Rereview Summaries for Acid Orange 3, Chloroxylenol, Erythorbic Acid, Glyceryl Diesters, Hexamidine & Hexamidine Diiesthionate, Mink Oil, and Sodium Lauryl Sulfoacetate

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NOTE: Rereview Summaries reflect recent Panel deliberations of previously reviewed cosmetic ingredients by the Expert Panel for Cosmetic Ingredient Safety. Panel generally rereviews ingredients on a 15-year cycle, but priorities in a given year may bring forward ingredients for rereview at any time. Rereview Summaries are shortened and updated assessments based on the original assessment and reflecting recent changes made by the Panel to better highlight any new information.

The Expert Panel for Cosmetic Ingredient Safety members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; David E. Cohen, M.D.; Curtis D. Klaassen, Ph.D.; Allan E. Rettie, Ph.D.; David Ross, Ph.D.; Thomas J. Slaga, Ph.D.; Paul W. Snyder, D.V.M., Ph.D.; and Susan C. Tilton, Ph.D. Previous Panel members involved in this assessment: Daniel C. Liebler, Ph.D.; Lisa A. Peterson, Ph.D.; and Ronald C. Shank, Ph.D. The Cosmetic Ingredient Review (CIR) Executive Director is Bart Heldreth, Ph.D. These rereview summary assessments were prepared by CIR Analysts and Writers for the Expert Panel.

1620 L Street, NW, Suite 1200 ♢ Washington, DC 20036-4702 ♢ ph 202.331.0651
cirinfo@cir-safety.org

ACID ORANGE 3

The Expert Panel for Cosmetic Ingredient Safety (Panel) first published the Final Report on the Safety Assessment of Acid Orange 3 in 2000.[1] The Panel concluded that this ingredient is safe for use in hair dye formulations at concentrations ≤ 0.2%.

Because it has been at least 15 years since the final report was published, in accordance with Cosmetic Ingredient Review (CIR) Procedures, the Panel determined whether the safety assessment should be reopened. At the September 2022 meeting, the Panel considered updated 2022 information regarding product types and ingredient use frequencies as reported in the US Food and Drug Administration (FDA) Voluntary Cosmetic Registration Program (VCRP) database[2] and maximum use concentrations provided by the Personal Care Products Council (Council).[3] According to 2022 VCRP survey data, Acid Orange 3 is used in one formulation; it is reported to be used in a nail polish and enamel.[2] The results of the concentration of use survey provided by the Council in 2022 reported no uses for this ingredient.[3] When the original safety assessment was published in 2000, Acid Orange 3 was reported to be used in 4 hair dye formulations (data acquired in 1997).[1] At that time, concentrations of use were no longer reported by the FDA; however, data available from the FDA in 1984 indicated that Acid Orange 3 was used in one hair dye formulation at a concentration between 10% and 25% and 33 hair dye formulations at ≤ 1%.

An extensive search of the world's literature was performed for studies dated 1997 forward, and new data were found.[4-7] The Panel agreed that an updated search of the published literature did not reveal toxicity data that warrant re-evaluation of the safety of this ingredient in cosmetic products. The Panel did note that the European Union has banned Acid Orange 3 for use in cosmetic products; however, this ban is due to a lack of safety test data and not because of any toxicological findings.

The Panel remarked on the reported use in a non-coloring cosmetic product (nail polish and enamel). The Federal Food, Drug and Cosmetic Act (FD&C Act) mandates that color additives must be approved by FDA for their intended use before they are used. Acid Orange 3 is an unapproved color additive in cosmetics products, and thereby, such use is not permitted. This use is not within the purview of this Panel.

However, due to the "coal-tar hair dye exemption" of the FD&C Act, hair dye products labeled with the following caution statement do not require FDA approval prior to use:

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

Thus, use of this ingredient in hair dye products is permitted and is within the purview of this Panel.

Finally, Acid Orange 3 is a secondary amine; a concern is the conversion of secondary amines (R1-NH-R2) into N-nitrosamines that may be carcinogenic.[8] The Panel cautions that this ingredient should not be used in cosmetic products in which *N*-nitroso compounds can be formed.

