested for deletion because it's already, I guess, in the other one.

I thought about this in another way which is, we face this problem of what are we putting our emphasis on when we talk about, for example, some of these zinc compounds where we have a counter -- undecylenate for example. So, we reviewed this component of it in some other report as a zinc salt, and now do we talk about it in here?

That caused me to think about, well, what are the concerns across this category? Because essentially, all of these are large molecular weight as far as I know. We get to verify that large molecular weight. The concerns I would have, from a toxicology point of view, would be really in common across all of them; to me, it doesn't really matter if they're cross polymers or if there's styrene stuffed into the mix.

It's like filing a paper where there are multiple things in there; and in every note I can use tags and I don't care where they're filed, but I lose it in one note because it's in some folder for this but it has that. It's a similar problem and I don't know.

Where I landed on this was, as monstrous as it feels to put all of these together under one umbrella, create subcategories like we did for the polysaccharides report, because the concerns that we would be looking at, from a toxicology point of view, I think are in common across all of them. Adding these fluorinated ones that we just talked about and see if -- I don't' know that there are any unique things. But I also get Carol's point of view completely.

In terms of staff effort, that's on your radar when -- I mean, I think about that. But in terms of the day to day operation, that's you and Monice and the staff members who I'm thinking are trembling. We're talking about 100 group of polymers with a lot of different monomers.

DR. HELDRETH: I think the resources are certainly there for the CIR staff to do it. I know it will be a pretty big burden on industry to go out and survey hundreds of ingredients for one report. That may be something to think about when strategizing this; that if we do make a huge report like this and include all the acrylates polymers, that it may take a significant amount of time to get the survey completed and include that in the report later.

DR. MARKS: So, if we're not in any rush and we know one of them is going to pop up for the 2019 anyway -- or the next cycle -- it's not on this group, right?

DR. EISENMANN: If you include it in this report, it will be in this report. But I presume glyceryl polyacrylate belongs in this report in addition to glyceryl polymethacrylate.

DR. HILL: Yes, that other orphan. And so, what I was suggesting is think about making one big report. You all take your time getting it put together, and when you have all the information, then bring it back. Because this isn't a draft report at this stage, right? This is really a guidance solicitation if I understand correctly.

DR. HELDRETH: Right, when it comes back, then it would be a draft report. This is really just a strategy document at this point.

DR. HILL: That was my impression.

DR. MARKS: Right, this is not -- we aren't going to land on an amended tentative report today. It's just making the decision to reopen. And then we had the discussion, at this point we have the 65 ingredients plus the 33 in the previous report. And those or maybe more.

Let me read what Ron Shank had to say because I think it's important as we move forward. Can we state that the 65 potential add-ons are of such as large molecule size as to preclude their penetration through the skin and therefore not enter the circulation? If so, we do not need to consider systemic toxic effects of the copolymers. For those ingredients that are to be used in lipstick where ingestion may occur, potential systemic toxicity may be a concern.

And then his next paragraph; do we have any toxicity information on the monomers used to produce the 65 potential add-ons that haven't already been considered in the 2002 report? It appears that the following monomers used to prepare some of the potential add-ons were not part of the 2002 report. And he had, ethoxylated palm alcohol, T-butyl methacrylate, butyl acrylate, cyclohexyl methacrylate, 2-ethylhexyl-methacrylate, and acyloyloxy propylene glycol methacrylate. He says, let the chemists sort these out before the toxicologists work on the monomer issue. So, there you go, Bart.

Page 9 table, highlighted ingredients have functions other than those included in the original reviews, that are new functions. That's Ron's comments to take note as we move forward in this.

DR. HELDRETH: And that's certainly another option, is to treat this like a very traditional re-review; only potentially adding no brainers into it and moving forward with it that way. But again, the prerogative is up to the panel.

DR. HILL: I don't know what would be the no brainers here, because I always start with that.

DR. MARKS: And so, in that case I think we're doing a real review of these, not just reopen and add.

Okay. Tomorrow, I presume, I'm going to be seconding a reopening of these 33 acrylic copolymers with the intent to add 65 ingredients, maybe more. Maybe we will handle them, as you suggest Ron Hill, to create subcategories and see where that takes us. And address Ron Shank's questions too. Sound good, Ron, Tom?

DR. SLAGA: Sounds good.

DR. MARKS: It is 11:55. We have the zinc salts next. Should we adjourn for lunch? Looking at Tom Slaga has already closed his computer, the answer is, yes. We are not going to proceed without the whole team. We don't have the whole team, but even one less, we're not going to proceed without you, Tom. Thank you.

ACRYLATES COPOLYMERS – ORIGINAL REVIEW

April 3-4, 1997

Special presentations to the Panel on … and on Acrylate Copolymers (by Dr. Ian Cottrell) were made during the closed session. Dr. Bergfeld thanked Dr. McEwen for making arrangements for these presentations. She remarked that the Panel found the information relating to … acrylate copolymers in cosmetic products very helpful.

June 5, 1997

At the June 5, 1997 Team meetings, informal data requests on this group of ingredients were made by both the Belsito and Schroeter Teams. The combined list of data requested from industry is included below:

1. Current concentration of use data
2. (Chemical properties and method of manufacture; including impurities data, especially unreacted monomers, precursors, catalysts, plasticizers, etc.
3. Dependent on the amount of unreacted monomer, etc., dermal reproductive/developmental toxicity data may be needed
4. Ocular irritation data at concentration of use, if available
5. Skin irritation and sensitization data on Acrylates Copolymer and/or Styrene Acrylates at concentrations of use
6. Two genotoxicity studies, one using a mammalian system, on Acrylates Copolymer of Styrene Acrylates Copolymer and on Acrylates/VA Copolymer; if positive, a two-year dermal carcinogenicity assay performed using NTP methods is needed

In response to the above data requests, the following types of studies were received prior to (but after meeting materials had been mailed) the present meeting: impurities analysis, acute oral toxicity, acute inhalation toxicity, dermal irritation, ocular irritation, repeated insult patch test, and Ames mutagenicity test. Having briefly reviewed these studies for the first time on the preceding day, the Panel noted that data on Acrylates/VA Copolymer are needed for each type of study in the list of informal data requests. The Panel also noted that the amount of methyl methacrylate in Acrylates Copolymer is of concern, and that additional studies may be needed.

The Panel voted unanimously in favor of tabling the Draft Report on Acrylates Copolymer until the December 8-9, 1997 Panel meeting. This action was based on the fact that the Panel did not have an opportunity to review the large submission of new data prior to the present meeting.

December 8-9, 1997

Dr. Belsito said that a significant amount of information was received in response to the informal data requests issued at the June 5-6, 1997 Panel meeting. However, skin irritation data on the Acrylates/VA Copolymer were not included in the submission. Dr. Belsito noted that data already included in the CIR Draft Report indicate that this ingredient was quite irritating to the skin, perhaps, primarily, because it appeared to have been used full-strength. Dr. Belsito said that the data also indicate that Acrylates/VA Copolymer is extremely toxic to the eye.

Dr. Belsito noted that his Team determined that the available data are still insufficient for evaluating the safety of this group of ingredients, and that the following data are needed: (1) Current concentration of use data, especially on the Acrylates/VA Copolymer, (2) Impurities data, including precursors, catalysts, and plasticizers, and other ingredients, (3) Skin irritation data, at the concentration of use, on the Acrylates/VA Copolymer, and (4) Ocular irritation data, at the concentration of use, on the Acrylates/VA Copolymer, if available.

Dr. McEwen said that the Panel has reviewed irritating chemicals before, and has not frequently expressed the need for data at a concentration that is less than irritating. However, he noted that the Panel has stated than an ingredient cannot be irritating in formulation, and did not see why the Panel could not address Acrylates/VA Copolymer in a similar manner.

Dr. Schroeter said that his Team recognized that industry is eliminating the unreacted monomer from Acrylates/VA Copolymer, and, if this is the case, then the need for data becomes much less demanding in terms of irritation and sensitization. Thus, Dr. Schroeter's Team asserted that the Acrylates Copolymer ingredient family is safe as used.

Dr. Belsito said that, typically, when the Panel has used the terminology safe as used, the function of the ingredient and its use concentration range have been known, and the ingredient was not irritating or sensitizing or was not sufficiently absorbed within the use concentration range. Dr. Belsito said that the Panel does not know the use concentration range for Acrylates/VA Copolymer in cosmetics and does not have data indicating the concentration of Acrylates/VA Copolymer that does not cause skin irritation. Dr. Belsito also said that data in the Draft Report indicate that Acrylates/VA Copolymer is corrosive when placed on the skin. Thus, even though Acrylates/VA Copolymer is low in unreacted monomer, it can be extremely irritating.

Dr. Bailey made comments relating to the issue of composition and impurities (monomers and other contaminants that may be present). Initially, he referred to a risk assessment on acrylamide and the polyacrylamides that was done in Sweden. He said that he was somewhat hesitant to mention this because he was unsure of its relevance. However, he said that in understanding that acrylic acid can be derived from acrylamide, the risk assessment is relevant and also points to some of the other issues relative to styrene residues etc. in setting a specification. A fairly detailed risk assessment on acrylamide and polyacrylamides was conducted

in Sweden. Basically, it is a worst case risk assessment where the investigators considered exposure not only from one product, but from all products that an individual may be using at any given time. Dr. Bailey noted that a risk of 2×10^{-3}, which is fairly significant if one accepts it, was determined.

Dr. Bailey noted that in the risk assessment mentioned above, the investigators are assuming a level at a specification of 0.01% of residues of acrylamide in the polymer. Thus, he said that the Panel may wish to consider not only the issue of acrylamide residues, but also styrene and other contaminants that could be present. Dr. Bailey recalled that data from either one or two companies are represented in the risk assessment, and that whether of not the data are representative of what is on the market is questionable.

Dr. Bailey added that, in his opinion, the available data in the CIR report are fairly incomplete in terms of providing the Panel with what it needs to know about contaminant residues.

Dr. Shank noted that the Acrylates/VA Copolymer is not being used in cosmetics.

Dr. Bergfeld said that it could be stated in the report discussion that the data are insufficient for evaluating the safety of Acrylates/VA Copolymer in cosmetics.

Dr. McEwen said that the Panel has data on VA Copolymer, and that these data indicate that this ingredient is severely irritating, but that the irritation is reversible.

Dr. Belsito recalled that at the June 5-6, 1997 Panel meeting, a variety of impurities was requested, and that the only information received was on the level of monomer impurities. He wanted to know if the Panel is now concluding that the remainder of the information is no longer needed.

Dr. McEwen noted that mutagenicity data, reproductive toxicity data, and other toxicity data are available on acrylates other than Acrylates Copolymer.

Dr. Belsito reiterated that his Team concluded that the available data are insufficient for determining safety and that the following data are needed:

1. Current concentration of use data, especially on the Acrylates/VA Copolymer
2. Impurities data, including precursors, catalysts, and plasticizers, and other ingredients
3. Skin irritation data at the concentration of use on the Acrylates/VA Copolymer
4. Ocular irritation data at the concentration of use on the Acrylates/VA Copolymer, if available.

Dr. Belsito said that a modification of this conclusion would be a statement to the effect that these ingredients are safe for use in cosmetic products, if formulated to avoid irritant levels of the Acrylate Copolymers.

Ms. Fise wanted to know how the issue of impurities would be dealt with.

Dr. Belsito said that one would assume that the Panel does not need to be concerned about impurities, based on the other toxicology data that are available.

Dr. Shank said that if the Panel is willing to use the available data on several, but not all, of the ingredients, then the Panel has sufficient toxicological data to indicate that the ingredients are not a toxicological problem, whether or not impurities are present.

Dr. Slaga said that it could still be emphasized in the report discussion that impurities (any of the catalysts, initiators, monomers etc.) should be kept at a minimum.

Dr. Belsito wanted to know if the information on levels of the monomer, received from Chemir Polytech Laboratories, should be included in the report discussion. This would be done to indicate that the level of monomer present is very small, and would provide further support for a safe as used conclusion.

Dr. Slaga said that limiting levels of the monomer should not be the only concern, because in order to reduce levels of the monomer, the levels of catalyst and initiators have to be increased to make sure that the reaction goes to completion. Therefore, all of the impurities related to leftover monomers, catalysts, and initiators have to be kept at a minimum.

Dr. Bailey said that if the Panel's conclusion on the safety of the Acrylates Copolymer ingredient family is premised on a limited amount of data indicating that some manufacturers are taking steps to produce a product that is freer of contaminants, then this should be captured in the report discussion and, possibly, in the conclusion.

Dr. McEwen did not see the need for inclusion of such a statement in the report conclusion. He said that it is understood that a manufacturer is going to produce an ingredient that is as free of impurities as possible.

Ms. Fise said that if this is the case, why doesn't industry supply the data.

Dr. Bailey noted that one company has stated that residues of the monomer are present at concentrations of $\leq$ 20 ppm. He said that perhaps, either in the report discussion or conclusion (or in both), it should be stated that the initiators, plasticizers, etc. should be kept at a minimum, since no data are available on this.

Based on the Panel's discussion, Dr. Belsito proposed the following conclusion for the Acrylates Copolymer ingredient family: Safe for use in cosmetics when the concentration of copolymer is adjusted (or designed) to minimize irritation and when the level of unreacted monomers, catalysts, and other impurities are kept at a minimum.

Dr. Shank wanted to know what the minimum is.

Dr. Belsito said that this information was requested from industry, but was not received.

Dr. Slaga said that it would be better if the Panel could establish specific restrictions on impurities, but this is not possible.

Dr. Shank said that the issue of impurities should be handled in the report discussion, but not in the conclusion.

Drs. Shank and Slaga agreed that a statement to the effect that impurities should be kept at a level that is as low as analytically possible should be included in the report.

Dr. Carlton noted that Acrylates/VA Copolymer is a very irritating substance when undiluted, and that the Panel needs data indicating the concentrations at which skin irritation is not observed. He favored issuing a Tentative Report with an insufficient data conclusion, with the data needed to complete the safety assessment listed in the report discussion.

Dr. Belsito said that the issue now is how the Panel should deal with unreacted monomer and catalysts.

Dr. Shank said that the Panel has dealt with this issue through its review of a variety of toxicological tests that yielded negative results for the ingredients tested. He said that if levels of impurities were a problem, this would have been evident in test results.

Dr. Bergfeld said that the preceding statement by Dr. Shank should be included in the report discussion.

The Panel voted unanimously in favor of issuing a Tentative Report with the following conclusion: Based on the available data, the Acrylates Copolymer group of ingredients is safe for use in cosmetics when formulated to avoid skin irritation. The ingredients included in this group are:

Acrylates Copolymer
Ammonium Acrylates Copolymer
Ammonium VA/Acrylates Copolymer
Sodium Acrylates Copolymer,
Ethylene/Acrylic Acid Copolymer,
Ethylene/Calcium Acrylate Copolymer,
Ethylene/Magnesium Acrylate Copolymer,
Ethylene/Sodium Acrylate Copolymer,
Ethylene/Zinc Acrylate Copolymer,
Ethylene/Acrylic Acid/VA Copolymer,
Acrylates/PVP Copolymer,
Acrylates/VA Copolymer, Steareth-10 Allyl Ether/Acrylates Copolymer,
Acrylates/Steareth-50 Acrylate Copolymer,
Acrylates/Steareth-20 Methacrylate Copolymer,
Acrylates/Ammonium Methacrylate Copolymer, Styrene/Acrylates Copolymer,
Styrene/Acrylates/Ammonium Methacrylate Copolymer,
Ammonium Styrene/Acrylates Copolymer,
Sodium Styrene/Acrylates Copolymer,
Acrylates/Hydroxyesters Acrylates Copolymer,
Methacryloyl Ethyl Betaine/Acrylates Copolymer,
Lauryl Acrylate/VA Copolymer,
VA/Butyl Maleate/Isobornyl Acrylate Copolymer,
Ethylene/Methacrylate Copolymer,
Vinyl Caprolactam/PVP/Dimethylaminoethyl Methacrylate Copolymer,
Sodium Acrylates/Acrolein Copolymer,
PVP/Dimethylaminoethylmethacrylate Copolymer, AMP-Acrylates Copolymer,
Polyacrylic Acid, Ammonium Polyacrylate,
Potassium Aluminum Polyacrylate,
Potassium Polyacrylate,
Sodium Polyacrylate

Dr. Bergfeld said that a report discussion addressing the issues discussed during the open session, skin irritation and impurities, will be developed.

At Dr. Bergfeld's request, Dr. Bailey agreed to make the report that he mentioned earlier (risk assessment on acrylamide and polyacrylamides) available to the Panel.

May 18-19, 1998

Dr. Belsito recalled that at the December 8-9, 1997 Panel meeting, the Panel concluded that these ingredients are safe for use in cosmetics when formulated to avoid skin irritation. He also noted that during the public comment period for the Tentative Report, several submissions on mutagenicity and carcinogenicity testing were received. Dr. Belsito said that the study on the dermal oncogenicity of 2-ethyl- hexyl acrylate (one of the monomer units of Acrylates VA Copolymer) that was received was perhaps of most concern to the Panel. In that study, 43% and 83% concentrations of this chemical induced skin cancer. However, in reviewing the document, the Belsito Team concluded that the most likely mechanism for this finding was the chronic, very intense irritation of the skin. This opinion was based on the fact that when the 43% treatment group was discontinued after 24 weeks and the animals were observed throughout their lifetime, there was no evidence of skin cancer. Furthermore, Dr. Belsito noted that an additional group in this study was dosed with 2.5% 2-ethylhexyl acrylate, and that there was no evidence of skin cancer at this concentration.

In addition to the above comments, Dr. Belsito said that in a presentation to the Panel that was made by Dr. Ian Cottrell, it was stated that the acrylates are polymerized, virtually to 100%. Referring to information in the CIR report, he also noted that acrylate copolymers would typically contain ≤ 20 ppm of unreacted monomer, which is well below the 2.5% dose that was found to be safe in the above study. After considering the dermal carcinogenicity study as well as the presentation to the Panel that had been made by Dr. Ian Cottrell, Dr. Belsito's Team determined that a conclusion of safe for use in cosmetics, with a restriction of ≤ 20 ppm unreacted monomer, could be issued.

Dr. Schroeter noted that members of his Team disagreed, stating that it cannot be concluded that the Acrylates Copolymer group of ingredients is safe because of the data discussed by Dr. Belsito. He added that the 2-ethylhexyl ester is difficult to quantify, and that his Team expressed concern over its presence. Furthermore, Dr. Schroeter said that there are no available data that could be used to arrive at a safe concentration for this impurity.

Dr. Slaga said that there was some concern that the 21% dose of 2-ethylhexyl acrylate induced a higher incidence of carcinoma than did the 86.5% dose in the dermal carcinogenicity study. Based on these results, he noted that the Schroeter Team was unable to establish a safe concentration.

Dr. Belsito said that there were four test groups in the dermal carcinogenicity study (2.5, 21, 43, and 86.5% 2-ethylhexyl acrylate, respectively). He recalled that the group dosed with 43% 2-ethylhexyl acrylate was dropped from the study after 24 weeks and subsequently reverted back to normal. Furthermore, the 21% dose group that was allowed to continue beyond the 24 weeks also had carcinomas.

Dr. Shank said that the test results make it difficult for one to conclude that 2.5% 2-ethylhexyl acrylate is a safe concentration.

Dr. McEwen disagreed. He said that if one looks closely at the dermal carcinogenicity data, these data are indicative of a physical irritation phenomenon. Dr. McEwen proposed that the reason why 43% 2-ethylhexyl acrylate did not cause skin tumors is because dosing was discontinued before the skin irritation progressed to tumor stages. He also asked the Panel to review the changes in the skin that were observed prior to tumor formation, which included not only hyperkeratosis, but other types of lesions.

Regarding the skin changes noted prior to discontinuation of treatment with 43% 2-ethylhexyl acrylate, Dr. Slaga said that limited application of almost any carcinogen will cause these changes, regardless of whether it is genotoxic or irritating.

Dr. McEwen noted that the 43% concentration was applied for 24 weeks and that 2.5% was applied for a lifetime. Comparatively speaking, he said that the mice tested with the 43% concentration over a period of 24 weeks received the higher dose.

Dr. Slaga emphasized that 20 carcinomas were reported for the group that received 21% 2-ethylhexyl acrylate, versus 14 carcinomas for the group that received 86.5% 2-ethylhexyl acrylate. With this in mind, he said that the Schroeter Team did not know how to judge these results in terms of establishing a threshold concentration for the induction of skin tumors.

Dr. Shank said that irritation is one possible explanation for the results of the dermal carcinogenicity study, but is not the only explanation.

Dr. McEwen said that irritation (erythema) was not the only skin effect noted; trauma was also observed.

Dr. Belsito wanted to know whether the reduction in carcinoma incidence at the highest concentration tested (86.5% 2-ethylhexyl acrylate) was suggestive of the fact that it was so irritating that it was actually toxic.

Dr. Slaga said that it was not possible to determine a dose response in the study. Furthermore, he said that if the results at the highest test concentration (reduction in carcinoma incidence noted) were indicative of a toxic effect, then there could be a lower dose that could yield more tumors.

Dr. Belsito noted that the limitation established by his Team, ≤ 20 ppm of unreacted monomer, is much lower than the 2.5% concentration of 2-ethylhexyl acrylate that did not cause skin tumors in the dermal carcinogenicity study.

Dr. Slaga wanted to know the origin of the ≤ 20 ppm limitation.

Dr. Belsito recalled that Dr. Ian Cottrell had indicated in his presentation to the Panel that industry allows the polymerization reaction to progress to nearly 100%, primarily because the monomers have an unwanted odor. Dr. Belsito also referred to the following statement in the impurities section of the Acrylates Copolymer Draft Report: A company reported that in its production of Acrylates Copolymer, it controls impurities in the form of residual, unreacted monomer (i.e. ethyl acrylate, methyl methacrylate, methacrylic acid, and acrylic acid) to ≤ 20 ppm.

Dr. McEwen said that ≤ 20 ppm unreacted monomer is not an industry standard, but is a limitation that the Panel could propose and announce to the public for comment.

Dr. Shank said that this limitation is acceptable only if there are data to substantiate that ≤ 20 ppm is well below toxic levels for the monomer, and that the Panel does not have these data. He also said that ≤ 20 ppm monomer is based on what industry says that it has achieved, and not on safety.

Dr. Shank said that he does not know the mechanism of action of the carcinogen and cannot rely on the negative results for 2.5% 2-ethylhexyl acrylate in the dermal carcinogenicity study. He also said that the mechanism of action proposed by Dr. McEwen is plausible, but that there are others as well.

Dr. McEwen said that the no-effect-level is 2500 ppm.

Dr. Shank said that when one is dealing with a carcinogen and there is a no-effect-level in an eighty-mouse study (80 mice at that one level), it cannot be said that level is a level that has been proven to be safe.

Dr. Belsito said that a number of negative mutagenicity studies, with the exception of the mouse lymphoma assay, are included in the Draft Report on Acrylates Copolymer. He also noted that oral carcinogenicity studies on acrylic acid and ethyl acrylate were negative, and that the dermal carcinogenicity study on 2-ethylhexyl acrylate was the only study in the Draft Report over which his Team had expressed concern.

Dr. Shank said that his Team had no concerns about the safety of acrylic acid, but that the safety of 2-ethylhexyl acrylate is definitely a concern.

Dr. Klaassen noted that at a concentration of 2500 ppm, 2-ethylhexyl acrylate was not carcinogenic in mice (group of 80). However, at higher concentrations, carcinomas were observed. He asked for any suggestions as to what could be done in order to establish an acceptable limitation.

Dr. Shank said that if it could be established that 2-ethylhexyl acrylate is carcinogenic through irritation only, then a threshold could be argued.

Dr. Klaassen wanted to know how suitable the ATGC transgenic mouse is for determining promoters.

Dr. Slaga said that this strain is good for promoters, but not as good for complete carcinogens.

Dr. Bailey said that in a situation such as this, FDA would typically do a quantitative risk assessment to actually extrapolate from the available data to a risk, and determine whether or not that risk is acceptable.

Dr. McEwen said that the problem with doing a risk assessment is making a determination as to the method of action of the purported carcinogen. He also said that if the Panel believes that the method of action is a physical phenomenon, then a threshold-type risk assessment should be performed. If it is not believed to be a physical phenomenon, then an EPA-type risk assessment should be performed.

Dr. McEwen also said that the concern that he would have is that the Panel does not seem to be comfortable with the proposition that the method of action in the dermal carcinogenicity study on 2-ethylhexyl acrylate is a physical phenomenon, and, therefore, is being forced into doing a risk assessment based on data that are not believed to show a genotoxic carcinogen.

Dr. Belsito asked Dr. Shank if a negative genotoxicity study on 2-ethylhexyl acrylate would increase his comfort level.

Dr. Shank said that if it could be established that there is no basis for genotoxicity, he would feel more comfortable. He also indicated that he has not concluded that 2-ethylhexyl acrylate is unsafe, but that the Panel does not have sufficient data for concluding that it is safe.

Dr. Shank also said that after paying close attention to the monomer issue and reviewing the available data more closely, he concluded that of the 34 ingredients that are being reviewed in the Draft Report on Acrylates Copolymer, a reasonable amount of data are available on only four ingredients. Furthermore, he said that he does not favor including all 34 ingredients in one report or agree that the data that are available on four ingredients can be used to sufficiently evaluate the safety of all 34. Dr. Shank recommended that a decision be made as to which ingredients should remain in the present safety assessment, and that the Panel should be very careful in determining exactly which data on these compounds are needed.

The Panel voted in favor of tabling the Draft Report on Acrylates Copolymer. Drs. Belsito and Carlton voted against the motion to table.

Dr. Shank noted that the report is being tabled such that 34 ingredients can be placed into groups and the Panel can determine how much information is actually available. He said that the Panel will find that there are data only on the following three ingredients: Acrylates Copolymer, Polyacrylic Acid, Sodium Polyacrylate. Additionally, Dr. Shank noted that the Panel has fairly good impurities data on these ingredients and that this is not the case for the remaining 31 ingredients. He suggested requesting impurities data (unreacted copolymers included) on each ingredient for which no impurities data have been made available.

Dr. Shank indicated that he is not in favor of regrouping the 34 ingredients in the safety assessment and creating individual group reports, but wants to analyze the group of 34 ingredients differently, compared to what has been done in the past.

Dr. Belsito asked if Dr. Shank wants, e.g., all of the information on Acrylates Copolymer grouped within the document.

Dr. Shank said that, at least, the information should be looked at in that way, even if there is no physical grouping of information within the document.

Dr. Andersen said that the types of data available on each ingredient will be listed in a table.

Dr. Bergfeld asked what should be done concerning the issue of 2-ethylhexyl acrylate carcinogenicity.

Dr. Schroeter said that as justification for tabling the report, he had suggested that a risk assessment be done on 2-ethylhexyl acrylate. He also said that if there are individuals or groups that have information that would assist the Panel in making a decision, then such information should be made available.

In light of the Panel's discussion, Dr. Bergfeld noted that, possibly, a risk assessment will be done and that the Panel will again request information on the safety of these polymers from industry. She also suggested that the Panel discussion that led to the decision to do a risk assessment should be captured in the minutes.

Concerning Acrylates/VA Copolymer, Dr. Shank said that, perhaps, 2-ethylhexyl acrylate is not present in the finished product and that industry may be able to prove this. In other words, it may be that 2-ethylhexyl acrylate is not included in the chemical process of synthesizing a copolymer. Dr. Shank noted that the name, Acrylates/VA Copolymer has the name of the carcinogen in it, and that the Panel has asked for but not received information on this compound. He said that without any information, one has to assume, based on the name, that unreacted carcinogen is present.

Dr. Belsito noted that Acrylates/VA Copolymer is a copolymer of vinyl acetate and 2-ethylhexyl acrylate copolymer. He said that the reason why he originally wanted information on Acrylates/VA Copolymer is because, in irritation studies, it was the most irritating. At a concentration of 100%, it was extremely corrosive to skin. Dr. Belsito also noted that this same effect was reported in the dermal carcinogenicity study on 2-ethylhexyl acrylate.

Dr. Ian Cottrell said that most of the polymers don't contain 2-ethylhexyl acrylate. He wanted to know if the Panel is only concerned about this monomer.

In response to Dr. Bergfeld's request, Dr. Cottrell agreed to supply data on some of the polymers indicating that 2-ethylhexyl acrylate is not present. He said that he could supply the Panel with a package of information on the polymers with which he is familiar within four to six weeks.

Dr. Bailey said that if the Panel is going to invite an expert to discuss the mechanism (mechanism for 2-ethylhexyl acrylate-induced dermal carcinogenicity) issue, it is his recommendation that the Panel be involved in the selection of this person such that there will be an independent opinion. Dr. Bailey recommended that the scientist be from academia.

Dr. Slaga said that mutagenicity data on 2-ethylhexyl acrylate would be helpful.

Dr. McEwen wanted to know the types of mutagenicity studies that would be sufficient.

Dr. Shank said that the usual mutagenicity profile (2 mutagenicity assays, one in a mammalian system) that has been requested in the past for other compounds would be sufficient.

Dr. Bergfeld confirmed that mutagenicity data will be requested in order to resolve the issue of mechanism (i.e., is the mechanism for 2-ethylhexyl acrylate-induced dermal carcinogenicity related to genotoxicity or irritation?).

Dr. Bronaugh made a comment relating to the family of acrylates being reviewed. He said that he recently noticed that there is an acrylamide sodium acrylate copolymer that is used in some products according to FDA's voluntary reporting system. Dr. Bronaugh wanted to know if this compound should be included in the family of acrylates that is being reviewed.

Dr. Bergfeld said that Dr. Belsito's Team had considered the addition of this ingredient.

Dr. Belsito said that the Panel was appreciative of the FDA submission on the risk assessment of acrylamide monomer and polyacrylamide. He also said that his Team specifically wanted to be assured that there no polyacrylamides would be included in the family of ingredients being reviewed, because the polyacrylamides would need to be addressed on a very specific basis. Dr. Belsito added that based on the risk assessment that was received from FDA, his Team was very specific to exclude any of the polyacrylamides from the safety assessment of the Acrylates Copolymer ingredient family.

Dr. Bronaugh noted that the ingredient that he was referring to is not a polyacrylamide. It is an acrylamide sodium acrylate copolymer.

Dr. Belsito said that the reason for concern over polyacrylamide is the presence of acrylamide monomer, which could be present in acrylamide sodium acrylate copolymer. Therefore, any copolymer with acrylamide would be removed from the Acrylates Copolymer ingredient family and reviewed specifically.

Ms. Fise asked if acrylamides are on the CIR priority list as a separate group, and when the Panel might be expected to review this group.

Dr. Andersen said that the Panel has completed the safety assessment on polyacrylamide, and FDA's risk assessment was not part of that evaluation. Therefore, Dr. Andersen said that he would like to use these data to reopen the Panel's discussion on Polyacrylamide.

Dr. Bergfeld asked Dr. Andersen to comment on how the Panel will proceed with its review of the Acrylates Copolymer ingredient family at the next Panel meeting.

Dr. Andersen said that the CIR staff will present a description of the data included in the Draft Report, as a function of each ingredient (i.e., how much data are actually available on each ingredient) in tabular form. He also said that the CIR staff will also attempt, with assistance as needed, to perform a risk assessment and present that analysis to the Panel. As recommended by Dr. Bailey, Dr. Andersen noted that outside academic assistance will be utilized, as needed, in order to complete the risk assessment. He added that exposure assessment is going to be part of any risk assessment, and that the information on monomer residues may be accessible only from industry. Therefore, there are some limits in terms of how this information can be factored in.

Dr. Andersen also stated that a number of possibilities was presented to industry as ways of helping to resolve the issue of potential 2-ethylhexyl acrylate-induced dermal carcinogenicity, which included the conduct of genotoxicity tests. The genotoxicity tests normally described by the Panel would include at least one in a mammalian system, and, in this case, the goal is to characterize the genotoxicity potential of 2-ethylhexyl acrylate. Dr. Andersen noted that another possibility was a description of the chemistry of copolymers containing 2-ethylhexyl acrylate, with a goal of showing that there may actually be no monomer left in the final material.

Dr. Andersen stated that his comments (stated immediately above) relate to possibilities that industry may consider as ways of assisting in the resolution of the issue of potential 2-ethylhexyl acrylate-induced dermal carcinogenicity.

Dr. Shank wanted to know which ingredient will be evaluated in the risk assessment, 2-ethylhexyl acrylate (monomer) or Acrylates/VA Copolymer.

Dr. Andersen said that the risk assessment will be done on the monomer, with some assumptions that may have to be made, if actual values are not available, on how much of that compound is actually going to be in a cosmetic formulation and how much of that cosmetic formulation is going to contact the user's skin.

Dr. Bergfeld said that if the polymerization is complete and there is no residue left, then the Panel's data needs would be greatly reduced.

Dr. Shank wanted to know if there is any information on how free the monomer is to migrate from the polymer into the skin. He also wanted to know if one should assume that all of the monomer is going to migrate out.

Dr. Cottrell said that one cannot assume that all of the monomer is going to migrate from the polymer. He added that it may only be used at a very small percentage in the final formulation that contacts the skin. Dr. Cottrell also noted that much skin irritation data is available on Acrylates Copolymer, and that he is willing to provide the Panel with these data.

Noting that many ingredients are being reviewed in the present report, Dr. Slaga said that, in the future, it may be a good idea to break any large group of ingredients down into smaller groups. He said that this would make the review process a lot easier.

In summary, the Panel asked for a risk assessment based on the carcinogenic potential of 2-ethylhexyl acrylate, one of the monomers used to create one of the copolymers in the Acrylates Copolymer ingredient family. The concern could be resolved if it were understood that the mechanism of action in the dermal carcinogenicity study is likely physical (e.g. genotoxicity tests in bacterial and mammalian systems are negative). Additional information on the specific copolymers that could contain 2-ethylhexyl acrylate as a monomer was also requested from industry, along with any other information on monomer residues that would help make the report more complete.

Furthermore, as stated earlier, the Panel voted in favor of tabling the Draft Report on Acrylates Copolymer. Drs. Belsito and Carlton voted against the motion to table.

June 14-15, 1999

Dr. Belsito noted that, at the December 8-9, 1997 Panel meeting, the Panel concluded that these ingredients are safe for use in cosmetics when formulated to avoid skin irritation. He also mentioned that the following two caveats are included in the report discussion: (1) The levels of unreacted monomer should be kept at a minimum, consistent with good manufacturing practices and (2) Based on the information that was provided, hydroquinone is completely removed before the acrylates are used in the production of a cosmetic product.

Dr. Schroeter said that his Team expressed concern about the following two issues relating to acrylates copolymer: (1) the cocarcinogenicity of 2-ethylhexyl acrylate, one of the monomers in Acrylates /VA Copolymer - Dr. Schroeter said that 2-ethylhexyl acrylate does have carcinogenic activity, and, therefore, may be unsafe. (2) the carcinogenicity of acrylic acid, which is a monomer in many of the copolymers. There is a concern that acrylic acid is unsafe based on the data that have been supplied. 1% acrylic acid showed no significant effect, while 4% acrylic acid induced two tumors in 30 animals. Acrylic acid is said to be found in Sodium Polyacrylate at concentrations almost as high as 4%. Furthermore, according to an IARC report on acrylic acid that the Panel has not seen, it is possible that this chemical may be a human carcinogen.

Dr. Schroeter said that in light of the absence of data from IARC and the other data that are in question, perhaps the Panel should table the review of this ingredient group, pending the Panel's review of the IARC report on acrylic acid.

Dr. McEwen recalled that, on the preceding day, the Panel was informed that acrylic acid has been classified as a category III chemical, meaning that IARC was unable to arrive at a conclusion on its carcinogenicity, not that there was evidence that acrylic acid might be a carcinogen.

The Panel voted in favor of tabling the report on Acrylates Copolymer. Drs. Slaga and Shank opposed the motion to table.

Mr. McLaughlin made the following comments: IARC completed its review on acrylic acid, ethyl acrylate and ethylhexyl acrylate last year. Additional data are included in the EPA IRIS report (acrylic acid reviewed), which will be provided. ECETOC (European Chemical Council) completed a review on acrylic acid as well, and this will be provided along with all relevant data addressing genotoxicity and carcinogenicity. A large body of data from the mouse lymphoma assay exists. Information will be provided on monomers in this assay, including those that have been tested in product studies and shown to be negative for carcinogenicity.

Dr. Belsito wanted to know why the mutagenicity of 2-ethylhexyl acrylate is still an issue. He thought that this issue had been resolved by the Panel's suggestion that the weak mutagenic effect reported was probably due to an irritant effect of the chemical. He recalled that, except for the mouse lymphoma assay, the mutagenicity data were relatively clean. He also recalled that 43% ethylhexyl acrylate induced excess irritation in mice to the point where application was discontinued, and that the mice went on to heal without the subsequent development of tumors.

Dr. Slaga recalled that 2.5% ethylhexyl acrylate was also positive (an irritant).

Dr. Shank noted that there is a possibility that 2-ethylhexyl acrylate is a weak mutagen, and that the Panel has not seen the genotoxicity data on this chemical. He acknowledged that there is no evidence that 2-ethylhexyl acrylate is a strong mutagen, but also said that if there is any doubt surrounding the mutagenicity data, one cannot say that the mutagenicity data exclude a possible genotoxic mechanism. Therefore, the Panel has to be confident that the chemical is carcinogenic only because it is an irritant.

Dr. Klaassen said that he is not concerned about the mutagenicity of 2-ethylhexyl acrylate. However, he noted that an IARC document on acrylic acid has just been reviewed, and that the CIR report could possibly be made stronger by including studies from the IARC report.

Dr. Shank said that, at this point, it would be very difficult to develop a report discussion that explains why the Panel is saying that chemicals that cause skin cancer (acrylic acid, ethyl acrylate, and 2-ethylhexyl acrylate) are safe as used. He also noted that the Panel has not had an opportunity to review the mutagenicity data.

Dr. Bailey said that it would be reasonable for the Panel to request any additional data on residues of these monomers in the ingredients being reviewed. He recalled from yesterday's Team discussions that the data submitted thus far are not really reflective of what is actually in the material, and that such data exist. He said that the Panel would benefit from asking for these data again.

Dr. Andersen said that the fact that the discussion of this ingredient report was tabled will be included in the announcement of the results of this meeting. It will be explained that the basis for tabling was to allow receipt of additional data that may in-clude an IARC report, other industry data on genotoxicity, and, at Dr. Bailey's request, a request for any additional information on monomer residues that may be present in any of the copolymers that are being considered will be added to the list.

Dr. Bailey requested that any data on monomer residues should be on cosmetic grade materials.

As noted earlier, the Panel voted in favor of tabling the report on the Acrylates Copolymer ingredient family, pending the Panel's review of the IARC report on acrylic acid. Assuming that the IARC report may be a lengthy document, Dr. Belsito requested that this document be mailed to Panel members as soon as it is received, rather than holding it until the mail date for meeting materials.

December 20-21, 1999

Dr. Bergfeld thanked Dr. Clay Frederick, Basic Acrylic Monomer Manufacturers, for assisting the Panel with its review of the Acrylates Copolymer ingredient family.

Dr. Belsito recalled that a Tentative Report with a conclusion indicating that these ingredients are safe for use in cosmetics when formulated to avoid skin irritation was issued two years ago. He also said that over the past two years, the Panel has struggled with reports on the carcinogenic potential of 2-ethylhexyl acrylate, which is said to be a trace component of one of the acrylate copolymers that is being reviewed.

Dr. Belsito noted that the Panel recently received information on the extreme sensitivity, but lack of specificity, of the mouse lymphoma assay for genotoxicity and also received another report (Mellert et al., 1994) on the carcinogenicity of 2-ethylhexyl acrylate in different mouse strains (C3H and NMRI). In the latter strain, in spite of some irritation that was observed, the induction of carcinogenicity was not observed. Carcinogenicity was induced in the C3H strain.

Dr. Belsito said that the Panel has also had an opportunity to review risk assessment data based on use concentrations of the Acrylate Copolymers in cosmetics, working under the assumption by the Panel that monomer will be present in amounts < 1,000

ppm. He also recalled that the concentration that induced skin cancer, even when assuming that this was an effect of 2-ethylhexyl acrylate in that solution, was 210,000 ppm. Dr. Belsito said that this concentration is 210-fold higher than any amount of monomer that would be expected, even if it were used in pure form in a cosmetic product. Thus, Dr. Belsito concluded that based on the animal and clinical data included in the CIR report, all of the Acrylates Copolymer included in this review are safe as used when formulated to avoid irritation.

The Panel voted unanimously in favor of issuing a Final Report with the conclusion stated in the preceding paragraph.

Dr. Schroeter confirmed that Dr. Belsito's comments will be included in the report discussion. These relate to the reasoning behind the Panel's evaluation of the carcinogenicity of Acrylates Copolymer.

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September 2011 – Full Panel

Going on to the next blue final which is the crosslinked acrylates. Dr. Marks?

DR. MARKS: At the March meeting of this year we were concerned about the possibility of residual benzene in these cosmetic ingredients, and with that in mind we have before us a draft final safety assessment on crosslinked alkyl acrylates with the conclusion that the ingredients listed below are safe in the present practices use and concentration described in this safety assessment except when they are polymerized in benzene and that the available data are insufficient to make a determination of safety for these ingredients when polymerized in benzene and then the caveat about if they were not in use. So I've move that this conclusion as stated in this memorandum be a final safety assessment.

DR. BELSITO: Second.

DR. BERGFELD: Second. Are there any comments or other discussion?

DR. BELSITO: Just to discuss why they're insufficient. I'll let Paul speak to it further, but the issue was whose safety assessment on benzene do you accept? We received several different ones, one with a borderline safe margin the other with a margin that clearly was unsafe. It was unclear to us how much benzene one might expect in a trade product and therefore how much one might expect to get into a finished product. I think that was why we felt this was insufficient. We just didn't have that data or that level of confidence in terms of doing risk analysis for a carcinogenic end point.

DR. BERGFELD: Paul?

DR. SNYDER: I'd second Don's comments. We felt that the uncertainty factors are very complex and there was not unanimous agreement on that which led our team to not have very confidence in the risk assessments and which one to pick or how to approach that.

DR. BERGFELD: Ron Shank and then Tom?

DR. SHANK: I would like to suggest changing in the discussion, replacing the last two sentences in the fourth paragraph, the sentences that begin if residual benzene were present and then all those numbers. Dr. Heldreth had made a very good statement which I think could replace that, and that statement was since it cannot be predicted with certainty what quantity of benzene would be volatilized or leached from the cross-polymers during manufacture, formulation or product use, the panel determined that the data are insufficient are to conclude that cross-polymers polymerized in benzene are safe.

DR. BERGFELD: Thank you. Tom?

DR. SLAGA: I agree.

DR. BERGFELD: Ron Hill? Dan?

DR. LIEBLER: I'm fine with that.

DR. BERGFELD: Curt?

DR. KLAASSEN: Yes.

DR. BERGFELD: Don?

DR. BELSITO: Then we need to do what is the respiratory boilerplate for this one.

DR. BERGFELD: Do you have a suggestion?

DR. ANDERSEN: I think certainly as of now we are offering the blanket comfort that they're non-respirable and that clearly needs to change.

DR. BELSITO: Right.

DR. ANDERSEN: We talked yesterday about what the full presentation of an argument on the safety of ingredients that are used in products that may be aerosolized. Jay expanded a short while ago on one aspect of that which is sprays enter a breathing zone, don't enter a breathing zone and there are issues of how much gets in that are independent of what's the particle size. A small percentage of particles can get in but there is not that much material. I guess you parlay those two pieces of information into an argument that it's unlikely that inhalation is going to be a significant route of exposure for systemic toxicity so I think that gets captured. Then it's a matter of looking at the individual chemicals to see what's the use concentration and that's another factor that deserves mentioning. If that's low, it's another factor in the right direction that there is no concern. In the document if there are oral systemic repeated dose toxicity data that are say it's simply clean and in particular no evidence of lung damage, that's a further factor. If there is reproductive and developmental tox data that are negative, that's another factor, genotox, down through while they're not inhalation toxicity end points, they add to that picture of what do we know about the particular ingredient. Paul commented yesterday that over the long term those are all things that we've looked at every single time anyway. Now we would potentially be putting them into a way of capturing that for the reader now to see in the discussion. So instead of that one lonesome little sentence that says don't worry about it, it becomes a more expanded and I think robust discussion, but it must be tailored to each individual ingredient. I'd like to think that there's a boilerplate but I think it's a way of presenting the data and if they're there, we include it, if they're not, we don't include it.

DR. BERGFELD: What are you proposing for this ingredient?

DR. ANDERSEN: I think for this ingredient that single sentence that says don't worry about inhalation because particles won't be inhaled gets replaced with a paragraph that goes through those factors.

DR. BELSITO: The same with TA.

DR. ANDERSEN: I think so.

DR. BERGFELD: Is this going to come back to us to look at or is this going to be automatically placed and this sent out? What is the procedure here?

DR. ANDERSEN: I think if the panel is comfortable with the pattern -- which one are we talking about?

DR. BERGFELD: We're talking about crosslinked.

DR. ANDERSEN: Alkyl acrylates. This is something that since I'd rather have this issued as a final, I think we can develop that discussion language and run it by the chair and the two team leaders and proceed.

DR. BERGFELD: Is that acceptable?

DR. MARKS: Alan, I would suggest since it's easy, the electrons, run it by all the panel members and not just the chair, just the team leaders.

DR. ANDERSEN: Can do.

DR. BERGFELD: We'll have an email signoff of the inhalation statement in the discussion. We've had a motion made and seconded to go forward with safe with some caveats here at the N-nitroso. I think that is in this one too.

Yes.

DR. HILL: So if the minutes could reflect that we're going to do that and then when we approve the minutes next time that will say we did it.

DR. BERGFELD: Yes. The minutes on these are being taken as we speak. Can we move the question now or is there further discussion? Move the question. All those in favor then of this conclusion please raise your hands.

Unanimous.

September 2011 – Belsito Team

going back to the cross-linked acrylates in which the last time we said that data were insufficient for those that had a benzene derivitization, and we've got

two margins of safety; one that Ivan put together, one that the scientific committee put together. The scientific committee is saying oh, it doesn't matter if it comes from benzene and margins of safety, so fine, and Ivan's margins of safety are a little bit different. So, duke it out, guys.

DR. BOYER: Well, the PCPC actually compared their exposure estimates to a value that was derived what EPA states is a concentration of benzene in drinking water that would represent the 10-6 risk, and that's considered de minimis. And, actually, they made a statement that if you assume that 10 percent of the residual benzene ingredient volatilizes during the manufacturing of a cosmetic product, the body lotion, for instance, that, in fact, the risks, looking at it that way would be below the 10-6 risk level of 0 de minimis.

And, actually, if you do that, the concentration approaches the upper range of concentration as it represents 10-6 risk, and so, it doesn't look like much, it's marginally above those concentrations of that concentration range.

So, what I did was to do a standard EPA risk assessment, calculating the upper bound cancer risk estimate based on standard EPA protocols for doing those risk assessments, and I used the slope factors that EPA has issued for benzene, and unlike almost every other substance that I've seen when EPA's addressed them this way, EPA has issued two slope factors for benzene, and

what they want to see is a risk estimate that lies between the risk estimates that those slope factors represent.

So, I started from scratch, I took one of the highest concentrations of benzene in the ingredient, in the polymer, together with the highest concentration of the polymer used in these products, and used these slope factors to calculate risk estimates. And what I found was that when you look at it that way, the risk estimates are substantially greater than 10-6, 20-fold higher than 10-6, 25-fold and so forth, and that's assuming again, conservatively. This has to be considered to be a screening level kind of risk assessment conservatively, upper 95 percent exposure levels. And daily use throughout an entire lifetime.

Okay, so, basically, we don't know to what extent the residual benzene concentrations in the ingredients are actually volatized when the products are manufactured using those ingredients. PCPC has shown 10 percent, and based on the calculations that I did, it seems as though you would have to reduce that residual benzene concentration by 96 percent or 8 percent or so forth, depending on what your assumptions are, your exposure assumptions are.

So, we still don't have sufficient information to result, to refine the risk assessments to show definitively that the use of these products at a relatively high rate would result in a 10-6 risk or an exposure that lies between that acceptable range.

DR. BELSITO: But did you calculate a level at which benzene could be present, assuming your calculations where the risk would be 10-6 or lower?

DR. BOYER: Yes, I calculated based on the assumptions, PCPC's assumptions in particular. I calculated just how much of the benzene would

have to be volatilized to bring those cancer risk estimates down to 10-6. And we're talking about not 10 percent, but closer to 90 percent or so. But we don't have the data. Another part of this is that --

DR. BELSITO: Just let me step back. From your calculations, do we not have the data to say that cross-linked alkyl acrylates that are derived from benzene are safe as used if the residual benzene contents are less than or equal to a certain number?

