

# Annual Review of Cosmetic Ingredient Safety Assessments: 2007-2010

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## Keywords

cosmetics, hair dyes, review, safety

This Annual Review of Cosmetic Ingredient Safety Assessments updates and affirms the findings of the Cosmetic Ingredient Review (CIR) Expert Panel's assessment of almost 30 compounds used in cosmetic ingredients. The review also summarizes new findings from epidemiology studies of hair dyes.

The CIR Expert Panel's re-review process is intended to uncover any new data since the last safety assessment. In some cases, newly available data are largely redundant compared with the data available in the original safety assessment. In other cases, new data present new safety issues. If after considering the newly available information, the CIR Expert Panel decides to not reopen a safety assessment, this finding, along with any background material, is summarized and announced publicly. To assure that the scientific community is aware of any new information and the decision not to reopen, this Annual Review of Cosmetic Ingredient Safety Assessments is prepared.

A list of reference sources is provided after each ingredient re-review summary that updates the available published literature and includes any unpublished data made available since the original safety assessment.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 CIR Expert Panel has assessed the safety of over 2100 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*.

The ingredients the CIR Expert Panel reconsidered during the 2007-2010 period and did not reopen are:

Acetamide MEA  
5-Bromo-5-nitro-1,3-dioxane  
Butyl benzyl phthalate  
*t*-Butyl hydroquinone (TBHQ)  
Chlorhexidine, chlorhexidine dihydrochloride, chlorhexidine digluconate, chlorhexidine diacetate  
2-Chloro-*p*-phenylenediamine and 2-chloro-*p*-phenylenediamine sulfate

2,4-Diaminophenol and 2,4-diaminophenol dihydrochloride  
Diisopropylamine  
Disperse blue 1  
Disperse violet 1  
Ethyl hexanediol  
HC Blue No. 2  
HC Red No. 3  
HC Yellow No. 2  
Hydroxybenzomorpholine  
Isopropyl isostearate  
Lauramine oxide and stearamine oxide  
Methenamine  
1-Naphthol  
Phenoxyethanol  
Phenyl methyl pyrazolone  
*N*-Phenyl-*p*-phenylenediamine  
Polyoxymethylene urea  
Polyquaternium-7  
Quaternium-22  
Shellac  
Sodium and potassium bromate  
Stearpyrium chloride and lapyrium chloride

Among these are several cosmetic ingredients used in hair dye products (2-chloro-*p*-phenylenediamine and 2-chloro-*p*-phenylenediamine sulfate, 2,4-diaminophenol and 2,4-diaminophenol dihydrochloride, disperse blue 1, disperse violet 1, HC Blue No. 2, HC Red No. 3, HC Yellow No. 2, 1-naphthol, phenyl methyl pyrazolone, and *N*-phenyl-*p*-phenylenediamine).

## Hair Dye Epidemiology

As part of its continuing assessment of cosmetic ingredient safety, the CIR Expert Panel reviews all epidemiology studies

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on hair dyes. While the safety of individual hair dye ingredients are not addressed in epidemiology studies that seek to determine links, if any, between hair dye use and disease, such studies do provide broad information. The CIR Expert Panel has developed an approach in which a given hair dye ingredient is categorized into groupings that are relevant to the epidemiology data; for example, permanent or oxidative versus semipermanent or nonoxidative.

The epidemiology studies reviewed by the Expert Panel are summarized on the CIR Web site (<http://www.cir-safety.org/findings.shtml>); only a summary of these data are provided in a safety assessment of a specific hair dye ingredient.

Summaries of these studies the Panel reviewed during 2007-2010 are presented by the outcome studied.

### Bladder Cancer

Bolt and Golka<sup>1</sup> reviewed the published literature on bladder cancer risk and personal use of hair dyes (17 publications) or occupation as a hairdresser and/or barber (23 publications) and concluded that, based on these studies, there seems to be no relevant bladder cancer risk from the use of oxidative hair dyes currently available. The authors could not rule out a bladder cancer risk in hairdressers who worked with oxidative hair dyes available decades ago.

Kelsh et al<sup>2</sup> conducted meta-analyses of primary epidemiology studies of hair dye use and bladder cancer and performed their own meta-analysis that examined regular use of hair dye, including permanent hair dye, gender, duration of use, lifetime extent of use, and use of dark hair dye. No association was found between any use of hair dye and bladder cancer among women, men, or both sexes. No statistically significant differences were found for permanent hair dye; duration of any use; duration of permanent hair dye use or lifetime application of any hair dye, permanent hair dye, or dark color hair dye.

### Lymphoma and Leukemia

Chiu et al<sup>3</sup> evaluated non-Hodgkin lymphoma subtypes defined according to the presence or absence of t(14:18) translocation from samples taken from a case-control study conducted in Nebraska during 1983-1986. Exposures in 65 t(14:18)-positive cases and 107 t(14:18)-negative cases were compared with those among 1432 controls. Among women, hair dye use was not associated with either t(14:18)-positive or t(14:18)-negative subtypes. (There were too few cases for meaningful analysis of hair dye use among men.) The use of permanent hair dye was associated with a 40% higher risk of the t(14:18)-negative subtype (odds ratio [OR] of 1.4). Hair dye use was not associated with follicular lymphoma or diffuse large B-cell lymphoma in either sex.