The Panel reviewed 2022 frequency and concentration of use data, in addition to any new, available, relevant safety data, and reaffirmed the 2000 conclusion regarding the safety of Acid Orange 3 in hair dye formulations.

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CHLOROXYLENOL

The Expert Panel for Cosmetic Ingredient Safety (Panel) first published the Final Report on the Safety Assessment of Chloroxylenol in 1985.[1] The Panel concluded that Chloroxylenol is safe as used in cosmetics, as described in the safety assessment. Upon re-review, the Panel reaffirmed the original conclusion, as published in 2006.[2]

Because it has been at least 15 years since the prior re-review was published, in accordance with Cosmetic Ingredient Review (CIR) Procedures, the Panel again determined whether the safety assessment should be reopened. At the September 2022 meeting, the Panel considered updated (2022) information regarding product types and ingredient use frequencies as reported in the US Food and Drug Administration (FDA) Voluntary Cosmetic Registration Program (VCRP) database[3] and maximum use concentrations provided in response to the survey conducted by the Personal Care Products Council.[4] The frequency of use of Chloroxylenol increased slightly. In 2002, Chloroxylenol was reported to be used in 43 formulations.[2] According to 2022 VCRP data, Chloroxylenol is now reported to be used in 51 formulations. The maximum reported concentration of use, 0.05%, has not changed since the last review. The cumulative frequency and concentration of use data are presented in Table 1.

An extensive search of the world's literature was performed for studies dated 2000 forward, and new data were found.[5-18] The Panel agreed, however, that the published literature did not reveal toxicity or other data that warrant re-evaluation of the safety of this ingredient in cosmetic products. The Panel noted depigmentation following dermal exposure to undiluted Chloroxylenol and an antiseptic formulation containing predominantly Chloroxylenol. Depigmentation/skin lightening is considered a drug effect, and therefore evaluation of this effect is not within the purview of the Panel; however, manufacturers should take caution when formulating cosmetic products containing Chloroxylenol to ensure that skin lightening is not a side effect. Furthermore, concern for this endpoint with the use of this ingredient in cosmetics was mitigated in that the concentrations the subjects were exposed to when depigmentation was observed were much higher than what is used in cosmetics.

The Panel reviewed 2022 frequency and concentration of use data, in addition to any new, available, relevant safety data, and once again reaffirmed the 1985 conclusion regarding the safety of Chloroxylenol in cosmetics.

Table 1. Frequency (2022; 2002) and concentration (2022; 2003) of use according to duration and exposure

	# of Uses		***Max Conc of Use (%)***	
	2022[3]	**2002[2]**	**2022[4]**	**2003[2]**
Totals*	**51**	**43**	**0.1 – 0.5**	**0.1 – 0.5**
Duration of Use				
Leave-On	*40*	*20*	*0.1 – 0.3*	*0.1 – 0.2*
Rinse-Off	*10*	*23*	*0.2 – 0.5*	*0.4 – 0.5*
Diluted for (Bath) Use	*1*	*NR*	*NR*	*NR*
Exposure Type				
Eye Area	8	1	NR	NR
Incidental Ingestion	NR	NR	NR	0.4
Incidental Inhalation-Spray	20[a]; 5[b]	7[a]; 2[b]	NR	0.1[s]; 0.2[b]
Incidental Inhalation-Powder	5[b]	2[b]	0.1 – 0.3[c]	0.2[b]; 0.1[c]
Dermal Contact	40	31	0.1 – 0.5	0.1 – 0.5
Deodorant (underarm)	NR	1[a]	NR	NR
Hair - Non-Coloring	4	12	0.3	NR
Hair-Coloring	NR	NR	NR	NR
Nail	NR	NR	NR	NR
Mucous Membrane	4	12	0.2 – 0.5	0.4
Baby Products	NR	NR	0.1 – 0.3	0.1

*Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.
[a] It is possible these products are sprays, but it is not specified whether the reported uses are sprays.
[b] Not specified whether a spray or a powder, but it is possible the use can be as a spray or a powder, therefore the information is captured in both categories
[c] It is possible these products are powders, but it is not specified whether the reported uses are powders.
NR – not reported

