

Annual Review of Cosmetic Ingredient Safety Assessments—2004/2005¹

The Cosmetic Ingredient Review (CIR) program Expert Panel has assessed the safety of almost 1300 cosmetic ingredients since its inception in 1976. These safety assessments were published in the *Journal of Environmental Pathology and Toxicology* in 1980, the *Journal of the American College of Toxicology*, from 1982 to 1996, and since then in the *International Journal of Toxicology*.

Because information relevant to the safety of ingredients may have become available since early safety assessments were published, the CIR Expert Panel has initiated a re-review process. If new information is thought to be available or if a long period of time has passed, the CIR Expert Panel may initiate a search for relevant new data.

In some cases, newly available data are largely redundant with the data available in the original safety assessment. In other cases, there are new safety data. If the CIR Expert Panel decides to not reopen a safety assessment, this finding is summarized and announced publicly. To assure that the scientific community is aware of any new information and the decision to not reopen, this *Annual Review of Cosmetic Ingredient Safety Assessments* is prepared.

A reference list is provided that updates the available published literature and includes any unpublished data made available since the original safety assessment. The re-review also captures information on the industry's current practices of ingredient use, updating the data available in the earlier report. Although this material provides the opinion of the CIR Expert Panel regarding the new data described, it does not constitute a full safety review.

The ingredients the CIR Expert Panel reconsidered in 2004/2005, and decided not to reopen are

Benzethonium Chloride and Methylbenzethonium Chloride
2-Bromo-2-Nitropropane-1,3-Diol
Butylated Hydroxyanisole (BHA)
Butylene Glycol, Hexylene Glycol, Ethoxydiglycol, and Dipropylene Glycol
Cetearyl Octanoate (Ceteraryl Ethylhexanoate)
Cholesterol

Chloroxylenol
Diisopropanolamine, Isopropanolamine, Triisopropanolamine, and Mixed Isopropanolamines
Dioctyl Adipate and Diisopropyl Adipate
Formaldehyde
Hydrolyzed Collagen
p-Hydroxyanisole
Isostearyl Neopentanoate
2-Nitro-*p*-Phenylenediamine and 4-Nitro-*o*-Phenylenediamine
Oleic Acid, Lauric Acid, Palmitic Acid, Myristic Acid, Stearic Acid
Panthenol and Pantothenic Acid
p-Phenylenediamine
Phenyl Trimethicone
Propylene Carbonate
Propyl Gallate
Polyvinylpyrrolidone/Vinyl Acetate Copolymer
Safflower Oil
Sodium Borate and Boric Acid
Sodium Dehydroacetate and Dehydroacetic Acid
Sodium Lauryl Sulfoacetate
Sodium Sesquicarbonate, Sodium Bicarbonate, and Sodium Carbonate
Stearyl Alcohol, Oleyl Alcohol, and Octyl Dodecanol
Toluene
Toluenesulfonamide/Formaldehyde Resin
Tragacanth Gum
Vinyl Acetate/Crotonic Acid Copolymer
Zinc Phenolsulfonate

BENZETHONIUM CHLORIDE AND METHYLBENZETHONIUM CHLORIDE

A safety assessment of Benzethonium Chloride and Methylbenzethonium Chloride was published in 1985 with the conclusion that these ingredients are safe at concentrations of 0.5% in cosmetics applied to the skin, and up to 0.02% for cosmetics used in the eye area (Elder 1985). New studies, along with the updated information below regarding types and concentrations of use, were considered by the CIR Expert Panel. The Panel determined to not reopen this safety assessment.

Benzethonium Chloride is a quaternary ammonium salt used as an antimicrobial agent, cosmetic biocide, deodorant

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TABLE 1
 Historical and current cosmetic product uses and concentrations for Benzethonium Chloride and historical uses of
 Methylbenzethonium Chloride

Product category	1981 uses (Elder 1985)	2002 uses (FDA 2002)	1981 concentrations (Elder 1985) %	2003 concentrations (CTFA 2003) %
<i>Benzethonium Chloride</i>				
Baby care*	1	—	>0 1–1	—
Bath*	1	—	≤0 1	—
Eye makeup				
Eyeliners	2	—	>0 1–1	—
Fragrances				
Colognes and toilet waters	6	—	>0 1–1	—
Perfumes	3	—	>0 1–1	—
Powders	1	—	>0 1–1	—
Noncoloring hair care				
Conditioners	2	—	>0 1–1	—
Sprays/aerosol fixatives	1	—	≤0 1	—
Rinses	3	—	≤0 1	—
Shampoos	1	—	>0 1–1	—
Tonics, dressings, etc	1	2	≤0 1	—
Wave sets	1	—	≤0 1	—
Other noncoloring hair care	2	3	≤0 1	—
Makeup				
Other makeup	—	—	—	0 03
Personal hygiene				
Underarm deodorants	11	6	≤0 1	0 05
Douches	7	1	>0 1–5	—
Feminine deodorants	3	1	≤0 1	—
Other personal hygiene	7	5	≤1	0 1–0 3
Shaving				
Aftershave lotions	2	3	≤0 1	—
Mens talcum	2	—	≤1	0 1
Preshave lotions	1	—	>0 1–1	—
Other	—	1	—	—
Skin care				
Cleansing creams, lotions, etc	5	2	≤1	0 2%
Face and neck skin care	7**	1	≤1**	—
Body and hand skin care	—	5	—	—
Foot powders and sprays	—	2	—	0 1
Moisturizers	2	1	≤0 1	≤0 1
Paste masks/mud packs	2	—	≤0 1	—
Skin fresheners	13	—	≤1	—
Other skin care	3	4	≤0 1	—
Suntan products				
Suntan gels, creams, liquids and sprays	2	2	≤0 1	—
Indoor tanning preparations	1	—	≤0 1	—
Total uses/ranges for Benzethonium Chloride	93	39	≤5	0 03–0 3
<i>Methylbenzethonium Chloride</i>				
Baby Care				
Lotions, oils, powders, and creams	2	—	≤1	—

TABLE 1
Historical and current cosmetic product uses and concentrations for Benzethonium Chloride and historical uses of Methylbenzethonium Chloride (*Continued*)

Product category	1981 uses (Elder 1985)	2002 uses (FDA 2002)	1981 concentrations (Elder 1985) %	2003 concentrations (CTFA 2003) %
Fragrances				
Colognes and toilet waters	1	—	≤0.1	—
Noncoloring hair care				
Conditioners	1	—	≤0.1	—
Sprays/aerosol fixatives	6	—	≤0.1	—
Personal hygiene				
Underarm deodorants	5	—	≤1	—
Douches	1	—	>0.1–1	—
Feminine deodorants	2	—	≤0.1	—
Other personal hygiene	1	—	≤0.1	—
Shaving				
Aftershave lotions	4	—	≤1	—
Other shaving	1	—	≤0.1	—
Skin care				
Cleansing creams, lotions, etc	1	—	≤0.1	—
Face and neck creams, lotions, powder and sprays	1	—	≤0.1	—
Moisturizers	1	—	≤0.1	—
Skin fresheners	3	—	≤0.1	—
Suntan				
Suntan gels, creams, liquids and sprays	2	—	≤0.1	—
Other suntan	1	—	≤0.1	—
Total uses/ranges for Methylbenzethonium Chloride	33	—	≤1.0	—

*No details were provided describing specific product categories

**These categories were combined and have since been separated

agent, or surfactant—suspending agent in cosmetics. In voluntary reports provided by industry to the Food and Drug Administration (FDA) in 1981, Benzethonium Chloride was used in 93 cosmetic products, with a maximum concentration up to 5% (Elder 1985). In 2002, information provided by industry to FDA indicated that Benzethonium Chloride was used in 39 cosmetic products (FDA 2002). A survey conducted by the Cosmetic, Toiletry, and Fragrance Association (CTFA) found that the maximum use concentration for Benzethonium Chloride was 5% in douches (CTFA 2003). The current and historical data on use as a function of product category are given in Table 1. The most recent information now constitutes the present use of this ingredient.

Newly available unpublished toxicology data were considered supportive of the original conclusion. The CIR Expert Panel did consider an analysis by Blumenthal et al. (1995), in which a margin of safety was calculated for Benzethonium Chloride as an antibacterial agent in consumer handsoaps as follows:

- Soap usage of 15 g/day (90th percentile of human use = 10×1.5 g)
- Maximum use concentration of 5%

- 1% of soap remaining on human skin after washing
- human dermal absorption of Benzethonium Chloride from hand soap formulations = 50%
- Average body weight 40 kg
- No observable effect level (NOEL) of 12.5 mg/kg day⁻¹ for systemic toxicity from an NTP 13-week dermal study

Exposure calculation

$$1.5 \text{ g/day} \times 5\% \times 1\% \times 50\% = 3.75 \text{ mg/day}$$

$$3.75 \text{ mg/day} / 40 \text{ kg} = 0.09375 \text{ mg/kgday}^{-1} \text{ maximum possible exposure}$$

The NOEL value divided by the maximum possible exposure yielded a margin of safety of 113 for Benzethonium Chloride.

Methylbenzethonium Chloride is also a quaternary ammonium salt with functions in cosmetics that include antimicrobial agent, antistatic agent, cosmetic biocide, and deodorant agent. In the earlier safety assessment, Methylbenzethonium Chloride was used in 33 cosmetic products, at a maximum concentration up to 1% in baby lotions, oils, powders, and creams, and

in underarm deodorants, douches, and aftershave lotions (Elder 1985). Industry reported no uses to the FDA in 2002 (FDA 2002) and CTFA found no uses in its survey (CTFA 2003).

The historical data on use of Methylbenzethonium Chloride as a function of product category are given in Table 1. Were this ingredient to be used in the future, the CIR Expert Panel expects that it would be used at concentrations and in product types similar to those in the original safety assessment.

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²Available for review: Director, Cosmetic Ingredient Review (CIR), 1101 17th Street, NW, Suite 412, Washington, DC 20036-4702, USA

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- 2-BROMO-2-NITROPROPANE-1,3-DIOL (BRONOPOL)**
- A safety assessment of 2-Bromo-2-Nitropropane-1,3-Diol was published in 1980 with the conclusion that this preservative is safe as a cosmetic ingredient at concentrations up to and including 0.1% except under circumstances where its action with amines or amides can result in the formation of nitrosamines or nitrosamides (Elder 1980)
- In 1984, a report addendum considered newly available data that use concentrations were reported at levels up to 1%. In addition, the action of 2-Bromo-2-Nitropropane-1,3-Diol as a nitrosating agent was emphasized and data provided demonstrating that it was present in formulations with amines such as Triethanolamine. The CIR Expert Panel reaffirmed the concentration limitation at 0.1% and the need to avoid use where nitrosamines or nitrosamides could be formed (Elder 1984)
- Studies available since the addendum was completed, along with the updated information regarding uses and use concentrations, were considered by the CIR Expert Panel. The Panel determined to not reopen this safety assessment.
- 2-Bromo-2-Nitropropane-1,3-Diol was used in 323 products in 1976 (Elder 1980), with the largest single use in makeup fixatives at concentrations of $\leq 0.1\%$. Frequency of use data provided by industry to FDA in 2002 indicated that 2-Bromo-2-Nitropropane-1,3-Diol was used in only one noncoloring hair preparation (FDA 2002). Use concentration data provided from an industry survey in 2003 indicated use in several other product categories (CTFA 2003). The current maximum use concentration was 0.1%. Complete information is included in Table 2.
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³Available for review Director, Cosmetic Ingredient Review (CIR), 1101 17th Street, NW, Suite 412, Washington, DC 20036-4702, USA

TABLE 2

Historical and current cosmetic product uses and concentrations for 2-Bromo-2-Nitropropane-1,3-Diol

Product category	1976 use (Elder 1980)	2002 use (FDA 2002)	1976 concentrations (Elder 1980) %	2003 concentrations (CTFA 2003) %
Bath				
Bath oils, tablets, and salts	1	—	≤0.1	—
Bubble baths	4	—	≤0.1	—
Bath soaps and detergents	1	—	≤0.1	—
Other bath	5	—	≤0.1	—
Eye makeup				
Eyebrow pencil	14	—	≤0.1	—
Eyeliner	11	—	≤0.1	—
Eye shadow	3	—	≤0.1	0.1
Eye makeup remover	—	—	—	0.05
Mascara	6	—	≤0.1	—
Other eye makeup	2	—	≤0.1	—
Fragrances				
Colognes and toilet waters	—	—	—	0.03
Perfumes	—	—	—	0.1
Other fragrances	2	—	>0.1–1	—
Noncoloring hair care				
Hair conditioners	22	—	≤0.1–1	—
Rinses	6	—	≤0.1–1	—
Shampoos	9	—	≤0.1	—
Hair tonics dressings, etc	3	—	≤0.1–1	—
Wave sets	1	—	≤0.1	—
Other noncoloring hair care	1	1	≤0.1	—
Hair coloring				
Hair dyes and colors	3	—	>0.1–1	—
Shampoos	6	—	≤0.1	—
Makeup				
Blushers	20	—	≤0.1	0.1
Foundations	6	—	≤0.1	—
Leg and body paints	2	—	≤0.1	—
Lipstick	—	—	—	0.1
Makeup bases	3	—	≤0.1	—
Makeup fixatives	134	—	≤0.1	—
Other makeup	1	—	≤0.1	—
Personal hygiene				
Underarm deodorants	2	—	≤0.1	—
Shaving				
Aftershave lotion	1	—	≤0.1	0.03
Skin care				
Cleansing creams, lotions, etc	17	—	≤0.1	0.02
Depilatories				
Face and neck skin care preparations	3*	—	>0.1–1*	—
Body and hand skin care preparations	—	—	—	—
Moisturizers	9	—	≤0.1	—
Night skin care preparations	3	—	≤0.1	—
Paste masks/mud packs	8	—	≤0.1	—
Skin fresheners	3	—	≤0.1	0.01
Other skin care	6	—	≤0.1	0.009
Suntan preparations				
Suntan gels, creams, and liquids	3	—	≤0.1–1	0.05
Indoor tanning preparations	1	—	≤0.1	—
Other suntan	1	—	≤0.1	—
Total uses/ranges for 2-Bromo 2-Nitropropane-1,3-Diol	323	1	≤0.1–1	≤0.1

*These categories were originally combined, but are now separate

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BUTYLATED HYDROXYANISOLE (BHA)

A safety assessment of Butylated Hydroxyanisole was published in 1984 with the conclusion that this ingredient is safe as a cosmetic ingredient in the practices of use (Elder 1984) New studies, along with updated information regarding types and concentrations of use, were considered by the CIR Expert Panel The Panel determined to not reopen this safety assessment

The name of Butylated Hydroxyanisole as listed in the *International Cosmetic Ingredient Dictionary and Handbook* has been changed to BHA (Pepe et al 2002)

BHA functions in cosmetics include antioxidant and fragrance ingredient It was used in 3217 cosmetic products in 1981, with the largest use occurring in lipstick at concentrations of ≤10% (Elder 1984) In 2002, BHA was used in 1224 cosmetic products (FDA 2002), at a maximum use concentration of 0.2% in colognes, toilet waters, and perfumes (CTFA 2003) Table 3 presents the available use information for BHA The most recent information now constitutes the present use of this ingredient

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TABLE 3
Historical and current cosmetic product uses and concentrations for BHA

Product category	1981 uses (Elder 1984)	2002 uses (FDA 2002)	1981 concentrations (Elder 1984) %	2003 concentrations (CTFA 2003) %
Baby care				
Lotions, oils, powders, and creams	1	1	>0 1–1	0 0001
Bath				
Oils, tablets, and salts	20	4	≤0 1	0 0004
Bubble baths	7	—	≤0 1	0 00001
Bath soaps and detergents	2	5	≤0 1	0 000004
Other bath	10	3	≤1	0 0001
Eye makeup				
Eyebrow pencil	33	51	≤1	0 0001
Eyeline	75	399	≤1	0 1
Eye shadow	410	38	≤5	0 002
Eye lotion	2	2	≤0 1	—
Eye makeup remover	11	6	≤0 1	0 02
Mascara	65	18	≤1	0 1
Other eye makeup	39	10	≤1	0 001
Fragrances				
Colognes and toilet waters	97	18	≤1	0 2
Perfumes	62	6	≤1	0 2
Powders	12	2	≤0 1	0 0002
Sachets	21	—	≤0 1	—
Other fragrances	24	10	≤1	0 004
Noncoloring hair care				
Conditioners	8	5	≤0 1	0 0002
Sprays	1	—	—	0 0001
Shampoos	6	—	≤0 1	0 0005
Tonics, dressings, etc	10	8	≤1	0 02
Wave sets	1	—	—	—
Other noncoloring hair care	—	—	—	0 05
Hair coloring				
Other hair coloring	5	1	≤0 1	—
Makeup				
Blushers	176	26	≤5	0 2
Face powders	98	11	≤1	0 005
Makeup foundations	119	30	≤0 1	0 05
Lipstick	1256	279	≤25	0 2
Makeup bases	64	4	≤1	0 005
Rouges	48	1	≤1	0 04
Makeup fixatives	10	—	≤0 1	—
Other makeup	106	23	≤5	0 05
Nail care				
Basecoats and undercoats	1	3	≤0 1	—
Cuticle softeners	2	2	≤0 1	0 001
Creams and lotions	4	1	≤0 1	—
Polish and enamel	—	—	—	0 06
Polish and enamel remover	1	—	≤0 1	—
Other nail care	2	4	≤0 1	0 004

TABLE 3
Historical and current cosmetic product uses and concentrations for BHA (Continued)

Product category	1981 uses (Elder 1984)	2002 uses (FDA 2002)	1981 concentrations (Elder 1984) %	2003 concentrations (CTFA 2003) %
Oral hygiene				
Dentifrices	—	—	—	0.01
Personal hygiene				
Underarm deodorants	1	1	≤0.1	0.002
Other personal hygiene	2	4	≤1	0.002
Shaving				
Aftershave lotions	11	2	≤1	0.006
Preshave lotions	3	—	—	—
Shaving cream	8	10	≤0.1	0.0003
Shaving soap	1	—	>0.1–1	—
Other shaving	3	—	≤1	0.0003
Skin care				
Cleansing creams, lotions, etc	51	23	≤1	0.05
Face and neck skin care	77*	15	≤1*	0.1
Body and hand skin care	—	72	—	0.1
Hormone skin care**	1	**	—	**
Foot powders and sprays	—	1	—	0.004
Moisturizers	111	51	≤1	0.06
Night skin care	30	26	≤1	0.04
Paste masks/mud packs	6	3	≤1	0.004
Skin lighteners**	11	**	≤0.1	**
Skin fresheners	6	2	≤0.1	—
Wrinkle smoothers**	6	**	≤0.1	**
Other skin care	42	30	≤1	0.03
Suntan				
Suntan gels, creams, and liquids	27	7	≤1	0.1
Indoor tanning	2	1	≤0.1	—
Other suntan	9	5	≤0.1	—
Total uses/ranges for BHA	3217	1224	≤0.1–25	0.000004–0.2

*These categories were combined, but now are listed separately

**No longer listed as product categories

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BUTYLENE GLYCOL, HEXYLENE GLYCOL, ETHOXYDIGLYCOL, AND DIPROPYLENE GLYCOL

A safety assessment was published in 1985 with the conclusion that these ingredients are safe as presently used in cosmetics (Elder 1985). New studies, along with updated information regarding types and concentrations of use, were considered by the CIR Expert Panel. The Panel determined to not reopen this safety assessment.