DR. BOYER: We do have sufficient information from those calculations.

DR. BELSITO: From your calculations --

DR. BOYER: Right.

DR. BELSITO: -- being more conservative than PCPC's.

DR. BOYER: Being done more in accordance with the standard risk assessment protocol.

DR. BELSITO: Okay, so, would industry have a problem if we went ahead and said safe as used, and we could use Ivan's restrictions, which are more stringent than industry's, or do you people on the panel who are more knowledgeable about benzene have further concerns or less concerns?

DR. LIEBLER: So, I think that's actually the best you'd probably get out of me because my first reaction to this was the PCPC's SSCs or risk assessment came in a little below, and then Ivan's calculations came in well above them, and, to me, that suggests that there was insufficient evidence to suggest that the -- to

(inaudible) the safety in the ingredients containing benzene.

DR. BOYER: Well, and there is an explanation for that. I mean, if you'll look at the daily intake, it looks like a small increment. Actually, I do find that (inaudible) concentration of daily exposure, there is an exceedance. But when you actually calculate the risk, that's amplified. Just daily exposure that results in the substantial daily --

DR. LIEBLER: Is that where this slope factor comes in?

DR. BOYER: The slope factor, it represents the risk per unit dose.

DR. LIEBLER: Okay. I mean, that was one characteristic of your calculation. It wasn't the SSC, right? It was not in the SSC?

DR. ANSELL: Well, I think it depends on what you do with the EPA risk assessment. They had a lower dose and an upper dose, a lower slope factor and a higher slope factor. If you use the range that EPA gives as it relates to drinking water with a 10-6 risk, becomes somewhere in the middle, but we're not at the lowest or we're below the highest.

I guess the question that comes though is: Can we take the EPA risk assessment and start just using bits and pieces of it? We have an extremely conservative risk assessment, but I don't think our numbers are substantially different, it's what risk?

If we use California Prop 65, then all these numbers are okay. If we use the EPA water number, they're not okay. So, what do we consider to be appropriate in this case? The staff estimate would qualify pharmaceutical grade materials, which the USP establishes at.2. So,

it's what do we consider acceptable, the numbers, whether they range from 10-6, 7.2 times 10-6, or 2.7 times 10-6, absent some idea of what ultimately is acceptable becomes very problematic. And these are all, we felt, reasonable estimates.

DR. LIEBLER: All "reasonable estimates."

DR. ANSELL: I don't know how you --

DR. LIEBLER: Right. I mean, you're making relatively small differences in the beginning assumptions, you've basically between the SSC and Ivan's, you essentially have done several similar slight different variations of these calculations, and, to me, you still come out around this limit, which is the EPA intake, and, to me, you keep coming out around this limit, more it gets above the limit than below the limit. That's what bothered me. That's where I came out on this, right, because I realize you can fill with this how much evaporates during preparation of the product versus how much is absorbed, et cetera, which slope you use, all those things. To me, if I step back and look at it, I say most of these estimates are coming in slightly below or somewhat above that value that was used as a reference for unacceptable, and since most of those calculations come above that, I came to the conclusion that there's insufficient evidence to support the safety of the product that uses that material with benzene in it.

DR. BELSITO: Okay, so, your argument is because Ivan's would further lower the number and that scientific committee for PCPC came at a higher level of benzene contamination that still would be safe within or insufficient. So, I understand what you're saying there, but for the purposes of argument, are you uncomfortable that even Ivan's assumptions could be wrong and,

therefore, we would, using his calculations, if we set a limit of benzene in those products that we still might be too high with the benzene?

DR. LIEBLER: I hadn't even thought about that.

DR. BELSITO: See, my point was saying --

DR. LIEBLER: Yes.

DR. BELSITO: Safe as used in using Ivan's calculations to set benzene limits in those alkyl acrylates that are benzene-derived.

DR. KLAASSEN: How are you determining here the daily benzene exposure?

DR. BOYER: Okay, we have data actually from the survey which point like PCPC's as far as the daily usage of body lotions.

DR. KLAASSEN: Okay.

DR. BOYER: And body lotions are, in fact, a product that have the highest afforded concentration of polymer in the survey. So, we used that plus the concentration was the higher concentration of benzene in the polymer to estimate the daily exposure to benzene. And what PCPC -- he did at that point was to compare that daily exposure to the daily exposure that you would get from drinking water if you used the highest drinking water concentration with benzene in EPA's range that represents 10-6 risk. And that range actually originates from slope factor.

DR. KLAASSEN: Right.

DR. BOYER: So, what I did, and, again, EPA has two slope factors for benzene, and what I

did was use both of those slope factors and actually calculate the risk, which is typically what FDA does, typically what EPA does, other regulatory agencies do. They'll do a risk assessment, they'll estimate cancer risk. It minerally is an upper bound risk; it represents at most what the risk might be. It could very well be that any actual risk lies well below that, but, often, it is the basis for making regulatory decisions.

DR. KLAASSEN: Yes, okay.

DR. BOYER: Okay, so, we took the dose of the allowable concentration, which would be calculated from the range that EPA provided, and it was 2 to 20, and our calculation comes in at 12. And felt that based on the typical reported concentration of benzene, not the actual loss, and felt that if this represented a worst case -- it assumed no material was going to be lost during processing, it didn't look at the exposure. It looked at the exposure, but it didn't assume that any material was lost, although we used the typical concentration and not the specification, which was.4 and not.5, and figured that if it came in between 2 and 20 and we came in at 12, based on the EPA risk assessment that going through and taking an extremely conservative risk assessment, which is already a linear model, already has something approaching 100,000-fold safety factor in it, that we probably didn't need to go farther. If we do need to go farther, I would argue that the benzene concentration has to be based on exposures and not the amount of raw material.

SPEAKER: Well, the problem is that the 12 micrograms per day is based on the assumption of a 50th percentile exposure to the lotion, whereas typically, the starting point for a risk assessment is the 90th percentile, and when you do it that way, the daily exposure exceeds 20

micrograms per day.

DR. KLAASSEN: This is a difficult thing. Risk assessment isn't the real science. When you do science, you have to use data within the points and you don't extrapolate almost nothing, and this is unfortunately what we are doing in this country at this time. So, I guess my toxicological feeling is that there's absolutely no problem here. And I would put this on my skin and my grandchildren's skin and everybody else forever and don't think I have problem.

But where the real problem is, is the potential public perception, just like we had with arsenic on Dr. Oz last week, that with arsenic, those of you -- and, again, this is trying to -- this whole risk assessment business, you get to the feeling and the public gets to the impression that this number is real, and it's not a real number, it's a hypothetical number, and just as Ivan said, it could be off by 1,000-fold. And -- but how do you come to grips with all of this? And especially from a cosmetic standpoint, but with public relations standpoint, we are letting people put this stuff on their baby's skin after they take a bath, yet we wouldn't let them drink it or have it in the bathwater. Right? Can you see this on Dr. Oz?

DR. ANSELL: Yes, although what goes on in the press, I mean, has no bearing on -- if we take California's number instead of the EPA's number, we'd come up with a completely different answer.

DR. KLAASSEN: So, what do they use?

DR. ANSELL: 10-5.

DR. KLAASSEN: Oh, they go 10-5 instead of 10-6?

DR. ANSELL: Right. In which case, everything would have been fine. We felt that using the EPA was just one example. But that's really the issue, so I'd be happy with some conclusion that manufacturers are aware of it and they should control to the minimum amount consistent with GMP's. We could try to calculate a number, but you're going to end up in the same place as for what model you're going to use. I mean, there's a lot of disagreement that this is the right model to begin with. I mean, EPA uses it because it's hyper conservative.

DR. BELSITO: Right, but, I mean, so that's getting back to my point. I mean, you used a less conservative model that would allow us to just simply come out and say safe as used with, what is it, 5 percent benzene that's been reported potentially in the products up to 5 percent?

SPEAKER: .5 percent.

DR. ANSELL: .5 percent.

DR. BELSITO: .5, okay. So, it's been a long week, a long day, a long month. Ivan has come up with the most conservative estimate that if these products contained what level did you assume?

DR. BOYER: We did it with.41 percent and the.5 percent.

DR. BELSITO: But if you backtracked your calculations, how much could be in there and still be safe?

DR. ANSELL: Well, you'd have to reduce it to.02.

DR. BOYER: That sounds right.

DR. BELSITO: .02.

DR. KLAASSEN: From 0.5 to 0.02?

DR. ANSELL: Right.

DR. BOYER: Right.

DR. ANSELL: Right, but we don't think --

DR. KLAASSEN: Which is probably not easily done.

DR. ANSELL: Well, or not relevant because what we wanted to do was absent processing, absent any of that stuff, just doesn't look okay, and we felt that that was our worst case scenario. We didn't start cherry-picking the EPA risk assessment. And, so, if you want to come in and argue that the 10-6 risk at the user level is acceptable, I mean, I think we would look at that. Well, I'd have to find out what that number comes out to be, but that's what we've done in the past.

DR. BELSITO: Well, but that's what Ivan is saying, that a 10-6 risk at the user level the way that EPA and he would do the calculations is.02 percent.

DR. ANSELL: No, that's what would be in the raw material. It would not result --

DR. BELSITO: Right.

DR. ANSELL: What I would like to do is if the panel believes the 10-6 is the right number and can agree upon a model, then we would calculate from that the amount of exposure that a

person would be allowed per day. And then put it to the manufacturer to process the material accordingly, but not go back to the raw material and saw the raw material has to be at.02 because the USP grade is.2.

DR. BOYER: Well, the USP is based on the application of topical medications and so forth, so the exposure, the amount that one's exposed to, is going to be very different. So, I mean, I actually did the risk assessment on theirs, assuming that someone would use that kind of medication as they would a body lotion, and the risk estimate comes to about 2 times to the -6, and I think it's clear that simply taking into consideration the smaller amounts that someone would use even on a daily basis, that you're below that 10-6 threshold.

DR. BELSITO: Well, it could be used in multiple products several times per day. We're not talking about an OTC, where you're not likely to use an antibiotic ointment, different antibiotic ointments all over the body several times a day.

DR. ANSELL: Well, our suggestion to resolve this would be to put in a proviso that when formulated, 2 percent less than 10-6 risk to the user.

DR. BELSITO: But you can't do that, Jay. So, I'm Proctor & Gamble and I have formulated product X to propose less than 10-6 risk of user, and I'm another company and I formulated another product that's going to be used at the same time on the same individual and my product poses less than 10-6. But when combined, the two products used together on the same individual now have a risk greater than 10-6, also, so --

DR. ANSELL: How does setting any specification result in that problem?

DR. BELSITO: Because I think if we use Ivan's calculation, is based off of maximum daily use of cosmetic product in a high-end user, no?

DR. BOYER: Correct. Well, the other way to approach this is to obtain that data that would be needed to -- the uncertainty in the risk assessment --

DR. BELSITO: Yes.

DR. BOYER: -- to refine the risk assessment using more reasonable estimates.

DR. SNYDER: I think that's a good point. I think that's where we're at. I think we're at the same conclusion we were last time. I think it's still insufficient with benzene --

SPEAKER: Right.

DR. SNYDER: -- manufacturer of the (inaudible). I think for the others, were safe as used, but for the benzene (inaudible) I think we're -- I mean, I don't think we want to push to unsafe. I don't think that's where we want to go, but I do think that we are insufficient because I think there's just too many uncertainties, and the best we can do is to say insufficient.

DR. LIEBLER: It's insufficient because the risk assessment simply does not resolve the question.

DR. SNYDER: I mean, I think we're just chasing our tail here and (inaudible).

DR. ANSELL: Yes, but if I come back and say.04, is that.2? I'm not sure that it's going to resolve the question as it relates to the

uncertainty of the risk assessments?

DR. LIEBLER: But you can't come back and say that because that's not what the concentration is in the ingredient. We've been given a range of concentrations, and the ingredient goes up to.41 percent.

DR. ANSELL: Well, suppose we were to say.2 is safe. I mean, that's ultimately where we're trying to go, is some number. And it's how are we going to judge that number?

DR. BOYER: Well, if you base it on a (inaudible) level assessment that is entirely based upon very conservative exposure assumptions, then you can set a level that you're fairly certain does 5 represent over 10-6 risk? If you can refine that risk assessment, refine the exposure assessment, you may be able to go up a little bit higher. It really is a matter of just how much uncertainty you're willing to commit with as risk manager.

DR. LIEBLER: There's so much uncertainty in all of these. When you just tweak a few (inaudible) you've got about four tweak-ables that we've talked about so far that I can recall, and, you know, if you let any of those five at a half or five whole, and you can make this number move around quite a bit. So, I think, to me, that suggests that anyway you do this risk assessment, you come out close to an area where you're uncertain about the safety, and as long as that's the case, we are insufficient.

SPEAKER: All right.

DR. SNYDER: Yes, I mean, the whole discussion is leading me toward an area of not very high confidence in the safety conclusion of the risk assessment.

DR. KLAASSEN: Do we have, and I don't know, have we ever used this type of a carcinogen risk assessment for a chemical and have this problem? For the cosmetic ingredient review?

SPEAKER: No.

MS. FIUME: We haven't done a risk assessment. In carbomers, which is what industry asked us to look at, is it refers back to the EPA safe level and says, for example, that EPA has established for drinking water that 10-6 risk level for cancers between 1 and 10 micrograms per liter. But now with using those numbers in our risk assessment, then we're looking at how we can shift them.

So, as the writer sitting here and not the expert, I mean, everything I'm hearing is if we move this number or if we assume this much is volatilized, and that was one of the problems when CIR was looking at the risk assessment, is we don't know how much is in the finished product. Assumptions were made on what happens during the manufacture, and that's not been measured. We're asked to use this number, but then when it's skewed, well, here, let's look at a different number. So, I think what the panel is saying --

DR. SNYDER: I think in our previous (inaudible) we had better numbers, we had more certainties as to what --

MS. FIUME: For the carbomer?

DR. SNYDER: No, for --

MS. FIUME: Other things, yes.

DR. SNYDER: -- the risk assessments.

DR. BOYER: And, you know, the other

problem is if you do a risk assessment and the number's clearly above 10-6 or clearly below, there's really no issue. It's fairly easy to answer that question, but in this case, in that range, you've got some values, some estimates that are right above that range and some within the range. So, that's why this is a little bit more difficult.

DR. BELSITO: Okay, so, what I am hearing is, again, Curt saying insufficient, we just don't have the dataset skills that we need to assess the relative level of safety in benzene.
Curt, what are you thinking?

DR. KLAASSEN: Well, I have mixed emotions on this one. I guess I would, first of all, like to know what dose people really are being exposed to. I mean, what you're doing is taking the number from your manufactured product and how much of that is really in the product that you put on the skin? We don't know.
And, secondly, what you put on the skin, how much gets into the blood of the person? We don't know. So, I mean, I think all of those could be refined.
Now, my real problem is --

DR. BELSITO: But then if it needs to be refined, the data is still insufficient. So, it's insufficient for how much gets on and how much gets absorbed.

DR. KLAASSEN: Right, so, that's insufficient. Now, I question if we should use an EPA risk assessment model for cosmetics period. I mean, there is a huge question right now if this linearized -- well, there has been since it was started, this linearized, multistage model that EPA uses should be used for anything, including for the EPA. And this is really based on the fact that everybody thinks that radiation cancer is

linear down to one molecule, in essence, and now it's turning out that a person that got a Nobel Prize for this many years ago with radiation, that even his data shows that that's not true.

So, this whole thing is evolving and will continue to evolve, but it is being used by EPA at the present time for drinking water and for a number of other things. This is going on and on. But, at the same time, our legislators are saying that if we want to have an economy, we can't have all of these ridiculous regulations, so.

DR. LIEBLER: That's the TEA group, Curt. I think you're getting ahead of yourself. (Laughter)

DR. ANSELL: Well, EPA is now having an enormously hard time getting these estimates through IRIS because the assessments are routinely coming in with acceptable exposure levels below (inaudible) care, below background --

DR. KLAASSEN: But it's a tough one, but I think we can go with the insufficient.

DR. BELSITO: Okay, so, that's where we're going. I think we need to cut out the further discussion --

DR. KLAASSEN: I agree.

DR. BELSITO: -- on this at this point. So, insufficient data for benzene concentrations, what we would like to know would be how much benzene is actually in the trade product, how much gets absorbed through the skin, and all of this information that allows us to not really be able to do current risk assessments.

DR. MARKS: Yes. Next we're to the Crosslinked Alkyl Acrylates.

So at the March meeting we were concerned about the residual benzene that may be present in these crosspolymers and issued an insufficient data announcement requesting impurity data. At the June meeting it was confirmed that there was benzene and a 0.5 residual level. And then we were -- issued a tentative safety announcement that it's safe as used except when they are polymerized with benzene.

So one thing we could do is handle the benzene to make an effort to reduce the benzene to the lowest possible level or else we can amend the conclusion insufficient if polymerized in benzene. How does the team want to go? And I have -- is Ivan here? Because I wanted Ivan to talk about that but he doesn't -- he's not present.

MS. FIUME: Actually, yes, I would like Ivan to be here for the risk assessment talk also because this was mostly his work on the risk assessment. But I have a feeling they might still be discussing formaldehyde.

DR. MARKS: So shall we come back to this then since I actually -- thank you, Monice, because I had Ivan starred here to put this in perspective.

So I think what we'll do until Ivan becomes available -- how are we going to identify to bring him? If not now, after lunch. Is anybody in the visitor's -- does your time schedule not permit us to delay discussing these ingredients? Okay.

DR. BERGFELD: Can I ask a question? Is that the only pivotal point that you need to clarify in this document? Because you could move to clear up everything else if there is something

and leave that as the only pivotal point to be clarified.

DR. HILL: I thought we were down to -- I thought we were down to that.

DR. BERGFELD: Okay. That's what I wanted --

DR. MARKS: Yeah, that's the way I felt, too.

DR. BERGFELD: Could I make a comment again? I mentioned in my introductory remarks about components. Instead of the word reactive ingredients, precursor chemical, whatever you might say as in combination with other chemicals what you get, they're now referred to as components. Is that a term that is used? I didn't think so.

DR. HILL: You could say component acids and everybody will know what you're talking about if we're talking about amides. So it is used in that way. But to say components, I don't think even Dan would believe that that was a technically accurate way to reference it so we might need to be a little more careful with the wording. If you say structural moiety, then that's perfectly accurate and it doesn't roll off the tongue quite as well. But I think if we say component acid in an amide as an example, I think that's clear and it's appropriate use. It just might be how the sentences are structures might need to be more cautiously exercise.

DR. SLAGA: But in this case it would be considered just a residue, right?

DR. BERGFELD: Residue, yeah. In this particular case you would call it residue, what is left behind?

DR. SLAGA: Yeah, it's a residual part --

DR. BERGFELD: Yeah.

DR. SLAGA: -- of the reaction. Right?

DR. BERGFELD: Yeah.

DR. HILL: If we're talking about it as an impurity --

DR. BERGFELD: The byproducts, I mean, what, yeah.

DR. HILL: But in many cases when we've got the information on an additional component it's with the conjecture that it could be metabolized back to that component. And the problem with using the word "residue," although I don't have a real problem with it because when we digest protein we say imino acid residues and everybody knows what that means. It's just that if we're thinking about residue as something as there is an impurity, which it could be from process but we're also -- then that's one thing. If we're also considering it as a potential metabolite that might have toxicological relevance, that's another thing. So I think it's in the way that word is used.

DR. BERGFELD: Do we have use to figure that out?

MS. FIUME: The Crosslinked Alkyl Acrylates report, Dr. Bergfeld? Is that the report you're on with (inaudible).

DR. BERGFELD: I had written this in the front. I'm not sure if I just kept reading it and I thought that wasn't a proper citation or

component.

MS. FIUME: I know I haven't in the others.

DR. BERGFELD: Yeah.

MS. FIUME: I believe in this report I have that benzene is a residual, that there's residual monomer left or residual solvent. So do I have a term used incorrectly in the crosslinked alkyl acrylates that I need to correct? Or is -- I know it's in the other reports but I just want to make sure I'm not missing anything in this report.

DR. BERGFELD: It may be that I just had an epiphany there because I'd been reading it and not liking it.

Here it has monomer component on page -- it looks like it starts on 33. Is that okay?

DR. HILL: The monomer component would be a perfectly reasonable way to use that.

DR. BERGFELD: Okay.

DR. HILL: Because everybody will know technically exactly what that means.

DR. BERGFELD: Okay.

DR. HILL: At least in my opinion.

DR. BERGFELD: Okay.

DR. MARKS: I'm going to refer to page 39 in the discussion and I want the two Rons and Tom to comment on the next to the last paragraph where it says "if residual benzene was present at a 0.5." There are a lot of percentages there -- 5 percent, 0.025 percent benzene, 0.025 percent

benzene. Do you like the way that -- when that sentence -- or couple of sentences referring about the residual benzene is worded?

DR. SHANK: No.

DR. MARKS: Okay.

DR. SHANK: Are we going to discuss this now or wait for Ivan?

DR. MARKS: Ivan. Okay. So we'll come back to that. I think --

DR. SHANK: I thought, well, I think we should add both of the risk assessments to the report so we can refer to them in the discussion. And then Dr. Heldreth worded it very, very nicely I thought. I would replace the sentence you referred to, Jim, with one based on what Dr. Heldreth had in -- that he gave us last time. But we can wait until Dr. Boyer is here.

DR. MARKS: So we're going to go back but move forward. Is that possible? And we're going to -- Ivan, we've been anxiously awaiting you, Dr. Boyer, to elucidate the issue of benzene impurity in the compounds which are formulated with benzene as a solvent as I recollect. Is that right? There's some crosslinked acrylic acrylates which do not have benzene used in its manufacturer and others who do.

DR. BOYER: And in terms of numbers, I think that there are more that don't involve the use of benzene.

DR. MARKS: Right. So we were struggling with, as I recollect, with the team, the idea do we find safe only those crosslink alkyl acrylates that are not manufactured with benzene? Or do we include the benzene ones and

deal with the benzene residual in trying to determine a safety assessment which would make those crosslink alkyl acrylates that we feel are safe for cosmetic ingredients.

DR. BOYER: Okay. I think one of the first issues to consider is the association of residual benzene with the polymer. And we're not sure exactly what the character of that association is. And just how leachable the benzene might be from those polymers and how available they might be to evaporation. We just don't have that information. We do know something about the levels, the concentrations of benzene in the ingredient in the polymer as an ingredient. And the risk assessments that PCPC did and that I elaborated on were based on those residual levels. Assuming that during the manufacturing process none of that benzene evaporates and also repeating the calculations assuming that about 10 percent or so evaporates from the ingredient during the manufacturing and during the formulation of the actual product. And here the rationale is benzene is highly volatile. It is processed typically. It's -- the ingredient, the polymer is mixed up to produce the products, the body lotions and so forth at a relatively elevated temperature, and so there could be at least 10 percent evaporation during the manufacturing process.

When we compare -- do the simple comparison to EPA's drinking water levels, the levels that they say are associated with a 10-6 risk, a de minimis cancer risk, we find that conservative standard screening risk assessment protocols result in risk estimates that are somewhat elevated compared to that 10-6 threshold. And that's taking into consideration the possible evaporation of benzene from the product. Without having any data, again, about just how much might be leached out of the polymer into the rest of the product, the body lotion, for instance, we don't have a good feel for how much of it would be

available for absorption through the skin. We know that when it's applied neat to the skin it's absorbed into the blood stream at a relatively low level. On the other hand, a large component of that is the evaporation of benzene on the skin. It occurs very quickly. So to some extent benzene in an actual body lotion may be available for absorption longer than the simple application of benzene to the skin. On the other hand, it may not be available at all or to a minor extent if it's basically trapped in a polymer in some way.

So those were the issues that went into the risk assessments. The risk assessment that I did was an actual risk assessment starting with the EPA's cancer slope factors. Typically, EPA issues a single slow factor -- cancer slope factor for a chemical. Benzene has two slope factors, and the guidance we get from EPA in a case is that you want to be outside of that range. You want to be outside of the range of risk estimates that calculate using both of those slope factors. And so far we simply don't have the information that would enable us to refine the risk assessment and to ensure that the risks are the maximal risks, the upper bound risks that we calculate would be within that range.

DR. MARKS: Okay. Thank you.

DR. EISENMANN: One comment on the polymer. It's my understanding it starts as a powder and then you put it in warm water and it starts to uncoil. And then you add -- you neutralize it and it completely uncoils which would probably release all the benzene because I was also looking at the analytical methods and the first step is uncoiling the polymer to measure the benzene. So if, you know, in other words, I think -- of course, you can't say how much you can evaporate because it's a large vat and a small amount of benzene but I don't think it's going to be part of the polymer because --

DR. HILL: Uncoiling the polymer in water would not necessarily release the benzene. It's a high chance it will stay absorbed to the aromatic moieties and the acrylates.

DR. BOYER: And also we did some calculations. I think you have them in your Wave 2 package to show that, you know, 96 percent of the benzene would have to evaporate. Eighty percent of the benzene would have to evaporate to bring those benzene levels down -- the benzene levels in the product down to what would be associated with the 10-6 risk. So it's a substantial evaporation that would be necessary.

DR. MARKS: So Ron, Tom, and Ron, do you still like the conclusion where we say there's insufficient data? Hearing what Ivan said, it doesn't sound like you've reassured us very much actually -- that insufficient when these ingredients are polymerized in benzene? If you remember, Monice puts in her memo here that we heard there was a 0.5 percent residual benzene could be present in the raw material of one product. So do you still like the conclusion where we call attention to the --

DR. BERGFELD: Or is it unsafe?

DR. MARKS: Well, that's what I'm asking. Do you like that conclusion or should we have a different conclusion, and as Wilma suggests, make it unsafe?

DR. SHANK: Me? Okay. I think the conclusion is okay, but the discussion has to change.

DR. MARKS: Okay.

DR. SHANK: First, I would add the SCC's

risk assessment and Dr. Boyer's, I think very important works on that. They have to go together. And then in the discussion refer to the need to assume a loss of benzene if we use risk assessment. And then Dr. Heldreth, in one of the documents I read, I think stated it very, very well. I think I'm paraphrasing it. Rather than having the last two lines in the discussion in the second to the last paragraph, the last two lines begin "if residual benzene was present." I would take those two sentences out where all the numbers are and say "since it cannot be predicted with certainty, what quantity of benzene would be volatilized or leached from the crosspolymers during manufacture, formulation, or product use? The panel determined that the data are insufficient to conclude that crosspolymers polymerized in benzene are safe for use in cosmetic products." And leave out all of these numbers. These are assumptions and things.

DR. MARKS: Yes. That's what I was -- obviously, before you came in I've been asking about. So we would move that this become a final safety assessment with those changes in the discussion.

DR. HILL: And by the way, when I said aromatic moieties into polymer, I meant unsaturated, not aromatic. There are no aromatic moieties in the polymer.

DR. EISENMANN: Question. If I'm hearing you right, so if a company actually measured benzene in the final product and it was below the 10-6 risk level, that would be okay? Is that what you're saying?

DR. SHANK: Not explicitly, no. We would have to see the data.

DR. SLAGA: Right.

DR. SHANK: That's what we're saying.

DR. SLAGA: It's insufficient.

DR. SHANK: We haven't said that we automatically default to the EPA water standard.

DR. EISENMANN: Well, he's not using the water standard because the water standard is in the middle. Correct?

DR. BOYER: It's in the middle.

DR. EISENMANN: And they set that standard because that's technically achievable if I remember correctly.

DR. SHANK: The problem is we anticipate --

DR. EISENMANN: So you're setting it lower than the EPA water standard based on the lowest EPA risk level? You're not standing in the middle?

DR. SHANK: No, we're now going to a level that would have to be lower than the EPA standard.

DR. EISENMANN: And you're talking about the lower 10-6 risk level that Ivan has pointed out?

DR. SHANK: Yes.

DR. EISENMANN: Okay.

DR. SHANK: However, we're also saying that the volatilization of benzene from the finished product probably varies -- vary greatly with the product itself and the use conditions.

DR. EISENMANN: Well, I think I'm discussing more the volatilization while either making the product --

DR. SHANK: No.

DR. EISENMANN: -- as they heat it -- well --

DR. SHANK: We're not there. We're at the consumer level. That's where we're --

DR. EISENMANN: But if you measure -- if you measured it in the final product and the level was still below 10-6 in the final product after you've heated it and mixed it and do whatever they're going to do to it to make the product and it was below the 10-6 level, would you be okay with it?

DR. SHANK: It would depend on how much product is used. The drinking water standard is based on drinking two liters of water a day. Okay? Now, to use that concentrate --

DR. EISENMANN: I'm not saying a concentration. I'm saying a risk level. So they would have to -- they would have to do a risk assessment like Ivan did but instead of using the level that we calculated as an estimate in the product you'd have an actual measured level. And then you did the -- finished doing the risk assessment. If it was below 10-6 would you be okay with it?

DR. SLAGA: I think the way we have it, insufficient, until we see the data is the way -- you know, you're stating more of a hypothetical and we -- we're saying we want to see the data before we make that decision. We probably would agree with what you're saying.

DR. EISENMANN: Okay.

DR. MARKS: Okay. So tomorrow I'm going to move that we issue a final safety assessment on these crosslink alkyl acrylates with a conclusion that they're safe except when they're polymerized in benzene and that the available data are insufficient to make a determination of safety for these ingredients when polymerized and benzene has its data on page 39. It's going to be a very robust discussion in this final safety assessment of which Ron Shank, I may ask you to discuss tomorrow if need be. But that's been captured. The SCC. Dr. Boyer's risk assessment and then Ron, those comments you made in terms of ordering the discussion.

Is there -- I don't know if there's precedent set. Since there's a number of changes in the discussion, one would say that's editorial but does the expert panel need to see the final discussion before it's sent to the Journal?

DR. BERGFELD: No.

DR. MARKS: Good.

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going on to the crosslinked alkyl acrylates and that is Dr. Marks again.

DR. MARKS: So, in March of this year's meeting, the panel issued an insufficient data announcement asking for impurity data and what we were concerned about was benzene as the impurity in these crosslink alkyl acrylates, which are 23 compounds, and we had extensive discussion on how to deal with this benzene impurity, whether or not we should try and set limits to what should be in a cosmetic product and where would those limits be

derived from. Would it be from the California Prop 65 limits? Would it be EPA drinking water limits of benzene? And how we finally ended up is feeling, since a number of these crosslink alkyl acrylates are -- benzene is not used in the manufacturing process, we felt that a reasonable conclusion would be safe, however insufficient data for leave-ons having benzene impurity within it.

DR. BERGFELD: And that's a motion?

DR. MARKS: That's a motion. I'm sure there will be discussion.

DR. BERGFELD: Discussion? Belsito response?

DR. BELSITO: Yeah, we, in the draft discussion, in the third -- fourth paragraph, the next to the last sentence, it says, "For example, a worse case for benzene as an impurity would be 0.5 max times 6 percent maximum use concentration in the ingredient for a final level of 0.03 percent in a cosmetic formulation. Such a trace amount presents no safety issue," and then just deleted that last sentence.

So, the feeling of my panel members was that 0.03 percent did not represent a safety issue.

DR. MARKS: So, Ron Shank actually did the calculations on this comparing it to the EPA water level of 10 microns -- I'll tell you what, Ron, why don't you go through your calculations with the 10 micrograms if you drank 2 liters of water -- and then he calculated in a cosmetic ingredient that you could apply 1 gram and get a third of that potentially.

DR. SHANK: Right. I took the maximum concentration of a polymer in cosmetics is 6

percent and 1 gram of that cosmetic applied, which would give 60 micrograms of the polymer. If that's a half percent benzene, that would produce 300 micrograms of benzene per gram of formula -- formulation. That 300 micrograms is 30 times higher than the EPA maximum benzene drinking water standard of 5 micrograms per liter. Assuming an adult drinks 2 liters, that would be 10 micrograms of benzene per day. The cosmetic formulation would provide 300 micrograms per day. So, the benzene concentration is too high. And that's for one gram of cosmetic applied to the skin.

DR. BELSITO: I mean, we obviously had concerns with benzene as did you. I mean, I don't really have a problem with your conclusion. I mean, that's what we're all trying to get at is the restriction of benzene. So, I mean --

DR. LIEBLER: So, I think the calculation's valid. The question I have is, drinking water, obviously you're ingesting it and that means you're ingesting all the benzene in the calculation in the drinking water side. With a cosmetic ingredient you're applying an ingredient, and the question remains, how much of that ingredient -- of the benzene in that ingredient would actually be absorbed. And, you know, you would certainly be losing it -- if it's there, you'd be losing it to evaporation as well as absorbing whatever you could absorb. So, I mean, the difference you point out is high, except that the amount that you'd actually get into the body would be much lower -- lower fraction of what's presented to the body.

DR. SHANK: But you have to know how much.

DR. MARKS: And that's what we struggle with, and that's only one gram, Dan. If we applied this total body to an adult it would be 30

grams, and there are some baby products here, so if you did total body application, it could be not 300 in an adult, but exposure to 30 times that and then we don't know what percentage of that -- I agree, that's why we struggle trying to figure out how we could set a limit. And then we ended up with insufficient for leave-on just because we couldn't determine the limit and we didn't know how much absorption would occur. And we even asked the manufacturers how much benzene would be free within these acrylate ingredients and we couldn't come up with an answer to that.

DR. LIEBLER: It's insufficient for leave-on at a given concentration of benzene? Is that what you said?

DR. MARKS: Yes, insufficient data for leave-ons having benzene impurity within it. We're told that a number of these acryl acrylates are actually manufactured without benzene, so.

DR. SLAGA: As a solvent.

DR. MARKS: Yeah, as a solvent, so it would -- if it's not manufactured with benzene as a solvent, then it's a nonissue. It's only those ones in which benzene is a solvent.

DR. BELSITO: So, you need to be careful how you craft that because what you're saying is that it's -- the data are sufficient to support the safety for leave-on and rinse-off products, however, the assumption is that the leave-on products will not be manufactured with the use -- or however you want to say it -- of benzene.

DR. MARKS: Yeah, that's correct, Don. That's essentially it. However, insufficient data for leave-ons having benzene impurity.

DR. BRONAUGH: Could I just add that 1

gram of product probably, you know, that would cover 1,000 square centimeters of a baby. You couldn't get much more than one gram on --

DR. SHANK: It's still, at this concentration of a half a percent, it's still more benzene for a baby than would be allowed if the baby had that benzene in drinking water.

DR. BERGFELD: You're going out as insufficient in the leave-ons, did you want to modify?

DR. BELSITO: Only if the product is manufactured with benzene.

DR. MARKS: Correct.

DR. BERGFELD: Is there another way of stating that where it would be fine or safe if benzene-free leave- ons, but unsafe or insufficient for those who contain benzene?

DR. MARKS: That's exactly what we said.

DR. BELSITO: Have we ever set a limit for benzene?

DR. MARKS: Well, we tried doing that, Don, and if we can -- you know, as this goes out, issuing a tentative report, one of the data needs we would want for the insufficient data is establish a limit. We struggled with that so we would ask industry to help us with establishing a limit and a margin of safety calculation.

DR. BERGFELD: Would you restate your motion then again and --

DR. MARKS: We would move to issue a tentative report on these ingredients, and I have noted that there are 23 of them, that they're

safe; however, insufficient data for leave-ons having benzene impurity.

DR. BERGFELD: Is there a second?

DR. BELSITO: Second.

DR. BERGFELD: Second. Any further discussion?

DR. BELSITO: Yeah, what we would need would be, as Jim said, for -- they may be safe if they have a benzene impurity, but what is the level and what's the margin of safety?

DR. BERGFELD: All right. Calling the question then, all those in favor of this motion?
Approved, thank you.

DR. MARKS: And let me just reference one thing we did consider and look at was the 1987 report on toluene and actually in that conclusion it was that that ingredient would be benzene free, but we decided not to go to that extent that it had to be benzene free.

DR. BERGFELD: Any other points that need to be made at this time?

DR. KLAASSEN: Yes, I think it's very important that we don't say something like that, that it -- and if we said that for toluene before we should all be spanked.

DR. MARKS: Well, you can review the report. We pulled it up yesterday.

DR. KLAASSEN: I believe you, but we made a mistake.

DR. BELSITO: Last comment was we were asked whether if other chain length molecular

weight acrylate crosspolymers came on could we do like what we did with PEGs and just say safe if they're used in the same way? And our group felt we could not, we would like to see each individually.

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DR. BELSITO: Okay. So, we're going back now to acrylates crosspolymers, is that correct? Okay. So, the title has now been generalized to crosslinked alkyl acrylates. In March, insufficient data asking for impurities with a focus on residual benzene. Those have been provided and incorporated into the report. The panel -- so, basically that's what we're looking at. We have, just to remind you, the highest concentration -- at least, this is my scribble -- 6 percent leave-on n-hexane at.2 and benzene at.5 percent were the maxes that I scribbled down.

So, assuming that Curt and Paul and Dan are okay with those levels, safe as used for this acrylate copolymer group.

DR. BERGFELD: Before you go there, could I have you remind me about how you felt about the human sensitization, irritation? Are you using -- trying to look at this particular document, how it's arranged? But anything but particle size or size of molecule? There's not a lot here.

DR. BELSITO: You mean because of the acrylic component to them or what?

DR. BERGFELD: Yeah. Well, and just the fact that there's little information on it.

DR. BELSITO: It's Table 5. There's quite a bit of information in Table 5.

DR. BERGFELD: Non-human.

DR. BELSITO: No irritation, no sensitization. I mean, it's only summarized in two short lines in the text, but the table has quite a bit of data.

DR. BERGFELD: Yeah, you're right. It is.

MS. FIUME: I did just want to point out so it's not missed, on Panel Book page 49, the calculation for the amount of benzene that could be in cosmetic formulations has an extra zero after the decimal point. It's actually.03 percent, not.003.

DR. BELSITO: What line is this, Monice?

MS. FIUME: Fourth line from the bottom, very left.

DR. BELSITO: Okay, 0.03, not --

MS. FIUME: Yes.

DR. SNYDER: I had a question. Are we okay with that language, that last sentence there? That care should be taken to minimize the amount of residual benzene?

DR. BELSITO: Why? What is your concern with that?

DR. SNYDER: I mean, I think we could -- I think because it is such a significant toxicant that we probably should be a little bit more --

DR. BERGFELD: Specific --

DR. SNYDER: -- specific as to what we mean by minimize. I mean, it --

DR. LIEBLER: Well, I think you just said in the sentence prior to that, such a trace amount presents no safety issues.

DR. BERGFELD: Why don't you just end there?

DR. LIEBLER: I would recommend deleting the last sentence.

DR. KLAASSEN: I would, too. It kind of sounds the opposite.

DR. BELSITO: Yeah, so --

DR. EISENMANN: But did you catch it's 03 not 003. That's --

DR. BELSITO: .03 percent.

DR. EISENMANN: Right.

DR. BELSITO: You're okay with that?

DR. SNYDER: I'm asking that also, I guess. As to what level -- if we're comfortable with that level.

DR. KLAASSEN: Well, one thing with benzene is that we know it's a human carcinogen. And thus, people get very excited about it. But the amount of benzene that it takes to be a human carcinogen actually is very high. So, I have no concern with this concentration in this compound or class of compounds.

DR. BELSITO: Okay.

DR. LIEBLER: I agree.

DR. BELSITO: Okie-doke. So, safe as

used.

DR. SNYDER: Monice, had a comment on Table 6. When you compile the tables like this, which are highly informative, like on Page 71? If you look under acrylic acid, under toxicological studies, there's an inhalation study there that says lesions were observed in rats and mice in 4-day, 2-week, 20-day, and 13-week studies. But there's no dose information. And particularly if we could just at least have the doses that were tested, and if there was any way to calculate an NOAEL. And the same thing down on methyl methacrylate, toxicological studies: Single dose, oral, produced gastric lesions, but there's no indication of what doses to give us some idea. And likewise, even in the negative studies, like the repro studies, did not produce teratogenic or reproductive effects in rats. But I'd like to really know the doses that they tested.

MS. FIUME: Can I ask, if there's multiple studies, do you want me to just pick the one that had the lowest or -- you know, that was most representative for that amount? How do you want that handled?

DR. SNYDER: Certainly a study that could derive an NOAEL is the most -- going to be the most informative.

DR. BRESLAWEC: Keeping in mind that these are components, not the actual ingredients that we're talking about.

DR. EISENMANN: I have one thing in the discussion. This sentence, "The panel indicated that competence in these assumptions would be bolstered by data from well-conducted absorption penetration studies on, for example," and it continues. I don't remember you guys saying that, and these things are -- I am -- it's in the second

paragraph, last -- or the third paragraph, actually, the last sentence.

DR. LIEBLER: "The panel indicated that confidence in these assumptions would be bolstered," that sentence?

DR. EISENMANN: Yes.

DR. LIEBLER: Yeah, I flagged that, also. And I asked whether it suggests that we want or expect to see these data.

DR. EISENMANN: I mean --

DR. LIEBLER: That was my question.

DR. EISENMANN: These are -- they're just so large. At least the ones that you have in the molecular weight information are just so large that I don't know why you would need any information at all.

DR. LIEBLER: I agree with that view.

MS. FIUME: So just delete that sentence?

DR. LIEBLER: Yes, right?

MR. DEMARIA: Anything else?

DR. SNYDER: I have just a kind of global editorial thing. That in all of these reports, when we talk about the ingredients and their use in cosmetics, we use various terms like are used, "may function as," "can function as." And I think what we're really talking about, "as they're reportedly used," because that's what it's based on, correct?

DR. BRESLAWEC: Right. We've tried to

standardize that language. And instead of saying "used as," we're trying to say, "reported to function as." So that's the language we're trying to move toward.

DR. SNYDER: Yeah, because it is a reported use to us and that's what we base all of our conclusions on. So I think it's really important that we are accurate on what it is. Not that they can or may or --

DR. BELSITO: I'd like the "reported to function as." Comments? Monice, you have everything you need from us for this one?

MS. FIUME: Yes, thank you.

DR. BELSITO: Okay.

DR. BERGFELD: The only passing comment is on page 7, where you -- alternative studies. Under mucosal irritation, there you have a bunch of eye studies. They're a little bit tough to pull out, if you're just looking for eye. And in other documents, it was non-human eye or eye toxicity. I'm not sure what you're going to do about that, but this is inconsistent now with several documents.

MS. FIUME: So you're looking for eye.

DR. BERGFELD: And frequently look for eye, because of irritation.

MS. FIUME: So you would prefer the term "ocular" versus "mucosal?"

DR. BERGFELD: No. I prefer "eye" appear somewhere in the title so I can find it. That's basically what I'm saying.

DR. BRESLAWEC: Got it. What we occasionally come up with is that we have more

headings than text, and then we go through this heading removal exercise. And I think this is a victim -- fell victim to that.

June 2011 – Marks Team

Next is the Pink Book, acrylic crosspolymers or crosslinked alkyl acrylates. In March of this year, the panel issued an insufficient data announcement asking for impurities particularly focusing on residual benzene. Data has been provided and it's found in the report. Ron or Tom? How do you feel?

DR. SHANK: On page 49 of the book, page 9 of the report near the very bottom, it says that in worst case for benzene concentrations 0.003 percent, that's not correct. There is one too many zeros. So multiply that by 10 and it's 0.03 percent. And I calculated that if the maximum concentration of the polymer in a cosmetic formulation is 6 percent, for every gram of formulation would produce three- tenths of a milligram of benzene. And the EPA water standard for benzene is a maximum of 5 micrograms per liter, so this works out that an adult would be exposed to 10 micrograms per liter in drinking water as a maximum. The cosmetic concentration would be 30 times above that. So I think we need to say something about limiting the benzene concentration in the polymer.

DR. BRESLAWEC: Dr. Loretz, do you want to comment on that? There is some discussion about how it's lodged in and that the 6-percent concentration actually could be more like 1 percent.

DR. LORETZ: I think this is the supplier that provided information suggesting that the maximum concentration that they were aware of in use was less than that, so this is the worst

case in the course of the study minus the zero. So I think this is the highest concentration and higher than you would see, and then they've raised the issue of benzene when you mix it, et cetera, as it's volatile and expect to get some amount although we don't have anything.

DR. SHANK: I did a calculation based on 1 gram of cosmetic applied to the skin, that a concentration limit for benzene of 0.016 percent would be the same exposure as the EPA drinking water standard just as a reference. What we want to say is up to everybody. That would be 167 PPM in the cosmetic formulation. In the polymer, pardon me.

DR. MARKS: And the benzene is the only issue at this point with the safety of these ingredients. Ron, how would you work that in the conclusion then? I am presenting it so I'm going to ask you have you figured out how you'd like to work this?

DR. SHANK: No, I have not.

DR. MARKS: It obviously would be safe as used as long as the crosslinked alkyl acrylates have less than X- amount of benzene impurity or something to that effect. Is that what you were thinking, Ron, the way we'd do this, that we would in the conclusion state that we want a maximum amount of benzene impurity in it?

DR. SHANK: I was trying to find out in other ingredients we have reviewed. Have we asked this question before, a limitation on the amount of free benzene in an ingredient? Unfortunately, my access to the website doesn't work again, so I tried to do it through the compendium and I couldn't find anything, fortunately, the compendium we have online. So perhaps we have already asked this question about free benzene in

other ingredients and refer to that. Otherwise we'll have to discuss what basis we want to -- I just took the EPA drinking water standard because it was an easy number to find, but maybe there's a better way to do this.

MS. FIUME: I have a question per the discussions. Last night I pulled up the NIOSH and the OSHA limitations, but if we were to use EPA drinking water, in the discussion we currently say that we don't really expect it to absorb so the rationale for using the discussion of using an oral limitation versus something else, what type of wording would you want for something like that?

DR. SHANK: If the benzene in the ingredient polymer is free, then it will be absorbed through the skin. So that's why using an oral -- the polymer stays behind, but the benzene would be absorbed into the blood.

DR. SLAGA: In the past we always discussed the level of impurity is the word to make sure that benzene between 5 or less. Wouldn't just be as easy based on your calculation?

DR. SHANK: Putting 5 percent I think is too high.

DR. MARKS: Right.

DR. SHANK: Because.6 percent of 6 percent is 300 micrograms of benzene per gram of formulation. You can check my calculations. So 1 gram of formulation would give 300 micrograms of benzene. Two liters of drinking water at the maximum EPA limit would give you 10 micrograms of benzene. So 1 gram of cosmetic formulation at 6 percent polymer content would be 30 times above the EPA water standard.

DR. MARKS: That's assuming you only apply 1 gram.

DR. SHANK: Yes.

DR. MARKS: In a normal application if you're doing total body it would be 30 grams.

DR. LORETZ: It would depend on the product type, too.

DR. MARKS: Exactly. It could be significantly more than just 1 gram applied. Again, on page 49, you took one of the zeros for a final level of 0.03 percent of benzene? Is that what you said, Ron?

DR. SHANK: Yes.

DR. MARKS: Such trace amounts presents no safety issues. You want that sentence struck obviously.

DR. SHANK: Yes, please.

DR. MARKS: And now the question is such trace amounts may present a safety issue might be the better way of doing it since you have the EPA level. The panel did caution that care should be taken to minimize the amount of residual benzene. We're sort of addressing it with that but we haven't set a level.

DR. SLAGA: What level would you suggest?

DR. SHANK: As a starter for discussion tomorrow I guess, that application of the formulation would provide no more than 10 micrograms of benzene. That would be equivalent to 2 liters of drinking water. That's the

rationale. I'm sure the others will find that worthy of comment.

DR. BRESLAWEC: And that is based on the EPA drinking water standard?

DR. SHANK: This is the EPA drinking water standard and that standard is a maximum concentration of 5 micrograms of benzene per liter of water assuming an adult drinks 2 liters of water a day.

DR. BRESLAWEC: I'm sorry. Could you repeat that definition?

DR. SHANK: The EPA standard is a maximum concentration of benzene in drinking water of 5 micrograms of benzene per liter, and the assumption is that an adult would drink 2 liters of water a day. So the total exposure would be 10 micrograms per day of benzene.

MS. FIUME: Dr. Shank, out of my own curiosity, I've gotten lost in the numbers. That's my own fault. The California Prop 65 limits, are they higher or lower than the EPA that was listed in the text?

DR. SHANK: They would not be higher. If anything, they would be lower.

MS. FIUME: They would be lower. There is 6.4 micrograms per day.

DR. SHANK: So that would be lower.