Morton et al<sup>4</sup> conducted a US population-based case-control study of non-Hodgkin lymphoma. In 1321 cases and 1057 controls, hair dye use included when hair dye use first occurred, use of permanent versus semipermanent dyes, frequency of use, color (black, brown, red, blonde) and intensity

of dye used (light vs dark), and total lifetime use. Blood samples obtained from 773 cases and 668 controls and buccal cell samples from 399 cases and 314 controls were used to extract DNA for analyzing *NAT1* and *NAT2* genotypes and *NAT2* acetylation phenotype.

The authors reported no evidence of increased non-Hodgkin lymphoma risk among women, who began hair dye use in or after 1980, or in men. For women whose year of first use was prior to 1980, the odds ratio (OR) for any permanent hair dye use was 1.3 (95% confidence interval [CI] 0.9-1.9); for permanent dark hair dye use was 1.3 (95% CI 0.9-2.0); and for intense tone (ie, black, dark brown, and dark blonde) permanent hair dye use was 1.6 (95% CI 0.9-2.7). For women whose year of first use was 1980 or later, the ORs, for each of the 3 groups listed above, were 0.9 (95% CI 0.6-1.4), 1.2 (95% CI 0.7-1.7), and 0.6 (95% CI 0.4-1.1), respectively.

The risk did not increase consistently with frequency of use, duration of use, or total lifetime use. Women with the *NAT2* slow acetylator phenotype or who had no copies of the *NAT1\*10* allele and used intense tone permanent hair dyes before 1980 did not have an increased risk of non-Hodgkin lymphoma (OR 1.5; 95% CI 0.6-3.6 and OR 1.5; 95% CI 0.7-3.3, respectively), but women with the *NAT2* rapid/intermediate acetylator phenotype or those carrying 1 or 2 copies of the *NAT1\*10* allele did have an increased risk (OR 3.3; 95% CI 1.3-8.6 and OR 2.5; 95% CI 0.9-7.6, respectively).

Zhang et al<sup>5</sup> concluded that there was an increased risk of non-Hodgkin lymphoma in women who started using hair dyes before 1980, but not in women who started use after 1980. They performed an evaluation of pooled data from 4 previous studies in which information on sex, duration of use, number of applications, dates of use, and type and color of the hair dye used was available and in which non-Hodgkin lymphoma was classified by histologic type. A total of 4461 cases and 5799 controls were included. In the analysis of non-Hodgkin lymphoma subtypes, there was an increased risk of follicular lymphoma and chronic lymphocytic leukemia/small lymphocytic lymphoma mainly in users who began use before 1980, but no increased risk of diffuse large B-cell lymphoma, marginal-zone lymphoma, or T cell lymphoma. For women who began use after 1980, an increased risk of follicular lymphoma only was suggested for users of dark hair dyes. Other comparisons failed to show the differences between risks of dark versus light hair dyes and permanent versus semipermanent hair dyes. In the analysis of subtypes, similar failures to show differences were present in the data.

Koutros et al<sup>6</sup> found no association between hair dye use and myeloma risk, semipermanent hair dye use, permanent dye use, or dark permanent hair dye use. The authors also reported no significant association of myeloma with use of hair dyes before age 30 years, use begun before 1980, >240 lifetime uses, or use of dark permanent dyes for  $\geq 28$  years. They conducted a population-based case-control study of 175 cases of multiple myeloma with 679 matched controls. Information on type and color of hair-coloring product, age at first use, age when the use

was stopped, duration of use, and frequency of use per year were obtained from interviews.

### Reproductive and Developmental Outcomes

Axmon and Rylander<sup>7</sup> conducted a cohort study of Swedish women, who had attended vocational schools for hairdressers (3137), and their sisters (3952) based on data obtained from Swedish national registries. Low-birth-weight (less than 2500 g), small for gestational age, and large for gestational age data were gathered from Swedish birth registries of infants born to the hairdressers (6223 infants) and their sisters (8388 infants). The authors reported no association between occupation as a hairdresser and increased risk of low-birth-weight or small for gestational age parameters. Among the infants born to the hairdressers' sisters, the distribution of birth weights were wider than that among the infants born to the hairdressers. For "large for gestational age" data, there was a reduced risk of women who had actually worked as hairdressers during at least 1 pregnancy. The infants born to these women also had a significantly lower mean birth weight (3387 g vs 3419 g;  $P = .033$ ).