Butylene Glycol was reported to be used in 165 cosmetic preparations in 1981, with the greatest use occurring in mascara, and at concentrations that ranged from less than 0.14% to greater than 50% (Elder 1985). In 2002, industry reports to FDA indicated that Butylene Glycol was used in 813 preparations (FDA 2002). An industry survey of use concentrations in

TABLE 4

Historical and current cosmetic product uses and concentrations for Butylene Glycol, Hexylene Glycol, Ethoxydiglycol, and Dipropylene Glycol

Product category	1981 uses (Elder 1985)	2002 uses (FDA 2002)	1981 concentrations (Elder 1985) %	2003 concentrations (CTFA 2003) %
<i>Butylene Glycol</i>				
Baby care				
Lotions, oils, powders, and creams	—	2	—	13
Other baby care	—	—	—	3–4
Bath				
Oils, tablets, and salts	1	3	5–10	0.08
Soaps and detergents	1	10	5–10	0.02–1
Other bath	4	20	5–>50	1
Eye makeup				
Eyebrow pencils	—	1	—	0.007
Eyeliners	3	12	1–5	3–12
Eye shadow	13	3	5–25	2
Eye lotions	—	5	—	3–8
Eye makeup remover	4	16	1–5	5
Mascara	34	14	1–10	0.00007–3
Other eye makeup	1	19	1–5	7
Fragrances				
Colognes and toilet waters	3	5	0.1–25	4
Perfumes	2	4	1–5	—
Powders	—	4	—	—
Other fragrances	1	18	5–10	2
Noncoloring hair care				
Conditioners	5	10	≤1–10	<1–3
Sprays/aerosol fixatives	—	—	—	3
Permanent waves	—	2	—	1
Shampoos	1	9	≤0.1	1–4
Tonics, dressings, etc	1	11	1–5	0.02–5
Other noncoloring hair care	—	12	—	<1–6
Makeup				
Blushers	7	—	1–25	—
Face powders	1	2	1–5	2
Foundations	19	66	5–25	6–9
Lipsticks	—	4	—	0.2–3
Makeup bases	1	12	5–10	6
Rouges	2	—	5–>50	—
Makeup fixatives	—	3	—	6
Other makeup	2	15	5–25	3–4
Nail care				
Cuticle softeners	1	3	5–10	—
Creams and lotions	—	2	—	—
Nail polishes and enamels	—	5	—	—
Other nail care	—	2	—	—
Oral hygiene				
Other oral hygiene	—	—	—	0.01
Personal hygiene				
Underarm deodorants	1	14	10–25	20–30
Other personal hygiene	1	1	1–5	—

(Continued on next page)

TABLE 4

Historical and current cosmetic product uses and concentrations for Butylene Glycol, Hexylene Glycol, Ethoxydiglycol, and Dipropylene Glycol (*Continued*)

Product category	1981 uses (Elder 1985)	2002 uses (FDA 2002)	1981 concentrations (Elder 1985) %	2003 concentrations (CTFA 2003) %
Shaving				
After shave lotions	4	8	0.1–5	0.05–7
Shaving cream	—	5	—	1
Other shaving	—	5	—	—
Skin care				
Cleansing creams, lotions, etc	13	66	≤0.1–10	0.05–20
Depilatories	—	—	—	4
Face and neck skin care	8*	30	≤0.1–>50*	3–7
Body and hand skin care	—	43	—	0.01–14
Foot powders and sprays	—	4	—	—
Moisturizers	13	171	≤0.1–>50	0.02–13
Night skin care	1	23	≤0.1	3–8
Paste masks/mud packs	3	27	0.1–10	3–12
Skin fresheners	6	16	≤0.1–5	2–6
Other skin care	7	78	≤0.1–10	4–89
Suntan products				
Suntan gels, creams, liquids, and sprays	1	7	1–5	2–5
Indoor tanning	—	18	—	0.5–20
Other suntan	—	3	—	5
Total uses/ranges for Butylene Glycol	165	813	≤0.1–>50	0.00007–89
<i>Hexylene Glycol</i>				
Baby care				
Other baby care	—	—	—	1
Bath				
Oils, tablets, and salts	4	1	5–25	—
Soaps and detergents	3	3	1–5	—
Bubble baths	3	2	0.1–5	—
Other bath	—	2	—	—
Eye makeup				
Eye lotions	—	2	—	2
Eye makeup remover	1	20	0.1–1	2
Mascara	—	1	—	0.1
Other eye makeup	—	3	—	0.8
Fragrances				
Colognes and toilet waters	—	—	—	0.03
Other	—	1	—	—
Noncoloring hair care				
Conditioners	7	3	0.1–10	4
Permanent waves	1	2	10–25	—
Rinses	1	—	10–25	—
Shampoos	29	12	≤0.1–10	—
Tonics, dressings, etc	—	2	—	4
Wave sets	—	1	—	—
Other noncoloring hair care	—	2	—	—
Hair coloring				
Dyes and colors	20	179	1–25	—

TABLE 4

Historical and current cosmetic product uses and concentrations for Butylene Glycol, Hexylene Glycol, Ethoxydiglycol, and Dipropylene Glycol (*Continued*)

Product category	1981 uses (Elder 1985)	2002 uses (FDA 2002)	1981 concentrations (Elder 1985) %	2003 concentrations (CTFA 2003) %
Rinses	—	2	—	—
Bleaches	1	1	1–5	—
Makeup				
Foundations	—	4	—	0.3
Lipsticks	—	—	—	0.003
Makeup bases	—	1	—	—
Makeup fixatives	—	—	—	1
Nail care				
Nail polish and enamel removers	—	1	—	—
Personal hygiene				
Underarm deodorants	2	—	0.1–1	0.002
Other personal hygiene	—	1	—	0.0009
Shaving				
Aftershave lotions	—	—	—	0.1–2
Shaving cream	—	1	—	—
Other shaving	—	—	—	2
Skin care				
Cleansing creams, lotions, etc	4	22	0.1–5	0.005–6
Face and neck skin care	1*	5	1–5*	0.001–4
Body and hand skin care	—	1	—	0.0009–1
Moisturizers	3	7	0.1–5	1
Night skin care	—	2	—	1–4
Paste masks/mud packs	1	6	5–10	0.3
Skin fresheners	3	2	0.1–5	—
Other skin care	1	6	1–5	3
Suntan				
Suntan gels, creams, liquids, and sprays	—	6	—	0.01
Other suntan	—	2	—	—
Total uses/ranges for Hexylene Glycol	85	306	≤0.1–25	0.0009–6
<i>Ethoxydiglycol</i>				
Baby care				
Shampoos	—	—	—	<1
Lotions, oils, powders, and creams	—	—	—	<0.5
Bath				
Oils, tablets, and salts	—	3	—	—
Soaps and detergents	—	—	—	0.6
Bubble baths	—	2	—	0.006
Eye makeup				
Eye lotions	—	—	—	0.0001–2
Eye makeup remover	—	1	—	—
Mascara	1	7	0.1–1	—
Other eye makeup	—	1	—	—
Fragrances				
Colognes and toilet waters	3	—	0.1–10	1
Perfumes	—	—	—	1

TABLE 4

Historical and current cosmetic product uses and concentrations for Butylene Glycol, Hexylene Glycol, Ethoxydiglycol, and Dipropylene Glycol (*Continued*)

Product category	1981 uses (Elder 1985)	2002 uses (FDA 2002)	1981 concentrations (Elder 1985) %	2003 concentrations (CTFA 2003) %
Other fragrances	—	2	—	—
Noncoloring hair care				
Conditioners	4	11	0 1–5	0 04
Sprays/aerosol fixatives	—	4	—	0 00008
Rinses	—	1	—	—
Shampoos	1	15	0 1–1	0 02–1
Tonics, dressings, etc	—	4	—	0 03
Wave sets	1	1	1–5	—
Other noncoloring hair care	—	4	—	0 4
Hair coloring				
Dyes and colors	14	495	1–10	—
Tints	13	—	1–5	—
Bleaches	5	6	1–5	—
Other hair coloring	1	2	1–5	—
Makeup				
Blushers	—	—	—	0 0006
Face powders	—	—	—	0 0008
Foundations	—	1	—	0 005
Lipsticks	—	—	—	0 00004
Makeup bases	—	—	—	0 008
Rouges	—	—	—	0 05
Other	—	—	—	0 04
Nail care				
Basecoats and undercoats	—	1	—	—
Nail polish and enamel removers	1	—	5–10	—
Other nail care	—	—	—	42
Personal hygiene				
Underarm deodorants	—	—	—	0 2
Douches	—	—	—	0 1
Other personal hygiene	—	—	—	0 3
Shaving				
Aftershave lotions	2	2	0 1–1	0 6
Preshave lotions	—	—	—	0 0005
Shaving cream	—	2	—	5
Other shaving	—	2	—	—
Skin care				
Cleansing creams, lotions, etc	14	10	≤0 1–> 50	0 02–80
Depilatories	—	—	—	2
Face and neck skin care	3*	5	≤0 1–1*	0 2–15
Body and hand skin care	—	6	—	0 1–0 5
Moisturizers	3	3	1–10	0 04–3
Night skin care	2	—	≤0 1–5	0 09–10
Paste masks/mud packs	3	2	0 1–25	0 002–8
Skin fresheners	3	—	1–5	5–8
Other skin care	5	14	0 1–10	0 05–53
Skin lighteners**	1	—*	—	—

TABLE 4

Historical and current cosmetic product uses and concentrations for Butylene Glycol, Hexylene Glycol, Ethoxydiglycol, and Dipropylene Glycol (*Continued*)

Product category	1981 uses (Elder 1985)	2002 uses (FDA 2002)	1981 concentrations (Elder 1985) %	2003 concentrations (CTFA 2003) %
Suntan				
Suntan gels, creams, liquids, and sprays	—	5	—	—
Indoor tanning	—	10	—	1–5
Other suntan	—	—	—	0 2–9
Total uses/ranges for Ethoxydiglycol	80	622	≤0 1–> 50	0 00004–80
<i>Dipropylene Glycol</i>				
Baby care				
Lotions, oils, powders, and creams	—	1	—	—
Bath				
Oils, tablets, and salts	1	3	>50	—
Soaps and detergents	—	4	—	0 8
Bubble baths	—	1	—	0 03
Eye makeup				
Eye lotions	—	2	—	0 1–4
Eye makeup remover	—	1	—	—
Mascara	—	7	—	—
Fragrances				
Colognes and toilet waters	2	—	5–10	7–9
Perfumes	12	4	0 1–> 50	0 01–20
Powders	—	5	—	—
Sachets	1	—	>50	—
Other fragrances	1	5	>50	4
Noncoloring hair care				
Conditioners	—	8	—	0 2
Sprays/aerosol fixatives	1	—	≤0 1	0 6
Rinses	—	—	—	0 004
Shampoos	1	6	5–10	0 4
Tonics, dressings, etc	1	3	10–25	0 4
Wave sets	4	4	5–10	—
Hair coloring				
Dyes and colors	—	10	—	—
Other hair coloring	—	2	—	—
Makeup				
Blushers	—	1	—	0 08
Foundations	—	5	—	0 2
Lipsticks	4	15	≤0 1–10	0 03
Makeup bases	1	4	1–5	0 05
Rouges	—	—	—	0 08
Other makeup	—	2	—	0 2–7
Nail care				
Nail polish and enamel removers	—	—	—	0 004
Personal hygiene				
Underarm deodorants	4	25	1–5	8–50
Other personal hygiene	—	13	—	1

(Continued on next page)

TABLE 4
Historical and current cosmetic product uses and concentrations for Butylene Glycol, Hexylene Glycol, Ethoxydiglycol, and Dipropylene Glycol (*Continued*)

Product category	1981 uses (Elder 1985)	2002 uses (FDA 2002)	1981 concentrations (Elder 1985) %	2003 concentrations (CTFA 2003) %
Shaving				
Aftershave lotions	2	2	0.1–5	3–5
Preshave lotions	—	—	—	0.6
Shaving cream	—	—	—	0.07
Skin care				
Cleansing creams, lotions, etc	4	38	≤0.1	0.01–12
Face and neck skin care	3*	24	1–5*	2
Body and hand skin care	—	19	—	0.1–9
Foot powders and sprays	1	—	0.1–1	—
Moisturizers	4	39	1–10	7
Night creams, lotions, powder, and sprays	—	4	—	2–3
Paste masks/mud packs	—	14	—	0.02–0.03
Skin fresheners	2	3	0.1–25	2
Other skin care	1	18	5–10	1–2
Suntan				
Suntan gels, creams, liquids and sprays	—	5	—	—
Indoor tanning	—	4	—	1
Other suntan	—	3	—	—
Total uses/ranges for Dipropylene Glycol	50	304	≤0.1–>50	0.004–50

*This category was combined when the original safety assessment was performed and is now two separate categories

**No longer included as a cosmetic product category

2003 found concentrations of use ranging from 0.00007% to 89% (CTFA 2003)

Hexylene Glycol was reported to be used in 85 preparations in 1981, with the largest use in shampoos, and at concentrations ranging from less than 0.1% to 25% (Elder 1985). In 2002, Hexylene Glycol was reported to be used in 306 preparations, with the greatest use in hair dyes and colors (FDA 2002). Concentrations of use in 2003 ranged from 0.0005% to 6% (CTFA 2003).

Ethoxydiglycol was reported to be used in 80 preparations in 1981, with the largest uses in hair dyes and colors as well as skin cleansing creams, lotions, liquids, and pads. The concentration of use ranged from less than 0.1% to greater than 50% (Elder 1985). In 2002, Ethoxydiglycol was used in 622 preparations (FDA 2002) and at concentrations ranging from 0.0004% to 80% (CTFA 2003).

Dipropylene Glycol was reported to be used in 50 preparations in 1981, with the largest single use occurring in perfumes, and at concentrations ranging from less than 0.1% to greater than 50% (Elder 1985). In 2002, Dipropylene Glycol was reported to be used in 304 preparations (FDA 2002) at concentrations ranging from 0.004% to 50% (CTFA 2003).

Table 4 presents the available use and concentration information. The most recent information now constitutes the present practices of use.

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CETEARYL OCTANOATE (CETEARYL ETHYLHEXANOATE)

A safety assessment of Cetearyl Octanoate was published in 1982 with the conclusion that this ingredient is safe as a cosmetic ingredient in the present practices of use (Elder 1982). Studies available since that safety assessment was completed have been considered by the CIR Expert Panel, along with updated information regarding uses and use concentrations. The Panel determined to not reopen this safety assessment.

The terminology for this ingredient in the *International Cosmetic Ingredient Dictionary and Handbook* has changed—Ceteraryl Ethylhexanoate is the current terminology (Pepe et al 2002).

Significant among the new data were data on 2-ethylhexanoic acid (2-EHA), which has been shown to be a liver and developmental toxicant in animal studies at high dose levels. 2-EHA is a possible metabolite of Cetearyl Ethylhexanoate.

In developmental toxicity studies, it has been postulated that 2-EHA maternal liver toxicity begins a cascade of effects that includes metallothionein (MT) induction, zinc accumulation in the liver due to MT binding, and a resulting zinc deficiency in the developing embryo. In this model, it is the zinc deficiency in the developing embryo that causes developmental toxicity. Support for this mechanism of action come from several sources. Animal studies have demonstrated that dietary zinc supplementation reduces this toxic effect and that further zinc deficiency makes 2-EHA more toxic. In vitro studies using embryo cultures have demonstrated that either zinc-deficient or 2-EHA-treated sera produced developmental toxicity. Zinc supplementation of either/both sera eliminated the effect.

To further examine this question, di-2-ethylhexyl terephthalate (DEHT), a 2-EHA precursor, was chosen as a model that would result in 2-EHA exposures without liver toxicity, MT induction, etc. DEHT is metabolized in the gut and liver to 2-ethylhexanol (2-EH) and terephthalate. Two moles of 2-EH are produced per mole of DEHT. Subsequent hydrolysis of 2-EH produces 2-EHA. It can be hypothesized that this pathway to 2-EHA production from a precursor would not give rise to acute

liver toxicity, MT induction, zinc sequestration, and developmental toxicity.

In a reproductive and developmental toxicity study, 0%, 0.3%, 0.6%, and 1% DEHT was provided in the feed of rats. The doses were calculated to be 614 to 823 mg/kg day⁻¹ for males and 783 to 1021 mg/kg day⁻¹ for females. Neither reproductive toxicity or developmental toxicity were seen at any dose level. These findings suggest that the process of metabolic conversion of DEHT to 2-EH, and subsequent hydrolysis to 2-EHA results in a time course of 2-EHA appearance that allows clearance before sufficient levels can arise to produce acute liver toxicity.

Although this study was undertaken to understand 2-EHA developmental toxicity, the Panel considered that it is relevant to the assessment of Cetearyl Ethylhexanoate. Like DEHT, Cetearyl Ethylhexanoate must undergo conversion in order to produce 2-EHA. In addition, Cetearyl Ethylhexanoate, as used in cosmetics, would have to pass through the stratum corneum and the epidermis before entering the blood stream, further moderating the time course of 2-EHA appearing in the liver. The Panel recognized that Cetearyl Ethylhexanoate is used in lipsticks and that ingestion is possible from that use. It was the view of the CIR Expert Panel that these considerations would preclude any possibility that Cetearyl Ethylhexanoate in cosmetics could present a risk of developmental toxicity.

Cetearyl Ethylhexanoate was used in 243 cosmetic products in 1976 (Elder 1982). The highest concentrations were in eye makeup, makeup, and skin care preparations. Currently there are 229 reported uses of Cetearyl Ethylhexanoate reported to FDA (FDA 2002), with the highest concentrations (up to 35%) in makeup (CTFA 2002). Although current use concentrations have increased compared to those reported in 1976, available skin irritation data show no irritation at concentrations up to 30%.

Table 5 presents the available use and concentration information. The most recent information now constitutes the present practices of use.

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⁶ Available for review: Director, Cosmetic Ingredient Review (CIR), 1101 17th Street, NW, Suite 412, Washington, DC 20036-4702, USA.

TABLE 5
 Historical and current cosmetic product uses and concentrations for Cetearyl Ethylhexanoate

Product category	1976 uses (Elder 1982)	2002 uses (FDA 2002)	1976 concentrations (Elder 1982) %	2002 concentrations (CTFA 2002a) %
Baby care				
Lotions, oils, powders, and creams	—	1	—	—
Bath				
Oils, tablets, and salts	1	—	Unknown	—
Capsules	—	—	—	9
Other bath	2	—	1–10	—
Eye makeup				
Eyeliners	1	—	0 1–1	—
Eye shadows	22	4	0–25	26–28
Mascara	6	—	0 1–1	0 07
Other eye makeup	2	3	0 1–5	3–5
Fragrances				
Powders	—	2	—	—
Other fragrances	—	12	—	—
Noncoloring hair care				
Conditioners	5	—	0–5	—
Sprays (aerosol fixatives)	5	5	0–5	—
Straighteners	1	—	0 1–1	—
Rinses	1	—	0 1–1	—
Shampoos	—	—	—	0 2
Tonics, dressings, etc	1	32	0 1–1	0 1
Wave sets	1	—	1–5	—
Other noncoloring hair	3	2	0–5	—
Makeup				
Blushers	19	3	1–25	3
Face powders	10	6	0 1–1	1–4
Foundations	—	5	—	0 1–34
Lipstick	—	4	—	0 1–8
Makeup bases	25	—	0 1–5	—
Rouges	2	—	5–25	—
Makeup fixatives	1	—	5–10	—
Other makeup	10	—	0 1–5	35
Nail care				
Nail creams and lotions	1	—	10–25	—
Personal hygiene				
Underarm deodorants	—	—	—	3
Feminine deodorants	1	—	1–5	—
Shaving				
Aftershave lotion	—	2	—	—
Mens talcum	—	1	—	—
Preshave lotions	1	—	1–5	—
Other shaving	1	—	1–5	—
Skin care				
Cleansing creams, lotions, etc	15	7	>0–10	13
Face and neck skin care	35*	21	>0–25*	3
Body and hand skin care	—	38	—	3–10
Moisturizers	39	23	0 1–25	2–34
Night skin care	16	13	0 1–10	2–7
Paste masks/mud packs	3	8	0 1–5	—
Skin fresheners	1	2	0 1–1	—
Other skin care	4	21	1–25	6
Suntan				
Suntan gels, creams, and liquids	7	9	0–5	0 5–9
Indoor tanning	—	2	—	3
Other suntan	1	3	5–10	—
Total uses/ranges for Cetearyl Ethylhexanoate	243	229	0–25	0 07–35

*This category was combined when the original safety assessment was performed and is now two separate categories

- Consumer Product Testing Co 1996b Primary ocular irritation in rabbits Unpublished data submitted by CTFA August 5, 2002 7 pages⁶
- Consumer Product Testing Co 1996c Primary dermal irritation in rabbits Unpublished data submitted by CTFA August 5 2002 6 pages⁶
- Consumer Product Testing Co 1996d Comedogenicity assay in rabbits Unpublished data submitted by CTFA August 5 2002 10 pages⁶
- Consumer Product Testing Co 1998 48 hour patch test in humans (dermal irritation study) Unpublished data submitted by CTFA March 22 2002 8 pages⁶
- Consumer Product Testing Co 1999a Skin irritation by MatTex Epiderm Skin Model Unpublished data submitted by CTFA March 22, 2002 14 pages⁶
- Consumer Product Testing Co 1999b Eye irritation by MatTek Epiocular Model Unpublished data submitted by CTFA March 22, 2002 14 pages⁶
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CHOLESTEROL

A safety assessment of Cholesterol was published in 1986 with the conclusion that this ingredient is safe as presently used in cosmetic products (Elder 1986). The CIR Expert Panel reviewed new studies available since that time, along with updated information regarding types and concentrations of use, and determined to not reopen this safety assessment.

According to the entry in the *International Cosmetic Ingredient Dictionary and Handbook*, Cholesterol functions as an emulsion stabilizer, miscellaneous skin-conditioning agent, and nonaqueous viscosity-increasing agent in cosmetic products (Gottschalck and McEwen 2004).

Frequency of use data provided by industry to FDA for 2002 show that cholesterol is used in 258 cosmetic products (FDA 2002), an increase compared to 145 uses reported in 1981 (Elder 1986). In 1981, Cholesterol use concentrations (again, as reported by industry to FDA) ranged from $\leq 0.1\%$ to 5% (Elder 1986). A survey by the Cosmetic, Toiletry, and Fragrance Association (CTFA) in 2004 found the range of use concentrations to be 0.002% to 3% , with majority of products around 0.1% .

Historical and current cosmetic product uses and concentrations for Cholesterol are given in Table 6. The most recent information now constitutes the present practices of use.

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CHLOROXYLENOL

A safety assessment of Chloroxylenol was published in 1985 with the conclusion that this ingredient was safe as a cosmetic ingredient in the practices of use at that time (Elder 1985). New studies, along with the updated information below regarding types and concentrations of use, were considered by the CIR Expert Panel. The Panel determined not to reopen this safety assessment.

As given in the *International Cosmetic Ingredient Dictionary and Handbook*, the functions of Chloroxylenol in cosmetic products are now described as a cosmetic biocide, deodorant agent, and preservative (Gottschalck and McEwen 2006).

