BUFF BOOK 1

Memo

Agenda

Minutes

Boilerplates

CIR EXPERT PANEL MEETING

MARCH 3-4, 2011

Cosmetic Ingredient Review

Commitment . . . Credibility
Since 1976

C I R

MEMORANDUM

To:	CIR Expert Panel Members and Liaisons
From:	Director, CIR
Subject:	118th Meeting of the CIR Expert Panel — Thursday and Friday, March 3-4, 2011
Date:	February 10, 2011

Enclosed are the agenda and accompanying materials for the 118th CIR Expert Panel Meeting, to be held Thursday and Friday, March 3-4, 2011 at the Madison Hotel, 1177 Fifteenth Street, NW, Washington, DC 20005. Phone: (202) 862-1600. Fax: (202) 785-1255.

The agenda includes consideration of 9 ingredient groups, along with an initial review of boilerplates, precedents, and formats in current use.

Schedule and Hotel Accommodations

We will reserve rooms for the nights of Wednesday, March 2, and Thursday, March 3 at the Madison. If you have any problems, please contact me on my cell phone at 301-512-7846.

Team Meetings - remember, breakfast buffet on day 1 is at 8:30 am and meeting starts at 9:00 am.

Re-review summary - buff cover - you'll also be able to review the re-review summary of the Disperse Blue 1.

Draft reports - there are 4 reports under green cover.

1. Acrylate Cross Polymers – This group is headlined by Acrylates/C10-30 alkyl acrylate crosspolymer with 1606 current uses, mostly in leave-on products. When this ingredient was included on the priority list, it was contemplated that it would be expanded to include other crosslinked alkyl acrylates in which the co-monomers are comprised of at least one of: acrylic acid, sodium acrylate, methacrylic acid, or alkyl acrylate. That brings the group up to 23 individual cosmetic ingredients that appear to share the same lack of chemical reactivity, i.e., they are nearly impervious to degradation. The Scientific Literature Review (SLR) for Acrylate Cross Polymers was announced in December, 2010. The teams should review the draft report to determine if additional data are needed.

2. DEA and Related DEA-Containing Ingredients – at the last meeting, the Panel agreed to reopen the safety assessment of DEA separate from MEA and TEA. With that strategy, the Panel reasoned that DEA-containing ingredients could be included in the reopened report. There are 69 ingredients in this report, including DEA. The teams should review the draft report to determine if additional data are needed.

3. Formaldehyde and Methylene Glycol – at the last meeting, the Panel agreed to reopen the safety assessment of formaldehyde to address the uses of this ingredient in hair smoothing products and to add methylene glycol to the reopened report. We have used a focused approach to identify the issues, leaning heavily on the information provided in a very complete, draft EPA risk assessment of formaldehyde. Details of the use of these ingredients in hair smoothing products are scarce. The teams should review the draft report to determine if additional data are needed.

4. Silylates and Surface Modified Siloxysilicates - CIR announced the SLR for 4 silylate ingredients in December, 2010. Comments from industry have been addressed and unpublished data have been incorporated. The teams should review the draft report to determine if additional data are needed.

Draft final reports - there are 2 reports under blue cover. Each of these had been issued as a tentative report at the December meeting. After reviewing these drafts, especially the rationale in the discussion section, the Panel should issue them as final reports.

1. C12-15 Alkyl Benzoate and related Alkyl Benzoates. Technical comments from the Personal Care Products Council have been addressed. These 17 ingredients were found safe in the present practices of use and concentration.

2. Plant-Derived Fatty Acid Oils. The Council has continued to provide needed data. Fatty acid profiles appear to be in hand for 241 of the 244 plant-derived fatty acid oils and a determination of safe as used for these ingredients should be made. Chemical composition data, particularly fatty acid profiles, are absent for 3 of the oils; suggesting insufficient data for a determination of safety.

New data – recent data suggest a significant association between quaternium-15 and formaldehyde allergy, suggesting that quaternium-15 may be a formaldehyde releaser, yet other analyses of the data suggest the converse. These data should be discussed and a determination made regarding the need to reopen the recently amended safety assessment of quaternium-15 (safe up to 0.2%).

Boilerplate language – from the extensive discussion of hair dye epidemiology data to the differentiation between rinse-off and leave-on, CIR makes use of boilerplate language in its safety assessments to avoid having re-craft new language each time an issue presents itself. This is an opportunity for the Panel to review these established approaches and make any necessary changes.

Full Panel Meeting - remember, breakfast buffet at 8:00 am and meeting starts at 8:30 am on day 2.

The Panel will consider the 2 reports to be issued as final safety assessments, followed by the 4 reports under green covers and the remaining items on the agenda.

It is likely that the full Panel session will conclude before lunch time on day 2, so plan your travel accordingly. Have a safe journey.

Future Planning - in the short term, it appears as if we will celebrate CIR's 35th anniversary at the June 27-28, 2011 meeting of CIR Expert Panel. As for all CIR anniversary events, your spouses are invited to join you in traveling to Washington for the meeting and participating in the gala celebration the evening of June 27th. CIR staff and their spouses also will participate.

In the longer term, I want to remind you that the 2012 meeting dates have been established. Yes, 2012 (next year)! They are March 5-6, 2012 (Mon-Tues); June 11-12, 2012 (Mon-Tues); September 10-11, 2012 (Mon-Tues); and December 10-11, 2012 (Mon-Tues). If you are up for 2013 planning, we can talk about that at this upcoming meeting.

118th Cosmetic Ingredient Review Expert Panel Meeting
March 3-4, 2011

Madison Hotel
1177 Fifteenth Street, NW
Washington, DC 20005
Phone: (202) 862-1600
Fax: (202) 785-1255

Thursday, March 3, 2011

8:30 am	**Breakfast**	
9:00 am	**WELCOME TO THE 118th EXPERT PANEL TEAM MEETINGS**	**Drs. Bergfeld/Andersen**
9:30 am	**TEAM MEETINGS**	**Drs. Marks/Belsito**

Dr. Belsito Team		**Dr. Marks Team**	
Buff (MF)	Disperse Blue 1 – re-review summary	Buff (HB)	CIR boilerplate language review
Green (MF)	DEA and Related DEA-Containing Ingredients	Green (IB/BAH/FAA)	Formaldehyde and Methylene Glycol
Green (MF)	Acrylate Cross Polymers	Green (LB)	Silylates and Surface Modified Siloxysilicates
Blue (CLB/MF)	Plant-Derived Fatty Acid Oils	Blue (LB)	C12-15 Alkyl Benzoate and related Alkyl Benzoates
Blue (LB)	C12-15 Alkyl Benzoate and related Alkyl Benzoates	Buff (LB)	Quaternium-15 – new data
Green (LB)	Silylates and Surface Modified Siloxysilicates	Buff (MF)	Disperse Blue 1 – re-review summary
Buff (LB)	Quaternium-15 – new data	Green (MF)	DEA and Related DEA-Containing Ingredients
Green (IB/BAH/FAA)	Formaldehyde and Methylene Glycol	Green (MF)	Acrylate Cross Polymers
Buff (HB)	CIR boilerplate language review	Blue (CLB/MF)	Plant-Derived Fatty Acid Oils

Noon	**Lunch**
1:00 pm	**TEAM MEETINGS (continued as needed)**
5:00 pm	**ADJOURN DAY 1 SESSION**

NOTE: The order of presentation and discussion of each topic will be maintained. However, the scheduled times may be accelerated or delayed depending upon the time required for the Expert Panel to complete its review of each subject.

Friday, March 4, 2011			
8:00 am	**Breakfast**		
8:30 am	**WELCOME TO THE 118th FULL CIR EXPERT PANEL MEETING**		
8:45 am	**MINUTES OF THE December 13-14, 2010 EXPERT PANEL MEETING** (Buff)		**Dr. Bergfeld**
8:55 am	**DIRECTOR'S REPORT**		**Dr. Andersen**
9:00 am	**FINAL REPORTS, REPORTS ADVANCING TO THE NEXT LEVEL, and RE-REVIEWS**		
Final Reports			
	Blue (CLB/MF)	Plant-Derived Fatty Acid Oils - Dr. Belsito reports	
	Blue (LB)	C12-15 Alkyl Benzoate and related Alkyl Benzoates - Dr. Marks reports	
Reports Advancing			
	Green (LB)	Silylates and Surface Modified Siloxysilicates - Dr. Belsito reports	
	Green(IB/BAH/FAA)	Formaldehyde and Methylene Glycol - Dr. Marks reports	
	Green (MF)	DEA and Related DEA-Containing Ingredients- Dr. Belsito reports	
	Green (MF)	Acrylate Cross Polymers - Dr. Marks reports	
Re-Review Summary			
	Buff (MF)	Disperse Blue 1- Dr. Belsito reports	
New Data			
	Buff (LB)	Quaternium-15 – Dr. Marks reports	
Boilerplate Language	Buff (HB)		

ADJOURN - Next meeting *Monday and Tuesday, June 27-28, 2011 – Celebration of CIR's 35th Anniversary*

Cosmetic Ingredient Review

Commitment . . . Credibility

Since 1976

C I R

ONE HUNDRED SEVENTEENTH MEETING

OF THE

EXPERT PANEL

December 13-14, 2010

Embassy Suites Washington D.C. – Convention Center

Washington, D.C.

Expert Panel Members	Liaison Representatives
Wilma F. Bergfeld, M.D., Chairman	Consumer
Donald V. Belsito, M.D.	Rachel Weintraub, Esq.
Ronald A. Hill, Ph.D.	
Curtis D. Klaassen, Ph.D.	Industry
Daniel C. Liebler, Ph.D.	John Bailey, Ph.D.
James G. Marks, Jr., M.D.	
Ronald C. Shank, Ph.D.	
Thomas J. Slaga, Ph.D.	Government
Paul W. Snyder, D.V.M., Ph.D.	Linda Katz, MD., M.P.H.

_____

Adopted (Date)

_____

Wilma F. Bergfeld, M.D.

Others Present at Meeting

F. Alan Andersen	CIR
David Andrews	EWG
Jay Ansell	The Council
Dan Bagley	Colgate
Lillian Becker	CIR
Ivan Boyer	CIR
Halyna Breslawec	CIR
Robert Bronaugh	FDA
Christina Burnett	CIR
Jon Busch	American Chemistry Council
Kapal Dewa	FDA
Robert Finking	BASF
Monice Fiume	CIR
Darren Gilbert	Vivimed Labs
Don Havery	FDA
Bart Heldreth	CIR
Wilbur Johnson, Jr.	CIR
Kenji Mori	Kanebo
Thomas Re	L'Oreal USA
Josephine Robinson	CIR
Diego Rua	FDA
Noriko Shibuya	Shiseido
Ryuji Sugai	Kanebo cosmetics
David Steinberg	Steinberg & Associates
Jane Vergnes	ISP
Perry Wang	FDA
Shontell Wright	FDA

MINUTES FROM THE 117TH CIR EXPERT PANEL MEETING

CHAIRMAN'S OPENING REMARKS

The 117th meeting of the CIR Expert Panel was called to order by Dr. Bergfeld at 8:00 a.m on Tuesday, December 14, 2010. Dr. Bergfeld noted that 13 ingredient groups comprising an unusually large number of ingredients were reviewed in Teams on the preceding day, and congratulated the CIR staff for all of the work that was done in preparation for this Expert Panel meeting. Some of the discussions on the preceding day addressed the use of read-across information in CIR safety assessments as part of the database for evaluating the safety of cosmetic ingredients, and similar discussions will continue today. Dr. Bergfeld expressed the need for the Panel to focus on the consistency of CIR's boilerplate conclusions and discussion items, taking into consideration any necessary revisions to ensure that all information is consistent with current knowledge. As a starting point, Dr. Breslawec agreed to review CIR's list of boilerplate conclusions and discussion items (e.g., relating to hair dyes, plant pesticides, etc.).

APPROVAL OF MINUTES

The minutes of the August 30-31, 2010 CIR Expert Panel meeting were unanimously approved, without any corrections.