DR. MARKS: So one part would be in the discussion we're explaining the rationale based on the EPA 2 liters of water adjusted daily in that total of 10 micrograms of benzene. The other is going to be how we word the conclusion that these crosslinked alkyl acrylates are safe as used as

long as the limit of benzene is no greater than 10 micrograms total daily exposure or something like that. How do you like that, Ron or Tom?

DR. SLAGA: That sounds good.

DR. SHANK: The rationale is the EPA drinking water standard. I should know this. The Prop 65 limit is 6 micrograms.

MS. FIUME: 6.4 micrograms per day orally.

DR. SHANK: Oral?

MS. FIUME: Yes. That's actually in there.

DR. SHANK: Does that mean if a cosmetic formulation has 10 that it can't be sold in California which is 10 percent of the U.S. population?

DR. SLAGA: They probably use more cosmetics out there.

DR. MARKS: What was California?

MS. FIUME: 6.4 micrograms per day for oral exposure and 13 for inhalation.

DR. SHANK: I don't know that I would recommend using the California Prop 65. I won't comment further. I wouldn't use that as the standard.

MS. FIUME: I would imagine that suppliers have had to do something because the European limits are very different. There are different limits for the amount of residual benzene based on where they're supplying to. Europe has a level of.1 so certainly they can't

use that in their jurisdiction.

DR. SHANK: .1 microgram?

MS. FIUME: .1 percent.

DR. LORETZ: .1 percent.

DR. SHANK: .1 percent.

DR. SLAGA: That adds up to impurities?

DR. LORETZ: They showed that the loss they looked at, it range and I think the highest was.41 and that some fall well below that.

MS. FIUME: I tried to find what Europe's rationale was for the limit and I wasn't able to find it to really pinpoint what they were basing their number on.

DR. LORETZ: We would assume that somebody selling it in California is aware of that and in compliance with Prop 65 but we don't have any more information.

DR. MARKS: So you don't have a problem, Ron, with saying we're going to limit it to 10 even though California has 6.4?

MS. FIUME: Actually in the memo it does say that formulators that sell products in California must comply with California's Prop 65 which limits benzene exposure from a product to 6.4 micrograms per day for oral exposure. So the information that did come from industry does state that they are aware of what California's limit is and that they have to comply.

DR. MARKS: I would say we go to 6.4.

DR. SLAGA: It's easier for the formula

based on the lowest.

DR. MARKS: Yes.

DR. SLAGA: You don't have to mention California.

DR. SHANK: You'd have to mention why is it 6. --

DR. SLAGA: That's true.

MS. FIUME: Provide it just in case you --

DR. MARKS: Then we get into we think that EPA is better than the California Prop 65. I don't know. I just see that if I were a formulator a conflict when I look at the CIR recommendation of 10, although maybe that happens all the time. I'm not sure. We can certainly leave it at 10. You're our California representative here, Dr. Shank. So it's going to be safe?

DR. SLAGA: Industry will probably try to keep it below Proposition 65, I'd guess.

MS. FIUME: Because there's multiple solvents.

DR. BRESLAWEC: And that.1 percent, how does that compare to the 10 micrograms per day?

DR. MARKS: Let me see. I think I'm the one proposing, so tomorrow I'm going to move that we issue a tentative report on the crosslinked.

MS. FIUME: Insufficient?

DR. MARKS: Yes. It was insufficient. So a tentative report on -- yes, I know the subject says tentative report, but actually it's

what we're moving. A tentative report on crosslinked alkyl acrylates as safe as used as long as the benzene impurity limit is no greater than 10 micrograms of benzene total exposure daily or daily total exposure. Does that sound like the way to handle it?

DR. SLAGA: Total from all sources or cosmetics?

DR. MARKS: We say there that in cosmetics safe for cosmetics. So you think somebody would interpret the conclusion total or should we be more specific and say 10 micrograms of total exposure? Now you get into all the other issues we have like the phthalates in nail. We limited in the nail cosmetic but we're not limiting it to all phthalate exposure from --

DR. SLAGA: Any source.

DR. MARKS: Yes.

DR. SHANK: I haven't reviewed the EPA document for some time, but I would be -- I'm fairly sure that they considered other sources of exposure because it's an additive to gasoline. People who pump gasoline are exposed by inhalation to benzene. There are several sources of benzene in the environment and I'm pretty sure the EPA water standard took that into account. So I would put the benzene limitation as 10 micrograms per cosmetic exposure or however you word that.

DR. MARKS: Personal care product.

DR. SHANK: Personal care product.

DR. MARKS: Personal care product exposure.

DR. LORETZ: That's a little complicated

as to you don't know if -- still in theory so if you're putting in your five and he's putting his five, it gets challenging that way.

DR. MARKS: Another nuance.

MS. FIUME: And that will be in the conclusion and not just the discussion?

DR. SHANK: It would have to be in the discussion to say how we arrived at that number.

DR. MARKS: But the conclusion would limit.

DR. SHANK: The limit would be in the conclusion, yes.

DR. MARKS: Right.

DR. SHANK: Is there some way to scan previous documents to see if we've asked this question about limited benzene before?

DR. LORETZ: There's one coming up on today's agenda that refers to benzene free.

DR. SHANK: For benzyl alcohol?

DR. LORETZ: It must be in that.

DR. BRESLAWEC: I'm not particularly aware that we've limited it per product exposure before. I think, and I honestly can't say this with 100 percent certainty, but I think it's always been concentration in the ingredient because we're looking at an ingredient and not the product.

DR. MARKS: Right.

DR. BRESLAWEC: So I would urge you to

characterize it in a way that focuses on the level of impurity in the ingredient rather than in the product.

DR. SLAGA: In this specific ingredient.

DR. MARKS: This is for the specific ingredient.

DR. SLAGA: Not in personal care products.

MS. FIUME: But I think it was just PEG alkyl ethers that there was concern over some of the residual solvents or residual components. In the discussion it was worded a certain way without specifics, but I would have to go back and look at it because I want to think it was the alkyl PEG ethers that addressed that. Same type of concept.

DR. MARKS: What do we do with heavy metals, aflatoxins and that sort of thing? We don't do limits do we?

DR. BRESLAWEC: We have in the past.

DR. SLAGA: We have a boilerplate.

DR. MARKS: Right. A boilerplate.

DR. BRESLAWEC: But it's based on the ingredient.

DR. MARKS: Right.

MS. BECKER: Dr. Marks? It's in the silylate report in the report on toluene. The CIR Expert Panel has stated that all cosmetic ingredients should be benzene free.

DR. BRESLAWEC: But there was a comment from industry where they questioned where CIR had

stated that, so that's an issue we need to address.

MS. BECKER: I can go get my computer and pull it up.

DR. BRESLAWEC: Let's do that.

DR. SHANK: It's hard to say because I based my calculations on 1 gram, but that was arbitrary, so I guess it depends on what the product is and how much is applied to the skin. So how do you set a limit on the concentration in the ingredient based on the maximum amount you apply to the skin and what would that be? I have no idea.

DR. BRESLAWEC: I think you can help us on that.

DR. MARKS: Because here we have -- I mean there's a lot of leave-on use. For the C-10 to 30 acrylates there are over 1,300 leave-on products.

MS. FIUME: Another complicating factor and I think Linda was alluding to this earlier is that from that manufacturer under that trade name they state that they're aware of it being used at a maximum of 1 percent, but the problem is we don't have the concentration of use breakdown by trade name, it's by INCI name. So they may only be using it at 1 percent and we're using it at 6 percent as the worst-case scenario, so it also complicates what is actually being put in. In one of my reports there's actually a calculation of how much is exposed based on product type. I don't know if this is helpful, but in the TEA report a company actually came up with an exposure of consumers. It's on page 6 of the report.

DR. SHANK: Of the report. Yes?

MS. FIUME: And then on page 6, the third full paragraph down, it --

DR. SLAGA: What page, ma'am?

MS. FIUME: Page 6 of the report, which is Panel Book page 25, and that's TEA.

DR. MARKS: It's a different book.

MS. FIUME: Yes.

DR. MARKS: TEA.

DR. SLAGA: Yes, I have that.

MS. FIUME: I don't know if that's helpful at all.

DR. SHANK: So there is some kind of algorithm to use?

MS. FIUME: That was submitted to us. And I know calculations have been done for things like the diluted products, how much is actually exposed per day, but I don't know of any other products if there's been calculations as to what type of product, how much exposure actually occurs per day.

DR. MARKS: I think we saw that with the RFL presentations on fragrance exposure and they did it with various product categories.

DR. LORETZ: And we've published. There are a lot of publications.

MS. FIUME: It sounds familiar because I know the diluted ones, if that would be referred to more often in the report. Yes, that

calculation actually came from an OECD SIDS document that was their calculation that was included in their report.

DR. SHANK: Okay.

DR. LORETZ: I know the Expert Panel has used the Prop 65 levels before. I guess this one's just more complicated because if you take the worst case then you start getting into a different --

DR. MARKS: Here we go. On toluene it says that was the question actually I was going to ask, and I don't know whether it can be answered, can these acrylics be manufactured free of benzene?

DR. LORETZ: I think benzene is just way of making it. It's not necessarily a common way. It's just one way.

DR. MARKS: So if it isn't a common way then to me the way to solve it would be that we recommend there be no benzene.

DR. LORETZ: I think it's a certain product type that some people find have some benefits.

DR. SHANK: I'm perfectly happy with this. What year was this written? Back in the day.

DR. MARKS: Do you want to read it? I like the second sentence under the discussion I guess it is or the summary.

DR. SHANK: This is on the toluene document in the 1980s I guess, "One possible impurity, benzene, is a carcinogen. Therefore, cosmetic products formulated with toluene should

be benzene free." That's the best way for us to go if that doesn't cripple the manufacturer if there are other solvents that can be used.

DR. MARKS: Is there anybody from -- of course that's not going to influence our decision on safety other than to say is that an issue with the manufacturer.

DR. LORETZ: I think what the manufacturer said is that is an issue, that they do sell that product and that product has value, so I guess that's why they -- you know, we think it would be a safety assessment on the benzene levels rather than just a flat-out ban.

MR. LABA: Dennis Laba from PRESPERSE. PRESPERSE represents one manufacturer that makes products. These products were originally precipitated in benzene and they have been moving more and more environmentally friendly solvents and toxicity safe solvents. But the whole industry has not moved as fast as the manufacturers though these other products have been available. People who have been using these for years have not changed all of their products over to the other ones. There is one particular manufacturer that has most of the market and they would probably be the ones most upset about that, saying that there can't be any benzene, but the alternatives are out there certainly.

DR. SHANK: Thank you.

DR. SLAGA: Let's proceed then.

DR. SHANK: So the precedent if the benzene document is that we say benzene free.

DR. BRESLAWEC: The toluene, yes.

DR. SHANK: Toluene document. Thank

you.

DR. MARKS: I like safe. And then in the discussion because that's the way it is in the toluene document, in the discussion we say that it's benzene free, that we're concerned about benzene and unless there's an alternative way of arriving at a safe limit which we've discussed, it doesn't sound like that's going to be easy.

DR. LORETZ: I guess I have some real concerns about benzene free because that implies a zero tolerance which, I mean, when you look at like traces in things that are like in Annex 2 in Europe, I mean, they, you know, qualify that as a good manufacturing practice, et cetera. It's not a true zero. So, but to me benzene free taken literally is a true zero which is --

DR. SHANK: The original toluene document is dated 1987, so that must have gone through re-review. So if we could find the re-review to see -- because I'm sure we've handled this before.

DR. MARKS: So we're back to safe, and then in the conclusion do we mention there it should be benzene free or should we put that in the discussion? Because in the toluene document it's in the discussion, is it not?

DR. SLAGA: Not in the conclusion.

DR. MARKS: Right.

DR. SLAGA: We ought to be consistent depending on what the re-review was.

DR. MARKS: Then the question also there is do we want to as you suggested what may create heartburn, but from a safety point of view do we want to be benzene free? Because obviously what

we've struggled is if we don't say it's benzene free, what is the limit we're going to set?

DR. SLAGA: In the original discussion we were talking about benzene that's trapped.

DR. BRESLAWEC: I think that was a misunderstanding on my part.

DR. SLAGA: I'm sorry. We'd have to have had some kind of linkage wouldn't we to keep

DR. SHANK: It's a polymer so it could be physically trapped, not chemically trapped.

DR. LORETZ: I think benzene is referred to a monomer at some point in here and that's not correct.

DR. SLAGA: I think in reality we're worried about the total exposure of benzene so maybe we're going into cosmetic and looking for environmentally safe alternative solvents here, then it seems to me that's as good a case.

DR. LORETZ: While that may be the ideal, does it make sense if your product is in compliance with Prop 65 and you specify that that's what you recognize is your safe level?

DR. SLAGA: That means that we would be going beyond Proposition 65.

DR. LORETZ: Right.

DR. SLAGA: We can't say we're excepting Prop 65.

DR. SHANK: Another way is to take the EPA water standard for a total exposure of 10 and that cosmetic personal product care use should contribute no more than half of that, so that

would be 5 micrograms?

DR. BRESLAWEC: At what level?

DR. SLAGA: That's getting a little wishy.

DR. SHANK: Somebody else try it.

DR. SLAGA: This is toluene sulfonamide formaldehyde residue and that was straight toluene in that one.

DR. SHANK: Yes.

DR. LORETZ: I think for consistency I'm concerned about again setting a zero standard because we're going risk based throughout and not just benzene.

MS. FIUME: I'm trying to think about in the past with the wording where is a maximum is allowed per day, but you could have multiple exposures how we've worded it in the conclusion. Peppermint oil might be one because I think peppermint oil didn't have a maximum that should be allowed per day and I don't know if the discussion handled that at all or not.

DR. SHANK: What was it called?

DR. MARKS: That was a sensitivity issue.

MS. FIUME: Peppermint oil.

DR. MARKS: Let me see. I'm trying to think. Again, I come back to the phthalates because there was the concern that nail polish would add to the total burden of phthalates, but I think we just did a safe because our margin of

safety calculation with that showed that it would be --

DR. SLAGA: Wouldn't have been very large.

DR. MARKS: -- a very small contribution by nail. Whereas this potentially --

DR. SLAGA: We've added significant with our approval.

DR. MARKS: Yes. This with your calculation, Ron, would give a significant amount of exposure.

DR. LORETZ: Would you maybe then be going to ask industry for more information on use levels and risk to defend the risk assessment?

DR. SHANK: It's a genotoxic carcinogen.

DR. MARKS: The way we could proceed is to with the benzene free and that goes out as a tentative report which means industry can react to it. And if they can show us some margin-of-safety calculation that is reassuring -- we're obviously struggling with coming up with establishing a limit. Maybe industry could suggest a limit.

DR. SLAGA: We'll have the discussion tomorrow.

DR. SHANK: The limit on aflatoxin is a lot more potent carcinogen than benzene by far. That limitation is based on the fact that in certain things you can't get it any lower so you just have to live with it. Even FDA allows it in food at a certain level because it's associated with the use of peanuts. You can't get it to zero. But here if it's used a solvent, you can get it to zero by not using it as a solvent.

DR. SLAGA: Let's go with benzene free because at least we have the toluene document to base it on.

DR. LORETZ: I guess I'm still struggling with the free and that meaning zero and that being kind of a scary precedent. Would it maybe make more sense or would it be just as well to say benzene should not be used as a solvent and then leave open the door for industry to come back with some kind of a risk assessment to defend it?

DR. MARKS: If they don't use it as a solvent, there won't be any benzene. Correct?

DR. SLAGA: Yes.

DR. LORETZ: I guess I'm struggling again with the zero because benzene free to me is too absolute.

DR. BRESLAWEC: Perhaps we can say something alone the lines of benzene no higher than a safe level as determined by a risk assessment and then expect the risk assessment to come in from industry to provide a level that the panel would consider safe at its next deliberation. Bart Heldreth is here.

DR. SHANK: Benzene in crosslinked polymer.

DR. MARKS: Alkyl acrylates.

DR. SHANK: Alkyl acrylates. Is the benzene that's a solvent physically trapped in the polymer so that it can't be absorbed?

DR. HELDRETH: That potentially could be the case. We don't have any data from industry saying that they used it as a solvent and during

the crosslinking it got trapped in there. Potentially, sure. Anytime you do crosslinking you could trap the solvent or anything else that's in the solution inside small spaces inside the polymer. Whether that's the case here we don't know.

The other thing, once you have a polymer, especially a crosslinked polymer, there's also the possibility of the solvent absorbing into the polymer even though it didn't get tracked on crosslinking and residing in there and even upon heating and doing lyophilization to try to get things out of there, it could stay in there a little longer than you would expect. Whether that's the case here, though, we don't have any data on that, but there is that potential.

DR. SHANK: Thank you. I guess we can say in the discussion that benzene should not be used as a solvent. Then the question is what do you put in the conclusion.

DR. MARKS: If we do what you suggest, it was a draft tentative report, we could issue a tentative report with insufficient and out concern about benzene and let industry come back and provide sufficient information to declare it safe. That would be another tact, move forward with a formal insufficient report.

DR. SHANK: Could you go sufficient for a crosspolymer that is made without benzene and insufficient for a crosspolymer that is made with benzene?

DR. MARKS: That's another option.

DR. SHANK: Because if a lot of this product is made without benzene, it seems unfair to put it all into insufficient.

DR. BRESLAWEC: I think there's only one

polymer that we have data on.

DR. SHANK: We've never done that before, split it.

DR. BRESLAWEC: You're making a distinction on the method of manufacture rather than levels of something in the ingredients.

DR. MARKS: Ron, we've been struggling here. We've only gotten to the third ingredient. The first two we did not reopen, HC Red No. 1 and the glutaral. Where we're struggling with the crosslinked alkyl acrylates is the benzene impurity, benzene using a solvent. If we go on page 49, Ron pointed out that the actual calculation there in the next to the last paragraph should be 0.03 percent of benzene in cosmetic formulations. Is that correct, Ron?

DR. SHANK: Yes.

DR. HILL: Is that by the California numbers?

DR. MARKS: No.

DR. SHANK: It's based on industry data and it was calculated --

DR. HILL: Five times formula 6.

DR. SHANK: Right.

DR. HILL: There it is.

DR. MARKS: Ron further calculated that if we had the maximum concentration and we applied 1 gram of a cosmetic ingredient, all the benzene in this polymer was released and that would be equivalent of 300 micrograms. Did I recall that

correctly?

DR. SHANK: Correct.

DR. MARKS: Which is 30 times -- in the EPA and drinking 2 liters of water a day. So assuming all this benzene is absorbed or even a large portion of it, we've exceeded the EPA limits for exposure to benzene systemically. So we're struggling on in the one case trying to set a limit based on the EPA drinking water or the California Prop or going back to a 1987 report on toluene which in the discussion it was stated that toluene should be benzene free. So we're exploring the idea of having this document saying safe but in the discussion put benzene free. That gets into the issues that some of these products apparently are now made without benzene as a solvent. Should we go that strict and say benzene free or should we try and establish some sort of a limit and what is that limit going to be? Do we move forward by issuing a tentative report splitting out these product whether they have benzene or not benzene and safe for benzene free, obviously insufficient for benzene containing or just go to an insufficient tentative report?

So that's sort of where we were and we're struggling with how to present this tomorrow. Does that pretty much summarize where we are?

DR. SHANK: Yes.

MS. FIUME: As a suggestion, if somehow the discussion or the risk assessment can be written in giving industry the option to either bring in information or send information with a safe as used conclusion and then the comments came in, as long as it didn't become more restrictive, that wording in the discussion can change based on the industry comments and it could still go as a final report next time as long as it didn't change

the conclusion and the main point of the discussion. Not that that's a reason to do it one way or the other, but that is a consideration as you write the conclusion as to the next step of the report.

DR. MARKS: Tom and Ron, do you think there is a safe limit that benzene could be used or exposure? It seems like there is since the EPA has set a safe limit. So I guess, yes, you could put safe and then the challenge will be somehow crafting a way of setting that limit. What you're doing is helping facilitate so the next time if there are any changes you can move right on to a final. I'm not quite so sure that procedurally that's -- even though that's expeditious, I'm not sure it sends the right message that it's safe, but we really have concerns.

MS. FIUME: I was thinking is that we have items that are sensitizers. We don't set a limit. It's formulated so that they're not sensitizing, so if it was formulated so that the amount of benzene isn't above safe limits, because when I searched benzene using our SciFinder and you hit regulations, there are so many different numbers. There was page after page after page. So I think trying to find a specific number is going to be difficult.

DR. BRESLAWEC: You could specify in the discussion which standard and you could say to the EPA standard.

DR. SHANK: You can't formulated to be non- carcinogenic.

DR. MARKS: Here are some more complications. We don't get hell from the re-review. It doesn't mention benzene in the re-review Lillian tells us.

DR. SLAGA: We didn't re-review it did we?

DR. SHANK: Toluene.

DR. MARKS: Toluene.

DR. BRESLAWEC: There should have been probably two by now.

DR. MARKS: Which year is this?

MS. BECKER: This is 2005.

DR. MARKS: So it's the most recent one.

DR. SLAGA: We didn't re-review it. We didn't reopen it did we?

MS. BECKER: No.

DR. SLAGA: So that's the reason.

DR. SHANK: We agreed with the benzene free.

DR. MARKS: Right.

DR. SLAGA: I think we ought to use that. Don't you?

DR. MARKS: Obviously industry didn't have a problem with benzene free.

DR. HILL: Yes, but the catch to that there's no such thing as benzene-free toluene. What you're really dealing with is a detection limit issue and now with the mass specs available I think that would be way down there compared to whatever year that was sent. There's no such thing as benzene-free toluene.

DR. SLAGA: Approaching benzene free.

DR. BRESLAWEC: I actually think that it might be worth asking FDA whether FDA has a benzene limit.

MS. DEWAN: Not that I'm aware of as far as know.

DR. HILL: And these California standards are for ingestion. Right?

MS. FIUME: One is oral and one is inhaled.

DR. HILL: Inhalation and oral, but we don't have any dermal.

DR. MARKS: No, and one of the problems we have with that, Ron, is that when Ron Shank was calculating, he was using an EPA standard with a 10. With California Prop 65 the limit is 6.5 for oral exposure. So it's actually lower.

DR. HILL: 6.5.

DR. MARKS: Yes, 6.5.

DR. HILL: That's practically nothing. It's about the same.

DR. SLAGA: And we're assuming that it all gets absorbed.

DR. MARKS: I shouldn't have written this many notes over here because I still have to make a motion tomorrow and I'm not sure what motion I'm going to make.

DR. HILL: In the EU the raw material has to be.1 percent or less. Do I remember that

correctly?

DR. MARKS: Yes.

DR. BRESLAWEC: To me it seems as if you are lacking data to make a decision.

DR. MARKS: I wait.

MS. FIUME: Actually that's not raw material. It's mixtures I think so that it should be final product.

DR. MARKS: Right.

DR. HILL: In the final product makes your point. Is that right? I don't trust my memory.

MS. FIUME: A constituent of other substances or in mixtures. So that would be final product. Correct?

DR. HILL: My impression was it was in the raw material.

DR. LORETZ: That was my understanding as well.

DR. HILL: Again, lots of water has flowed under the bridge.

DR. MARKS: I don't know how that is calculating now.

DR. LORETZ: That sounds fine in the final product.

DR. HILL: The final product?

DR. LORETZ: No, I said that sounds fine in the final product.

DR. HILL: Yes.

MS. FIUME: Other directive. As a constituent of other substances or in mixtures in concentrations equal to or greater than 0.1 percent by weight.

DR. MARKS: That seems like a higher limit than micrograms of drinking water. Options? We can't take this. We've got to move it forward.

DR. SLAGA: No, we have to move it forward.

DR. MARKS: So the next is, and we've already had a draft, we had the insufficient data announcement, so we're into a tentative report and the options there are safe, insufficient, unsafe. We aren't at unsafe. That's for sure. So do we do safe and address the benzene impurity in the discussion? Or do we put insufficient and ask industry to help us reach a margin of safety?

DR. HILL: My impression is that if the EU sets the standard which again I interpret to be a raw material number, that it's possible to achieve that and that maybe people are formulating with a less-expensive grade, we've talked about and that maybe better grades either because it's not pulverized in benzene in the first place or because it's processed more to get rid of the benzene more thoroughly, then it's available to them. But I also realize whenever you say somebody has to reformulate a product that's a big deal.

DR. SLAGA: There are a number of products that don't use benzene as a solvent.

DR. HILL: That's what I'm saying. They use either hexane/ethyl acetate or something

unspecified.

DR. MARKS: We could do the safe and in the discussion mention that a number of products do not use benzene. The ones who use the benzene, the panel is concerned about its toxicity and then elaborate on that. Then if we can get a margin of safety in and have a suggested limit it would be good, but we could certainly reference the California Prop and the EPA. So that might be another way of handling it. I know that gets to what you said in terms of let's do safe and move forward, but that would be another way of handling it.

DR. SLAGA: We're discussing all the possibilities.

MS. FIUME: That's right, and there are at least four solvents that are available for that one ingredient which is the one trade name.

DR. MARKS: Tom, how do you want to proceed?

DR. SLAGA: I would go with that. I definitely don't want to table it.

DR. MARKS: No.

DR. SLAGA: And I'm just thinking what the other group would do. None of them would say it's safe too.

DR. MARKS: I think we'll find out tomorrow when I make our team's move and our team needs to feel comfortable with that. It is a little bit different knowing that we really feel it's safe when it's benzene free. That's the easiest way of looking at it.

DR. SLAGA: When benzene is not used as

a solvent.

DR. MARKS: Right.

DR. SHANK: I'm not at ease calling it safe if our calculations are that it can contain levels of benzene that have been found in excess of several regulatory bodies' standards. So I don't like saying it's safe alone unless it's qualified. Polymers made with solvents other than benzene are safe, and then in the discussion say why we say that. If you're going go safe I'd put in there for those polymers that are not made with benzene. That's not saying benzene free or anything.

DR. HILL: To me that seems overly restrictive given the fact, although I'm not thoroughly familiar with what happens to small, small amounts of benzene when it gets into the skin or an even smaller amount if it entered the nasopharyngeal region than was suggested, I would think those kinds of levels if we were within the European limits of.1 percent and then formulate it a maximum of 6 percent if we're going to put it way down in the levels of benzene, I wouldn't think anything systemic would be any problem. Are there any dermal carcinogenesis sorts of things that one needs to worry about with that small an amount of benzene?

DR. SLAGA: It's extremely weak activity.

DR. HILL: I used to wash my hands in it.

DR. SHANK: I don't think that's the problem. I think the problem is setting the concentration limit in personal care products.

DR. HILL: Right. I know. I get that.

DR. SHANK: Finding the number.

DR. HILL: We don't have the information that lets us do that.

DR. SHANK: That's correct.

DR. MARKS: So we could go forward with insufficient.

DR. HILL: Insufficient with anything with benzene in it?

DR. MARKS: Just insufficient. We keep coming back to saying either there is no benzene or there is a benzene limit and we have a problem with finding what the benzene limit is and determining that.

DR. LORETZ: You're not comfortable with splitting them into insufficient for the benzene and asking for further information and safe for the others?

DR. MARKS: We could say, yes, the conclusion could be safe and as we've done -- this would be the first we've had the same ingredient and said they're safe when they're done one way and insufficient in another way. We've done that for ingredients within groups where there are different ingredients, some are safe and some are insufficient.

DR. HILL: But I'm thinking why not?

DR. MARKS: Yes, that's an interesting -- precedent setting, but maybe that's the way it should be.

DR. SHANK: I favor that. Safe for rinse-off, safe for leave-ons when the polymer is

made with solvents other than benzene, insufficient for leave-on when the polymer is made with benzene.

DR. SLAGA: That could start a discussion tomorrow.

DR. SHANK: That will start a discussion.

DR. HILL: It sure will. Were there any concerns about the residual ester monomers at.5 percent when we're talking alkyl acrylates? I'm looking at page 3 at the bottom. Did anybody have any concerns related to those? I'm looking at Panel Book page 43, which is draft report page 3, talking about.5 percent residual ester in the C-10 and C-30 alkyl acrylates. So in formulation that would be again down in the.03 percent range or something like that, but we are talking alkyl acrylates.

DR. SHANK: I think our only concern was acrylic acid itself and the concentration is below our concern.

DR. HILL: Okay.

DR. SHANK: The larger ones were not our concern.

DR. HILL: I was thinking that the esters might be more problematic than the acids. I don't know that for a fact, but that was my sense is the esters could be thermally absorbed. I'm not sure how much the acid would penetrate past upper stratum corneum, but the esters might. I think defenses such as glutathione would take this out pretty effectively, but I wondered if anybody else even thought about that. And I'm guessing it was thought about -- it wasn't this that was the original review, but the other alkyl

acrylate polymers there was discussion of monomers. We don't have that report, but I at least glanced at it.

DR. MARKS: I'm going to summarize where I think we are, and Tom, Ron and Ron just be sure I'm on the same page with you. Tomorrow I'll move that we issue a tentative report on the crosslinked alkyl acrylates, that they're safe, but they're insufficient for leave-on products having benzene impurities.

DR. LORETZ: You don't want to say polymerized with benzene just for clarity?

DR. MARKS: No, I think benzene impurity.

DR. HILL: Yes, because in principle that's the only place it could come from, but it would be good either way.

DR. MARKS: Safe, however insufficient.

DR. HILL: I suppose it's polymerized in the other solvent, but then recrystallized with benzene and you'd have the possibility of getting the benzene active. I don't know anybody would do that, but then I've done a lot of crystallization in my life and sometimes --

DR. MARKS: Leave-ons having benzene impurities. That can be refined, but does that catch it?

DR. SHANK: Yes. That's okay. I can be wordsmithed.

DR. MARKS: Then the insufficient data is we need a margin-of-safe calculation with a limit and establish a limit so if industry came back and showed us a margin of safety with

establishing a limit for benzene impurity on a leave-on then we'd feel comfortable. Does that capture it? Do you think this is going to make an interesting discussion on the conclusion in this tentative report and then of course the discussion is going to go all around what we just talked about, the EPA limits, the California Prop 65, the European and all that and their concern that benzene is a carcinogen. Does that sound good?

DR. SHANK: I'm going to change my flight tomorrow.

DR. MARKS: We haven't even gotten to the formaldehydes.

DR. BRESLAWEC: Apparently the other group is still on formaldehydes.

DR. MARKS: Who knows? Maybe ours will go quicker. At any rate, are there any other discussions? Safe, however insufficient data for leave-ons having benzene impurities and that's how we're going to deal with the benzene impurity and deal with that the industry can help us with this. Ron Shank? Be prepared tomorrow. I'm going to say, Ron, would you make comments on this?

March 2011 – Full Panel

Going on to the next Green Book, and that's the acrylate crosspolymers, Dr. Marks presenting.

DR. MARKS: A scientific literature review for these cosmetic ingredients were issued in December of last year. Our team reviewed the available data. This is the first time we saw it, and we moved to issue a tentative report that these ingredients are safe as used in cosmetics.

DR. BERGFELD: Second or comments?

DR. BELSITO: Comment?
DR. BERGFELD: Yes, go ahead.
DR. BELSITO: We were struck on page 3 or Panel Book page 9 by the benzine impurities in carbachol 1342. The specifications state that it can contain 0.5 percent max of residual benzine. Monice was nice enough to pull a material safety data sheet on carbachol 1342, and it indicates that to -- it can be produced at 0.1 percent maximum as benzine -- as required by Canada, the EU, and Korea with no further information there. But this is only from one manufacturer. So, we had actually thought that we would like to go insufficient on these acrylate crosspolymers at this time to get clarification regarding the level of benzine. Dr. Bailey had indicated that that was perhaps an old manufacturing method that was no longer applicable to the current way that these cross-linked acrylate polymers are produced. But this is the first time we're seeing it. So, we would like to go insufficient for impurities, specifically benzine.
DR. BERGFELD: Tom?
DR. SLAGA: I agree that would be worthwhile doing.
DR. MARKS: I withdraw our team's motion. And we'll second the motion of Dr. Belsito's team.
DR. BERGFELD: To go insufficient? John Bailey?
DR. BAILEY: Why can't we go with Monice's find on the MSDS sheet, which was.01 percent, right?
DR. BELSITO: 0.1.
DR. BAILEY: 0.1.
MS. FIUME: For the EU. It didn't give for the U.S. For the U.S., the main impurity specification says.5 max with a footnote from EU, Canada, and Korea. So that.5 max is sort of hanging out there in the air, unless it's addressed in a different manner.

DR. BAILEY: But if the panel issues a tentative report that restricts benzine impurities to 0.1 percent, then it's not hanging in the air anymore.

DR. BELSITO: You know, we certainly could do that. I mean, the highest level of use is 6 percent in an eye care product. So that's the highest. So, I don't -- I'm not a benzine toxicologist, so I throw that out. So.1 percent benzine in the product, maximum use at 6 percent is -- does anyone perceive that that would be a problem?

If not, then hopefully we can get the data to support that and we can go ahead with the safe as used conclusion.

DR. BERGFELD: Ron Hill?

DR. HILL: Yes, I wanted to raise one more while we were on the subject of impurities On same page of the book, under impurities. The last sentence in the first section says the residual monomer content of acrylates, blah, blah, blah, blah, is typically less than 2,500 ppm acrylic acid and 500 ppm residual ester. So, it has the word "typically." And I had a note that I wrote here that said, we really need this information for all the acrylates because acrylate esters are not something we want to be having dermally absorbed in high concentrations, I think. And we didn't really have that.

So, from -- I wondered if anybody else had that same concern.

DR. MARKS: I thought we had addressed that. We were going to address it in a discussion, we didn't get to editorial comments. But the -- would be monomer impurities, and that they've been addressed in previous CIR reports.

DR. HILL: Okay, I think that's the way it was dealt with, yes. I just --

DR. MARKS: So that was going to be in the discussion. But if we still go back to how are we going to move forward, and the -- Don, you made the motion to insufficient. Do we want to

change that? Our team made a motion to safe. Do we want to do a safe with a limit of benzine?
DR. BELSITO: I think --
DR. BERGFELD: Either way, you have to withdraw the motion.
DR. BELSITO: I didn't make the motion.
DR. BERGFELD: Yes, you did. Insufficient was the motion. And Jim was seconding it.
DR. BELSITO: Okay.
DR. BERGFELD: No one seconded his --
DR. BELSITO: No, Dr. Marks' initial motion was safe as used.
DR. BERGFELD: Nobody seconded.
DR. BELSITO: Oh, okay. Someone seconded mine?
DR. MARKS: Yes, I did.
DR. BELSITO: Oh, good. Okay. (Laughter) Whoa, okay. So, again, I throw it -- it's not my area of expertise. I'm telling you that they -- in Europe, they can limit to 0.1. We don't have any information as to how they came up with that magic number, though the maximum concentration of use is limited here, 6 percent in eye products.
So those of you who know about benzine toxicity, if you're prepared to do the math today and sign off on it, I'm comfortable with it. In terms of skin sensitization, yadda, yadda, yadda, I'm comfortable. I can't comment on benzine toxicity at that level.
DR. SLAGA: Can't we --
DR. BERGFELD: Tom.
DR. SLAGA: -- look at the data, continue with this motion but get the European data -- the EU data and look at why they came up with.1?
I mean, first thought -- you know, 6 percent of.1 is very, very small and more likely

would have no carcinogenic or any other effect. But they probably already made the calculation. And why don't we just look at it?

DR. BELSITO: So, do you want to go safe as used when benzine impurity in the material is less than.1, or do you want to go insufficient --

DR. SLAGA: Insufficient until we get comparison --

DR. BELSITO: I'm fine --

DR. SLAGA: -- and see what kind of calculations they made.

DR. BELSITO: I'm fine either way. I think there are probably no safety issues, so delaying the final on this report -- I think, don't think --

DR. SLAGA: Right --

DR. BELSITO: -- it's going to be a big deal.

DR. BERGFELD: Ron Shank?

DR. SHANK: So, your motion is --

DR. BELSITO: Insufficient for impurities, specifically benzine.

DR. SHANK: -- insufficient for -- and what do you want? Is --

DR. BELSITO: I want to know what --

DR. SHANK: How much is in there or how much --

DR. BELSITO: How much is in there, and I want some benzine toxicity brought in. I want information as to why the Europeans decided to regulate it at.1. Where they got that information that allowed them to set that limit.

DR. SHANK: Okay.

DR. BERGFELD: Ron Hill, okay? Dan?

DR. LIEBLER: Yes, I like that approach.

DR. BERGFELD: Paul? Curt?

DR. KLAASSEN: Yes.

DR. BERGFELD: How about John Bailey?

DR. BAILEY: You know, I hate to continue this on for another meeting, but I think it's a reasonable request and we'll certainly do our best to get the information.

21 DR. BERGFELD: Thank you. So, we have a
22 motion. We had a second. Any other discussion?
1 Seeing none -- yes, Monice.
2 MS. FIUME: I just want to clarify. So
3 it's an insufficient data announcement --
4 DR. BELSITO: Right.
5 DR. BERGFELD: Call for the question.
6 All those in favor, raise your hands. Thank you,

March 2011- Belsito Team

he next one we're looking at would be acrylate
14 cross-polymers. Now, you were going to hand out a
15 hard copy of something that you had e-mailed to
16 us, is that correct, Monice?
17 MS. FIUME: Yeah. Table 1 was
18 corrected. There was a structure that was
19 missing, and there was a structure that was
20 incorrect. We've just redone the entire table.
21 You might --
22 DR. BELSITO: Sure.
1 MS. FIUME: And then also -- sorry.
2 DR. BELSITO: I looked at this.
3 MS. FIUME: I have about 16 of these.
4 Does anyone else need a copy? And then for you,
5 Dr. Belsito. I updated the data profile. The one
6 in the bag matched what came in with wave 2.
7 They're sort of hard to see, but the X is in red.
8 DR. BELSITO: Yes, yes.
9 MS. FIUME: Here's the updated
10 information for wave 2.
11 DR. BELSITO: Right, which is mainly all
12 dermal, and a --
13 MS. FIUME: Little bit monomer.
14 DR. BELSITO: -- little bit of monomer
15 content.
16 MS. FIUME: I only made one -- I have a
17 couple of copies if anyone else would like one.
18 DR. BELSITO: Okay. And when I looked
19 at the changes in table 1, they didn't really seem
20 -- I mean, it was just really more editorial

corrections than anything of substance. Is that a good, correct assumption?

MS. FIUME: Look at the -- the one structure was incorrect, and my structure was missing. But it was more substance. We were e-mailing it to Dr. Liebler electronically, so I wanted to make sure you were included.

DR. BELSITO: Oh, thank you. Okay, so the acrylate cross-polymers -- this is the first time we're looking at the report. We've previously looked at acrylate copolymers and found them to be safe as used when formulated to avoid skin irritation. The cross-polymers theoretically should be even safer, because they're going to be even larger molecules with less chance of penetration and less reactive monomer content, and the cross-polymers we're looking at probably number about 20. They're listed on page 1 of the book or page 7 of the Panel Book.

And beyond that, I really had no substantive comments. I was comfortable with the report. I thought it was very well put together. We got a whole wave of second data dealing with skin irritation and sensitization, and that was all negative. So, I really had no comments on this report. I love that little circular structure, the theoretical magnified view of the cross-linked --

MS. FIUME: (inaudible) having a chemist on (inaudible).

DR. LIEBLER: We did that.

DR. BELSITO: I don't have a clue how you would do that, but I thought it was phenomenal.

DR. LIEBLER: Yeah, I wanted to also second that, because I think that was a very effective way to portray the chemical nature of these above and beyond just the structure that would be on the table, and it worked very nicely also in the silylates report as well. So, this is a nice innovation. It really helps to bring the chemistry to the non-chemist audience I think

19 better, so nice idea.
20 DR. SNYDER: Can I add one question on
21 the impurities on page 3?
22 DR. KLAASSEN: Yes, the benzene?
1 DR. SNYDER: Yeah, the benzene. So, we
2 recognize that a product can -- one product does
3 have residual benzene, and we do have leave-on in
4 the baby/infant use, so is that an issue?
5 DR. BELSITO: Where are you, Paul, on --
6 DR. SNYDER: Carbopol 1342, the product
7 specification states that the acrylates C10 to C30
8 -- acrylate cross-polymer continue --
9 DR. BELSITO: 0.5 percent max.
10 MR. SNYDER: Okay.
11 MS. FIUME: And the baby product is.2
12 percent use.
13 DR. BELSITO: Okay.
14 MS. FIUME: In that entire product,
15 leave-on is.0002 to 5 percent. But the baby
16 product is.2.
17 DR. BELSITO: Okay.
18 DR. SNYDER: All right.
19 DR. BELSITO: Is that okay?
20 DR. SNYDER: Yeah, I mean, I just wanted
21 to point it out and make sure that we considered
22 it. I mean, is there anything in the manufacture
1 that other ones would contain higher levels than
2 that?
3 MS. FIUME: I haven't included anything
4 that I either found through industry or MSDS that
5 had residual levels, and that's why I broke it out
6 by trade name, because they did have different
7 amounts. Even though it was the same ingredient,
8 the trade names did have different specifications.
9 DR. KLAASSEN: Well, where did you find
10 this up to 5 percent?
11 DR. BELSITO: 0.5.
12 DR. KLAASSEN: Did you say 5 percent
13 someplace else?
14 MS. FIUME: Oh, the max leave-on use is
15 percent.
16 DR. KLAASSEN: Oh, the max leave-on use,

17 okay, not the amount of benzene.
18 DR. BELSITO: No. Well, is this
19 something that we need to put into the discussion?
20 DR. SNYDER: I think so.
21 DR. KLAASSEN: Yes.
22 DR. SNYDER: I think so.
1 DR. KLAASSEN: Yes, I noted it also.
2 DR. BELSITO: And how would you address
3 that?
4 DR. SNYDER: That we noted it in the
5 method of manufacture that benzene can be an
6 impurity in that process based on the information
7 that we have that it's at a low level in the
8 product and at the low exposure rates that is not
9 a concern, I guess, or something along that line
10 saying --
11 DR. BELSITO: Well, how specific do you
12 want to be about not a concern? I mean, so we're
13 saying -- are we saying it shouldn't contain more
14 than 0.5 crystal benzene?
15 DR. SNYDER: Well, I actually queried to
16 say should we limit the amount of benzene. I
17 don't know what we've done in -- with been benzene
18 in other reports, because I have that tagged as
19 have we limited benzene in other --
20 DR. BELSITO: I don't remember ever
21 specifically discussing a limit on benzene. I
22 don't.
1 MS. FIUME: Yeah, I can't recall off the
2 top of my head.
3 DR. SNYDER: I don't recall it either.
4 I'm checking the report on sodium
5 dodecylbenzenesulfonate to see if we did anything.
6 You know, up above there it said that when they
7 make these cross-polymers, they can make them in
8 apple acetate cycle hexane mixture or may also be
9 polymerized in benzene. So, some of them might
10 not have any.
11 DR. ANDERSEN: When I think a question
12 that while wouldn't specifically be directed but
13 the producer of the material should be aware that
14 the question has come up, and while 0.5 percent

may be the maximum, what's the normal expected level, and if that is what I would think would be significantly lower than that they just put a max to cover the possibility, then that gives some more information.

DR. BELSITO: Well, I guess, you know, if we're going to -- I mean, we obviously -- the issue is raised. We obviously feel it needs to go in the discussion. I think from my point of view, and again this is not my area of expertise -- benzene toxicity applied to the skin. If we're going to say that it shouldn't contain more than 0.5 percent, it would seem to me that we would have to have a rationale as to why it couldn't, why we're limiting it at 0.5, because maybe it could be 1 percent, you know? Maybe it could be 2.5.

So, I guess the question becomes we're obviously concerned that at some point benzene could be an issue. But what's that point, and since we can either table it to get to that point, give a specific -- and that's not going to happen -- or if we say, you know, safe as used in the current yadda, yadda, yadda, does that mean that the assumption is it won't contain more than 0.5 percent benzene max? I mean, we don't have all of the manufacturers here.

MS. FIUME: I found what I could find on the internet.

DR. BELSITO: Right.

DR. ANDERSEN: Yeah. Perhaps we could provide some additional clarification on this. This is a report from 15 years ago. Benzene is an industrial solvent for purposes of polymerization and is, you know, somewhat old style, so let us see if we can provide some guidance. But we were also aware of the report that they have established a maximum for this particular grade of 0.5 percent, but that seems like a lot.

DR. KLAASSEN: Yeah, it might not even be used anymore.

DR. BELSITO: Okay, so then looking at

these acrylate cross-polymers, I mean, essentially safe as used but we need to deal with this benzene in some fashion, and so do we table it to hear back from industry about current methods of manufacture? Does a "safe as used" -- does that mean that we're assuming there would be no more than 0.5 percent benzene? Because if we start getting into specifics in the discussion about that, then I think we need to justify why we put that limit, and we don't have the data to do that

DR. SNYDER: Well, benzene is not an insignificant toxicant.

DR. BELSITO: Right.

DR. SNYDER: I mean it's -- and so -- I mean, I think that we have information that it is an impurity, and in one product it can -- you know, they say it maxes at.05 percent. But, again, we also have --

DR. BELSITO: 0.5.

DR. SNYDER: 0.5 percent. And we also have information, though, that it is used in a polymerization, or has been historically used in a polymerization. So, I think this --

DR. BELSITO: Then maybe we should table it and hear what industry has to say about current methods of manufacture? I mean, because that's -- I mean, basically if there's no benzene or if every product on the market is less than 0.5 percent, we're comfortable going ahead with "safe as is," is that correct?

DR. SNYDER: Correct.

DR. KLAASSEN: Right.

DR. BELSITO: But right now we don't know that. We have one company saying their max is 0.5, but we don't know who the manufacturers are, and we're not prepared to do a risk assessment on benzene.

DR. KLAASSEN: I suggest we wait for this information.

DR. SNYDER: I concur.

DR. ANDERSEN: There's two ways of waiting -- passively waiting and aggressively

waiting. (Laughter) The aggressive stance would be to issue an insufficient data announcement to -- for clarification of benzene levels in these products period. We just -- that's what you need to know.

DR. BELSITO: I'm an aggressive guy. Let's go with that if you're comfortable. I mean, insufficient, further information on levels of benzene.

DR. ANDERSEN: I mean, it's -- you would expect that you will get a response. So, it's not like it's sending it to insufficient limbo, and once you have the information, you can easily issue the safety assessment as a tentative the next time we meet.

DR. KLAASSEN: Fine.

DR. BELSITO: I like that better than tabling, yeah. Puts a time limit on it. Okay, good.

So, then, Dan, you comfortable with that?

DR. LIEBLER: Yeah, I am.

DR. BELSITO: We're going to go insufficient, further information about levels of benzene and the acrylate cross-polymers. Otherwise, once we get that if the information is less than.5 percent, we'll go ahead with the safe as used.

DR. SNYDER: I have another question. So, the inhalation data. So, we go through our respiratory boilerplate, and I quite didn't know how to correlate with -- we have known industrial exposure limits. So, it is respirable, and so how does -- it comes up in another report, too, where we actually have inhalation data where they actually dosed animals and it was -- it did have an effect. And so the use of the boilerplate usually says "in the absence of data," but could -- we have data that says it is respirable -- I'm kind of conflicted there as to what does that -- how are we dealing with that or --

DR. ANDERSEN: I think, Paul, the issue

of respirable/not respirable really relates more to the class of products called cosmetics. As aerosols are produced in the cosmetics industry, they are not blockbuster particles but they're bigger than what's respirable in general, and we simply capture that. I don't have any question that the technology exists to make smaller particles, which would be respirable, but you aren't going to find it in cosmetics. And so there's been limits established for respiratory levels, and that's fine. They wouldn't have been needed for cosmetics.

DR. BELSITO: Okay.

DR. SNYDER: I have one editorial suggestion on report page 2 right under the virtual -- well, virtual molecule structure. It says, "Due to the multitude of possible reaction conditions" -- this is under chemistry and structure, a definition and structure -- "Due to multitude of possible reaction conditions and methods, the properties of a single ingredient" blah-blah-blah. And then the sentence -- two sentences after that, "Nonetheless, the polymers in this group share the same lack of chemical activity." These are really discussions of properties. So, they should be moved down under "Physical and Chemical Properties." And I actually reworded the sentence about the polymers having a lack of chemical reactivity to read, "The polymers in this group share a general lack of chemical reactivity that renders them nearly impervious to degradation." So, this is very clearly outlined in my annotated version.

DR. BELSITO: Anything else?

DR. ANDERSEN: No.

DR. BELSITO: Okay, so we're going "Insufficient, for further information" on the benzene content, residual benzene content.