⁷Available for review: Director, Cosmetic Ingredient Review (CIR), 1101 17th Street, NW, Suite 412, Washington, DC 20036-4702, USA

TABLE 6
Historical and current cosmetic product uses and concentrations for Cholesterol

Product category	1981 uses (Elder 1984)	2002 uses (FDA 2002)	1981 concentrations (Elder 1984) %	2004 concentrations (CTFA 2004) %
Bath				
Soaps and detergents	—	2	—	—
Eye makeup				
Eyeliners	6	1	>0 1-1	—
Eye shadow	15	—	<0 1-1	0 01
Eye lotions	—	1	—	0 04-0 3
Eye makeup remover	—	—	—	0 002
Mascara	16	2	>0 1-5	—
Other eye makeup	3	4	>0 1-5	—
Fragrances				
Other fragrances	1	2	>0 1-1	—
Noncoloring hair care				
Conditioners	7	13	≤0 1-1	0 3
Straighteners	—	—	—	0 003
Rinses	—	1	—	—
Shampoos	1	5	>0 1-1	—
Tonics, dressings, etc	—	3	—	2
Other noncoloring hair care	—	4	—	0 2
Hair coloring				
Dyes and colors	—	27	—	—
Makeup				
Face powders	—	3	—	—
Foundations	7	7	≤0 1-1	3
Lipsticks	—	5	—	0 1
Makeup bases	12	3	≤0 1-1	0 02
Rouges	—	1	—	—
Makeup fixatives	—	2	—	—
Other makeup	14	4	≤0 1-1	—
Nail care				
Cuticle softeners	—	1	—	0 1
Nail polish and enamel removers	—	1	—	—
Shaving				
Aftershave lotions	1	3	>0 1-1	0 1
Shaving cream	—	—	—	0 1
Other shaving	1	—	>0 1-1	—
Skin care				
Cleansing creams, lotions, etc	5	11	≤0 1-1	1
Face and neck skin care	—	22	—	0 3-2
Body and hand skin care	11*	19	≤0 1-5*	0 01-0 5
Foot powders and sprays	—	3	—	0 5
Moisturizers	19	61	≤0 1-5	0 005-1
Night skin care	15	24	≤0 1-5	0 1-1
Wrinkle smoothers**	2	—	≤0 1-5	—
Paste masks/mud packs	—	4	—	0 5
Skin fresheners	—	3	—	—
Other skin care	8	13	≤0 1-5	—
Suntan				
Suntan gels, creams, liquids, and sprays	1	1	>0 1-1	0 02-0 4
Indoor tanning	—	—	—	0 005
Other suntan	—	2	—	—
Total uses/ranges for Cholesterol	145	258	≤0 1-5	0 002-3

*This category was combined when the original safety assessment was performed and is now two separate categories

**No longer listed as product categories

In 1984, Chloroxylenol was used as an antimicrobial compound in 93 cosmetic products, with the maximum concentrations at up to 5% in fragrance powders, noncoloring shampoos, and other hair preparations (Elder 1985). In 2002, industry reports of Chloroxylenol use to the FDA included 43 cosmetic products (FDA 2002). Based on an industry survey, CTFA (2002) reported that Chloroxylenol was used in cosmetic products at a maximum concentration of use of 0.5% in skin cleansing products.

Table 7 summarizes these data. The most recent information now constitutes the present practices of use.

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DIISOPROPANOLAMINE, ISOPROPANOLAMINE, TRIISOPROPANOLAMINE, AND MIXED ISOPROPANOLAMINES

A safety assessment of Diisopropanolamine, Triisopropanolamine, Isopropanolamine, and Mixed Isopropanolamines was published in 1987 with the conclusion that these ingredients are safe as cosmetic ingredients in the present practices of use and concentration, if not used in products containing N-nitrosating agents (Elder 1987). The CIR Expert Panel considered new studies, along with updated information regarding types and concentrations of use. The Panel determined not to reopen this safety assessment.

No uses of Mixed Isopropanolamines were reported in the original safety assessment, in frequency of use data collected by FDA in 2002 (FDA 2002) or in a recent industry survey (CTFA 2004).

Diisopropanolamine reportedly was used in 66 products in 1981, at concentrations of $\leq 10\%$, and in 33 products in 2002, at concentrations of up to 0.7% (from the 2004 survey).

Isopropanolamine was used in 11 cosmetic products in 1981, at concentrations of $\leq 1\%$, and in 27 products in 2002, at the same concentrations (from the 2004 survey).

Triisopropanolamine had 36 cosmetic uses in 1981, at concentrations of $\leq 5\%$, and 25 uses in 2002, at concentrations up to 1% (from the 2004 survey).

Table 8 summarizes the historical and recent uses of Diisopropanolamine, Isopropanolamine, and Triisopropanolamine in

⁸Available for review: Director, Cosmetic Ingredient Review, 1101 17th Street, NW Suite 412, Washington, DC 20036-4702, USA

TABLE 7
Historical and current cosmetic product uses and concentrations for Chloroxylenol

Product category	1979 uses (Elder 1985)	2002 uses (FDA 2002)	1979 concentrations (Elder 1985) %	2003 concentrations (CTFA 2004) %
Baby care				
Lotions, oils, powders, and creams	—	—	—	0.1
Bath				
Soaps and detergents	2	1	>0.1–1	—
Eye makeup				
Eye shadow	—	1	—	—
Eye makeup remover	2	—	≤1	—
Fragrances				
Powders	2	—	>1–5	—
Noncoloring hair care				
Conditioners	8	3	≤1	—
Straighteners	4	—	>0.1–1	—
Shampoos	29	3	≤5	—
Tonics, dressings, etc	3	6	>0.1–1	—
Wave sets	1	—	≤0.1	—
Other noncoloring hair care	3	—	≤5	—
Hair coloring				
Dyes and colors	1	—	≤1	—
Rinses	2	—	>0.1–1	—
Makeup				
Blushers	1	—	>0.1–1	—
Rouges	—	1	—	—
Makeup fixatives	1	—	>0.1–1	—
Other makeup	—	5	—	—
Nail care				
Basecoats and undercoats	1	—	≤1	—
Cuticle softeners	1	—	>0.1–1	—
Oral hygiene				
Other oral hygiene	—	—	—	0.4
Personal hygiene				
Underarm deodorants	1	1	>0.1–1	—
Feminine deodorants	1	—	≤0.1	—
Other personal hygiene	8	11	≤1	—
Shaving				
Shaving cream	—	1	—	—
Skin care				
Cleansing creams, lotions, etc	5	4	≤1	0.5
Depilatories	1	—	>0.1–1	—
Face and neck skin care	7*	—	≤1*	0.2
Body and hand skin care	—	2	—	—
Moisturizers	—	1	—	0.1
Paste masks/mud packs	2	—	≤1	—
Skin fresheners	1	—	≤1	—
Other skin care	5	3	≤1	—
Suntan products				
Suntan gels, creams, liquids and sprays	1	—	0.1–1	—
Total uses/ranges for Chloroxylenol	93	43	≤5	0.1–0.5

*This category was combined when the original safety assessment was performed and is now two separate categories

TABLE 8

Historical and current uses and use concentrations for Diisopropanolamine, Isopropanolamine, and Triisopropanolamine in cosmetic products

Product category	1981 uses (Elder 1985)	2002 uses (FDA 2002)	1981 concentrations (Elder 1985) %	2004 concentrations (CTFA 2004) %
<i>Diisopropanolamine</i>				
Fragrances				
Colognes and toilet waters	2	1	≤0.1	—
Other fragrances	13	10	≤1	—
Noncoloring hair care				
Conditioners	1	1	>0.1–1	—
Sprays	1	—	>1–5	—
Permanent waves	7	3	>0.1–10	—
Tonics, dressings, etc	2	5	≤1	0.7
Wave sets	1	1	>0.1–1	—
Other noncoloring hair care	2	1	>1–5	—
Hair coloring				
Hair dyes and colors	—	3	—	—
Makeup				
Makeup foundations	2	—	>1–5	—
Other makeup	5	—	>0.1–5	—
Shaving				
Aftershave lotion	4	2	≤1	—
Other shaving	2	3	≤1	—
Skin care preparations				
Cleansing creams, lotions, etc	—	—	—	<0.01
Face, body, and hand skin care	10	—	>0.1–1	—
Moisturizers	4	—	≤5	—
Night skin care	1	—	>0.1–1	—
Paste masks/mud packs	2	1	>0.1–5	—
Skin fresheners	2	1	≤1	—
Wrinkle smoothers**	1	—**	>0.1–1	—**
Other skin care	1	1	>0.1–1	—
Suntan preparations				
Suntan gels, creams, and liquids	2	—	>0.1–1	—
Indoor tanning	1	—	>0.1–1	—
Total uses/ranges for Diisopropanolamine	66	33	≤10	<0.01–0.7
<i>Isopropanolamine</i>				
Eye makeup				
Eyeliner	—	1	—	—
Mascara	3	22	≤1	—
Noncoloring hair care				
Tonics, dressings, etc	1	1	≤0.1	—
Hair coloring				
Hair dyes and colors	—	—	—	1
Shaving				
Aftershave lotions	2	—	>0.1–1	—
Skin care				
Depilatories	1	—	≤0.1	—
Body and hand skin care	—	1	—	—
Moisturizers	3	1	≤1	—

(Continued on next page)

TABLE 8

Historical and current uses and use concentrations for Diisopropanolamine, Isopropanolamine, and Triisopropanolamine in cosmetic products (*Continued*)

Product category	1981 uses (Elder, 1985)	2002 uses (FDA, 2002)	1981 concentrations (Elder, 1985) %	2004 concentrations (CTFA, 2004) %
Suntan				
Suntan gels, creams, and lotions	1	1	≤0.1	—
Total uses/ranges for Isopropanolamine	11	27	≤1	1
<i>Triisopropanolamine</i>				
Baby care				
Lotions, oils, powders, and sprays	1	—	>0.1–1	—
Noncoloring hair care				
Conditioners	4	—	>0.1–5	—
Sprays	9	9	≤1	0.4
Tonics, dressings, etc	13	12	≤5	0.7
Wave sets	2	3	>0.1–1	—
Other hair care	2	1	>0.1–1	1*
Skin care				
Cleansing creams, lotions, etc	1	—	>1–5	—
Face and neck skin care preparations	1***	—	>0.1–1***	—
Body and hand skin care preparations	—	—	—	—
Moisturizers	3	—	>0.1–1	—
Total uses/ranges for Triisopropanolamine	36	25	≤5	0.4–1

*Nonaerosol pump spray

**No longer a cosmetic product category

***This category was combined when the original safety assessment was performed and is now two separate categories

cosmetic products. The most recent information now constitutes the present practices of use.

The CIR Expert Panel did note that Diisopropanolamine has a structure that is related to diethanolamine (DEA), which has been implicated as an animal carcinogen. Data were provided suggesting a mechanism for DEA carcinogenicity in animals is related to choline metabolism. Data also were provided demonstrating that Diisopropanolamine does not act by the same mechanism. It was suggested, therefore, that Diisopropanolamine is unlikely to present any risk of carcinogenicity.

The Panel acknowledged the use of Diisopropanolamine in hair sprays. The effects of inhaled aerosols depend on the specific chemical species, the concentration, the duration of exposure, and site of deposition (Jensen and O'Brien 1993) within the respiratory system. Particle size is the most important factor affecting the location of deposition. The mean aerodynamic diameter of pump hair spray particles is approximately 80 μm , and diameter of anhydrous hair spray particles is 60 to 80 μm . Typically, less than 1% are below 10 μm , which is the upper limit for respirable particles (Bowen 1999). Based on the particle size, Diisopropanolamine would not be respirable in formulation. Therefore, exposure of the lung by inhalation was not considered likely.

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⁹Available for review: Director, Cosmetic Ingredient Review, 1101 17th Street, NW, Suite 412, Washington, DC 20036-4702, USA.

TABLE 9
 Historical and current uses and use concentrations for Diethylhexyl Adipate and Diisopropyl Adipate

Product category	1981 uses (Elder 1984)	2002 uses (FDA 2002)	1981 concentrations (Elder 1984) %	2003 concentrations (CTFA 2003) %
<i>Diethylhexyl Adipate</i>				
Bath				
Oils, tablets, salts	4	—	>10–25	—
Eye makeup				
Lotion	—	—	—	0.6
Other eye makeup	—	2	—	0.4–2
Fragrances				
Colognes and toilet waters	6	—	>1–5	—
Other fragrance	—	5	—	—
Makeup				
Blushers	1	3	≥0.1	13
Foundations	4	2	>0.1–10	16
Makeup bases	—	6	—	6
Lipsticks	5	1	>1–5	—
Other makeup	1	2	>1–5	—
Nail care				
Nail polish & enamel remover	2	—	>1–5	—
Nail creams and lotions	—	1	—	—
Cuticle softeners	—	1	—	—
Personal hygiene				
Underarm deodorants	1	—	>0.1–1	8
Other personal hygiene	—	4	—	—
Shaving				
Aftershave lotions	1	—	>1–5	1
Shaving cream	—	5	—	—
Skin care				
Face and neck skin care	1*	2	>1–5*	—
Body and hand skin care	—	2	—	—
Moisturizers	—	4	—	—
Other skin care	—	5	—	—
Suntan				
Suntan gels, creams, and liquids	—	1	—	38
Indoor tanning	—	2	—	12
Other suntan	1	1	—	—
Total uses/ranges for Diethylhexyl Adipate	27	49	≥0.1–25	0.4–38
<i>Diisopropyl Adipate</i>				
Bath				
Oils, tablets, and salts	7	5	>1–25	5
Bubble baths	1	—	>1–5	—
Other bath	—	1	—	8
Eye makeup				
Eyeliners	1	—	>1–5	—
Eye shadow	1	—	>10–25	—
Fragrances				
Colognes and toilet waters	15	16	>0.1–5	8
Perfumes	20	14	>1–10	8

(Continued on next page)

TABLE 9
Historical and current uses and use concentrations for Diethylhexyl Adipate and Diisopropyl Adipate (*Continued*)

Product category	1981 uses (Elder 1984)	2002 uses (FDA 2002)	1981 concentrations (Elder 1984) %	2003 concentrations (CTFA 2003) %
Sachets	1	—	>10–25	—
Other fragrances	9	2	>0 1–25	15
Noncoloring hair care				
Conditioners	3	—	≥0 1–1	0 1
Sprays	1	1	>1–5	3
Tonics, dressings, etc	4	2	>1–5	—
Wave sets	2	—	>0 1–5	—
Makeup				
Blushers	1	—	>1–5	—
Face powders	1	—	>1–5	—
Foundations	1	—	>0 1–1	5
Nail care				
Nail polish and enamel removers	—	1	—	3
Personal hygiene				
Underarm deodorants	—	—	—	0 01
Other personal hygiene	1	—	>0 1–1	—
Shaving				
Aftershave lotions	16	10	>1–5	1
Preshave lotions	1	—	>5–10	5
Skin care				
Cleansing creams, lotions, etc	5	1	>0 1–1	—
Face and neck skin care	—*	1	—*	—
Body and hand skin care	—	1	—	2–3
Foot powders and sprays	1	—	>0 1–1	—
Moisturizers	2	5	>0 1–5	0 2
Night skin care	1	—	>5–10	—
Skin fresheners	11	2	—	—
Other skin care	2	—	>1–10	4
Suntan				
Suntan gels, creams, and liquids	2	3	>5–10	4
Indoor tanning	2	—	>1–5	—
Other suntan	—	1	—	—
Total uses/ranges for Diisopropyl Adipate	112	66	≥0 1–25	0 1–15

*This category was combined when the original safety assessment was performed and is now two separate categories

Stott W T 2004 CIR Board diisopropanolamine review presentation on research by Dow Chemical Company Dec 2 2004⁹

Wigfield Y Y M D Lacroix M Lanouette, and N P Gurprasad 1988 Gas chromatographic determination of *N* nitrosodialkanolamines I herbicide di or trialkanolamine formulations *J Assoc Off Anal Chem* 71:328–333

DIOCTYL ADIPATE AND DIISOPROPYL ADIPATE

A safety assessment of Dioctyl Adipate and Diisopropyl Adipate was published in 1984 with the conclusion that these ingredients are safe as presently used in cosmetics (Elder 1984). New studies, along with updated information regarding types

and concentrations of use, were considered by the CIR Expert Panel. The Panel determined to not reopen this safety assessment.

The name of Dioctyl Adipate as listed in the *International Cosmetic Ingredient Dictionary and Handbook* has been changed to Diethylhexyl Adipate (Pepe et al 2002).

Diethylhexyl Adipate, according to information provided by industry to FDA under a voluntary reporting program, was used in 27 cosmetic products in 1981, with the maximum use concentration at 25%. Use increased in 2002 to 49 cosmetic products. As reported in an industry survey, the maximum use concentration increased to 38% in 2003.

Diisopropyl Adipate was used in 112 cosmetic products in 1981, with the maximum use concentration in the 10% to 25% range. Use decreased to 66 reported uses in 2002. The maximum use concentration was 15% in 2003, consistent with that reported in 1981.

Table 9 gives the available use and concentration data for Dioctyl Adipate and Diisopropyl Adipate. The most recent data now constitute the present practices of use.

The CIR Expert Panel noted that Dioctyl Adipate and Diisopropyl Adipate are used in cosmetic products that may be incidentally inhaled during use (e.g., hair sprays). The effects of inhaled aerosols depend on the specific chemical species, the concentration, the duration of exposure, and site of deposition (Jensen and O'Brien 1993) within the respiratory system. Particle size is the most important factor affecting the location of deposition.

The mean aerodynamic diameter of pump hair spray particles is approximately 80 μm , and diameter of anhydrous hair spray particles is 60 to 80 μm . Typically, less than 1% are below 10 μm , which is the upper limit for respirable particles (Bowen 1999). Based on the particle size, these ingredients would not be respirable in formulation. Therefore, exposure of the lung by inhalation was not considered likely.

The increase in the maximum concentration of use to 38% (in suntan lotion) was considered in the context of newly available reproductive and developmental toxicity data suggesting that Diethylhexyl Adipate can be fetotoxic in animal studies. This was a threshold effect and the systemic dose at which no adverse effects were seen (NOAEL) was 200 mg/kg day⁻¹. Using an estimated use of 40 g per day of suntan lotion containing Diethylhexyl Adipate at 38%, a 60-kg person would receive a dermal dose of 250 mg/kg day⁻¹. Given that Diethylhexyl Adipate is soluble in organic solvents, but not in water, dermal penetration of Diethylhexyl Adipate is likely to be less than 1%, yielding a maximum possible systemic dose of <2.5 mg/kg day⁻¹, well below the level demonstrated to have no fetotoxic effect.

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FORMALDEHYDE

A safety assessment of Formaldehyde was published in 1984 (Elder 1984) with the conclusion that this ingredient is safe in cosmetic products to the great majority of consumers, however, because of skin sensitivity of some individuals to this agent, the formulation and manufacture of a cosmetic product should be such as to ensure use at the minimal effective concentration of formaldehyde, not to exceed 0.2% measured as free formaldehyde. Furthermore, it cannot be concluded that formaldehyde is safe in cosmetic products intended to be aerosolized. An extensive number of new studies, along with updated information regarding types and concentrations of use, were considered by the CIR Expert Panel. The Panel determined to not reopen this safety assessment.

Data reported to the FDA by industry in 1981 indicated that Formaldehyde was used in a total of 805 cosmetic products, but that figure decreased to 120 reported uses in 2002. The maximum use concentration reported to FDA in 1981 was in the ≤0.1% to 10% range. Data from an industry use concentration survey in 2003 indicate a maximum use concentration of 0.08%.

Table 10 presents the recent and historical frequency of use and concentration of use data as a function of product category.

The discussion section in the original safety assessment acknowledged that Formaldehyde can be a skin irritant and sensitizer in clinical tests, and a developmental toxin, a genotoxin, and a neoplastic agent in experimental animal studies. The new clinical studies confirmed that Formaldehyde can be a skin irritant and sensitizer, but at levels higher than the 0.2% free Formaldehyde upper limit established by the CIR Expert Panel.

The developmental toxicity, genotoxicity, and carcinogenicity of high doses of Formaldehyde was also confirmed in the new studies. These studies demonstrate that there is a threshold effect, that is, high doses are required before any effect is seen. Again, the limit on the amount of free Formaldehyde established by the CIR Expert Panel precludes any risk as a result of use of cosmetic products containing Formaldehyde.