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ERYTHORBIC ACID and SODIUM ERYTHORBATE

The Expert Panel for Cosmetic Ingredient Safety (Panel) first published a Final Report on the Safety Assessment of Erythorbic Acid and Sodium Erythorbate, as part of a larger group of ingredients, in 1999.[1] The Panel concluded that these ingredients are safe for use as cosmetic ingredients in the present practices of use. It should be noted that Ascorbyl Palmitate, Ascorbyl Dipalmitate, and Ascorbyl Stearate, which were a part of the original review, were added to a grouping of ethers and esters of ascorbic acid for which a safety assessment was published in 2017, and therefore, are not included as part of this rereview.

Because it has been at least 15 years since the final report was published, in accordance with Cosmetic Ingredient Review (CIR) Procedures, the Panel determined whether the safety assessment should be reopened. At the September 2022 meeting, the Panel considered updated (2022) information regarding product types and ingredient use frequencies as reported in the US Food and Drug Administration (FDA) Voluntary Cosmetic Registration Program (VCRP) database[2] and the maximum use concentrations provided in response to the survey conducted by the Personal Care Products Council.[3] In the original 1999 report, there were 727 reported uses for Erythorbic Acid, which has since decreased to 300 reported uses in 2022. Similarly, the overall reported concentrations of use have decreased for both ingredients. In both the historical and 2022 data, the bulk of reported uses are for non-coloring hair preparations. Sodium Erythorbate, which was reported to be used in hair coloring preparations at > 50% in 1984, is reported to be used at up to 0.3% in hair dyes and colors in 2022. The cumulative frequency and concentration of use data are presented in Table 1.

An extensive search of the world's literature was performed for studies dated 1994 forward, and minimal new published data was found.[4-15] One noteworthy finding included a local lymph node assay performed in female mice in which Sodium Erythorbate was tested at 5, 10, or 25% in propylene glycol.[15] The stimulation index for the maximum concentration tested (25%) was 1.29; all stimulation index values were < 3, and indicating that Sodium Erythorbate is not a sensitizer.

The Panel reviewed 2022 frequency and concentration of use data, in addition to any new, available, relevant safety data, and reaffirmed the 1999 conclusion that these ingredients are safe for use as cosmetic ingredients in the present practices of use.

Table 1. 2022 and historical frequency and concentration of use of Erythorbic Acid and Sodium Erythorbate according to duration and exposure

	# of Uses		Max Conc of Use (%)		# of Uses		Max Conc of Use (%)	
	Erythorbic Acid				Sodium Erythorbate			
	2022[2]	1996[1]	2022[3]	1984[1]	2022[2]	1996[1]	2022[3]	1984[1]
Totals*	**300**	**727**	**0.1-0.7**	**1****	**6**	**19**	**0.3**	**> 50****
Duration of Use								
Leave-On	*2*	*1*	*0.1*	**	*NR*	*NR*	*NR*	**
Rinse-Off	*298*	*726*	*0.2-0.7*	**	*6*	*19*	*0.3*	**
Diluted for (Bath) Use	*NR*	*NR*	*NR*	**	*NR*	*NR*	*NR*	**
Exposure Type								
Eye Area	1	NR	0.1	**	NR	NR	NR	**
Incidental Ingestion	NR	1	NR	**	NR	NR	NR	**
Incidental Inhalation-Spray	1[a]	1[a]	0.1[a]; 0.1[b]	**	NR	NR	NR	**
Incidental Inhalation-Powder	NR	NR	0.1[b]	**	NR	NR	NR	**
Dermal Contact	2	NR	0.1	**	NR	NR	NR	**
Deodorant (underarm)	NR	NR	NR	**	NR	NR	NR	**
Hair - Non-Coloring	NR	4	NR	**	NR	NR	NR	**
Hair-Coloring	298	721	0.2-0.7	**	6	19	0.3	>50**
Nail	NR	1	NR	**	NR	NR	NR	**
Mucous Membrane	NR	1	NR	**	NR	NR	NR	**
Baby Products	NR	NR	NR	**	NR	NR	NR	**

*Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.
**At the time of the 1999 safety assessment, concentration of use data were not reported. However, data provided to the FDA in 1984 data were presented; use categories were not indicated.
[a] It is possible these products are sprays, but it is not specified whether the reported uses are sprays.
[b] Not specified whether a spray or a powder, but it is possible the use can be as a spray or a powder, therefore the information is captured in both categories
NR – not reported

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GLYCERYL DIESTERS

The Expert Panel for Cosmetic Ingredient Safety (Panel) first issued a final report on the safety of glyceryl diesters in 2002, with an insufficient data conclusion.[1] Subsequently, the necessary data were received, and in 2007 the Panel published an amended final report on the safety of the glyceryl diester ingredients (listed below).[2] The Panel concluded that these ingredients are safe as cosmetic ingredients in the present practices of use and concentrations described in the safety assessment provided that the content of 1,2-diesters is not high enough to induce epidermal hyperplasia. Glyceryl Dimyristate was originally a part of this group, but has since been reviewed with Myristic Acid ingredients, and is therefore not included in this rereview.

Glyceryl Dilaurate
Glyceryl Diarachidate
Glyceryl Dibehenate
Glyceryl Dierucate
Glyceryl Dihydroxystearate
Glyceryl Diisopalmitate
Glyceryl Diisostearate
Glyceryl Dilinoleate
Glyceryl Dioleate
Glyceryl Diricinoleate
Glyceryl Dipalmitate
Glyceryl Dipalmitoleate
Glyceryl Distearate
Glyceryl Palmitate Lactate
Glyceryl Stearate Citrate
Glyceryl Stearate Lactate
Glyceryl Stearate Succinate

Because it has been at least 15 years since the amended final report was published, in accordance with Cosmetic Ingredient Review (CIR) Procedures, the Panel determined whether the safety assessment should be reopened. At the September 2022 meeting, the Panel considered updated (2022) information regarding product types and ingredient use frequencies as reported by the US Food and Drug Administration (FDA) Voluntary Cosmetic Registration Program (VCRP) database[3] and the maximum use concentrations provided in response to the survey conducted by the Personal Care Products Council.[4] Generally, there has been an increase in frequency of use since the last review in 2007. As of 2022, Glyceryl Distearate and Glyceryl Stearate Citrate were reported to be used in baby products, when there were no reported uses for glyceryl diesters in this product category previously. Glyceryl Stearate Citrate, which had no reported uses in the original report, is reported to have 164 uses, at a maximum concentration of use of 4% in non-spray moisturizing products, in 2022. Additionally, although the number of reported uses of Glyceryl Diisostearate in lipstick increased, the maximum reported concentrations of use for this product category significantly decreased, from 43% in 1999 to 0.54% in 2022. The cumulative frequency and concentration of use data are presented in Table 1. Ingredients with no reported use are listed in Table 2.

An extensive search of the world's literature was performed for studies dated 2002 forward, and new data were found.[5-27] The Panel considered new chronic toxicity,[14,18] developmental and reproductive toxicity,[19-21] and carcinogenicity/tumor promotion studies.[22-25] In addition to these studies having negative results, the FDA-approved use of Glyceryl Dibehenate and Glyceryl Distearate as inactive ingredients in oral capsule formulations,[26] as well as the approved use of diacylglycerol oil and diglycerides as food additives, reassured the Panel of safety.[27]

The Panel reviewed 2022 frequency and concentration of use data, in addition to any new, available, relevant safety data, and reaffirmed the 2007 conclusion regarding the safety of glyceryl diesters in cosmetics.