DIRECTOR'S REPORT

♦ Dr. Andersen thanked the CIR staff for all of the hard work that was done in preparation for this Panel meeting.
♦ Again, CIR final reports will be published in 3 issues of the *International Journal of Toxicology* this year. As encouraged by the journal editor, studies previously categorized as acute, short-term, subchronic, and chronic toxicity are now categorized as acute and repeated dose toxicity studies.
♦ Christina Burnett is now the very proud mother of a beautiful baby boy, Alexander Burnett, and both are doing well.
♦ Dr. Ivan Boyer, Senior Toxicologist, was introduced as a new member of the CIR staff on the preceding day. The addition of an information technition, Ms. Julia Linthicum, to the CIR staff was also announced. Further expansion of the staff to include an additional technical writer is among the plans for the upcoming year.
♦As reported at the recent Personal Care Products Board of Directors meeting, CIR is on track to issue safety assessments on over 750 ingredients this year. The team approach for report development is working rather well. In keeping with this approach, a Pre-Production Package (chemical structures + other relevant information) will be developed for each safety assessment assigned. As time goes on, the Pre-Production Package will be expanded to include input from the Senior Toxicologist concerning the significant toxicological issues identified for each chemical, contributing to the efficiency of report development.
♦CIR will continue to publish its Compendium as an electronic document (pdf), offered for sale at the Personal Care Products Council's website. Additionally, the Personal Care Products Council will be issuing a compendium of cosmetic ingredients that are actually in use.

Dr. Andersen was congratulated and received a warm round of applause for his leadership of the CIR program.

APPROVAL OF FINAL REPORTS

Dicarboxylic Acids and Their Salts and Esters

Dicarboxylic acids function in cosmetics primarily as pH adjusters, whereas the esters have a wide range of functions, including skin conditioning agents, plasticizers, solvents, and emollients. While gaps in the available safety data exist for some of the dicarboxylic acids, salts, and esters, the data on many of the ingredients are sufficient, and similar structural activity relationships, biologic functions, and cosmetic product usage, suggest that the available data may be extrapolated to the entire group. For example, a concern regarding the extent of dermal absorption for certain long-chain, branched diesters is addressed , because dermal penetration of long chain alcohols is likely to be low and the dermal penetration for the diesters is likely to be even lower, inferring toxicity characteristics from ingredients where toxicity data were available was appropriate.

The Panel concluded that dicarboxylic salts and their salts and the esters are safe for use in cosmetic products in the present practices of use and concentration. Were the ingredients not in current use (as indicated by *) to be used in the future, the expectation is that they would be used in product categories and at concentrations comparable to others in these groups. The following 12 dicarboxylic acids and salts are included:

Malonic Acid*,	Sodium Succinate,	Glutaric Acid*,
Succinic Acid,	Disodium Succinate,	Adipic Acid,

Azelaic Acid,
Dipotassium Azelate*,
Disodium Azelate*,
Sebacic Acid,
Disodium Sebacate*, and
Dodecanedioic Acid*

The 44 following esters of dicarboxylic acids are included:

Diethyl Malonate,
Decyl Succinate,
Dimethyl Succinate*,
Diethyl Succinate*,
Dicapryl Succinate,
Dicetearyl Succinate*,
Diisobutyl Succinate*,
Diethylhexyl Succinate,
Dimethyl Glutarate,
Diisobutyl Glutarate*,
Diisostearyl Glutarate*,
Dimethyl Adipate,
Diethyl Adipate*,
Dipropyl Adipate*,
Dibutyl Adipate,
Dihexyl Adipate,
Dicapryl Adipate,
Di-C12-15 Alkyl Adipate*,
Ditridecyl Adipate*,
Dicetyl Adipate*,
Diisopropyl Adipate,
Diisobutyl Adipate,
Diethylhexyl Adipate,
Diisooctyl Adipate*,
Diisononyl Adipate*,
Diisodecyl Adipate,
Dihexyldecyl Adipate*,
Diheptylundecyl Adipate,
Dioctyldodecyl Adipate,
Diisocetyl Adipate*,
Diisostearyl Adipate,
Isostearyl Sebacate,
Diethyl Sebacate,
Dibutyl Sebacate*,
Dicaprylyl/Capryl Sebacate*,
Diisopropyl Sebacate,
Diethylhexyl Sebacate,
Dibutyloctyl Sebacate*,
Diisooctyl Sebacate,
Dihexyldecyl Sebacate*,
Dioctyldodecyl Sebacate,
Diisostearyl Sebacate*,
Dioctyldodecyl Dodecanedioate, and
Diisocetyl Dodecanedioate

Dimethiconol and its Esters and Reaction Products

Most of these ingredients function as skin conditioning agents and/or hair conditioning agents in cosmetics. In addition to Dimethiconol itself, there are two subgroups, end-capped homopolymers and copolymers. The end-capped homopolymers consist of polymers chains made from dimethyl siloxyl monomers, wherein each end of the polymer chain is capped with an ester side chain (e.g, dimethiconol behenate, a dimethyl siloxyl polymer which terminates on each end with the behenate ester). The copolymers consist of at least two monomers polymerized together. The Panel noted gaps in the available safety data for some of the ingredients in this safety assessment. The available data on many of the ingredients are sufficient, however, and similar structural activity relationships, biologic functions, and cosmetic product usage, suggests that the available data may be extrapolated to support the safety of the entire group. For example, while there is an absence of data on reproductive and developmental toxicity and limited tumorigenicity and metabolism data; the Panel reached consensus that these ingredients would not be absorbed through the skin, thereby obviating further concern over potential reproductive and developmental toxicity or carcinogenicity.

The CIR Expert Panel concluded that these 28 ingredients are safe in the present practices of use and concentration described in the safety assessment. Were ingredients in this group not in current use (as indicated by *) to be used in the future, the expectation is that they would be used in product categories and at concentrations comparable to others in the group.

Dimethiconol
Dimethiconol Arginine,
Dimethiconol Beeswax,
Dimethiconol Behenate,
Dimethiconol Borageate*,
Dimethiconol Candelillate*,
Dimethiconol Carnaubate*,
Dimethiconol Cysteine,
Dimethiconol Dhupa Butterate*,
Dimethiconol Hydroxystearate*,
Dimethiconol Illipe Butterate*,
Dimethiconol Isostearate*,
Dimethiconol Kokum Butterate*,
Dimethiconol Lactate*,
Dimethiconol Meadowfoamate,
Dimethiconol Methionine,
Dimethiconol Mohwa Butterate*,
Dimethiconol Panthenol,
Dimethiconol Sal Butterate*, and
Dimethiconol Stearate;

Hydrolyzed Collagen PG-Propyl Dimethiconol*,
Dimethiconol/Methylsilanol/Silicate Crosspolymer*,
Dimethiconol/Silica Crosspolymer*,
Dimethiconol/Silsesquioxane Copolymer,
Dimethiconol/Stearyl Methicone/Phenyl Trimethicone Copolymer*,
Isopolyglyceryl-3 Dimethiconol*,
Trimethylsiloxysilicate/Dimethiconol Crosspolymer, and
Acrylates/Dimethiconol Acrylate Copolymer

Isoparaffins

Isoparaffinic hydrocarbons (isoparaffins) are branched alkanes that function mostly as solvents in personal care products. The CIR Expert Panel evaluated additional data provided by industry, noting that most of these additional studies could be added to the safety assessment simply by stating “reported similar effects” in the appropriate section and giving the citation, so that the report represents a complete record of the data considered. The Panel noted gaps in the available safety data for some of the isoparaffins in this safety

assessment. The available data on many of the isoparaffins are sufficient, however, and similar structural activity relationships, biologic functions, and cosmetic product usage, suggests that the available data may be extrapolated to support the safety of the entire group.

The Panel concluded that the 24 isoparaffin ingredients are safe for use in cosmetics when formulated to be non-irritating. Those ingredients not in current use are indicated with an asterisk.

C7-8 Isoparaffin,
C8-9 Isoparaffin,
C9-11 Isoparaffin,
C9-12 Isoparaffin*,
C9-13 Isoparaffin*,
C9-14 Isoparaffin*,
C9-16 Isoparaffin*,
C10-11 Isoparaffin,
C10-12 Isoparaffin*,
C10-13 Isoparaffin,
C11-12 Isoparaffin,
C11-13 Isoparaffin,
C11-14 Isoparaffin*,
C12-14 Isoparaffin,
C12-20 Isoparaffin*,
C13-14 Isoparaffin,
C13-16 Isoparaffin,
C18-70 Isoparaffin,
C20-40 Isoparaffin*,
C15-35 Isoparaffin/Isoalkylcycloalkanes*,
Isododecane,
Isoeicosane,
Isohexadecane, and
Isooctane

Triclosan

In cosmetics, Triclosan functions as a cosmetic biocide, preservative, or deodorant agent. The CIR Expert Panel focused on Triclosan sourcing and the need to limit dioxin impurities, photostability, carcinogenicity, endocrine disruption, and potential for bacterial resistance from the use of triclosan in cosmetics. The Panel noted that data from the Skin Deep Cosmetics Safety Database were not a reliable source of Triclosan usage. The Panel also considered a recently published study that reported that Triclosan, as measured in urine, was associated with an increased incidence of hay fever in individuals less than 18 years of age. The Panel determined that, while this study should be included, it did not demonstrate a causal relationship between the endpoint and Triclosan usage. The Panel also noted that a risk assessment using an appropriate no-observable-adverse-effect-level and considering exposures to triclosan from all product sources, including OTC drugs, also supported safety.The CIR Expert Panel concluded that Triclosan is safe as a cosmetic ingredient in the present practices of use and concentration of this safety assessment, even were all products types to contain Triclosan and used concurrently, on a daily basis.

FINAL AMENDED SAFETY ASSESSMENTS

Alkyl PEG Ethers

Alkyl PEG ethers are alkyl terminated polyethers that function primarily as surfactants in cosmetic formulations. The Panel noted gaps in the available safety data for some of the alkyl PEG ethers in this safety assessment. The available data on many of the alkyl PEG ethers are sufficient, however, and similar structural activity relationships, biologic functions, and cosmetic product usage, suggests that the available data may be extrapolated to support the safety of the entire group. For example, a concern was expressed regarding the extent of dermal absorption for certain long-chain, branched alkyl PEG ethers because of a lack of information on dermal absorption and metabolism. The consensus of the Panel was, that because, dermal penetration of long chain alcohols is likely to be low, and the dermal penetration for alkyl PEG ethers is likely to be even lower, inferring toxicity characteristics from ingredients where toxicity data were available was appropriate.

The CIR Expert Panel concluded that the alkyl PEG ethers, listed below, are safe in the present practices of use and concentration described in this safety assessment when formulated to be non-irritating. This assessment is also intended to address future alkyl PEG ether cosmetic ingredients that vary from those ingredients recited herein only by the number of ethylene glycol repeat units. Those ingredients not in current use are indicated with an asterisk. The 369 ingredients included in this safety assessment are:

Arachideth-20*
Beheneth-2*
Beheneth-5*
Beheneth-10
Beheneth-15*
Beheneth-20
Beheneth-25
Beheneth-30
C9-11 Pareth-3*
C9-11 Pareth-4 *
C9-11 Pareth-6
C9-11-Pareth-8
C9-15 Pareth-8*
C10-16 Pareth-1*
C10-16 Pareth-2 *
C11-13 Pareth-6*
C11-13 Pareth-9*
C11-13 Pareth-10*
C11-15 Pareth-3
C11-15 Pareth-5
C11-15 Pareth-7
C11-15 Pareth-9
C11-15 Pareth-12*
C11-15 Pareth-15*
C11-15 Pareth-20*
C11-15 Pareth-30*
C11-15 Pareth-40
C11-21-Pareth-3*
C11-21-Pareth-10*
C12-13 Pareth-1