Gallicchio et al<sup>8</sup> conducted a study of cosmetologists to determine whether they are at increased risk of poor pregnancy outcomes compared with women of the same age who are not cosmetologists. Participants were self-selected through mass mailing of questionnaires. Respondents to the survey had to be between 21 and 55 years of age and not have had a hysterectomy or oophorectomy. A cohort of 350 cosmetologists and 397 women in other occupations who self-reported that they met the inclusion criteria and had 5 or fewer singleton pregnancies were included. Outcome measures were miscarriage, stillbirth, and occurrence of maternal health conditions during pregnancy (preeclampsia, high blood pressure, and diabetes), hospitalization or physician-ordered bed rest during pregnancy, preterm labor, and premature delivery (before 37 weeks at delivery). The authors reported no statistically significant associations between occupation as a cosmetologist and any pregnancy outcomes after adjustment for age, race, education, and smoking and alcohol use at the time of pregnancy.

Halliday-Bell et al<sup>9</sup> identified all singleton births to hairdressers (10 662) and cosmetologists (2490) from the 1990-2004 Finnish Medical Birth Registry. Singleton births to teachers (18 594) were used as the control population. Data were obtained from the confidential registry on the parameters of sex distribution, low-birth-weight, small for gestational age, preterm delivery, and perinatal death. In comparing occupation as a hairdresser to that of a teacher, the authors reported a higher incidence of low-birth-weight, small for gestational age, preterm delivery, and perinatal death, but no difference in sex distribution. In comparing occupation as a cosmetologist to that of a teacher, the authors reported a higher incidence of small for gestational age and perinatal death but no difference in sex distribution, incidence of low birth weight, or preterm delivery. The authors concluded that occupation as a hairdresser or cosmetologist may reduce fetal growth and that occupation as a

hairdresser may also increase the incidence of preterm delivery and perinatal death.

Herd-Lojavio et al<sup>10</sup> conducted a retrospective cohort study of cosmetologists (15 003) compared with realtors (4246) or compared with the general population (12 171) using birth records in New York State from 1997 to 2003. From the birth records, the authors obtained information on low-birth-weight, small for gestational age, and preterm birth. The incidence of low-birth-weight (1500-2499 g) was higher for cosmetologists compared with realtors but not when compared with the general population. For nonwhite cosmetologists, the incidence of low-birth-weight was higher compared with realtors and the general population. No statistically significant differences were reported for any comparison of small for gestational age or preterm births.

Baste et al<sup>11</sup> conducted a cross-sectional study among women in Hordaland county in Norway. Among 10 512 women providing information by self-report, 221 were hairdressers. An association between occupation as a hairdresser and increased risk of infertility (OR 1.3; 95% CI 1.08-1.55) or spontaneous abortion (OR 1.31; 95% CI 1.07-1.60) were found. These associations were found primarily among those individuals who reported that they were never smokers.

### Other Outcomes

Mendelsohn et al<sup>12</sup> examined personal hair dye use and cancer risk in a prospective cohort of 73 366 Chinese women (29 076 hair dye users and 44 290 nonusers). Cancer diagnoses were ascertained through the Shanghai Cancer Registry in 1536 nonusers and 901 hair dye users. Self-administered questionnaires followed by interviews were used to gather data on use of hair dyes over the past 3 years, with follow-up questions about frequency of use over the past year and years of use for those individuals who answered "yes" to the initial question about recent hair dye use; the authors noted that hair dye color was not determined, but that most hair dye use would be expected to be dark hair dyes. The authors reported no significant association with hair dye use and overall cancer or for several common cancers, including breast cancer, lung cancer, stomach cancer, bladder cancer, hematopoietic cancer, including subtypes of non-Hodgkin lymphoma, multiple myeloma, and leukemia. The authors cautioned that the study is limited by small numbers of certain cancer types.

### Exposure Assessment

Ambrosone et al<sup>13</sup> evaluated DNA adducts in breast ductal epithelial cells isolated from breast milk obtained from 64 women. A questionnaire was used to determine prior hair dye use, meat intake, and tobacco exposure. The following were reported:

- 2-Amino-6-phenylimidazo[4,5-*b*]pyridine (PhIP)-DNA adducts (30 participants, mean detectable level of  $4.7 \pm 1.7$  adducts/107 nucleotides),

- Benzo[*a*]pyrene-7,8-diol-9,10-epoxide (BPDE)-adducts (13 participants, mean detectable level of  $1.7 \pm 0.7$  adducts/10 nucleotides), and
- 4-Amino biphenyl (4-ABP)-DNA adducts (18 participants, mean detectable level of  $4.7 \pm 2.2$  adducts/107 nucleotides).

No association was reported between PhIP-DNA adducts or BPDE-DNA adducts and either meat consumption or tobacco exposure. The authors did not present PhIP-DNA or BPDE-DNA adduct data as a function of hair dye exposure. The authors reported that the presence of 4-ABP-DNA adducts were associated with use of hair dyes in the previous year but the association was not statistically significant. Among the hair dye users, the OR for use 6 to 12 months prior to sample collection was 5.42 (95% CI 0.49-59.74) and for 0 to 6 months, the OR was 11.17 (95% CI 1.14-109.19).