Table 1. 2022 and historical frequency and concentration of use according to duration and exposure

	# of Uses		Max Conc of Use (%)		# of Uses		Max Conc of Use (%)	
	Glyceryl Dibehenate				Glyceryl Diisostearate			
	2022[3]	2002[2]	2022[4]	1999[2]	2022[3]	2002[2]	2022[4]	1999[2]
Totals*	**32**	**NR**	**1**	**NR**	**139**	**97**	**0.54**	**18-43**
Duration of Use								
Leave-On	*32*	*NR*	*1*	*NR*	*138*	*97*	*0.54*	*18-43*
Rinse-Off	*NR*	*NR*	*NR*	*NR*	*1*	*NR*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	8	NR	NR	NR	NR	NR	NR	NR
Incidental Ingestion	1	NR	NR	NR	124	93	0.54	43
Incidental Inhalation-Spray	5[a]; 12[b]	NR	1[a]	NR	3[a]; 3[b]	1; 1[a]; 1[b]	NR	18
Incidental Inhalation-Powder	12[b]	NR	NR	NR	3[b]	1[b]	NR	NR
Dermal Contact	26	NR	1	NR	15	3	NR	18
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	1	NR	NR	NR	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	2	NR	NR	NR	NR	1	NR	NR
Mucous Membrane	1	NR	NR	NR	124	93	0.54	43
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

Table 1. 2022 and historical frequency and concentration of use according to duration and exposure

	# of Uses		Max Conc of Use (%)		# of Uses		Max Conc of Use (%)	
	Glyceryl Dilaurate				Glyceryl Dioleate			
	2022[3]	2002[2]	2022[4]	1999[2]	2022[3]	2002[2]	2022[4]	1999[2]
Totals*	**27**	**35**	**1-4**	**0.02-5**	**10**	**1**	**NR**	**0.8-2**
Duration of Use								
Leave-On	*26*	*27*	*1-4*	*2-5*	*10*	*1*	*NR*	*0.8-2*
Rinse-Off	*1*	*8*	*NR*	*0.02-5*	*NR*	*NR*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	NR	NR	NR	2	1	NR	NR	NR
Incidental Ingestion	NR	1	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	22[a]; 4[b]	8[a]; 13[b]	NR	5[a]; 2-4[b]	5[a]; 1[b]	NR	NR	2[a]; 0.8[b]
Incidental Inhalation-Powder	4[b]	13[b]	1.5[c]	2-4[b]	1; 1[b]	NR	NR	0.8[b]
Dermal Contact	27	34	1-4	0.02-5	10	1	NR	0.8-2
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	4	NR	0.02	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR
	Glyceryl Dipalmitate				Glyceryl Distearate			
	2022[3]	2002[2]	2022[4]	1999[2]	2022[3]	2002	2022[4]	1999[2]
Totals*	**NR**	**NR**	**1.1**	**NR**	**16**	**NR**	**0.05-4.4**	**0.00003-7**
Duration of Use								
Leave-On	*NR*	*NR*	*1.1*	*NR*	*14*	*NR*	*0.05-4.4*	*0.00003-7*
Rinse-Off	*NR*	*NR*	*NR*	*NR*	*2*	*NR*	*0.3-2.2*	*0.0003-6*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	NR	NR	NR	NR	2	NR	2.3	0.003-0.5
Incidental Ingestion	NR	NR	NR	NR	1	NR	NR	7
Incidental Inhalation-Spray	NR	NR	NR	NR	6[a]; 2[b]	NR	2.9[a]	0.00003-7[a]; 0.2-7[b]
Incidental Inhalation-Powder	NR	NR	1.1[c]	NR	2[b]	NR	0.22-4.4[b]	0.2-7[b]
Dermal Contact	NR	NR	1.1	NR	12	NR	0.05-4.4	0.00003-7
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	3	NR	0.3-0.55	6
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	0.02
Mucous Membrane	NR	NR	NR	NR	1	NR	NR	7
Baby Products	NR	NR	NR	NR	NR	NR	0.55-1.1	NR
	Glyceryl Stearate Citrate				Glyceryl Stearate Lactate			
	2022[3]	2002[2]	2022[4]	1999[2]	2022[3]	2002[2]	2022[4]	1999[2]
Totals*	164	NR	0.5-4	NR	NR	NR	NR	5
Duration of Use								
Leave-On	*142*	*NR*	*0.5-4*	*NR*	*NR*	*NR*	*NR*	*5*
Rinse-Off	*21*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Diluted for (Bath) Use	*1*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	6	NR	1.2	NR	NR	NR	NR	NR
Incidental Ingestion	1	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	1;53[a]; 61[b]	NR	NR	NR	NR	NR	NR	5[a]; 5[b]
Incidental Inhalation-Powder	61[b]; 4[c]	NR	0.5-2[c]	NR	NR	NR	NR	5[b]
Dermal Contact	157	NR	0.5-4	NR	NR	NR	NR	5
Deodorant (underarm)	4[a]	NR	NR	NR	NR	NR	NR	5[a]
Hair - Non-Coloring	6	NR	NR	NR	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	6	NR	NR	NR	NR	NR	NR	NR
Baby Products	5	NR	2	NR	NR	NR	NR	NR