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TABLE 10
Historical and recent uses and use concentrations of Formaldehyde in cosmetic products

Product category	1981 uses (Elder 1984)	2002 uses (FDA 2002)	1981 concentrations (Elder 1984) %	2003 concentrations (CTFA 2003) %
Baby care				
Shampoos	7	—	≤ 0.1–1	—
Lotions, oils, powders and creams	1	—	> 0.1–1	—
Bath				
Soaps and detergents	5	5	≤ 0.1–1	< 0.002–0.08
Oils, tablets and salts	10	6	≤ 0.1–1	0.08
Bubble baths	109	4	≤ 0.1–1	0.08
Other bath	24	1	≤ 0.1–5	0.08
Eye makeup				
Mascara	1	—	≤ 0.1	0.0002
Other eye makeup	3	—	≤ 0.1–1	—
Fragrance				
Sachets	2	—	≤ 0.1–1	—
Other fragrance	—	—	—	0.02
Noncoloring hair care				
Conditioners	95	11	≤ 0.1–5	—
Permanent waves	11	2	≤ 0.1–1	—
Rinses	32	2	≤ 0.1–1	—
Shampoos	316	59	≤ 0.1–5	< 0.005–0.08
Tonics, dressings, etc	21	9	≤ 0.1–10	< 0.005
Wave sets	37	8	≤ 0.1–10	—
Other hair	13	3	≤ 0.1–5	—
Hair coloring				
Dyes and colors	5	—	≤ 0.1	—
Shampoos	3	2	≤ 0.1–1	—
Makeup				
Face powders	1	—	> 0.1–1	—
Foundations	2	—	≤ 0.1–1	—
Leg and body paints	—	—	—	0.02
Makeup bases	3	—	≤ 0.1–1	—
Other makeup	—	—	—	0.01
Nail care				
Cuticle softeners	1	—	≤ 0.1	—
Nail creams and lotions	1	1	≤ 0.1	—
Other manicuring	—	1	—	2*
Oral hygiene				
Dentifrices	—	—	—	0.04
Mouthwashes and breath fresheners	2	—	≤ 0.1–1	—
Personal hygiene				
Underarm deodorants	7	—	> 0.1–1	—
Feminine hygiene deodorants	1	—	> 1–5	—
Other personal cleanliness	1	1	≤ 0.1	0.07–0.08
Shaving				
Aftershave lotions	1	—	> 0.1–1	—
Shaving creams	2	1	≤ 0.1	—
Other shaving	1	—	> 1–5	—

(Continued on next page)

TABLE 10
Historical and recent uses and use concentrations of Formaldehyde in cosmetic products (*Continued*)

Product category	1981 uses (Elder 1984)	2002 uses (FDA 2002)	1981 concentrations (Elder 1984) %	2003 concentrations (CTFA 2003) %
Skin care				
Cleansing creams, lotions, etc	13	1	≤0.1–1	<0.0001–0.002
Face and neck skin care	47**	—	≤0.1–1**	—
Body and hand skin care	—	2	—	<0.0001
Foot powders and sprays	1	—	>0.1–1	—
Moisturizers	11	1	≤0.1–1	—
Night skin care	5	—	≤0.1–1	—
Paste masks/mud packs	3	—	≤0.1–1	—
Skin fresheners	1	—	>0.1–1	—
Other skin care	4	—	>0.1–1	0.06
Suntan				
Suntan gels, creams, and liquids	2	—	≤0.1–1	—
Total uses/ranges for Formaldehyde	805	120	≤0.1–10	<0.0001–0.08

*This product was sold only in Europe and no longer marketed

**This category was combined when the original safety assessment was performed and is now two separate categories

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HYDROLYZED COLLAGEN

A safety assessment of Hydrolyzed Collagen concluded that this ingredient is safe as a cosmetic ingredient in the present practices of use and concentration (Elder 1985). New studies, along with the updated information regarding types and concentrations of use, were considered by the CIR Expert Panel. The Panel determined not to reopen this safety assessment.

Data reported to the FDA by industry in 1981 indicated that Hydrolyzed Collagen was used in 936 cosmetic products at concentrations ranging from $\leq 0.1\%$ to $>50\%$ (Elder 1985). Uses reported to FDA in 2002 (Hydrolyzed Animal Protein and Hydrolyzed Animal Collagen) were listed in this FDA database decreased to 569 (FDA 2002) and an industry survey of use concentrations yielded a maximum use concentration of 1% (CTFA 2004).

Table 11 presents the historical and recent uses and concentrations of Hydrolyzed Collagen in cosmetic products. The most recent data now constitute the present practices of use and concentration.

The CIR Expert Panel did note that the description of Hydrolyzed Collagen has been expanded recently to include specific mention of animal and fish collagen as the source material (Hydrolyzed Collagen is the hydrosylate of animal or fish collagen derived by acid, enzyme, or other method of hydrolysis) (Gottschalck and McEwen 2004).

The CIR Expert Panel is aware of the concerns about infectious prions in products obtained from mammalian tissues. As with all animal-derived ingredients, the use of Hydrolyzed Collagen should comply with FDA regulations to ensure that this ingredient is free of infectious agents, including bovine spongiform encephalopathy.

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ISOSTEARYL NEOPENTANOATE

A safety assessment of Isostearyl Neopentanoate concluded that this ingredient is safe as a cosmetic ingredient in the present practices of use and concentration (Elder 1985). One new study, along with the updated information regarding types and concentrations of use, were considered by the CIR Expert Panel. The Panel determined not to reopen this safety assessment.

Data reported to the FDA by industry in 1981 indicated that Isostearyl Neopentanoate was used in 208 cosmetic products at concentrations $>1\%$ to 50% (Elder 1985). Uses reported to FDA in 2002 decreased to 71 (FDA 2002) and an industry survey of use concentrations yielded a use concentration range from 0.2% to 14% (CTFA 2003).

Table 12 presents the historical and recent uses of Hydrolyzed Collagen in cosmetic products. The most current data are now considered the present practices of use.

The CIR Expert Panel did note a new use in lipsticks at concentrations of use of 9% to 14%. Oral toxicity studies in the original report suggest no concerns relating to this new use.

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¹² Available for review: Director, Cosmetic Ingredient Review, 1101 17th Street, NW, Suite 412, Washington, DC 20036-4702, USA

¹³ Available for review: Director, Cosmetic Ingredient Review, 1101 17th Street, NW, Suite 412, Washington, DC 20036-4702, USA

TABLE 11
Historical and recent uses and use concentrations of Hydrolyzed Collagen in cosmetic products

Product category	1981 uses (Elder 1985)	2002 uses (FDA 2002)	1981 concentrations (Elder 1985) %	2004 concentrations (CTFA 2004) %
Baby care				
Shampoos	1	—	≤0.1	—
Bath				
Oils, tablets and salts	2	—	>1–5	—
Bubble baths	2	2 ^a	>0.1–1	—
Soaps and detergents	3	13 ^a	>0.1–5	0.1
Other bath	2	2 ^a	>0.1–1	—
Eye makeup				
Eyebrow pencils	—	1 ^a , 1	—	—
Eyeliners	1	1 ^a	≤0.1	1
Eye shadow	6	7 ^a	≤1	—
Eye lotion	—	—	—	3
Eye makeup remover	—	1 ^a	—	—
Mascara	28	9 ^a	≤1	0.02–1
Other eye makeup	5	1 ^a	≤5	0.000004
Noncoloring hair				
Hair conditioners	174	126 ^a	>50	—
Hair sprays/aerosol fixatives	7	3 ^a	≤1	—
Hair Straighteners	7	7 ^a	>0.1–1	—
Permanent waves	70	13 ^a	≤25	0.05
Rinses	34	7 ^a	≤10	—
Shampoos	224	116 ^a	≤10	0.02
Hair tonics, dressings, etc	35	40 ^a	>50	—
Wave sets	39	4 ^a	≤25	—
Other noncoloring hair	18	15 ^a	≤10	0.03–0.2
Hair coloring				
Tints	14	2 ^a	≤5	—
Rinses	24	—	≤0.1	—
Shampoos	—	2 ^a	—	—
Bleaches	7	—	≤5	—
Other hair coloring	1	—	>0.1–1	—
Makeup				
Blushers	5	2 ^a	>0.1–1	0.5
Face powders	5	4 ^a	≤1	0.5
Foundations	10	7 ^a	≤1	0.5–4
Lipsticks	15	7 ^a	≤1	1
Makeup bases	15	4 ^a	≤1	—
Other makeup	—	—	—	0.2
Nail care				
Basecoats	—	1 ^a	—	—
Cuticle softeners	3	2 ^a	≤1	—
Creams and lotions	6	5 ^a	≤50	—
Polishes and enamels	1	—	>1–5	—
Polish and enamel removers	2	—	≤0.1	—
Other nail care	6	1 ^a	≤5	—
Personal hygiene				
Other personal hygiene	—	4 ^a	—	—

TABLE 11
Historical and recent uses and use concentrations of Hydrolyzed Collagen in cosmetic products (*Continued*)

Product category	1981 uses (Elder 1985)	2002 uses (FDA 2002)	1981 concentrations (Elder 1985) %	2004 concentrations (CTFA 2004) %
Shaving				
Aftershave lotions	3	1 ^a	>0.1–1	0.007
Other shaving	—	1 ^a	—	0.007
Skin Care				
Cleansing creams, lotions, etc	27	17 ^a	≤5	—
Face and neck skin care	46 ^c	18 ^a	≤10 ^c	0.06–6
Body and hand skin care		20 ^a		1
Moisturizers	43	36 ^a	≤25	1
Night skin care	11	15 ^a	>0.1–25	0.02
Paste masks/mud packs	6	8 ^a	≤5	0.008
Skin fresheners	7	8 ^a	≤5	—
Wrinkle smoothers ^d	1	— ^d	>1–5	— ^d
Other skin care preparations	7	27 ^a	≤0.1–5	0.5
Suntan Preparations				
Suntan gels, creams and liquids	—	7 ^a	—	0.000004
Other suntan preparations	—	2 ^a	—	0.05
Total uses/ranges for Hydrolyzed Collagen	923	569^a, 1^b	≤0.1–>50	000004–6

^aIngredient identified as “Hydrolyzed Animal Protein” in the FDA database

^bIngredient identified as “Hydrolyzed Animal Collagen” in the FDA database

^cThis category was combined when the original safety assessment was performed and is now two separate categories

^dNo longer a cosmetic product category

Food and Drug Administration (FDA) 2002. Frequency of use of cosmetic ingredients. *FDA database*. Washington, DC: FDA.

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2-NITRO-*p*-PHENYLENEDIAMINE AND 4-NITRO-*o*-PHENYLENEDIAMINE

A safety assessment of 2-Nitro-*p*-Phenylenediamine and 4-Nitro-*o*-Phenylenediamine was published in 1985 with the conclusion “for those persons not sensitized, the Expert Panel concludes that 2-Nitro-*p*-Phenylenediamine and 4-Nitro-*o*-Phenylenediamine are safe as hair dye ingredients at the current concentration of use” (Elder 1985). Studies available since that safety assessment was completed, along with updated information regarding uses and use concentrations, were considered by the CIR Expert Panel. The Panel determined to not reopen this safety assessment.

2-Nitro-*p*-Phenylenediamine was reported to be used in 28 hair dyes and colors in 1981 at concentrations from ≤0.1% to 1% (Elder 1985). In 2002, voluntary reports provided by industry to FDA indicated that 2-Nitro-*p*-Phenylenediamine was used in 113 hair dyes and colors (FDA 2002). Use concentration data

from a survey of industry practices by the Cosmetic, Toiletry, and Fragrance Association (CTFA) indicated use at concentrations from 0.1% to 1% in cosmetic products (CTFA 2003).

4-Nitro-*o*-Phenylenediamine was reported to be used in 26 hair dyes and colors in 1981, at concentrations of ≤0.1% to 1% (Elder 1985). Industry reports to FDA in 2002 included 22 uses as hair dyes and colors. Use concentration data from an industry survey in 2003 indicated use at concentrations of 0.1% to 0.2% (CTFA 2003).

The available use and concentration as a function of product type is given in Table 13. The most recent information now constitutes the current practices of use and concentration.

In 2003, an updated review of the available hair dye epidemiology literature was prepared (Helzlsouer et al 2003). 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 with an exposure assessment that included hair dye type, color, and frequency or duration of use, which found associations between personal hair dye use and development of bladder cancer, non-Hodgkin’s lymphoma, and multiple myeloma. These findings, however, were not consistently observed across studies.

In considering all these 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. The Panel stated that use of direct

TABLE 12
Historical and recent uses and use concentrations of Isostearyl Neopentaoate in cosmetic products

Product category	1981 uses (Elder 1985)	2002 uses (FDA 2002)	1981 concentrations (Elder 1985) %	2003 concentrations (CTFA 2003) %
Eye makeup				
Eyeliner	5	—	>5–10	8–13
Eye shadow	135	5	>1–10	1–13
Eye makeup remover	1	1	>10–25	—
Eye lotion	—	—	—	2
Other eye makeup preparations	3	1	>1–10	13
Fragrances				
Perfumes	—	1	—	—
Powders	—	1	—	—
Other fragrances	—	4	—	—
Makeup				
Blushers	20	8	>1–50	2–10
Foundations	10	9	>1–10	—
Face powders	—	2	—	3–6
Lipstick	—	3	—	9–14
Foundations	—	—	—	1–10
Makeup bases	16	9	>1–50	1–2
Rouges	2	—	>1–5	—
Other makeup	1	4	>10–25	0.2–12
Skin care				
Cleansing creams, lotions, etc	1	2	>5–10	3–8
Face and neck skin care	1*	1	>1–5*	4
Body and hand skin care	—	1	—	2–5
Body and hand sprays	—	—	—	6
Moisturizers	8	11	>0.1–10	—
Night skin care	1	1	>1–5	—
Paste masks/mud packs	—	1	—	4
Other skin care	1	5	>1–5	1–7
Suntan				
Suntan gels, creams, and liquids	2	—	>1–5	2–4
Indoor tanning	—	1	—	—
Other suntan	1	—	>1–5	—
Total uses/ranges for Isostearyl Neopentaoate	208	71	>0.1–50	0.2–14

*This category was combined when the original safety assessment was performed and is now two separate categories

TABLE 13
Historical and current uses and use concentrations for 2-Nitro-*p*-phenylenediamine and 4-Nitro-*o*-phenylenediamine

Product category	1981 use (Elder 1980)	2002 use (FDA 2002)	1981 concentrations (Elder 1980) %	2003 concentrations (CTFA 2003) %
2-Nitro- <i>p</i> -phenylenediamine				
Hair dyes and colors	28	113	≤0.1–1	0.1–1
Total uses/ranges for 2-Nitro-<i>p</i>-phenylenediamine	28	113	≤0.1–1	0.1–1
4-Nitro- <i>o</i> -phenylenediamine				
Hair dyes and colors	26	22	≤0.1–1	0.1–0.2
Total uses/ranges 4-Nitro-<i>o</i>-phenylenediamine	26	22	≤0.1–1	0.1–0.2

hair dyes, although not the focus in all investigations, appears to have little evidence of an association with adverse events as reported in epidemiology studies. However, direct hair dyes are a diverse group of chemicals and the determination of safety may hinge on other safety test data.

Discussion of the most recent available hair dye epidemiology data is available at <http://www.cir-safety.org/findings.shtml>

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OLEIC ACID, LAURIC ACID, PALMITIC ACID, MYRISTIC ACID, AND STEARIC ACID

A safety assessment of the Oleic Acid group was published in 1987 with a conclusion that these ingredients are safe in present practices of use and concentration in cosmetics New studies regarding these fatty acids available since then, along with updated information regarding uses and use concentrations, were considered by the CIR Expert Panel The Panel determined to not reopen this safety assessment

Oleic Acid usage increased from 424 in 1981 to 1131 in 2002, based on industry voluntary reports provided to FDA (Elder 1987, FDA 2002) An industry survey in 2004 indicated that use concentrations range from 0.00004% to 20%, within the range reported in 1981 (Elder 1987)

Lauric Acid usage increased from 22 in 1981 to 121 in 2002, based on industry voluntary reports provided to FDA (Elder 1987, FDA 2002) An industry survey in 2004 indicated that use concentrations range from 0.00003% to 11%, within the range reported in 1981 (Elder 1987)

Palmitic Acid usage increased from 29 in 1981 to 132 in 2002, based on industry voluntary reports provided to FDA (Elder 1987, FDA 2002) An industry survey in 2004 indicated that use concentrations range from 0.00006% to 20%, within the range reported in 1981 (Elder 1987)

Myristic Acid usage increased from 36 in 1981 to 73 in 2002, based on industry voluntary reports provided to FDA (Elder 1987, FDA 2002) An industry survey in 2004 indicated that use concentrations range from 0.00001% to 38%, within the range reported in 1981 (Elder 1987)

Stearic Acid usage decreased from 2465 in 1981 to 2133 in 2002, based on industry voluntary reports provided to FDA (Elder 1987, FDA 2002) An industry survey in 2004 indicated that use concentrations range from 0.000002% to 43%, within the range reported in 1981 (Elder 1987)

The available use and concentration data are given in Table 14 The most recent information now constitutes the present practices of use and concentration

The newly available studies reported findings consistent with the data in the original safety assessment One area not covered in the original report was reproductive and developmental toxicity One new study was available that demonstrated little or no toxicity to sperm cells by Oleic Acid, Palmitic Acid, and Stearic Acid

These fatty acids may be plant derived In such cases, established limits for pesticide and heavy metal residues should not be exceeded (lead ≤ 10 ppm, arsenic ≤ 3 ppm, mercury ≤ 1 ppm, total PCB/pesticide ≤ 40 ppm, with ≤ 10 ppm for any specific pesticide residue)

These fatty acids may also be derived from animal sources, including beef The Panel agrees with the Food and Drug Administration's position that tallow derivatives, including these fatty acids, would not present any risk of transmissible encephalopathies

TABLE 14

Historical and current cosmetic product uses and concentrations for Oleic Acid, Lauric Acid, Palmitic Acid, Myristic Acid, and Stearic Acid

Product category	1981 uses (Elder 1987)	2002 uses (FDA 2002)	1981 concentrations (Elder 1987) %	2004 concentrations (CTFA 2005) %
<i>Oleic Acid</i>				
Baby care				
Shampoos	1	1	>10–25	—
Lotions, oils, powders, and creams	1	1	>1–5	1
Other baby care	2	4	>1–25	2
Bath				
Oils, tablets, and salts	1	1	>5–10	—
Soaps and detergents	5	20	>1–10	0 000004–15
Other bath	—	10	—	—
Eye makeup				
Eyeliners	16	10	>0 1–25	0 1–3
Eye shadow	5	—	>0 1–5	0 4
Eye makeup remover	2	—	>1–5	—
Mascara	41	38	>0 1–10	1–4
Other eye makeup	1	1	>1–5	2–5 ^a
Fragrances				
Colognes and toilet waters	—	—	—	0 001
Sachets	4	2	>0 1–1	—
Other fragrances	8	5	>0 1–5	—
Noncoloring hair care				
Conditioners	1	—	>25–50	—
Permanent waves	1	2	≤0 1	—
Rinses	—	1	—	—
Shampoos	9	5	>1–25	0 000007
Tonics, dressings, etc	1	1	>0 1–1	0 6
Other noncoloring hair care	—	—	—	20 ^b
Hair coloring				
Dyes and colors	205	946	≤0 1–25	19
Tints	14	9	>1–25	—
Shampoos	7	—	>0 1–5	—
Color sprays	—	1	—	—
Lighteners with color	1	1	>1–5	—
Bleaches	8	17	>1–50	—
Makeup				
Blushers	10	2	>1–5	0 4
Face powders	1	—	>0 1–1	0 0001
Foundations	20	9	>0 1–5	0 4–2
Lipsticks	1	5	>5–10	16
Makeup bases	5	3	≤0 1–5	0 4
Rouges	—	1	—	0 00005
Other makeup	4	3	>0 1–25	2
Nail care				
Basecoats and undercoats	1	1	>10–25	—
Nail polish and enamels	—	—	—	0 0008
Other nail care	—	1	—	—

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TABLE 14
 Historical and current cosmetic product uses and concentrations for Oleic Acid, Lauric Acid, Palmitic Acid,
 Myristic Acid, and Stearic Acid (*Continued*)

Product category	1981 uses (Elder 1985)	2002 uses (FDA 2002)	1981 concentrations (Elder 1985) %	2004 concentrations (CTFA 2005) %
Personal hygiene				
Underarm deodorants	—	—	—	0 0007–0 6
Other personal hygiene	3	4	>1–10	6 ^e
Shaving				
Aftershave lotions	3	—	≤0 1–1	0 00008
Shaving cream	2	3	>1–5	0 7–4
Skin care				
Cleansing creams, lotions, etc	10	5	>0 1–5	0 00002–9
Face and neck skin care	11 ^c	—	>0 1–25 ^c	2
Body and hand skin care	—	2	—	0 2–0 4
Moisturizers	14	7	>0 1–5	0 2–0 4
Night skin care	—	—	—	0 5
Other skin care	2	3	>0 1–5	—
Hormone preparations ^d	1	NA ^d	>1–5	NA ^d
Suntan products				
Suntan gels, creams, liquids, and sprays	2	5	>1–5	0 02
Indoor tanning preparations	—	1	—	—
Total uses/ranges for Oleic Acid	424	1131	≤0 1–50	0 000004–20
<i>Lauric Acid</i>				
Bath				
Soaps and detergents	—	16	—	0 1–8
Other bath	—	20	—	2–11
Noncoloring hair care				
Conditioners	—	1	—	0 000004–4
Sprays	—	—	—	0 00002
Shampoos	3	1	>1–25	0 2–0 5
Tonics, dressings, etc	3	5	>0 1–1	0.00003
Fragrances				
Colognes and toilet waters	—	—	—	0 001
Perfumes	—	—	—	0 00002
Hair coloring				
Dyes and colors	—	43	—	—
Makeup				
Foundations	—	—	—	1
Lipsticks	—	1	—	0 00003
Personal hygiene				
Underarm deodorants	5	3	≤0 1–1	0 3
Other personal hygiene	4	3	≤0 1–10	5 ^e
Shaving				
Aftershave lotions	—	—	—	0 0003
Shaving cream	3	1	>1–10	0 003
Other shaving	—	—	—	0 2 ^g
Skin care				
Cleansing creams, lotions, etc	3	25	>1–5	—
Face and neck skin care	— ^c	—	— ^c	—
Body and hand skin care	—	—	—	0 00006
Moisturizers	1	2	>0 1–1	—

TABLE 14

Historical and current cosmetic product uses and concentrations for Oleic Acid, Lauric Acid, Palmitic Acid, Myristic Acid, and Stearic Acid (*Continued*)