For temporary hair dye users, the OR was 9.47 (95% CI 0.46-195.04) and for permanent hair dye users the OR was 8.20 (95% CI 0.94-71.83). Use of light hair dye colors had an OR of 18.12 (95% CI 1.45-226.83), medium colors had an OR of 5.61 (95% CI 0.35-90.35), and dark colors had an OR of 2.57 (95% CI 0.10-64.31).

The authors reported that rapid *NAT1* and *NAT2* genotypes were associated with an increase in PhIP-DNA adducts and 4-ABP-DNA adducts, compared with slow acetylator genotypes, and that the level of 4-ABP-DNA adducts was higher for rapid *NAT2* genotypes compared to rapid *NAT1* genotypes.

The authors did not provide data on BPDE-DNA adducts as a function of *NAT* genotype. The authors also did not present data on 4-ABP-DNA adducts as a function of meat consumption or tobacco exposure. The authors acknowledged that the small sample size resulted in wide CIs and limited the statistical power of the results.

Hueber-Becker et al<sup>14</sup> monitored the exposure of hairdressers to oxidative hair dyes under controlled conditions to determine whether the process of oxidative hair dye use produces measurable external and/or systemic exposure, and, if so, which parts of the process are responsible. [<sup>14</sup>C]-*p*-Phenylenediamine dihydrochloride was combined with a commercial product containing *p*-phenylenediamine dihydrochloride (4%), resorcinol (2%), and *m*-aminophenol (2%) in the dye component and a cream formulation developer with hydrogen peroxide (6%). In addition to the task of hair dye preparation and dyeing, the study monitored exposure during shampooing, rinsing, and conditioning and during hair cutting and drying. Six artificial human training heads with implanted human hair were used in a given day. One hairdresser performed the hair dye preparation and dyeing, a second hairdresser did the shampooing, and so on, and a third hairdresser did the cutting and drying—on all 6 heads. This process was repeated 6 times, involving a total of 18 hairdressers and 36 artificial human heads. Other than the mixing bowl, hair wash, and hair, recoveries were all less than 0.5% and most <0.1%.

Urinary excretion of radioactivity in the 18 hairdressers determined over 3 intervals (0-12 hours, 12-24 hours, and

24-48 hours) resulted in excretion values (all values below the limit of detection were given the value of the limit of detection) of  $<8.8 \pm 4.4$ ;  $<6.8 \pm 4.6$ , and  $<9.7 \pm 6.0$  mg [<sup>14</sup>C] *p*-phenylenediamine dihydrochloride equivalent. Excretion values per working day (including 6 complete procedures) was  $<25.3 \pm 5.2$  mg [<sup>14</sup>C] *p*-phenylenediamine dihydrochloride equivalent. For a 71-kg individual, the exposure was calculated to be  $<0.36$  mg/kg per day. The authors expressed uncertainty as to the source of this low level of measured systemic exposure. The authors noted that detectable air levels of radioactivity were found during the preparation and dyeing phase and the hair-cutting phase but not in the washing phase. In those individuals exposed to detectable air levels, urinary excretion was not elevated compared to individuals exposed to air samples with no detectable radioactivity.

### International Agency for Research on Cancer

In 2008, International Agency for Research on Cancer (IARC) issued new working group observations on bladder cancer and hematological cancers.<sup>15</sup> The working group considered 82 studies involving personal use of hair dyes and 85 studies of occupational exposures. They concluded that the data are insufficient (quality, consistency, or statistical power) to conclude the presence or absence of a causal link between personal use of hair dyes and cancer. They also reviewed animal studies and cited major limitations (qualitative and quantitative) that preclude concluding that hair dyes have carcinogenic effects in animals. Occupational exposure as a hairdresser, barber, or beautician was also assessed. The working group noted that such occupations may involve exposure to hair dyes, but that any risk cannot be attributed to hair dye exposure, but is linked to all exposures that individuals may experience in these occupations. With that caveat, the working group did find that exposures experienced in these occupations are probably carcinogenic.

### Discussion

In considering these data on many different end points, 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 end points based on lack of strength of the associations and inconsistency of findings. The Panel stated that use of direct hair dyes, while 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.

### Author's Note

All unpublished sources cited in these re-reviews are available from the Director, Cosmetic Ingredient Reivew, 1101 17th St., NW Suite 412 Washington, D.C. 20036 USA

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# Acetamide MEA

## Conclusion

In a 1993 safety assessment of acetamide monoethanolamine (MEA), the Cosmetic Ingredient Review (CIR) Expert Panel stated that acetamide MEA is considered safe up to a concentration of 7.5% in leave-on products and at the current practices of use in rinse-off products.<sup>1</sup> The Expert Panel reviewed updated information regarding product types and concentrations of use. No new information on acetamide MEA was found, and the Panel did not reopen this safety assessment. The Panel confirmed that acetamide MEA is safe as a cosmetic ingredient at concentrations not to exceed 7.5% in leave-on products and is safe in rinse-off products in the practices of use and concentration as given in Table 1.