March 2011 – Marks Team

DR. MARKS: "After penetration" --
delete. Okay. Acrylate Cross Polymers.
Let's go to acrylate cross polymers,
Green Book, titled "Crosslinked Alkyl Acrylates."
And then we got another electronic transmission of
changes in the Table 1, "Definitions, Functions,
Structures."
This is the first time we've seen this
report, the first time for us to review these
cosmetic ingredients. So we have the draft report
in front of us.
And I'll ask the old team, Tom and Ron,
are there any needs from your vantage point? And,
also -- I think I have that.
MS. FIUME: Okay.
DR. MARKS: I printed it out. Thanks.
MS. FIUME: I will give you this. This
is just the updated data profile. The red is what
was new.
DR. MARKS: Oh, okay. Thank you.
DR. SHANK: I have no data needs.
DR. SLAGA: Same here. It's a very
stable -- probably even more so than the original
document on just the (inaudible).
DR. MARKS: So we would issue a
tentative report "safe?"
DR. SLAGA: Yep.
DR. SHANK: Right.
DR. MARKS: I saw no issues. And --
okay. Safe. Shall we move on without Ron Hill
being here?
DR. SHANK: (Inaudible).
DR. MARKS: Yes, I agree. This would
actually be good armor in warfare?
DR. SHANK: Yes -- oh.
DR. MARKS: So one thing I highlighted
on page 74, it is used in baby products. There's
no -- again, it doesn't raise any issues from that
point of view. It's used in baby lotions, oils,
powders and creams. That -- still -- safe.

DR. SHANK: Well, I think in the "Discussion," we should have discussion that the monomers could be impurities, but the monomers have already been reviewed by the panel? And we should wait for Dr. Hill?

DR. MARKS: Yes -- will do. They've already been addressed in previous CIR reports. And, obviously, they were addressed as being safe, or else we would be concerned about the monomers' being present.

DR. SHANK: Well, the maximum use-concentration --

DR. MARKS: Right.

DR. SHANK: -- for the polymers is (inaudible). So the un-reacted monomer's going to be small.

DR. MARKS: Right. So, Ron, we've already decided that we have enough data, and we can issue a tentative report with a "safe" conclusion. And this is for the crosslinked --

DR. HILL: Yes.

DR. MARKS: -- alkyl acrylates. But we didn't want to finalize that until we got your input. We didn't want you to be surprised tomorrow when I moved to make this --

DR. HILL: No, I think that's where I came to. I'm just trying to remember if there were any --

DR. MARKS: Monomer impurities are addressed in previous -- so that would be in the discussion. Yes.

DR. HILL: I think most of my things in here were all editorial. So --

DR. MARKS: Okay.

DR. BERGFELD: May I ask a question? Some of the special tox studies were not here. If you're using the monomer studies, is that adequate? The genotox, the reproductive? You know, there's nothing on this group, crosslinked acrylates.

DR. SHANK: These won't be absorbed.

DR. BERGFELD: So they won't be

absorbed. So that's -- you don't need that.
So you'll put that in the discussion, as
well?
DR. MARKS: Yes.
DR. BERGFELD: Okay. So they've very
big.
DR. HILL: Who was the report writer
here?
MS. FIUME: I am.
DR. HILL: Okay. Yes, I have quite a
bit of -- it falls in the category of editorial
things. But in the structures table, and --
MS. FIUME: Oh, I just gave you a new
structures table --
DR. HILL: You gave me a new --
MS. FIUME: -- that has a corrected
structure, and one that was missing.
DR. HILL: Well, there are quite a few
places where I made notations concerning the
structures. And it doesn't affect anything in
terms of conclusion. And it's probably, in many
cases, traceable to dictionary errors. But -- so
--
DR. MARKS: Okay. So tomorrow I'll move
to issue a tentative report with a "safe as used"
conclusion. And the discussion will say that
these ingredients are not absorbed, hence the lack
of some of the data points needed. And that the
monomer impurities have been addressed in previous
CIR reports.
DR. HILL: The only other question I had
was will Table 5 -- it is intended that Table 5
will be maintained in the final report? I'm
hoping yes.
MS. FIUME: Yes, Table 5 will replace
that "Dermal Irritation and Sensitization" -- the
text will be replaced by Table 5.
DR. HILL: Okay. But Table 5 is planned
for the final report?
MS. FIUME: Yes.
DR. HILL: Yes? Great.

POLYMETHYL METHACRYLATE (PMMA) REPORT

June 28-29, 2010

The CIR Expert Panel utilized data from FDA approvals of PMMA medical devices including: intraocular lenses (IOLs), bone cement, dental fillers, and dermal fillers. Available data on PMMA used in cosmetics demonstrated the equivalence to that used in devices. The Panel deleted Sodium polymethacrylate from the report because it is not a methyl methacrylate polymer.

The CIR Expert Panel concluded that these three ingredients are safe in the practices of use and concentration as given in the safety assessment.

April 5-6, 2010

A new approach was used in the assessment of the safety of PMMA. PMMA is used in several implanted medical devices that have been approved by the Food and Drug Administration (FDA) including: intraocular lenses (IOLs), bone cement, dental fillers, and dermal fillers. Because FDA has examined these devices for safety far beyond the risks posed by use in cosmetic applications, the CIR Expert Panel concluded that FDA's approval is sufficient for a conclusion of safety for cosmetic uses.

The CIR Expert Panel had sought better characterizations of the PMMA used in cosmetics. These data were received and were consistent with those data available that characterized the PMMA approved by FDA (the data on which was a primary basis for this safety assessment). The Panel asked that additional information about the characterization of the PMMA material as used in devices be included.

The CIR Expert Panel concluded that these ingredients are safe in the practices of use and concentration as given in the safety assessment.

December 7-8, 2009

The CIR Expert Panel agreed that the approach taken by CIR to evaluate these ingredients was acceptable, but determined that certain additional data are needed. Additional data needs include evaluation of:

- Level of monomer in methyl methacrylate/glycol dimethacrylate crosspolymer

In addition, CIR staff will gather relevant data on methyl methacrylate sensitization for incorporation into the draft report.

CARBOMERS

Original minutes were not available.

Amended Safety Assessment of Acrylates Copolymers as Used in Cosmetics

Status:	Draft Final Amended Report for Panel Review
Release Date:	November 9, 2018
Panel Meeting Date:	December 3-4, 2018

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The 2018 Cosmetic Ingredient Review Expert Panel members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Ronald A. Hill, Ph.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; James G. Marks, Jr., M.D., Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The CIR Executive Director is Bart Heldreth, Ph.D. This safety assessment was prepared by Monice M. Fiume, Senior Director.

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ABSTRACT

The Cosmetic Ingredient Review (CIR) Expert Panel (Panel) assessed the safety of 126 acrylates copolymers; 56 of these ingredients were previously reviewed by the Panel, and 70 are reviewed herein for the first time. Many of these ingredients are reported to have several functions in cosmetics, with the function of film former being the most commonly reported cosmetic function for members of this family; many of the ingredients also may function in cosmetics as viscosity increasing agents. The Panel reviewed relevant new data, including frequency and concentration of use, and considered the data from previous CIR reports. The Panel concluded the 126 acrylates copolymers named in this report are safe in cosmetics in the present practices of use and concentration described in the safety assessment when formulated to be non-irritating.

INTRODUCTION

CIR published the Final Report on the Safety Assessment of Acrylates Copolymer and 33 Related Cosmetic Ingredients in 2002.[1] Based on the available data, the Panel concluded that the acrylates copolymers named in that report are safe for use in cosmetics when formulated to avoid irritation.

According to its Procedures, the CIR evaluates the conclusions of previously-issued reports every 15 years. As part of the re-review process, in addition to reassessing the existing conclusion, CIR also determines whether other ingredients are appropriate for inclusion in the re-review document. The Panel determined that it is appropriate to include all the copolymers (including crosslinked copolymers (i.e., crosspolymers)) prepared from monomers that comprise, in part, acrylic acid and/or methacrylic acid; the methyl, ethyl, propyl, or butyl ester(s) of these acids; or the salts of one or both of these two acids, with a few exceptions, as described below. Based on this rationale, the 126 ingredients described below, and listed in Table 1, are included in this re-review.

Some of the ingredients deemed appropriate for inclusion have previously been reviewed by CIR in other assessments. In 2017, the Panel published a safety assessment with the conclusion that 23 crosslinked alkyl acrylates included in the safety assessment are safe in the present practices of use and concentration, except when polymerized in benzene; Acrylates C10-30 Alkyl Acrylate Crosspolymer may be polymerized in benzene, and the available data were insufficient to make a determination of safety for this ingredient when polymerized in benzene.[2] Because the data were insufficient for Acrylates C10-30 Alkyl Acrylate Crosspolymer polymerized in benzene, this assessment will only review the safety of Acrylates C10-30 Alkyl Acrylate Crosspolymer in solvents other than benzene.

In 2011, the Panel published a safety assessment of Polymethyl Methacrylate (PMMA), Methyl Methacrylate Crosspolymer, and Methyl Methacrylate/Glycol Dimethacrylate Crosspolymer, and concluded that these ingredients are safe in the practices of use and concentration that were described in the report.[3] The Food and Drug Administration (FDA) had made a determination of safety of PMMA use in several medical devices, which included human and animal safety data. The Panel used that information as the basis of safety of PMMA and related polymers as used in cosmetics.

Another report on similar ingredients is the 1982 CIR Final Report on the Safety Assessment of Carbomers-934, -910, -934P, 940, -941, and -962; the Panel concluded that these ingredients are safe in the present practices of use and concentration that were described in that report.[4] These ingredient names no longer exist as INCI names. Instead, they are now identified in the web-based *International Cosmetic Ingredient Dictionary and Handbook* (wINCI; *Dictionary*) as technical names for one ingredient, Carbomer.[5] In 2003, the Panel reaffirmed that Carbomer is safe as used.[6]

In addition to the ingredients that have been previously reviewed by the Panel, an additional 70 acrylates copolymers that have not yet been reviewed are named in the *Dictionary*.[5] These ingredients are also included in this safety assessment.

The Panel determined that it was appropriate to exclude five ingredients that were part of the initial safety assessment on the Acrylates Copolymers in this re-review because they are either already part of a recent or a concurrent safety assessment. Sodium Styrene/Acrylates Copolymer and Styrene/Acrylates Copolymer were reviewed in 2014 (and found safe as used in cosmetics),[7] and the safety of Acrylates/VP Copolymer, Vinyl Caprolactam/VP/Dimethylaminoethyl Methacrylate Copolymer, and VP/Dimethyl-aminoethylmethacrylate Copolymer are part of the concurrent safety assessment of Vinylpyrrolidone Polymers.

According to the *Dictionary*, the ingredients included in this report have an array of functions in cosmetics, with the function of film former being the most commonly reported cosmetic function for members of this family (Table 2).[5] Many of the ingredients also may function in cosmetics as viscosity increasing agents.

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

Excerpts from the summaries of previous reports on Acrylates Copolymer and related ingredients, and all other previously-reviewed ingredients, are disseminated throughout the text of this re-review document, as appropriate, and are identified by *italicized text*. (This information is not included in the tables or the summary section.) Additionally, the Discussions from these reports are also included in this document. For complete and detailed information, please refer to the original documents, which are available on the CIR website (https://www.cir-safety.org/ingredients). Please note that information on the monomers is found in several of the original reports, but not in this document.

Much of the new data included in this safety assessment was published by Australia's National Industrial Chemicals Notification and Assessment Scheme (NICNAS).[8-14] Please note that NICNAS provides summaries of information generated by industry, and it is that summary data that are brought into this safety assessment when NICNAS is cited.

CHEMISTRY

Definition and Structure

The definitions and structures of the ingredients included in this report are provided in Table 2.

Copolymers are polymers synthesized from two or more different monomers, and crosspolymers are copolymers that are crosslinked (i.e., individual polymer chains are connected by bridging molecules [crosslinking agents]).[2] As stated in the Introduction, this report comprises a large number of copolymers and crosspolymers, most of which are prepared from monomers that include, in part, acrylic acid and/or methacrylic acid; the methyl, ethyl, propyl, or butyl ester(s) of these acids; or the salts of one or both of these two acids (Figure 1).

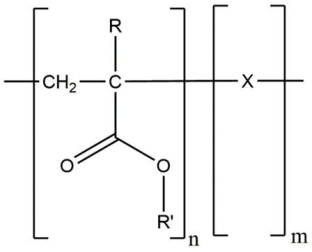


Figure 1. Acrylates copolymers, wherein R is hydrogen or methyl; R' is hydrogen, methyl, ethyl, propyl, butyl, or a salt cation (e.g., sodium); and X is one or more co-monomer residues.

However, a few of these ingredients are the polymerization products of monomers that comprise acrylate esters that are not methyl, ethyl, propyl, or butyl; but instead, these esters are the products of different alkoxyl or polyalkoxyl groups (Figure 1). Also, these other ingredients are all essentially homopolymers.

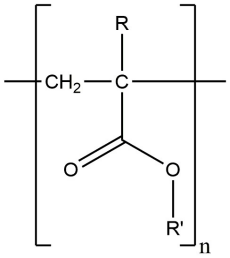


Figure 2. Other polyacrylates, wherein R is hydrogen or methyl; and R' is alkoxyl or polyalkoxyl (e.g., PEG-23).

Physical and Chemical Properties

From the Safety Assessment of Crosslinked Alkyl Acrylates[2]

Crosslinked polymers are generally less chemically reactive and less soluble (if not totally insoluble) than their respective non-crosslinked counterparts. Because of the manner in which these polymers are created and the mixture of monomers and cross-linking agents that can be used, 2 polymers that have the same INCI name can have very different physical consistencies.

Physical and chemical properties of several acrylates copolymers are described in Table 3. Primarily, physical form is identified therein.

Methods of Manufacture

From the Original Safety Assessment of Acrylates Copolymers[1]

Linear polymers of acrylic acid are produced by combining the monomer with a free-radical initiator, which is generally largely consumed by the reaction. The size of the polymer is determined by controlling the environment in which the polymerization occurs. Polymers of acrylic acid are characterized by their average molecular weight, but many species of greater and lesser molecular weight are present and unreacted monomer and catalysts can also be present. Additionally, hydroquinone and monomethyl ester of hydroquinone are often incorporated into acrylic acid and its esters as an inhibitor.[1]

Specific method of manufacture information for several ingredients is found in the original report.

From the Safety Assessment of Crosslinked Alkyl Acrylates[2]

Cross-linked alkyl acrylates are typically produced via free radical, head-to tail chain propagation polymerization. Ethyl acetate + cyclohexane, water, n-hexane, and benzene are all named as solvents.

From the Safety Assessment of PMMA and related ingredients[3]

The manufacturing process for PMMA beads used in medical devices and in cosmetic products is the same. The only difference is the size of the PMMA spheres, which are provided according to the specifications of the purchaser. Polymethyl methacrylate beads or powders in cosmetics are precipitated out from a polymerization reaction. The average bead size can be controlled within the 4 to 50 µm specifications. In nail products, polymer powders are made from methyl or ethyl methacrylate or their copolymers. [Please note: these types of beads are being phased out in many jurisdictions, including the US.]

From the Safety Assessment of [Carbomer][4]

Carbomer is manufactured by reflux polymerization of acrylic acid in an inert solvent in the presence of a catalyst. In doing this, a closed system, free of oxygen and water, is used.

Acrylates Copolymer

Acrylates Copolymer, as a fully polymerized copolymer of methyl methacrylate and ethyl acrylate, with a quantitative composition described as poly(ethyl acrylate-co-methyl methacrylate) 2:1, is produced by emulsion polymerization.[15] A redox-initiated polymerization of the monomers ethyl acrylate and methyl methacrylate occurs through the use of a free radical donor redox initiator system. Polyethylene glycol monostearyl ether is used as an emulsifier in the process, and an alkyl mercaptan is used as a chain modifying agent. At the end of the process, an emulsifier is added to reduce foaming. Residual monomers and excess water are removed by water vapor distillation, and the pH of the reaction mixture is adjusted with sodium hydroxide.

A similar emulsion polymerization process is used to synthesize Acrylates Copolymer as a fully polymerized copolymer of methyl acrylate, methyl methacrylate, and methacrylic acid, with a quantitative composition described as poly(methyl acrylate-co-methyl methacrylate-co-methacrylic acid) 7:3:1 in an aqueous (aq.) medium.[16] Polymerization is by means of a free radical initiator. Sodium lauryl sulfate (SLS) and polysorbate 80 are used as emulsifiers, and an alkyl mercaptan is used as a chain-modifying agent. Small amounts of dimethicone (polydimethyl siloxane) are added to reduce foam formation. Water vapor distillation removes the residual monomers to a level of less than 100 mg/kg total. After the reaction product is cooled and filtered, the dry substance content is approximately 30%.

Composition/Impurities

From the Original Safety Assessment of Acrylates Copolymers[1]

Linear polymers of acrylic acid may contain unreacted starting material and catalysts. Ten companies representing the majority of the production of polymers sold for cosmetic use indicated that residual acrylic acid concentrations in polymers are typically between 10 and 1000 ppm, with an upper limit of 1500 ppm.

One source reported Acrylates Copolymer can contain residual amounts of ≤ 20 ppm ethyl acrylate, methyl methacrylate, methacrylic acid, and acrylic acid; another source reported that three samples analyzed using gas chromatography (GC) contained < 0.2 to 0.8 ppm acrylic acid, 0.8 to 2.6 ppm methyl methacrylate, and 1.3 to 3.9 ppm ethylene glycol dimethacrylate. Additionally, it was reported to CIR that two polymers, both defined as Acrylates Copolymer, contained different residual monomers; the first contained 36, 20, and 45 ppm n-butyl acrylate, methyl methacrylate, and methacrylic acid, respectively, and the second contained 1500 and 200 ppm stearyl acrylate and methacrylic acid, respectively. Acrylates/VA Copolymer can contain, as reported by two polymer producers, 100 to 1000 ppm residual 2-ethylhexyl acrylate. However, the 10 respondents of the survey described previously reported that they did not produce acrylate polymers with 2-ethylhexyl acrylate for use in the cosmetic industry. Using UV spectroscopy with a limit of detection of 300 mg/kg (ppm), acrylic acid was detected in Polyacrylic Acid at 195 nm. A 90,000-Da molecular weight sodium hydroxide-neutralized Polyacrylic Acid contained 77.5% Sodium Polyacrylate, 3.3% free acrylic acid, and 18.1% water, whereas a 4500-Da molecular weight compound contained 43.3% solids and 0.09% residual monomer.

From the Safety Assessment of Crosslinked Alkyl Acrylates[2]

Small amounts of residual monomer and/or solvent may be present in the crosspolymers.

From the Safety Assessment of PMMA and related ingredients[3]

The impurity of concern in PMMA is the monomer, methyl methacrylate (MMA). Analysis of PMMA beads used in cosmetic formulations found MMA to be present at < 100 ppm. The Nail Manufacturers Council reported that the residual monomer is typically < 1.5%; averages of 0.7% and 1.2% have been reported. Residual MMA in Methyl Methacrylate Crosspolymer is similar to that found in PMMA, i.e., < 100 ppm.

From the Safety Assessment of [Carbomer][4,6]

Reported impurities for the Carbomer resins include water, benzene, propionic acid, acetic acid, acrylic acid, heavy metals, iron, arsenic, and lead. The Panel calls attention to the presence of benzene as an impurity in Carbomer and recommends that every effort be made to reduce it to the lowest possible value. However, when the safety of Carbomer was reassessed in 2003, the Panel acknowledged the industry practice of removing benzene from Carbomer.

Acrylates Copolymer

Specifications for Acrylates Copolymer (as a fully polymerized copolymer of methyl methacrylate and ethyl acrylate) state that it contains < 100 mg/kg total monomer (sum of methyl methacrylate and ethyl acrylate); 0.7% residual emulsifier (polyethylene glycol monostearyl ether); < 0.5% ethanol; and < 0.1% methanol.[17] Additionally, limits on heavy metals are: < 2 mg/kg arsenic; < 2 mg/kg lead; < 2 mg/kg mercury; < 10 mg/kg zinc; and < 10 mg/kg copper.

Approximately 0.3% SLS and 1.2% polysorbate 80, both w/w based on the solid substance, are residual in the polymer as a result of the emulsion polymerization process used to synthesize Acrylates Copolymer as a fully polymerized copolymer of methyl acrylate, methyl methacrylate, and methacrylic acid.[16]

Acrylates/Steareth-20 Methacrylate Copolymer

Acrylates/Steareth-20 Methacrylate Copolymer contains < 100 ppm residual monomer.[18]

Polyacrylate-1 Crosspolymer

Polyacrylate-1 Crosspolymer is reported to be 99% pure.[12] (No other details were available.)

VA/Butyl Maleate/Isobornyl Acrylate Copolymer

A copolymer of vinyl acetate, butyl maleate and isobornyl acrylate in ethanol is reported to be at least 95.3% pure.[8] Impurities are reported as < 0.4% acetone dimethylformaldehyde; < 0.1% vinyl acetate; < 0.1% monobutyl maleate; and < 0.1% isobornyl acrylate. The maximum percentage of low molecular weight species (molecular weight < 1000) is < 2%.

USE

Cosmetic

The safety of the cosmetic ingredients addressed in this report is evaluated based on data received from the US FDA and the cosmetics industry on the expected use of these ingredients in cosmetics. Use frequencies of individual ingredients in cosmetics are collected from manufacturers and reported by cosmetic product category in FDA's Voluntary Cosmetic Registration Program (VCRP) database. Use concentration data are submitted by the cosmetic industry in response to a survey, conducted by the Personal Care Products Council (Council), of maximum reported use concentrations by product category.

According to information received in 2018 from the VCRP and the Council survey, 66 of the 126 ingredients assessed in this report are in use.[19-24] Carbomer has the highest frequency of use; according to 2018 VCRP data, it is used in 6434 cosmetic formulations (with 6175 uses under the name Carbomer and 259 uses listed under various tradenames), and most of these uses (5336) are in leave-on products (Table 4).[24] Acrylates Copolymer and Acrylate/C10-30 Alkyl Acrylate Crosspolymer (solvent not specified) have the next highest frequencies of use, with 3177 and 3135 reported uses, respectively. Many of the other in-use acrylates copolymers have hundreds of use, although some have just a few.

The results of concentration of use surveys conducted by the Council in 2018 indicate that Acrylates Copolymer has the highest maximum use concentration; it is used at up to 98.6% in nail extenders; use in product categories other than nail products is not as high, but Acrylates Copolymer is used at up to 25% in products that result in dermal contact (face and neck products).[19] Ingredients with the next highest reported concentrations of use are Acrylates/VA Copolymer (at 50%, in "other" skin care formulations)[19] and Polymethyl Methacrylate (at up to 44.6%, in face powders).[23]

Numerous ingredients named in this report have been reviewed previously by the Panel. For many of the previously-reviewed ingredients, the frequency of use has increased since the time of the original review, with some increases being quite significant. For example, the frequency of use of Acrylates Copolymer increased from 227 uses in 1998[1] to 3177 uses in 2018,[24] and the frequency of use of Carbomer increased from 1504 uses in 2001[6] to 6434 uses in 2018.[24] Concentrations of use were not reported by the FDA at the time of the original assessment of Acrylates Copolymer and related ingredients, so it is not known if the concentrations of use have changed for those ingredients. For the other previously-reviewed ingredients, there were no notable increases in concentrations of use.

In some cases, reports of uses were received from the FDA VCRP, but no concentration of use data were provided. For example, Potassium Carbomer is reported to be used in 73 formulations, but no use concentration data were submitted in response to the Council survey. In several other cases, no uses were reported to the VCRP, but a maximum use concentration was provided by industry. It should be presumed that for those ingredients, there is at least one use in each category for which a concentration was reported.

Many of the acrylates copolymers are used in products that can be used near the eye (e.g., 30% Acrylates/Ethylhexyl Acrylate Copolymer in mascara),[20] or are used in products that could result in incidental ingestion (e.g., 16.1% Polymethyl Methacrylate in lipstick formulations).[23] Additionally, some of these ingredients are used in cosmetic sprays and could possibly be inhaled; for example, VA/Butyl Maleate/Isobornyl Acrylate Copolymer is reported to be used at a maximum concentration of 10% in aerosol hair sprays). In practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters > 10 µm, with propellant sprays yielding a greater fraction of droplets/particles < 10 µm compared with pump sprays.[25,26] Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and thoracic regions of the respiratory tract and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.[27,28]

Sodium Polyacrylate has reported use in an aerosol deodorant at a concentration of 2.9%.[19] There is some evidence indicating that deodorant spray products can release substantially larger fractions of particulates having aerodynamic equivalent diameters in the range considered to be respirable.[28] However, the information is not sufficient to determine whether significantly greater lung exposures result from the use of deodorant sprays, compared to other cosmetic sprays. Additionally, some of the acrylates copolymers are reportedly used in loose powders; for example, Polymethyl Methacrylate is used at concentrations up to 44.6% in face powders,[23] and could possibly be inhaled. Conservative estimates of inhalation exposures to respirable particles during the use of loose powder cosmetic products are 400-fold to 1000-fold less than protective regulatory and guidance limits for inert airborne respirable particles in the workplace.[29-31]

The acrylates copolymers that are not reported to be in use, according to 2018 FDA VCRP and 2018 Council survey data, are listed in Table 5.

With the exception of AMP-Acrylates Copolymer, the acrylates copolymers described in this safety assessment are not restricted from use in any way under the rules governing cosmetic products in the European Union (EU).[32] AMP-Acrylates Copolymer is restricted by a maximum secondary amine content of 5% in ready for use preparations.

Non-Cosmetic

From the Safety Assessment of PMMA and related ingredients[3]

Polymethyl methacrylate bone cement has been approved by the FDA as a class II (special controls) medical device that requires premarket notification and adherence to standards. Polymethyl methacrylate beads are incorporated into collagen as dermal fillers. Intraocular lenses are made of PMMA.

Several of the ingredients reviewed in this report are approved for use as secondary direct food additives or as indirect food additives. (See Table 6.) Additionally, Polymethyl Acrylate is a prior-sanctioned food ingredient as a substances used in the manufacture of paper and paperboard products used in food packaging. [21CFR181.30]

Acrylates Copolymer

Acrylates Copolymer (as a fully polymerized copolymer of methyl methacrylate and ethyl acrylate[15] and as a fully polymerized copolymer of methyl acrylate, methyl methacrylate, and methacrylic acid[16]) is used as an excipient in the preparations for oral tablets as a glazing/coating agent to permit the pH-independent delayed release of active ingredients.

TOXICOKINETIC STUDIES

Dermal Penetration

From the Safety Assessment of PMMA and related ingredients[3]

Polymethyl methacrylate-based cosmetic ingredients are large molecules and remain in particulate form (dispersed) in final preparations and thus will not likely cross the stratum corneum to induce systemic toxicity.

Absorption, Distribution, Metabolism, and Excretion (ADME)

Animal

Oral

Acrylates Copolymer

Five male rats were administered 55 - 75 mg/animal of Acrylates Copolymer (as a fully polymerized copolymer of methyl methacrylate and ethyl acrylate; supplied as a dried film labeled with ^{14}C with a specific activity of 0.17 µCi/mg) by gavage.[15] Urine and feces were collected for 5 days prior to dosing (to establish background radioactivity levels), and for 7 days following dosing. Animals were then killed, and tissue samples were collected and assessed for radioactivity. An additional 9 male rats were also given a single oral dose of the test article, and 3 animals were killed 1, 3, or 14 days after dosing, and tissue samples were collected. The mean total recovery of radioactivity over a period of 5 days following administration of the labeled substance was in excess of 90% of the administered dose. More than 97% of the radioactivity was recovered in the feces, primarily with 48 h of dosing. Little radioactivity (0.0092%) was excreted in the urine. Levels of radioactivity in the blood and tissues did not significantly differ between treated and control animals. The researchers concluded that less than 0.02% of the administered test article was absorbed from the gastrointestinal tract, and that any material that was absorbed was rapidly excreted.

Three groups of 4 male and 4 female Sprague-Dawley rats were dosed by gavage for 13 days with Acrylates Copolymer (as a fully polymerized copolymer of methyl acrylate, methyl methacrylate, and methacrylic acid; dose not stated), followed by a single dose of radiolabeled test material (10 µCi per animal; ^{14}C-labeled at the free carboxyl group of the methacrylic acid moiety).[16] One group was killed at 24 h, and one at 72 h, after the last dose. The last group was kept for 10 days, and urine and feces were collected. The majority of the dose was excreted in the feces; with 94% collected within 72 h of dosing. Little or no radioactivity (< 0.1%) was recovered in urine. Tissues and tissue contents accounted for < 0.01% of the total recovery, and levels of radioactivity in the carcass were below limits of detection.

TOXICOLOGICAL STUDIES

From the Safety Assessment of PMMA and related ingredients[3]

The Panel saw no need to review systemic toxicity data on PMMA and related polymers applied to the skin as the safety of this route of exposure can be extrapolated from data on use of these polymers as medical devices, which had already been reviewed and found safe by the FDA.

Acute Toxicity Studies

From the Original Safety Assessment of Acrylates Copolymers[1]

The following LD_{50} values were reported for Acrylates Copolymer: > 16 g/kg (dermal, rabbits), > 16 ml/kg (dermal), >9 g/kg (dermal), 9 g/kg (dermal, rats), > 5.2 mg/l (rats). Ethylene/Acrylic Acid Copolymer had a" low order of acute toxicity" following dermal and oral administration to rats; the oral LD_{50} was > 5 g/kg. The oral LD_{50} for rats of an ammonium salt of Ethylene/Acrylic Acid was 41.5 ml/kg. In an acute inhalation study, 0 of 6 rats exposed to an aqueous emulsion of the ammonium salt of Ethylene/Acrylic Acid polymer died. The dermal LD_{50} for rabbits and the oral LD_{50} for rats of Vinyl Acetate/Maleate/Acrylate Copolymer solution was > 5 g/kg. For rats, the oral LD_{50} values of Polyacrylic Acid and Sodium Polyacrylate were 2.5 and > 40 g/kg, respectively; and 0.34 and 2.59 ml/kg, respectively, for male rats.

From the Safety Assessment of Crosslinked Alkyl Acrylates[2]

Little toxicity data were available. Acute dermal toxicity data for Acrylates/C10-30 Alkyl Acrylate Crosspolymer and Acrylates/Vinyl Neodecanoate Crosspolymer in rabbits (LD_{50}s > 2.0 g/kg and > 5.0 g/kg, respectively) and oral LD_{50} values in rats for Acrylates/C10-30 Alkyl Acrylate Crosspolymer (>10 g/kg), Acrylates/ Vinyl Isodecanoate Crosspolymer (2 g/kg), Acrylates/Vinyl Neodecanoate Crosspolymer (> 5 g/kg), and Sodium Acrylates Crosspolymer-2(> 2 g/kg indicated that these ingredients are not very toxic. Additionally, the inhalation LC_{50} of Acrylates/Vinyl Neodecanoate Crosspolymer in rats is > 16.34 mg/l air (1 h).

From the Safety Assessment of [Carbomer][4]

Acute oral studies with rats, guinea pigs, mice, and dogs showed that Carbomer has low toxicity when ingested. The inhalation LC_{50} of Carbomer in albino rats was 1.71 mg/l. The dermal LD_{50} of rats exposed to Carbomer was > 3 g/kg.

The acute toxicity studies summarized here are described in Table 7. Dermal LD_{50}s of > 2 g/kg[13] and > 5 g/kg[14] were reported for Acrylates Copolymer in rats, and in rabbits, an LD_{50} of > 2 g/kg was reported for VA/Butyl Maleate/Isobornyl Acrylate Copolymer in ethanol.[8] The dermal LD_{50}s of Acrylates/Beheneth-25 Methacrylate Copolymer[10] and Acrylates/Hydroxyesters Acrylates Copolymer (product containing < 50%) in rats[14] were > 5 g/kg. Acute oral studies were conducted on Acrylates Copolymer; the LD_{50}s in rats and dogs were > 25.2 g dry copolymer/kg bw and > 7.95 g dry copolymer/kg bw, respectively.[15] In oral studies in rats, LD_{50}s of > 5 g/kg were reported for Acrylates/ Beheneth-25 Methacrylate Copolymer,[10] Acrylates/Hydroxyesters Acrylates Copolymer (product containing < 50%),[14] and VA/Butyl Maleate/Isobornyl Acrylate Copolymer in ethanol.[8] For Polyacrylate-1 Crosspolymer, the oral LD_{50} in rats was > 2 g/kg.[12] In an acute inhalation study in rats, a 4-h exposure resulted in an LC_{50} of > 3960 mg/l Acrylates Copolymer.[15]

Short-Term Toxicity Studies

From the Original Safety Assessment of Acrylates Copolymers[1]

Pulmonary lesions were observed in rats used in short-term inhalation studies of acrylic acid polymers.

From the Safety Assessment of [Carbomer][4]

Feeding of rats with doses up to 5.0 g/kg/day Carbomer (49 days) and of rats and dogs with up to 5.0% Carbomer in the diet (21 days) resulted in lower than normal body weights.

Oral

Acrylates Copolymer

Groups of 10 male and 10 female rats were dosed by gavage with 500, 1000, and 2000 mg/kg bw/day of dry Acrylates Copolymer (as a fully polymerized copolymer of methyl methacrylate and ethyl acrylate) for 35 days.[15] Two recovery groups of 5 males and 5 females were dosed with 0 or 2000 mg dry copolymer/kg bw/d and were used for a recovery period of 14 days without dosing. The control group received distilled water. No animals died during the study. Differences in hematology and clinical chemistry parameters and in organ weights that were observed between treated and control animals were not considered related to the test article because a dose-response was not observed. There were no changes in urinary parameters reported. The no-observed-adverse effect level (NOAEL) was 2000 mg/kg bw/day.

In a 28-day study, groups of 3 male and 3 female Göttingen minipigs were administered Acrylates Copolymer (as a fully polymerized copolymer of methyl methacrylate and ethyl acrylate) via coating on cellulose pellets containing 22.7% copolymer.[15] The animals received the coated cellulose pellets at dose levels of 500, 1000, and 2000 mg/kg bw/d, which corresponded to dose levels of 113, 227, and 454 mg/kg bw/d expressed as dry copolymer. Clinical signs were observed and feed consumption was measured daily, body weights were measured weekly, and hematology, clinical chemistry, urinalysis, and fecal parameters were evaluated. No treatment-related deaths were observed. There were no toxicologically relevant changes in body weight, food consump-

tion, clinical observations, ophthalmoscopy, clinical pathology, urinalysis, fecal analysis, or in organ weights. Microscopic examination revealed instances of mucosal/submucosal edema in the cecum and colon of one male receiving 454 mg dry copolymer/kg bw/d and in the caecum of one male dosed at 227 mg dry copolymer/kg bw/d; the researcher commented that the influence of the high doses is unclear, and the finding may be a physiological reaction of the intestine to the high amounts of non-soluble or non-degradable particles resulting in osmotic imbalance. No toxicological relevance was attributed to this change. Centrilobular yellow/brown pigmentation and mild fibrosis was apparent in the liver of a single female dosed at 454 mg dry copolymer/kg bw/d. The NOAEL was determined to be 227 mg dry copolymer/kg bw/d.

Subchronic Toxicity Studies

From the Original Safety Assessment of Acrylates Copolymers[1]

In a subchronic inhalation toxicity study of Acrylates Copolymer, alveolar histiocytosis was observed at a concentration of 30 mg/m^3. Pulmonary lesions were observed in rats used in subchronic inhalation studies of acrylic acid polymers.

From the Safety Assessment of [Carbomer][4]

Subchronic feeding of rats and dogs with up to 5.0% Carbomer in the diet (90 days) resulted in lower than normal body weights. In rats fed Carbomer at dietary levels of 5.0% for 90 days, absolute liver weights and liver to body and brain weight ratios were reduced, but no pathological changes were observed.

Chronic Toxicity Studies

From the Original Safety Assessment of Acrylates Copolymers[1]

In a chronic inhalation study of respirable polyacrylate particles, compound-related pulmonary lesions were not observed.

From the Safety Assessment of [Carbomer][4]

Rats fed Carbomer at dietary levels of 0.1%, 0.5%, or 5.0% for 6.5 months exhibited various organ weight changes. In dogs fed 0.5 or 1.0 g/kg/day Carbomer for 6.5 months, gastrointestinal irritation and marked pigment deposition within Kupffer cells of the liver were observed. In another study, there were no significant effects in dogs fed up to 1.0 g/kg/day Carbomer for 32 months.

Oral

Acrylates Copolymer

A 40% Acrylates Copolymer (as a fully polymerized copolymer of methyl methacrylate and ethyl acrylate) dispersion was sprayed onto powdered diet at a ratio of 1:10, and the coated diet was mixed with basal diet and administered to groups of 20 male and 20 female Sprague-Dawley rats for 26 wks.[15] Once mixed with basal diet, the dose levels were 500 and 2000 mg dry copolymer/kg bw/day. A control group of 20 males and 20 females received diet prepared by spraying with water and subsequent drying. The test was performed in accord with the Organisation for Economic Co-operation and Development (OECD) test guideline (TG) 408. Clinical signs were evaluated and feed consumption was measured daily, body weights were determined weekly, and clinical chemistry, hematology, and urinalysis parameters were evaluated at several intervals. All animals were killed at study termination. None of the animals died during the study, and no clinical signs of toxicity were observed. No treatment-related findings were observed. The NOAEL was ≥ 2000 mg dry copolymer/ kg bw/day.

A similar study was conducted using coated pellets containing approximately 22.7% Acrylates Copolymer (as a fully polymerized copolymer of methyl methacrylate and ethyl acrylate), and the pellets were placed into gelatin capsules and administered to groups of 4 male and 4 female Beagle dogs for 26 wks.[15] The dose levels used were 50, 125, and 250 mg dry copolymer/kg bw/d, which were equivalent to 200, 500, and 1000 mg test material/kg bw/d. A control group of 4 males and 4 females were given empty capsules. An additional 3 male and 3 female animals were included with both the control and high dose groups, and these animals were allowed to recover for 3 wks after the termination of dosing. Examinations were made as described above. High-dose animals had lower body weight gains as compared to controls, and the difference became statistically significant at wk 12. Males of the low- and mid-dose groups had slightly lower body weights compared to controls; no changes were observed in the body weights of females of these groups. Relative heart and right thyroid weights in treated females were increased, but these changes were not considered treatment-related because no differences were observed microscopically. Other observations were not considered toxicologically significant, and the NOAEL was determined to be 250 mg dry copolymer/kg bw/d.

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY STUDIES

From the Original Safety Assessment of Acrylates Copolymers[1]

Reproductive effects were not observed in a study in which rats were dosed orally with 4500- or 90,000-Da molecular weight (MW) Sodium Polyacrylate. In this study, groups of 30 gravid rats were dosed with up to 3000 mg/kg/day of the low MW test article in distilled water on days 6-15 of gestation, and the animals were killed on day 19 of gestation. Groups of 28-29 gravid rats were dosed with up to 1125 mg/kg/day of the high MW test article in distilled water; 8 animals/group were dosed on days 6-13 of gestation and killed on day 13, and the remaining animals in each high MW-test article group were dosed on days 6-15 of gestation, and killed on day 10 of gestation.

Oral

Acrylates Copolymer

Two studies were conducted in which an Acrylates Copolymer (as a fully polymerized copolymer of methyl methacrylate and ethyl acrylate) dispersion was sprayed onto powdered diet at a ratio of 1:10, and the coated diet was mixed with basal diet for testing.[15] In the first study, groups of 20 mated female Wistar rats were fed 0, 500, or 2000 mg dry copolymer/ kg bw/day on days 6 through 15 of gestation, and the gravid rats were killed on day 19 of gestation. In the second study, groups of 10 mated female New Zealand White rabbits were given the same dosages on days 6 to 18 of gestation, and killed on day 29 of gestation. There were no signs of maternal toxicity in rats or rabbits, and there were no reproductive or developmental effects observed for either species. The NOAELs for dams and fetuses were 2000 mg/kg bw/day in both rats and rabbits.

GENOTOXICITY STUDIES

From the Original Safety Assessment of Acrylates Copolymers[1]

Acrylates Copolymer was not mutagenic in Ames tests. A mixture containing 30% Ammonium Acrylates Copolymer was not mutagenic in a modified Ames test. Sodium Polyacrylate was not mutagenic in an Ames assay, a plate test, a mouse lymphoma assay, chromosomal aberration assays, an unscheduled DNA syntheses (UDS) assay, or an in vivo mouse micronucleus assay.

From the Safety Assessment of Crosslinked Alkyl Acrylates[2]

The little genotoxicity data that were available for the crosslinked alkyl acrylates reported negative results in Ames tests.

The genotoxicity studies summarized here are described in Table 8. Acrylates Copolymer (comprised of various monomer combinations) was not genotoxic in Ames tests (up to 5000 µg dry copolymer/plate), mouse lymphoma L5178Y cell mutation assays (up to 6250 µg dry copolymer/ml), or a chromosomal aberration assay (up to 9000 µg dry copolymer/ml in human lymphocytes), and it was not genotoxic in the mouse micronucleus test in which mice were dosed with up to 2000 mg dry copolymer/kg bw.[13,15,16] Acrylates/Hydroxyesters Acrylates Copolymer (in a product containing < 50%) was also not mutagenic in the Ames test.[14] Details were missing from many of these studies.

CARCINOGENICITY STUDIES

Published carcinogenicity studies on the acrylates copolymers were not discovered in the published literature, and unpublished data were not submitted.

DERMAL IRRITATION AND SENSITIZATION STUDIES

From the Original Safety Assessment of Acrylates Copolymers[1]

In dermal irritation studies using rabbits, Acrylates Copolymer was non- to mildly irritating. In one study, it produced signs of an irritant property. However, in a study in which the patches adhered to the skin, very slight to well-defined erythema, and severe erythema in one animal, were observed at 72 hours. A mixture containing 30% Ammonium Acrylates Copolymer was practically nonirritant, and an aqueous emulsion of the ammonium salt of an Ethylene/Acrylic Acid polymer produced minor irritation. Acrylates/VA Copolymer produced moderate to severe but reversible dermal irritation, Vinyl Acetate/ Maleate/Acrylate Copolymer solution had a primary irritation index of 4.4. Sodium Polyacrylate did not produce irritation. Acrylates Copolymer was not a sensitizer to guinea pigs in maximization studies or a Buehler sensitization test.

A 25% aq. dilution of Acrylates Copolymer was not an irritant or a sensitizer in a human repeated insult patch test (HRIPT; 47 subjects). In clinical testing, Acrylates Copolymer, 30% solids, was not an irritant or sensitizer, and neither was Acrylates Copolymer (100% solids) tested as a 15% solution in ammonia water or a 25% solution in acetone. Undiluted Sodium Polyacrylate did not produce irritation or sensitization in 50 subjects.

From the Safety Assessment of Crosslinked Alkyl Acrylates[2]

In an alternative method study, Acrylates/Vinyl Neodecanoate Crosspolymer was predicted to be a nonirritant. Studies in rabbits, guinea pigs, and humans reported no to slight irritation with undiluted and weak sensitization with 2% aq, Acrylates/C10-30 Alkyl Acrylate Crosspolymer, no irritation with Acrylates Crosspolymer at 30% in olive oil, and no irritation or sensitization with Sodium Acrylates Crosspolymer 2 (concentration not specified). Mostly, human testing with undiluted Acrylates/C10-30 Alkyl Acrylate Crosspolymer, Acrylates Crosspolymer, and Acrylates/Ethylhexyl Acrylate Crosspolymer, up to 2.5% aq. Acrylates/Vinyl Isodecanoate Crosspolymer, 1% aq. dilutions of formulations containing 2% Acrylates/Vinyl Neodecanoate Crosspolymer, and formulations containing up to 2.6% Lauryl Methacrylate/Glycol Dimethacrylate Crosspolymers do not indicate any dermal irritation or sensitization. The only exception was a weak irritant response noted during an intensified Shelanski HRIPT with undiluted Acrylates/C10-30 Alkyl Acrylate Crosspolymer.

While the residual monomer (MMA) has the potential to induce sensitization, the levels in these ingredients were reported to be well below the levels that would induce sensitization to MMA, thus resolving the Panel's concern about sensitization.

From the Safety Assessment of PMMA and related ingredients[3]

PMMA was not a dermal irritant to rabbits. PMMA was not irritating or sensitizing at 6.8% in an HRIPT test using 52 participants. The same result was obtained in another HRIPT test of PMMA at 2.0% (n = 106).

From the Safety Assessment of [Carbomer][4]

Rabbits showed minimal skin irritation when tested with 100% Carbomer. Clinical studies with Carbomer and its various salts showed low potential for skin irritation and sensitization at concentrations of 0.5%, 5%, 10%, and 100%. When tested on humans at 1.0% concentration, Carbomer and its various salts also demonstrated low potential for skin irritation and sensitization. Further, formulations containing up to 0.25% Carbomer demonstrated low potential for human skin irritation, sensitization, phototoxicity, and photo-contact allergenicity.

The dermal irritation and sensitization studies summarized here are described in Table 9; details were not available for many of the studies. In animal studies, Acrylates/Beheneth-25 Methacrylate Copolymer[10] and Acrylates/Hydroxyesters Acrylates Copolymer (in a product containing < 50%)[14] were classified as slightly irritating to rabbit skin. Acrylates Copolymer[13,15] and VA/Butyl Maleate/Isobornyl Acrylate Copolymer in ethanol[8] were not irritating to rabbit skin. Acrylates Copolymer was not classified as a sensitizer in a local lymph node assay (LLNA),[13] or in a Buehler test using guinea pigs.[15] VA/Butyl Maleate/Isobornyl Acrylate Copolymer in ethanol, tested neat, was not irritating or sensitizing in a Buehler test in guinea pigs [8] In clinical testing, VA/Butyl Maleate/Isobornyl Acrylate Copolymer (as a slurry in ethanol) produced slight erythema in 20% of the 25 subjects tested in a 48-h patch test.[8] In an HRIPT, Acrylates/Hydroxyesters Acrylates Copolymer (as a product containing < 50%) was not a sensitizer, and it was concluded that VA/Butyl Maleate/Isobornyl Acrylate Copolymer in 10% ethanol not likely to be a sensitizer (109 subjects); erythema was observed in a few subjects at both induction and challenge.[8]

Phototoxicity/Photosensitization

Human

VA/Butyl Maleate/Isobornyl Acrylate Copolymer

The phototoxicity of VA/Butyl Maleate/Isobornyl Acrylate Copolymer was evaluated in 10 fair-skinned subjects.[8] Patches with 0.2 ml of the copolymer in 10% ethanol were applied to both volar forearms of each subject for 24 h. One arm was irradiated with long-wave ultraviolet (UVA) for 15 minutes (total dose = 3.3 J); an untested site on this arm served as an irradiated control. The other arm was not irradiated and was protected from light, including sunlight, by either a mitten or a long sleeve. Immediately after irradiation and at 48 and 72 h, both arms were graded for reactions. Minimal erythema at the test site, which occurred immediately after irradiation, was observed in one subject; no other reactions were reported. It was concluded that the test article "is not likely to be phototoxic in humans" at the concentration tested.

In a photosensitization study, 24-h patches applied with 0.2 ml of VA/Butyl Maleate/Isobornyl Acrylate Copolymer in 10% ethanol were applied to both volar forearms of 28 fair-skinned subjects twice a week for 3 wks.[8] At 24 hours, the test sites of both arms were examined and graded. One arm was then irradiated with ultraviolet UVA for 15 minutes, followed by medium-wave ultraviolet (UVB) irradiation. The dose of UVB irradiation administered was determined separately for each subject and was based on skin type and the minimal erythema dose (MED), which was established on the control arm prior to the first irradiation. The MED used in the study was set at the lesser of either the time that was sufficient to achieve a 1.0 score, or 120 seconds. An untreated site on the irradiated arm served as the irradiated control. Each test site was graded immediately after irradiation. The other treated arm was not irradiated. After a 2–wk non-treatment period, challenge patches were applied to previously untreated sites for 24 h, and the irradiated arm was exposed to UVA only.

During induction, transient effects such as minimal erythema, slight edema, and tanning were observed; most of the responses reported were seen at the irradiated treated and non-treated sites. No responses were reported on the non-irradiated arm. Following challenge, 3 subjects exhibited positive responses on the treated and irradiated arm, including minimal erythema, slight edema, skin dryness, or a combination of these symptoms. Two of these subjects also showed similar symptoms on the treated but non-irradiated arm. No reactions were observed on the non-treated irradiated forearm. It was concluded that VA/Butyl Maleate/ Isobornyl Acrylate Copolymer in 10% ethanol was "not likely to be photoallergenic or photosensitizing."