Table 1. 2022 and historical frequency and concentration of use according to duration and exposure

	# of Uses		Max Conc of Use (%)		# of Uses		Max Conc of Use (%)	
	Glyceryl Stearate Succinate							
	2022[3]	2002[2]	2022[4]	1999[2]				
Totals*	1	NR	NR	NR				
Duration of Use								
Leave-On	*1*	*NR*	*NR*	*NR*				
Rinse-Off	*NR*	*NR*	*NR*	*NR*				
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*				
Exposure Type								
Eye Area	NR	NR	NR	NR				
Incidental Ingestion	NR	NR	NR	NR				
Incidental Inhalation-Spray	NR	NR	NR	NR				
Incidental Inhalation-Powder	NR	NR	NR	NR				
Dermal Contact	1	NR	NR	NR				
Deodorant (underarm)	NR	NR	NR	NR				
Hair - Non-Coloring	NR	NR	NR	NR				
Hair-Coloring	NR	NR	NR	NR				
Nail	NR	NR	NR	NR				
Mucous Membrane	NR	NR	NR	NR				
Baby Products	NR	NR	NR	NR				

*Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.
[a] It is possible these products are sprays, but it is not specified whether the reported uses are sprays.
[b] Not specified whether a spray or a powder, but it is possible the use can be as a spray or a powder, therefore the information is captured in both categories
[c] It is possible these products are powders, but it is not specified whether the reported uses are powders.
NR – not reported

Table 2. Ingredients not reported to be in use (2022)[3,4]

Glyceryl Diarachidate
Glyceryl Dierucate
Glyceryl Dihydroxystearate
Glyceryl Diisopalmitate
Glyceryl Dilinoleate
Glyceryl Diricinoleate
Glyceryl Dipalmitoleate
Glyceryl Palmitate Lactate

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HEXAMIDINE AND HEXAMIDINE DIISETHIONATE

The Expert Panel for Cosmetic Ingredient Safety (Panel) first published the Final Report on the Safety Assessment of Hexamidine and Hexamidine Diisethionate in 2007.[1] The Panel concluded that Hexamidine and Hexamidine Diisethionate are safe for use in cosmetics in the practices and concentrations of use as described in the safety assessment if used at concentrations less than or equal to 0.10%.

Because it has been at least 15 years since the final report was published, in accordance with Cosmetic Ingredient Review (CIR) Procedures, the Panel determined whether the safety assessment should be reopened. At the September 2022 meeting, the Panel considered updated (2022) information regarding product types and ingredient use frequencies as reported in the US Food and Drug Administration (FDA) Voluntary Cosmetic Registration Program (VCRP) database,[2] and maximum use concentrations provided in response to the survey conducted by the Personal Care Products Council.[3] The frequency of use of Hexamidine Diisethionate has increased from 38 uses in 2002[1] to 52 uses in 2022. The concentration of use of this ingredient has remained the same (≤ 0.1%). There were previously, and are currently, no reported uses for Hexamidine. The cumulative frequency and concentration of use data are presented in Table 1.

An extensive search of the world's literature was performed for studies dated 2000 forward, and new data were found.[4-9] The Panel agreed, however, that the published literature did not reveal toxicity or other data that warrant re-evaluation of the safety of these ingredients in cosmetic products. The Panel noted the clinical studies in which hypersensitivity was observed; however, these studies were performed in previously determined atopic individuals; therefore, concern for this endpoint was mitigated.