## Discussion

The CIR Expert Panel noted that a safety assessment of MEA had been performed,<sup>2</sup> with the conclusion that MEA should be used only in rinse-off products at concentrations up to 5%. The Panel contrasted that conclusion with that of acetamide MEA for which leave-on use is considered safe up to a concentration of 7.5%. Because acetamide MEA is a stable ingredient on the skin, however, the Panel determined that the restriction to rinse-off products of MEA would not be applicable to acetamide MEA. The Panel agreed that the available skin sensitization studies at 7.5% supported leave-on use of acetamide MEA up to that concentration.

The Panel considered the possibility that the available data could support the safety of chemically similar ingredients.

**Table 1** Historical and Current Cosmetic Product Uses and Concentrations for Acetamide MEA

Product Category	1992 Uses <sup>1</sup>	2007 Uses <sup>3</sup>	1992 Concentrations, <sup>1</sup> %	2008 Concentrations, <sup>4</sup> %
Bath products				
Soaps and detergents	—	2	—	—
Other	3	—	—	—
Noncoloring hair care products				
Conditioners	60	69	25	0.01-3
Sprays/aerosol fixatives	—	11	—	—
Rinses	—	2	—	0.5
Shampoos	14	21	5	0.0001
Tonics, dressings, etc	12	16	10	0.03-0.3
Wave sets	7	2	5	—
Other <sup>a</sup>	3	9	—	0.2-5
Nail care products				
Other	—	1	—	—
Personal hygiene products				
Underarm deodorants	—	9	—	0.7
Skin care products				
Skin cleansing creams, lotions, liquids, and pads	—	4	—	0.06
Face and neck creams, lotions, powder, and sprays	— <sup>b</sup>	—	— <sup>b</sup>	0.2-3
Body and hand creams, lotions, powder, and sprays	—	7	—	—
Moisturizers	3	1	—	—
Night creams, lotions, powder, and sprays	—	3	—	—
Skin fresheners	—	1	—	—
Total uses/ranges for acetamide MEA	102	159	5-25	0.0001-5

<sup>a</sup> 0.2% in a leave-on conditioner; 0.7% in an oil treatment; 3% in a hair mask; and 5% in a nonaerosol hair spray.

<sup>b</sup> This category was combined when the original safety assessment was performed and is now 2 separate categories.

Because skin sensitization and skin penetration data are not available for these chemically similar ingredients, however, the decision was made that the safety test data in the original safety assessment support the safety of acetamide MEA only.

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## 5-Bromo-5-Nitro-1,3-Dioxane

### Conclusion

In its 1990 safety assessment of 5-bromo-5-nitro-1,3-dioxane,<sup>1</sup> the Cosmetic Ingredient Review (CIR) Expert Panel stated that this ingredient 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. The CIR Expert Panel considered newly available studies<sup>2,3</sup> and reviewed current usage,<sup>4</sup> including use concentrations.<sup>5</sup> The Expert Panel confirmed the safety of 5-bromo-5-nitro-1,3-dioxane at concentrations  $\leq 0.1\%$ , except under circumstances where its action with amines or amides can

result in the formation of nitrosamines or nitrosamides and did not reopen this safety assessment.

### Discussion

Current and historical usage and use concentration data are presented in Table 1. In 1988, it was reported by industry (to the US Food and Drug Administration [FDA] voluntary product reporting program) that 5-bromo-5-nitro-1,3-dioxane was used in 46 product formulations<sup>1</sup> at concentrations up to and including 1%. Currently, its use in 34 product formulations in specific product

**Table 1.** Historical and Current Cosmetic Product Uses and Concentrations for 5-Bromo-5-Nitro-1,3-Dioxane

Product Category	1988 Uses (Total Number of Products in Category) <sup>1</sup>	2007 Uses (Total Number of Products in Category) <sup>4</sup>	1988 Use Concentration Ranges <sup>1</sup> (%)	2007 Use Concentrations <sup>5</sup> (%)
Baby products				
Shampoos	–	1 (38)	–	–
Bath products	19 (1008)		≤0.1 and >0.1-1	–
OILS, tablets, and salts	–	1 (207)		–
Bubble baths	–	1 (256)		–
Noncoloring hair care products	24 (1315)		≤0.1 and >0.1-1	
Conditioners	–	6 (715)	–	–
Rinses	–	1 (46)	–	–
Shampoos	–	16 (1022)	–	0.04
Hair coloring products				
Dyes and colors	–	1 (1600)	–	–
Other	–	4 (73)	–	–
Skin care products	3 (2004)			
Personal hygiene products				
Soaps and detergents	–	2 (594)	–	–
Feminine hygiene products				
Other	–	1 (390)	–	–
Totals	46	38	≤0.1 and >0.1-1	0.04

Categories<sup>4,5</sup> is reported to FDA and an industry survey produced use concentration, 0.04%.