OCULAR IRRITATION STUDIES

From the Original Safety Assessment of Acrylates Copolymers[1]

In two chorioallantoic membrane vascular assays (CAMVAs), Acrylates Copolymer was predicted to be non-irritating, and in two bovine corneal opacity and permeability (BCOP) test, it was predicted to be a mild irritant. In ocular irritation studies using rabbits, Acrylates Copolymer was generally non- to mildly irritating. In two other studies, Acrylates Copolymer (containing 1500 and 200 ppm stearyl acrylate and methacrylic acid, respectively) was an eye irritant but not corrosive according to OECD guidelines, by considered minimally irritating according to the methods of Kay and Calandra. A mixture containing 30% Ammonium Acrylates Copolymer was practically nonirritating. An aqueous emulsion of the ammonium salt of an Ethylene/Acrylic Acid polymer produced trace corneal injury. Acrylates/VA Copolymer produced severe but reversible ocular irritation, and Vinyl Acetate/Maleate/ Acrylate Copolymer solution produced moderate to severe but reversible ocular irritation. In a Draize eye test, the greatest tolerated concentration of Sodium Polyacrylate was 13% to 20% and 20% to 30% for unrinsed and rinsed eyes, respectively. In an irritant

threshold test, the greatest concentration of Sodium Polyacrylate that did not produce irritation in three or more of five rabbits was 2%.

From the Safety Assessment of Crosslinked Alkyl Acrylates[2]

Alternative test methods for ocular irritation indicated that Acrylates/Vinyl Isodecanoate Crosspolymer and a formulation containing 1% Lauryl Methacrylate/Glycol Dimethacrylate Crosspolymer are not likely ocular irritants. In studies using rabbits, undiluted Acrylates/C10-30 Alkyl Acrylate Crosspolymer produced minimal to moderate irritation, and it was considered a borderline irritant in unrinsed rabbit eyes. Acrylates Crosspolymer, at 50% in olive oil, and Sodium Acrylates Crosspolymer 2 did not appear to be ocular irritants in rabbit eyes.

From the Safety Assessment of PMMA and related ingredients[3]

In an EpiOcular test, PMMA had a Draize ocular irritation score of 0. PMMA was mildly irritating in rabbit eyes.

From the Safety Assessment of [Carbomer][4]

Rabbits showed zero to moderate eye irritation when tested with Carbomer and/or its various salts at concentrations of 0.20 - 100%.

The ocular irritation studies summarized here are described in Table 10. All of the studies were performed in rabbits; details were not available for several of the studies. Acrylates Copolymer was not an ocular irritant in one study,[15] and was slightly irritating in another.[13] Acrylates/Beheneth-25 Methacrylate Copolymer[10] and Acrylates/Hydroxyesters Acrylates Copolymer (as a product containing < 50%)[14] were slightly irritating to rabbit eyes, and VA/Butyl Maleate/Isobornyl Acrylate Copolymer in ethanol (tested undiluted) was a moderate to severe eye irritant.[8]

CLINICAL STUDIES

Occupational Exposure

From the Original Safety Assessment of Acrylates Copolymers[1]

In examining the effects of workplace exposures, employees exposed to a variety of acrylic polymer dusts (as well as other materials) did not have an excess of chest x-ray abnormalities, especially those suggestive of diffuse pulmonary fibrosis. Additionally, they did not have an excess of pulmonary function testing (PFT) abnormality.

Risk Assessment

From the Safety Assessment of Crosslinked Alkyl Acrylates[2]

Two different risk assessments evaluating the carcinogenic endpoint for benzene that may be present in Acrylates/C10-30 Alkyl Acrylates Crosspolymer resulted in different lifetime risk. One found that the risk was within the range associated with a 10^6 cancer risk, while the other reported a 20-fold greater risk.

SUMMARY

The Panel has previously issued a Final Report on Acrylates Copolymer and 33 Related Cosmetic Ingredients in 2002, concluding that the acrylates copolymers named in that report are safe for use in cosmetics when formulated to avoid irritation. The Panel also reviewed the safety of numerous similar ingredients in several other reports. The Panel determined that it is appropriate to include all the copolymers in one assessment, including crosslinked copolymers (i.e., crosspolymers) prepared from monomers that comprise, in part, acrylic acid and/or methacrylic acid; the methyl, ethyl, propyl, or butyl ester(s) of these acids; or the salts of one or both of these two acids. Additionally, the Panel determined that three acrylates copolymers that were included in the original report should be excluded here because these are already under review in a concurrent safety assessment. As a result, this is a safety assessment of 126 similar copolymers that are commonly reported to function as film formers and viscosity increasing agents.

According to FDA VCRP data and the results of the Council use survey, 66 of the 126 ingredients assessed in this report are in use. According to VCRP data, Carbomer has the highest frequency of use; it is reported to be used in 6434 cosmetic formulations, and most of these uses (5336) are in leave-on products. Acrylates Copolymer and Acrylate/C10-30 Alkyl Acrylate Crosspolymer (solvent not specified) also have very high frequency of use, with 3177 and 3135 reported uses, respectively.

The results of concentration of use surveys conducted by the Council in 2018 indicate that Acrylates Copolymer has the highest maximum use concentration; it is used at up to 98.6% in nail extenders; use in product categories other than nail products is not as high, but Acrylates Copolymer is used at up to 25% in products that result in dermal contact (face and neck products). Ingredients with the next highest reported concentrations of use are Acrylates/VA Copolymer (at 50%, in “other” skin care formulations) and Polymethyl Methacrylate (at up to 44.6%, in face powders).

In ADME studies of Acrylates Copolymer (either as a fully polymerized copolymer of methyl methacrylate and ethyl acrylate or as a fully polymerized copolymer of methyl acrylate, methyl methacrylate, and methacrylic acid), most of the test substance was excreted in the feces. Very little radioactivity was recovered in the urine or in the carcass.

Dermal LD_{50}s of > 2 g/kg and > 5 g/kg were reported for Acrylates Copolymer in rats, and in rabbits, an LD_{50} of > 2 g/kg was reported for VA/Butyl Maleate/Isobornyl Acrylate Copolymer in ethanol. The dermal LD_{50}s of Acrylates/ Beheneth-25

Methacrylate Copolymer and Acrylates/Hydroxyesters Acrylates Copolymer (product containing < 50%) in rats were > 5 g/kg. Acute oral studies were conducted on Acrylates Copolymer; the LD_{50}s in rats and dogs were > 25.2 g dry copolymer/kg bw and > 7.95 g dry copolymer/kg bw, respectively. In oral studies in rats, LD_{50}s of > 5 g/kg were reported for Acrylates/Beheneth-25 Methacrylate Copolymer, Acrylates/Hydroxyesters Acrylates Copolymer (product containing < 50%), and VA/Butyl Maleate/Isobornyl Acrylate Copolymer in ethanol. For Polyacrylate-1 Crosspolymer, the oral LD_{50} in rats was > 2 g/kg. In an acute inhalation study of Acrylates Copolymer in rats, the LC_{50} was > 3960 mg/l.

In a gavage study, rats were dosed with 500, 1000, and 2000 mg/kg bw/day of dry Acrylates Copolymer (as a fully polymerized copolymer of methyl methacrylate and ethyl acrylate) for 35 days. There were no notable findings, and the NOAEL was 2000 mg/kg bw/day. In a 28-day dietary study in which rats were fed Acrylates Copolymer-coated cellulose pellets at a dose up to 2000 mg/kg bw/d. There were no toxicologically relevant changes in body weight, food consumption, clinical observations, ophthalmoscopy, clinical pathology, urinalysis, fecal analysis, or in organ weights. In this study, the NOAEL was determined to be 227 mg dry copolymer/kg bw/d. In similar studies in which rats and dogs were fed Acrylates Copolymer-coated pellets for 26 weeks, the NOAEL was ≥ 2000 mg dry copolymer/kg bw/day for rats, and it was determined to be 250 mg dry copolymer/kg bw/d for dogs. These were the highest doses tested in the 26 wk studies.

In two dietary studies in which an Acrylates Copolymer (as a fully polymerized copolymer of methyl methacrylate and ethyl acrylate) dispersion was sprayed onto powdered diet and administered at a dose up to 2000 mg dry copolymer/kg bw/day and fed to pregnant rats (on days 6 – 15 of gestation) and rabbits (on days 6 – 18 of gestation), there were no signs of maternal toxicity in rats or rabbits, and there were no reproductive or developmental effects observed for either species. The NOAELs for dams and fetuses were 2000 mg/kg bw/day in both rats and rabbits.

Acrylates Copolymer (comprised of various monomer combinations) was not genotoxic in Ames tests (up to 5000 µg dry copolymer/plate), mouse lymphoma L5178Y cell mutation assays (up to 6250 µg dry copolymer/ml), or a chromosomal aberration assay (up to 9000 µg dry copolymer/ml in human lymphocytes), and it was not genotoxic in the mouse micronucleus test in which mice were dosed with up to 2000 mg dry copolymer/kg bw. Acrylates/Hydroxyesters Acrylates Copolymer (in a product containing < 50%) also was not mutagenic in the Ames test.[14] Details were not available for many of these studies.

Carcinogenicity data were neither found in the published in the publically available literature, nor were unpublished studies submitted.

In animal studies, Acrylates/Beheneth-25 Methacrylate Copolymer and Acrylates/Hydroxyesters Acrylates Copolymer (in a product containing < 50%) were classified as slightly irritating to rabbit skin. Acrylates Copolymer and VA/Butyl Maleate/Isobornyl Acrylate Copolymer in ethanol were not irritating to rabbit skin. Acrylates Copolymer was not classified as a sensitizer in a LLNA, or in a Buehler test using guinea pigs. VA/Butyl Maleate/Isobornyl Acrylate Copolymer in ethanol, tested neat, was not irritating or sensitizing in a Buehler test in guinea pigs. In clinical testing, VA/Butyl Maleate/Isobornyl Acrylate Copolymer (as a slurry in ethanol) produced slight erythema in 20% of the 25 subjects tested in a 48-h patch test. In an HRIPT, Acrylates/Hydroxyesters Acrylates Copolymer (as a product containing < 50%) was not a sensitizer, and it was concluded that VA/Butyl Maleate/Isobornyl Acrylate Copolymer in 10% ethanol not likely to be a sensitizer (109 subjects); erythema was observed in a few subjects at both induction and challenge.

In study in which the phototoxicity of VA/Butyl Maleate/Isobornyl Acrylate Copolymer in 10% ethanol was evaluated in 10 fair-skinned subjects following 24 h patches, it was concluded that the test article "is not likely to be phototoxic in humans." In a similar test in which 24-h patches were applied to 28 fair-skinned subjects twice a week for 3 wks, VA/Butyl Maleate/Isobornyl Acrylate Copolymer in 10% ethanol was "not likely to be photoallergenic or photosensitizing."

Ocular irritation studies were performed in rabbits; details were not available for several of the studies. Acrylates Copolymer was not an ocular irritant in one study, and was slightly irritating in another. Acrylates/Beheneth-25 Methacrylate Copolymer and Acrylates/Hydroxyesters Acrylates Copolymer (as a product containing < 50%) were slightly irritating to rabbit eyes, and VA/Butyl Maleate/Isobornyl Acrylate Copolymer in ethanol (tested undiluted) was a moderate to severe eye irritant.

DISCUSSION

In accordance with its procedures, CIR evaluates the conclusions of previously-issued reports approximately every 15 years. In 2002, the Panel reviewed the safety of Acrylates Copolymer and 33 related cosmetic ingredients, and concluded that those ingredients were safe for use in cosmetics when formulated to avoid irritation. The Panel has issued three other reports on related copolymers and crosspolymer prepared from monomers that comprise, in part, acrylic acid or methacrylic acid (as well as appropriate salts and esters of these acids). In addition to those acrylates copolymers previously reviewed, the Panel determined that it was appropriate to include 70 acrylates copolymers that have not yet been reviewed. Subsequently, there are a few copolymers that fit the description for this family that are not included in this report because they were recently included in other reports, and there are some that will warrant a review of their own in in the near future because of frequency of use.

The Panel recognized the large number of ingredients in this safety assessment, and the fact that these polymers are comprised of many different monomeric building blocks. Nonetheless, these polymers are uniformly large molecules and are produced in chemical reactions that leave very little residual monomer. For these reasons, the Panel concluded that it is reasonable to consider these ingredients as a group, and the collection of these 126 ingredients in one report enables the assembly of reinforcing and complementary test data.

Acrylates Copolymer is used at up to 98.6% in nail extenders; however, concentrations of use in products that result in dermal exposure are lower (i.e., 50% or less). Because these copolymers are generally large molecules, significant dermal absorption is not expected. Therefore, topical application of these ingredients is not expected to result in systemic toxicity. Additionally, the existing data support a lack of sensitization potential; consequently, the Panel was satisfied that the data included in this report (as well as those data described in the previous reports) supported the safety of the acrylates copolymers as used in cosmetics.

The Panel discussed the concern of residual monomer that might be present in these polymers. In most cases, taking into consideration the low amount of residual monomer in the polymers, the Panel was not concerned that the presence of residual monomer would result in adverse effects. However, the Panel did stress that manufacturers should continue to use good manufacturing processes to ensure the amount of residual monomer is kept to a minimum.

The Panel also discussed the issue of residual solvent that might be present. Again, the Panel stressed that the amount of residual solvent should be minimized. However, the Panel was particularly concerned with polymerization in benzene. It cannot be predicted with certainty what quantity of benzene would be volatilized/leached from a polymer during manufacture, formulation, or use; while some benzene is inevitably volatilized during manufacture, some benzene may be trapped in the polymer matrix and may leach out during formulation and use. Because of this uncertainty, the Panel stipulated that these ingredients should not be polymerized in benzene.

The Panel remarked that the potential exists for dermal irritation with the use of products formulated using the ingredients named in this assessment. Therefore, the Panel specified that products containing the acrylates copolymers named in this assessment must be formulated to be non-irritating.

Finally, because some of the acrylates copolymers are used in cosmetic sprays and powders (e.g., VA/Butyl Maleate/Isobornyl Acrylate Copolymer is reported to be used at a maximum concentration of 10% in aerosol hair sprays and Polymethyl Methacrylate is used at concentrations up to 44.6% in face powders) and could possibly be inhaled, the Panel discussed the issue of potential inhalation toxicity. As discussed in the initial assessment on Acrylates Copolymer, the acrylic acid monomer can be a nasal irritant; however, exposure to the monomer from use of these polymers in cosmetic formulations would be less than the established threshold limit value for nasal irritation. Also, the Panel noted that in aerosol products, 95% – 99% of droplets/particles would not be respirable to any appreciable amount. Furthermore, droplets/particles deposited in the nasopharyngeal or bronchial regions of the respiratory tract present no toxicological concerns based on the chemical and biological properties of these ingredients. Coupled with the small actual exposure in the breathing zone and the concentrations at which the ingredients are used, the available information indicates that incidental inhalation would not be a significant route of exposure that might lead to local respiratory or systemic effects. A detailed discussion and summary of the Panel's approach to evaluating incidental inhalation exposures to ingredients in cosmetic products is available at https://www.cir-safety.org/cir-findings.

CONCLUSION

The Panel issued a tentative amended report for public comment with the conclusion that the 126 acrylates copolymers named below are safe in cosmetics in the present practices of use and concentration described in the safety assessment when formulated to be non-irritating.

Acrylates Copolymer
Acrylates Crosspolymer
Acrylates Crosspolymer-3
Acrylates Crosspolymer-4
Acrylates Crosspolymer-5*
Acrylates/Ammonium Methacrylate Copolymer
Acrylates/Beheneth-25 Methacrylate Copolymer
Acrylates/Beheneth-25 Methacrylate/Steareth-30 Methacrylate Copolymer*
Acrylates/C10-30 Alkyl Methacrylate Copolymer
Acrylates/C10-30Alkyl Acrylate Crosspolymer
Acrylates/C12-13 Alkyl Methacrylates/Methoxyethyl Acrylate Crosspolymer*
Acrylates/C12-22 Alkyl Methacrylate Copolymer
Acrylates/C26-28 Olefin Copolymer*
Acrylates/C5-8 Alkyl Acrylate Copolymer*
Acrylates/Ceteareth-20 Methacrylate Crosspolymer*
Acrylates/Ceteareth-20 Methacrylate Crosspolymer-2*
Acrylates/Ceteth-20 Methacrylate Copolymer*
Acrylates/Ethylhexyl Acrylate Copolymer
Acrylates/Ethylhexyl Acrylate Crosspolymer
Acrylates/Ethylhexyl Acrylate/Glycidyl Methacrylate Crosspolymer*
Acrylates/Hydroxyesters Acrylates Copolymer
Acrylates/Hydroxyethyl Acrylate/Lauryl Acrylate Copolymer*
Acrylates/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer*
Acrylates/Laureth-25 Methacrylate Copolymer*
Acrylates/Lauryl Methacrylate Copolymer*
Acrylates/Lauryl Methacrylate/Tridecyl Methacrylate Crosspolymer*
Acrylates/Methoxy PEG-4 Methacrylate Copolymer*
Acrylates/Methoxy PEG-15 Methacrylate Copolymer*
Acrylates/Methoxy PEG-23 Methacrylate Copolymer
Acrylates/Methoxy PEG-90 Methacrylate Crosspolymer*
Acrylates/Palmeth-25 Acrylate Copolymer
Acrylates/PEG-4 Dimethacrylate Crosspolymer*
Acrylates/Steareth-20 Methacrylate Copolymer
Acrylates/Steareth-20 Methacrylate Crosspolymer
Acrylates/Steareth-30 Methacrylate Copolymer
Acrylates/Steareth-50 Acrylate Copolymer*
Acrylates/Stearyl Methacrylate Copolymer
Acrylates/VA Copolymer
Acrylates/VA Crosspolymer
Acrylates/Vinyl Isodecanoate Crosspolymer

Acrylates/Vinyl Neodecanoate Crosspolymer
Acrylic Acid/C12-22 Alkyl Acrylate Copolymer*
Acrylic Acid/Stearyl Acrylate Copolymer
Allyl Methacrylate/Glycol Dimethacrylate Crosspolymer*
Allyl Methacrylates Crosspolymer
Ammonium Acrylates Copolymer
Ammonium Acrylates/Ethylhexyl Acrylate Copolymer*
Ammonium Acrylates/Methyl Styrene/Styrene Copolymer
Ammonium Polyacrylate
Ammonium Styrene/Acrylates Copolymer
Ammonium Styrene/Acrylates/Ethylhexyl Acrylate/Lauryl Acrylate Copolymer*
Ammonium VA/Acrylates Copolymer*
AMP-Acrylates Copolymer
Behenyl Methacrylate/t-Butyl Methacrylate Copolymer
Butyl Acrylate/Cyclohexyl Methacrylate Copolymer*
Butyl Acrylate/Ethylhexyl Methacrylate Copolymer*
Butyl Acrylate/Glycol Dimethacrylate Crosspolymer
Butyl Acrylate/Hydroxyethyl Methacrylate Copolymer*
Butyl Methacrylate/Acryoyloxy PG Methacrylate Copolymer*
C12-22 Alkyl Acrylate/Hydroxyethylacrylate Copolymer
C8-22 Alkyl Acrylates/Methacrylic Acid Crosspolymer*
Calcium Potassium Carbomer*
Carbomer
Cyclohexyl Methacrylate/Ethylhexyl Methacrylate Copolymer*
Ethylene/Acrylic Acid Copolymer
Ethylene/Acrylic Acid/VA Copolymer*
Ethylene/Calcium Acrylate Copolymer*
Ethylene/Magnesium Acrylate Copolymer*
Ethylene/Methacrylate Copolymer
Ethylene/Sodium Acrylate Copolymer
Ethylene/Zinc Acrylate Copolymer*
Ethylhexyl Acrylate/Methoxy PEG-23 Methacrylate/Vinyl Acetate Copolymer*
Ethylhexyl Acrylate/Methyl Methacrylate Copolymer
Glycol Dimethacrylate Crosspolymer*
Glycol Dimethacrylate/Vinyl Alcohol Crosspolymer*
Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer*
Lauryl Acrylate Crosspolymer
Lauryl Acrylate/VA Copolymer*
Lauryl Acrylate/VA Crosspolymer*
Lauryl Methacrylate/Glycol Dimethacrylate Crosspolymer
Lauryl Methacrylate/Sodium Methacrylate Crosspolymer
Methacrylic Acid/PEG-6 Methacrylate/PEG-6 Dimethacrylate Crosspolymer*
Methacryloyl Ethyl Betaine/Acrylates Copolymer
Methoxy PEG-23 Methacrylate/Glyceryl Diisostearate Methacrylate Copolymer
Methyl Methacrylate Crosspolymer
Methyl Methacrylate/Glycol Dimethacrylate Crosspolymer
Methyl Methacrylate/PEG/PPG-4/3 Methacrylate Crosspolymer
PEG/PPG-5/2 Methacrylate/Methacrylic Acid Crosspolymer*
Poly C10-30 Alkyl Acrylate
Poly(Methoxy PEG-9 Methacrylate)*
Polyacrylate-14
Polyacrylate-29*
Polyacrylate-34*
Polyacrylate-1 Crosspolymer
Polyacrylic Acid
Polybutyl Acrylate*
Polybutyl Methacrylate*
Polyethylacrylate
Polyhydroxyethylmethacrylate*
Polyisobutyl Methacrylate*
Polymethyl Acrylate
Polymethyl Methacrylate
Polypropyl Methacrylate*
Polystearyl Methacrylate*
Potassium Acrylate Crosspolymer*
Potassium Acrylates Copolymer
Potassium Acrylates/C10-30 Alkyl Acrylate Crosspolymer
Potassium Acrylates/Ethylhexyl Acrylate Copolymer*
Potassium Aluminum Polyacrylate*
Potassium Carbomer
Potassium Polyacrylate*
Sodium Acrylate/Acrolein Copolymer*
Sodium Acrylate/Vinyl Alcohol Copolymer
Sodium Acrylates Copolymer
Sodium Acrylates Crosspolymer-2
Sodium Acrylates/Beheneth-25 Methacrylate Crosspolymer*
Sodium Acrylates/C10-30 Alkyl Acrylate Crosspolymer
Sodium Acrylates/Ethylhexyl Acrylate Copolymer*
Sodium Acrylates/Vinyl Isodecanoate Crosspolymer
Sodium Carbomer
Sodium Polyacrylate
Sodium Polymethacrylate
Steareth-10 Allyl Ether/Acrylates Copolymer
Stearyl/Lauryl Methacrylate Crosspolymer*
Styrene/Acrylates/Ammonium Methacrylate Copolymer
VA/Butyl Maleate/Isobornyl Acrylate Copolymer

**Not reported to be in current use. Were ingredients in this group not in current use to be used in the future, the expectation is that they would be used in product categories and at concentrations comparable to others in this group*.

TABLES

Table 1. List of 126 ingredients included in this re-review

Acrylates Copolymer
Acrylates Crosspolymer
Acrylates Crosspolymer-3
Acrylates Crosspolymer-4
Acrylates Crosspolymer-5
Acrylates/Ammonium Methacrylate Copolymer
Acrylates/Beheneth-25 Methacrylate Copolymer
Acrylates/Beheneth-25 Methacrylate/Steareth-30 Methacrylate Copolymer
Acrylates/C10-30 Alkyl Methacrylate Copolymer
Acrylates/C10-30Alkyl Acrylate Crosspolymer
Acrylates/C12-13 Alkyl Methacrylates/Methoxyethyl Acrylate Crosspolymer
Acrylates/C12-22 Alkyl Methacrylate Copolymer
Acrylates/C26-28 Olefin Copolymer
Acrylates/C5-8 Alkyl Acrylate Copolymer
Acrylates/Ceteareth-20 Methacrylate Crosspolymer
Acrylates/Ceteareth-20 Methacrylate Crosspolymer-2
Acrylates/Ceteth-20 Methacrylate Copolymer
Acrylates/Ethylhexyl Acrylate Copolymer
Acrylates/Ethylhexyl Acrylate Crosspolymer
Acrylates/Ethylhexyl Acrylate/Glycidyl Methacrylate Crosspolymer
Acrylates/Hydroxyesters Acrylates Copolymer
Acrylates/Hydroxyethyl Acrylate/Lauryl Acrylate Copolymer
Acrylates/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer
Acrylates/Laureth-25 Methacrylate Copolymer
Acrylates/Lauryl Methacrylate Copolymer
Acrylates/Lauryl Methacrylate/Tridecyl Methacrylate Crosspolymer
Acrylates/Methoxy PEG-4 Methacrylate Copolymer
Acrylates/Methoxy PEG-15 Methacrylate Copolymer
Acrylates/Methoxy PEG-23 Methacrylate Copolymer
Acrylates/Methoxy PEG-90 Methacrylate Crosspolymer
Acrylates/Palmeth-25 Acrylate Copolymer
Acrylates/PEG-4 Dimethacrylate Crosspolymer
Acrylates/Steareth-20 Methacrylate Copolymer
Acrylates/Steareth-20 Methacrylate Crosspolymer
Acrylates/Steareth-30 Methacrylate Copolymer
Acrylates/Steareth-50 Acrylate Copolymer
Acrylates/Stearyl Methacrylate Copolymer
Acrylates/VA Copolymer
Acrylates/VA Crosspolymer
Acrylates/Vinyl Isodecanoate Crosspolymer
Acrylates/Vinyl Neodecanoate Crosspolymer
Acrylic Acid/C12-22 Alkyl Acrylate Copolymer
Acrylic Acid/Stearyl Acrylate Copolymer
Allyl Methacrylate/Glycol Dimethacrylate Crosspolymer
Allyl Methacrylates Crosspolymer
Ammonium Acrylates Copolymer
Ammonium Acrylates/Ethylhexyl Acrylate Copolymer
Ammonium Acrylates/Methyl Styrene/Styrene Copolymer
Ammonium Polyacrylate
Ammonium Styrene/Acrylates Copolymer
Ammonium Styrene/Acrylates/Ethylhexyl Acrylate/Lauryl Acrylate Copolymer
Ammonium VA/Acrylates Copolymer
AMP-Acrylates Copolymer
Behenyl Methacrylate/t-Butyl Methacrylate Copolymer
Butyl Acrylate/Cyclohexyl Methacrylate Copolymer
Butyl Acrylate/Ethylhexyl Methacrylate Copolymer
Butyl Acrylate/Glycol Dimethacrylate Crosspolymer
Butyl Acrylate/Hydroxyethyl Methacrylate Copolymer
Butyl Methacrylate/Acryoyloxy PG Methacrylate Copolymer
C12-22 Alkyl Acrylate/Hydroxyethylacrylate Copolymer
C8-22 Alkyl Acrylates/Methacrylic Acid Crosspolymer
Calcium Potassium Carbomer
Carbomer
Cyclohexyl Methacrylate/Ethylhexyl Methacrylate Copolymer
Ethylene/Acrylic Acid Copolymer
Ethylene/Acrylic Acid/VA Copolymer
Ethylene/Calcium Acrylate Copolymer
Ethylene/Magnesium Acrylate Copolymer
Ethylene/Methacrylate Copolymer
Ethylene/Sodium Acrylate Copolymer
Ethylene/Zinc Acrylate Copolymer
Ethylhexyl Acrylate/Methoxy PEG-23 Methacrylate/Vinyl Acetate Copolymer
Ethylhexyl Acrylate/Methyl Methacrylate Copolymer
Glycol Dimethacrylate Crosspolymer
Glycol Dimethacrylate/Vinyl Alcohol Crosspolymer
Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer
Lauryl Acrylate Crosspolymer
Lauryl Acrylate/VA Copolymer
Lauryl Acrylate/VA Crosspolymer
Lauryl Methacrylate/Glycol Dimethacrylate Crosspolymer
Lauryl Methacrylate/Sodium Methacrylate Crosspolymer
Methacrylic Acid/PEG-6 Methacrylate/PEG-6 Dimethacrylate Crosspolymer
Methacryloyl Ethyl Betaine/Acrylates Copolymer
Methoxy PEG-23 Methacrylate/Glyceryl Diisostearate Methacrylate Copolymer
Methyl Methacrylate Crosspolymer
Methyl Methacrylate/Glycol Dimethacrylate Crosspolymer
Methyl Methacrylate/PEG/PPG-4/3 Methacrylate Crosspolymer
PEG/PPG-5/2 Methacrylate/Methacrylic Acid Crosspolymer
Poly C10-30 Alkyl Acrylate
Poly(Methoxy PEG-9 Methacrylate)
Polyacrylate-14
Polyacrylate-29
Polyacrylate-34
Polyacrylate-1 Crosspolymer
Polyacrylic Acid
Polybutyl Acrylate
Polybutyl Methacrylate
Polyethylacrylate
Polyhydroxyethylmethacrylate
Polyisobutyl Methacrylate
Polymethyl Acrylate
Polymethyl Methacrylate
Polypropyl Methacrylate
Polystearyl Methacrylate
Potassium Acrylate Crosspolymer
Potassium Acrylates Copolymer
Potassium Acrylates/C10-30 Alkyl Acrylate Crosspolymer
Potassium Acrylates/Ethylhexyl Acrylate Copolymer
Potassium Aluminum Polyacrylate
Potassium Carbomer
Potassium Polyacrylate
Sodium Acrylate/Acrolein Copolymer
Sodium Acrylate/Vinyl Alcohol Copolymer
Sodium Acrylates Copolymer
Sodium Acrylates Crosspolymer-2
Sodium Acrylates/Beheneth-25 Methacrylate Crosspolymer
Sodium Acrylates/C10-30 Alkyl Acrylate Crosspolymer
Sodium Acrylates/Ethylhexyl Acrylate Copolymer
Sodium Acrylates/Vinyl Isodecanoate Crosspolymer
Sodium Carbomer
Sodium Polyacrylate
Sodium Polymethacrylate
Steareth-10 Allyl Ether/Acrylates Copolymer
Stearyl/Lauryl Methacrylate Crosspolymer
Styrene/Acrylates/Ammonium Methacrylate Copolymer
VA/Butyl Maleate/Isobornyl Acrylate Copolymer

Ingredients in blue type were included in the original Safety Assessment of Acrylates Copolymer and 33 Related Cosmetic Ingredients[1]
Ingredients in green type were reviewed in the Safety Assessment of Cross-Linked Alkyl Acrylates[2]
Ingredients in pink type were reviewed in the safety assessment of Polymethyl Methacrylate and other ingredients[3]
The ingredient in gray type was reviewed in the safety assessment of Carbomers[4]
Prior to this assessment, the ingredients in black type had not yet been reviewed by CIR

Table 2. Definitions, Structures, and Functions of the ingredients reviewed in this report[5]

Ingredients (CAS Nos.)*	Definitions and Structures	Function(s)
Acrylates Copolymer 159666-35-0; 25035-69-2; 25212-88-8; 25685-29-4	a copolymer of two or more monomers consisting of acrylic acid, methacrylic acid or one of their simple esters	adhesives; artificial nail builders; binders; dispersing agents - nonsurfactant; film formers; hair fixatives; skin-conditioning agents - emollient; skin-conditioning agents - miscellaneous
Acrylates Crosspolymer 26794-61-6; 74464-10-1	a copolymer of acrylic acid, methacrylic acid or one of its simple esters, crosslinked with glycol dimethacrylate	absorbents
Acrylates Crosspolymer-3	a copolymer of acrylic acid, methacrylic acid or one of its simple esters, crosslinked with trimethylolpropane triacrylate and trimethylolpropane diallyl ether	film formers; hair fixatives; viscosity increasing agents - aqueous
Acrylates Crosspolymer-4	a copolymer of acrylic acid, methacrylic acid or one of its simple esters, crosslinked with trimethylolpropane triacrylate	emulsion stabilizers; film formers; surfactants - dispersing agents; viscosity increasing agents - aqueous
Acrylates Crosspolymer-5	a copolymer of acrylic acid, methacrylic acid or one of their simple esters, crosslinked with an allyl ether of pentaerythritol	viscosity increasing agents - aqueous
Acrylates/Ammonium Methacrylate Copolymer	a copolymer of ammonium methacrylate and one or more monomers of acrylic acid, methacrylic acid or one of their simple esters	binders; film formers; hair fixatives
Acrylates/Beheneth-25 Methacrylate Copolymer	a copolymer of the ester of methacrylic acid and Beheneth-25 and one or more monomers of acrylic acid, methacrylic acid, or one of their simple esters	viscosity increasing agents - aqueous
Acrylates/Beheneth-25 Methacrylate/Steareth-30 Methacrylate Copolymer	a copolymer of beheneth-25 methacrylate, steareth-30 methacrylate and one or more monomers consisting of acrylic acid, methacrylic acid or one of their simple esters	film formers
Acrylates/C10-30 Alkyl Methacrylate Copolymer	the copolymer of C10-30 alkyl methacrylate and one or more monomers of acrylic acid, methacrylic acid, or one of their simple esters	viscosity increasing agents - aqueous
Acrylates/C10-30Alkyl Acrylate Crosspolymer	a copolymer of C10-30 alkyl acrylate and one or more monomers of acrylic acid, methacrylic acid or one of their simple esters crosslinked with an allyl ether of sucrose or an allyl ether of pentaerythritol	emulsion stabilizers; viscosity increasing agents - aqueous; viscosity increasing agents - nonaqueous
Acrylates/C12-13 Alkyl Methacrylates/Methoxy-ethyl Acrylate Crosspolymer	a copolymer of C12-13 alkyl methacrylates, methoxyethyl acrylate, and one or more monomers of acrylic acid, methacrylic acid or one of their simple esters, crosslinked with vinyloxazoline	hair fixatives
Acrylates/C12-22 Alkyl Methacrylate Copolymer	the copolymer of C12-22 alkyl methacrylate and one or more monomers of acrylic acid, methacrylic acid, or one of their simple esters	film formers
Acrylates/C26-28 Olefin Copolymer	a polymer of C26-28 olefins and one or more monomers of acrylic acid, methacrylic acid or one of their simple esters	viscosity increasing agents - nonaqueous
Acrylates/C5-8 Alkyl Acrylate Copolymer	copolymer of C5-8 alkyl acrylate and one or more monomers of acrylic acid, methacrylic acid, or one of their simple esters	emulsion stabilizers; film formers; viscosity increasing agents - aqueous
Acrylates/Ceteareth-20 Methacrylate Crosspolymer	copolymer of the ester of methacrylic acid and Ceteareth-20 and one or more monomers of acrylic acid, methacrylic acid, or one of their simple esters, crosslinked with ethylene glycol dimethacrylate	viscosity increasing agents - aqueous
Acrylates/Ceteareth-20 Methacrylate Crosspolymer-2	a copolymer of the ester of methacrylic acid and ceteareth-20 and one or more monomers of acrylic acid, methacrylic acid, or one of their simple esters, crosslinked with diallyl maleate	bulking agents; chelating agents; emulsion stabilizers; opacifying agents; viscosity increasing agents - aqueous
Acrylates/Ceteth-20 Methacrylate Copolymer	a copolymer formed from the ester of methacrylic acid and ceteth-20 , and one or more monomers consisting of acrylic acid, methacrylic acid or one of their simple esters	viscosity increasing agents - aqueous
Acrylates/Ethylhexyl Acrylate Copolymer	a copolymer of ethylhexyl acrylate and one or more monomers of acrylic acid, methacrylic acid or one of their simple esters	film formers
Acrylates/Ethylhexyl Acrylate Crosspolymer	a copolymer of 2-ethylhexylacrylate and one or more monomers of acrylic acid, methacrylic acid or one of their simple esters, crosslinked with ethylene glycol dimethacrylate	binders
Acrylates/Ethylhexyl Acrylate/Glycidyl Methacrylate Crosspolymer	a copolymer of 2-ethylhexyl acrylate, glycidyl methacrylate and one or more monomers consisting of acrylic acid, methacrylic acid or one of their simple esters, crosslinked with triethylene glycol dimethacrylate	film formers

Table 2. Definitions, Structures, and Functions of the ingredients reviewed in this report[5]

Ingredients (CAS Nos.)*	Definitions and Structures	Function(s)
Acrylates/Hydroxyesters Acrylates Copolymer 25035-89-6	a copolymer of one or more monomers consisting of acrylic acid, methacrylic acid, or their simple esters, and one or more monomers of hydroxyacrylate esters	film formers
Acrylates/Hydroxyethyl Acrylate/Lauryl Acrylate Copolymer	a copolymer of hydroxyethyl acrylate, lauryl acrylate, and one or more monomers of acrylic acid, methacrylic acid or one of their simple esters	film formers
Acrylates/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer	a copolymer of hydroxyethyl acrylate, butyl acrylate and methoxyethyl acrylate	film formers
Acrylates/Laureth-25 Methacrylate Copolymer	the copolymer of laureth-25 methacrylate and one or more monomers of acrylic acid, methacrylic acid, or one of their simple esters	viscosity increasing agents - aqueous
Acrylates/Lauryl Methacrylate Copolymer	a copolymer of lauryl methacrylate and one or more monomers consisting of acrylic acid, methacrylic acid or one of their simple esters	film formers
Acrylates/Lauryl Methacrylate/Tridecyl Methacrylate Crosspolymer	a copolymer of lauryl methacrylate, tridecyl methacrylate and one or more monomers consisting of acrylic acid, methacrylic acid or one of their simple esters, crosslinked with vinyloxazoline	film formers
Acrylates/Methoxy PEG-4 Methacrylate Copolymer	a copolymer of methoxy PEG-4 methacrylate and one or more monomers of acrylic acid, methacrylic acid or one of their simple esters	hair conditioning agents
Acrylates/Methoxy PEG-15 Methacrylate Copolymer	a copolymer of methoxy PEG-15 methacrylate and one or more monomers of acrylic acid, methacrylic acid or one of their simple esters	dispersing agents - nonsurfactant
Acrylates/Methoxy PEG-23 Methacrylate Copolymer	a copolymer of methoxy PEG-23 methacrylate and one or more monomers of acrylic acid, methacrylic acid or one of their simple esters	film formers
Acrylates/Methoxy PEG-90 Methacrylate Crosspolymer 957645-61-3	a copolymer of methoxy PEG-90 methacrylate and one or more monomers of acrylic acid, methacrylic acid or one of their simple esters crosslinked by glycol dimethacrylate	skin protectants
Acrylates/Palmeth-25 Acrylate Copolymer	a copolymer of the ester of acrylic acid and ethoxylated palm alcohol with an average of 25 moles of ethylene oxide and one or more monomers of acrylic acid, methacrylic acid or one of their simple esters	viscosity increasing agents - aqueous
Acrylates/PEG-4 Dimethacrylate Crosspolymer 50657-38-0	a copolymer of one or more monomers of acrylic acid, methacrylic acid or one of their simple esters crosslinked by PEG-4 dimethacrylate	film formers
Acrylates/Steareth-20 Methacrylate Copolymer	a copolymer of the ester of methacrylic acid and steareth-20 and one or more monomers of acrylic acid, methacrylic acid or one of their simple esters	viscosity increasing agents - aqueous
Acrylates/Steareth-20 Methacrylate Crosspolymer	a copolymer of steareth-20 methacrylate and one or more monomers consisting of acrylic acid, methacrylic acid or one of their simple esters, crosslinked with an allyl ether of pentaerythritol or an allyl ether of trimethylolpropane	dispersing agents - nonsurfactant; film formers
Acrylates/Steareth-30 Methacrylate Copolymer 75760-37-1	a copolymer of the ester of methacrylic acid and steareth-30 and one or more monomers of acrylic acid, methacrylic acid, or one of their simple esters	viscosity increasing agents - aqueous
Acrylates/Steareth-50 Acrylate Copolymer	a copolymer of the ester of acrylic acid and steareth-50 and one or more monomers of acrylic acid, methacrylic acid or one of their simple esters	viscosity increasing agents - aqueous
Acrylates/Stearyl Methacrylate Copolymer	a copolymer of stearyl methacrylate and one or more monomers of acrylic acid, methacrylic acid or one of their simple esters	emulsion stabilizers; viscosity increasing agents - aqueous
Acrylates/VA Copolymer	a copolymer of vinyl acetate and one or more monomers of acrylic acid, methacrylic acid or one of their simple esters	binders; film formers; hair fixatives
Acrylates/VA Crosspolymer	a copolymer of vinyl acetate and one or more monomers of acrylic acid, methacrylic acid or one of their simple esters crosslinked with triallylisocyanurate	film formers
Acrylates/Vinyl Isodecanoate Crosspolymer	a copolymer of the ester of vinyl isodecanoate and one or more monomers of acrylic acid, methacrylic acid or one of their simple esters crosslinked with polyalkenyl polyether	dispersing agents - nonsurfactant; emulsion stabilizers; viscosity increasing agents - aqueous
Acrylates/Vinyl Neodecanoate Crosspolymer	a copolymer of vinyl neodecanoate and one or more monomers of acrylic acid, methacrylic acid or one of their simple esters crosslinked with an allyl ether of trimethylolpropane or pentaerythritol	emulsion stabilizers; film formers; viscosity increasing agents - aqueous
Acrylic Acid/C12-22 Alkyl Acrylate Copolymer	a copolymer of acrylic acid and C12-22 alkyl acrylate	binders; emulsion stabilizers; viscosity increasing agents - nonaqueous

Table 2. Definitions, Structures, and Functions of the ingredients reviewed in this report[5]

Ingredients (CAS Nos.)*	Definitions and Structures	Function(s)
Acrylic Acid/Stearyl Acrylate Copolymer 36120-03-3	a polymer of acrylic acid and stearyl acrylate monomers	emulsion stabilizers; film formers; surfactants - emulsifying agents
Allyl Methacrylate/Glycol Dimethacrylate Crosspolymer 779327-42-3	a highly crosslinked polymer of allyl methacrylate and ethylene glycol dimethacrylate	oral care agents; skin protectants; skin-conditioning agents - emollient; skin-conditioning agents - miscellaneous
Allyl Methacrylates Crosspolymer 182212-41-5	a copolymer of allyl methacrylates crosslinked with glycol dimethacrylate	emulsion stabilizers; opacifying agents; viscosity increasing agents - nonaqueous
Ammonium Acrylates Copolymer	the ammonium salt of a polymer of two or more monomers consisting of acrylic acid, methacrylic acid or one of their simple esters	binders; film formers; viscosity increasing agents - aqueous
Ammonium Acrylates/Ethylhexyl Acrylate Copolymer	a copolymer of ethylhexyl acrylate and the ammonium salt of one or more monomers consisting of acrylic acid, methacrylic acid, or one of their simple esters	film formers
Ammonium Acrylates/Methyl Styrene/Styrene Copolymer	a copolymer consisting of ammonium acrylate, methyl styrene and styrene monomers	film formers
Ammonium Polyacrylate 9003-03-6	the ammonium salt of Polyacrylic Acid	emulsion stabilizers; film formers
Ammonium Styrene/Acrylates Copolymer	the ammonium salt of a polymer of styrene and a monomer consisting of acrylic acid, methacrylic acid or one of their simple esters	dispersing agents - nonsurfactant; film formers
Ammonium Styrene/Acrylates/Ethylhexyl Acrylate/Lauryl Acrylate Copolymer	ammonium salt of Styrene/Acrylates/Ethylhexyl Acrylate/Lauryl Acrylate Copolymer	film formers
Ammonium VA/Acrylates Copolymer	the ammonium salt of a polymer of vinyl acetate and two or more monomers consisting of acrylic acid, methacrylic acid or their simple ester	binders; dispersing agents - nonsurfactant; film formers; hair fixatives
AMP-Acrylates Copolymer 1203962-19-9	the aminomethyl propanol salt of Acrylates Copolymer	film formers
Behenyl Methacrylate/t-Butyl Methacrylate Copolymer	a copolymer of behenyl methacrylate and t-butyl methacrylate monomers	film formers
Butyl Acrylate/Cyclohexyl Methacrylate Copolymer	a copolymer of butyl acrylate and cyclohexyl methacrylate	film formers
Butyl Acrylate/Ethylhexyl Methacrylate Copolymer	a copolymer of butyl acrylate and 2-ethylhexyl methacrylate monomers	film formers; hair fixatives
Butyl Acrylate/Glycol Dimethacrylate Crosspolymer	a homopolymer of butyl acrylate crosslinked with glycol dimethacrylate	absorbents; film formers
Butyl Acrylate/Hydroxyethyl Methacrylate Copolymer	a copolymer consisting of n-butyl acrylate and 2-hydroxyethyl methacrylate monomers	film formers
Butyl Methacrylate/Acryoyloxy PG Methacrylate Copolymer 1431551-12-0	a polymer of butyl methacrylate and acryloyloxy propylene glycol methacrylate monomers	film formers
C12-22 Alkyl Acrylate/Hydroxyethylacrylate Copolymer	a copolymer of C12-22 alkyl acrylate and hydroxyethylacrylate	binders; emulsion stabilizers; viscosity increasing agents - nonaqueous
C8-22 Alkyl Acrylates/Methacrylic Acid Crosspolymer	a copolymer of C8-22 alkyl acrylate and methacrylic acid crosslinked with hexanediol diacrylate	film formers; hair fixatives; hair-waving/straightening agents
Calcium Potassium Carbomer	the calcium potassium salt of Carbomer	emulsion stabilizers; film formers; viscosity increasing agents - aqueous
Carbomer 9003-01-4; 9007-16-3; 9007-17-4; 9062-04-8; 76050-42-5	a homopolymer of acrylic acid crosslinked with an allyl ether of pentaerythritol, an allyl ether of sucrose, or an allyl ether of propylene	emulsion stabilizers; viscosity increasing agents - aqueous
Cyclohexyl Methacrylate/Ethylhexyl Methacrylate Copolymer 82227-04-1	a copolymer of cyclohexyl methacrylate and ethylhexyl methacrylate	film formers
Ethylene/Acrylic Acid Copolymer 9010-77-9	a copolymer of ethylene and acrylic acid monomers	binders; film formers; viscosity increasing agents - nonaqueous
Ethylene/Acrylic Acid/VA Copolymer 26713-18-8	a copolymer of ethylene, acrylic acid and vinyl acetate monomers	binders; film formers; viscosity increasing agents - nonaqueous
Ethylene/Calcium Acrylate Copolymer 26445-96-5	a copolymer of ethylene and calcium acrylate monomers	binders; film formers
Ethylene/Magnesium Acrylate Copolymer 27515-37-3	a copolymer of ethylene and magnesium acrylate monomers	binders; film formers
Ethylene/Methacrylate Copolymer 25103-74-6	a copolymer of ethylene and methyl methacrylate monomers	film formers
Ethylene/Sodium Acrylate Copolymer 25749-98-8; 25750-82-7	a copolymer of ethylene and sodium acrylate monomers	binders; film formers; viscosity increasing agents - aqueous

Table 2. Definitions, Structures, and Functions of the ingredients reviewed in this report[5]