C12-13 Pareth-2*
C12-13 Pareth-3
C12-13 Pareth-4*
C12-13 Pareth-5*
C12-13 Pareth-6*
C12-13 Pareth-7
C12-13 Pareth-9*
C12-13 Pareth-10*
C12-13 Pareth-15*
C12-13 Pareth-23
C12-14 Pareth-3
C12-14 Pareth-5*
C12-14 Pareth-7*
C12-14 Pareth-9*
C12-14 Pareth-12
C12-15 Pareth-2*
C12-15 Pareth-3
C12-15 Pareth-4*
C12-15 Pareth-5*
C12-15 Pareth-7
C12-15 Pareth-9
C12-15 Pareth-10*
C12-15 Pareth-11*
C12-15 Pareth-12
C12-16 Pareth-5*
C12-16 Pareth-7
C12-16 Pareth-9
C13-15 Pareth-21*
C14-15 Pareth-4*
C14-15 Pareth-7*
C14-15 Pareth-8*
C14-15 Pareth-11*
C14-15 Pareth-12*
C14-15 Pareth-13*
C20-22 Pareth-30*
C20-40 Pareth-3
C20-40 Pareth-10
C20-40 Pareth-24*
C20-40 Pareth-40
C20-40 Pareth-95
C22-24 Pareth-33
C30-50 Pareth-3*
C30-50 Pareth-10*
C30-50 Pareth-40*
C40-60 Pareth-3*
C40-60 Pareth-10*
C11-15 Sec-Pareth-12*
C12-14 Sec-Pareth-3*
C12-14 Sec-Pareth-5
C12-14 Sec-Pareth-7
C12-14 Sec-Pareth-8*
C12-14 Sec-Pareth-9*
C12-14 Sec-Pareth-12*
C12-14 Sec-Pareth-15*
C12-14 Sec-Pareth-20*
C12-14 Sec-Pareth-30*
C12-14 Sec-Pareth-40*
C12-14 Sec-Pareth-50*
Capryleth-4*
Capryleth-5*
Ceteareth-2
Ceteareth-3
Ceteareth-4
Ceteareth-5
Ceteareth-6
Ceteareth-7
Ceteareth-8*
Ceteareth-9*
Ceteareth-10
Ceteareth-11*
Ceteareth-12
Ceteareth-13*
Ceteareth-14*
Ceteareth-15
Ceteareth-16*
Ceteareth-17
Ceteareth-18*
Ceteareth-20
Ceteareth-22
Ceteareth-23*
Ceteareth-24*
Ceteareth-25
Ceteareth-27*
Ceteareth-28*
Ceteareth-29*
Ceteareth-30
Ceteareth-33
Ceteareth-34*
Ceteareth-40*
Ceteareth-50
Ceteareth-55*
Ceteareth-60*
Ceteareth-80*
Ceteareth-100*
Ceteth-1
Ceteth-2
Ceteth-3
Ceteth-4*
Ceteth-5*
Ceteth-6
Ceteth-7*
Ceteth-10
Ceteth-12
Ceteth-13*
Ceteth-14*
Ceteth-15
Ceteth-16
Ceteth-17*
Ceteth-18*
Ceteth-20
Ceteth-23*
Ceteth-24
Ceteth-25
Ceteth-30*
Ceteth-40*
Ceteth-45*
Ceteth-150*
Cetoleth-2*
Cetoleth-4*
Cetoleth-5*
Cetoleth-6*
Cetoleth-10*
Cetoleth-11*
Cetoleth-15*
Cetoleth-18*
Cetoleth-20*
Cetoleth-22*
Cetoleth-24*
Cetoleth-25
Cetoleth-30*
Coceth-3*
Coceth-5*
Coceth-6*
Coceth-7
Coceth-8
Coceth-10
Coceth-20*
Coceth-25*
Deceth-3
Deceth-4*
Deceth-5
Deceth-6*
Deceth-7
Deceth-8
Deceth-9
Deceth-10*
Decyltetradeceth-5*
Decyltetradeceth-10*
Decyltetradeceth-15*
Decyltetradeceth-20*
Decyltetradeceth-25*
Decyltetradeceth-30*
Hexyldeceth-2*
Hexyldeceth-20*
Hydrogenated Dimer Dilinoleth-20*
Hydrogenated Dimer Dilinoleth-30*
Hydrogenated Dimer Dilinoleth-40*
Hydrogenated Dimer Dilinoleth-60*
Hydrogenated Dimer Dilinoleth-80*
Hydrogenated Laneth-5*
Hydrogenated Laneth-20*
Hydrogenated Laneth-25*
Hydrogenated Talloweth-12*
Hydrogenated Talloweth-25*
Isoceteth-5*
Isoceteth-7*
Isoceteth-10
Isoceteth-12*
Isoceteth-15*
Isoceteth-20
Isoceteth-25
Isoceteth-30*
Isodeceth-4*
Isodeceth-5*
Isodeceth-6
Isolaureth-3*
Isolaureth-6
Isolaureth-10*
Isomyreth-3*
Isomyreth-9*
Isosteareth-2
Isosteareth-3
Isosteareth-5

Isosteareth-8*
Isosteareth-10
Isosteareth-12*
Isosteareth-15*
Isosteareth-16*
Isosteareth-20
Isosteareth-22*
Isosteareth-25*
Isosteareth-50*
Laneth-5
Laneth-10*
Laneth-15
Laneth-16
Laneth-20
Laneth-25
Laneth-40
Laneth-50*
Laneth-60*
Laneth-75*
Laureth-1
Laureth-2
Laureth-3
Laureth-4
Laureth-5
Laureth-6
Laureth-7
Laureth-8
Laureth-9
Laureth-10
Laureth-11
Laureth-12
Laureth-13*
Laureth-14
Laureth-15*
Laureth-16
Laureth-20
Laureth-21
Laureth-23
Laureth-25
Laureth-30
Laureth-38*
Laureth-40*
Laureth-50*
Methoxy PEG-7*
Methoxy PEG-10*
Methoxy PEG-16
Methoxy PEG-25*
Methoxy PEG-40*
Methoxy PEG-100*
Myreth-2 *
Myreth-3
Myreth-4
Myreth-5*
Myreth-10
Noneth-8*
Octyldodeceth-2*
Octyldodeceth-5*
Octyldodeceth-10*
Octyldodeceth-16
Octyldodeceth-20
Octyldodeceth-25
Octyldodeceth-30*
Oleth-2
Oleth-3
Oleth-4
Oleth-5
Oleth-6*
Oleth-7*
Oleth-8
Oleth-9*
Oleth-10
Oleth-11*
Oleth-12
Oleth-15
Oleth-16
Oleth-20
Oleth-23*
Oleth-24*
Oleth-25
Oleth-30
Oleth-35*
Oleth-40*
Oleth-44*
Oleth-45*
Oleth-50
Oleth-82
Oleth-100*
Oleth-106
Palmeth-2*
PEG-16 Cetyl/Oleyl/Stearyl/Lanolin Alcohol Ether*
PEG-Cetyl Stearyl Diether*
PEG-4 Distearyl Ether
PEG-4 Ditallow Ether*
PEG-15 Jojoba Alcohol*
PEG-26 Jojoba Alcohol*
PEG-40 Jojoba Alcohol*
PEG-3 Methyl Ether*
PEG-4 Methyl Ether*
PEG-6 Methyl Ether*
PEG-7 Methyl Ether*
PEG-7 Propylheptyl Ether
PEG-8 Propylheptyl Ether
Steareth-1*
Steareth-2
Steareth-3*
Steareth-4
Steareth-5*
Steareth-6
Steareth-7*
Steareth-8*
Steareth-10
Steareth-11*
Steareth-13*
Steareth-14*
Steareth-15*
Steareth-16
Steareth-20
Steareth-21
Steareth-25
Steareth-27*
Steareth-30
Steareth-40*
Steareth-50
Steareth-80*
Steareth-100
Steareth-200
Steareth-60 Cetyl Ether*
Talloweth-4
Talloweth-5
Talloweth-6
Talloweth-7*
Talloweth-18*
Trideceth-2*
Trideceth-3
Trideceth-4*
Trideceth-5
Trideceth-6
Trideceth-7
Trideceth-8
Trideceth-9
Trideceth-10
Trideceth-11*
Trideceth-12
Trideceth-15*
Trideceth-18*
Trideceth-20*
Trideceth-21*
Trideceth-50*
Undeceth-3
Undeceth-5
Undeceth-7*
Undeceth-8*
Undeceth-9*
Undeceth-11
Undeceth-40*
Undecyleneth-6*

Cocamidopropyl Betaine and Related Amidopropyl Betaines as used in Cosmetics

Cocamidopropyl betaine (CAPB) and related amidopropyl betaines are zwitterions used mainly as surfactants in cosmetics. These cosmetic ingredients are similar in their chemistry, in particular with respect to the presence of 3,3-dimethylaminopropylamine (DMAPA) and fatty acid amidopropyl dimethylamine (amidoamine) impurities, which are known sensitizers. The CIR Expert Panel accepted that a quantitative risk assessment approach would be appropriate, but acknowledged that actual RIPT data demonstrating an absence of sensitization also is appropriate

To address concerns about sensitization reactions from the use of products containing these ingredients, the CIR Expert Panel concluded that these 31 ingredients are safe in the present practices of use and concentration in cosmetics, as long as they are formulated to be non-sensitizing, which may be based on a quantitative risk assessment. Those ingredients not in current use are indicated with an asterisk.

Cocamidopropyl Betaine,
Almondamidopropyl Betaine,
Apricotamidopropyl Betaine*,
Avocadamidopropyl Betaine*,
Babassuamidopropyl Betaine,
Behenamidopropyl Betaine*,
Canolamidopropyl Betaine*,
Capryl/Capramidopropyl Betaine,
Coco/Oleamidopropyl Betaine*,
Coco/Sunfloweramidopropyl Betaine,
Cupuassuamidopropyl Betaine*,
Isostearamidopropyl Betaine*,
Lauramidopropyl Betaine,
Meadowfoamamidopropyl Betaine*,
Milkamidopropyl Betaine*,
Minkamidopropyl Betaine*,
Myristamidopropyl Betaine,
Oatamidopropyl Betaine,
Oleamidopropyl Betaine*,
Olivamidopropyl Betaine,
Palmamidopropyl Betaine*,
Palmitamidopropyl Betaine*,
Palm Kernelamidopropyl Betaine,
Ricinoleamidopropyl Betaine*,
Sesamidopropyl Betaine*,
Shea Butteramidopropyl Betaine,
Soyamidopropyl Betaine,
Stearamidopropyl Betaine*,
Tallowamidopropyl Betaine*,
Undecyleneamidopropyl Betaine, and
Wheat Germamidopropyl Betaine*

Trimoniums

These quaternary ammonium salts, including alkyl chain, alkanol, and polymer derivatives are used in cosmetics mainly as surfactant-cleansing agents, antistatic agents, hair conditioning agents, and antistatic agents. The Panel noted gaps in the available safety data for some of the trimoniums in this safety assessment. The available data on many of the trimoniums are sufficient, however, and similar structural activity relationships, biologic functions, and cosmetic product usage, suggests that the available data may be extrapolated to support the safety of the entire group. The CIR Expert Panel noted that pesticide or other residues that might be of concern in those ingredients obtained from plant sources, were not a concern because of the extensive processing to extract the alkyl chains.

These 52 ingredients were found to be safe in the present practices of use and concentration described in the safety assessment when formulated to be non-irritating. Those ingredients not in current use are indicated with an asterisk.

Behentrimonium Chloride,
Ceteartrimonium Chloride*,
Cetrimonium Chloride,
Choline Chloride*,
Cocotrimonium Chloride,
Dodecylhexadecyltrimonium Chloride*,
Hydrogenated Palmtrimonium Chloride*,
Hydrogenated Tallowtrimonium Chloride*,
Laurtrimonium Chloride*,
Octacosatrimonium Chloride*,
Octyldodecyltrimonium Chloride*,
Soytrimonium Chloride,
Stearoxypropyltrimonium Chloride*,
Steartrimonium Chloride,
Tallowtrimonium Chloride
Cetrimonium Bromide
Laurtrimonium Bromide,
Myrtrimonium Bromide,
Steartrimonium Bromide*,
Behentrimonium Methosulfate*,
Cetrimonium Methosulfate,
Cocoylcholine Methosulfate*,
Cocotrimonium Methosulfate,
Lauroyl Ethyltrimonium Methosulfate*,
Myristoyl Ethyltrimonium Methosulfate*,
Palmitoyl Ethyltrimonium Methosulfate*,
Stearoyl Ethyltrimonium Methosulfate*,
Steartrimonium Methosulfate*,
Acetyl Carnitine*,
Acetyl Carnitine HCl,
Carnitine,
Carnitine HCl,
Carnitine Hydroxycitrate,
Carnitine PCA*,
Palmitoyl Carnitine,
Acrylamide/Ethyltrimonium Chloride* Acrylate/Ethalkonium Chloride Acrylate Copolymer,
Acrylamidopropyl Trimonium Chloride/Acrylamide Copolymer*,
Acrylamidopropyl-Trimonium Chloride/Acrylates Copolymer
Polyquaternium-14*,
Polyquaternium-28,
Polyquaternium-32,
Polyquaternium-33*,
Polyquaternium-35,
Polyquaternium-36,
Polyquaternium-37,
Polyquaternium-45*,
Polyquaternium-47*,
Polyquaternium-48*,
Polyquaternium-53*,
Polyquaternium-63*,

Polyquaternium-73*,

Polyquaternium-91*,

TENTATIVE SAFETY ASSESSMENTS

Alkyl Benzoates

The alkyl benzoate ingredients are esters of benzoic acid and a corresponding alcohol used in cosmetics mostly as skin-conditioning agents, preservatives, solvents, and plasticizers. The CIR Expert Panel reviewed additional data regarding dermal penetration of lower molecular weight ingredients in this group. Newly provided dermal irritation and sensitization data also were reviewed, along with new reproductive and developmental toxicity data. The existing carcinogenicity data for benzoic acid and several alcohols were considered adequate. The Panel noted gaps in the available safety data for some of the alkyl benzoates in this safety assessment. The available data on many of the alkyl benzoates are sufficient, however, and similar structural activity relationships, biologic functions, and cosmetic product usage, suggests that the available data may be extrapolated to support the safety of the entire group.