Product category	1981 uses (Elder 1985)	2002 uses (FDA 2002)	1981 concentrations (Elder 1985) %	2004 concentrations (CTFA 2005) %
Night skin care	—	—	—	0.00003–0.5
Other skin care	—	—	—	2–3
Suntan				
Suntan gels, creams and liquids	—	—	—	1
Total uses/ranges for Lauric Acid	22	121	≤0.1–25	0.000004–11
<i>Palmitic Acid</i>				
Bath				
Soaps and detergents	1	10	>5–10	0.3–10
Other	—	11	—	0.000006–2
Eye makeup				
Eyeliners	—	—	—	0.1–0.7
Eye shadow	1	—	>5–10	0.006–0.3
Eye lotion	—	—	—	0.05
Mascara	—	1	—	0.02–4
Other eye makeup	—	2	—	0.003
Fragrance				
Colognes and toilet waters	—	—	—	0.01–0.8
Other fragrances	—	1	—	3
Noncoloring hair care				
Conditioners	—	1	—	0.00002–0.4
Shampoos	2	26	>1–5	0.001–3
Tonics, dressings, etc	—	—	—	0.00003–2
Other noncoloring hair care	—	3	—	—
Hair coloring				
Other hair coloring	—	1	—	—
Makeup				
Blushers	—	—	—	0.008–0.2
Face powders	—	1	—	0.01–1
Foundations	2	10	>0.1–5	0.3–2
Lipsticks	—	1	—	0.2–16
Rouges	—	1	—	0.00005
Makeup fixatives	—	1	—	—
Other makeup	—	—	—	0.01–2
Nail care				
Nail polishes and enamels	—	—	—	0.02–0.03
Personal hygiene				
Underarm deodorants	—	1	—	0.09–3
Other personal hygiene	—	—	—	0.3–4
Shaving				
Aftershave lotions	—	—	—	0.006
Shaving cream	4	11	>0.1–10	2–20
Shaving soap	—	—	—	0.4–8
Other shaving	—	17	—	10
Skin care				
Cleansing creams, lotions, etc	8	8	>1–25	0.03–7
Depilatories	—	—	—	4

(Continued on next page)

TABLE 14
 Historical and current cosmetic product uses and concentrations for Oleic Acid, Lauric Acid, Palmitic Acid,
 Myristic Acid, and Stearic Acid (*Continued*)

Product category	1981 uses (Elder 1985)	2002 uses (FDA 2002)	1981 concentrations (Elder 1985) %	2004 concentrations (CTFA 2005) %
Face and neck skin care	3 ^c	1	>0 1–5 ^c	0 2–3
Body and hand skin care	—	3	—	0 05–7
Foot powders and sprays	—	1	—	—
Moisturizers	3	8	>0 1–5	0 2–2
Night skin care	3	—	>1–25	0 05–1
Paste masks/mud packs	—	—	—	0 02
Skin fresheners	—	1	—	—
Other skin care	1	4	>1–5	0 2–2
Suntan				
Suntan gels, creams, liquids, and sprays	1	5	>10–25	0 0009–3
Indoor tanning	—	1	—	—
Other suntan	—	1	—	—
Total uses/ranges for Palmitic Acid	29	132	>0 1–25	0 000006–20
<i>Myristic Acid</i>				
Bath				
Soaps and detergents	3	7	>5–25	0 005–19
Other bath	—	11	—	0 00001–14
Eye makeup				
Mascara	2	—	>0 1–1	0 005–0 8
Fragrances				
Colognes and toilet waters	—	—	—	0 001
Other fragrances	—	1	—	—
Noncoloring hair care				
Conditioners	—	1	—	—
Shampoos	2	3	>1–5	0 00006–0 2
Tonics, dressings, etc	—	—	—	0 00002–0 08
Makeup				
Face powders	—	—	—	0 05
Foundations	—	2	—	0 4
Lipsticks	—	1	—	—
Rouges	—	—	—	0 00005
Other makeup	—	—	—	0 00004
Oral hygiene				
Dentifrices	—	—	—	0 0003
Personal hygiene				
Underarm deodorants	—	1	—	—
Other personal hygiene	2	1	>10–25	1–38 ^f
Shaving				
Aftershave lotions	—	—	—	0 00008
Beard softeners	2	—	>25–50	—
Shaving cream	16	13	>1–10	3–33
Shaving soap	—	—	—	2
Other shaving	1	3	>0 1–1	—
Skin care				
Cleansing creams, lotions, etc	5	26	1–25	0 0005–12
Depilatories	—	—	—	12
Face and neck skin care	2 ^c	—	>0 1–5 ^c	14
Body and hand skin care	—	1	—	0 5–10
Moisturizers	1	1	>0 1–1	0 0002–1

TABLE 14

Historical and current cosmetic product uses and concentrations for Oleic Acid, Lauric Acid, Palmitic Acid, Myristic Acid, and Stearic Acid (*Continued*)

Product category	1981 uses (Elder 1985)	2002 uses (FDA 2002)	1981 concentrations (Elder 1985) %	2004 concentrations (CTFA 2005) %
Night skin care	—	—	—	0 0003
Other skin care	—	1	—	0 003–15
Total uses/ranges for Myristic Acid	36	73	>0 1–50	0 00001–38
<i>Stearic Acid</i>				
Baby care				
Shampoos	—	—	—	2
Lotions, oils, powders, and creams	9	11	>0 1–10	2–3
Other baby care	1	7	>10–25	0 1–2
Bath				
Soaps and detergents	13	41	>1–25	0 2–19
Bubble baths	—	1	—	1–2
Other bath	3	13	>0 1–5	0 000007–7 ^h
Eye makeup				
Eyebrow pencils	9	12	>5–25	0 009–15
Eyeliners	55	74	>0 1–50	0 7–22
Eye shadow	128	4	>0 1–5	0 3–16
Eye lotions	1	4	>1–5	0 05–3
Eye makeup remover	1	3	>0 1–1	0 1–0 5
Mascara	139	95	>0 1–50	1–21
Other eye makeup	26	32	>0 1–10	1–14
Fragrances				
Colognes and toilet waters	3	—	>1–5	1
Perfumes	3	—	>0 1–10	—
Sachets	32	4	>0 1–10	—
Other fragrances	34	31	>0 1–10	16
Noncoloring hair care				
Conditioners	18	7	≤0 1–5	0 000002–0 5
Sprays/aerosol fixatives	1	—	>1–5	—
Straighteners	6	8	>0 1–10	—
Shampoos	17	10	>0 1–25	0 000007–7
Tonics, dressings, etc	18	4	≤0 1–>50	0 01–2
Hair coloring				
Dyes and colors	76	132	>1–5	—
Tints	—	1	—	—
Rinses	—	1	—	—
Color sprays	—	1	—	—
Bleaches	4	—	>0 1–5	—
Other hair coloring	8	2	>10–25	—
Makeup				
Blushers	47	4	>0 1–10	0 8–3
Face powders	2	6	>0 1–1	0 1–1
Foundations	190	119	>0 1–25	1–5
Lipsticks	27	40	>0 1–25	0 02–9
Makeup bases	263	35	>0 1–25	2–3
Rouges	9	—	>0 1–10	0 00005–0 1
Makeup fixatives	1	4	>1–5	—
Other makeup	20	22	>0 1–25	0 01–6

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TABLE 14
 Historical and current cosmetic product uses and concentrations for Oleic Acid, Lauric Acid, Palmitic Acid, Myristic Acid, and Stearic Acid (*Continued*)

Product category	1981 uses (Elder 1985)	2002 uses (FDA 2002)	1981 concentrations (Elder 1985)%	2004 concentrations (CTFA 2005)%
Nail care				
Cuticle softeners	10	8	>0 1–25	1–4
Creams and lotions	6	5	> 1–5	3–5
Nail polishes and enamels	—	—	—	0 04
Other nail care	2	—	> 1–10	0 05–4
Personal hygiene				
Underarm deodorants	8	21	> 1–25	0 2–9
Other personal hygiene	8	6	> 1–25	5–6 ^e
Shaving				
Aftershave lotions	5	9	>0 1–5	0 5–2
Shaving cream	100	100	>0 1–50	1–43
Shaving soap	1	1	>25–50	0 4–2
Other shaving	6	4	> 1–25	0 5–8
Skin care				
Cleansing creams, lotions, etc	173	168	≤0 1–25	1–25
Depilatories	—	—	—	7
Face and neck skin care		84		3–7
Body and hand skin care	432 ^c	320	>0 1–50 ^c	0 1–16
Foot powders and sprays	—	5	—	4
Moisturizers	327	356	≤1–50	0 3–10
Night skin care	67	62	≤0 1–25	0 4–2
Paste masks/mud packs	15	55	> 1–25	0 4–8
Skin fresheners	4	4	> 10–25	—
Skin lighteners ^d	11	— ^d	> 1–25	— ^d
Hormone preparations ^d	3	— ^d	> 1–25	— ^d
Wrinkle smoothers ^d	4	— ^d	> 1–5	— ^d
Other skin care	55	133	>0 1–25	0 0005–5
Suntan				
Suntan gels, creams, liquids, and sprays	48	42	>0 1–25	—
Indoor tanning	3	9	>0 1–1	0 3–2
Other suntan	13	13	>0 1–5	—
Total uses/ranges for Stearic Acid	2465	2133	≤0 1–>50	0 000007–43

^aThe 5% concentration was for a definer

^bA hair care protective oil

^cThese categories were combined in 1981, but are now separate

^dNo longer considered as a cosmetic ingredient category

^eA hand wash product

^fThe highest concentration was for a hand wash product

^gThe 0 2% concentration was specifically reported in a shave lubricant product

^hThe 7% concentration was for a body scrub product

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PANTHENOL AND PANTOTHENIC ACID

A safety assessment of Panthenol and Pantothenic Acid was published in 1987 with the conclusion that these ingredients are safe as presently used in cosmetics (Elder 1987). Studies published since the last assessment, along with updated information concerning frequency of use and use concentrations, were considered by the CIR Expert Panel. The Panel determined to not reopen the safety assessment.

The safety assessment applies to Panthenol in both the D and the DL form.

The available use and concentration information is provided in Table 15. The most recent information now constitutes the present use of these ingredients.

Panthenol reported usage increased from 284 in 1981 to 1538 in 2002, based on industry voluntary reports provided to FDA (Elder 1987, FDA 2002). An industry survey in 2004 indicated that use concentrations range from 0.00005% to 6%, which is lower than the maximum use concentration range reported in 1981 (Elder 1987).

Pantothenic Acid was not reportedly used in cosmetics in 1981 (Elder 1987), but industry voluntary reports provided to FDA in 2002 included three uses in eye makeup and skin care products (FDA 2002). An industry survey in 2004 indicated that use concentrations range from 0.00001% to 0.01% in those product categories and in makeup and shaving preparations (categories in which no uses were reported to FDA).

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TABLE 15
Historical and current cosmetic product uses and concentrations for Panthenol and Pantothenic Acid

Product category	1981 uses (Elder 1987)	2002 uses (FDA 2002)	1981 concentrations (Elder 1987) %	2004 concentrations (CTFA 2004) %
<i>Panthenol</i>				
Baby care				
Lotions, oils, powders, and creams	—	3	—	—
Bath				
Oils, tablets and salts	—	—	—	2
Soaps and detergents	—	15	—	0.05–4
Bubble baths	—	3	—	0.01–2
Capsules	—	1	—	—
Other bath	—	11	—	0.3–2
Eye makeup				
Eyebrow pencils	—	3	—	0.01–2
Eyeliner	5	—	>0.1–1	0.01–0.05
Eye shadow	23	—	>0.1–1	0.5–1
Eye lotions	—	5	—	0.01–0.6
Eye makeup remover	2	8	>0.1–1	0.001–1
Mascara	10	70	>0.1–5	0.1–2
Other eye makeup	2	14	>0.1–1	0.3–0.5
Fragrances				
Colognes and toilet waters	1	5	>0.1–1	0.003–0.1
Perfumes	—	—	—	1
Powders	—	3	—	—
Other fragrances	—	11	—	1
Noncoloring hair care				
Conditioners	33	264	≤0.1–5	0.09–6
Sprays/aerosol fixatives	17	82	≤0.1–1	0.01–5
Straighteners	—	1	—	—
Permanent waves	2	6	>0.1–1	5
Rinses	1	6	>0.1–1	0.1–0.5
Shampoos	25	206	≤0.1–5	0.01–5
Tonics, dressings, etc	11	187	≤0.1–1	0.01–5
Wave sets	31	12	≤0.1–5	0.9–1
Other noncoloring hair care	6	93	≤0.1–1	0.01–1*
Hair coloring				
Dyes and colors	—	52	—	0.01–0.1
Tints	—	1	—	—
Color sprays	—	2	—	—
Bleaches	—	1	—	0.5
Other hair coloring	—	6	—	0.00005–1
Makeup				
Blushers	3	2	>0.1–1 >10–25	0.2–1
Face powders	1	1	>0.1–1	0.02–1
Foundations	8	45	≤0.1–1	0.2–1
Lipsticks	27	6	≤0.1–5	0.01–2
Makeup bases	1	8	≤0.1	0.5
Rouges	1	—	>0.1–1	—
Other makeup	2	4	>0.1–1	<1–6

TABLE 15

Historical and current cosmetic product uses and concentrations for Panthenol and Pantothenic Acid (*Continued*)

Product category	1981 uses (Elder 1987)	2002 uses (FDA 2002)	1981 concentrations (Elder 1987) %	2004 concentrations (CTFA 2004) %
Nail care				
Basecoats and undercoats	—	9	—	0.03–0.2
Cuticle softeners	1	4	>0.1–1	0.1–0.2
Creams and lotions	1	1	>0.1–1	0.05–0.5
Polishes and enamels	—	10	—	0.2–1
Polish and enamel removers	—	5	—	0.03–0.5
Other nail care	—	11	—	0.1–0.2
Personal hygiene				
Underarm deodorants	1	3	>0.1–1	0.05–0.5
Douches	—	—	—	0.1–0.8
Other personal hygiene	—	8	—	0.1
Shaving				
Aftershave lotions	3	14	≤0.1–1	0.03–3
Preshave lotions	1	—	>0.1–1	—
Shaving cream	—	1	—	0.1–0.3
Other shaving	1	2	>0.1–1	0.4–1
Skin care				
Cleansing creams, lotions, etc	5	38	>0.1–1	0.05–3
Depilatories	—	—	—	1
Face and neck skin care	—	29	—	0.001–6
Body and hand skin care	8**	32	≤0.1–1**	0.1–5
Body and hand sprays	—	—	—	2
Foot powders and sprays	—	—	—	0.5
Moisturizers	22	98	≤0.1–5	0.1–3
Night skin care	14	29	>0.1–1	0.08–2
Paste masks/mud packs	1	24	≤0.1	0.1–5
Skin fresheners	2	15	>0.1–1	0.01–3
Other skin care	5	46	≤0.1–1	0.1–5
Suntan				
Suntan gels, creams, liquids, and sprays	5	10	>0.1–1	0.1–2
Indoor tanning	—	2	—	0.1–2
Other suntan	2	10	>0.1–1	0.5
Total uses/ranges for Panthenol	284	1538	≤0.1–25	0.00005–6
<i>Pantothenic Acid</i>				
Eye makeup				
Mascara	—	—	—	0.001–0.01
Other eye makeup	—	1	—	—
Makeup				
Face powders	—	—	—	0.001
Foundations	—	—	—	0.002
Shaving				
Aftershave lotions	—	—	—	0.001
Shaving cream	—	—	—	0.00001
Skin Care				
Moisturizers	—	1	—	0.003
Other skin care	—	1	—	0.001
Total uses/ranges for Pantothenic Acid	—	3	—	0.00001–0.01

*Includes two non-aerosol hair sprays

**These categories were combined originally, but are now separate

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p-PHENYLENEDIAMINE

A safety assessment on *p*-Phenylenediamine was published in 1985 in which the CIR Expert Panel acknowledged that *p*-Phenylenediamine is a known sensitizer and some persons may be sensitized under intended conditions of use For those persons not sensitized, the Expert Panel concluded that *p*-Phenylenediamine is safe as a hair dye ingredient at the current concentrations of use (Elder 1985) Studies available since that safety assessment was completed, along with updated informa-

tion regarding uses and use concentrations, were considered by the CIR Expert Panel The Panel determined to not reopen the safety assessment

Although the safety of *p*-Phenylenediamine as a hair dye ingredient was reaffirmed, the Panel did agree with FDA that other uses of this dye are unapproved The Panel expressed particular concern over the practice of combining *p*-Phenylenediamine with henna (so-called dark henna) for use in temporary tattoos—*p*-Phenylenediamine is a known sensitizer, highly inappropriate for such use as evidenced by reports of severe adverse skin reactions to dark henna temporary tattoos The Panel urged users to report adverse reactions to the FDA (for more information see the FDA website at <http://www.cfsan.fda.gov/~dms/cosatt.html>) The Panel also will work with the Consumer Federation of America to help the public understand the need to avoid using such unapproved and potentially dangerous products

The CIR Expert Panel also reviewed hair dye epidemiology data In 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/permanent 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

In 2003, an updated review of the available epidemiology literature was prepared (Helzlsouer et al 2003) This review considered 83 literature citations available since the IARC review The authors found insufficient evidence to support a causal association between personal hair dye use and a variety of tumors and cancers

In considering this information, the CIR Expert Panel agrees that the available epidemiology studies are insufficient to conclude there is a causal relationship between hair dye use and cancer and other end points described in the Helzlsouer et al (2003) review

The Panel also stated that use of direct hair dyes, although not the focus in all investigations, appear to have little evidence of an association with adverse events as reported in epidemiology studies However, direct hair dyes are a diverse group of chemicals and the determination of safety may hinge on other safety test data

p-Phenylenediamine was used in 500 hair-coloring products in 1981, at concentrations of $\leq 0.1\%$ to 5% In 2002, *p*-Phenylenediamine was used in 1178 hair-coloring products and in 2 nail care products Use concentration data provided in 2000 indicated use at concentrations of $\leq 0.014\%$ to $\leq 4\%$ in hair coloring products The 2004 use concentration data were provided by CTFA (CTFA 2004)

Available use and concentration information is shown in Table 16 The most recent information now constitutes the present practices of use

TABLE 16
Historical and current cosmetic product uses and concentrations for *p*-Phenylenediamine

Product category	1981 uses (Elder 1985)	2002 uses (FDA 2002)	1981 concentrations (Elder 1985) %	2004 concentrations (CTFA 2005) %
Hair coloring				
Dyes and colors	493	1167	≤0.1–5	≤4
Tints	7	9	≤0.1	—
Rinses	—	—	—	≤0.0014
Color sprays	—	1	—	—
Lighteners with color	—	1	—	—
Nail care				
Basecoats and undercoats	—	2	—	—
Total uses/ranges for <i>p</i>-Phenylenediamine	500	1180	≤0.1–5	≤0.0014–≤4

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PHENYL TRIMETHICONE

In 1986, the CIR Expert Panel found that Phenyl Trimethicone is safe as a cosmetic ingredient in the present practices of use and concentration (Elder 1986). A review of the recent literature uncovered no new studies regarding Phenyl Trimethicone

but the Panel did consider updated information regarding uses and use concentrations. The Panel determined to not reopen the safety assessment.

Phenyl Trimethicone uses have increased from 169 in 1981 to 279 in 2002, based on industry voluntary reports provided to FDA (Elder 1986, FDA 2002). An industry survey in 2003 indicated that use concentrations range from 0.0075% to 36% (CTFA 2004). The maximum value in that range is higher than the maximum use concentration of 5% reported in 1981 (Elder 1986). Table 17 presents the available use and concentration information for Phenyltrimethicone. The most recent information now represents the present practice of use and concentration.

The Panel considered the increased use concentrations in the context of the reproductive and developmental toxicity data in the original safety assessment. Phenyl Trimethicone was not teratogenic at 500 mg/kg/day in rats and rabbits. For a 70-kg person, this dose corresponds to 35 g/day. At the current maximum use in lipsticks and the amount of lipstick used in a typical day, a dose of Phenyl Trimethicone was estimated to be 10 mg/day. This dose was 3500× lower than the observable effect level.

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PROPYLENE CARBONATE

A safety assessment of Propylene Carbonate was published in 1987 with the conclusion that it is safe as a cosmetic ingredient in the present practices of use and concentration (Elder 1987). Studies published since the last assessment were reviewed along with updated information concerning frequency of use and use concentrations. The CIR Expert Panel determined to not reopen the safety assessment.

Based on voluntary reports provided by industry to FDA, there were 295 reported uses in 1981 (Elder 1987) and 178 reported uses in 2002 (FDA 2002). Use concentrations from an industry survey (CTFA 2003) ranged from 0.003% to 6%, not very different from the use concentration range reported in 1981 of ≤0.1% to >5% (Elder 1987).

Table 18 presents the available use and concentration information for Propylene Carbonate. The most recent information constitutes present practices of use and concentration.

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POLYVINYLPIRROLIDONE/VINYL ACETATE COPOLYMER

In 1983, the CIR Expert Panel concluded that this ingredient is safe as a cosmetic ingredient under the present practices of product and concentration use (Elder 1983). New studies available since that review have been considered by the Expert Panel,

¹⁸ Available for review: Director, Cosmetic Ingredient Review, 1101 17th Street, NW, Suite 412, Washington, DC 20036-4702, USA.

¹⁹ Available for review: Director, Cosmetic Ingredient Review, 1101 17th Street, NW, Suite 412, Washington, DC 20036-4702, USA.