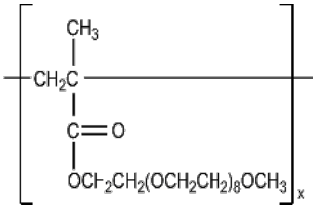
Ingredients (CAS Nos.)*	Definitions and Structures	Function(s)
Ethylene/Zinc Acrylate Copolymer 28208-80-2; 59650-68-9	a copolymer of ethylene and zinc acrylate monomers	film formers
Ethylhexyl Acrylate/Methoxy PEG-23 Methacrylate/Vinyl Acetate Copolymer 137455-77-7	a copolymer of methoxy PEG-23 methacrylate, vinyl acetate, and ethylhexyl acrylate	hair fixatives
Ethylhexyl Acrylate/Methyl Methacrylate Copolymer	a copolymer of ethylhexyl acrylate and methyl methacrylate	film formers
Glycol Dimethacrylate Crosspolymer	a crosslinked polymer of glycol dimethacrylate	slip modifier
Glycol Dimethacrylate/Vinyl Alcohol Crosspolymer	a crosslinked copolymer of vinyl alcohol and glycol dimethacrylate	film formers
Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer	the copolymer of hydroxyethyl acrylate and methoxyethyl acrylate	film formers
Lauryl Acrylate Crosspolymer	a polymer of lauryl acrylate crosslinked with divinylbenzene	hair fixatives
Lauryl Acrylate/VA Copolymer	a copolymer of lauryl acrylate and vinyl acetate monomers	film formers
Lauryl Acrylate/VA Crosspolymer	a copolymer of lauryl acrylate and vinyl acetate crosslinked with divinylbenzene	abrasives
Lauryl Methacrylate/Glycol Dimethacrylate Crosspolymer	a crosslinked copolymer of lauryl methacrylate and ethylene glycol dimethacrylate monomers	film formers; hair fixatives
Lauryl Methacrylate/Sodium Methacrylate Crosspolymer	a copolymer of lauryl methacrylate and sodium methacrylate crosslinked with ethylene glycol dimethacrylate	slip modifiers; surface modifiers
Methacrylic Acid/PEG-6 Methacrylate/PEG-6 Dimethacrylate Crosspolymer	a copolymer of methacrylic acid and PEG-6 methacrylate crosslinked with PEG-6 dimethacrylate	film formers
Methacryloyl Ethyl Betaine/Acrylates Copolymer	a polymer of methacryloyl ethyl betaine and two or more monomers of methacrylic acid or its simple esters	dispersing agents - nonsurfactant; film formers; hair fixatives
Methoxy PEG-23 Methacrylate/Glyceryl Diisostearate Methacrylate Copolymer	a copolymer of methoxy PEG-23 methacrylate and glyceryl diisostearate methacrylate monomers	skin protectants
Methyl Methacrylate Crosspolymer 25777-71-3	a copolymer of methyl methacrylate crosslinked with glycol dimethacrylate	bulking agent; film former; viscosity increasing agent - nonaqueous
Methyl Methacrylate/Glycol Dimethacrylate Crosspolymer 25777-71-3	a crosslinked copolymer of methyl methacrylate and ethylene glycol dimethacrylate monomers	film formers
Methyl Methacrylate/PEG/PPG-4/3 Methacrylate Crosspolymer	a random copolymer of methyl methacrylate and PEG/PPG-4/3 methacrylate crosslinked with ethylene glycol dimethacrylate	film formers
PEG/PPG-5/2 Methacrylate/Methacrylic Acid Crosspolymer	copolymer of methacrylic acid and polyethylene glycol, polypropylene glycol methacrylate containing an average of 5 moles of ethylene oxide and 2 moles of propylene oxide, crosslinked with glycol dimethacrylate	film formers
Poly C10-30 Alkyl Acrylate	a polymer of the ester of acrylic acid and C10-30 alcohol	binders; emulsion stabilizers; viscosity increasing agents - nonaqueous
Poly(Methoxy PEG-9 Methacrylate)	the polymer that conforms generally to the formula: 	film formers; skin-conditioning agents - humectant; skin-conditioning agents - occlusive
Polyacrylate-14	a copolymer of PEG-25 C10-30 alkyl ether methacrylate, PEG-20 PPG-5 allyl ether and one or more monomers consisting of acrylic acid, methacrylic acid or one of their simple esters	film former
Polyacrylate-29	A copolymer of stearyl methacrylate, methoxy PEG-9 methacrylate and methacrylic acid	film formers; skin-conditioning agents - miscellaneous; surfactants - emulsifying agents
Polyacrylate-34	a copolymer of octoxy PEG-8 PPG-6 methacrylate, PPG-9 methacrylate, PPG-6 acrylate and 2-methoxyethylacrylate monomers	hair fixative
Polyacrylate-1 Crosspolymer	a copolymer of one or more simple esters of acrylic or methacrylic acid, C1-4 dialkylamino C1-6 alkyl methacrylate, PEG/PPG-30/5 allyl ether, PEG 20-25 C10-30 alkyl ether methacrylate, hydroxy C2-6 alkyl methacrylate crosslinked with ethylene glycol dimethacrylate	film formers; hair conditioning agents; hair fixatives; viscosity increasing agents - aqueous

Table 2. Definitions, Structures, and Functions of the ingredients reviewed in this report[5]

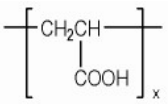
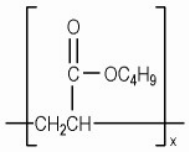
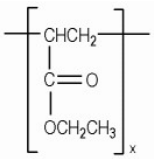
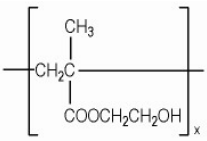
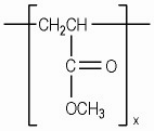
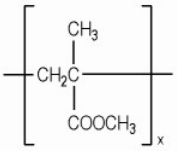
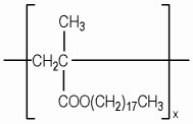
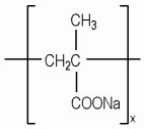
Ingredients (CAS Nos.)*	Definitions and Structures	Function(s)
Polyacrylic Acid 9003-01-4	the polymer of acrylic acid that conforms generally to the formula: 	binders; emulsion stabilizers; film formers; viscosity increasing agents - aqueous
Polybutyl Acrylate 9003-49-0	a polymer of n-butyl acrylate that conforms generally to the formula: 	binders; film formers
Polybutyl Methacrylate 9003-63-8	the homopolymer of butyl methacrylate	film formers
Polyethylacrylate 9003-32-1	the polymer of ethyl acrylate that conforms generally to the formula: 	binders; dispersing agents - nonsurfactant; film formers; hair fixatives
Polyhydroxyethylmethacrylate 25249-16-5	the organic compound that conforms to the formula: 	binders
Polyisobutyl Methacrylate 9011-15-8	the homopolymer of isobutyl methacrylate	film formers
Polymethyl Acrylate 9003-21-8	the polymer that conforms to the formula: 	film formers
Polymethyl Methacrylate 9011-14-7	the polymer of methyl methacrylate that conforms to the formula: 	bulking agents; film formers
Polypropyl Methacrylate	the homopolymer of propyl acrylate	film formers
Polystearyl Methacrylate	the polymer of stearyl methacrylate that conforms to the formula: 	film formers
Potassium Acrylate Crosspolymer 86416-97-9 (sodium salt)	the potassium salt of a polymer of acrylic acid crosslinked with *N*,*N*'-methylenebisacrylamide	absorbents; slip modifiers
Potassium Acrylates Copolymer	the potassium salt of a polymer consisting of acrylic acid, methacrylic acid or one of their simple esters	binders; film formers
Potassium Acrylates/C10-30 Alkyl Acrylate Crosspolymer	the potassium salt of Acrylates/C10-30 Alkyl Acrylate Crosspolymer	film formers
Potassium Acrylates/Ethylhexyl Acrylate Copolymer	the potassium salt of Acrylates/Ethylhexyl Acrylate Copolymer	film formers
Potassium Aluminum Polyacrylate	a mixture of the potassium and aluminum salts of Polyacrylic Acid	absorbents; binders; viscosity increasing agents - aqueous
Potassium Carbomer	the sodium salt of Carbomer	emulsion stabilizers; film formers; viscosity increasing agents - aqueous

Table 2. Definitions, Structures, and Functions of the ingredients reviewed in this report[5]

Ingredients (CAS Nos.)*	Definitions and Structures	Function(s)
Potassium Polyacrylate 25608-12-2	the potassium salt of Polyacrylic Acid	emulsion stabilizers; viscosity increasing agents - aqueous
Sodium Acrylate/Acrolein Copolymer	a polymer consisting of sodium acrylate and acrolein monomers	binders; film formers; viscosity increasing agents - aqueous
Sodium Acrylate/Vinyl Alcohol Copolymer 27599-56-0; 58374-38-2	a polymer of sodium acrylate and vinyl alcohol monomers	binders; emulsion stabilizers; film formers; viscosity increasing agents - aqueous
Sodium Acrylates Copolymer 25549-84-2	the sodium salt of a polymer consisting of acrylic acid, methacrylic acid or one of their simple esters	binders; film formers; viscosity increasing agents - aqueous
Sodium Acrylates Crosspolymer-2	the sodium salt of a copolymer of acrylic acid, methacrylic acid or one or more of its simple esters crosslinked with ethylene glycol diglycidyl ether	absorbents
Sodium Acrylates/Beheneth-25 Methacrylate Crosspolymer	the sodium salt of a copolymer of acrylic acid, methacrylic acid or one or more of its simple esters and beheneth-25 methacrylate, crosslinked with methylene bis-acrylamide	dispersing agents - nonsurfactant; skin-conditioning agents - miscellaneous; viscosity increasing agents - aqueous
Sodium Acrylates/C10-30 Alkyl Acrylate Crosspolymer	the sodium salt of Acrylates/C10-30 Alkyl Acrylate Crosspolymer	film formers
Sodium Acrylates/Ethylhexyl Acrylate Copolymer	a copolymer of ethylhexyl acrylate and the sodium salt of one or more monomers consisting of acrylic acid, methacrylic acid or one of their simple esters	film formers
Sodium Acrylates/Vinyl Isodecanoate Crosspolymer	the sodium salt of Acrylates/Vinyl Isodecanoate Crosspolymer	dispersing agents - nonsurfactant; emulsion stabilizers; viscosity increasing agents - aqueous
Sodium Carbomer 1401207-41-7; 73298-57-4	sodium salt of Carbomer	emulsion stabilizers; film formers; viscosity increasing agents - aqueous
Sodium Polyacrylate 25549-84-2; 9003-04-7	the sodium salt of Polyacrylic Acid	absorbent; emulsion stabilizer; film former; hair fixative; skin-conditioning agent - emollient; viscosity increasing agent - aqueous
Sodium Polymethacrylate 25086-62-8; 54193-36-1	the polymer that conforms generally to the formula:  	binders; emulsion stabilizers; film formers; viscosity increasing agents - aqueous
Steareth-10 Allyl Ether/Acrylates Copolymer 109292-17-3	a copolymer of the allyl ether of steareth-10 and one or more monomers consisting of acrylic acid, methacrylic acid or one of their simple esters	film formers; viscosity increasing agents - nonaqueous
Stearyl/Lauryl Methacrylate Crosspolymer	a copolymer of stearyl methacrylate and lauryl methacrylate crosslinked with ethylene glycol dimethacrylate	skin-conditioning agents - miscellaneous
Styrene/Acrylate/Ammonium Methacrylate Copolymer	a polymer of styrene, ammonium methacrylate and a monomer consisting of acrylic acid, methacrylic acid or one of their simple esters	dispersing agents - nonsurfactant; film formers
VA/Butyl Maleate/Isobornyl Acrylate Copolymer	a copolymer of vinyl acetate, butyl maleate and isobornyl acrylate monomers	film formers

***Ingredients in blue type were included in the original Safety Assessment of Acrylates Copolymer and 33 Related Cosmetic Ingredients[1]**
Ingredients in green type were reviewed in the Safety Assessment of Cross-Linked Alkyl Acrylates[2]
Ingredients in pink type were reviewed in the safety assessment of Polymethyl Methacrylate and other ingredients[3]
The ingredient in gray type was reviewed in the safety assessment of Carbomers[4]
Prior to this assessment, the ingredients in black type had not yet been reviewed by CIR

Table 3. Physical and Chemical Properties

Property	Value	Reference
Acrylates Copolymer		
Physical Form	white beads [as 2-propenoic acid, 2-methyl-, polymer with butyl 2-methyl-2-propenoate, ethyl 2-methyl-2-propenoate and ethyl 2-propenoate] liquid in commercial form; forms a film when dried	13 15,16
Color	milky white	15,16
Odor	"characteristic"	15,16
Molecular Weight (g/mol)	100,000 (wt avg) [as 2-propenoic acid, 2-methyl-, polymer with butyl 2-methyl-2-propenoate, ethyl 2-methyl-2-propenoate and ethyl 2-propenoate] 600,000 (avg) [as a fully polymerized copolymer of methyl methacrylate and ethyl acrylate] 280,000 (avg) [as a fully polymerized copolymer of methyl acrylate, methyl methacrylate, and methacrylic acid]	13 15 16
Density/Specific Gravity (@ 20 ºC)	1.37 – 1.047 [as a fully polymerized copolymer of methyl methacrylate and ethyl acrylate]	17
Water Solubility (g/L)	miscible in water	15,16
Acrylates/Beheneth-25 Methacrylate Copolymer		
Physical Form	opaque flowing dispersion	10
Color	white	10
Melting Point (ºC)	> 100	10
Water Solubility (@ pH 2 – 3) (@ pH 6 – 8)	insoluble soluble	10
Acrylates/C12-22 Alkyl Methacrylate Copolymer		
Physical Form	aq. emulsion	9
Odor	acrylic	9
Water Solubility (g/L @ 20 ºC)	1000	9
Acrylates/Hydroxyesters Acrylates Copolymer		
Physical Form	emulsion	33
Color	white	14
Molecular Weight (g/mol)	~ 60,000	33
Acrylates/Palmeth-25 Acrylate Copolymer		
Physical Form	opaque emulsion	11
Color	white	11
Water Solubility (g/L @ 20 ºC)	1000	11
Acrylates/Steareth-20 Methacrylate Copolymer		
Physical Form	liquid	18
Color	milky white	18
Polyacrylate-1 Crosspolymer		
Physical Form	solid	12
Color	pale brown	12
Density (kg/m^3 @ 25 ºC)	1160	12
Melting Point (ºC)	47.35	12
VA/Butyl Maleate/Isobornyl Acrylate Copolymer in ethanol		
Physical Form	clear viscous liquid	8
Odor	ethanolic	8
Molecular Weight (g/mol)	79,000 – 154,000 (wt avg)	8
Vapor pressure (mmHg @ 20ºC)	44.48	8
Water Solubility (g/L)	< 1; if the ethanol is allowed to evaporate, the remaining polymer is stated to be water insoluble	8

Table 4. Current and historical (where applicable) frequency and concentration of use, according to duration and exposure

	# of Uses		Max Conc of Use (%)		# of Uses		Max Conc of Use (%)	
	Acrylates Copolymer				Acrylates Crosspolymer			
	2018[24]	1998[1]	2018[19]	1998[1]	2018[24]	2011[2]	2018[21]	2011[2]
Totals*	**3177**	**227**	**0.00025-98.6**	**	**5**	**2**	**0.15-4.5**	**0.1-4**
Duration of Use								
Leave-On	*2050*	*207*	*0.00025-98.6*	**	*5*	*2*	*1-4.5*	*0.1-4*
Rinse-Off	*1106*	*20*	*0.00052-4.2*	**	*NR*	*NR*	*0.15-2.7*	*0.3-0.8*
Diluted for (Bath) Use	*21*	*NR*	*0.9-2.4*	**	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	702	33	0.00025-18.4	**	1	NR	1	0.8
Incidental Ingestion	453	36	0.0003-3	**	NR	NR	NR	4
Incidental Inhalation-Spray	53; 107[a]; 58[b]	3; 5[a]; 3[b]	0.36-4.9; 0.12-2.6[a]	**	1[a]; 2[b]	NR	NR	NR
Incidental Inhalation-Powder	45; 58[b]	35; 3[b]	0.015-1.4; 0.045-25[c]	**	2[b]	NR	NR	2
Dermal Contact	1884	104	0.00025-25	**	4	2	1-4.5	0.1-4
Deodorant (underarm)	2[a]	3[a]	NR	**	NR	NR	NR	NR
Hair - Non-Coloring	184	3	0.00052-4.9	**	NR	NR	NR	NR
Hair-Coloring	17	14	0.36-3.6	**	NR	NR	0.15	NR
Nail	436	53	0.54-98.6	**	1	NR	NR	NR
Mucous Membrane	1297	36	0.0003-4.2	**	NR	NR	2.2-2.7	4
Baby Products	14	NR	0.26-1.4	**	NR	NR	NR	NR
	Acrylates Crosspolymer-3				Acrylates Crosspolymer-4			
	2018[24]		2018[20]		2018[24]		2018[20]	
Totals*	**4**		**1.6**		**16**		**3.1**	
Duration of Use								
Leave-On	*3*		*1.6*		*NR*		*3.1*	
Rinse-Off	*1*		*NR*		*16*		*NR*	
Diluted for (Bath) Use	*NR*		*NR*		*NR*		*NR*	
Exposure Type								
Eye Area	1		NR		NR		NR	
Incidental Ingestion	NR		NR		NR		NR	
Incidental Inhalation-Spray	2[a]		1.6[a]		NR		NR	
Incidental Inhalation-Powder	NR		NR		NR		3.1[c]	
Dermal Contact	NR		NR		16		NR	
Deodorant (underarm)	NR		NR		NR		NR	
Hair - Non-Coloring	3		1.6		NR		NR	
Hair-Coloring	NR		NR		NR		NR	
Nail	NR		NR		NR		NR	
Mucous Membrane	NR		NR		16		NR	
Baby Products	NR		NR		NR		NR	
	Acrylates/Ammonium Methacrylate Copolymer				Acrylates/Beheneth-25 Methacrylate Copolymer			
	2018[24]	1998[1]	2018[19]	1998[1]	2018[24]		2018[20]	
Totals*	**26**	**1**	**0.00063-10**	**	**91**		**0.05-1.7**	
Duration of Use								
Leave-On	*11*	*1*	*0.002-10*	**	*53*		*0.3-1.7*	
Rinse-Off	*15*	*NR*	*0.00063-0.0025*	**	*37*		*0.05-1*	
Diluted for (Bath) Use	*NR*	*NR*	*NR*	**	*1*		*NR*	
Exposure Type								
Eye Area	NR	1	NR	**	NR		NR	
Incidental Ingestion	1	NR	NR	**	NR		NR	
Incidental Inhalation-Spray	4[a]; 3[b]	NR	NR	**	48[a]		1.7; 0.95-1.1[a]	
Incidental Inhalation-Powder	3[b]	NR	0.002[c]	**	NR		0.3-0.8[c]	
Dermal Contact	25	NR	0.00063-0.005	**	34		0.3-8	
Deodorant (underarm)	NR	NR	NR	**	NR		NR	
Hair - Non-Coloring	NR	NR	NR	**	46		0.05-1.7	
Hair-Coloring	NR	NR	NR	**	11		0.2-1	
Nail	NR	NR	10	**	NR		NR	
Mucous Membrane	7	NR	0.00062	**	10		NR	
Baby Products	NR	NR	NR	**	NR		NR	

Table 4. Current and historical (where applicable) frequency and concentration of use, according to duration and exposure

	# of Uses		Max Conc of Use (%)		# of Uses		Max Conc of Use (%)	
	Acrylates/C10-30 Alkyl Methacrylate Copolymer				**Acrylates/C10-30Alkyl Acrylate Crosspolymer (†polymerized in solvents other than benzene)**			
	2018[24]		**2018[20]**		**2018[24]**	**2011[2] †**	**2018[21] †**	**2011[2] †**
Totals*	**NR**		**0.0001-1.1**		**3135**	**1696**	**0.000045-3**	**0.0002-5**
Duration of Use								
Leave-On	*NR*		*0.0001-1.1*		*2577*	*1365*	*0.000045-3*	*0.0002-5*
Rinse-Off	*NR*		*0.0005-0.001*		*546*	*313*	*0.1-1.8*	*0.002-5*
Diluted for (Bath) Use	*NR*		*NR*		*12*	*18*	*0.15*	*1*
Exposure Type								
Eye Area	NR		NR		215	132	0.12-0.9	0.003-2
Incidental Ingestion	NR		NR		1	3	0.6	0.5
Incidental Inhalation-Spray	NR		0.0001		176; 1167[a]; 770[b]	70[a]	0.08-2; 0.11-0.2[a]	0.03-2
Incidental Inhalation-Powder	NR		NR		77[b]; 4[c]	6	0.000045-0.6; 0.07-2[c]	0.0002-0.1
Dermal Contact	NR		0.15-0.3		2992	1591	0.000045-3	0.0002-5
Deodorant (underarm)	NR		NR		3[a]	1[a]	0.15-0.5 (not spray) 0.2 (spray)	0.001[a]
Hair - Non-Coloring	NR		0.0001-1.1		95	77	0.19-2	0.1-2
Hair-Coloring	NR		NR		35	11	0.19-1.8	0.4-5
Nail	NR		NR		8	9	0.05-1	0.1-1
Mucous Membrane	NR		NR		175	111	0.15-0.6	0.002-3
Baby Products			0.15		17	10	0.3	0.2
	Acrylates/C12-22 Alkyl Methacrylate Copolymer				**Acrylates/Ethylhexyl Acrylate Copolymer**			
	2018[24]		**2018[20]**		**2018[24]**		**2018[20]**	
Totals*	**9**		**0.23-1.4**		**60**		**0.25-30**	
Duration of Use								
Leave-On	*9*		*0.23-1.4*		*60*		*0.25-30*	
Rinse-Off	*NR*		*NR*		*NR*		*NR*	
Diluted for (Bath) Use	*NR*		*NR*		*NR*		*NR*	
Exposure Type								
Eye Area	1		0.23		53		0.9-30	
Incidental Ingestion	NR		NR		NR		NR	
Incidental Inhalation-Spray	5[a]; 1[b]		1; 0.9[a]		NR		NR	
Incidental Inhalation-Powder	1[b]		0.45-1.4[c]		NR		0.25[c]	
Dermal Contact	9		0.23-1.4		19		0.25-20.1	
Deodorant (underarm)	NR		NR		NR		NR	
Hair - Non-Coloring	NR		NR		NR		NR	
Hair-Coloring	NR		NR		NR		NR	
Nail	NR		NR		2		NR	
Mucous Membrane	NR		NR		NR		NR	
Baby Products	NR		NR		NR		NR	
	Acrylates/Ethylhexyl Acrylate Crosspolymer				**Acrylates/Hydroxyesters Acrylates Copolymer**			
	2018[24]	**2011[2]**	**2018[21]**	**2011[2]**	**2018[24]**	**1998[1]**	**2018[19]**	**1998[1]**
Totals*	**3**	**NR**	**1-5.4**	**4-6**	**35**	**NR**	**0.71-6**	**
Duration of Use								
Leave-On	*3*	*NR*	*1-5.4*	*4-6*	*30*	*NR*	*0.71-6*	**
Rinse-Off	*NR*	*NR*	*NR*	*NR*	*5*	*NR*	*NR*	**
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	**
Exposure Type								
Eye Area	NR	NR	NR	6	8	NR	0.8	**
Incidental Ingestion	1	NR	NR	NR	NR	NR	NR	**
Incidental Inhalation-Spray	NR	NR	NR	NR	15; 5[a]; 1[b]	NR	0.71-6	**
Incidental Inhalation-Powder	NR	NR	1-3.1; 4.5[c]	NR	NR	NR	NR	**
Dermal Contact	NR	NR	1-5.4	4-6	2	NR	NR	**
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	**
Hair - Non-Coloring	NR	NR	NR	NR	25	NR	0.71-6	**
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	**
Nail	2	NR	NR	NR	NR	NR	NR	**
Mucous Membrane	1	NR	NR	NR	NR	NR	NR	**
Baby Products	NR	NR	NR	NR	NR	NR	NR	**

Table 4. Current and historical (where applicable) frequency and concentration of use, according to duration and exposure

	# of Uses		Max Conc of Use (%)		# of Uses		Max Conc of Use (%)	
	Acrylates/Methoxy PEG-23 Methacrylate Copolymer				**Acrylates/Palmeth-25 Acrylate Copolymer**			
	2018[24]		**2018[20]**		**2018[24]**		**2018[20]**	
Totals*	**NR**		**0.4-1.4**		**9**		**0.53-1.3**	
Duration of Use								
Leave-On	*NR*		*0.4-1.4*		*2*		*NR*	
Rinse-Off	*NR*		*NR*		*7*		*0.53-1.3*	
Diluted for (Bath) Use	*NR*		*NR*		*NR*		*NR*	
Exposure Type								
Eye Area	NR		NR		NR		NR	
Incidental Ingestion	NR		NR		NR		NR	
Incidental Inhalation-Spray	NR		1.4; 0.4[a]		1[b]		NR	
Incidental Inhalation-Powder	NR		NR		1[b]		NR	
Dermal Contact	NR		NR		6		1.3	
Deodorant (underarm)	NR		NR		NR		NR	
Hair - Non-Coloring	NR		0.4-1.4		NR		NR	
Hair-Coloring	NR		NR		3		0.53	
Nail	NR		NR		NR		NR	
Mucous Membrane	NR		NR		2		NR	
Baby Products	NR		NR		NR		NR	
	Acrylates/Steareth-20 Methacrylate Copolymer				**Acrylates/Steareth-20 Methacrylate Crosspolymer**			
	2018[24]	**1998[1]**	**2018[19]**	**1998[1]**	**2018[24]**	**2011[2]**	**2018[21]**	**2011[2]**
Totals*	**65**	**35**	**0.06-2**	**	**4**	**NR**	**0.37-2.3**	**0.1-2**
Duration of Use								
Leave-On	*22*	*10*	*0.06-0.5*	**	*2*	*NR*	*2.3*	*0.1-2*
Rinse-Off	*43*	*24*	*0.3-2*	**	*2*	*NR*	*0.37-1.6*	*1*
Diluted for (Bath) Use	*NR*	*1*	*NR*	**	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	2	NR	0.11-0.21	**	NR	NR	NR	NR
Incidental Ingestion	1	NR	NR	**	NR	NR	NR	NR
Incidental Inhalation-Spray	2; 4[a]; 9[b]	2; 7[a]	0.06-0.5	**	1[a]; 1[b]	NR	2.3[a]	NR
Incidental Inhalation-Powder	9[b]	NR	0.09[c]	**	1[b]	NR	NR	NR
Dermal Contact	36	14	0.06-1.8	**	1	NR	1.6	0.1-1
Deodorant (underarm)	NR	NR	NR	**	NR	NR	NR	NR
Hair - Non-Coloring	19	15	0.45-0.5	**	1	NR	2.3	2
Hair-Coloring	9	5	0.54-2	**	2	NR	0.37	NR
Nail	NR	1	NR	**	NR	NR	NR	NR
Mucous Membrane	7	2	0.3	**	NR	NR	NR	1
Baby Products	1	2	NR	**	NR	NR	NR	NR
	Acrylates/Steareth-30 Methacrylate Copolymer				**Acrylates/Stearyl Methacrylate Copolymer**			
	2018[24]		**2018[20]**		**2018[24]**		**2018[20]**	
Totals*	**NR**		**0.03-2.1**		**NR**		**0.014-0.04**	
Duration of Use								
Leave-On	*NR*		*0.03-0.87*		*NR*		*0.014-0.04*	
Rinse-Off	*NR*		*1.8-2.1*		*NR*		*0.02-0.04*	
Diluted for (Bath) Use	*NR*		*NR*		*NR*		*NR*	
Exposure Type								
Eye Area	NR		0.03		NR		NR	
Incidental Ingestion	NR		NR		NR		NR	
Incidental Inhalation-Spray	NR		0.2-0.6; 0.87[a]		NR		0.014-0.04[a]	
Incidental Inhalation-Powder	NR		NR		NR		NR	
Dermal Contact	NR		0.15-2.1		NR		0.04	
Deodorant (underarm)	NR		NR		NR		NR	
Hair - Non-Coloring	NR		0.2-0.87		NR		0.014-0.04	
Hair-Coloring	NR		NR		NR		NR	
Nail	NR		NR		NR		NR	
Mucous Membrane	NR		2.1		NR		NR	
Baby Products	NR		NR		NR		NR	

Table 4. Current and historical (where applicable) frequency and concentration of use, according to duration and exposure

	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	Acrylates/VA Copolymer				**Acrylates/VA Crosspolymer**			
	2018[24]	**1998[1]**	**2018[19]**	**1998[1]**	**2018[24]**		**2018[20]**	
Totals*	**1**	**NR**	**2.5-50**	**	**1**		**25**	
Duration of Use								
Leave-On	*1*	*NR*	*2.5-50*	**	*1*		*25*	
Rinse-Off	*NR*	*NR*	*NR*	**	*NR*		*NR*	
Diluted for (Bath) Use	*NR*	*NR*	*NR*	**	*NR*		*NR*	
Exposure Type								
Eye Area	1	NR	2.5	**	NR		NR	
Incidental Ingestion	NR	NR	NR	**	NR		NR	
Incidental Inhalation-Spray	NR	NR	NR	**	NR		NR	
Incidental Inhalation-Powder	NR	NR	NR	**	NR		NR	
Dermal Contact	NR	NR	50	**	NR		NR	
Deodorant (underarm)	NR	NR	NR	**	NR		NR	
Hair - Non-Coloring	NR	NR	NR	**	NR		NR	
Hair-Coloring	NR	NR	NR	**	NR		NR	
Nail	NR	NR	NR	**	1		25	
Mucous Membrane	NR	NR	NR	**	NR		NR	
Baby Products	NR	NR	NR	**	NR		NR	
	Acrylates/Vinyl Isodecanoate Crosspolymer				**Acrylates/Vinyl Neodecanoate Crosspolymer**			
	2018[24]	**2011[2]**	**2018[21]**	**2011[2]**	**2018[24]**	**2011[2]**	**2018[21]**	**2011[2]**
Totals*	**30**	**33**	**0.2-0.4**	**0.2-0.5**	**14**	**10**	**NR**	**2**
Duration of Use								
Leave-On	*22*	*25*	*0.25-0.4*	*0.3-0.5*	*3*	*4*	*NR*	*2*
Rinse-Off	*8*	*8*	*0.2*	*0.2-0.5*	*5*	*4*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*6*	*2*	*NR*	*NR*
Exposure Type								
Eye Area	1	NR	NR	NR	1	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	8[a]; 10[b]	NR	0.34-0.4[a]	0.4	2[a]	NR	NR	NR
Incidental Inhalation-Powder	10[b]	NR	0.25[c]	NR	NR	NR	NR	NR
Dermal Contact	30	33	0.2-.0.4	0.2-0.5	14	10	NR	2
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	NR	NR	NR	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	10	6	NR	2
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR
	Acrylic Acid/Stearyl Acrylate Copolymer				**Allyl Methacrylates Crosspolymer**			
	2018[24]		**2018[20]**		**2018[24]**	**2011[2]**	**2018[21]**	**2011[2]**
Totals*	**NR**		**0.1-2**		**31**	**48**	**0.0034-2**	**0.003-2**
Duration of Use								
Leave-On	*NR*		*0.1-2*		*27*	*44*	*0.0034-2*	*0.003-2*
Rinse-Off	*NR*		*0.25*		*4*	*4*	*0.075-1*	*0.1*
Diluted for (Bath) Use	*NR*		*NR*		*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	NR		NR		NR	4	0.0034	4
Incidental Ingestion	NR		NR		7	16	0.034	16
Incidental Inhalation-Spray	NR		0.1; 2[a]		7[a]; 4[b]	2[a]	1[a]	2[a]
Incidental Inhalation-Powder	NR		NR		4[b]	2	2; 0.4-2[c]	2
Dermal Contact	NR		NR		23	31	0.0034-2	31
Deodorant (underarm)	NR		NR		NR	NR	NR	NR
Hair - Non-Coloring	NR		0.1-2		1	NR	NR	NR
Hair-Coloring	NR		NR		NR	NR	NR	NR
Nail	NR		NR		NR	NR	NR	NR
Mucous Membrane	NR		NR		7	16	0.034	16
Baby Products	NR		NR		NR	NR	NR	NR

Table 4. Current and historical (where applicable) frequency and concentration of use, according to duration and exposure

	# of Uses		Max Conc of Use (%)		# of Uses		Max Conc of Use (%)	
	Ammonium Acrylates Copolymer				**Ammonium Acrylates/Methyl Styrene/Styrene Copolymer**			
	2018[24]	**1998[1]**	**2018[19]**	**1998[1]**	**2018[24]**		**2018[20]**	
Totals*	**60**	**21**	**0.0057-19.5**	**	**5**		**0.9**	
Duration of Use								
Leave-On	*60*	*21*	*0.3-19.5*	**	*5*		*0.9*	
Rinse-Off	*NR*	*NR*	*0.0057-0.046*	**	*NR*		*NR*	
Diluted for (Bath) Use	*NR*	*NR*	*NR*	**	*NR*		*NR*	
Exposure Type								
Eye Area	47	21	0.8-19.5	**	5		0.9	
Incidental Ingestion	NR	NR	NR	**	NR		NR	
Incidental Inhalation-Spray	1[b]	NR	NR	**	NR		NR	
Incidental Inhalation-Powder	1[b]	NR	NR	**	NR		NR	
Dermal Contact	20	3	0.0057-19.5	**	5		0.9	
Deodorant (underarm)	NR	NR	NR	**	NR		NR	
Hair - Non-Coloring	NR	NR	NR	**	NR		NR	
Hair-Coloring	NR	NR	NR	**	NR		NR	
Nail	10	NR	0.3-7.8	**	NR		NR	
Mucous Membrane	NR	NR	NR	**	NR		NR	
Baby Products	NR	NR	NR	**	NR		NR	
	Ammonium Polyacrylate				**Ammonium Styrene/Acrylates Copolymer**			
	2018[24]	**1998[1]**	**2018[19]**	**1998[1]**	**2018[24]**	**1998[1]**	**2018[19]**	**1998[1]**
Totals*	**15**	**NR**	**0.000001-1.8**	**	**2**	**NR**	**0.052-16.5**	**
Duration of Use								
Leave-On	*14*	*NR*	*0.00018-1.8*	**	*2*	*NR*	*0.052-16.5*	**
Rinse-Off	*1*	*NR*	*0.000001-0.0005*	**	*NR*	*NR*	*NR*	**
Diluted for (Bath) Use	*NR*	*NR*	*NR*	**	*NR*	*NR*	*NR*	**
Exposure Type								
Eye Area	2	NR	0.0022	**	1	NR	NR	**
Incidental Ingestion	NR	NR	NR	**	NR	NR	NR	**
Incidental Inhalation-Spray	3[a]; 6[b]	NR	NR	**	1[a]	NR	NR	**
Incidental Inhalation-Powder	6[b]	NR	0.00018[c]	**	NR	NR	0.052	**
Dermal Contact	14	NR	0.000001-1.8	**	2	NR	0.052	**
Deodorant (underarm)	NR	NR	NR	**	NR	NR	NR	**
Hair - Non-Coloring	NR	NR	NR	**	NR	NR	NR	**
Hair-Coloring	NR	NR	NR	**	NR	NR	NR	**
Nail	1	NR	NR	**	NR	NR	16.5	**
Mucous Membrane	1	NR	NR	**	NR	NR	NR	**
Baby Products	NR	NR	NR	**	NR	NR	NR	**
	AMP-Acrylates Copolymer				**Behenyl Methacrylate/t-Butyl Methacrylate Copolymer**			
	2018[24]	**1998[1]**	**2018[19]**	**1998[1]**	**2018[24]**		**2018[20]**	
Totals*	**31**	**NR**	**0.00084-8**	**	**5**		**NR**	
Duration of Use								
Leave-On	*28*	*NR*	*0.00084-8*	**	*5*		*NR*	
Rinse-Off	*3*	*NR*	*0.51*	**	*NR*		*NR*	
Diluted for (Bath) Use	*NR*	*NR*	*NR*	**	*NR*		*NR*	
Exposure Type								
Eye Area	1	NR	0.3	**	2		NR	
Incidental Ingestion	NR	NR	NR	**	3		NR	
Incidental Inhalation-Spray	12; 14[a]	NR	0.44-8; 0.00084-1.1[a]	**	NR		NR	
Incidental Inhalation-Powder	NR	NR	NR	**	NR		NR	
Dermal Contact	1	NR	0.035-0.64	**	2		NR	
Deodorant (underarm)	NR	NR	NR	**	NR		NR	
Hair - Non-Coloring	29	NR	0.00084-8	**	NR		NR	
Hair-Coloring	NR	NR	NR	**	NR		NR	
Nail	1	NR	NR	**	NR		NR	
Mucous Membrane	NR	NR	NR	**	3		NR	
Baby Products	NR	NR	NR	**	NR		NR	

Table 4. Current and historical (where applicable) frequency and concentration of use, according to duration and exposure

	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	Butyl Acrylate/Glycol Dimethacrylate Crosspolymer				**C12-22 Alkyl Acrylate/Hydroxyethylacrylate Copolymer**			
	2018[24]	**2011[2]**	**2018[21]**	**2011[2]**	**2018[24]**		**2018[20]**	
Totals*	**1**	**NR**	**4.2-10**	**NR**	**NR**		**3**	
Duration of Use								
Leave-On	*1*	*NR*	*4.2-10*	*NR*	*NR*		*3*	
Rinse-Off	*NR*	*NR*	*NR*	*NR*	*NR*		*NR*	
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*		*NR*	
Exposure Type								
Eye Area	NR	NR	8.3-8.5	NR	NR		NR	
Incidental Ingestion	NR	NR	NR	NR	NR		NR	
Incidental Inhalation-Spray	1[a]	NR	NR	NR	NR		NR	
Incidental Inhalation-Powder	NR	NR	4.2	NR	NR		NR	
Dermal Contact	1	NR	4.2-10	NR	NR		3	
Deodorant (underarm)	NR	NR	NR	NR	NR		NR	
Hair - Non-Coloring	NR	NR	NR	NR	NR		NR	
Hair-Coloring	NR	NR	NR	NR	NR		NR	
Nail	NR	NR	NR	NR	NR		NR	
Mucous Membrane	NR	NR	NR	NR	NR		NR	
Baby Products	NR	NR	NR	NR	NR		NR	
	C8-22 Alkyl Acrylates/Methacrylic Acid Crosspolymer				**Carbomer**			
	2018[24]	**2011[2]**	**2018[21]**	**2011[2]**	**2018[24 #]**	**2001[6 ##]**	**2018[22]**	**2001[6]**
Totals*	**2**	**NR**	**NR**	**NR**	**6434**	**1504**	**0.00001-15**	**0.001-2**
Duration of Use								
Leave-On	*2*	*NR*	*NR*	*NR*	*5336*	*1167*	*0.0012-15*	*0.001-2*
Rinse-Off	*NR*	*NR*	*NR*	*NR*	*1093*	*330*	*0.00001-2.5*	*0.003-2*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*5*	*7*	*0.18-0.3*	*0.1-1*
Exposure Type								
Eye Area	NR	NR	NR	NR	301	65	0.2-1.5	0.2-2
Incidental Ingestion	NR	NR	NR	NR	95	6	0.048-9	0.1-0.7
Incidental Inhalation-Spray	1[b]	NR	NR	NR	16; 2565[a]; 1870[b]	50; 347[a]; 412[b]	0.003-1; 0.048-2.5[a]	0.3-1; 0.003-2[a]; 0.05-1[b]
Incidental Inhalation-Powder	1[b]	NR	NR	NR	2; 1870[b]; 30[c]	1; 412[b]; 5[c]	0.0012-0.88 0.1-15[c]	0.3; 0.05-1[b]; 0.2-0.8[c]
Dermal Contact	1	NR	NR	NR	5601	1335	0.00001-15	0.001-2
Deodorant (underarm)	NR	NR	NR	NR	3[a]	NR	0.25 (not spray) 0.18 (spray)	NR
Hair - Non-Coloring	1	NR	NR	NR	490	96	0.0084-2.5	0.3-1.5
Hair-Coloring	NR	NR	NR	NR	222	57	0.2-2.5	0.7-2
Nail	NR	NR	NR	NR	12	7	0.003-0.87	0.2-2
Mucous Membrane	NR	NR	NR	NR	200	26	0.048-9	0.003-2
Baby Products	NR	NR	NR	NR	36	15	0.15-0.69	0.2-0.8
	Ethylene/Acrylic Acid Copolymer				**Ethylene/Methacrylate Copolymer**			
	2018[24]	**1998[1]**	**2018[19]**	**1998[1]**	**2018[24]**	**1998[1]**	**2018[19]**	**1998[1]**
Totals*	**316**	**6**	**0.001-16.5**	**	**60**	**5**	**0.0003-0.83**	**
Duration of Use								
Leave-On	*306*	*6*	*0.001-16.5*	**	*60*	*5*	*0.0003-0.83*	**
Rinse-Off	*NR*	*NR*	*0.001-0.5*	**	*NR*	*NR*	*NR*	**
Diluted for (Bath) Use	*NR*	*NR*	*NR*	**	*NR*	*NR*	*NR*	**
Exposure Type								
Eye Area	181	NR	0.001-16.5	**	29	NR	0.0003-0.74	**
Incidental Ingestion	3	NR	NR	**	NR	NR	0.3-0.59	**
Incidental Inhalation-Spray	18[a]; 7[b]	NR	0.25	**	2[a]; 1[b]	NR	NR	**
Incidental Inhalation-Powder	23; 7[b]	NR	0.5; 0.001-8[c]	**	9; 1[b]	NR	0.3;0.037-0.53[c]	**
Dermal Contact	298	6	0.001-16.5	**	42	5	0.037-0.83	**
Deodorant (underarm)	NR	NR	NR	**	NR	NR	NR	**
Hair - Non-Coloring	1	NR	NR	**	NR	NR	NR	**
Hair-Coloring	NR	NR	NR	**	NR	NR	NR	**
Nail	4	NR	4	**	NR	NR	NR	**
Mucous Membrane	3	NR	NR	**	NR	NR	0.3-0.59	**
Baby Products	NR	NR	NR	**	NR	NR	NR	**

Table 4. Current and historical (where applicable) frequency and concentration of use, according to duration and exposure

	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	Ethylene/Sodium Acrylate Copolymer				**Ethylhexyl Acrylate/Methyl Methacrylate Copolymer**			
	2018[24]	**1998[1]**	**2018[19]**	**1998[1]**	**2018[24]**		**2018[20]**	
Totals*	**1**	**1**	**NR**	**	**5**		**7**	
Duration of Use								
Leave-On	*NR*	*1*	*NR*	**	*5*		*7*	
Rinse-Off	*1*	*NR*	*NR*	**	*NR*		*NR*	
Diluted for (Bath) Use	*NR*	*NR*	*NR*	**	*NR*		*NR*	
Exposure Type								
Eye Area	NR	1	NR	**	5		NR	
Incidental Ingestion	NR	NR	NR	**	NR		NR	
Incidental Inhalation-Spray	NR	NR	NR	**	NR		NR	
Incidental Inhalation-Powder	NR	NR	NR	**	NR		NR	
Dermal Contact	1	1	NR	**	5		7	
Deodorant (underarm)	NR	NR	NR	**	NR		NR	
Hair - Non-Coloring	NR	NR	NR	**	NR		NR	
Hair-Coloring	NR	NR	NR	**	NR		NR	
Nail	NR	NR	NR	**	NR		NR	
Mucous Membrane	NR	NR	NR	**	NR		NR	
Baby Products	NR	NR	NR	**	NR		NR	
	Lauryl Acrylate Crosspolymer				**Lauryl Methacrylate/Glycol Dimethacrylate Crosspolymer**			
	2018[24]		**2018[20]**		**2018[24]**	**2011[2]**	**2018[21]**	**2011[2]**
Totals*	**NR**		**1.2**		**99**	**63**	**1.1-3.2**	**0.06-3**
Duration of Use								
Leave-On	*NR*		*1.2*		*90*	*56*	*1.1-3.2*	*0.06-3*
Rinse-Off	*NR*		*NR*		*9*	*7*	*NR*	*0.2-3*
Diluted for (Bath) Use	*NR*		*NR*		*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	NR		NR		25	9	NR	0.1-3
Incidental Ingestion	NR		NR		19	8	1.3	0.06-2
Incidental Inhalation-Spray	NR		1.2[a]		6; 2[b]	NR	NR	0.3
Incidental Inhalation-Powder	NR		NR		6; 2[b]	8	1.1; 3[c]	0.01-1
Dermal Contact	NR		NR		79	53	1.1-3.2	0.06-3
Deodorant (underarm)	NR		NR		NR	1[a]	NR	0.3[a]
Hair - Non-Coloring	NR		1.2		NR	NR	NR	NR
Hair-Coloring	NR		NR		NR	NR	NR	NR
Nail	NR		NR		1	1	NR	NR
Mucous Membrane	NR		NR		19	8	1.3	0.06-2
Baby Products	NR		NR		NR	NR	NR	NR
	Lauryl Methacrylate/Sodium Methacrylate Crosspolymer				**Methacryloyl Ethyl Betaine/Acrylates Copolymer**			
	2018[24]	**2011[2]**	**2018[21]**	**2011[2]**	**2018[24]**	**1998[1]**	**2018[19]**	**1998[1]**
Totals*	**4**	**1**	**0.081-7.7**	**0.004-4**	**12**	**NR**	**0.00015-11**	**
Duration of Use								
Leave-On	*3*	*1*	*1.3-7.7*	*0.1-4*	*3*	*NR*	*0.09-11*	**
Rinse-Off	*1*	*NR*	*0.081*	*0.004-0.1*	*9*	*NR*	*0.00015-2.7*	**
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	**
Exposure Type								
Eye Area	NR	NR	NR	NR	NR	NR	NR	**
Incidental Ingestion	NR	NR	NR	NR	NR	NR	NR	**
Incidental Inhalation-Spray	NR	NR	1.3	NR	3[a]	NR	0.09-3.6; 5.1-11[a]	**
Incidental Inhalation-Powder	NR	NR	7.7[c]	NR	NR	NR	NR	**
Dermal Contact	4	1	0.081-7.7	0.004-4	NR	NR	NR	**
Deodorant (underarm)	NR	NR	4.6 (not spray)	NR	NR	NR	NR	**
Hair - Non-Coloring	NR	NR	NR	NR	4	NR	0.09-11	**
Hair-Coloring	NR	NR	NR	NR	8	NR	0.00015-2.7	**
Nail	NR	NR	NR	NR	NR	NR	NR	**
Mucous Membrane	1	NR	0.081	NR	NR	NR	NR	**
Baby Products	NR	NR	NR	NR	NR	NR	NR	**

Table 4. Current and historical (where applicable) frequency and concentration of use, according to duration and exposure

	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	Methyl Methacrylate Crosspolymer				**Methyl Methacrylate/Glycol Dimethacrylate Crosspolymer**			
	2018[24]	**2008[3]**	**2018[23]**	**2009[3]**	**2018[24]**	**2008[3]**	**2018[23]**	**2009[3]**
Totals*	**423**	**144**	**0.0001-13**	**0.1-14**	**38**	**7**	**0.39-1.6**	**0.1-3**
Duration of Use								
Leave-On	*417*	*142*	*0.0001-13*	*0.1-14*	*38*	*7*	*0.39-1.6*	*0.1-3*
Rinse-Off	*6*	*2*	*0.12*	*NR*	*N R*	*NR*	*NR*	*0.1*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	53	15	2-13	0.5-10	2	NR	1.4	NR
Incidental Ingestion	38	15	2	1-10	NR	NR	NR	NR
Incidental Inhalation-Spray	5; 46[a]; 39[b]	1; 24[a]; 16[b]	0.12-0.38; 0.0069[a]	0.1-0.6; 0.8-3[a]; 0.1-3[b]	5[a]; 11[b]	1[a]	NR	0.5[a]; 0.2[b]
Incidental Inhalation-Powder	36; 39[b]	17; 16[b]	7.6-12; 0.5-8[c]	0.8-8; 0.1-3[b]	1; 11[b]	NR	0.65; 1-1.5[c]	3; 0.2[b]
Dermal Contact	370	127	0.0069-13	0.1-14	38	7	0.39-1.6	3
Deodorant (underarm)	1[a]	NR	2 (not spray)	0.9[a]	NR	NR	NR	NR
Hair - Non-Coloring	1	NR	NR	0.1	NR	NR	NR	NR
Hair-Coloring	7	NR	0.12	NR	NR	NR	NR	NR
Nail	2	1	0.0001-4	1	NR	NR	NR	NR
Mucous Membrane	38	15	2	1-10	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

	Methyl Methacrylate/PEG/PPG-4/3 Methacrylate Crosspolymer		**Poly C10-30 Alkyl Acrylate**	
	2018[24]	**2018[20]**	**2018[24]**	**2018[20]**
Totals*	**1**	**NR**	**19**	**0.5-3.2**
Duration of Use				
Leave-On	*1*	*NR*	*19*	*0.5-3.2*
Rinse-Off	*NR*	*NR*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*
Exposure Type				
Eye Area	NR	NR	2	3.2
Incidental Ingestion	NR	NR	3	0.52-1.2
Incidental Inhalation-Spray	NR	NR	9[a]; 3[b]	NR
Incidental Inhalation-Powder	NR	NR	3[b]	2[c]
Dermal Contact	1	NR	15	0.5-2
Deodorant (underarm)	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR
Nail	NR	NR	NR	NR
Mucous Membrane	NR	NR	3	0.5-1.2
Baby Products	NR	NR	NR	NR

	Polyacrylate-14		**Polyacrylate-1 Crosspolymer**	
	2018[24]	**2018[20]**	**2018[24]**	**2018[20]**
Totals*	**3**	**NS**	**14**	**0.2-2**
Duration of Use				
Leave-On	*2*	*NS*	*4*	*NR*
Rinse-Off	*1*	*NS*	*10*	*0.2-2*
Diluted for (Bath) Use	*NR*	*NS*	*NR*	*NR*
Exposure Type				
Eye Area	NR	NS	NR	NR
Incidental Ingestion	NR	NS	NR	NR
Incidental Inhalation-Spray	1[a]	NS	1[a]; 3[b]	NR
Incidental Inhalation-Powder	NR	NS	NR	NR
Dermal Contact	NR	NS	11	0.2-2
Deodorant (underarm)	NR	NS	NR	NR
Hair - Non-Coloring	3	NS	3	NR
Hair-Coloring	NR	NS	NR	NR
Nail	NR	NS	NR	NR
Mucous Membrane	NR	NS	6	1.5
Baby Products	NR	NS	NR	NR