The Panel reached the tentative conclusion that these 17 ingredients are safe in the present practices of use and concentration as given in the report. Were ingredients in this group not in current use (marked with an *) to be used in the future, the expectation is that they would be used in product categories and at concentrations comparable to others in the group.

Methyl Benzoate,
Ethyl Benzoate,
Propyl Benzoate*,
Butyl Benzoate*,
Amyl Benzoate*,
Lauryl/ Myristyl Benzoate*,
C12-15 Alkyl Benzoate,
C16-17 Alkyl Benzoate,
Stearyl Benzoate,
Behenyl Benzoate*,
Isopropyl Benzoate*,
Isobutyl Benzoate,
Isostearyl Benzoate,
Ethylhexyl Benzoate,
Butyloctyl Benzoate*,
Hexyldecyl Benzoate*, and
Octyldodecyl Benzoate

Caprylyl Glycol and Other 1,2-Glycols

The 1,2-glycols function mostly as skin and hair conditioning agents and viscosity increasing agents in cosmetics; caprylyl glycol and pentylene glycol also function as preservatives. Concern was expressed that the lipophilicity of 1,2-glycols with greater than 12 carbons in the chain may alter the dermal penetration of these ingredients and that the available metabolic modeling may not be relevant. The Panel reached a consensus, however, that there were ample data demonstrating that the lower chain length 1,2-glycols penetrate the skin readily and that repeat dose systemic toxicity data are available demonstrating the safety of these ingredients. The available data on these are sufficient, and similar structural activity relationships, biologic functions, and cosmetic product usage, suggests that the available data may be extrapolated to support the safety of the entire group.

Accordingly, the Panel reached the tentative conclusion that the 16 ingredients in the report are safe in the present practices of use and concentration. Were ingredients in this group not in current use (marked with an *) to be used in the future, the expectation is that they would be used in product categories and at concentrations comparable to others in the group:

Caprylyl Glycol
Arachidyl Glycol*
Cetyl Glycol*
Hexacosyl Glycol*
Lauryl Glycol*
Myristyl Glycol*
Octacosanyl Glycol*
Stearyl Glycol*
Decylene Glycol*
Pentylene Glycol
1,2-Butanediol*
1,2-Hexanediol
C14-18 Glycol*
C15-18 Glycol
C18-30 Glycol*
C20-30 Glycol*

Plant-Derived Fatty Acid Oils

Plant-derived fatty acid oils, which are the glyceryl esters of fatty acid (triglycerides) normally found in plants, including those which have been hydrogenated to reduce or eliminate unsaturation, are used in cosmetics primarily for their skin conditioning, occlusive, emollient, and moisturizing properties. The CIR Expert Panel determined that these triglycerides, based on their similar fatty acid profiles, also are similar in structural activity relationships, biologic functions, and cosmetic product usage. In a small number of cases, however, the basic information on which fatty acids are found in these triglycerides was not available. Accordingly, the Panel

reached a tentative conclusion stating that data are insufficient for the following 10 ingredients due to the lack of chemical composition data, specifically fatty acid profiles:

Arctium Lappa Seed Oil
Citrus Paradisi (Grapefruit) Seed Oil
Coix Lacryma-Jobi (Job's Tears) Seed Oil
Fragaria Chiloensis (Strawberry Seed Oil
Fragaria Vesca (Strawberry) Seed Oil
Fragaria Virginiana (Strawberry) Seed Oil
Lycium Barbarum Seed Oil
Morinda Citrifolia Seed Oil
Orbignya Speciosa Kernel Oil
Schinziophyton Rautanenii Kernel Oil

The Panel reached a tentative conclusion that the additional 234 plant-derived fatty acid oils included in this review, listed below, are safe in the present practices of use and concentration described in this safety assessment. The Panel did note that while the fatty acid profiles of Oryza Sativa (Rice) Germ Oil and Sclerocarya Birrea Seed Oil state that arachidonic acid, an ingredient previously found by the Panel to have insufficient data for safety, is one of the components of these ingredients, the amount of arachadonic acid in the oil is low and the concentration of use of these ingredients was sufficiently low as to not warrant concern. Were the ingredients not in current use (as indicated by *) to be used in the future, the expectation is that they would be used in product categories and concentrations comparable to others in these groups. The ingredients found safe are:

Actinidia Chinensis (Kiwi) Seed Oil
Adansonia Digitata Oil
Adansonia Digitata Seed Oil*
Aleurites Moluccanus Bakoly Seed Oil*
Aleurities Moluccana Seed Oil
Amaranthus Hypochondriacus Seed Oil*
Anacardium Occidentale (Cashew) Seed Oil
Arachis Hypogaea (Peanut) Oil
Argania Spinosa Kernel Oil
Astrocaryum Murumuru Seed Butter
Avena Sativa (Oat) Kernel Oil
Babassu Acid*
Bassia Butyracea Seed Butter*
Bassia Latifolia Seed Butter
Bertholletia Excelsa Seed Oil
Borago Officinalis Seed Oil
Brassica Campestris (Rapeseed) Oil Unsaponifiables*
Brassica Campestris (Rapeseed) Seed Oil
Brassica Napus Seed Oil*
Brassica Oleracea Acephala Seed Oil*
Brassica Oleracea Italica (Broccoli) Seed Oil
Butyrospermum Parkii (Shea) Butter
Butyrospermum Parkii (Shea) Butter Unsaponifiables
Butyrospermum Parkii (Shea) Oil
Camelina Sativa Seed Oil
Camellia Japonica Seed Oil
Camellia Kissi Seed Oil
Camellia Oleifera Seed Oil
Camellia Sinensis Seed Oil
Canarium Indicum Seed Oil*
Canola Oil
Canola Oil Unsaponifiables
Carica Papaya Seed Oil
Carthamus Tinctorius (Safflower) Seed Oil
Carya Illinoensis (Pecan) Seed Oil*
Caryocar Brasiliense Fruit Oil
Chenopodium Quinoa Seed Oil
Citrullus Lanatus (Watermelon) Seed Oil
Citrus Aurantifolia (Lime) Seed Oil*
Citrus Aurantifolia (Lime) Seed Oil Unsaponifiables*
Citrus Aurantium Dulcis (Orange) Seed Oil*
Citrus Aurantium Dulcis (Orange) Seed Oil Unsaponifiables*
Citrus Grandis (Grapefruit) Seed Oil Unsaponifiables*
Citrus Limon (Lemon) Seed Oil*
Coconut Acid
Cocos Nucifera (Coconut) Oil
Cocos Nucifera (Coconut) Seed Butter*
Corn Acid*
Corylus Americana (Hazel) Seed Oil
Corylus Avellana (Hazel) Seed Oil
Cottonseed Acid*
Crambe Abyssinica Seed Oil
Cucumis Sativus (Cucumber) Seed Oil
Cucurbita Pepo (Pumpkin) Seed Oil
Cynara Cardunculus Seed Oil*
Elaeis (Palm) Oil*
Elaeis Guineensis (Palm) Butter*
Elaeis Guineensis (Palm) Kernel Oil
Elaeis Guineensis (Palm) Oil
Elaeis Oleifera Kernel Oil
Euterpe Oleracea Fruit Oil
Fragaria Ananassa (Strawberry) Seed Oil*
Garcinia Indica Seed Butter
Genuina Avellana Seed Oil
Gevuina Avellana Oil
Glycine Soja (Soybean) Oil
Glycine Soja (Soybean) Oil Unsaponifiables
Gossypium Herbaceum (Cotton) Seed Oil
Guizotia Abyssinica Seed Oil*
Helianthus Annuus (Sunflower) Seed Oil
Helianthus Annuus (Sunflower) Seed Oil Unsaponifiables
Hippophae Rhamnoides Fruit Oil
Hippophae Rhamnoides Oil
Hippophae Rhamnoides Seed Oil*
Hydrogenated Adansonia Digitata Seed Oil*
Hydrogenated Apricot Kernel Oil
Hydrogenated Apricot Kernel Oil Unsaponifiables*
Hydrogenated Argania Spinosa Kernel Oil*
Hydrogenated Avocado Oil
Hydrogenated Black Currant Seed Oil*
Hydrogenated Camelina Sativa Seed Oil*
Hydrogenated Camellia Oleifera Seed Oil
Hydrogenated Canola Oil
Hydrogenated Coconut Acid
Hydrogenated Coconut Oil
Hydrogenated Cottonseed Oil

Hydrogenated Cranberry Seed Oil*
Hydrogenated Evening Primrose Oil
Hydrogenated Grapefruit Seed Oil*
Hydrogenated Grapefruit Seed Oil Unsaponifiables*
Hydrogenated Grapeseed Oil
Hydrogenated Hazelnut Oil*
Hydrogenated Kukui Nut Oil*
Hydrogenated Lime Seed Oil*
Hydrogenated Lime Seed Oil Unsaponifiables*
Hydrogenated Macadamia Seed Oil*
Hydrogenated Meadowfoam Seed Oil*
Hydrogenated Olive Oil
Hydrogenated Olive Oil Unsaponifiables
Hydrogenated Orange Seed Oil*
Hydrogenated Orange Seed Oil Unsaponifiables*
Hydrogenated Palm Acid*
Hydrogenated Palm Kernel Oil
Hydrogenated Palm Oil
Hydrogenated Passiflora Edulis Seed Oil*
Hydrogenated Peach Kernel Oil*
Hydrogenated Peanut Oil
Hydrogenated Pistachio Seed Oil*
Hydrogenated Pumpkin Seed Oil*
Hydrogenated Punica Granatum Seed Oil*
Hydrogenated Rapeseed Oil*
Hydrogenated Raspberry Seed Oil
Hydrogenated Rice Bran Oil*
Hydrogenated Rosa Canina Fruit Oil*
Hydrogenated Safflower Seed Oil*
Hydrogenated Sesame Seed Oil*
Hydrogenated Shea Butter
Hydrogenated Soybean Oil
Hydrogenated Sunflower Seed Oil
Hydrogenated Sweet Almond Oil
Hydrogenated Sweet Almond Oil Unsaponifiables*
Hydrogenated Vegetable Oil
Hydrogenated Wheat Germ Oil*
Hydrogenated Wheat Germ Oil Unsaponifiables*
Irvingia Gabonensis Kernel Butter
Juglans Regia (Walnut) Seed Oil
Limnanthes Alba (Meadowfoam) Seed Oil
Linseed Acid
Linum Usitatissimum (Linseed) Seed Oil
Luffa Cylindrica Seed Oil
Lupinus Albus Oil Unsaponifiables*
Lupinus Albus Seed Oil
Macadamia Integrifolia Seed Oil
Macadamia Ternifolia Seed Oil
Magnesium Cocoate
Mangifera Indica (Mango) Seed Butter
Mangifera Indica (Mango) Seed Oil
Moringa Oleifera Seed Oil
Moringa Pterygosperma Seed Oil
Oenothera Biennis (Evening Primrose) Oil
Olea Europaea (Olive) Husk Oil*
Olea Europaea (Olive) Oil Unsaponifiables
Olea Europea (Olive) Fruit Oil
Olive Acid*
Orbignya Cohune Seed Oil
Orbignya Oleifera Seed Oil
Oryza Sativa (Rice) Bran Oil
Oryza Sativa (Rice) Germ Oil
Oryza Sativa (Rice) Seed Oil*
Palm Acid
Palm Kernel Acid
Passiflora Edulis Seed Oil
Peanut Acid*
Perilla Ocymoides Seed Oil
Persea Gratissima (Avocado) Butter
Persea Gratissima (Avocado) Oil
Persea Gratissima (Avocado) Oil Unsaponifiables
Pistacia Vera Seed Oil
Plukenetia Volubilis Seed Oil
Potassium Babassuate*
Potassium Cocoate
Potassium Cornate*
Potassium Hydrogenated Cocoate*
Potassium Hydrogenated Palmate*
Potassium Olivate
Potassium Palm Kernelate
Potassium Palmate
Potassium Peanutate
Potassium Rapeseedate*
Potassium Safflowerate*
Potassium Soyate*
Prunus Amygdalus Dulcis (Sweet Almond) Oil
Prunus Amygdalus Dulcis (Sweet Almond) Oil Unsaponifiables*
Prunus Armeniaca (Apricot) Kernel Oil
Prunus Armeniaca (Apricot) Kernel Oil Unsaponifiables*
Prunus Avium (Sweet Cherry) Seed Oil
Prunus Domestica Seed Oil
Prunus Persica (Peach) Kernel Oil
Punica Granatum Seed Oil
Pyrus Malus (Apple) Seed Oil
Rapeseed Acid*
Ribes Nigrum (Black Currant) Seed Oil
Ribes Rubrum (Currant) Seed Oil*
Rice Bran Acid*
Rosa Canina Fruit Oil
Rubus Chamaemorus Seed Oil
Rubus Idaeus (Raspberry) Seed Oil
Safflower Acid*
Sclerocarya Birrea Seed Oil
Sesamum Indicum (Sesame) Oil Unsaponifiables
Sesamum Indicum (Sesame) Seed Butter*
Sesamum Indicum (Sesame) Seed Oil
Silybum Marianum Seed Oil [Thistle]
Sodium Astrocaryum Murumuruate
Sodium Avocadoate
Sodium Babassuate
Sodium Cocoa Butterate*
Sodium Cocoate
Sodium Grapeseedate
Sodium Hydrogenated Cocoate*
Sodium Hydrogenated Palmate*
Sodium Macadamiaseedate*
Sodium Mangoseedate
Sodium Olivate
Sodium Palm Kernelate
Sodium Palmate
Sodium Peanutate*