The CIR Expert Panel noted that safety concerns about 1,4-dioxane, which may be an impurity in some cosmetic ingredient preparations, do not exist for 5-bromo-5-nitro-1,3-dioxane because 1,4-dioxane is not an impurity, nor is it a breakdown product.

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# Butyl Benzyl Phthalate

## Conclusion

In a 1992 safety assessment of butyl benzyl phthalate, the Cosmetic Ingredient Review (CIR) Expert Panel<sup>1</sup> stated that this ingredient is safe as a cosmetic ingredient in the present practices of use and concentration. The Expert Panel reviewed newly available studies since that assessment,<sup>2-73</sup> along with statements/data from the cosmetics industry and the Food and Drug Administration indicating that butyl benzyl phthalate is not currently being used in cosmetic products. The Panel noted that though butyl benzyl phthalate is not being used in cosmetics, it would be considered safe in the current practices of use and concentration and did not reopen this safety assessment.

## Discussion

The Panel considers that this ingredient has been used as a plasticizer in cosmetic products. Butyl benzyl phthalate was used in 2 hair sprays (aerosol fixatives) in 1989, based on voluntary reports submitted to Food and Drug Administration (FDA)<sup>1</sup> by industry, with concentrations of use <1%. In 2006, there were no reported uses of butyl benzyl phthalate.<sup>74</sup> Similarly, data from an industry survey in 2007 indicated no reported uses of this ingredient.<sup>75</sup>

The available use and concentration data are given in Table 1 as a function of product category.

The Expert Panel recognizes that though there are no reported uses of butyl benzyl phthalate, it could be a

**Table I.** Historical and Current Cosmetic Product Uses and Concentrations for Butyl Benzyl Phthalate

Product Category (FDA 2006) <sup>74</sup>	1989 Uses <sup>1</sup>	Total Products in Category <sup>1</sup>	2006 Uses <sup>74</sup>	Total Products in Category <sup>74</sup>	1989 Concentrations <sup>1</sup> (%)	2007 Concentrations <sup>75</sup> (%)
Hair sprays (aerosol fixatives)	2	261	a	294	<1.0	b
Total uses/ranges for butyl benzyl phthalate	2		a		<1.0	b

Abbreviation: FDA, Food and Drug Administration.

<sup>a</sup> In FDA's voluntary reporting system, no uses reported for this category in 2006.

<sup>b</sup> In industry survey, no use concentrations reported for this category in 2007.

contaminant of other phthalates (ie, dimethyl phthalate, diethyl phthalate, and dibutyl phthalate) in cosmetic products due to the migration of butyl benzyl phthalate from the plastic container.

In consideration of the numerous studies on butyl benzyl phthalate (a reproductive toxicant) identified in the published literature since the final report on this ingredient was issued by the Expert Panel, studies relating to endocrine activity, reproductive toxicity, developmental toxicity, and carcinogenicity were of particular concern. The Panel noted that weak effects were reported in these studies, all of which were observed at high doses, compared to exposure to use concentrations of <1% butyl benzyl phthalate that have been associated with hair sprays and considered nontoxic. Regarding reproductive and developmental toxicities, the Panel considered that these studies demonstrate a no observable effect level. The Panel noted that these data, combined with recent information indicating that trace amounts (up to 100 ppm) of butyl benzyl phthalate have been detected in cosmetic products, suggest a wide margin of safety (MOS) that would preclude any risks to the health of consumers. An MOS calculation for butyl benzyl phthalate and the considerations used in determining the MOS<sup>75</sup> are discussed below.

The most appropriate no observable adverse effect level (NOAEL) is for developmental effects identified by the National Toxicology Program (NTP) Center for the Evaluation of Risks to Human Reproduction (CERHR).<sup>76</sup> The NOAEL for butyl benzyl phthalate, 182 mg/kg per d (mice) is from a study that was conducted by the NTP (1990),<sup>77</sup> and this NTP study is summarized in the published CIR final report on butyl benzyl phthalate.<sup>1</sup> It is important to note that an NOAEL of 185 mg/kg per d in Wistar rats<sup>78</sup> was also cited by Kavlock et al (2002).<sup>76</sup> However, the NOAEL of 182 mg/kg per d was used in the MOS calculation.