TABLE 17
 Historical and current cosmetic product uses and concentrations for Phenyl Trimethicone

Product category	1981 uses (Elder 1986)	2002 uses (FDA 2002)	1986 concentrations (Elder 1986) %	2003 concentrations (CTFA 2004) %
Baby Care	1*	—	>0 1-1*	—
Bath				
Oils, tablets and salts	1	1	>0 1-1	—
Other bath	2	—	>1-5	—
Eye Makeup				
Eyeliners	—	1	—	2-6
Eye shadow	1	77	≤0 1-5	4-13
Eye lotions	—	—	—	0 008-1
Mascara	1	1	>0 1-1	0 1-0 4
Other eye makeup	1	4	>0 1-1	6-15
Fragrances				
Colognes and toilet waters	—	—	—	0 5
Perfumes	—	1	—	—
Powders	—	1	—	—
Other fragrances	—	—	—	0 5
Noncoloring hair care				
Conditioners	10	8	≤0 1-5	0 3-2
Sprays	25	23	≤0 1-1	0 1-18
Straighteners	1	—	>1-5	—
Rinses	1	—	>0 1-1	—
Shampoos	—	—	—	1
Tonics, dressings, etc	9	31	≤0 1-5	5-11
Wave sets	2	—	>0 1-5	—
Other noncoloring hair care	1	7	>0 1-1	0 5-2
Makeup				
Blushers	11	1	>1-5	2-15
Face powders	2	9	>0 1-1	0 1-8
Foundations	2	17	>1-5	2-22
Leg and body paints	—	—	—	2
Lipsticks	2	34	>1-5	0 08-36
Makeup bases	2	8	≤0 1-5	—
Rouges	—	2	—	—
Other makeup	—	13	—	0 0075-22
Nail care				
Creams and lotions	—	—	—	0 5
Polishes and enamels	7	—	>0 1-1	—
Personal hygiene				
Underarm deodorants	—	1	—	—
Other personal hygiene	—	1	—	—
Shaving				
Aftershave lotions	—	1	—	0 5-2
Preshave lotions	6	1	>0 1-5	2
Other shaving	—	—	—	0 5
Skin care				
Cleansing creams lotions, etc	—	4	—	2-4
Face and neck skin care	8**	3	≤0 1-1**	4-6
Body and hand skin care	—	4	—	0 2-18
Moisturizers	7	15	≤0 1-5	0 8-3
Night skin care	1	—	≤0 1	2
Other skin care	1	—	>1-5	2
Suntan				
Suntan gels creams, liquids and sprays	6	2	—	0 5-9
Indoor tanning	1	8	—	0 2-5
Other suntan	1	—	>1-5	2
Total uses/ranges for Phenyl Trimethicone	113	279	≤0 1-5	0 0075-36

*Product categories within the group not given

**These categories were combined originally, but are now separate

TABLE 18
Current and historical uses and concentrations of Propylene Carbonate in cosmetics

Product category	1981 uses (Elder 1984)	2002 uses (FDA 2002)	1981 concentrations (Elder 1984) %	2003 concentrations (CTFA 2003) %
Bath				
Oils, tablets and salts	1	1	>1-5	—
Eye makeup				
Eyebrow pencils	6	6	>1-5	0.3
Eyeliners	17	15	>1-5	0.2-0.6
Eye shadow	42	10	>0.1-5	0.4-1
Eye lotions	1	—	>1-5	—
Eye makeup remover	—	3	—	—
Mascara	34	22	>0.1-5	2-4
Other eye makeup	9	12	>0.1-5	0.5
Fragrances				
Colognes and toilet waters	5	—	>1-5	—
Perfumes	4	—	>1-5	—
Noncoloring hair care				
Conditioners	1	—	>1-5	—
Tonics, dressings, etc	—	1	—	—
Hair Coloring				
Other hair coloring	3	1	>1-5	—
Makeup				
Blushers	13	1	≤0.1-5	1-2
Face powders	1	—	>1-5	0.4
Foundations	11	3	>0.1-5	0.6-2
Rouges	—	—	—	0.1
Lipsticks	95	35	≤0.1-5	0.03-2
Makeup bases	13	4	>0.1-1	—
Makeup fixatives	1	2	>1-5	—
Other makeup	9	20	>0.1-5	1
Nail care				
Creams and lotions	1	—	>1-5	—
Polish and enamel	—	—	—	0.003
Polish and enamel removers	—	6	—	1
Other nail care	—	—	—	4
Personal hygiene				
Underarm deodorants	—	2	—	0.2-5
Other personal hygiene	4	26	≤0.1-5	—
Skin care				
Cleansing creams, lotions, etc	9	1	>1-5	0.1
Face and neck skin care	1*	—	>0.1-1*	—
Body and hand skin care	—	—	—	—
Moisturizers	2	4	>1-5	0.02-0.2
Night skin care	4	1	>1-5	—
Paste masks/mud packs	—	1	—	0.3-2
Skin fresheners	1	—	>0.1-1	—
Suntan preparations				
Suntan gels, creams, and liquids	6	1	>1-5	0.08-0.2
Other suntan preparations	1	—	>1-5	—
Total uses/ranges for Propylene Carbonate	295	178	≤0.1-5	0.003-5

*These categories were combined originally, but are now separate

along with the most current information available on use and concentration. The Panel noted that most of the newly available data concern Vinyl Acetate. The Panel determined to not reopen this safety assessment.

As given in the 9th edition of the *International Cosmetic Ingredient Dictionary and Handbook*, the name of this ingredient has been changed to VP/VA Copolymer (Pepe et al. 2002).

Based on voluntary reports provided by industry to FDA, there were 114 reported uses of this ingredient in 1976 (Elder 1983) and 210 reported uses in 2002 (FDA 2002). Use concentrations from an industry survey (CTFA 2003) ranged from 0.3% to 68%, but these data were clarified to note that the product reported to contain 68% is no longer on the market. The actual current use concentration range is 0.3% to 12%, which is in the range of >0.1% to >50% reported in 1976 (Elder 1983).

Table 19 presents the available use and use concentration information. The most current data now represent the present practices of use.

The Panel acknowledged that inhalation of Vinyl Acetate is associated with nasopharyngeal carcinoma. The mechanism of action appears to be an irritant-hyperproliferative type which requires a threshold dose. Two factors suggest that threshold doses could not be achieved from inhalation of cosmetics. First, the VP/VA Copolymer is stable, even under adverse environmental conditions, so that there will be little, if any, Vinyl Acetate actually present, especially since the maximum use concentration is 12%. Second, the effects of inhaled aerosols depend on the specific chemical species, the concentration, the duration of exposure, and site of deposition (Jensen and O'Brien 1993) within the respiratory system. Particle size is the most important factor affecting the location of deposition. The mean aerodynamic diameter of pump hair spray particles is approximately 80 μm , and diameter of anhydrous hair spray particles is 60 to 80 μm . Typically, less than 1% are below 10 μm , which is the upper limit for respirable particles (Bowen 1999). Based on the particle size, VP/VA Copolymers would not be respirable in formulation.

TABLE 19
Historical and current uses and use concentrations for VP/VA Copolymer

Product category	1976 uses (Elder 1983)	2002 uses (FDA 2002)	1976 use concentrations (Elder 1983) %	2003 use concentrations (CTFA 2003) %
Eye makeup				
Eyeliner	—	—	—	0.3
Eye shadow	—	—	—	2
Mascara	2	2	>1–5	6–9
Other eye makeup	—	8	—	—
Noncoloring hair care				
Hair conditioners	17	12	>1–50	0.3
Hair sprays	27	26	>0.1–10	2–4
Permanent waves	1	—	>0.1–1	—
Shampoos	2	1	>0.1–50	7
Tonics, dressings, etc	6	87	>0.1–25	4–12
Wave sets	50	12	>0.1–>50	7
Other noncoloring hair care	4	52	>5–25	8
Hair coloring				
Color sprays	—	1	—	0.5
Bleaches	1	2	>1–5	—
Makeup				
Foundations	—	—	—	0.5
Makeup fixatives	1	—	>0.1–1	4
Other makeup	1	4	>0.1–1	2
Nail care				
Cuticle softeners	1	—	>1–5	—
Skin care				
Body and hand skin care	—	1	—	—
Paste masks/mud packs	—	2	—	10
Other skin care preparations	1	—	>1–5	68*
Total uses/ranges of VP/VA Copolymer	114	210	>0.1–>50	0.3–12

*This product no longer is marketed, so this use concentration is not included in the total range.

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SAFFLOWER OIL

In 1985 the CIR Expert Panel concluded that this ingredient is safe as a cosmetic ingredient in the present practices of use (Elder 1985). Studies available since that safety assessment was completed, along with the updated information regarding uses and use concentrations were considered by the CIR Expert Panel. The Panel determined not to reopen this safety assessment.

The terminology for this ingredient in the *International Cosmetic Ingredient Dictionary and Handbook* (Gottschalk and McEwen 2004) has changed. Safflower Oil is currently *Carthamus Tinctorius* (Safflower) Seed Oil.

Carthamus Tinctorius (Safflower) Seed Oil was used in 94 products in 1981, based on voluntary reports provided to FDA by industry, and use concentrations ranged from less than 0.1% to greater than 50% (Elder 1985). In 2002 there were 142 uses (FDA 2002) and according to an industry survey the current range of use concentrations is 0.00005% to 84% (CTFA 2004).

Table 20 presents the available use information. The most recent information is now considered to be the present practices of use and concentration.

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SODIUM BORATE AND BORIC ACID

In 1983, the CIR Expert Panel concluded that Sodium Borate and Boric Acid, at concentrations $\leq 5\%$, are safe as cosmetic ingredients when used as currently recommended, but that cosmetic formulations containing free Sodium Borate or Boric Acid should not be used on infant or injured skin (Elder 1983). Studies available since that safety assessment was completed, along

²⁰ Available for review: Director, Cosmetic Ingredient Review, 1101 17th Street, NW, Suite 412, Washington, DC 20036-4702, USA

²¹ Available for review: Director, Cosmetic Ingredient Review, 1101 17th Street, NW, Suite 412, Washington, DC 20036-4702, USA

TABLE 20
 Historical and current cosmetic product uses and concentrations for *Carthamus Tinctorius* (Safflower) Seed Oil

Product category	1981 uses (Elder 1985)	2002 uses (FDA 2002)	1981 concentrations (Elder 1985) %	2003 concentrations (CTFA 2004) %
Baby care				
Lotions, oils, powders, and creams	—	—	—	10
Bath				
Oils, tablets, and salts	1	—	>0 1–1	7
Other bath	2	1	>0 1–1	—
Eye makeup				
Eye makeup remover	1	—	>10–25	2
Mascara	—	—	—	1
Other eye makeup	1	5	>0 1–1	6
Fragrances				
Other fragrances	—	1	—	5
Noncoloring hair care				
Conditioners	—	15	—	—
Sprays/aerosol fixatives	1	2	>5–10	—
Rinses	—	1	—	—
Shampoos	—	5	—	—
Tonics, dressings, etc	—	5	—	0 00005–27
Hair coloring				
Other hair coloring	—	—	—	1
Makeup				
Blushers	—	—	—	2
Foundations	6	2	>0 1–5	0 02–27
Lipsticks	4	18	≤0 1–5	0 1–60
Makeup bases	5	3	—	—
Other makeup	3	1	>1–5	—
Nail care				
Creams and lotions	—	1	—	—
Other nail care	—	—	—	84
Shaving				
Shaving cream	—	—	—	0 01
Skin Care				
Cleansing creams, lotions, etc	7	3	≤0 1–10	0 001–5
Face and neck skin care	15*	4	≤0 1–50*	0 5–8
Body and hand skin care	—	16	—	0 3–4
Foot powders and sprays	—	—	—	—
Moisturizers	28	17	≤0 1– >50	0 2–20
Night skin care	3	5	>1–50	—
Paste masks/mud packs	1	3	>5–10	72
Skin fresheners	1	1	>0 1–1	—
Wrinkle smoothers**	1	—	>25–50	—
Other	7	16	≤0 1– >50	0 03
Suntan products				
Suntan gels, creams, liquids and sprays	7	16	>0 1–>50	0 1
Indoor tanning preparations	—	1	—	—
Total uses/ranges for <i>Carthamus Tinctorius</i> (Safflower) Oil	94	142	≤0 1–>50	0 00005–84

*These categories were combined in 1981, but since have been separated

**No longer a cosmetic product category

with the updated information regarding uses and use concentrations were considered by the CIR Expert Panel. The Panel determined to not reopen this safety assessment.

Sodium Borate was used in 488 products in 1981, based on voluntary reports provided to FDA by industry, use concentrations ranged from less than 0.1% to greater than 50% (Elder 1983). In 2002 there were 280 uses (FDA 2002) and according to an industry survey the current range of use concentrations is 0.1% to 3% (CTFA 2002).

Boric Acid was used in 142 ingredients in 1981, based on voluntary reports provided to FDA by industry, and use concentrations ranged from less than 0.1% to greater than 50% (Elder 1985). In 2002 there were 77 uses (FDA 2002) and according to an industry survey the current range of use concentrations is 0.1% to 2% (CTFA 2002).

Table 21 presents the available usage and use concentration information as a function of cosmetic product category for both ingredients.

Significant among the new studies considered by the CIR Expert Panel are those on the reproductive and developmental toxicity of Boric Acid. Under the auspices of the National Toxicology Program, Fail et al. (1991) reported results of a reproductive assessment by continuous breeding protocol in which Boric Acid administered to rats in their feed was determined to be a reproductive toxicant. The NOAEL was suggested to be 110 mg/kg day⁻¹ and the LOAEL was 598 mg/kg day⁻¹. Price et al. (1997) reported results of another rat feeding study with a NOAEL of 10 mg/kg day⁻¹ and a LOAEL of 13 mg/kg day⁻¹ for decreased fetal body weight per litter. Yoshizaki et al. (1999) reported that an oral study using rats resulted in a NOAEL of 50 mg/kg day⁻¹ and a LOAEL of 150 mg/kg day⁻¹ for reduced sperm counts and the same NOAEL and LOAEL values for reduced implants and viable embryos.

The CIR Expert Panel considered that these findings do not suggest any reason for concern in the context of current use concentrations and the low dermal absorption through intact skin. These findings reinforce the Panel's prior determination that these ingredients should not be used on damaged skin, i.e., skin in which the barrier function has been compromised by disease or injury.

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²² Available for review: Director, Cosmetic Ingredient Review, 1101 17th Street, NW, Suite 412, Washington, DC 20036-4702, USA.

TABLE 21
 Historical and current uses and use concentrations for Sodium Borate and Boric Acid

Product category	1981 uses (Elder 1983)	2002 uses (FDA 2002)	1981 use concentrations (Elder 1983) %	2002 use concentrations (CTFA 2002) %
<i>Sodium Borate</i>				
Baby care				
Lotions, oils, powders, creams	1	—	0.1–1	—
Bath				
Soaps and detergents	1	1	>0–0.1	20 ^a
Bath oils, tablets, salts	3	—	1–50	—
Bubble baths	10	—	10–50	—
Eye makeup				
Eyeliners	14	1	0.1–5	—
Eye shadow	—	—	—	0.2
Eye lotion	2	—	0.1–1	—
Eye makeup remover	5	2	>0–5	—
Mascara	24	12	0.1–10	0.6
Other eye makeup	4	1	0.1–1	2
Fragrances				
Other fragrances	4	1	>0–1	—
Noncoloring Hair Care				
Conditioners	3	2	0.1–1	0.6
Sprays	1	—	1–5	—
Straighteners	2	—	1–5	—
Permanent waves	16	5	0.1–10	—
Shampoos	2	1	0.1–1	—
Tonics, dressings, etc	13	7	>0–5	—
Wave sets	3	—	>0–1	—
Other hair care	3	1	0.1–10	—
Hair coloring				
Other hair coloring	3	—	0.1–1	—
Makeup				
Blushers	2	2	0.1–1	0.2
Face powders	—	1	—	—
Foundations	4	3	0.1–1	0.2–0.5
Lipstick	1	—	0.1–1	—
Makeup bases	19	15	0.1–5	—
Other makeup	1	—	0.1–1	1
Nail care				
Cuticle softeners	—	1	—	—
Nail creams and lotions	2	—	0.1–1	—
Oral hygiene				
Dentifrices	—	3	—	—
Mouthwashes and breath fresheners	—	1	—	—
Personal hygiene				
Underarm deodorants	2	—	>0–1	—
Other personal hygiene	8	6	5–>50	0.1
Shaving				
Aftershave lotions	2	—	>0–0.1	—
Shaving cream	4	8	0.1–5	—
Other shaving	1	1	0.1–1	—

TABLE 21
 Historical and current uses and use concentrations for Sodium Borate and Boric Acid (*Continued*)

Product category	1981 uses (Elder 1983)	2002 uses (FDA 2002)	1981 use concentrations (Elder 1983) %	2002 use concentrations (CTFA 2002) %
Skin care				
Cleansing creams, lotions, etc	144	68	>0-5	0.4-1
Depilatories	1	—	0.1-1	—
Face and neck skin care	71 ^b	11	>0-5 ^b	—
Body and hand skin care		32		0.4-0.8
Moisturizers	47	31	>0-5	0.3-1
Night skin care	37	22	>0-1	0.4-0.9
Paste masks/mud packs	3	6	1-5	0.2-3
Fresheners	12	4	>0-1	0.3
Other skin care	1	23	>0->50	0.6-0.8
Skin lighteners ^c	1	NA ^c	0.1-1	NA ^c
Hormone products ^c	2	NA ^c	0.1-5	NA ^c
Wrinkle smoothing ^c	4	NA ^c	0.1-5	NA ^c
Suntan				
Suntan gels, creams, liquids	5	5	0.1-1	0.4
Other suntan	—	3	—	—
Total uses/ranges for Sodium Borate	488	280	>0->50	0.1-3
		<i>Boric Acid</i>		
Baby Care				
Baby shampoos	1	—	0.1-1	—
Bath				
Soaps and detergents	1	—	1-5	—
Oils, tablets, and salts	1	1	0.1-1	—
Bubble baths	—	1	—	—
Eye makeup				
Eye lotion	1	—	1-5	—
Eye makeup remover	3	4	0.1-5	—
Fragrances				
Powders	13	7	0.1-5	—
Other fragrances	1	—	0.1-1	—
Noncoloring hair care				
Conditioners	—	1	—	2
Permanent waves	13	5	0.1-5	—
Rinses	1	—	1-5	—
Shampoos	13	8	0.1-5	—
Tonics, dressings, etc	3	1	>0-1	—
Wave sets	2	3	>0-5	—
Other hair care	3	—	0.1-5	—
Hair coloring				
Coloring rinses	14	—	1-10	—
Bleaches	—	3	—	—
Other hair coloring	3	—	0.1-5	—
Makeup				
Blushers	2	—	0.1-1	—
Face powders	1	1	0.1-1	—
Rouges	1	—	0.1-1	—
Makeup fixatives	2	2	1-5	—

(Continued on next page)

TABLE 21
Historical and current uses and use concentrations for Sodium Borate and Boric Acid (*Continued*)

Product category	1981 uses (Elder 1983)	2002 uses (FDA 2002)	1981 use concentrations (Elder 1983) %	2002 use concentrations (CTFA 2002) %
Oral hygiene				
Mouthwashes and breath fresheners	5	—	>0–5	—
Personal hygiene				
Underarm deodorants	5	2	1–10	—
Douches	5	1	>50	10 ^c
Other personal hygiene	1	2	0 1–1	—
Shaving				
Aftershave lotions	5	5	>0–5	0 4
Preshave lotions	1	—	>0–0 1	—
Shaving cream	6	4	0 1–5	0 1–1
Other shaving	1	1	0 1–1	—
Skin care				
Cleansing creams, lotions, etc	4	2	0 1–5	—
Face and neck skin care	5 ^b	—	0 1–5 ^b	—
Body and hand skin care	—	9	—	—
Foot powders and sprays	—	1	—	—
Moisturizers	4	2	0 1–5	0 5
Night skin care	1	1	0 1–1	—
Paste masks/mud packs	3	3	0 1–5	—
Skin fresheners	17	6	>0–5	—
Other skin care	—	1	—	—
Total uses/ranges of Boric Acid	142	77	>0–>50	0 1–2

^aDiluted to about 0 3% Sodium Borate during use

^bThese categories were combined in 1981 but are now separate

^cNo longer considered as cosmetic product categories

^dPowder dissolved in water to produce a solution of about 0 1% Boric Acid before use

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SODIUM DEHYDROACETATE AND DEHYDROACETIC ACID

A safety assessment of Sodium Dehydroacetate and Dehydroacetic Acid was published in 1985 with the conclusion that these ingredients are safe as cosmetic ingredients in the present practices of use and concentration (Elder 1985). Studies available since that safety assessment was completed, along with updated information regarding uses and use concentrations were considered by the CIR Expert Panel. The Panel determined to not reopen this safety assessment.

Sodium Dehydroacetate was used in 260 products in 1981, based on voluntary reports provided to FDA by industry, use concentrations ranged from less than 0.1% to 1% (Elder 1985). In 2002 there were 325 uses (FDA 2002) and according to an industry survey the current range of use concentrations is 0.00003% to 0.5% (CTFA 2002).

Dehydroacetic Acid was used in 139 products in 1981, based on voluntary reports provided to FDA by industry, use concentrations ranged from less than 0.1% to 1% (Elder 1985). In 2002 there were 88 uses (FDA 2002) and according to an industry survey the current range of use concentrations is 0.007% to 0.7% (CTFA 2002).

Table 22 presents the available use and concentration information. The most recent information now constitutes the present practices of use.

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SODIUM LAURYL SULFOACETATE

A safety assessment on Sodium Lauryl Sulfoacetate was published in 1987 with the conclusion “On the basis of the available data presented in this report, the Expert Panel concludes that Sodium Lauryl Sulfoacetate is safe as a cosmetic ingredient in the present practices of use and concentration” (Elder 1987). Studies available since that safety assessment was completed, along with updated information regarding uses and use concentrations, were considered by the CIR Expert Panel. After reviewing the available data, the Panel determined to not reopen this safety assessment.

Sodium Lauryl Sulfoacetate was used in 93 products in 1981, based on voluntary reports provided to FDA by industry, use concentrations ranged from >0.1% to >50% (Elder 1985). In 2002 there were 68 uses (FDA 2002) and according to an industry survey in 2004 the current range of use concentrations is 0.6% to 21% (CTFA 2004).

Table 23 presents the available use and concentration information. The most recent information now constitutes the present practices of use.