Sodium Rapeseedate*
Sodium Safflowerate*
Sodium Sesameseedate
Sodium Soyate*
Sodium Sweet Almondate
Sodium Theobroma Grandiflorum Seedate*
Solanum Lycopersicum (Tomato) Fruit Oil
Solanum Lycopersicum (Tomato) Seed Oil
Soy Acid*
Sunflower Seed Acid*
Theobroma Cacao (Cocoa) Seed Butter
Theobroma Grandiflorum Seed Butter
Torreya Nucifera Seed Oil*
Triticum Aestivum (Wheat) Germ Oil*
Triticum Vulgare (Wheat) Germ Oil
Triticum Vulgare (Wheat) Germ Oil Unsaponifiables*
Vaccinium Corymbosum (Blueberry) Seed Oil*
Vaccinium Macrocarpon (Cranberry) Seed Oil
Vaccinium Myrtillus Seed Oil
Vaccinium Vitis-Idaea Seed Oil
Vegetable (Olus) Oil
Vitis Vinifera (Grape) Seed Oil
Wheat Germ Acid
Zea Mays (Corn) Germ Oil
Zea Mays (Corn) Oil
Zea Mays (Corn) Oil Unsaponifiables

RE-REVIEWS

Disperse Blue 1- Not Reopened

In 1995, the CIR Expert Panel concluded that disperse blue 1 was safe for use in hair dyes at concentrations up to 1%. The Panel focused on and further discussed the existing carcinogenicity data on disperse blue 1 and considered risk assessment input from FDA and industry. Based on these inputs, CIR developed an overall risk assessment which demonstrated a margin of safety were Disperse Blue 1 to be used as a hair dye at a concentration of 1%. The Panel noted that Disperse Blue 1 is not in current use. The CIR Expert Panel determined to not reopen the safety assessment of disperse blue 1.

Formaldehyde – Reopened

The CIR Expert Panel acknowledged the recent reports about high levels of formaldehyde measured in "Brazilian" hair smoothing products. FDA has asked CIR to consider the safety of formaldehyde in these products and to address the safety of methylene glycol in cosmetics. The Personal Care Products Council has supported such an effort. The Professional Beauty Association has joined in that support. In its previous safety assessment of formaldehyde, the Panel stated that free formaldehyde should be minimized, but in no case should free formaldehyde be >0.2%; and it can't be concluded that formaldehyde is safe in cosmetic products intended to be aerosolized.

The Panel determined that the safety assessment of formaldehyde should be reopened to address three issues: (1) the complex chemistry between formaldehyde and methylene glycol in water; (2) the safety of methylene glycol as used in cosmetics, especially in these hair smoothing products; and (3) the adequacy of the current limit on free formaldehyde, given that the process of using hair smoothing products appears to involve drying and heating, both of which may tend to drive the formaldehyde/methylene glycol equilibrium towards formaldehyde gas and/or produce methylene glycol gas.

MEA, DEA, and TEA – Reopened

In 1983, the CIR Expert Panel issued a final report on the safety of TEA, DEA, and MEA as one document. While newly available information concerning the safety of these ingredients as used in cosmetics did not raise significant concerns, new data are available that should be formally reviewed. Accordingly, the Panel determined it would re-open this document. Additionally, the Expert Panel determined that it would consider adding ingredients such as related salts to each. To facilitate such consideration, CIR will create three separate draft amended safety assessments, one each for TEA, DEA, and MEA.

NEWLY SUBMITTED DATA FOR HUMAN UMBILICAL EXTRACT

The CIR Expert Panel considered new data provided by a manufacturer intended to address an earlier insufficient data finding for Human Umbilical Extract. Those data likely would not reverse the finding of insufficient data. The Panel, however, reached a consensus that the patented ingredient actually is Human Umbilical Serum Extract, an ingredient not previously reviewed. The Panel also noted that the implications in product literature that this ingredient would have some health benefit could mean that the U.S. Food and Drug Administration's Center for Biologics Evaluation and Research might consider the product to be a biologic product that should be cleared by FDA before marketing. This information will be provided to the company.

Cosmetic Ingredient Review
Commitment . . . Credibility
Since 1976

CIR

MEMORANDUM

To:	CIR Expert Panel Members and Liaisons
From:	Deputy Director, CIR
Subject:	CIR Boilerplates, Precedents and Formats
Date:	February 10, 2011

Attached is a copy of the CIR Boilerplates, Precedents, and Formats which have been derived from a compilation of issues previously discussed by the CIR Expert Panel, along with language developed to articulate the Panels thinking. This collection has been around for a long time; tweaked as appropriate along the way, but is now brought together in one place.

The current version has three sections. The first is a collection of general issues; some include a background and boilerplate section, and others only include previous examples of how the Panel described its reasoning. The second section summarizes the formats CIR uses in crafting sections of the report. The third section provides standardized formats for certain commonly used charts.

We expect to expand this document to include the rationale and reasoning behind other Panel practices and decisions, for example, information on the VCRP, and how the current use and concentration summary table is compiled. The existence of the compilation will allow CIR reports to be more concise with regard to certain issues. For example, almost every report currently includes a several paragraph discussion on aerosol and spray particle sizes and why their size makes them non respirable and not a safety concern. With the reasoning behind this decision publicly available, a lengthy discussion will no longer be necessary in each report.

We are bringing the CIR Precedents to your attention for the following reasons:

1. While the rationale and the wording included in this compilation has been made public in many of the CIR Expert Reports, we want to make sure that the Public is aware that many of the issues addressed in single reports have an impact on other findings and that the Panel strives to apply consistent reasoning wherever possible.
2. The issues included are not exhaustive. We would ask the Panel to identify other issues it believes need to be included in this compilation.
3. Recent Panel discussions and decisions have resulted in changes to a number of the boilerplates (Transmission of Disease; Nitrosamines; Aerosol). Older versions are “boxed” in the text to provide historical content.

If the Panel believes any of the issues need further discussion, we will capture those and they will be scheduled for future Panel Meetings.

We welcome your thoughts and comments.

COSMETIC INGREDIENT REVIEW

CIR Precedents

Boilerplates, Precedents and Formats

2/10/2011

This document is a compilation of issues discussed by the CIR Expert Panel along with boilerplate language used in CIR Reports to articulate the Panel's views. Standard formats for Tables used in Panel Reports are also provided. This is intended to provide background on issues and serve as a reference to the reasoning behind previous Panel decisions.

Precedents and Boilerplates

Contents

1. **Boilerplates and Precedents**

Aerosols

Aerosol Propellant Dilution

As aerosols, Isobutane, Propane, Isopentane, and n-Butane are so greatly diluted when discharged that the amount coming into contact with the skin is much less than the stated amounts used in the clinical tests. Since alkanes are highly volatile and have low water solubility, it is estimated that, as propellants, they would remain on the skin no longer than 10 seconds. Such a short period of contact makes the absence of sensitization, phototoxicity, and photosensitization studies relatively unimportant.

Sprays/aerosols – particle size

Draft Update 2/2011

BACKGROUND

For ingredients used in cosmetic sprays and aerosols, it is important to consider inhalation safety. (Fragrance Preparations, Hair Sprays, Hair Color Sprays and Foot Powders and Sprays are examples of categories of cosmetics that are sprays and aerosols). Safety of inhaled aerosols depends on the ingredient, the concentration, the duration of the exposure and where they are deposited within the respiratory system.[1] The site of deposition is associated most with the particle size and density of the particle being inhaled. Absorption of gases and vapors by inhalation is determined by the partitioning of the compound between the blood and the gas phase along with its solubility and tissue reactivity. The important characteristics that affect absorption after exposure to aerosols are the aerosol size and water solubility of any chemical present in the aerosol. In general, the smaller the particle, the further into the respiratory tree the particle will deposit and the greater the impact on the respiratory system.

The parameter most closely associated with this regional deposition is the aerodynamic diameter, d_a, defined as the diameter of a sphere of unit density possessing the same terminal settling velocity as the particle in question. In humans, particles with an aerodynamic diameter of ≤ 10 µm are respirable. Particles with a d_a from 0.1 – 10 µm settle in the upper respiratory tract and particles with a d_a < 0.1 µm settle in the lower respiratory tract.[2,3] Nanoparticles have the potential to deliver high amounts of particulates to the lung.[4]

Particle diameters of 60-80 µm and ≥80 µm have been reported for anhydrous hair sprays and pump hairsprays, respectively.[5] In practice, aerosols should have at least 99% of their particle diameters in the 10 – 110 µm range and the mean particle diameter in a typical aerosol spray has been reported as ~38 µm.[6] Therefore, most aerosol particles are deposited in the nasopharyngeal region and are not respirable.

The Panel has discussed this issue and has decided that in the absence of inhalation toxicity data on a specific ingredient, they will consider the ingredient particle size in determining its inhalation safety.

REFERENCES

1. Jensen PA, O'Brien D. Industrial Hygiene. In: Willeke K, Baron PA, eds. *Aerosol Measurement: Principles Techniques and Applications*. New York: John Wiley and Sons, Inc.; 1993;538-540.
2. James AC, Stahlhofen W, Rudolf G et al. Annexe D. Deposition of inhaled particles. *Annals of the ICRP.* 1994;24(1-3):231-2.
3. Oberdorster G, Oberdorster E, Oberdorster J. Nanotoxicology: An Emerging Discipline Evolving from Studies of Ultrafine Particles. *Environmental Health Perspectives.* 2005;113(7):823-839.
4. Lehman-McKeeman LD. Absorption, Distribution, and Excretion of Toxicants. In: Klassen CD, ed. *Casarett and Doull's Toxicology: The Basic Science of Poisons*. 7 ed. New York: McGraw-Hill Companies, Inc.; 2008;131-159.
5. Bower D. Unpublished information on hair spray particle sizes provided at the September 9, 1999 CIR Expert Panel meeting. 1999.

6. Johnson MA. The Influence of Particle Size. *Spray Technology and Marketing.* 2004;November:24-27.

Boilerplate language for specific report sections:

Cosmetic Use Section

[INGREDIENT] is used in [LIST TYPE OF COSMETIC INGREDIENT, eg hair spray], and effects on the lungs that may be induced by aerosolized products containing this ingredient, are of concern. The particle size of aerosol hair sprays is and pump hair sprays is around 38 µm and >80 µm, respectively, and is large compared to respirable particle sizes (≤10 µm). Therefor, because of their size, most aerosol particles are deposited in the nasopharyngeal region and are not respirable.

Previous Version in Cosmetic Use Section:

[INGREDIENT] is used in hair sprays, and effects on the lungs that may be induced by aerosolized products containing this ingredient, are of concern.

The aerosol properties that determine deposition in the respiratory system are particle size and density. The parameter most closely associated with deposition is the aerodynamic diameter, d_a, defined as the diameter of a sphere of unit density possessing the same terminal settling velocity as the particle in question. In humans, particles with an aerodynamic diameter of ≤ 10µm are respirable. Particles with a d_a from 0.1 - 10µm settle in the upper respiratory tract and particles with a d_a < 0.1 µm settle in the lower respiratory tract.[2,3]

Particle diameters of 60-80 µm and ≥80 µm have been reported for anhydrous hair sprays and pump hairsprays, respectively.[5] In practice, aerosols should have at least 99% of their particle diameters in the 10 – 110 µm range and the mean particle diameter in a typical aerosol spray has been reported as ~38 µm.[6] Therefore, most aerosol particles are deposited in the nasopharyngeal region and are not respirable.