The Panel reviewed 2022 frequency and concentration of use data, in addition to any new, available, relevant safety data, and reaffirmed the 2007 conclusion regarding the safety of Hexamidine and Hexamidine Diisethionate in cosmetics.

Table 1. 2022 and historical frequency and concentration of use according to duration and exposure

	# of Uses		*Max Conc of Use (%)*	
	Hexamidine Diisethionate			
	2022[2]	**2002[1]**	**2022[3]**	**2004[1]**
Totals*	**52**	**38**	**0.036 – 0.1**	**0.03 – 0.1**
Duration of Use				
Leave-On	*34*	*23*	*0.036 – 0.1*	*0.03 – 0.1*
Rinse-Off	*18*	*15*	*NR*	*0.05 – 0.06*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*
Exposure Type				
Eye Area	2	1	NR	NR
Incidental Ingestion	NR	NR	NR	NR
Incidental Inhalation-Spray	9[a]; 8[b]	9[a]; 5[b]	NR	0.1[a]; 0.05[b]
Incidental Inhalation-Powder	1; 8[b]; 3[c]	5[b]; 3[c]	0.036[c]	0.05[b]
Dermal Contact	37	32	0.036 – 0.1	0.04 – 0.1
Deodorant (underarm)	3[a]	NR	0.05	0.1[a]
Hair - Non-Coloring	14	5	NR	NR
Hair-Coloring	1	NR	NR	NR
Nail	NR	NR	NR	0.03
Mucous Membrane	1	NR	NR	NR
Baby Products	5	5	0.036	NR

[a] It is possible these products are sprays, but it is not specified whether the reported uses are sprays.
[b] Not specified whether a spray or a powder, but it is possible the use can be as a spray or a powder, therefore the information is captured in both categories
[c] It is possible these products are powders, but it is not specified whether the reported uses are powders.
NR – no reported use

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MINK OIL

The Expert Panel for Cosmetic Ingredient Safety (Panel) first published a review on the safety of Mink Oil in 1998, with an insufficient data conclusion.[1] Subsequently, the Panel's data needs were met, and in 2005 a final amended report was published with the conclusion that Mink Oil is safe as a cosmetic ingredient in the practices of use and concentration described in that safety assessment.[2]

Because it has been at least 15 years since the final amended report was published, in accordance with CIR Procedures, the Panel considered whether the safety assessment should be reopened. At the September 2022 meeting, the Panel considered updated (2022) information regarding product types and ingredient use frequencies as reported in the US Food and Drug Administration (FDA) Voluntary Cosmetic Registration Program (VCRP) database[3] and maximum use concentrations provided in response to the survey conducted by the Personal Care Products Council.[4] Since the final amended report was issued, there is one new use category reported in 2022 (hair-coloring). The frequency of use has decreased, from 100 reported uses in 2001 to 32 uses in 2022, and the maximum concentration of use for Mink Oil has decreased from 3% in 2001 to 0.1% in 2022. The cumulative frequency and concentration of use data are presented in Table 1.

An extensive search of the world's literature was performed for studies dated 2000 forward, and no new data were found.

The Panel reviewed 2022 frequency and concentration of use data, in addition to any new, available, relevant safety data, and reaffirmed the 2005 conclusion regarding the safety of Mink Oil in cosmetics.

Table 1. Frequency and concentration of use (2022; 2001) according to duration and exposure

	# of Uses		*Max Conc of Use (%)*	
	2022[3]	**2001[2]**	**2022[4]**	**2001[2]**
Totals*	**32**	**100**	**0.1**	**0.001-3**
Duration of Use				
Leave-On	*22*	*63*	*0.1*	*0.001-2*
Rinse-Off	*5*	*36*	*NR*	*3*
Diluted for (Bath) Use	*5*	*1*	*NR*	*0.1*
Exposure Type				
Eye Area	NR	2	NR	0.1-1
Incidental Ingestion	11	12	NR	0.001
Incidental Inhalation-Spray	5[a];3[c]	3;23[a];12[c]	NR	1;0.2-2[a];0.1-0.5[c]
Incidental Inhalation-Powder	1;3[c]	1;12[c]	NR	0.1;1[b];0.1-0.5[c]
Dermal Contact	19	48	0.1	0.1-2
Deodorant (underarm)	NR	NR	NR	NR
Hair - Non-Coloring	1	39	NR	3
Hair-Coloring	1	NR	NR	NR
Nail	NR	NR	NR	0.001-0.1
Mucous Membrane	16	13	NR	NR
Baby Products	NR	NR	NR	NR

*Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.
[a] It is possible these products are sprays, but it is not specified whether the reported uses are sprays.
[b] It is possible these products are powders, but it is not specified whether the reported uses are powders.
[c] Not specified whether a spray or a powder, but it is possible the use can be as a spray or a powder, therefore the information is captured in both categories
NR – no reported use

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SODIUM LAURYL SULFOACETATE

The Expert Panel for Cosmetic Ingredient Safety (Panel) first published the Final Report on the Safety Assessment of Sodium Lauryl Sulfoacetate in 1987.[1] The Panel concluded that this ingredient is safe as a cosmetic ingredient in the present practices of use and concentration. Upon re-review, the Panel reaffirmed the original conclusion, as published in 2006.[2]

Because it has been at least 15 years since the prior re-review was published, in accordance with Cosmetic Ingredient Review (CIR) Procedures, the Panel again determined whether the safety assessment should be reopened. At the September 2022 meeting, the Panel considered updated 2022 information regarding product types and ingredient use frequencies as reported in the US Food and Drug Administration (FDA) Voluntary Cosmetic Registration Program (VCRP) database[3] and maximum use concentrations provided by the Personal Care Products Council (Council).[4] Since the initial re-review was considered, the frequency of use has increased slightly, from 68 to 97 uses.[2,3] In 2004, the maximum concentration of use for this ingredient was reported to be 4% in leave-on products, 5% in rinse-off products, and 21% in products diluted for use.[2] Concentration of use provided by the Council in 2022 indicate that Sodium Lauryl Sulfoacetate is used at up to 2.5% in leave-on products (foot powders), up to 10.2% in rinse-off products (preshave lotions), and up to 8.4% in products diluted for use (bubble baths).[4] The cumulative frequency and concentration of use data are presented in Table 1.

An extensive search of the world's literature was performed for studies dated 2004 forward, and no new data were found.

The Panel reviewed 2022 frequency and concentration of use data, noted the lack of any new, available, relevant safety data, and once again reaffirmed the 1987 conclusion regarding the safety of Sodium Lauryl Sulfoacetate in cosmetics.

Table 1. Frequency (2022; 2002) and concentration (2022; 2004) of use according to duration and exposure

	# of Uses		*Max Conc of Use (%)*	
	2022[3]	**2002[2]**	**2022[4]**	**2004[2]**
Totals*	**87**	**68**	**0.00028-10.2**	**0.6-21**
Duration of Use				
Leave-On	*5*	*1*	*0.8-2.5*	*4*
Rinse-Off	*52*	*6*	*0.00028-10.2*	*5*
Diluted for (Bath) Use	*30*	*61*	*3-8.4*	*21*
Exposure Type				
Eye Area	NR	NR	NR	NR
Incidental Ingestion	NR	1	0.74	0.7
Incidental Inhalation-Spray	1[a]	1	1.5	2; 2[a]
Incidental Inhalation-Powder	1[a]	NR	2.5	1[b]; 2[a]
Dermal Contact	53	64	0.00028-10.2	0.6-21
Deodorant (underarm)	NR	NR	NR	NR
Hair - Non-Coloring	33	1	0.53-4.4	1-5
Hair-Coloring	1	2	3	NR
Nail	NR	NR	NR	4
Mucous Membrane	42	62	0.00028-10	0.6-21
Baby Products	1	NR	0.53	1

*Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.
[a] Not specified whether a spray or a powder, but it is possible the use can be as a spray or a powder, therefore the information is captured in both categories
[b] It is possible these products are powders, but it is not specified whether the reported uses are powders.
NR – no reported use

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