The CIR Expert Panel did note that Stepan Company had submitted robust summaries and test plans on Sodium Lauryl Sulfoacetate as part of EPA’s high production volume chemical testing program. This submission argued that the only missing data were reproductive and developmental toxicity data. The company proposed conducting such a study. Though the Panel noted that there are no data in the published literature,

²³Available for review: Director, Cosmetic Ingredient Review, 1101 17th Street, NW, Suite 412, Washington, DC 20036-4702, USA

TABLE 22
 Historical and current uses and use concentrations for Sodium Dehydroacetate and Dehydroacetic Acid

Product category	1981 uses (Elder 1985)	2002 uses (FDA 2002)	1981 concentrations (Elder 1985) %	2003 concentrations (CTFA 2003) %
<i>Sodium Dehydroacetate</i>				
Baby care				
Lotions, oils, powders & creams	—	—	—	0.6
Bath				
Soaps and detergents	—	2	—	0.0001
Oils, tablets, and salts	1	—	≤0.1	—
Eye makeup				
Eyebrow Pencil	—	—	—	0.2–0.3
Eyeliner	2	4	≤0.1–1	0.05–0.5
Eye shadow	56	74	≤0.1–1	0.05–0.3
Eye lotion	—	3	—	—
Eye makeup remover	—	1	—	0.05
Mascara	13	16	≤0.1–1	0.001–0.4
Other eye makeup	4	12	>0.1–1	0.0006–0.4
Fragrances				
Powders	1	3	>0.1–1	—
Colognes and toilet waters	—	—	—	0.001–0.5
Noncoloring hair care				
Conditioners	—	—	—	0.2
Shampoos	—	2	—	0.2
Tonics, dressings, etc	1	1	≤0.1	—
Other noncoloring hair care	—	4	—	—
Hair coloring				
Tints	—	1	—	—
Other hair coloring	—	2	—	—
Makeup				
Blushers	22	15	≤0.1–1	0.1–0.4
Face powders	23	31	≤0.1–1	0.05–0.4
Makeup foundations	8	10	≤0.1–1	0.0001–0.4
Makeup bases	14	6	>0.1–1	0.1
Leg and body paints	—	—	—	0.1
Lipstick	—	1	—	0.3
Rouges	2	—	≤0.1–1	—
Makeup fixatives	—	1	—	—
Other makeup	2	4	>0.1–1	0.0003–0.2
Nail care				
Basecoats and undercoats	—	—	—	0.02
Nail creams and lotions	—	3	—	—
Cuticle Softeners	4	2	>0.1–1	—
Creams and lotions	2	—	≤0.1–1	—
Polish and enamel	—	—	—	0.2
Other nail care	1	—	>0.1–1	0.2
Personal hygiene				
Underarm deodorants	—	2	—	—
Shaving				
Shaving cream	1	4	>0.1–1	—
Other shaving	1	1	>0.1–1	—
Aftershave lotions	1	1	≤0.1	0.0003

TABLE 22

Historical and current uses and use concentrations for Sodium Dehydroacetate and Dehydroacetic Acid (*Continued*)

Product category	1981 uses (Elder 1985)	2002 uses (FDA 2002)	1981 concentrations (Elder 1985) (%)	2003 concentrations (CTFA 2003) (%)
Skin care				
Skin-cleansing preparations	23	13	≤0.1–1	0.0003–0.3
Face and neck skin care	24*	4	≤0.1–1*	0.008–0.2
Body and hand skin care		20		0.00003–0.5
Moisturizers	27	39	≤0.1–1	0.001–0.3
Night skin care	7	5	≤0.1	0.003–0.2
Paste masks/mud packs	4	6	≤0.1–1	0.03–0.2
Fresheners	2	2	>0.1–1	—
Other skin care	—	25	—	0.00003–0.1
Skin lighteners**	2	—**	≤0.1–1	—**
Wrinkle smoothers**	1	—**	>0.1–1	—**
Suntan				
Suntan gels, creams, and liquids	5	1	>0.1–1	0.2
Indoor tanning preparations	3	2	≤0.1–1	0.4
Other suntan preparations	3	2	>0.1–1	0.1
Total uses/ranges for Sodium Dehydroacetate	260	325	≤0.1–1	0.00003–0.6
	<i>Dehydroacetic Acid</i>			
Bath				
Soaps and detergents	—	—	—	0.03
Oils, tablets and salts	1	—	≤0.1	—
Bubble baths	2	1	≤0.1	—
Eye makeup				
Eyeline	1	—	>0.1–1	0.1
Eye shadow	11	4	≤0.1–1	0.3
Eye lotion	—	—	—	0.2
Eye makeup remover	8	5	≤0.1–1	0.1
Mascara	1	—	>0.1–1	0.2
Other eye makeup	9	—	≤0.1–1	—
Fragrances				
Colognes and toilet waters	4	—	≤0.1	—
Perfumes	4	—	≤0.1	—
Noncoloring hair care				
Shampoos	2	—	≤0.1	0.02–0.03
Tonics, dressings, etc	2	1	≤0.1–1	—
Makeup				
Blushers	5	1	≤0.1–1	0.05–0.2
Face powders	6	3	≤0.1–1	0.7
Makeup foundations	13	3	≤0.1–1	0.1
Makeup bases	1	—	≤0.1	—
Rouges	1	1	>0.1–1	—
Lipstick	1	—	≤0.1	—
Other makeup	1	—	≤0.1	0.07
Nail care				
Cuticle softeners	—	1	—	—
Polish and enamel	—	1	—	—
Personal hygiene				
Other personal hygiene	—	—	—	0.03

(Continued on next page)

TABLE 22
Historical and current uses and use concentrations for Sodium Dehydroacetate and Dehydroacetic Acid (*Continued*)

Product category	1981 uses (Elder 1985)	2002 uses (FDA 2002)	1981 concentrations (Elder 1985) %	2003 concentrations (CTFA 2003) %
Skin care				
Cleansing creams, lotions, etc	15	8	≤0 1–1	0 007–0 02
Face and neck skin care	16*	11	≤0 1–1*	0 01–0 08
Body and hand skin care		9		0 03–0 05
Moisturizers	10	10	≤0 1–1	—
Night skin care	5	2	≤0 1–1	0 03
Paste masks/mud packs	3	6	≤0 1–1	—
Skin fresheners	2	—	≤0 1	—
Other skin care	9	16	≤0 1–1	0 03
Wrinkle smoothers**	2	—**	≤0 1	—**
Suntan				
Suntan gels, creams, and liquids	3	—	>0 1–1	0 2
Indoor tanning preparation	—	5	—	—
Other suntan preparations	1	—	>0 1–1	—
Total Uses/Ranges for Dehydroacetic Acid Totals	139	88	≤0 1–1	0 007–0 7

*These categories were combined in 1981 but are now separate

**No longer considered as cosmetic product categories

which suggest that the reproductive and developmental toxicity potential of Sodium Lauryl Sulfoacetate is an issue, it was agreed that the results of the proposed reproductive and developmental toxicity study would be considered when available

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SODIUM SESQUICARBONATE, SODIUM BICARBONATE, AND SODIUM CARBONATE

A safety assessment of Sodium Sesquicarbonate, Sodium Bicarbonate, and Sodium Carbonate was published in 1987 with the conclusion that these ingredients are safe as presently used in cosmetic products (Elder 1987) Studies available since that safety assessment was completed, along with updated information regarding uses and use concentrations, were considered by the CIR Expert Panel After reviewing the available data, the Panel determined to not reopen this safety assessment

Sodium Sesquicarbonate was used in 111 products in 1981, based on voluntary reports provided to FDA by industry; use concentrations ranged from >1% to 50% (Elder 1985) In 2002 there were 24 uses (FDA 2002) and according to an industry survey in 2004 the current range of use concentrations is 2 0% to 90% (CTFA 2004)

Sodium Bicarbonate was used in 45 products in 1981, based on voluntary reports provided to FDA by industry, use concentrations ranged from less than 0 1% to 50% (Elder 1985) In 2002 there were 70 uses (FDA 2002) and according to an industry survey in 2004 the current range of use concentrations is 0 006% to 95% (CTFA 2004)

Sodium Carbonate was used in 25 products in 1981, based on voluntary reports provided to FDA by industry; use concentrations ranged from less than 0 1% to 25% (Elder 1985) In 2002 there were 21 uses (FDA 2002) and according to an industry survey in 2004 the current range of use concentrations is 0 000002% to 51% (CTFA 2004)

Table 24 presents the available use and concentration information The most recent information now constitutes the present practices of use

²⁴Available for review: Director, Cosmetic Ingredient Review, 1101 17th Street, NW, Suite 412, Washington, DC 20036-4702, USA

TABLE 23
Historical and current cosmetic product uses and concentrations for Sodium Lauryl Sulfoacetate

Product category	1981 uses (Elder 1987)	2002 uses (FDA 2002)	1981 concentrations (Elder 1987) %	2004 concentrations (CTFA 2004) %
Baby care				
Lotions, oils, powders, and creams	—	—	—	1
Bath				
Oils, tablets and salts	1	13	>1–5	5–21
Soaps and detergents	—	—	—	0.6–4
Bubble baths	85	21	>1–>50	6–10
Other bath	—	27	—	6–10
Fragrances				
Other fragrances	—	1	—	2
Noncoloring hair care				
Shampoos	—	1	—	1–5
Hair coloring				
Bleaches	—	2	—	—
Nail care				
Other nail care	—	—	—	4
Oral hygiene				
Dentifrices	3	1	>0.1–5	—
Other oral hygiene	—	—	—	0.7*
Personal hygiene				
Douches	—	—	—	2
Other personal hygiene	1	—	>0.1–1	2
Shaving				
Shaving cream	—	—	—	2
Skin care products				
Cleansing creams, lotions, etc	2	2	>1–25	4
Body and hand skin care	—	—	—	2
Foot powders and sprays	—	—	—	3
Other skin care	1	—	>5–10	—
Total uses/ranges for Sodium Lauryl Sulfoacetate	93	68	>0.1–>50	0.6–21

*A denture cleanser

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²⁵ Available for review: Director, Cosmetic Ingredient Review, 1101 17th Street, NW, Suite 412, Washington, DC 20036-4702, USA

TABLE 24

Historical and current uses and use concentrations for Sodium Sesquicarbonate, Sodium Bicarbonate, and Sodium Carbonate

Product category	1981 uses (Elder 1987)	2002 uses (FDA 2002)	1981 concentrations (Elder 1987) (%)	2004 concentrations (CTFA 2004) (%)
<i>Sodium Sesquicarbonate</i>				
Bath				
Oils, tablets, and salts	24	16	>1–50	2–90
Soaps and detergents	—	2	—	—
Bubble baths	68	2	>5–50	18
Capsules	2	—	>10–25	—
Other bath	11	2	>5–50	10–35
Fragrances				
Other fragrances	1	1	>5–10	—
Noncoloring hair care				
Straighteners	1	—	>50	—
Permanent waves	2	—	>1–10	—
Personal hygiene				
Other personal hygiene	2	1	>5–10	—
Skin care				
Foot powders and sprays	—	—	—	35–59
Total uses/ranges for Sodium Sesquicarbonate	111	24	>1–50	2–90
<i>Sodium Bicarbonate</i>				
Baby care				
Lotions, oils, powders, and creams	—	1	—	5
Bath				
Oils, tablets, and salts	1	7	<5–10	30–64
Soaps and detergents	—	2	—	25–54
Bubble baths	4	—	>10–25	5–52
Capsules	—	—	—	49
Other bath	—	—	—	1–64
Eye makeup				
Eyebrow pencils	—	—	—	0 2
Eyeliner	2	1	≤0 1–1	0 04–0 1
Mascara	—	6	—	0 2
Other eye makeup	—	1	—	—
Fragrance				
Powders	5	9	>0 1–10	20
Noncoloring hair care				
Conditioners	—	—	—	5
Straighteners	1	—	>0 1–1	—
Permanent waves	5	3	≤0 1–1	10
Shampoos	—	—	—	0 09
Other noncoloring hair care	1	—	>1–5	—
Hair-coloring products				
Dyes and colors	—	8	—	—
Bleaches	1	—	>25–50	0 1–10
Makeup				
Foundations	—	—	—	0 09
Lipsticks	—	—	—	0 03–1
Nail care				
Other	—	—	—	39

TABLE 24

Historical and current uses and use concentrations for Sodium Sesquicarbonate, Sodium Bicarbonate, and Sodium Carbonate
(Continued)

Product category	1981 uses (Elder 1987)	2002 uses (FDA 2002)	1981 concentrations (Elder 1987) (%)	2004 concentrations (CTFA 2004) (%)
Oral hygiene				
Dentifrices	5	10	>1–50	3–95
Mouthwashes and breath fresheners	—	2	—	0 1
Other oral hygiene	—	1	—	0 5
Personal hygiene				
Underarm deodorants	2	—	>1–5	0 01–15
Douches	4	2	≤0 1–25	—
Feminine deodorants	—	2	—	—
Other personal hygiene	4	3	≤0 1–25	0 07–56
Shaving				
Shaving cream	—	—	—	0 006
Other shaving	1	1	≤0 1	—
Skin care				
Cleansing creams, lotions, etc	—	—	—	0 04–26
Face and neck skin care	—*	—	—*	0 01–7
Body and hand skin care	—	—	—	10
Foot powders and sprays	—	4	—	25–56
Moisturizers	—	—	—	0 4
Paste masks/mud packs	3	1	≤0 1–50	61
Skin fresheners	2	2	≤0 1–10	—
Other skin care	4	4	>10–25	2–5***
Suntan products				
Suntan gels, creams, liquids, and sprays	—	—	—	0 2
Total uses/ranges for Sodium Bicarbonate	45	70	≤0 1–50	0 006–95
	<i>Sodium Carbonate</i>			
Bath				
Oils, tablets, and salts	—	4	—	40–51
Soaps and detergents	2	1	>0 1–1	3–32
Bubble baths	4	—	>10–25	7–39
Other	—	—	—	0 009–39
Eye makeup				
Eyebrow pencils	—	—	—	0 2
Eye shadow	—	—	—	0 3
Eye lotions	—	—	—	0 004
Mascara	—	—	—	0 2
Fragrances				
Colognes and toilet waters	—	—	—	0 03
Noncoloring hair care				
Conditioners	1	2	>0 1–1	0 01
Straighteners	1	—	>1–5	—
Permanent waves	1	1	>1–5	—
Shampoos	2	1	>0 1–1	0 08
Tonics, dressings, etc	—	—	—	0 000002–0 01
Wave sets	—	—	—	1

(Continued on next page)

TABLE 24

Historical and current uses and use concentrations for Sodium Sesquicarbonate, Sodium Bicarbonate, and Sodium Carbonate
(Continued)

Product category	1981 uses (Elder 1987)	2002 uses (FDA 2002)	1981 concentrations (Elder 1987) (%)	2004 concentrations (CTFA 2004) (%)
Hair coloring				
Dyes and colors	1	2	>1–5	0.1–0.6
Rinses	—	—	—	0.02
Bleaches	2	—	>0.1–10	25
Other hair coloring	—	—	—	1
Makeup				
Blushers	—	—	—	0.03
Foundations	1	1	≤0.1	0.3
Lipsticks	—	3	—	—
Nail care				
Other nail care	—	—	—	0.6
Oral hygiene				
Dentifrices	—	—	—	2
Other oral hygiene	—	—	—	22***
Personal hygiene				
Underarm deodorants	—	—	—	0.002
Douches	1	—	>5–10	—
Other	3	2	>1–5	—
Skin care				
Cleansing creams, lotions, etc	2	1	≤0.1	0.02–0.2
Face and neck skin care	—*	—	—*	0.008
Body and hand skin care	—	1	—	—
Moisturizers	2	2	≤0.1	—
Skin fresheners	1	—	≤0.1	—
Hormone preparations**	1	N/A**	≤0.1	N/A**
Total uses/ranges for Sodium Carbonate	25	21	≤0.1–25	0.000002–51

*This category was combined when the original safety assessment was performed and is now two separate categories

**No longer included as a cosmetic product category

***Denture cleanser

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STEARYL ALCOHOL, OLEYL ALCOHOL, AND OCTYLDODECANOL

A safety assessment of Stearyl Alcohol, Oleyl Alcohol, and Octyldodecanol was published in 1985 with the conclusion "safe as currently used in cosmetic products" (Elder 1985). New studies, along with the updated information in Table 25 regarding uses and used concentrations, were considered by the CIR Expert Panel. The Panel determined not to reopen this safety assessment.

Stearyl Alcohol was used in 425 cosmetic products in 1981, based on voluntary reports provided to FDA by industry with concentrations ranging from $\leq 0.1\%$ to 50% (Elder 1985). In 2002, Stearyl Alcohol was reportedly used in 1063 cosmetic products (FDA 2002). Concentration of use data from an industry survey in 2003 indicated that Stearyl Alcohol was used in a range from 0.002% to 56% (CTFA 2003).

The Panel noted that the Hannuksela (1988) report reviewed the previous literature which included a report of positive patch test reactions to Stearyl Alcohol as high as 44% . Although this information raised some concern, Hannuksela (1988) did report current data with a frequency of 11 positive tests out of over 1000 patch tests performed, a low frequency consistent with current experience.

Oleyl Alcohol was used in 1018 cosmetic products in 1981, with concentrations ranging from $\leq 0.1\%$ to $>50\%$ (Elder 1985). In 2002, Oleyl Alcohol was used in 343 cosmetic products (FDA 2002). Concentration of use data from a 2003 survey indicated that Oleyl Alcohol was used in a range from 0.0002% to 18% (CTFA 2003).

Although Tosti et al. (1996) reported a high proportion of 34 patients as positive to Oleyl Alcohol in a patch test, the Panel indicated that such reactions are not seen in their experience.

Octyldodecanol was used in 371 cosmetic products in 1981, with concentrations ranging from $\leq 0.1\%$ to $>50\%$ (Elder 1985). In 2002, Octyldodecanol was used in 814 cosmetic products (FDA 2002). Concentration of use data from 2003 indicated that Octyldodecanol was used in a range from 0.006% to 85% (CTFA 2003).

Table 25 presents the available use information for Stearyl Alcohol, Oleyl Alcohol, and Octyldodecanol. The most current information now represents the present practices of use.

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TOLUENE

A safety assessment of Toluene was published in 1987 with the conclusion that Toluene "is safe for cosmetic use at the present practices of use and concentration" despite limited skin exposure data (Elder 1987). Since then a large number of studies

²⁶ Available for review: Director, Cosmetic Ingredient Review, 1101 17th Street, NW, Suite 412, Washington, DC 20036-4702, USA

TABLE 25

Historical and current cosmetic product uses and concentrations for Stearyl Alcohol, Oleyl Alcohol, and Octyldodecanol

Product category	1981 uses (Elder 1985)	2002 uses (FDA 2002)	1981 concentrations (Elder 1985) %	2003 concentrations (CTFA 2003) %
<i>Stearyl Alcohol</i>				
Baby care				
Lotions, oils, powders, and creams	2	9	>0 1–1	0 6–2
Other baby care	—	1	—	2
Bath				
Soaps and detergents	—	1	—	0 06
Bubble baths	—	—	—	2
Other bath	—	1	—	1–6
Eye makeup				
Eyebrow pencils	1	—	>1–5	3
Eyeliners	—	3	—	—
Eye shadow	24	6	≤0 1–1	8
Eye lotions	—	5	—	0 4–0 5
Eye makeup remover	—	—	—	0 9
Mascara	2	5	>0 1–1	0 2–2
Other eye makeup	2	9	≤0 1–1	5
Fragrances				
Perfumes	—	—	—	2
Powders	—	1	—	—
Sachets	26	1	>0 1–25	1
Other fragrances	—	8	—	2
Noncoloring hair care				
Conditioners	46	174	≤0 1–10	0 02–8
Straighteners	2	7	>0 1–1, >5–10	2
Permanent waves	5	4	≤0 1–1	3
Rinses	21	4	≤0 1–5	3–5
Shampoos	1	23	>0 1–1	0 1–5
Tonics, dressings, etc	—	9	—	1–5
Other noncoloring hair care	—	3	—	1–5
Hair coloring				
Dyes and colors	1	259	>0 1–1	—
Tints	—	—	—	4
Rinses	—	—	—	2–5
Lighteners with color	—	1	—	—
Bleaches	5	25	>0 1–5	—
Other hair coloring	2	1	>1–5	2
Makeup				
Blushers	15	—	≤0 1–1	2
Foundations	8	32	>0 1–1	0 8–3
Leg and body paints	3	—	>0 1–1	—
Lipsticks	3	2	≤0 1–1	0 2–3
Makeup bases	63	12	≤0 1–5	0 6
Rouges	1	1	≤0 1	—
Makeup fixatives	1	2	≤0 1	—
Other makeup	2	6	≤0 1–1	0 5–5
Nail care				
Cuticle softeners	2	1	>0 1–1	2

TABLE 25

Historical and current cosmetic product uses and concentrations for Stearyl Alcohol, Oleyl Alcohol, and Octyldodecanol
(Continued)