Discussion

Certain of the [ingredients] are used in cosmetic products that may be inhaled during their use. In practice, however the particle sizes produce by cosmetic aerosols are not respirable. [If inhalation toxicity data are available, they should be mentioned].

Previous Version in Discussion:

The potential adverse effects of inhaled aerosols depend on the specific chemical species, the concentration and the duration of the exposure and their site of deposition within the respiratory system. In practice, aerosols should have at least 99% of their particle diameters in the 10 – 110 µm range and the mean particle diameter in a typical aerosol spray has been reported as ~38 µm. Particles with an aerodynamic diameter of ≤ 10µm are respirable. In [THE ABSENCE OF/ADDITION TO] inhalation toxicity data, the panel determined that [INGREDIENT] can be used safely in hair sprays, because the product particle size is not respirable. NOTE: If there are inhalation toxicity data, mention them and present particle size discussion as “in addition”, not “in the absence”.

References previously included in Panel report:

James AC, Stahlhofen W, Rudolf G et al. Annexe D. Deposition of inhaled particles. *Annals of the ICRP* 1994;24(1-3):231-2.

Oberdorster G, Oberdorster E, Oberdorster J. Nanotoxicology: An Emerging Discipline Evolving from Studies of Ultrafine Particles. *Environmental Health Perspectives.* 2005;113(7):823-839.

Bower D. Unpublished information on hair spray particle sizes provided at the September 9,1999 CIR Expert Panel meeting. 1999.

Johnson MA. The Influence of Particle Size. *Spray Technology and Marketing.* 2004; November: 24-27.

Re-review summaries

The CIR Expert panel noted the absence of inhalation toxicity data. However, in the absence of

these data, the Panel determined that [INGREDIENT] can be used safely in hair sprays, because the product particle size is not respirable. The Panel reasoned that the particle size of aerosol hair sprays and pump hair sprays is large compared to respirable particle sizes (≤10 μm).

Botanicals

Plant extracts - equivalency

Concern, however, was expressed about alternative approaches to extraction that might not produce material with the same safety profile described in this safety assessment, especially if pesticides were used on the plants. While extracts from pesticide-free plants were not genotoxic and there do not appear to be any components that could be carcinogenic, pesticide residues could raise this issue. The Panel urged that manufacturers limit pesticide residues to the limit previously used for lanolin of not more than 40 ppm total pesticide residue, (with not more than 10 ppm for any one residue).

The conclusion regarding safety is valid only for extracts prepared in a manner that produces a similar chemical profile as that described in this report, particularly as regards diosgenin. Prepared in this manner, the Panel's conclusion is that these extracts do not have significant estrogenic activity. Extracts not prepared in a manner that produces a similar chemical profile, would be considered safe if they have a similar safety test profile.

Ingredients from Processed Botanical Sources

While plants are the source of some components in the ingredients of this report, they result from significant processing, and as such are not expected to contain residual pesticides or heavy metals.

ALSO See: Contaminants, Residues, Impurities: Aflatoxin, and Pesticide and Heavy Metals Boilerplates.

Contaminants, Residues, Impurities

Aflatoxin

While aflatoxin has been detected in [source of ingredient], the Panel believes that aflatoxin should not be present in botanical ingredients that are derived from *[source of ingredient]*; the Panel adopted the USDA designation of ≤ 15 ppb as corresponding to "negative" aflatoxin content.

1,4-Dioxane and Ethylene Oxide

eg 1: Also of concern to the Expert Panel was the possible presence of 1,4-dioxane and ethylene oxide impurities. They stressed that the cosmetics industry should continue to use the necessary procedures to remove these impurities from the [INGREDIENT] before blending them into cosmetic formulations.

eg 2: In its safety assessment on lower molecular weight Nonoxynols, the Panel reviewed data indicating that these compounds can contain up to 67 ppm ethylene oxide and up to 20 ppm 1,4-dioxane (both are carcinogenic). However, the Panel was not concerned about the toxicity of ethylene oxide in cosmetics containing Nonoxynols given that use of these products only in excessive amounts could yield an average exposure of 0.1 mg ethylene oxide/day. This level of exposure was

established (using chronic toxicity and carcinogenicity data) by the International Organization for Standardization (ISO) as the average residue limit for patient exposure to ethylene oxide (30 days to life) from each medical device. Although the ISO limitation was mentioned in the CIR report discussion on lower molecular weight Nonoxynols, it does not appear in the report conclusion because the Panel recognized that it is very unlikely that use of a cosmetic product could result in this level of exposure (0.1 mg /day) to ethylene oxide.

Pesticide and heavy metal limits

BACKGROUND:

The CIR Expert Panel has included specified limits for pesticides and heavy metals that may be present in botanical ingredients. Examples include:

eg 1: The CIR Expert Panel expressed concern about toxic metal residues that may be present in (ingredient name) and advised industry that this ingredient should not contain more than: 3 mg/kg of arsenic (as As), 1 ppm mercury (as Hg), and 0.1 mg/kg of lead (as Pb).

eg 2: In its safety assessment of Acid Violet 43 (Andersen 2001a), the CIR Expert Panel adopted limitations established by the Food and Drug Administration for certification of Ext. D & C No. 2 as a color additive (FDA 1976). In its safety assessment of the Lard Glycerides group of ingredients (Andersen 2001b), the CIR Expert Panel adopted the Food Chemicals Codex limit for lead in unhydrogenated lard (National Academy of Sciences 1996). The Panel recognizes that these limits were developed for uses other than cosmetics, but considers that such limits would assure that any cosmetic product with these ingredients can be used safely.

eg 3: In 2001, the Environmental Protection Agency established a limit of 10 ppb for arsenic in drinking water (40 CFR 141.6). The CIR Expert Panel considered this EPA determination as it might relate to cosmetics such as lipsticks that may be ingested. According to Loretz et al. (2005), the mean application per day of lipstick is 24 mg. Recognizing that not all of that application would be ingested and that not all ingredients in a lipstick product would contain arsenic up to 3 ppm, the Panel determined that the daily ingestion of arsenic from lipstick would be less than that received from the ingestion of 2 liters of drinking water per day at the 10 ppb level established by EPA.

More recently, the Panel has incorporated more general language, but limit specific language should be included where appropriate.:

Boilerplate <u>In Discussion Section:</u>

The Expert Panel expressed concern regarding pesticide residues and heavy metals that may be present in botanical ingredients. They stressed that the cosmetics industry should continue to use the necessary procedures to limit these impurities in the ingredient before blending into cosmetic formulation.

Hair Dyes

Hair dyes as "consumables"

(9/2009)

The Expert Panel noted that data supplied by industry indicate that during the hair dyeing procedure, Hydroquinone is a "consumable." This means that the actual concentration of Hydroquinone decreases sharply as the color-forming reaction proceeds. Therefore, the amount of Hydroquinone that may be absorbed during the hair dyeing process is limited both by the decreasing concentration of available Hydroquinone and by the length of time the hair dye is applied before being rinsed off.

Hair Dye Ingredients

(updated 9/2009)

Coal Tar Hair Dyes: BACKGROUND

Hair dye ingredients containing coal tar are not subject to the same FDA requirements as other hair dyes. Since 1938, FDA law exempts coal tar hair dye products from the principal adulteration and color additive provisions in sections 601 and 706 of the Federal Food, Drug, and Cosmetic Act, when the label bears a caution statement and patch test instructions for determining whether the product causes skin irritation (FDA, 1979). The caution statement reads as follows:

> Caution - this product contains ingredients which may cause skin irritation on certain individuals and a preliminary test according to accompanying directions should be made. This product must not be used for dyeing the eyelashes or eyebrows; to do so may cause blindness.

In 1991-1992, the Panel addressed the question of sensitization testing for coal tar hair dye products. There was a general consensus among dermatologists that screening of patients for sensitization (allergic contact dermatitis) should be conducted by the procedures used by the North American Contact Dermatitis Group and the International Contact Dermatitis Group (North American Contact Dermatitis Group 1980; Eiermann et al. 1982; Adams et al. 1985). Basically, these procedures state that the test material should be applied at an acceptable concentration to the patient, covered with an appropriate occlusive patch, and evaluated for sensitization at 48 and 72 hours after application. The CIR Expert Panel has cited the results of these studies in its safety assessments of cosmetic ingredients. The Panel advised the cosmetics industry to recommend that the open patch test be evaluated 48 hours after application of the test material.

REFERENCES

Adams, R.M., H.I. Maibach, W.W. Clendenning, et al. 1985. A five-year study of cosmetic reactions. *J Am Acad Dermatol* 13:1062-1069.
Eiermann, H.J. W. Larsen, H.I. Maibach, et al. 1982. Prospective study of cosmetic reactions: 1977-1980. *J Am Acad Dermatol* 6:909-917.

Food and Drug Administration (FDA). 1979. Cosmetic product warning statements: coal tar hair dyes containing 4-methoxy-m-phenylenediamine (2,4-diaminanisole) or 4-methoxy-m-phenylenediamine sulfate (2,4-diaminoanisole sulfate). *Federal Register* 44:59509-59510.
North American Contact Dermatitis Group. 1980. Patch testing in allergic contact dermatitis. Evaston IL:American Academy of Dermatology.

Boilerplate language for specific report sections:

> *DISCUSSION section;* **Hair dye adulteration exemption**:
> The Expert Panel recognizes that [INGREDIENT] is used as a hair dye ingredient and that irritation and sensitization data are not available in all cases. However, hair dyes containing [INGREDIENT], as coal tar hair dye products, are exempt from certain adulteration and color additive provisions of the Federal Food, Drug, and Cosmetic Act, when the label bears a caution statement and patch test instructions for determining whether the product causes skin irritation. The Expert Panel expects that following this procedure will identify prospective individuals who would have an irritation/sensitization reaction and allow them to avoid significant exposures.
>
> *COSMETIC USE section;* **Hair Dye Caution Statement - FDA labeling**
> **[INGREDIENT]** is considered a coal tar hair dye for which regulations require caution statements and instructions regarding patch tests in order to be exempt from certain adulteration and color additive provisions of the of the Federal Food, Drug, and Cosmetic Act. In order to be exempt, the following caution statement must be displayed on all coal tar hair dye products:
>
> > Caution - this product contains ingredients which may cause skin irritation on certain individuals and a preliminary test according to accompanying directions should be made. This

product must not be used for dyeing the eyelashes or eyebrows; to do so may cause blindness.

Product labels shall also bear a caution statement and patch test instructions for determining whether the product causes skin irritation. The CIR Expert Panel recommends that an open patch test be applied and evaluated by the beautician and/or consumer for sensitization 48 hours after application of the test material and prior to the use of a hair dye formulation.

Hair Dye Epidemiology

(updated 9/2009)

BACKGROUND

While the safety of individual hair dye ingredients are not addressed in epidemiology studies that seek to determine links, if any, between hair dye use and disease, such studies do provide broad information and have been exhaustively considered by the CIR Expert Panel, most recently in 2009. Included in the Panel's review were three large reviews on hair dye epidemiology:

- 1993, an International Agency for Research on Cancer (IARC) working group evaluated 78 epidemiology literature citations and concluded that "personal use of hair colourants cannot be evaluated as to its carcinogenicity" and that "occupation as a hairdresser or barber entails exposures that are probably carcinogenic" (IARC 1993). The IARC report did not distinguish between personal use of oxidative versus direct hair dyes, or distinguish among the multiple chemical exposures in addition to hair dyes to which a hairdresser or barber might be exposed.

- Rollison et al. (2006) reviewed the available epidemiology literature published from 1992 through February 2005. The authors found that hair dye exposure in the assessment ranged widely. The authors found insufficient evidence to support a causal association between personal hair dye use and a variety of tumors and cancers. The review highlighted well-designed studies which found associations between personal hair dye use and development of acute leukemia, bladder cancer, multiple myeloma, and non-Hodgkin's lymphoma. These findings, however, were not consistently observed across studies.

- In February 2008, an IARC Working Group re-evaluated the epidemiology literature including studies considered in the 1993 evaluation as well as all studies subsequently published. For personal use of hair colorants, the Working Group considered the epidemiological evidence inadequate and concluded that personal use of hair colorants is "not classifiable as to its carcinogenicity to humans". The Working Group considered the studies of occupational exposures in hairdressers and barbers as providing limited evidence of carcinogenicity and reaffirmed the previous conclusion made in 1993 that occupation as a hairdresser or barber entails exposures that are probably carcinogenic (Baan et al. 2008).