Table 4. Current and historical (where applicable) frequency and concentration of use, according to duration and exposure

	# of Uses		Max Conc of Use (%)		# of Uses		Max Conc of Use (%)	
	Polyacrylic Acid				Polyethylacrylate			
	2018[24]	1998[1]	2018[19]	1998[1]	2018[24]		2018[20]	
Totals*	**111**	**31**	**0.0012-4**	**	**4**		**NR**	
Duration of Use								
Leave-On	*96*	*27*	*0.0012-4*	**	*4*		*NR*	
Rinse-Off	*15*	*7*	*0.0049-0.4*	**	*NR*		*NR*	
Diluted for (Bath) Use	*NR*	*NR*	*0.36*	**	*NR*		*NR*	
Exposure Type								
Eye Area	8	NR	0.5-2.1	**	2		NR	
Incidental Ingestion	2	NR	0.0049-0.048	**	NR		NR	
Incidental Inhalation-Spray	1; 34[a]; 29[b]	3[a]; 14[b]	0.0049-0.62[a]	**	NR		NR	
Incidental Inhalation-Powder	29[b]	14[b]	0.0012; 0.25-4[c]	**	NR		NR	
Dermal Contact	95	28	0.0012-4	**	1		NR	
Deodorant (underarm)	NR	NR	NR	**	NR		NR	
Hair - Non-Coloring	3	1	0.4-1.2	**	NR		NR	
Hair-Coloring	NR	NR	NR	**	NR		NR	
Nail	11	2	NR	**	1		NR	
Mucous Membrane	3	2	0.0049-0.4	**	NR		NR	
Baby Products	NR	NR	0.15	**	NR		NR	
	Polymethyl Acrylate				Polymethyl Methacrylate			
	2018[24]		2018[20]		2018[24]	2008[3]	2018[23]	2009[3]
Totals*	**1**		**0.0014-5.9**		**922**	**892**	**0.0036-44.6**	**0.01-45**
Duration of Use								
Leave-On	*1*		*0.0014-5.9*		*896*	*879*	*0.0036-44.6*	*0.01-45*
Rinse-Off	*NR*		*NR*		*26*	*13*	*0.009-15.6*	*0.3-6*
Diluted for (Bath) Use	*NR*		*NR*		*0*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	NR		4-5.9		293	304	1-9.8	0.1-45
Incidental Ingestion	NR		2		72	60	0.16-16.1	3-20
Incidental Inhalation-Spray	1[a]		NR		4; 97[a]; 88[b]	6; 74[a]; 79[b]	0.1; 4-14.9[a]	0.5-20; 0.01-15[a]; 0.3-16[b]
Incidental Inhalation-Powder	NR		5		76; 88[b]	93; 79[b]	0.27-44.6; 0.23-8.6[c]	2-30 0.3-16[b]
Dermal Contact	1		0.5-5.9		807	806	0.009-44.6	0.01-45
Deodorant (underarm)	NR		NR		NR	NR	NR	4[a]
Hair - Non-Coloring	NR		NR		4	2	0.1-14.9	0.3-1
Hair-Coloring	NR		NR		9	1	15.6	2
Nail	NR		0.0014-.44		19	14	0.0036-19	0.7-30
Mucous Membrane	NR		2		78	62	0.16-16.1	3-20
Baby Products	NR		NR		NR	NR	NR	NR
	Potassium Acrylates Copolymer				Potassium Acrylates/C10-30 Alkyl Acrylate Crosspolymer			
	2018[24]		2018[20]		2018[24]	2011[2]	2018[21]	2011[2]
Totals*	**16**		**0.00031-1.3**		**2**	**NR**	**0.3**	**NR**
Duration of Use								
Leave-On	*10*		*1.3*		*2*	*NR*	*NR*	*NR*
Rinse-Off	*6*		*0.00031-0.31*		*NR*	*NR*	*0.3*	*NR*
Diluted for (Bath) Use	*NR*		*NR*		*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	NR		NR		1	NR	NR	NR
Incidental Ingestion	NR		NR		NR	NR	NR	NR
Incidental Inhalation-Spray	NR		NR		1[b]	NR	NR	NR
Incidental Inhalation-Powder	NR		1.3[c]		1[b]	NR	NR	NR
Dermal Contact	14		NR		2	NR	0.3	NR
Deodorant (underarm)	NR		NR		NR	NR	NR	NR
Hair - Non-Coloring	2		0.00031		NR	NR	NR	NR
Hair-Coloring	NR		NR		NR	NR	NR	NR
Nail	NR		NR		NR	NR	NR	NR
Mucous Membrane	1		NR		NR	NR	NR	NR
Baby Products	12		0.00031		NR	NR	NR	NR

Table 4. Current and historical (where applicable) frequency and concentration of use, according to duration and exposure

	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	Potassium Carbomer				**Sodium Acrylate/Vinyl Alcohol Copolymer**			
	2018[24]		**2018[20]**		**2018[24]**		**2018[20]**	
Totals*	**73**		**NR**		**NR**		**1.5**	
Duration of Use								
Leave-On	*56*		*NR*		*NR*		*NR*	
Rinse-Off	*13*		*NR*		*NR*		*1.5*	
Diluted for (Bath) Use	*4*		*NR*		*NR*		*NR*	
Exposure Type								
Eye Area	3		NR		NR		NR	
Incidental Ingestion	NR		NR		NR		NR	
Incidental Inhalation-Spray	25[a]; 27[b]		NR		NR		NR	
Incidental Inhalation-Powder	27[b]		NR		NR		NR	
Dermal Contact	73		NR		NR		NR	
Deodorant (underarm)	NR		NR		NR		NR	
Hair - Non-Coloring	NR		NR		NR		1.5	
Hair-Coloring	NR		NR		NR		NR	
Nail	NR		NR		NR		NR	
Mucous Membrane	6		NR		NR		NR	
Baby Products	NR		NR		NR		NR	
	Sodium Acrylates Copolymer				**Sodium Acrylates Crosspolymer-2**			
	2018[24]	**1998[1]**	**2018[19]**	**1998[1]**	**2018[24]**	**2011[2]**	**2018[21]**	**2011[2]**
Totals*	**179**	**5**	**0.005-18**	**	**NR**	**NR**	**0.47-1.8**	**0.8**
Duration of Use								
Leave-On	*170*	*NR*	*0.005-18*	**	*NR*	*NR*	*0.47-1.8*	*0.8*
Rinse-Off	*9*	*5*	*NR*	**	*NR*	*NR*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	**	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	20	NR	1.5	**	NR	NR	NR	NR
Incidental Ingestion	1	NR	NR	**	NR	NR	NR	NR
Incidental Inhalation-Spray	72[a]; 50[b]	NR	8[a]	**	NR	NR	NR	NR
Incidental Inhalation-Powder	50[b]; 2[c]	NR	0.5-1.2[b]	**	NR	NR	0.47-1.8[c]	NR
Dermal Contact	176	NR	0.005-18	**	NR	NR	0.47-1.8	0.8
Deodorant (underarm)	NR	NR	NR	**	NR	NR	NR	NR
Hair - Non-Coloring	1	NR	NR	**	NR	NR	NR	NR
Hair-Coloring	NR	5	NR	**	NR	NR	NR	NR
Nail	NR	NR	NR	**	NR	NR	NR	NR
Mucous Membrane	2	NR	NR	**	NR	NR	NR	NR
Baby Products	2	NR	NR	**	NR	NR	NR	NR
	Sodium Acrylates/C10-30 Alkyl Acrylate Crosspolymer				**Sodium Acrylates/Vinyl Isodecanoate Crosspolymer**			
	2018[24]	**2011[2]**	**2018[21]**	**2011[2]**	**2018[24]**	**2011[2]**	**2018[21]**	**2011[2]**
Totals*	**96**	**6**	**0.3**	**NR**	**NR**	**NR**	**0.55**	**NR**
Duration of Use								
Leave-On	*18*	*6*	*NR*	*NR*	*NR*	*NR*	*0.55*	*NR*
Rinse-Off	*78*	*NR*	*0.3*	*NR*	*NR*	*NR*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	2	NR	NR	NR	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	5[a]; 5[b]	1	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Powder	5[b]	NR	NR	NR	NR	NR	NR	NR
Dermal Contact	96	6	0.3	NR	NR	NR	0.55	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	NR	NR	NR	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
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

Table 4. Current and historical (where applicable) frequency and concentration of use, according to duration and exposure

	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	Sodium Carbomer				**Sodium Polyacrylate**			
	2018[24]		**2018[22]**		**2018[24]**	**1998[1]**	**2018[19]**	**1998[1]**
Totals*	**168**		**0.015-0.65**		**900**	**8**	**0.0001-29.7**	**
Duration of Use								
Leave-On	*146*		*0.015-0.65*		*782*	*5*	*0.0001-29.7*	**
Rinse-Off	*22*		*NR*		*118*	*3*	*0.0002-1.5*	**
Diluted for (Bath) Use	*NR*		*0.16*		*NR*	*NR*	*NR*	**
Exposure Type								
Eye Area	22		0.015		131	NR	0.9-29.7	**
Incidental Ingestion	NR		NR		3	NR	0.0095-0.09	**
Incidental Inhalation-Spray	76[a]; 39[b]		0.65[a]		1; 319[a]; 267[b]	1	0.0001-1.8 0.0005-0.0098[a]; 1.5[b]	**
Incidental Inhalation-Powder	39[b]		0.028-0.13[c]		7; 267[b]	NR	0.05; 1.5[b]; 0.0015-7[c]	**
Dermal Contact	166		0.015-0.16		774	5	0.0005-7	**
Deodorant (underarm)	NR		NR		NR	NR	1.5 (not spray) 2.9 (spray)	**
Hair - Non-Coloring	NR		0.65		83	NR	0.0001-1.8	**
Hair-Coloring	NR		NR		22	3	1.5	**
Nail	1		NR		1	NR	6	**
Mucous Membrane	1		0.16		16	2	0.0098-0.8	**
Baby Products	NR		NR		NR	NR	0.55	**
	Sodium Polymethacrylate				Steareth-10 Allyl Ether/Acrylates Copolymer			
	2018[24]		**2018[20]**		**2018[24]**	**1998[1]**	**2018[19]**	**1998[1]**
Totals*	**62**		**0.063-3.4**		**62**	**6**	**0.025-1.5**	**
Duration of Use								
Leave-On	*62*		*0.063-3.4*		*54*	*NR*	*0.025-1.5*	**
Rinse-Off	*NR*		*NR*		*8*	*6*	*1.5*	**
Diluted for (Bath) Use	*NR*		*NR*		*NR*	*NR*	*NR*	**
Exposure Type								
Eye Area	60		0.063-1.5		NR	NR	NR	**
Incidental Ingestion	NR		NR		NR	NR	NR	**
Incidental Inhalation-Spray	1[a]		NR		53[a]; 1[b]	NR	0.025-1.5[a]	**
Incidental Inhalation-Powder	NR		NR		1[b]	NR	NR	**
Dermal Contact	8		0.5-1.5		3	NR	NR	**
Deodorant (underarm)	NR		NR		NR	NR	NR	**
Hair - Non-Coloring	NR		3.4		53	NR	0.025-1.5	**
Hair-Coloring	NR		NR		6	6	NR	**
Nail	NR		NR		NR	NR	NR	**
Mucous Membrane	NR		NR		1	NR	NR	**
Baby Products	NR		NR		NR	NR	NR	**
	Styrene/Acrylates/Ammonium Methacrylate Copolymer				**VA/Butyl Maleate/Isobornyl Acrylate Copolymer**			
	2018[24]	**1998[1]**	**2018[19]**	**1998[1]**	**2018[24]**	**1998[1]**	**2018[19]**	**1998[1]**
Totals*	**106**	**1**	**1.2-38**	**	**2**	**5**	**1.3-10**	**
Duration of Use								
Leave-On	*102*	*1*	*1.2-38*	**	*2*	*5*	*1.3-10*	**
Rinse-Off	*4*	*NR*	*10*	**	*NR*	*NR*	*NR*	**
Diluted for (Bath) Use	*NR*	*NR*	*NR*	**	*NR*	*NR*	*NR*	**
Exposure Type								
Eye Area	99	1	1.2-22.6	**	NR	NR	NR	**
Incidental Ingestion	NR	NR	NR	**	NR	NR	NR	**
Incidental Inhalation-Spray	1[a]	NR	NR	**	1; 1[a]	NR	1.3-10	**
Incidental Inhalation-Powder	NR	NR	NR	**	NR	NR	NR	**
Dermal Contact	50	1	3.3-22.6	**	NR	NR	1.3-2	**
Deodorant (underarm)	NR	NR	NR	**	NR	NR	NR	**
Hair - Non-Coloring	NR	NR	NR	**	2	5	2.5-10	**
Hair-Coloring	4	NR	10	**	NR	NR	NR	**
Nail	1	NR	21-38	**	NR	NR	NR	**
Mucous Membrane	NR	NR	NR	**	NR	NR	NR	**
Baby Products	NR	NR	NR	**	NR	NR	NR	**

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

** Concentration of use data were not provided at the time of the review.

[#] This ingredient is listed in the VCRP as Carbomer (6175 used under the INCI name) and several tradenames (259 used listed under the tradenames)

[##] At the time of the original assessment, this ingredient was reported under several names. The use frequencies of use were combined for the purposes of this table; this may overestimate the actual 2001 frequency of use

[a] It is possible these products are sprays, but it is not specified whether the reported uses are sprays.

[b] Not specified whether a spray or a powder, but it is possible the use can be as a spray or a powder, therefore the information is captured in both categories.

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

NR – no reported use

NS – not yet surveyed

Table 5. Acrylates copolymers not reported to be used in cosmetics, according to 2018 FDA VCRP[24] and 2018 Council survey[19-23] data

Acrylates Crosspolymer-5	Cyclohexyl Methacrylate/Ethylhexyl Methacrylate Copolymer
Acrylates/Beheneth-25 Methacrylate/Steareth-30 Methacrylate Copolymer	Ethylene/Acrylic Acid/VA Copolymer
Acrylates/C12-13 Alkyl Methacrylates/Methoxyethyl Acrylate Crosspolymer	Ethylene/Calcium Acrylate Copolymer
	Ethylene/Magnesium Acrylate Copolymer
Acrylates/C26-28 Olefin Copolymer	Ethylene/Zinc Acrylate Copolymer
Acrylates/C5-8 Alkyl Acrylate Copolymer	Ethylhexyl Acrylate/Methoxy PEG-23 Methacrylate/Vinyl Acetate Copolymer
Acrylates/Ceteareth-20 Methacrylate Crosspolymer	
Acrylates/Ceteareth-20 Methacrylate Crosspolymer-2	Glycol Dimethacrylate Crosspolymer*
Acrylates/Ceteth-20 Methacrylate Copolymer	Glycol Dimethacrylate/Vinyl Alcohol Crosspolymer
Acrylates/Ethylhexyl Acrylate/Glycidyl Methacrylate Crosspolymer	Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer
Acrylates/Hydroxyethyl Acrylate/Lauryl Acrylate Copolymer	Lauryl Acrylate/VA Copolymer
Acrylates/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer	Lauryl Acrylate/VA Crosspolymer
Acrylates/Laureth-25 Methacrylate Copolymer	Methacrylic Acid/PEG-6 Methacrylate/PEG-6 Dimethacrylate Crosspolymer
Acrylates/Lauryl Methacrylate Copolymer	PEG/PPG-5/2 Methacrylate/Methacrylic Acid Crosspolymer
Acrylates/Lauryl Methacrylate/Tridecyl Methacrylate Crosspolymer	Poly(Methoxy PEG-9 Methacrylate)
Acrylates/Methoxy PEG-4 Methacrylate Copolymer	Polyacrylate-29*
Acrylates/Methoxy PEG-15 Methacrylate Copolymer	Polyacrylate-34*
Acrylates/Methoxy PEG-90 Methacrylate Crosspolymer	Polybutyl Acrylate
Acrylates/PEG-4 Dimethacrylate Crosspolymer	Polybutyl Methacrylate
Acrylates/Steareth-50 Acrylate Copolymer	Polyhydroxyethylmethacrylate
Acrylic Acid/C12-22 Alkyl Acrylate Copolymer	Polyisobutyl Methacrylate
Allyl Methacrylate/Glycol Dimethacrylate Crosspolymer	Polypropyl Methacrylate
Ammonium Acrylates/Ethylhexyl Acrylate Copolymer	Polystearyl Methacrylate
Ammonium Styrene/Acrylates/Ethylhexyl Acrylate/Lauryl Acrylate Copolymer	Potassium Acrylate Crosspolymer
	Potassium Acrylates/Ethylhexyl Acrylate Copolymer
Ammonium VA/Acrylates Copolymer	Potassium Aluminum Polyacrylate
Butyl Acrylate/Cyclohexyl Methacrylate Copolymer	Potassium Polyacrylate
Butyl Acrylate/Ethylhexyl Methacrylate Copolymer	Sodium Acrylate/Acrolein Copolymer
Butyl Acrylate/Hydroxyethyl Methacrylate Copolymer	Sodium Acrylates/Beheneth-25 Methacrylate Crosspolymer
Butyl Methacrylate/Acryoyloxy PG Methacrylate Copolymer	Sodium Acrylates/Ethylhexyl Acrylate Copolymer
C8-22 Alkyl Acrylates/Methacrylic Acid Crosspolymer	Stearyl/Lauryl Methacrylate Crosspolymer
Calcium Potassium Carbomer	

*not yet surveyed by the Council

Table 6. Acrylates Copolymers Approved for Use as Secondary Direct Food Additives and Indirect Food Additives

Secondary Direct Food Additives
21CFR173.310 - boiler water additives
Sodium Polyacrylate
Sodium Polymethacrylate
21CFR173.340 – defoaming agent
Sodium Polyacrylate
21CFR173.73 - polymer substances and polymer adjuvants for food treatment
Sodium Polyacrylate

Indirect Food Additives	
21CFR175.105 – adhesives	
Acrylates Copolymer	Polybutyl Acrylate
Ammonium Polyacrylate	Polybutyl Methacrylate
Ethylene/Calcium Acrylate Copolymer	Polyethylacrylate
Ethylene/Sodium Acrylate Copolymer	Sodium Polyacrylate
Ethylene/Zinc Acrylate Copolymer	Sodium Polymethacrylate
Polyacrylic Acid	
21CFR175.210 - acrylate ester copolymer coating	
Acrylates Copolymer	
21CFR175.300 - resinous and polymeric coatings	
Acrylates Copolymer	
Polyacrylic Acid	
Polyethylacrylate	
21CFR175.320 - resinous and polymeric coatings for polyolefin films	
Acrylates Copolymer	
Ethylhexyl Acrylate/Methyl Methacrylate Copolymer	
Polyacrylic Acid	
21CFR176.170 - components of paper and paperboard in contact with aqueous and fatty foods	
Acrylates Copolymer	Sodium Polyacrylate
Ethylene/Acrylic Acid Copolymer	Sodium Polymethacrylate
Polyacrylic Acid	
21CFR176.180 - components of paper and paperboard in contact with dry food	
Acrylates Copolymer	Polyethylacrylate
Acrylates VA Copolymer	Sodium Polyacrylate
Polyacrylic Acid	
21CFR176.200 - defoaming agents used in coatings	
Sodium Polyacrylate	
21CFR177.1010 acrylic and modified acrylic plastics, semi-rigid and rigid	
Ethylhexyl Acrylate/Methyl Methacrylate Copolymer	Polybutyl Methacrylate
Polybutyl Acrylate	Polyethylacrylate
21CFR177.1210 - closures with sealing gaskets for food containers	
Sodium Polyacrylate	
21CFR177.1310 – ethylene-acrylic acid copolymers	
Ethylene/Acrylic Acid Copolymer	
21CFR177.1520 - olefin polymers	
Polyethylacrylate	
21CFR178.3790 - polymer modifiers in semi-rigid and rigid vinyl chloride plastics	
Polybutyl Acrylate	
Polybutyl Methacrylate	
Polymethyl Methacrylate	

Table 7. Acute toxicity studies

Ingredient	Animals	No./Group	Vehicle	Concentration/Dose/Protocol	LD_{50}/LC_{50}/Results	Reference
DERMAL						
Acrylates/Beheneth-25 Methacrylate Copolymer	rats	not stated	not stated	details not provided	> 5 g/kg	[10]
Acrylates Copolymer [as 2-propenoic acid, 2-methyl-, polymer with butyl 2-methyl-2-propenoate, ethyl 2-methyl-2-propenoate and ethyl 2-propenoate]	rats	not stated	not stated	in accord with OECD TG 423; details not provided	> 2 g/kg	[13]
Acrylates/Hydroxyesters Acrylates Copolymer (product containing < 50%)	rats	not stated	not stated	in accord with OECD TG 402; details were not provided	>5 g/kg bw	[14]
VA/Butyl Maleate/Isobornyl Acrylate Copolymer in ethanol	NZW rabbits	3/sex	applied neat	occlusive patch of 2 g/kg of the test material was applied to intact and abraded skin for 24 h	> 2 g/kg	[8]
ORAL						
Acrylates/Beheneth-25 Methacrylate Copolymer	rats	not stated	not stated	details not provided	> 5 g/kg	[10]
Acrylates Copolymer (as a fully polymerized copolymer of methyl methacrylate and ethyl acrylate)	rats (strain not specified)	5/sex	copolymer dispersion was mixed with powdered diet	the copolymer dispersion was mixed with powdered diet to give a content of 20% of dry polymer substance; animals were given the treated feed for 24 h, and then observed for 4 wks	> 25.2 g dry copolymer/kg bw no mortality; no lesions observed at necropsy	[15]
Acrylates Copolymer (as a fully polymerized copolymer of methyl methacrylate and ethyl acrylate)	dogs (strain not specified)	2/sex	copolymer dispersion was mixed with powdered diet	the copolymer dispersion was mixed with powdered diet to give a content of 20% of dry polymer substance; fasted animals were fed 60 g formulated diet/kg bw, and then observed for clinical signs	> 7.95 g dry copolymer/kg bw no mortality; no lesions observed at necropsy	[15]
Acrylates/Hydroxyesters Acrylates Copolymer (product containing < 50%)	rats	not stated	not stated	in accord with OECD TG 425; details not provided	> 5 g/kg	[14]
Polyacrylate-1 Crosspolymer	rats	not stated	DMSO	in accord with OECD TG 423; details not provided	> 2 g/kg	[12]
VA/Butyl Maleate/Isobornyl Acrylate Copolymer in ethanol	Sprague-Dawley rats	5/sex	corn oil	5 g/kg by gavage	> 5 g/kg no mortality	[8]
INHALATION						
Acrylates Copolymer (as a fully polymerized copolymer of methyl methacrylate and ethyl acrylate)	Wistar rats	5/sex	the copolymer was dispersed with dry matter	single 4-h exposure (nose-only) to an aerosol of the copolymer dispersion with a dry matter content of 30.2%; the test was performed in accord with OECD TG 403	> 3960 mg/l no mortality; no observations of toxicity	[15]

Abbreviations: DMSO – dimethyl sulfoxide; NZW – New Zealand White; OECD – Organisation for Economic Co-operation and Development; TG – test guideline

Table 8. Genotoxicity Studies

Test Article	Concentration/Dose	Vehicle	Test System	Procedure	Results	Reference
			IN VITRO			
Acrylates Copolymer [as 2-propenoic acid, 2-methyl-, polymer with butyl 2-methyl-2-propenoate, ethyl 2-methyl-2-propenoate and ethyl 2-propenoate]	not provided	not provided	not provided	Ames test, in accord with OECD TG 471; details not provided	not mutagenic	13
Acrylates Copolymer (as a fully polymerized copolymer of methyl methacrylate and ethyl acrylate)	312.5 – 5000 µg dry copolymer/plate	acetone	*S. typhimurium* TA98, TA100, and TA1537	Ames test, with and without metabolic activation	not mutagenic	15
Acrylates Copolymer (as a fully polymerized copolymer of methyl methacrylate and ethyl acrylate)	40% dry substance 3 – 5000 µg dispersion/ plate (corresponds to 1.2 – 2000 µg dry copolymer/ plate	aq. dispersion	S. typhimurium TA98, TA100, TA102, TA1535, and TA1537	Ames test in accord with OECD TG 471, with and without metabolic activation	not mutagenic	15
Acrylates Copolymer (as a fully polymerized copolymer of methyl acrylate, methyl methacrylate, and methacrylic acid)	157 – 5000 µg dry copolymer/plate	DMSO	S. typhimurium TA98, TA100, TA1535, and TA1537; *E. coli* WP2uvrA	Ames test in accord with OECD TG 471 and 472, with and without metabolic activation	not mutagenic	16
Acrylates Copolymer [as 2-propenoic acid, 2-methyl-, polymer with butyl 2-methyl-2-propenoate, ethyl 2-methyl-2-propenoate and ethyl 2-propenoate]	not provided	not provided	not provided	mouse lymphoma cell assay; in accord with OECD TG 476; details not provided	not mutagenic	13
Acrylates Copolymer (as a fully polymerized copolymer of methyl methacrylate and ethyl acrylate)	195.3 – 6250 µg dry copolymer /ml	deionized water	mammalian L5178Y cells	mouse lymphoma L5178Y cell mutation assay in accord with OECD TG 476; cells were exposed to the test material for 4 h in the presence and absence of metabolic activation, or for 24 h without metabolic activation	not genotoxic	15
Acrylates Copolymer (as a fully polymerized copolymer of methyl acrylate, methyl methacrylate, and methacrylic acid)	14.5 - 5000 µg dry copolymer/ml	DMSO	mammalian L5178Y cells	mouse lymphoma L5178Y cell mutation assay in accord with OECD TG 476; cells were exposed to the test material for 4 h in the presence and absence of metabolic activation, or for 24 h without metabolic activation	not genotoxic	16
Acrylates Copolymer (as a fully polymerized copolymer of methyl acrylate, methyl methacrylate, and methacrylic acid)	≤ 1080 µg dry copolymer/ml (Exp. 1) ≤ 9000 µg dry copolymer/ml (Exp. 2)	DMSO	human lymphocytes	chromosomal aberration assay in accord with OECD TG 473 Exp 1: cells were exposed for 2 h with, and 3 h without, metabolic activation Exp. 2: cells were exposed for 24 h, with and without metabolic activation	not clastogenic	16
Acrylates/Hydroxyesters Acrylates Copolymer (product containing < 50%)	not provided	not provided	not provided	Ames test, in accord with OECD TG 471; details not provided	not mutagenic	14

Table 8. Genotoxicity Studies

Test Article	Concentration/Dose	Vehicle	Test System	Procedure	Results	Reference
IN VIVO						
Acrylates Copolymer (as a fully polymerized copolymer of methyl methacrylate and ethyl acrylate)	500, 1000, and 2000 mg dry copolymer/kg bw	sterile water	mice, 5/sex/group	mouse micronucleus test in accord with OECD TG 474; mice were dosed by gavage (10 ml/kg bw) and killed 24 h after dosing; a second high-dose group was killed 48 h after dosing	not genotoxic a minimal increase of MNPCE in male mice killed after 24 h was considered not biologically relevant, and was within historical range	15
Acrylates Copolymer (as a fully polymerized copolymer of methyl acrylate, methyl methacrylate, and methacrylic acid)	500, 1000, and 2000 mg dry copolymer/kg bw	1% aq CMC	mice, 5/sex/group	mouse micronucleus test in accord with OECD TG 474; mice were dosed by gavage (10 ml/kg bw) and killed 24 h after dosing; a second high-dose group was killed 48 h after dosing	not genotoxic	16

Abbreviations: CMC – carboxymethylcellulose; DMSO – dimethyl sulfoxide; MNPCE - micronucleated polychromatic erythrocytes; OECD – Organisation for Economic Co-operation and Development; TG – test guideline

Table 9. Dermal irritation and sensitization

Test Article	Dose/Concentration	Test Population	Procedure	Results	Reference
ANIMAL					
Acrylates/Beheneth-25 Methacrylate Copolymer	not stated	rabbits; # not stated	details not provided	classified as slightly irritating very slight to well-defined erythema and very slight edema were observed; erythema was resolved by day 7 and edema within 48 h	10
Acrylates Copolymer [as 2-propenoic acid, 2-methyl-, polymer with butyl 2-methyl-2-propenoate, ethyl 2-methyl-2-propenoate and ethyl 2-propenoate]	not stated	rabbits; # not stated	skin irritation test conducted in accord with OECD TG404; details not provided	not irritating	13
Acrylates Copolymer (as a fully polymerized copolymer of methyl methacrylate and ethyl acrylate)	0.5 ml	3 NZW rabbits	4-h semi-occlusive patch was applied to each animal, in accord with OECD TG 404; test sites were observed 1, 24, 48, and 72 h after patch removal	not an irritant	15
Acrylates Copolymer [as 2-propenoic acid, 2-methyl-, polymer with butyl 2-methyl-2-propenoate, ethyl 2-methyl-2-propenoate and ethyl 2-propenoate]	not stated	not stated; assumed to be mice	LLNA, in accord with OECD TG 429	not a sensitizer	13
Acrylates Copolymer (as a fully polymerized copolymer of methyl methacrylate and ethyl acrylate)	not stated; assumed neat	Dunkin-Hartley albino guinea pigs; 20 test and 10 control animals	Buehler test, performed in accord with OECD TG 406 induction: 6-h occlusive patches were applied 1 x/wk for 3 wks challenge: after a 2-wk non-treatment period, a 6-h occlusive patch was applied to an untreated site	not a sensitizer	15
Acrylates/Hydroxyesters Acrylates Copolymer (product containing < 50%)	not stated	rabbits; # not stated	skin irritation test conducted in accord with OECD TG404; details not provided	slightly irritating slight erythema observed at 1 and 24 h after patch removal; skin appeared normal after 48 h	14

Table 9. Dermal irritation and sensitization

Test Article	Dose/Concentration	Test Population	Procedure	Results	Reference
VA/Butyl Maleate/Isobornyl Acrylate Copolymer in ethanol	0.5 g	6 NZW rabbits	24 h occlusive patch of the test material moistened with 0.5 ml physiological saline applied to intact and abraded dorsal skin	not an irritant	[8]
VA/Butyl Maleate/Isobornyl Acrylate Copolymer in ethanol	Neat; 0.5 g	10 Hartley guinea pigs	Buehler test induction: 6-h occlusive patch applied 3x/wk for 3 wks challenge: after a 2-wk non-treatment period, patches were applied to the original test site, and to a previously untested site	not an irritant or a sensitizer	[8]
HUMAN					
Acrylates/Hydroxyesters Acrylates Copolymer (product containing < 50%)	not provided	# subjects not provided	HRIPT; details not provided	not a sensitizer	[14]
VA/Butyl Maleate/Isobornyl Acrylate Copolymer in ethanol	5 g; slurry in alcohol	25 subjects	48-h patch test	slight erythema observed in 20% of the subjects	[8]
VA/Butyl Maleate/Isobornyl Acrylate Copolymer	0.2 ml in 10% ethanol	109 subjects	HRIPT induction: 24-h patches 3x/wk for 3 wks challenge: after a 2-wk, non-treatment period, a 24-h patch was applied to a previously untreated site	not likely to be a sensitizer induction: minimal erythema in 3 subjects and hyperpigmentation in 1 subject; in 1 subject, edema and intense erythema with application 8 that did not recur when the patch was moved challenge: minimal erythema in the subject that had a reaction with the 8th induction patch; minimal erythema in 3 subjects that did not react during induction	[8]

Abbreviations: HRIPT – human repeated insult patch test; NZW – New Zealand White; OECD – Organisation for Economic Co-operation and Development; TG – test guideline

Table 10. Ocular irritation studies

Test Article	Concentration/Dose	Test Population	Procedure	Results	Reference
			ANIMAL		
Acrylates/Beheneth-25 Methacrylate Copolymer	not stated	rabbits; # not stated	details not provided	classified as slightly irritating transient conjunctival effects were observed; eyes were normal within 48 h	[10]
Acrylates Copolymer [as 2-propenoic acid, 2-methyl-, polymer with butyl 2-methyl-2-propenoate, ethyl 2-methyl-2-propenoate and ethyl 2-propenoate]	not stated	NZW rabbits; # not stated	in accord with OECD TG 405; details not provided	slightly irritating	[13]
Acrylates Copolymer (as a fully polymerized copolymer of methyl methacrylate and ethyl acrylate)	undiluted	3 NZW rabbits	0.1 ml was instilled into the conjunctival sac of one eye of each rabbits, in accord with OECD TG 405; test eyes were observed 1, 24, 48, and 72 h after patch removal	not an ocular irritant	[15]
Acrylates/Hydroxyesters Acrylates Copolymer (product containing < 50%)	not stated	rabbits; # not stated	details not provided	slightly irritating slight conjunctival irritation in treated eyes 1- and 24-h after instillation; irritation resolved within 48 h	[14]
VA/Butyl Maleate/Isobornyl Acrylate Copolymer in ethanol	undiluted	9 NZW rabbits	0.1 g was instilled into the conjunctival sac of one eye of each rabbits; the contralateral eye served as an untreated control. Following instillation, the eyes of 3 rabbits were immediately rinsed; the eyes of the remaining 6 rabbits were not rinsed.	moderate to severe eye irritant Slight corneal opacity, slight to moderate conjunctival redness, slight-to-severe conjunctival chemosis and slight to severe conjunctival discharge observed in the unwashed eyes; some degree of conjunctivitis observed in all unwashed eyes on day 7; within the first 3 days post-exposure, blistering of the conjunctiva was observed in 5 eyes that were not rinsed.	[8]

Abbreviations: NZW – New Zealand White; OECD – Organisation for Economic Co-operation and Development; TG – test guideline

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ACRYLATES COPOLYMER	01C - Other Baby Products	14
ACRYLATES COPOLYMER	02A - Bath Oils, Tablets, and Salts	1
ACRYLATES COPOLYMER	02B - Bubble Baths	19
ACRYLATES COPOLYMER	02D - Other Bath Preparations	1
ACRYLATES COPOLYMER	03A - Eyebrow Pencil	2
ACRYLATES COPOLYMER	03B - Eyeliner	82
ACRYLATES COPOLYMER	03C - Eye Shadow	381
ACRYLATES COPOLYMER	03D - Eye Lotion	9
ACRYLATES COPOLYMER	03F - Mascara	202
ACRYLATES COPOLYMER	03G - Other Eye Makeup Preparations	26
ACRYLATES COPOLYMER	04C - Powders (dusting and talcum, excluding aftershave talc)	7
ACRYLATES COPOLYMER	04E - Other Fragrance Preparation	12
ACRYLATES COPOLYMER	05A - Hair Conditioner	2
ACRYLATES COPOLYMER	05B - Hair Spray (aerosol fixatives)	40
ACRYLATES COPOLYMER	05F - Shampoos (non-coloring)	79
ACRYLATES COPOLYMER	05G - Tonics, Dressings, and Other Hair Grooming Aids	21
ACRYLATES COPOLYMER	05H - Wave Sets	19
ACRYLATES COPOLYMER	05I - Other Hair Preparations	23
ACRYLATES COPOLYMER	06A - Hair Dyes and Colors (all types requiring caution statements and patch tests)	1
ACRYLATES COPOLYMER	06B - Hair Tints	1
ACRYLATES COPOLYMER	06D - Hair Shampoos (coloring)	1
ACRYLATES COPOLYMER	06E - Hair Color Sprays (aerosol)	1
ACRYLATES COPOLYMER	06H - Other Hair Coloring Preparation	13
ACRYLATES COPOLYMER	07A - Blushers (all types)	18
ACRYLATES COPOLYMER	07B - Face Powders	38
ACRYLATES COPOLYMER	07C - Foundations	59
ACRYLATES COPOLYMER	07D - Leg and Body Paints	5
ACRYLATES COPOLYMER	07E - Lipstick	443
ACRYLATES COPOLYMER	07F - Makeup Bases	3
ACRYLATES COPOLYMER	07H - Makeup Fixatives	2
ACRYLATES COPOLYMER	07I - Other Makeup Preparations	80
ACRYLATES COPOLYMER	08A - Basecoats and Undercoats	31
ACRYLATES COPOLYMER	08C - Nail Creams and Lotions	4
ACRYLATES COPOLYMER	08D - Nail Extenders	29
ACRYLATES COPOLYMER	08E - Nail Polish and Enamel	318
ACRYLATES COPOLYMER	08G - Other Manicuring Preparations	51
ACRYLATES COPOLYMER	09C - Other Oral Hygiene Products	10
ACRYLATES COPOLYMER	10A - Bath Soaps and Detergents	561
ACRYLATES COPOLYMER	10B - Deodorants (underarm)	2
ACRYLATES COPOLYMER	10C - Douches	1
ACRYLATES COPOLYMER	10E - Other Personal Cleanliness Products	261
ACRYLATES COPOLYMER	11G - Other Shaving Preparation Products	2
ACRYLATES COPOLYMER	12A - Cleansing	137
ACRYLATES COPOLYMER	12B - Depilatories	16
ACRYLATES COPOLYMER	12C - Face and Neck (exc shave)	37
ACRYLATES COPOLYMER	12D - Body and Hand (exc shave)	21
ACRYLATES COPOLYMER	12F - Moisturizing	39
ACRYLATES COPOLYMER	12G - Night	8
ACRYLATES COPOLYMER	12H - Paste Masks (mud packs)	2
ACRYLATES COPOLYMER	12J - Other Skin Care Preps	34
ACRYLATES COPOLYMER	13B - Indoor Tanning Preparations	5
ACRYLIC-ACRYLATE COPOLYMER	08E - Nail Polish and Enamel	3
ACRYLATES CROSSPOLYMER	03D - Eye Lotion	1
ACRYLATES CROSSPOLYMER	08G - Other Manicuring Preparations	1
ACRYLATES CROSSPOLYMER	12C - Face and Neck (exc shave)	2
ACRYLATES CROSSPOLYMER	12J - Other Skin Care Preps	1
ACRYLATES CROSSPOLYMER-3	03F - Mascara	1
ACRYLATES CROSSPOLYMER-3	05G - Tonics, Dressings, and Other Hair Grooming Aids	2

ACRYLATES CROSSPOLYMER-3	05H - Wave Sets	1
ACRYLATES CROSSPOLYMER-4	10A - Bath Soaps and Detergents	16
ACRYLATES/AMMONIUM METHACRYLATE COPOLYMER	07C - Foundations	3
ACRYLATES/AMMONIUM METHACRYLATE COPOLYMER	07I - Other Makeup Preparations	1
ACRYLATES/AMMONIUM METHACRYLATE COPOLYMER	09C - Other Oral Hygiene Products	1
ACRYLATES/AMMONIUM METHACRYLATE COPOLYMER	10A - Bath Soaps and Detergents	6
ACRYLATES/AMMONIUM METHACRYLATE COPOLYMER	12A - Cleansing	8
ACRYLATES/AMMONIUM METHACRYLATE COPOLYMER	12C - Face and Neck (exc shave)	3
ACRYLATES/AMMONIUM METHACRYLATE COPOLYMER	12F - Moisturizing	2
ACRYLATES/AMMONIUM METHACRYLATE COPOLYMER	12G - Night	1
ACRYLATES/AMMONIUM METHACRYLATE COPOLYMER	12J - Other Skin Care Preps	1
ACRYLATES/BEHENETH-25 METHACRYLATE COPOLYMER	02D - Other Bath Preparations	1
ACRYLATES/BEHENETH-25 METHACRYLATE COPOLYMER	05A - Hair Conditioner	1
ACRYLATES/BEHENETH-25 METHACRYLATE COPOLYMER	05F - Shampoos (non-coloring)	8
ACRYLATES/BEHENETH-25 METHACRYLATE COPOLYMER	05G - Tonics, Dressings, and Other Hair Grooming Aids	28
ACRYLATES/BEHENETH-25 METHACRYLATE COPOLYMER	05H - Wave Sets	4
ACRYLATES/BEHENETH-25 METHACRYLATE COPOLYMER	05I - Other Hair Preparations	5
ACRYLATES/BEHENETH-25 METHACRYLATE COPOLYMER	06D - Hair Shampoos (coloring)	1
ACRYLATES/BEHENETH-25 METHACRYLATE COPOLYMER	06G - Hair Bleaches	2
ACRYLATES/BEHENETH-25 METHACRYLATE COPOLYMER	06H - Other Hair Coloring Preparation	8
ACRYLATES/BEHENETH-25 METHACRYLATE COPOLYMER	10A - Bath Soaps and Detergents	3
ACRYLATES/BEHENETH-25 METHACRYLATE COPOLYMER	10E - Other Personal Cleanliness Products	6
ACRYLATES/BEHENETH-25 METHACRYLATE COPOLYMER	11E - Shaving Cream	1
ACRYLATES/BEHENETH-25 METHACRYLATE COPOLYMER	12A - Cleansing	3
ACRYLATES/BEHENETH-25 METHACRYLATE COPOLYMER	12F - Moisturizing	20
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	01A - Baby Shampoos	3
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	01B - Baby Lotions, Oils, Powders, and Creams	4
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	01C - Other Baby Products	10
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	02A - Bath Oils, Tablets, and Salts	1
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	02B - Bubble Baths	7
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	02D - Other Bath Preparations	4
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	03A - Eyebrow Pencil	2
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	03B - Eyeliner	21
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	03C - Eye Shadow	3
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	03D - Eye Lotion	104
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	03E - Eye Makeup Remover	18
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	03F - Mascara	3
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	03G - Other Eye Makeup Preparations	64
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	04A - Cologne and Toilet waters	77
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	04B - Perfumes	1
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	04E - Other Fragrance Preparation	98
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	05A - Hair Conditioner	4
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	05F - Shampoos (non-coloring)	34
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	05G - Tonics, Dressings, and Other Hair Grooming Aids	53
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	05H - Wave Sets	1
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	05I - Other Hair Preparations	20
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	06A - Hair Dyes and Colors (all types requiring caution statements and patch tests)	24
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	06F - Hair Lighteners with Color	1
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	06G - Hair Bleaches	9
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	06H - Other Hair Coloring Preparation	1
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	07A - Blushers (all types)	2
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	07C - Foundations	9
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	07E - Lipstick	1

ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	07F - Makeup Bases	12
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	07I - Other Makeup Preparations	16
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	08B - Cuticle Softeners	7
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	08C - Nail Creams and Lotions	3
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	08E - Nail Polish and Enamel	2
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	08F - Nail Polish and Enamel Removers	1
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	08G - Other Manicuring Preparations	1
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	10A - Bath Soaps and Detergents	103
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	10B - Deodorants (underarm)	3
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	10C - Douches	1
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	10E - Other Personal Cleanliness Products	58
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	11A - Aftershave Lotion	67
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	11D - Preshave Lotions (all types)	3
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	11E - Shaving Cream	4
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	11G - Other Shaving Preparation Products	23
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	12A - Cleansing	212
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	12C - Face and Neck (exc shave)	368
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	12D - Body and Hand (exc shave)	402
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	12F - Moisturizing	996
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	12G - Night	89
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	12H - Paste Masks (mud packs)	48
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	12I - Skin Fresheners	7
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	12J - Other Skin Care Preps	134
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	13A - Suntan Gels, Creams, and Liquids	8
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	13B - Indoor Tanning Preparations	5
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	13C - Other Suntan Preparations	9
ACRYLATES/C12-22 ALKYL METHACRYLATE COPOLYMER	03D - Eye Lotion	1
ACRYLATES/C12-22 ALKYL METHACRYLATE COPOLYMER	07C - Foundations	1
ACRYLATES/C12-22 ALKYL METHACRYLATE COPOLYMER	07I - Other Makeup Preparations	1
ACRYLATES/C12-22 ALKYL METHACRYLATE COPOLYMER	12C - Face and Neck (exc shave)	1
ACRYLATES/C12-22 ALKYL METHACRYLATE COPOLYMER	12F - Moisturizing	1
ACRYLATES/C12-22 ALKYL METHACRYLATE COPOLYMER	13A - Suntan Gels, Creams, and Liquids	2
ACRYLATES/C12-22 ALKYL METHACRYLATE COPOLYMER	13C - Other Suntan Preparations	2
ACRYLATES/ETHYLHEXYL ACRYLATE COPOLYMER	03B - Eyeliner	11
ACRYLATES/ETHYLHEXYL ACRYLATE COPOLYMER	03C - Eye Shadow	1
ACRYLATES/ETHYLHEXYL ACRYLATE COPOLYMER	03F - Mascara	39
ACRYLATES/ETHYLHEXYL ACRYLATE COPOLYMER	03G - Other Eye Makeup Preparations	2
ACRYLATES/ETHYLHEXYL ACRYLATE COPOLYMER	07I - Other Makeup Preparations	3
ACRYLATES/ETHYLHEXYL ACRYLATE COPOLYMER	08E - Nail Polish and Enamel	2
ACRYLATES/ETHYLHEXYL ACRYLATE COPOLYMER	12J - Other Skin Care Preps	2
ACRYLATES/ETHYLHEXYL ACRYLATE CROSSPOLYMER	07E - Lipstick	1
ACRYLATES/ETHYLHEXYL ACRYLATE CROSSPOLYMER	08G - Other Manicuring Preparations	2
ACRYLATES/HYDROXYESTERS ACRYLATES COPOLYMER	03F - Mascara	8
ACRYLATES/HYDROXYESTERS ACRYLATES COPOLYMER	04B - Perfumes	1
ACRYLATES/HYDROXYESTERS ACRYLATES COPOLYMER	05B - Hair Spray (aerosol fixatives)	14
ACRYLATES/HYDROXYESTERS ACRYLATES COPOLYMER	05G - Tonics, Dressings, and Other Hair Grooming Aids	5
ACRYLATES/HYDROXYESTERS ACRYLATES COPOLYMER	05H - Wave Sets	5
ACRYLATES/HYDROXYESTERS ACRYLATES COPOLYMER	05I - Other Hair Preparations	1
ACRYLATES/HYDROXYESTERS ACRYLATES COPOLYMER	12D - Body and Hand (exc shave)	1
Acrylates/Methoxy PEG-23 Methacrylate Copolymer		0