## Expected Exposure

### Hair Spray<sup>79</sup>

- 5.18 g/d
- 1% butyl benzyl phthalate in hair spray<sup>1</sup>
- 20% skin contact; from Personal Care Products Council worst case estimate (used in the 2002 dibutyl phthalate exposure estimate)
- 30% dermal absorption<sup>80</sup> (rat study 30% is the amount excreted in 7 days)

$$5.18 \text{ g/d} \times 1\% \times 20\% \times 30\% = 3.1 \text{ mg/d per } 60 \text{ kg} = 0.052 \text{ mg/kg per d}$$

## Margin of Safety Calculation

$$182 \text{ mg/kg per d} / 0.052 \text{ mg/kg per d} = 3500$$

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## t-Butyl Hydroquinone

### Conclusion

In a 1991 addendum to the safety assessment of *t*-butyl hydroquinone (TBHQ),<sup>1</sup> the Cosmetic Ingredient Review (CIR) Expert Panel presented an amended conclusion that this ingredient may be safely used in cosmetics at concentrations  $\leq 0.1\%$ ; the original safety assessment had been published earlier by Elder.<sup>2</sup> In 2007, the CIR Expert Panel reviewed newly available studies since that addendum,<sup>3-41</sup> along with updated information regarding types and concentrations of use. The CIR Expert Panel confirmed the amended conclusion and did not reopen the safety assessment of TBHQ.

### Discussion

The CIR Expert Panel noted that *t*-butyl hydroquinone is now called TBHQ.<sup>42</sup>

*t*-Butyl hydroquinone was used in 266 products in 1981, with concentrations of use ranging from  $\leq 0.1\%$  to 1%, based on voluntary reports submitted to FDA by industry.<sup>43</sup> In 2006, TBHQ was reportedly used in 59 cosmetic products.<sup>44</sup> Data from an industry survey<sup>45</sup> in 2007 indicated that TBHQ was used at concentrations ranging from 0.008% to 0.2%.

Historical and current product usage and use concentration data as a function of product category are given in Table 1.

The Panel, aware of new co-carcinogenicity and tumor-promoting activity data, indicated an ongoing concern

regarding the safety of use levels greater than the 0.1% limit established in the original safety assessment (Note: 1 current use concentration of 0.2% in hair dyes and colors was noted and is above what the Panel finds acceptable). New genotoxicity studies using both bacterial and mammalian systems reaffirmed the safety of TBHQ at concentrations up to 0.1%.

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**Table 1.** Historical and Current Cosmetic Product Uses and Concentrations for TBHQ

Product Category	1981 Uses (Total Number of Products in Product Category) <sup>43</sup>	2005 Uses (Total Number of Products in Product Category) <sup>44</sup>	1981 Concentrations (%) <sup>43</sup>	2007 Concentrations (%) <sup>45</sup>
Bath preparations				
Soaps and detergents	— <sup>a</sup> (421)	— <sup>a</sup> (594)	— <sup>a</sup>	0.005%
Eye makeup preparations				
Eye shadow	1 (2582)	— <sup>a</sup> (1061)	$\leq 0.1$	—
Fragrance preparations				
Colognes and toilet waters	7 (1120)	— <sup>a</sup> (948)	$\leq 0.1$	—
Perfumes	3 (657)	— <sup>a</sup> (326)	$\leq 0.1$	—

(continued)

Table 1. (continued)

Product Category	1981 Uses (Total Number of Products in Product Category) <sup>43</sup>	2005 Uses (Total Number of Products in Product Category) <sup>44</sup>	1981 Concentrations (%) <sup>43</sup>	2007 Concentrations (%) <sup>45</sup>
Hair-coloring preparations				
Hair dyes and colors	- <sup>a</sup> (1690)	25 (1600)	- <sup>a</sup>	0.2% <sup>b</sup> (after dilution)
Makeup preparations				
Blushers	3 (819)	6 (459)	≤0.1	-
Foundations	- <sup>a</sup> (324)	- <sup>a</sup> (530)	- <sup>a</sup>	0.05%
Lipsticks	242 (3319)	- <sup>a</sup> (1681)	≤0.1-1	0.04%
Makeup bases	- <sup>a</sup> (141)	1 (273)	- <sup>a</sup>	-
Rouges	2 (211)	- <sup>a</sup> (115)	≤0.1	-
Other makeup preparations	3 (530)	- <sup>a</sup> (304)	≤0.1	-
Personal hygiene products				
Underarm deodorants	- <sup>a</sup> (247)	- <sup>a</sup> (281)	- <sup>a</sup>	0.05%
Other personal hygiene products	- <sup>a</sup> (308)	8 (390)	- <sup>a</sup>	-
Skin care preparations				
Skin cleansing creams, lotions, liquids, and pads	- <sup>a</sup> (775)	- <sup>a</sup> (1009)	- <sup>a</sup>	0.008%
Depilatories	1 (32)	- <sup>a</sup> (49)	>0.1-1	-
Face and neck skin care preparations	- <sup>a</sup> (310)	10 (546)	- <sup>a</sup>	-
Body and hand skin care preparations	- <sup>a</sup> (840)	- <sup>a</sup> (992)	- <sup>a</sup>	0.02%
Moisturizers	4 (747)	1 (1200)	≤0.1	-
Paste masks (mud packs)	- <sup>a</sup> (271)	- <sup>a</sup> (312)	- <sup>a</sup>	0.02%
Other skin care preparations	- <sup>a</sup> (725)	7 (915)	- <sup>a</sup>	0.04%
Suntan preparations				
Suntan gels, creams, and liquids	- <sup>a</sup> (131)	1 (138)	- <sup>a</sup>	0.004%
Total uses/ranges for TBHQ	266	59	≤0.1-1	0.004%-0.2%

Abbreviations: TBHQ, t-butyl hydroquinone; FDA, Food and Drug Administration.