Other studies addressing the possible link between hair dye use and bladder cancer, lymphoma and leukemia, other cancers, reproductive and developmental outcomes, and other endpoints published since the above reviews also have been considered. A detailed summary of the available hair dye epidemiology data is available at http://www.cir-safety.org/findings.shtml.

REFERENCES

Baan, R., K. Straif, Y. Grosse, et al. 2008. WHO International Agency for Research on Cancer Monograph Working Group: Carcinogenicity of some aromatic amines, organic dyes, and related exposures. *Lancet Oncol*. 9(4):322-3.

International Agency for Research on Cancer (IARC). 1993. IARC Monographs on the evaluation of carcinogenic risks to humans. Vol 57. Occupational exposures of hairdressers and barbers and personal use of hair colourants; some hair dyes, cosmetic colourants, industrial dyestuffs and aromatic amines. Lyon, France: IARC. (pages 43-118).

Rollison, D.E., K.J. Helzlsouer, and S.M. Pinney. 2006. Personal Hair Dye Use and Cancer: A Systematic Literature Review and Evaluation of Exposure Assessment in Studies Published Since 1992. *J. Toxicol. Environ. Health. Part B*. 9:413-439.

Boilerplate language for specific report sections:

Hair Dye Epidemiology section:

Hair dyes may be broadly grouped into oxidative (permanent) and direct (semipermanent) hair dyes. The oxidative dyes consist of precursors mixed with developers to produce color, while direct hair dyes are a preformed color. [INSERT INGREDIENT] is a/n [OXIDATIVE/DIRECT] hair dye ingredient. While the safety of individual hair dye ingredients are not addressed in epidemiology studies that seek to determine links, if any, between hair dye use and disease, such studies do provide broad information. A detailed summary of the available hair dye epidemiology data is available at http://www.cir-safety.org/findings.shtml.

Previously included in Hair Dye Epidemiology section:
The CIR Expert Panel is aware that the IARC (1993) concluded that personal use of hair colorants cannot be evaluated as to its carcinogenicity and that occupation as a hairdresser or barber entails exposures that are probably carcinogenic (IARC, 1993); that insufficient evidence exists to support a causal association between personal hair dye use and a variety of tumors and cancers such as acute leukemia, bladder cancer, multiple myeloma, and non-Hodgkin's lymphoma (Rollison et al. 2006); and that the epidemiological evidence for personal use of hair colorants is inadequate and is not classifiable as to its carcinogenicity to humans (Baan et al. 2008).

Summary Section:

The most recent comprehensive review of available epidemiology studies concluded that there is insufficient evidence to support a causal association between personal hair dye use and a variety of tumors and cancers.

Discussion Section:

In considering hair dye epidemiology data, the CIR Expert Panel concluded that the available epidemiology studies are insufficient to conclude there is a causal relationship between hair dye use and cancer and other endpoints, based on lack of strength of the associations and inconsistency of findings. Use of direct hair dyes, while not the focus in all investigations, appears to have little evidence of any association with adverse events as reported in epidemiology studies.

Leave-on and Rinse-off definitions

In response to the CIR Expert Panel's request for a statement discriminating between "rinse-off" and "leave-on" products, the following statement has been recommended by the CTFA Scientific Advisory Committee's Executive Committee:

A "rinse-off" product is one designed to be applied to the hair or body in diluted or undiluted form for a short period of time (less than 1 hour) followed by thorough rinsing. Operational examples include shampoos, hair conditioners, and depilitories.

A "leave-on" product is a product intended to be applied to the skin and left in place for a long enough time to achieve the desired benefit.

Nitrosamine formation

Revised draft; 10/2010

BACKGROUND:
Nitrosamines are compounds containing the R^1R^2N-NO functional group. Nitrosamides are compounds containing the $R^1C(O)R^2N$-NO functional group. Nitrosation is the process of converting organic compounds (e.g., alkyl and aryl amines and amides) into nitroso derivatives (e.g., nitrosamines and nitrosamides) by reaction with nitrosating agents. These agents include nitrous acid (HNO_2), oxides of nitrogen (e.g., nitrites, nitrates, and dinitrogen trioxide), and other compounds capable of generating a nitrosonium ion, NO^+.

Of concern in cosmetics is the conversion of secondary amines (R1-NH-R2) into *N*-nitrosamines that may be carcinogenic. Of the approximately 300 *N*-nitroso compounds that have been tested, 85% of the 209 nitrosamines and 92% of the 86 nitrosamides have been shown to produce cancer in laboratory animals **(Shank and Magee, 1981; NRC, 1981).** Nitrosation can occur under physiologic conditions. Depending on the nitrosating agent and the substrate, nitrosation can occur under acidic, neutral, or alkaline conditions. However, nitrosation occurs most commonly under acidic conditions. Atmospheric NO_2 may also participate in the nitrosation of amines in aqueous solution **(Challis et al., 1982).**

Another concern is when nitrosamines may be present in a cosmetic as an impurity of an ingredient. This concern became apparent during the safety assessment of morpholine (08/1989) wherein the CIR Expert Panel determined that, under conditions of cosmetic use, it is highly unlikely that morpholine is totally free of carcinogenic nitrosamines. Nitrosation of morpholine to form *N*-nitrosomorpholine occurs readily. Accordingly, concern was raised about the contamination of morpholine with *N*-nitrosomorphine.

Even though amines and amides may not be mutagenic or carcinogenic alone, in the presence of a nitrosating agent they may exhibit mutagenic and carcinogenic potential, due to the reactions recited above. While many secondary amines and amides are readily nitrosated to form isolatable nitrosamines and nitrosamides, primary alkyl and aryl amines ultimately yield diazonium salts, instead of nitrosamines. Tertiary alkyl amines also do not tend to react with nitrosating agents to form nitrosamines. While tertiary aryl amines do undergo nitrosation, the reaction occurs on the aromatic ring (i.e. not on the amine), and does not result in the formation of nitrosamines.

Consequently, the Panel generally cautions that cosmetic products containing secondary amines or amides should be free of nitrosating agents. Manufacturers can accomplish this by formulating these ingredients in a way that avoids the formation of nitrosamines, and by eliminating the presence of impurities that contain nitrosating agents.

References:
Mirvish, S., Sams J and P. Issenberg; CANCER RESEARCH 43, 2550-2554, June 1983]
The Nitrosating Agent in Mice Exposed to Nitrogen Dioxide: Improved Extraction Method and Localization in the Skin.
Rostkowska, K et al; *Polish Journal of Environmental Studies Vol.* 7, *No. 6 (1998), 321-325*
Review Formation and Metabolism of N-Nitrosamines.
Shank and Magee, 1981; NRC, 1981.
Challis et al., 1982.

BOILERPLATE (to be included in either the discussion, conclusion or summary sections of reports):

- The Expert Panel cautions that products containing these ingredients should be formulated to avoid the formation of nitrosamines.
-

Nitrosamine formation boilerplates: old versions
The nitrosamine formation caveat has been previously expressed as: ... <u>should not be used</u> with N-nitrosating agents

... should not be used in products containing N-nitrosating agents
...should not be used in products where N-nitroso compounds may be formed.
... should not contain N-nitroso impurities, nor should it be used in products where N-nitroso compounds may be formed.

pH Adjusters

While [INGREDIENT] may function in cosmetics as [LIST FUNCTIONS, including pH adjuster], this safety assessment considered only its use as a pH adjuster. The CIR Expert Panel recognized that while [INGREDIENT] itself may be a dermal and/or ocular irritant, its use as a pH adjuster in cosmetic formulations dictates that most of the acid will be neutralized into various [INGREDIENT] salts. Furthermore, the concentration of [INGREDIENT] used is dependent on the alkaline content of the formulations. Therefore, the concentration of free [INGREDIENT] is expected to be low, and systemic toxicity is not expected to be a concern. The safety of [INGREDIENT] as a pH adjustor should not be based on the concentration of use, but on the amount of free [INGREDIENT] that remains after neutralizing the formulation.

Phototoxicity

Fatty acid chain lengths

With increasing ethoxylation, the fatty acid components of the Stearic Acid moiety have less potential to produce phototoxicity and photosensitivity in humans and animals. Since there were no phototoxicity or photosensitivity reactions in subjects tested with PEG-2 Stearate and PEG-8 Stearate, the Panel concluded that it is reasonable to extrapolate these data to the higher molecular weight species (e.g. PEG-20, -32, -40, -50, -100, and -150 Stearates). The converse of this latter statement, that is, the extrapolation of high molecular weight species to lower molecular weight species, may or may not be true.

Unlikely UV absorbers

While no data were available, this ingredient would not be expected to have any significant ultraviolet (UV) absorption because it does not contain any of the functional groups commonly associated with UV absorption.

PEGs - damaged skin

Updated, 7/2010

The CIR Expert Panel discussed their concerns about the evidence of sensitization and nephrotoxicity in burn patients treated with a PEG-based antimicrobial cream. PEG was determined to be the causative agent in both animal and human studies. However, no evidence of systemic toxicity or sensitization occurred in studies with intact skin. Because of this, the Expert Panel qualified their conclusion on the safety of the PEGs to state that cosmetic formulations containing PEGs should not be used on damaged skin.

PEGs were re-reviewed in 2010 to address their use on damaged skin. Studies of extensively tape stripped skin demonstrated that the levels of PEGs that could penetrate in a worst case analysis are >100 times less than the renal toxicity no observable effect level, providing a margin of safety. As a result, the previous qualification regarding use of PEGs on damaged skin was removed.

Skin penetration studies

Study Design Preferences

The Panel stated that skin penetration studies using viable skin are preferable to those using cadaver skin. Studies using cadaver skin measure penetration of unmodified compounds only, and do not provide information on the influence of other factors such as skin metabolism. Therefore, studies using viable skin are more useful in assessing the safety of cosmetic ingredients.

Penetration Enhancement

> The Panel cautioned that [INGREDIENT] enhance the penetration of other chemicals or ingredients throught he skin, e.g., [GIVE EXAMPLE such as drug absorption].. The Panel cautioned that care should be taken in formulating cosmetic products that may contain these ingredients in combination with any ingredient that was found to be safe because it did not absorb dermally, or when dermal absorption was a concern. Care should be taken when creating formulations especially those products intended for use on infants.

Transmission of Infectious Disease

(BSE, HIV, Other) ***Updated 12/2010***

BACKGROUND:

The Panel has expressed concern about the inherent danger of transmission of infectious agents with use of human or animal derived cosmetic ingredients. For example, cosmetics may include cattle derived ingredients, including tallow and its derivatives, albumin, brain extract, brain lipid, cholesterol, fibronectin, sphingolipids, and collagen. Bovine Spongiform Encephalopathy (BSE) is an example of a pathogenic agent that may be transmitted through use of animal derived ingredients containing pathogenic viruses or infectious agents. For cosmetic ingredients of human origin, Human Immunodeficiency Virus (HIV), and Creutzfeld-Jacob disease (CJD) are examples of pathogenic agents that may be of concern.

In evaluating the safety of those cosmetic ingredients that are derived from animal or human sources, the specific sources, processing and manufacturing procedures and routes of potential exposure should be considered. The Panel believes that these ingredients must be free of detectible pathogenic viruses or infectious agents.

Not all animal or human derived cosmetic ingredients raise the same levels of concern. Tallow derivatives, particularly fatty acids and glycerin, are the predominant bovine ingredient used by the cosmetic industry. Tallow is an animal (mostly cattle) derived fat that is heat processed, during which the protein components and fat components are separated. The protein component is part of the insoluble impurities fraction that remains in the tallow after rendering. Any risk of disease transmission is a result of protein that is present as an impurity in the tallow. Tallow containing no more than 0.15 % hexane-insoluble impurities is considered to be protein-free tallow and is considered safe for consumption by animals. FDA concluded that tallow has negligible risk of transmitting BSE and that tallow derivatives, which undergo additional processing, do not pose a risk of transmitting the agent that causes BSE to humans.

CIR assessments of tallow containing ingredients do not need to include cautions about the transmission of infectious diseases. The reports, however, should refer to FDAs assessment that they do not pose a risk of transmitting disease .

In discussing the potential for transmission in CIR reports, the writer should take care to specify the source of the potentially infectious material, distinguish between human or animal derived cosmetic ingredients, and word the discussion accordingly.

REFERENCES

Federal Register: September 7, 2005 (Volume 7, Number 172).