ACRYLATES/PALMETH-25 ACRYLATE COPOLYMER	06A - Hair Dyes and Colors (all types requiring caution statements and patch tests)	3
ACRYLATES/PALMETH-25 ACRYLATE COPOLYMER	10E - Other Personal Cleanliness Products	2
ACRYLATES/PALMETH-25 ACRYLATE COPOLYMER	12A - Cleansing	1
ACRYLATES/PALMETH-25 ACRYLATE COPOLYMER	12B - Depilatories	1
ACRYLATES/PALMETH-25 ACRYLATE COPOLYMER	12C - Face and Neck (exc shave)	1
ACRYLATES/PALMETH-25 ACRYLATE COPOLYMER	12J - Other Skin Care Preps	1
ACRYLATES/STEARETH-20 METHACRYLATE COPOLYMER	01A - Baby Shampoos	1
ACRYLATES/STEARETH-20 METHACRYLATE COPOLYMER	03D - Eye Lotion	1
ACRYLATES/STEARETH-20 METHACRYLATE COPOLYMER	05B - Hair Spray (aerosol fixatives)	2
ACRYLATES/STEARETH-20 METHACRYLATE COPOLYMER	05G - Tonics, Dressings, and Other Hair Grooming Aids	3
ACRYLATES/STEARETH-20 METHACRYLATE COPOLYMER	05H - Wave Sets	1
ACRYLATES/STEARETH-20 METHACRYLATE COPOLYMER	05I - Other Hair Preparations	2
ACRYLATES/STEARETH-20 METHACRYLATE COPOLYMER	06H - Other Hair Coloring Preparation	6
ACRYLATES/STEARETH-20 METHACRYLATE COPOLYMER	07I - Other Makeup Preparations	2
ACRYLATES/STEARETH-20 METHACRYLATE COPOLYMER	10A - Bath Soaps and Detergents	1
ACRYLATES/STEARETH-20 METHACRYLATE COPOLYMER	10E - Other Personal Cleanliness Products	2
ACRYLATES/STEARETH-20 METHACRYLATE COPOLYMER	11E - Shaving Cream	1
ACRYLATES/STEARETH-20 METHACRYLATE COPOLYMER	12A - Cleansing	8
ACRYLATES/STEARETH-20 METHACRYLATE COPOLYMER	12F - Moisturizing	1
ACRYLATES/STEARETH-20 METHACRYLATE COPOLYMER	12H - Paste Masks (mud packs)	1
ACRYLATES-STEARETH-20 METHACRYLATE COPOLYMER	03E - Eye Makeup Remover	1
ACRYLATES-STEARETH-20 METHACRYLATE COPOLYMER	05F - Shampoos (non-coloring)	9
ACRYLATES-STEARETH-20 METHACRYLATE COPOLYMER	05I - Other Hair Preparations	1
ACRYLATES-STEARETH-20 METHACRYLATE COPOLYMER	06A - Hair Dyes and Colors (all types requiring caution statements and patch tests)	1
ACRYLATES-STEARETH-20 METHACRYLATE COPOLYMER	06H - Other Hair Coloring Preparation	2
ACRYLATES-STEARETH-20 METHACRYLATE COPOLYMER	07E - Lipstick	1
ACRYLATES-STEARETH-20 METHACRYLATE COPOLYMER	10A - Bath Soaps and Detergents	1
ACRYLATES-STEARETH-20 METHACRYLATE COPOLYMER	10E - Other Personal Cleanliness Products	2
ACRYLATES-STEARETH-20 METHACRYLATE COPOLYMER	12A - Cleansing	6
ACRYLATES-STEARETH-20 METHACRYLATE COPOLYMER	12C - Face and Neck (exc shave)	1
ACRYLATES-STEARETH-20 METHACRYLATE COPOLYMER	12F - Moisturizing	8
ACRYLATES/STEARETH-20 METHACRYLATE CROSSPOLYMER	05G - Tonics, Dressings, and Other Hair Grooming Aids	1
ACRYLATES/STEARETH-20 METHACRYLATE CROSSPOLYMER	06H - Other Hair Coloring Preparation	2
ACRYLATES/STEARETH-20 METHACRYLATE CROSSPOLYMER	12C - Face and Neck (exc shave)	1
Acrylates/Steareth-30 Methacrylate Copolymer		0
Acrylates/Stearyl Methacrylate Copolymer		0
ACRYLATES/VA COPOLYMER	03F - Mascara	1
ACRYLATES/VA CROSSPOLYMER	08G - Other Manicuring Preparations	1
ACRYLATES/VINYL ISODECANOATE CROSSPOLYMER	03D - Eye Lotion	1
ACRYLATES/VINYL ISODECANOATE CROSSPOLYMER	07I - Other Makeup Preparations	1
ACRYLATES/VINYL ISODECANOATE CROSSPOLYMER	12A - Cleansing	8
ACRYLATES/VINYL ISODECANOATE CROSSPOLYMER	12C - Face and Neck (exc shave)	5
ACRYLATES/VINYL ISODECANOATE CROSSPOLYMER	12D - Body and Hand (exc shave)	5
ACRYLATES/VINYL ISODECANOATE CROSSPOLYMER	12F - Moisturizing	3
ACRYLATES/VINYL ISODECANOATE CROSSPOLYMER	12G - Night	5

ACRYLATES/VINYL ISODECANOATE CROSSPOLYMER	12J - Other Skin Care Preps	2
ACRYLATES/VINYL NEODECANOATE CROSSPOLYMER	02A - Bath Oils, Tablets, and Salts	4
ACRYLATES/VINYL NEODECANOATE CROSSPOLYMER	02B - Bubble Baths	2
ACRYLATES/VINYL NEODECANOATE CROSSPOLYMER	03G - Other Eye Makeup Preparations	1
ACRYLATES/VINYL NEODECANOATE CROSSPOLYMER	10A - Bath Soaps and Detergents	2
ACRYLATES/VINYL NEODECANOATE CROSSPOLYMER	10E - Other Personal Cleanliness Products	2
ACRYLATES/VINYL NEODECANOATE CROSSPOLYMER	12A - Cleansing	1
ACRYLATES/VINYL NEODECANOATE CROSSPOLYMER	12F - Moisturizing	1
ACRYLATES/VINYL NEODECANOATE CROSSPOLYMER	12J - Other Skin Care Preps	1
Acrylic Acid/Stearyl Acrylate Copolymer		0
ALLYL METHACRYLATES CROSSPOLYMER	05G - Tonics, Dressings, and Other Hair Grooming Aids	1
ALLYL METHACRYLATES CROSSPOLYMER	07A - Blushers (all types)	2
ALLYL METHACRYLATES CROSSPOLYMER	07E - Lipstick	6
ALLYL METHACRYLATES CROSSPOLYMER	07I - Other Makeup Preparations	1
ALLYL METHACRYLATES CROSSPOLYMER	09A - Dentifrices	1
ALLYL METHACRYLATES CROSSPOLYMER	12A - Cleansing	1
ALLYL METHACRYLATES CROSSPOLYMER	12C - Face and Neck (exc shave)	4
ALLYL METHACRYLATES CROSSPOLYMER	12F - Moisturizing	2
ALLYL METHACRYLATES CROSSPOLYMER	12G - Night	3
ALLYL METHACRYLATES CROSSPOLYMER	12H - Paste Masks (mud packs)	2
ALLYL METHACRYLATES CROSSPOLYMER	12J - Other Skin Care Preps	7
ALLYL METHACRYLATES CROSSPOLYMER	13B - Indoor Tanning Preparations	1
AMMONIUM ACRYLATES COPOLYMER	03A - Eyebrow Pencil	2
AMMONIUM ACRYLATES COPOLYMER	03B - Eyeliner	12
AMMONIUM ACRYLATES COPOLYMER	03C - Eye Shadow	1
AMMONIUM ACRYLATES COPOLYMER	03D - Eye Lotion	1
AMMONIUM ACRYLATES COPOLYMER	03F - Mascara	30
AMMONIUM ACRYLATES COPOLYMER	03G - Other Eye Makeup Preparations	1
AMMONIUM ACRYLATES COPOLYMER	07I - Other Makeup Preparations	1
AMMONIUM ACRYLATES COPOLYMER	08E - Nail Polish and Enamel	10
AMMONIUM ACRYLATES COPOLYMER	12D - Body and Hand (exc shave)	1
AMMONIUM ACRYLATES COPOLYMER	12J - Other Skin Care Preps	1
AMMONIUM ACRYLATES/METHYL STYRENE/STYRENE COPOLYMER	03B - Eyeliner	5
AMMONIUM POLYACRYLATE	03D - Eye Lotion	2
AMMONIUM POLYACRYLATE	07G - Rouges	1
AMMONIUM POLYACRYLATE	08E - Nail Polish and Enamel	1
AMMONIUM POLYACRYLATE	10A - Bath Soaps and Detergents	1
AMMONIUM POLYACRYLATE	12C - Face and Neck (exc shave)	5
AMMONIUM POLYACRYLATE	12D - Body and Hand (exc shave)	1
AMMONIUM POLYACRYLATE	12F - Moisturizing	3
AMMONIUM POLYACRYLATE	12J - Other Skin Care Preps	1
AMMONIUM STYRENE/ACRYLATES COPOLYMER	03B - Eyeliner	1
AMMONIUM STYRENE/ACRYLATES COPOLYMER	13A - Suntan Gels, Creams, and Liquids	1
AMP-ACRYLATES COPOLYMER	03G - Other Eye Makeup Preparations	1
AMP-ACRYLATES COPOLYMER	05B - Hair Spray (aerosol fixatives)	12
AMP-ACRYLATES COPOLYMER	05F - Shampoos (non-coloring)	2

AMP-ACRYLATES COPOLYMER	05G - Tonics, Dressings, and Other Hair Grooming Aids	14
AMP-ACRYLATES COPOLYMER	05H - Wave Sets	1
AMP-ACRYLATES COPOLYMER	05I - Other Hair Preparations	5
AMP-ACRYLATES COPOLYMER	08E - Nail Polish and Enamel	1
BEHENYL METHACRYLATE/T-BUTYL METHACRYLATE COPOLYMER	03F - Mascara	2
BEHENYL METHACRYLATE/T-BUTYL METHACRYLATE COPOLYMER	07E - Lipstick	3
BUTYL ACRYLATE/GLYCOL DIMETHACRYLATE CROSSPOLYMER	12F - Moisturizing	1
C12-22 Alkyl Acrylate/Hydroxyethylacrylate Copolymer		0
C8-22 ALKYL ACRYLATES/METHACRYLIC ACID CROSSPOLYMER	05G - Tonics, Dressings, and Other Hair Grooming Aids	1
C8-22 ALKYL ACRYLATES/METHACRYLIC ACID CROSSPOLYMER	12C - Face and Neck (exc shave)	1
CARBOMER	01A - Baby Shampoos	2
CARBOMER	01B - Baby Lotions, Oils, Powders, and Creams	29
CARBOMER	01C - Other Baby Products	4
CARBOMER	02A - Bath Oils, Tablets, and Salts	4
CARBOMER	03A - Eyebrow Pencil	4
CARBOMER	03B - Eyeliner	2
CARBOMER	03C - Eye Shadow	6
CARBOMER	03D - Eye Lotion	169
CARBOMER	03E - Eye Makeup Remover	6
CARBOMER	03F - Mascara	14
CARBOMER	03G - Other Eye Makeup Preparations	89
CARBOMER	04E - Other Fragrance Preparation	9
CARBOMER	05A - Hair Conditioner	8
CARBOMER	05B - Hair Spray (aerosol fixatives)	3
CARBOMER	05C - Hair Straighteners	1
CARBOMER	05D - Permanent Waves	1
CARBOMER	05F - Shampoos (non-coloring)	237
CARBOMER	05G - Tonics, Dressings, and Other Hair Grooming Aids	161
CARBOMER	05H - Wave Sets	2
CARBOMER	05I - Other Hair Preparations	65
CARBOMER	06A - Hair Dyes and Colors (all types requiring caution statements and patch tests)	201
CARBOMER	06D - Hair Shampoos (coloring)	4
CARBOMER	06F - Hair Lighteners with Color	7
CARBOMER	06G - Hair Bleaches	6
CARBOMER	06H - Other Hair Coloring Preparation	4
CARBOMER	07A - Blushers (all types)	4
CARBOMER	07B - Face Powders	2
CARBOMER	07C - Foundations	57
CARBOMER	07D - Leg and Body Paints	13
CARBOMER	07E - Lipstick	2
CARBOMER	07F - Makeup Bases	16
CARBOMER	07G - Rouges	1
CARBOMER	07H - Makeup Fixatives	1
CARBOMER	07I - Other Makeup Preparations	31
CARBOMER	08A - Basecoats and Undercoats	1
CARBOMER	08B - Cuticle Softeners	5
CARBOMER	08C - Nail Creams and Lotions	1
CARBOMER	08E - Nail Polish and Enamel	1
CARBOMER	08G - Other Manicuring Preparations	4

CARBOMER	09A - Dentifrices	3
CARBOMER	09C - Other Oral Hygiene Products	87
CARBOMER	10A - Bath Soaps and Detergents	23
CARBOMER	10B - Deodorants (underarm)	3
CARBOMER	10E - Other Personal Cleanliness Products	73
CARBOMER	11A - Aftershave Lotion	75
CARBOMER	11D - Preshave Lotions (all types)	1
CARBOMER	11E - Shaving Cream	9
CARBOMER	11G - Other Shaving Preparation Products	14
CARBOMER	12A - Cleansing	246
CARBOMER	12B - Depilatories	4
CARBOMER	12C - Face and Neck (exc shave)	850
CARBOMER	12D - Body and Hand (exc shave)	924
CARBOMER	12E - Foot Powders and Sprays	6
CARBOMER	12F - Moisturizing	2112
CARBOMER	12G - Night	169
CARBOMER	12H - Paste Masks (mud packs)	102
CARBOMER	12I - Skin Fresheners	16
CARBOMER	12J - Other Skin Care Preps	247
CARBOMER	13A - Suntan Gels, Creams, and Liquids	8
CARBOMER	13B - Indoor Tanning Preparations	15
CARBOMER	13C - Other Suntan Preparations	13
CARBOMER EDT 2001	12D - Body and Hand (exc shave)	1
CARBOMER ULTREZ 10	12C - Face and Neck (exc shave)	1
CARBOMER ULTREZ 10	12D - Body and Hand (exc shave)	2
CARBOMER-934	01B - Baby Lotions, Oils, Powders, and Creams	1
CARBOMER-934	03B - Eyeliner	2
CARBOMER-934	03D - Eye Lotion	1
CARBOMER-934	03G - Other Eye Makeup Preparations	2
CARBOMER-934	05B - Hair Spray (aerosol fixatives)	1
CARBOMER-934	05G - Tonics, Dressings, and Other Hair Grooming Aids	6
CARBOMER-934	05H - Wave Sets	1
CARBOMER-934	05I - Other Hair Preparations	1
CARBOMER-934	06G - Hair Bleaches	1
CARBOMER-934	07C - Foundations	1
CARBOMER-934	10E - Other Personal Cleanliness Products	2
CARBOMER-934	11A - Aftershave Lotion	1
CARBOMER-934	11G - Other Shaving Preparation Products	1
CARBOMER-934	12A - Cleansing	11
CARBOMER-934	12C - Face and Neck (exc shave)	8
CARBOMER-934	12D - Body and Hand (exc shave)	20
CARBOMER-934	12F - Moisturizing	17
CARBOMER-934	12G - Night	1
CARBOMER-934	12H - Paste Masks (mud packs)	1
CARBOMER-934	12J - Other Skin Care Preps	15
CARBOMER-934	13A - Suntan Gels, Creams, and Liquids	3
CARBOMER-934P	12F - Moisturizing	2
CARBOMER-940	02D - Other Bath Preparations	1
CARBOMER-940	03E - Eye Makeup Remover	2
CARBOMER-940	03G - Other Eye Makeup Preparations	3
CARBOMER-940	05A - Hair Conditioner	2
CARBOMER-940	05B - Hair Spray (aerosol fixatives)	1
CARBOMER-940	05G - Tonics, Dressings, and Other Hair Grooming Aids	5
CARBOMER-940	05H - Wave Sets	1
CARBOMER-940	07A - Blushers (all types)	9
CARBOMER-940	07I - Other Makeup Preparations	1
CARBOMER-940	09A - Dentifrices	2
CARBOMER-940	10E - Other Personal Cleanliness Products	2
CARBOMER-940	12A - Cleansing	7
CARBOMER-940	12C - Face and Neck (exc shave)	23
CARBOMER-940	12D - Body and Hand (exc shave)	26

CARBOMER-940	12F - Moisturizing	17
CARBOMER-940	12G - Night	1
CARBOMER-940	12H - Paste Masks (mud packs)	9
CARBOMER-940	12J - Other Skin Care Preps	14
CARBOMER-940	13A - Suntan Gels, Creams, and Liquids	4
CARBOMER-941	03E - Eye Makeup Remover	2
CARBOMER-941	12A - Cleansing	4
CARBOMER-941	12C - Face and Neck (exc shave)	4
CARBOMER-941	12D - Body and Hand (exc shave)	4
CARBOMER-941	12F - Moisturizing	1
CARBOMER-941	12H - Paste Masks (mud packs)	1
CARBOMER-941	12J - Other Skin Care Preps	2
CARBOMER-941	13B - Indoor Tanning Preparations	1
CARBOMER-956	09C - Other Oral Hygiene Products	1
CARBOMER-980	03E - Eye Makeup Remover	1
CARBOMER-980	04E - Other Fragrance Preparation	3
CARBOMER-980	07C - Foundations	1
CARBOMER-980	11A - Aftershave Lotion	2
CARBOMER-980	11D - Preshave Lotions (all types)	3
CARBOMER-980	12C - Face and Neck (exc shave)	1
CARBOMER-980	12F - Moisturizing	4
ETHYLENE/ACRYLIC ACID COPOLYMER	03C - Eye Shadow	143
ETHYLENE/ACRYLIC ACID COPOLYMER	03D - Eye Lotion	14
ETHYLENE/ACRYLIC ACID COPOLYMER	03F - Mascara	10
ETHYLENE/ACRYLIC ACID COPOLYMER	03G - Other Eye Makeup Preparations	14
ETHYLENE/ACRYLIC ACID COPOLYMER	05G - Tonics, Dressings, and Other Hair Grooming Aids	1
ETHYLENE/ACRYLIC ACID COPOLYMER	07B - Face Powders	23
ETHYLENE/ACRYLIC ACID COPOLYMER	07C - Foundations	66
ETHYLENE/ACRYLIC ACID COPOLYMER	07E - Lipstick	3
ETHYLENE/ACRYLIC ACID COPOLYMER	07F - Makeup Bases	7
ETHYLENE/ACRYLIC ACID COPOLYMER	07G - Rouges	1
ETHYLENE/ACRYLIC ACID COPOLYMER	07H - Makeup Fixatives	1
ETHYLENE/ACRYLIC ACID COPOLYMER	07I - Other Makeup Preparations	3
ETHYLENE/ACRYLIC ACID COPOLYMER	08G - Other Manicuring Preparations	4
ETHYLENE/ACRYLIC ACID COPOLYMER	12C - Face and Neck (exc shave)	7
ETHYLENE/ACRYLIC ACID COPOLYMER	12F - Moisturizing	12
ETHYLENE/ACRYLIC ACID COPOLYMER	12G - Night	5
ETHYLENE/ACRYLIC ACID COPOLYMER	12J - Other Skin Care Preps	6
ETHYLENE/METHACRYLATE COPOLYMER	03A - Eyebrow Pencil	4
ETHYLENE/METHACRYLATE COPOLYMER	03B - Eyeliner	1
ETHYLENE/METHACRYLATE COPOLYMER	03C - Eye Shadow	2
ETHYLENE/METHACRYLATE COPOLYMER	03D - Eye Lotion	3
ETHYLENE/METHACRYLATE COPOLYMER	03F - Mascara	18
ETHYLENE/METHACRYLATE COPOLYMER	03G - Other Eye Makeup Preparations	1
ETHYLENE/METHACRYLATE COPOLYMER	07A - Blushers (all types)	6
ETHYLENE/METHACRYLATE COPOLYMER	07B - Face Powders	9
ETHYLENE/METHACRYLATE COPOLYMER	07C - Foundations	6
ETHYLENE/METHACRYLATE COPOLYMER	07F - Makeup Bases	3
ETHYLENE/METHACRYLATE COPOLYMER	07I - Other Makeup Preparations	3
ETHYLENE/METHACRYLATE COPOLYMER	12C - Face and Neck (exc shave)	1
ETHYLENE/METHACRYLATE COPOLYMER	12F - Moisturizing	2
ETHYLENE/METHACRYLATE COPOLYMER	12J - Other Skin Care Preps	1
ETHYLENE/SODIUM ACRYLATE COPOLYMER	12A - Cleansing	1
ETHYLHEXYL ACRYLATE/METHYL METHACRYLATE COPOLYMER	03B - Eyeliner	5

Lauryl Acrylate Crosspolymer		0
LAURYL METHACRYLATE/GLYCOL DIMETHACRYLATE CROSSPOLYMER	03B - Eyeliner	4
LAURYL METHACRYLATE/GLYCOL DIMETHACRYLATE CROSSPOLYMER	03C - Eye Shadow	19
LAURYL METHACRYLATE/GLYCOL DIMETHACRYLATE CROSSPOLYMER	03G - Other Eye Makeup Preparations	2
LAURYL METHACRYLATE/GLYCOL DIMETHACRYLATE CROSSPOLYMER	04E - Other Fragrance Preparation	6
LAURYL METHACRYLATE/GLYCOL DIMETHACRYLATE CROSSPOLYMER	07A - Blushers (all types)	2
LAURYL METHACRYLATE/GLYCOL DIMETHACRYLATE CROSSPOLYMER	07B - Face Powders	6
LAURYL METHACRYLATE/GLYCOL DIMETHACRYLATE CROSSPOLYMER	07C - Foundations	22
LAURYL METHACRYLATE/GLYCOL DIMETHACRYLATE CROSSPOLYMER	07E - Lipstick	19
LAURYL METHACRYLATE/GLYCOL DIMETHACRYLATE CROSSPOLYMER	07F - Makeup Bases	2
LAURYL METHACRYLATE/GLYCOL DIMETHACRYLATE CROSSPOLYMER	07G - Rouges	1
LAURYL METHACRYLATE/GLYCOL DIMETHACRYLATE CROSSPOLYMER	07I - Other Makeup Preparations	2
LAURYL METHACRYLATE/GLYCOL DIMETHACRYLATE CROSSPOLYMER	08G - Other Manicuring Preparations	1
LAURYL METHACRYLATE/GLYCOL DIMETHACRYLATE CROSSPOLYMER	12A - Cleansing	6
LAURYL METHACRYLATE/GLYCOL DIMETHACRYLATE CROSSPOLYMER	12C - Face and Neck (exc shave)	2
LAURYL METHACRYLATE/GLYCOL DIMETHACRYLATE CROSSPOLYMER	12H - Paste Masks (mud packs)	3
LAURYL METHACRYLATE/GLYCOL DIMETHACRYLATE CROSSPOLYMER	12J - Other Skin Care Preps	2
LAURYL METHACRYLATE/SODIUM METHACRYLATE CROSSPOLYMER	10E - Other Personal Cleanliness Products	1
LAURYL METHACRYLATE/SODIUM METHACRYLATE CROSSPOLYMER	12J - Other Skin Care Preps	3
METHACRYLOYL ETHYL BETAINE/ACRYLATES COPOLYMER	05G - Tonics, Dressings, and Other Hair Grooming Aids	3
METHACRYLOYL ETHYL BETAINE/ACRYLATES COPOLYMER	05H - Wave Sets	1
METHACRYLOYL ETHYL BETAINE/ACRYLATES COPOLYMER	06B - Hair Tints	8
METHYL METHACRYLATE CROSSPOLYMER	03A - Eyebrow Pencil	3
METHYL METHACRYLATE CROSSPOLYMER	03B - Eyeliner	10
METHYL METHACRYLATE CROSSPOLYMER	03C - Eye Shadow	19
METHYL METHACRYLATE CROSSPOLYMER	03D - Eye Lotion	5
METHYL METHACRYLATE CROSSPOLYMER	03F - Mascara	5
METHYL METHACRYLATE CROSSPOLYMER	03G - Other Eye Makeup Preparations	11
METHYL METHACRYLATE CROSSPOLYMER	04C - Powders (dusting and talcum, excluding aftershave talc)	3
METHYL METHACRYLATE CROSSPOLYMER	05H - Wave Sets	1
METHYL METHACRYLATE CROSSPOLYMER	06B - Hair Tints	2
METHYL METHACRYLATE CROSSPOLYMER	06E - Hair Color Sprays (aerosol)	5
METHYL METHACRYLATE CROSSPOLYMER	07A - Blushers (all types)	13
METHYL METHACRYLATE CROSSPOLYMER	07B - Face Powders	33
METHYL METHACRYLATE CROSSPOLYMER	07C - Foundations	109
METHYL METHACRYLATE CROSSPOLYMER	07E - Lipstick	38
METHYL METHACRYLATE CROSSPOLYMER	07F - Makeup Bases	6
METHYL METHACRYLATE CROSSPOLYMER	07G - Rouges	18
METHYL METHACRYLATE CROSSPOLYMER	07H - Makeup Fixatives	7
METHYL METHACRYLATE CROSSPOLYMER	07I - Other Makeup Preparations	28
METHYL METHACRYLATE CROSSPOLYMER	08E - Nail Polish and Enamel	2
METHYL METHACRYLATE CROSSPOLYMER	10B - Deodorants (underarm)	1
METHYL METHACRYLATE CROSSPOLYMER	11A - Aftershave Lotion	1
METHYL METHACRYLATE CROSSPOLYMER	11G - Other Shaving Preparation Products	1
METHYL METHACRYLATE CROSSPOLYMER	12A - Cleansing	2
METHYL METHACRYLATE CROSSPOLYMER	12C - Face and Neck (exc shave)	35
METHYL METHACRYLATE CROSSPOLYMER	12D - Body and Hand (exc shave)	3
METHYL METHACRYLATE CROSSPOLYMER	12F - Moisturizing	33
METHYL METHACRYLATE CROSSPOLYMER	12G - Night	11
METHYL METHACRYLATE CROSSPOLYMER	12I - Skin Fresheners	1
METHYL METHACRYLATE CROSSPOLYMER	12J - Other Skin Care Preps	15

METHYL METHACRYLATE CROSSPOLYMER	13B - Indoor Tanning Preparations	1
METHYL METHACRYLATE/GLYCOL DIMETHACRYLATE CROSSPOLYMER	03D - Eye Lotion	2
METHYL METHACRYLATE/GLYCOL DIMETHACRYLATE CROSSPOLYMER	07B - Face Powders	1
METHYL METHACRYLATE/GLYCOL DIMETHACRYLATE CROSSPOLYMER	07I - Other Makeup Preparations	16
METHYL METHACRYLATE/GLYCOL DIMETHACRYLATE CROSSPOLYMER	12C - Face and Neck (exc shave)	11
METHYL METHACRYLATE/GLYCOL DIMETHACRYLATE CROSSPOLYMER	12F - Moisturizing	4
METHYL METHACRYLATE/GLYCOL DIMETHACRYLATE CROSSPOLYMER	12G - Night	1
METHYL METHACRYLATE/GLYCOL DIMETHACRYLATE CROSSPOLYMER	12J - Other Skin Care Preps	3
METHYL METHACRYLATE/PEG/PPG-4/3 METHACRYLATE CROSSPOLYMER	03D - Eye Lotion	1
POLY C10-30 ALKYL ACRYLATE	03D - Eye Lotion	1
POLY C10-30 ALKYL ACRYLATE	03F - Mascara	1
POLY C10-30 ALKYL ACRYLATE	07E - Lipstick	3
POLY C10-30 ALKYL ACRYLATE	12C - Face and Neck (exc shave)	3
POLY C10-30 ALKYL ACRYLATE	12F - Moisturizing	5
POLY C10-30 ALKYL ACRYLATE	12G - Night	3
POLY C10-30 ALKYL ACRYLATE	12J - Other Skin Care Preps	2
POLY C10-30 ALKYL ACRYLATE	13A - Suntan Gels, Creams, and Liquids	1
POLYACRYLATE-14	05G - Tonics, Dressings, and Other Hair Grooming Aids	1
POLYACRYLATE-14	05H - Wave Sets	1
POLYACRYLATE-14	05I - Other Hair Preparations	1
POLYACRYLATE-1 CROSSPOLYMER	05F - Shampoos (non-coloring)	3
POLYACRYLATE-1 CROSSPOLYMER	10A - Bath Soaps and Detergents	6
POLYACRYLATE-1 CROSSPOLYMER	12A - Cleansing	1
POLYACRYLATE-1 CROSSPOLYMER	12C - Face and Neck (exc shave)	3
POLYACRYLATE-1 CROSSPOLYMER	12F - Moisturizing	1
POLYACRYLIC ACID	03B - Eyeliner	1
POLYACRYLIC ACID	03D - Eye Lotion	2
POLYACRYLIC ACID	03G - Other Eye Makeup Preparations	5
POLYACRYLIC ACID	04E - Other Fragrance Preparation	1
POLYACRYLIC ACID	05G - Tonics, Dressings, and Other Hair Grooming Aids	2
POLYACRYLIC ACID	05I - Other Hair Preparations	1
POLYACRYLIC ACID	07C - Foundations	1
POLYACRYLIC ACID	07E - Lipstick	1
POLYACRYLIC ACID	07F - Makeup Bases	1
POLYACRYLIC ACID	08B - Cuticle Softeners	1
POLYACRYLIC ACID	08E - Nail Polish and Enamel	4
POLYACRYLIC ACID	08G - Other Manicuring Preparations	6
POLYACRYLIC ACID	09C - Other Oral Hygiene Products	1
POLYACRYLIC ACID	10A - Bath Soaps and Detergents	1
POLYACRYLIC ACID	11A - Aftershave Lotion	1
POLYACRYLIC ACID	11E - Shaving Cream	1
POLYACRYLIC ACID	11G - Other Shaving Preparation Products	1
POLYACRYLIC ACID	12A - Cleansing	8
POLYACRYLIC ACID	12C - Face and Neck (exc shave)	17
POLYACRYLIC ACID	12D - Body and Hand (exc shave)	12
POLYACRYLIC ACID	12F - Moisturizing	29
POLYACRYLIC ACID	12G - Night	2
POLYACRYLIC ACID	12H - Paste Masks (mud packs)	3
POLYACRYLIC ACID	12I - Skin Fresheners	1

POLYACRYLIC ACID	12J - Other Skin Care Preps	8
POLYETHYLACRYLATE	03F - Mascara	2
POLYETHYLACRYLATE	07I - Other Makeup Preparations	1
POLYETHYLACRYLATE	08G - Other Manicuring Preparations	1
POLYMETHYL ACRYLATE	12F - Moisturizing	1
POLYMETHYL METHACRYLATE	03A - Eyebrow Pencil	13
POLYMETHYL METHACRYLATE	03B - Eyeliner	50
POLYMETHYL METHACRYLATE	03C - Eye Shadow	113
POLYMETHYL METHACRYLATE	03D - Eye Lotion	33
POLYMETHYL METHACRYLATE	03F - Mascara	11
POLYMETHYL METHACRYLATE	03G - Other Eye Makeup Preparations	73
POLYMETHYL METHACRYLATE	04B - Perfumes	1
POLYMETHYL METHACRYLATE	04C - Powders (dusting and talcum, excluding aftershave talc)	1
POLYMETHYL METHACRYLATE	04E - Other Fragrance Preparation	3
POLYMETHYL METHACRYLATE	05A - Hair Conditioner	1
POLYMETHYL METHACRYLATE	05G - Tonics, Dressings, and Other Hair Grooming Aids	3
POLYMETHYL METHACRYLATE	06B - Hair Tints	9
POLYMETHYL METHACRYLATE	07A - Blushers (all types)	58
POLYMETHYL METHACRYLATE	07B - Face Powders	75
POLYMETHYL METHACRYLATE	07C - Foundations	72
POLYMETHYL METHACRYLATE	07E - Lipstick	72
POLYMETHYL METHACRYLATE	07F - Makeup Bases	18
POLYMETHYL METHACRYLATE	07G - Rouges	3
POLYMETHYL METHACRYLATE	07H - Makeup Fixatives	3
POLYMETHYL METHACRYLATE	07I - Other Makeup Preparations	62
POLYMETHYL METHACRYLATE	08D - Nail Extenders	2
POLYMETHYL METHACRYLATE	08E - Nail Polish and Enamel	1
POLYMETHYL METHACRYLATE	08G - Other Manicuring Preparations	16
POLYMETHYL METHACRYLATE	10A - Bath Soaps and Detergents	2
POLYMETHYL METHACRYLATE	10E - Other Personal Cleanliness Products	4
POLYMETHYL METHACRYLATE	11A - Aftershave Lotion	6
POLYMETHYL METHACRYLATE	11E - Shaving Cream	1
POLYMETHYL METHACRYLATE	11G - Other Shaving Preparation Products	2
POLYMETHYL METHACRYLATE	12A - Cleansing	3
POLYMETHYL METHACRYLATE	12C - Face and Neck (exc shave)	65
POLYMETHYL METHACRYLATE	12D - Body and Hand (exc shave)	23
POLYMETHYL METHACRYLATE	12F - Moisturizing	65
POLYMETHYL METHACRYLATE	12G - Night	26
POLYMETHYL METHACRYLATE	12H - Paste Masks (mud packs)	4
POLYMETHYL METHACRYLATE	12J - Other Skin Care Preps	25
POLYMETHYL METHACRYLATE	13A - Suntan Gels, Creams, and Liquids	3
POTASSIUM ACRYLATES COPOLYMER	01A - Baby Shampoos	2
POTASSIUM ACRYLATES COPOLYMER	01C - Other Baby Products	10
POTASSIUM ACRYLATES COPOLYMER	10E - Other Personal Cleanliness Products	1
POTASSIUM ACRYLATES COPOLYMER	12A - Cleansing	3
POTASSIUM ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	03G - Other Eye Makeup Preparations	1
POTASSIUM ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	12C - Face and Neck (exc shave)	1
POTASSIUM CARBOMER	02A - Bath Oils, Tablets, and Salts	4
POTASSIUM CARBOMER	03D - Eye Lotion	1

POTASSIUM CARBOMER	03E - Eye Makeup Remover	1
POTASSIUM CARBOMER	03G - Other Eye Makeup Preparations	1
POTASSIUM CARBOMER	10A - Bath Soaps and Detergents	1
POTASSIUM CARBOMER	10E - Other Personal Cleanliness Products	1
POTASSIUM CARBOMER	11A - Aftershave Lotion	1
POTASSIUM CARBOMER	11G - Other Shaving Preparation Products	1
POTASSIUM CARBOMER	12A - Cleansing	9
POTASSIUM CARBOMER	12C - Face and Neck (exc shave)	4
POTASSIUM CARBOMER	12D - Body and Hand (exc shave)	23
POTASSIUM CARBOMER	12F - Moisturizing	23
POTASSIUM CARBOMER	12G - Night	1
POTASSIUM CARBOMER	12H - Paste Masks (mud packs)	1
POTASSIUM CARBOMER	12J - Other Skin Care Preps	3
Sodium Acrylate/Vinyl Alcohol Copolymer		0
SODIUM ACRYLATES COPOLYMER	01B - Baby Lotions, Oils, Powders, and Creams	2
SODIUM ACRYLATES COPOLYMER	03C - Eye Shadow	7
SODIUM ACRYLATES COPOLYMER	03D - Eye Lotion	3
SODIUM ACRYLATES COPOLYMER	03F - Mascara	1
SODIUM ACRYLATES COPOLYMER	03G - Other Eye Makeup Preparations	9
SODIUM ACRYLATES COPOLYMER	05G - Tonics, Dressings, and Other Hair Grooming Aids	1
SODIUM ACRYLATES COPOLYMER	07C - Foundations	3
SODIUM ACRYLATES COPOLYMER	07I - Other Makeup Preparations	1
SODIUM ACRYLATES COPOLYMER	09C - Other Oral Hygiene Products	1
SODIUM ACRYLATES COPOLYMER	10E - Other Personal Cleanliness Products	1
SODIUM ACRYLATES COPOLYMER	11A - Aftershave Lotion	8
SODIUM ACRYLATES COPOLYMER	12A - Cleansing	3
SODIUM ACRYLATES COPOLYMER	12C - Face and Neck (exc shave)	28
SODIUM ACRYLATES COPOLYMER	12D - Body and Hand (exc shave)	21
SODIUM ACRYLATES COPOLYMER	12E - Foot Powders and Sprays	1
SODIUM ACRYLATES COPOLYMER	12F - Moisturizing	62
SODIUM ACRYLATES COPOLYMER	12G - Night	6
SODIUM ACRYLATES COPOLYMER	12H - Paste Masks (mud packs)	4
SODIUM ACRYLATES COPOLYMER	12I - Skin Fresheners	2
SODIUM ACRYLATES COPOLYMER	12J - Other Skin Care Preps	14
SODIUM ACRYLATES COPOLYMER	13B - Indoor Tanning Preparations	1
Sodium Acrylates Crosspolymer-2		0
SODIUM ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	03D - Eye Lotion	1
SODIUM ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	03G - Other Eye Makeup Preparations	1
SODIUM ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	11A - Aftershave Lotion	5
SODIUM ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	12C - Face and Neck (exc shave)	5
SODIUM ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	12F - Moisturizing	4
SODIUM ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	12G - Night	1
SODIUM ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	12H - Paste Masks (mud packs)	78
SODIUM ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	12J - Other Skin Care Preps	1
Sodium Acrylates/Vinyl Isodecanoate Crosspolymer		0
SODIUM CARBOMER	03D - Eye Lotion	13
SODIUM CARBOMER	03F - Mascara	1
SODIUM CARBOMER	03G - Other Eye Makeup Preparations	8
SODIUM CARBOMER	08C - Nail Creams and Lotions	1
SODIUM CARBOMER	10E - Other Personal Cleanliness Products	1

SODIUM CARBOMER	11A - Aftershave Lotion	7
SODIUM CARBOMER	12A - Cleansing	16
SODIUM CARBOMER	12C - Face and Neck (exc shave)	26
SODIUM CARBOMER	12D - Body and Hand (exc shave)	12
SODIUM CARBOMER	12E - Foot Powders and Sprays	1
SODIUM CARBOMER	12F - Moisturizing	57
SODIUM CARBOMER	12G - Night	8
SODIUM CARBOMER	12H - Paste Masks (mud packs)	5
SODIUM CARBOMER	12J - Other Skin Care Preps	11
SODIUM CARBOMER	13C - Other Suntan Preparations	1
SODIUM POLYACRYLATE	03A - Eyebrow Pencil	1
SODIUM POLYACRYLATE	03B - Eyeliner	16
SODIUM POLYACRYLATE	03C - Eye Shadow	3
SODIUM POLYACRYLATE	03D - Eye Lotion	43
SODIUM POLYACRYLATE	03E - Eye Makeup Remover	2
SODIUM POLYACRYLATE	03F - Mascara	17
SODIUM POLYACRYLATE	03G - Other Eye Makeup Preparations	50
SODIUM POLYACRYLATE	04E - Other Fragrance Preparation	2
SODIUM POLYACRYLATE	05A - Hair Conditioner	17
SODIUM POLYACRYLATE	05B - Hair Spray (aerosol fixatives)	1
SODIUM POLYACRYLATE	05F - Shampoos (non-coloring)	21
SODIUM POLYACRYLATE	05G - Tonics, Dressings, and Other Hair Grooming Aids	23
SODIUM POLYACRYLATE	05I - Other Hair Preparations	21
SODIUM POLYACRYLATE	06A - Hair Dyes and Colors (all types requiring caution statements and patch tests)	21
SODIUM POLYACRYLATE	06D - Hair Shampoos (coloring)	1
SODIUM POLYACRYLATE	07B - Face Powders	7
SODIUM POLYACRYLATE	07C - Foundations	8
SODIUM POLYACRYLATE	07D - Leg and Body Paints	10
SODIUM POLYACRYLATE	07E - Lipstick	1
SODIUM POLYACRYLATE	07F - Makeup Bases	3
SODIUM POLYACRYLATE	07H - Makeup Fixatives	1
SODIUM POLYACRYLATE	07I - Other Makeup Preparations	3
SODIUM POLYACRYLATE	08G - Other Manicuring Preparations	1
SODIUM POLYACRYLATE	09A - Dentifrices	2
SODIUM POLYACRYLATE	10A - Bath Soaps and Detergents	1
SODIUM POLYACRYLATE	10E - Other Personal Cleanliness Products	12
SODIUM POLYACRYLATE	11A - Aftershave Lotion	9
SODIUM POLYACRYLATE	11E - Shaving Cream	2
SODIUM POLYACRYLATE	11G - Other Shaving Preparation Products	5
SODIUM POLYACRYLATE	12A - Cleansing	21
SODIUM POLYACRYLATE	12C - Face and Neck (exc shave)	128
SODIUM POLYACRYLATE	12D - Body and Hand (exc shave)	138
SODIUM POLYACRYLATE	12E - Foot Powders and Sprays	1
SODIUM POLYACRYLATE	12F - Moisturizing	230
SODIUM POLYACRYLATE	12G - Night	45
SODIUM POLYACRYLATE	12H - Paste Masks (mud packs)	13
SODIUM POLYACRYLATE	12I - Skin Fresheners	11
SODIUM POLYACRYLATE	12J - Other Skin Care Preps	52
SODIUM POLYACRYLATE	13A - Suntan Gels, Creams, and Liquids	4
SODIUM POLYACRYLATE	13B - Indoor Tanning Preparations	5
SODIUM POLYACRYLATE	13C - Other Suntan Preparations	1
SODIUM POLYMETHACRYLATE	03B - Eyeliner	4
SODIUM POLYMETHACRYLATE	03C - Eye Shadow	1
SODIUM POLYMETHACRYLATE	03F - Mascara	54
SODIUM POLYMETHACRYLATE	03G - Other Eye Makeup Preparations	1
SODIUM POLYMETHACRYLATE	12J - Other Skin Care Preps	1
SODIUM POLYMETHACRYLATE	13A - Suntan Gels, Creams, and Liquids	1

STEARETH-10 ALLYL ETHER/ACRYLATES COPOLYMER	05G - Tonics, Dressings, and Other Hair Grooming Aids	2
STEARETH-10 ALLYL ETHER/ACRYLATES COPOLYMER	05H - Wave Sets	1
STEARETH-10 ALLYL ETHER/ACRYLATES COPOLYMER	06A - Hair Dyes and Colors (all types requiring caution statements and patch tests)	1
STEARETH-10 ALLYL ETHER/ACRYLATES COPOLYMER	06B - Hair Tints	1
STEARETH-10 ALLYL ETHER/ACRYLATES COPOLYMER	06G - Hair Bleaches	2
STEARETH-10 ALLYL ETHER/ACRYLATES COPOLYMER	06H - Other Hair Coloring Preparation	2
STEARETH-10 ALLYL ETHER/ACRYLATES COPOLYMER	10E - Other Personal Cleanliness Products	1
STEARETH-10 ALLYL ETHER/ACRYLATES COPOLYMER	12C - Face and Neck (exc shave)	1
STEARETH-10 ALLYL ETHER/ACRYLATES COPOLYMER	12F - Moisturizing	1
STYRENE/ACRYLATES/AMMONIUM METHACRYLATE COPOLYMER	03B - Eyeliner	42
STYRENE/ACRYLATES/AMMONIUM METHACRYLATE COPOLYMER	03C - Eye Shadow	1
STYRENE/ACRYLATES/AMMONIUM METHACRYLATE COPOLYMER	03F - Mascara	51
STYRENE/ACRYLATES/AMMONIUM METHACRYLATE COPOLYMER	03G - Other Eye Makeup Preparations	5
STYRENE/ACRYLATES/AMMONIUM METHACRYLATE COPOLYMER	06A - Hair Dyes and Colors (all types requiring caution statements and patch tests)	4
STYRENE/ACRYLATES/AMMONIUM METHACRYLATE COPOLYMER	07I - Other Makeup Preparations	1
STYRENE/ACRYLATES/AMMONIUM METHACRYLATE COPOLYMER	08E - Nail Polish and Enamel	1
STYRENE/ACRYLATES/AMMONIUM METHACRYLATE COPOLYMER	12F - Moisturizing	1
VA/BUTYL MALEATE/ISOBORNYL ACRYLATE COPOLYMER	05B - Hair Spray (aerosol fixatives)	1
VA/BUTYL MALEATE/ISOBORNYL ACRYLATE COPOLYMER	05G - Tonics, Dressings, and Other Hair Grooming Aids	1

Personal Care Products Council
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Memorandum

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

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

DATE: September 18, 2018

SUBJECT: Draft Amended Report: Safety Assessment of Acrylates Copolymers as Used in Cosmetics (draft prepared for the September 24-25, 2018 CIR Expert Panel meeting)

The Council respectfully submits the following comments on the draft amended report, Safety Assessment of Acrylates Copolymers as Used in Cosmetics.

Key Issues

The memo states, that some of the Council comments have been addressed. It would have been helpful to the CIR Expert Panel to state the issues that have not been addressed.

There is a separate CIR report (finalized in 2014; not yet published) on styrene copolymers. Therefore, the styrene containing acrylate polymers should not be included in this report. This is especially true for ingredients in the styrene copolymers report and currently in the acrylates copolymers re-review, such as Acrylates/Styrene Copolymer.

If the styrene containing copolymers are left in the acrylates copolymers re-review, the styrene copolymer report needs to be mentioned in the Introduction of the acrylates copolymers re-review and summaries of information on the appropriate ingredients from the original styrene copolymer report need to be added to the acrylates copolymers re-review. At the time of the styrene copolymer report, industry provided unpublished information on Acrylates/Styrene Copolymer (some of which is apparently summarized in the NICNAS assessments [references 7 and 13 of the acrylates copolymer re-review]) which should be included in the acrylates copolymer re-review. In addition, the appropriate use information from the 2014 styrene copolymers report should be added to the acrylates copolymer report.

There are four ingredients (Glycol Dimethacrylate Crosspolymer, Polyacrylate-14, Polyacrylate-29 and Polyacrylate-34) for which a Council concentration of use survey has not been started. This is correctly indicated in Table 4 for Polyacrylate-14, but not indicated in

Table 5 for the other three ingredients which have no reported uses to the VCRP.

Concerning benzene in carbomer, the re-review should also note that in the 2003 re-review, the CIR Expert Panel stated: "Residual levels of benzene should be below those shown to have no risk to human health. For example, the EPA has established for drinking water that the 10^{-6} risk level for cancer is between 1 and 10 µg/L." Although no formal risk assessment was completed for Carbomer polymerized in benzene, this is essentially the same approach used for residual benzene in Acrylates/C10-30 Alkyl Acrylate Crosspolymer.

Carcinogenicity; Summary - The 2013 nomination of polyacrylates for consideration for listing in the NTP Report on Carcinogens (RoC) should be deleted unless more recent evidence can be found that this material is being considered for the RoC. The website on the RoC (at https://ntp.niehs.nih.gov/pubhealth/roc/index.html) does not list polyacrylates among the materials completed, under evaluation, or under consideration, although other materials from the 2013 *Federal Register* Notice are included in these lists.

Additional Considerations

Non-cosmetic Use - Which of the acrylates copolymers are approved for use as indirect food additives?

Acute, original acrylates copolymers summary - What was the dermal LD_{50} for Ethylene/Acrylic Acid Copolymer?

The information concerning the subchronic and chronic inhalation studies of Acrylates Copolymer do not belong in the Acute section.

Chronic, Oral, Acrylates Copolymer - It is not clear what the dose of the "test material" represent. Is this the dose of the pellets in gelatin capsules? It might be clearer if the doses of the "test material" (200, 500 and 1000) were presented before the doses of the copolymer (50, 125 and 250).

Dermal Irritation and Sensitization, summary Crosslinked Alkyl Acrylates - Does the paragraph concerning the residual monomer MMA belong in this section? It would be more appropriate for the summary of the PMMA and related ingredients report. What is meant by "these ingredients"?

Phototoxicity/Photosensitization - Please correct: "Each test sites were graded immediately after irradiation." (Either delete "Each" or change "test sites were" to "test site was")

Please add the units to "24" (likely hours)

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Memorandum

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

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

DATE: October 23, 2018

SUBJECT: Tentative Report: Amended Safety Assessment of Acrylates Copolymers as Used in Cosmetics (posted October 5, 2018)

The Council respectfully submits the following comments on the tentative report, Amended Safety Assessment of Acrylates Copolymers as Used in Cosmetics.

Key Issues

To acknowledge that Polymethyl Methacrylate has had use in cosmetics as "microbeads", please add the following to the Cosmetic Use section. "Based on environmental concerns, the use of microbeads in cosmetics is being phased out in many jurisdictions including the United States. Microbeads includes the Polymethyl Methacrylate beads described in the 2011 CIR report." FDA's web page on microbead-free waters act https://www.fda.gov/cosmetics/guidanceregulation/lawsregulations/ucm531849.htm provides additional details and appropriate references for this action in the United States.

Additional Considerations

Introduction - The following is not a complete sentence: "The Food and Drug Administration (FDA) determination of safety of PMMA use in several medical devices, which included human and animal safety data".

Methods of Manufacture, Acrylates Copolymer - Please revise: "After the reaction is cooled and filtered, the dry substance content is approximately 30%." The product of the reaction not the reaction is filtered.

Cosmetic Use - The second paragraph says that there were 6434 uses of Carbomer reported to the VCRP (agrees with Table 4), while the fourth paragraph says 3177 uses of Carbomer were reported.

Non-Cosmetic Use - Please state the copolymers with approved indirect food additive use, or provide an example. Please include the appropriate CFR citation(s).

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Acute, Crosslinked Alkyl Acrylate report summary - Please indicate the ingredient(s) for which there were data. For which ingredient was the lowest effect level reported?

Subchronic, Acrylates Copolymers report summary - Units of mg/m^3 should be called a "concentration" rather than "dose".

Chronic, Carbomer report summary - Were there two different 6.5 month dog studies? The first sentence says that there were no significant effects, while the next sentences describe effects in studies of the same duration. Please clearly state if there were multiple studies.

DART, Acrylates Copolymer report summary - Please state the doses used in the rat study.

Ocular Irritation, Acrylates Copolymers report and Crosslinked Alkyl Acrylate report summaries - Please include the concentrations that were tested.

Risk Assessment - As Acrylates/C10-30 Alkyl Acrylates Crosspolymer polymerized in benzene is not included in this report (as stated in the Introduction), the risk assessment concerning residual benzene in this polymer should be deleted from this report.

Summary - Please revise: "126 ingredients similar copolymers"

Unless a current reference can be found to indicate that NTP is still considering polyacrylates for the RoC, the statement concerning the 2013 nomination of polyacrylates should be deleted from the Summary.

Discussion - The following statement should be deleted: "and there are some that will warrant a review of their own in in the near future because of frequency of use." This statement is not necessary as it will become irrelevant after the review of the "other" ingredients is completed. In addition, there are always ingredients being added to the *Dictionary* for which a CIR review may become necessary.