Product category	1981 uses (Elder 1985)	2002 uses (FDA 2002)	1981 concentrations (Elder 1985) %	2003 concentrations (CTFA 2003) %
Creams and lotions	1	2	>1-5	1
Other nail care	—	1	—	6
Personal hygiene				
Underarm deodorants	3	8	>25-50	13-25
Douches	—	—	—	0 1
Other personal hygiene	10	66	>1-5, >10-25	—
Shaving				
Aftershave lotions	—	5	—	0 2-3
Beard softeners	1	—	>5-10	—
Preshave lotions	—	—	—	1
Shaving cream	6	7	>0 1-5	0 2-3
Other shaving	2	—	≤0 1-1	2
Skin care				
Cleansing creams, lotions, etc	39	52	≤0 1-10	0 5-8
Depilatories	6	1	>1-5	1
Face and neck skin care	36*	19	≤0 1-10*	1-8
Body and hand skin care	—	96	—	0 002-9
Foot powders and sprays	—	3	—	2-17
Moisturizers	50	106	≤0 1-10	0 002-56
Night skin care	12	14	≤0 1-5	0 002-3
Paste masks/mud packs	2	11	>0 1-5	0 8-6
Skin fresheners	1	2	>0 1-1	—
Other skin care	9	31	≤0 1-10	0 02-12
Skin lighteners**	6	NA**	>0 1-10	NA**
Suntan products				
Suntan gels, creams, liquids, and sprays	2	3	>0 1-1, >5-10	1-4
Indoor tanning preparations	1	19	>1-5	2-3
Other	—	1	—	0 3
Total uses/ranges for Stearyl Alcohol	425	1063	≤0 1-50	0 002-56
		<i>Oleyl Alcohol</i>		
Bath				
Oils, tablets, and salts	17	1	≤0 1-25	—
Soaps and detergents	—	2	—	0 0003
Bubble baths	1	—	>1-5	—
Capsules	1	—	>5-10	1-5
Other bath	3	—	>1-5	—
Eye makeup				
Eyebrow pencils	1	—	>5-10	—
Eyeliners	15	5	>1-25	0 4-0 5
Eye shadow	124	5	≤0 1-25	1
Mascara	26	2	>1-5	—
Other eye makeup	8	2	>0 1-25	—
Fragrances				
Colognes and toilet waters	2	—	>0 1-1	—
Perfumes	5	1	≤0 1, >1-5, >10-25	5
Sachets	2	1	>1-5	—
Other fragrances	9	1	>0 1-5	1-5

(Continued on next page)

TABLE 25

Historical and current cosmetic product uses and concentrations for Stearyl Alcohol, Oleyl Alcohol, and Octyldodecanol
(Continued)

Product category	1981 uses (Elder 1985)	2002 uses (FDA 2002)	1981 concentrations (Elder 1985) %	2003 concentrations (CTFA 2003) %
Noncoloring hair care				
Conditioners	9	26	>0 1–5	0 3–3
Sprays/aerosol fixatives	—	3	—	—
Straighteners	4	9	>1–5	1
Permanent waves	—	—	—	3
Rinses	—	—	—	18
Tonics, dressings, etc	4	6	>0 1–5	0 3–4
Other noncoloring hair care	1	2	>1–5	—
Hair coloring				
Dyes and colors	63	143	>1–5, >10–25	6–8
Tints	13	—	>10–25	—
Bleaches	2	2	>1–5	—
Other hair coloring	—	1	—	—
Makeup				
Blushers	13	2	>1–>50	1–10
Face powders	1	—	>1–5	—
Foundations	5	5	>0 1–5	0 5–5
Lipsticks	633	82	≤0 1–> 50	—
Makeup bases	2	—	>1–5, >10–25	—
Rouges	3	—	>1–5, >10–25	—
Other makeup	10	5	>5–25	—
Nail care				
Basecoats and undercoats	—	1	—	—
Nail polish and enamel removers	1	—	>1–5	—
Personal hygiene				
Underarm deodorants	2	—	>1–5	0 0005
Feminine deodorants	1	1	>25–50	0 1
Other personal hygiene	2	2	>0 1–5	—
Shaving products				
Aftershave lotions	2	2	>1–5	0 05
Preshave lotions	1	1	>0 1–1	—
Skin care				
Cleansing creams, lotions, etc	2	1	>1–5	—
Face and neck skin care	6*	2	≤0 1–10*	0 0002–3
Body and hand skin care	—	6	—	0 05
Foot powders and sprays	—	—	—	2
Moisturizers	8	9	≤0 1–25	4
Night skin care	2	1	>1–25	3
Paste masks/mud packs	2	2	≤0 1–5	—
Skin fresheners	2	6	≤0 1–1	—
Other skin care	4	—	≤0 1–25	3
Hormone preparations**	1	NA**	>10–25	NA**
Suntan products				
Suntan gels, creams, liquids and sprays	5	3	>0 1–10	—
Total uses/ranges for Oleyl Alcohol	1018	343	≤0 1–>50	0 0002–18

TABLE 25

Historical and current cosmetic product uses and concentrations for Stearyl Alcohol, Oleyl Alcohol, and Octyldodecanol
(Continued)

Product category	1981 uses (Elder 1985)	2002 uses (FDA 2002)	1981 concentrations (Elder 1985) %	2003 concentrations (CTFA 2003) %
<i>Octyldodecanol</i>				
Bath				
Oils, tablets, and salts	4	8	>5–10	1–30
Soaps and detergents	1	—	≤0.1	—
Eye makeup				
Eyebrow pencils	1	10	>5–10	4
Eyeliner	14	202	>0.1–10	3–7
Eye shadow	82	17	>1–25	0.1–15
Eye lotions	1	—	>25–50	—
Eye makeup remover	3	3	>1–5, >10–25	5
Mascara	1	—	>1–5	1–3
Other eye makeup	4	20	>5–25	0.1
Fragrances				
Perfumes	3	—	>25–50	—
Powders	4	—	>0.1–1	0.3
Sachets	6	—	>25–50	—
Other fragrances	1	1	>5–10	—
Noncoloring hair care				
Conditioners	3	11	>0.1–5	3–15
Sprays/aerosol fixatives	2	2	>0.1–5	—
Straighteners	—	—	—	0.5
Rinses	2	3	>0.1–1	4–6
Tonics, dressings, etc	—	—	—	0.5–20
Other noncoloring hair care	—	—	—	3
Hair coloring				
Dyes and colors	41	84	>5–25	10
Rinses	—	—	—	1
Color sprays	—	1	—	—
Other hair coloring	—	1	—	—
Makeup				
Blushers	6	9	>1–25	15–23
Face powders	6	6	>0.1–10	8
Foundations	—	20	—	5–16
Lipsticks	112	182	>0.1–>50	3–82
Makeup bases	1	1	>0.1–1	—
Rouges	1	2	>10–25	10–20
Makeup fixatives	1	—	>5–10	—
Other	2	23	>1–10	3–17
Nail care				
Polishes and enamels	—	—	—	2
Other nail care	—	—	—	0.06
Personal hygiene				
Underarm deodorants	1	3	>10–25	2–17
Douches	—	—	—	0.4
Other personal hygiene	1	2	>1–5	1

Continued on next page

TABLE 25

Historical and current cosmetic product uses and concentrations for Stearyl Alcohol, Oleyl Alcohol, and Octyldodecanol
(Continued)

Product category	1981 uses (Elder 1985)	2002 uses (FDA 2002)	1981 concentrations (Elder 1985) %	2003 concentrations (CTFA 2003) %
Shaving products				
Aftershave lotions	—	2	—	0.03–0.07
Preshave lotions	1	3	>0.1–1	—
Shaving cream	1	1	>0.1–1	0.4
Other	—	3	—	—
Skin care				
Cleansing creams, lotions, etc	9	22	≤0.1, >1–10	0.03–17
Face and neck skin care	23*	19	>0.1–50*	0.03–85
Body and hand skin care	14	59	≤0.1–25	0.006–6
Moisturizers	3	15	>1–5, >10–25	1
Night skin care	—	7	—	—
Paste masks/mud packs	7	24	>1–25	0.03–14
Other skin care	1	NA**	>1–5	NA**
Wrinkle smoothers**	4	NA**	>0.1–5	NA**
Skin lighteners**				
Suntan				
Suntan gels, creams, liquids, and sprays	3	9	>5–25	3–59
Other suntan	1	4	>1–5	—
Total uses/ranges for Octyldodecanol	371	814	≤ 0.1–>50	0.006–85

*This category was combined when the original safety assessment was performed and is now two separate categories

**No longer included as a cosmetic product category

have appeared in the scientific literature. These studies, along with updated information regarding uses and use concentrations, were considered by the CIR Expert Panel. Based on its consideration of the available data, the Panel decided to not reopen this safety assessment.

Toluene was used in 555 cosmetic products in 1981, based on voluntary reports provided to FDA by industry with concentrations ranging from >10%–50% (Elder 1987). In 2002, toluene was reportedly used in 59 cosmetic products (FDA 2002). Concentration of use data from an industry survey in 2003 indicated that Toluene was used in a range from 20% to 26% (CTFA 2004).

Table 26 provides the available data on usage and use concentration as a function of cosmetic product category. The most current information now represents the present practices of use.

Many of the newly available studies reported findings consistent with the data in the original safety assessment.

New findings of adverse effects included the following effects: Toluene was ototoxic for guinea pigs, interferes with performance and learning in neurotoxicity and behavior studies in animals, increased numbers of litters with low birth weights pups and adversely affected brain development, in cultured embryos exposed to Toluene, yolk sac diameter, crown-rump length, somite number, and protein concentration were significantly

TABLE 26

Historical and current cosmetic product uses and concentrations for Toluene

Product category	1984 uses (Elder 1987)	2002 uses (FDA 2002)	1984 concentrations (Elder 1987) %	2003 concentrations (CTFA 2004) %
Nail care				
Basecoats and undercoats	32	21	>10–50	—
Polishes and enamels	501	23	>10–50	20–25
Polish and enamel removers	—	2	—	—
Other nail care	22	13	>10–50	26
Total uses/ranges for Toluene	555	59	>10–50	20–26

reduced. A National Toxicology Program study concluded that there was no evidence of carcinogenic activity for Toluene in F344/N rats and B6C3F₁ mice.

The new adverse effects noted above appeared only at high exposures. They were found only when animals were exposed to Toluene vapor at a level of 10² to 10³ ppm. Such exposures, however, were not attainable in an exposure study of human subjects using nail polish—those values ranged from 1–4 ppm.

The Panel recognized that other data indicate adverse effects in the brain of Toluene abusers and in children born to mothers who inhaled Toluene during pregnancy. Again, the nature of these studies suggests high exposures and are not relevant to the use of Toluene in cosmetic products.

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TOLUENESULFONAMIDE/FORMALDEHYDE RESIN

A safety assessment of Toluenesulfonamide/Formaldehyde Resin (including Toluenesulfonamide/Formaldehyde Resin-80) was published in 1986 with the conclusion that these ingredients were safe as cosmetic ingredients in the present practices of use and concentration (Elder 1986). Studies available since that time, along with updated information regarding uses and use concentrations, were considered by the CIR Expert Panel. Based on its consideration of the available data, the Panel decided to not reopen this safety assessment.

The terminology for this ingredient in the *International Cosmetic Ingredient Dictionary and Handbook* has changed—Tosylamide/Formaldehyde Resin is the current terminology (Gottschalck and McEwen 2004).

TABLE 27

Historical and current cosmetic product uses and concentrations for Tosylamide/Formaldehyde Resin

Product category	1981 uses (Elder 1986)	2002 uses (FDA 2002)	1981 use concentrations (Elder 1986) %	2003 use concentrations (CTFA 2004) %
<i>Tosylamide/Formaldehyde Resin</i>				
Nail care products				
Basecoats and undercoats	31	—	1–10	8–11
Nail polishes and enamels	172	29	≤0 1–25	7–13
Other	8	—	1–10	7–8
Total uses/ranges for Tosylamide/Formaldehyde Resin	211	29	≤0 1–25	7–13
<i>Tosylamide/Formaldehyde Resin-80</i>				
Nail care products				
Basecoats and undercoats (44)	5	—	1–10	—
Nail polishes and enamels (767)	344	—	≤0 1–25	—
Other (50)	7	—	≤0 1–25	—
Total uses/ranges for Tosylamide/Formaldehyde Resin-80	356	29	≤0 1–25	—

Tosylamide/Formaldehyde Resin was used in 211 cosmetic products in 1981, based on voluntary reports provided to FDA by industry with concentrations ranging from ≤0 1%–25% (Elder 1986). In 2002, stearyl alcohol was reportedly used in 29 cosmetic products (FDA 2002). Concentration of use data from an industry survey in 2003 indicated that Toluene was used in a range from 7%–13% (CTFA 2004).

Tosylamide/Formaldehyde Resin-80 was used in 356 cosmetic products in 1981, based on voluntary reports provided to FDA by industry with concentrations ranging from ≤0 1%–25% (Elder 1986). In 2002, there were no reports of use (FDA 2002), nor did an industry survey in 2003 indicate any current use concentrations (CTFA 2004).

Table 27 provides the available data on usage and use concentration as a function of cosmetic product category. The most current information now represents the present practices of use and concentration.

Case reports of allergic reaction to nail care products containing Tosylamide/Formaldehyde Resin were consistent with the data in the original safety assessment.

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TRAGACANTH GUM

A safety assessment of Tragacanth Gum was published in 1987 with the conclusion that these ingredients were safe as cosmetic ingredients in the present practices of use and concentration (Elder 1987). Studies available since that time, along with updated information regarding uses and use concentrations, were considered by the CIR Expert Panel. Based on its consideration of the available data, the Panel decided to not reopen this safety assessment.

²⁸ Available for review: Director, Cosmetic Ingredient Review, 1101 17th Street, NW, Suite 412, Washington, DC 20036-4702, USA.

TABLE 28
Historical and current cosmetic product uses and concentrations for *Astragalus Gummifer* Gum

Product category	1981 uses (Elder 1987)	2002 uses (FDA 2002)	1981 concentrations (Elder 1987) %	2004 concentrations (CTFA 2004) %
Eye makeup				
Eye shadow	3	—	≤0.1	—
Noncoloring hair care				
Conditioners	—	1	≤0.1	—
Tonics, dressings, etc	1	2	>0.1–1	≤0.01
Wave Sets	—	1	—	—
Hair coloring				
Hair Bleaches	2	1	>1–5	≤3
Makeup				
Blushers	2	—	>1–5	—
Face Powders	6	—	≤0.1–1	—
Foundations	1	—	>0.1–1	—
Rouges	1	—	>0.1–1	—
Oral hygiene				
Dentifrices	2	2	>0.1–5	—
Shaving				
Aftershave lotions	1	—	>0.1–1	—
Pre shave lotions	1	—	>0.1–1	—
Skin care				
Cleansing creams, lotions, etc	1	—	>0.1–1	—
Face and neck skin care	—	—	—	—
Body and hand skin care	2*	—	>0.1–1*	—
Moisturizers	1	—	>0.1–1	—
Paste masks/mud packs	5	1	>0.1–10	—
Total uses/ranges for <i>Astragalus Gummifer</i> Gum	29	8	≤0.1–10	≤0.01%–≤3

*This category was combined when the original safety assessment was performed and is now two separate categories

The terminology for this ingredient in the *International Cosmetic Ingredient Dictionary and Handbook* has changed—*Astragalus Gummifer* Gum is the current terminology (Gottschalck and McEwen 2004).

Astragalus Gummifer Gum was used in 29 cosmetic products in 1981, based on voluntary reports provided to FDA by industry with concentrations ranging from ≤0.1% to 10% (Elder 1987). In 2002, stearyl alcohol was reportedly used in 8 cosmetic products (FDA 2002). Concentration of use data from an industry survey in 2004 indicated that *Astragalus Gummifer* Gum was used at concentrations from ≤0.01% to ≤3% (CTFA 2004).

Table 28 provides the available data on usage and use concentration as a function of cosmetic product category. The most current information now represents the present practices of use and concentration.

In the original safety assessment, this ingredient was described as derived from various *Astragalus* species, principally *Astragalus gummifer*. More recent information suggests that *Astragalus microcephalus* may be another source of this gum. The Panel suggested that the *International Cosmetic Ingredient Dictionary and Handbook* should be updated to include specific

mention of *Astragalus Microcephalus* Gum, and a new name adopted, if needed.

The Panel noted that pesticide impurities may form part of the composition of this plant-derived ingredient and has advised industry that the total (polychlorinated biphenyl) PCB/pesticide contamination should be limited to not more than 40 ppm, with not more than 10 ppm for any specific residue. The following limitations for other impurities were also recommended: arsenic (3 mg/kg max), heavy metals (0.002% max), and lead (5 mg/kg max).

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VINYL ACETATE/CROTONIC ACID COPOLYMER

A safety assessment of the Vinyl Acetate/Crotonic Acid Copolymer in 1983 concluded that this ingredient is considered safe as a cosmetic ingredient under present practices of product and concentration use (Elder 1983). New studies, along with updated information regarding types and concentrations of use, were considered by the CIR Expert Panel. The Panel determined to not reopen this safety assessment.

The terminology for this ingredient in the *International Cosmetic Ingredient Dictionary and Handbook* has changed—VA/Crotonates Copolymer is the current terminology (Gottschalk and McEwen 2004).

VA/Crotonates Copolymer was used in 55 cosmetic products in 1976, based on voluntary reports provided to FDA by industry with concentrations ranging from >0.01% to 25% (Elder 1986). In 2002, VA/Crotonates Copolymer was used in 38 cosmetic products (FDA 2002). Concentration of use data from an industry survey in 2003 indicated that this ingredient was used at concentrations from 0.05% to 11% (CTFA 2003).

Table 29 presents the available use information for VA/Crotonates Copolymer. The most recent information now constitutes the present practice of use and concentration.

The CIR Expert Panel acknowledged the use of Vinyl Acetate/Crotonic Acid Copolymer in aerosol hair sprays. The effects of inhaled aerosols depend on the specific chemical species, the concentration, the duration of exposure, and site of deposition within the respiratory system. Particle size is the most important factor affecting the location of deposition (Jensen and O'Brien 1993). The mean aerodynamic diameter of pump hair spray particles is $\geq 80 \mu$, and the diameter of anhydrous hair spray particles is 60 to 80μ . Typically less than 1% are below 10μ , which is the upper limit for respirable particles (Bower 1999). Based on the particle size, Vinyl Acetate/Crotonic Acid Copolymer would not be respirable in formulation. Therefore,

²⁹ Available for review: Director, Cosmetic Ingredient Review, 1101 17th Street, NW, Suite 412, Washington, DC 20036-4702, USA

TABLE 29
Historical and current cosmetic product uses and concentrations for VA/Crotonates Copolymer

Product category	1976 uses (Elder 1983)	2002 uses (FDA 2002)	1976 use concentrations (Elder 1983, 1976) (%)	2002 use concentrations (CTFA 2002b) (%)
Bath capsules	—	—	—	9
Eye makeup remover	—	—	—	9
Mascara	—	5	—	—
Hair conditioners	4	1	> 1–10	—
Hair sprays (aerosol fixatives)	30	9	> 01–25	2–11
Hair straighteners	—	1	—	—
Tonics, dressings, and other hair-grooming aids	2	10	> 1–5	0.05–4
Wave sets	9	3	> 1–5	2
Other hair preparations (noncoloring)	10	9	> 1–10	2–3
Hair dyes and colors (all types requiring caution statement and patch testing)	—	—	—	5
Moisturizing creams, lotions, and powders	—	—	—	2
Total uses/ranges for VA/Crotonates Copolymer	55	38	> 0.01–25	0.05–11

the Panel was not concerned about inhalation as a route of absorption.

Although there were reports associating vinyl acetate with nasopharyngeal carcinoma in rat inhalation studies, the amount of residual vinyl acetate monomer in VA/Crotonates Copolymer was below the no observed effect level. Additionally, studies show that the reported carcinogenicity of vinyl acetate in rats is through a nongenotoxic mechanism. Occupational studies in which workers were exposed to vinyl acetate ranging from 5 to 10 ppm, with intermittent exposures near 50 ppm and acute exposures to 300 ppm, showed no long-term chronic effects. These data support the CIR Expert Panel's confidence that vinyl acetate is not a concern in the safety of VA/Crotonates Copolymer.

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³⁰Available for review: Director, Cosmetic Ingredient Review, 1101 17th Street, NW, Suite 412, Washington, DC 20036-4702, USA.

TABLE 30
Historical and current cosmetic product uses and concentrations for Zinc Phenolsulfonate

Product category	1986 uses (CIR 1986)	2002 uses (FDA 2002)	1981 concentrations (CIR 1986) (%)	2004 concentrations (CTFA 2004) (%)
Fragrances				
Powders	5	1	>0 1–5	—
Personal hygiene				
Underarm deodorants	40	15	>0 1–5	4
Shaving				
Aftershave lotions	4	2	>0 1–5	—
Shaving cream	3	—	—	—
Skin care				
Skin cleansing creams, lotions, liquids, and pads	2		>0 1–5	—
Body and hand skin care preparations	—	2	—	—
Foot powders and sprays	—	1	—	3
Moisturizers	1	1	≤0 1	—
Paste masks/mud packs	1	—	>1–5	—
Skin fresheners	9	—	≤0 1–5	—
Other	2	1	1–5	—
Total uses/ranges for Zinc Phenolsulfonate	67	23	≤0 1–5	3–4

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ZINC PHENOLSULFONATE

A safety assessment of Zinc Phenolsulfonate published in 1986 concluded that this ingredient is considered safe as a cosmetic ingredient under present practices of product and concentration use (Elder 1986). New studies, along with updated information regarding types and concentrations of use, were considered by the CIR Expert Panel. The Panel determined to not reopen this safety assessment.

Zinc Phenolsulfonate was used in 67 cosmetic products in 1981, based on voluntary reports provided to FDA by industry

with concentrations ranging from ≤0.1 to 5% (Elder 1986). In 2002, Zinc Phenolsulfonate was used in 23 cosmetic products (FDA 2002). Concentration of use data from an industry survey in 2004 indicated that this ingredient was used at concentrations from 3 to 4% (CTFA 2004).

Table 30 presents the available use information for Zinc Phenolsulfonate. The most recent information now constitutes the present practice of use and concentration.

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³¹Available from the Director, Cosmetic Ingredient Review 1101 17th Street, NW Suite 412, Washington DC 20036, USA.