Boilerplate language for Discussion:

Animal derived cosmetic ingredients:

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

Human derived cosmetic ingredients:

[Human-derived substance]] is used in the manufacture of [INDREDIENT]. The Panel also concerned with the dangers inherent in using human-derived ingredients, namely the transmission of infectious agents. The CIR Expert Panel stressed that these ingredients must be free of detectible pathogenic viruses or infectious agents (e.g. Human Immunodeficiency Virus (HIV), and Creutzfeld-Jacob disease (CJD)). Suppliers and users of these ingredients must accept responsibility for assuring that these ingredients are risk-free. Tests to assure the absence of a pathogenic agent in the ingredients, or controls to assure derivation from pathogen-free sources are two approaches that should be considered.

Tallow derived cosmetic ingredients:

The CIR Expert Panel considered the dangers inherent in using animal-derived ingredients, namely the transmission of infectious agents. While tallow may be used in the manufacture of some ingredients in this safety assessment and is clearly animal-derived, the Expert Panel notes that tallow is highly processed and tallow derivatives even more so. The Panel agrees with determinations by the U.S. FDA that tallow derivatives are not risk materials for transmission of infectious agents.

Usage Data Gaps

Gaps in Frequency and Concentration of Use Data

Discussion Section:
The CIR Expert Panel recognizes that there are data gaps regarding frequency and concentration use of these ingredients. However, the overall information available on the types of products in which this ingredient is used and at what concentration indicate a pattern of use, which was considered by the Expert Panel in assessing safety. N**ote: put early in the Discussion section...**

Conclusion Section:
Were ingredients in this group not in current use to be used in the future, the expectation is that they would be used in product categories and at concentrations comparable to others in the group.

Data Gaps(and use of Read Across)

In abstract and in conclusion:
The Expert Panel noted gaps in the available safety data for some of the [ingredient group] in this safety assessment. The available data on many of the ingredients were sufficient, however, due to similar structural activity relationships, biologic functions and cosmetic product usage. . For example: *Provide example where read across was used in report.*
SEE ALSO SECTION 2, FORMAT.

2. Formats

Abstracts

BACKGROUND:
The International Journal of Toxicology limits abstracts to 150 words. To meet the 150 word limit and to convey relevant information in a consistent manner, the CIR Expert Panel has recommended that all Abstracts follow the same format. The abstract should include a description of the ingredient or group of ingredients that were reviewed, a statement that the Panel reviewed the relevant data, and a summary of the conclusion. In some cases, additional information may be included.

In describing the ingredient group, all reviewed ingredients do not need to be listed; they will be listed in the conclusion. For example, "Silica and the related cosmetic ingredients" rather than "Silica and the related cosmetic ingredients Alumina Magnesium Metasilicate, Aluminum Calcium Sodium Silicate, Aluminum Iron Silicate, Hydrated Silica, and Sodium Potassium Aluminum Silicate".

BOILERPLATES:

Safe as Used (Without restrictions) Conclusion:

Sentence 1: What was reviewed [NAME OF INGREDIENT OR INGREDIENT GROUP] and its FUNCTION.
Sentence 2: The Panel reviewed relevant animal and human data related to the ingredient.
Sentence 3: Optional, as needed.
Sentence 4: The Panel concluded that [NAME OF INGREDIENT OR INGREDIENT GROUP] was/were safe as cosmetic ingredients in the practices of use and concentration of this safety assessment.

NOTE: The Panel may ask to discuss a specific topic in the abstract. That discussion would comprise Sentence 3. The 150 word limit still applies.

For Safe with Qualifications Conclusion:

As above, but also include nature of and reason for qualification in Sentence 3.

For Insufficient Data Conclusion:

As above, but include short statement about the nature of the insufficiencies in Sentence 3. The report discussion will contain the detailed listing of data needs.

For Unsafe Conclusion:

As above, but:
Sentence 3 could include brief reason for unsafe decision, as stated in the conclusion.
Sentence 4 should read: The Panel concluded that [NAME OF INGREDIENT OR INGREDIENT GROUP] is/are not safe under its/their intended conditions of use.

When decision is based on read-across:

The Expert Panel noted gaps in the available safety data for some of the [ingredient group] in this safety assessment. The available data on many of the ingredients were sufficient, however, due to similar structural activity relationships, biologic functions and cosmetic product usage. For example: *Provide example where read across was used in report.*

Conclusions

Updated 12/2010

BOILERPLATES:

Safe as Used:

The CIR Expert Panel concluded that the following ingredients are safe in the present practices of use and concentration described in this safety assessment. Were ingredients in this group not in

current use (as indicated by an asterisk), 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.

[LIST ALL INGREDIENTS in bullet format]

Safe with Qualifications:

The CIR Expert Panel concluded that the [NAME OF INGREDIENT GROUP] ingredients are safe in the present practices of use and concentration described in this safety assessment when [LIST QUALIFICATION].

Examples of qualifications include:
…formulated to be non-irritating.
…formulated to avoid the formation of nitrosamines.
…formulated to be non-respirable.
…the concentration of [x] does not exceed [%].

Were ingredients in this group not in current use (as indicated by *) to be used in the future, the expectation is that they would be used in product categories and at concentrations comparable to others in this group.

Insufficient Data:

The CIR Expert Panel concluded that the available data or information are insufficient to make a determination that [LIST ALL INGREDIENTS] is/are safe under the intended conditions of use.

NOTE: A detailed description of the data needs should be included in the discussion section of the report, preferably in bulleted format.

Not Safe:

Based on the data included in this report, and [**provide brief summary of reason for decision**], the CIR Expert Panel concluded that [LIST ALL INGREDIENTS] is not safe for use as a cosmetic ingredient.

Examples of reasons for decision include:
…X is a potential human sensitizer at use concentrations,…
…X has been found to be a human carcinogen…

Where finding may apply to future cosmetic ingredients, add the following sentence:

This assessment is also intended to address future [LIST INGREDIENT GROUP] ingredients that vary from those ingredients recited herein only by the [LIST ACCEPTABLE ADD ONS].

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

Hybrid Conclusions:

If Panel determination is mixed, use following format:

The CIR Expert Panel concluded that [LIST ALL INGREDIENTS] is/are unsafe for use in leave-on products, and that the available data are insufficient to make a determination that [LIST ALL INGREDIENTS] is/are safe under the intended conditions of use.

If Decision is different than a previous CIR decision, add following statement:

This conclusion supersedes the earlier conclusion issued by the Expert Panel in [year of publication of previous decision].

NOTE: **If the number of ingredients in a group is five or less, list all ingredients in the conclusion sentence.**

Insufficient Data Announcement

Alternatives to "28-day dermal toxicity" study

Boilerplate for Insufficient Data Notice:
While the CIR Expert Panel has specified a "28-day dermal toxicity study", there is concern that specifying a type of study may inhibit those who want to gather data using other study designs. The types of data the Panel is seeking include the gross pathology and histopathology in skin and other major organ systems, along with certain other toxicity parameters, associated with repeated exposures. A 28-day dermal toxicity study would generate the needed data; but there are other approaches. For example, the Expert Panel would consider a dermal reproductive and developmental study in which gross pathology and histopathology data are gathered on the F_0 generation to be sufficient to meet both the "28-day dermal toxicity" and "reproductive and developmental toxicity" data requested, if done at or above current concentrations of use of the ingredient.

Read-Across Data

In abstract and in conclusion:
The Expert Panel noted gaps in the available safety data for some of the [ingredient group] in this safety assessment. The available data on many of the ingredients are sufficient, however, and similarity between structural activity relationships and biologic functions in cosmetic concentrations of use and can be extrapolated to support the safety of the entire group.

Re-Review Summaries for re-reviews not reopened.

First Paragraph
In a [YEAR] safety assessment of (insert name/names), the Cosmetic Ingredient Review (CIR) Expert Panel stated that (this ingredient/these ingredients) (is/are) safe as (then) used in cosmetic products (cite assessment). The Expert Panel reviewed newly available studies since that assessment, along with updated information regarding product types and concentrations of use, and did not reopen this safety assessment. The Panel confirmed that (insert name/names) (is/are) safe as (a) cosmetic ingredient(s) in the practices of use and concentration as given in Table 1.

3. Table Formats

Chemical and Physical Characteristics Table

Property	**Value**	**Reference**	**Background information**
Physical Form			at standard temperature and pressure (STP)
Color			
Odor			Not in a solvent
Molecular Weight g/mol			>1000 unlikely to be dermaly absorbed
Molecular Volume m^3/kmol			(Measure of molecular size)
Density/Specific Gravity @ ^oC			
Viscosity kg/(s x m)@ ^oC			kg/(seconds x meters)
Vapor pressure mmHg@ ^oC			As vapor pressure of a raw ingredient approaches atmospheric pressure (760 mmHg), its volatility increases, but in a formulation this property is concentration dependent.
Vapor Density mmHg			
Melting Point ^oC			Not in a solvent; relevance to possible physical form of ingredient.
Boiling Point ^oC			Not in a solvent
Water Solubility g/L @ ^oC & pH			
Other Solubility g/L @ ^oC & pH			
log K_{ow}			http://www.syrres.com/esc/chemfate.htm Log octanol/water partition coefficient may predict skin penetration
Disassociation constants (pKa, pKb) @^oC			
UV Absorption (λ) nm.			Reliable UV absorption spectra that shows the ingredient does not absorb in the UVA/UVB range may eliminate need for photosensitization testing using animals; alternatively, data can be presented as absorption maxima in the UVA/UVB wavelength range.

Frequency and Concentration of Use Table

TABLE 3. Use Table				
	# of Uses		***Conc. of Use (%)***	
	Ingredient Name			
data year		*2010*		*2010*
Totals				
Duration of Use				
Leave-On				
Rinse Off				
Exposure Type				
Eye Area				
Possible Ingestion				
Inhalation				
Dermal Contact				
Deodorant (underarm)				
Hair - Non-Coloring				
Hair-Coloring				
Nail				
Mucous Membrane				
Bath Products				
Baby Products				

Methodology for new frequency of use tables.

Frequency of Use Defined by Exposure		Frequency of Use Define by Duration	
Total # in Category VCRP Codes	***Exposure Type***	***Total # in Category VCRP Codes***	***Exposure Type***
3663	**Eye**	***23,788***	**Leave-On Uses**
3A-3G	Eye Makeup Preparations	1B, 1C	Baby Lotions, Other Baby Products
872	**Possible Ingestion**	3A-3D, 3F-3G	Eye Makeup, except Remover
7E	Lipstick	4A-4E	Fragrance Products
9A-9C	Oral Hygiene Products	5B, 5G, 5I	Hair Sprays; Tonics; Other
3447	**Inhalation**	6E	Hair Color Sprays
4A-4E	Fragrance Preparations	7A-7I	Makeup Preparations
5B	Hair Sprays	8A-8E, 8G	Manicuring Preparations, except Removers
6E	Hair Color Sprays	10B, 10D	Deodorants, Feminine Deodorants
12E	Foot Powders and Sprays	11A-11C	Aftershave Ltn, Beard Softener, Talcum
26,863	**Dermal**	12C-12G, 12I-12J	Skin Care, except cleans/depil/paste masks
1B,1C	Baby Lotions, Other Baby Products	13A-13C	Suntan Products
2A-2D	Bath Preparations		
3A-3E, 3G	Eye Makeup Preparations, except mascara	***13,020***	**Rinse-Off**
4A-4E	Fragrance Preparations	1A	Baby Shampoos
7A-7I	Makeup Preparations	2A-2D	Bath Preparations
10A-10E	Personal Cleanliness	3E	Eye Makeup Remover
11A-11G	Shaving Products	5A, 5C-5F, 5H	Non-Coloring Hair Prep except hair spray/tonics
12A-12J	Skin Care Preparations	6A-6D, 6F-6H	Hair Coloring Preps, except hair color sprays
13A-13C	Suntan Preparations	8F	Nail Polish and Enamel Removers
623	**Deodorant (Underarm)**	9A-9C	Oral Hygiene
10B	Deodorant (Underarm)	10A, 10C, 10E	Bath Soaps, Douches, Other
5687	**Hair - Non-Coloring**	11D-11G	Preshave Ltn, Shaving Crm, Shving Soap, Other
1A	Baby Shampoos	12A, 12B, 12H	Cleansing Prep, Depilatories, Paste Masks
5A-5I	Non-Coloring Hair Preparations		
2808	**Hair - Coloring**		
6A-6I	Hair Coloring Preparations		
674	**Nail**		
8A-8G	Manicuring Preparations		
3732	**Mucous Membranes**		
9A-9C	Oral Hygiene Products		
10A, 10C-10E	Personal Cleanliness, except Deodorants		
745	**Bath Products**		
2A-2D	Bath Preparations		
357	**Baby Products**		
1A-1C	Baby Products		