<sup>a</sup> Not reported. In some cases, ingredient uses were not reported to FDA in the voluntary industry product survey program; however, concentrations were provided. In other cases, the uses were reported, but no concentration was provided.

<sup>b</sup> The 0.2% concentration reported in hair dyes and colors exceeds panel recommendations.

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## Chlorhexidine, Chlorhexidine Diacetate, Chlorhexidine Dihydrochloride, and Chlorhexidine Digluconate

### Conclusion

In a 1993 safety assessment of chlorhexidine, chlorhexidine diacetate, chlorhexidine dihydrochloride, and chlorhexidine digluconate, the Cosmetic Ingredient Review (CIR) Expert Panel

stated that "chlorhexidine and its salts are safe for use in cosmetic products at concentrations up to 0.14% calculated as chlorhexidine free base; 0.19% as chlorhexidine diacetate; 0.20% as chlorhexidine digluconate; and 0.16% as chlorhexidine dihydrochloride."<sup>1</sup> The Expert Panel reviewed newly available

studies since that assessment (see references),<sup>2-24</sup> along with updated information regarding product types and concentrations of use and did not reopen this safety assessment. The Panel confirmed that chlorhexidine, chlorhexidine diacetate, chlorhexidine dihydrochloride, and chlorhexidine digluconate are safe as cosmetic ingredients in the practices of use and concentration as given in Table 1. Chlorhexidine diacetate is not currently reported to be used, but it is expected to be safe with similar use.

## Discussion

The CIR Expert Panel recognized the ongoing concern regarding potential hypersensitivity reactions to chlorhexidine-impregnated medical devices. These reactions are indicative of an immunoglobulin E (IgE)-mediated allergic reaction and are considered by the Panel as serious. The concentration limits imposed in the CIR Expert Panel safety assessment on these preservatives, however, are sufficient to ensure safety of their use in cosmetics.

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**Table 1.** Historical and Current Cosmetic Product Uses and Concentrations for Chlorhexidine, Chlorhexidine Dihydrochloride, and Chlorhexidine Digluconate

Product Category	1986 Uses (Total Number of Products in Product Category) <sup>a</sup>	2005 Uses (Total Number of Products in Product Category) <sup>25</sup>	1986 Concentrations <sup>a</sup>	2008 Concentrations <sup>26</sup>
<b>Chlorhexidine</b>				
Skin care preparations				
Skin fresheners	1 (184)	— <sup>b</sup> (212)	> 0.1%-1%	— <sup>b</sup>
Oral hygiene products				
Mouthwashes and breath fresheners	1 (53)	— <sup>b</sup> (57)	>1%-5%	— <sup>b</sup>
Other oral hygiene products	— <sup>b</sup> (6)	1 (10)	— <sup>b</sup>	0.13% <sup>1</sup>
<b>Chlorhexidine dihydrochloride</b>				
Noncoloring hair preparations				
Hair conditioners	— <sup>b</sup> (651)	26 (715)	— <sup>b</sup>	0.0001%-0.001%
Eye makeup preparations				
Eye makeup remover	— <sup>b</sup> (100)	2 (114)	— <sup>b</sup>	— <sup>b</sup>
Skin care preparations				
Cleansing	— <sup>b</sup> (775)	2 (1009)	— <sup>b</sup>	— <sup>b</sup>
Noncoloring hair preparations				
Hair conditioners	— <sup>b</sup> (651)	26 (715)	— <sup>b</sup>	— <sup>b</sup>
Shampoos	— <sup>b</sup> (884)	2 (1022)	— <sup>b</sup>	— <sup>b</sup>
Hair tonics, dressings, etc	— <sup>b</sup> (598)	1 (623)	— <sup>b</sup>	— <sup>b</sup>
Other noncoloring hair preparations	— <sup>b</sup> (277)	19 (73)	— <sup>b</sup>	— <sup>b</sup>
Hair-coloring preparations				
Bleaches	— <sup>b</sup> (120)	1 (103)	— <sup>b</sup>	— <sup>b</sup>
<b>Chlorhexidine digluconate</b>				
Baby products				
Lotions, oils, powders, and creams	— <sup>b</sup> (60)	4 (67)	— <sup>b</sup>	— <sup>b</sup>
Other baby products	— <sup>b</sup> (34)	1 (64)	— <sup>b</sup>	— <sup>b</sup>

(continued)

Table I. (continued)

Product Category	1986 Uses (Total Number of Products in Product Category) <sup>a</sup>	2005 Uses (Total Number of Products in Product Category) <sup>25</sup>	1986 Concentrations <sup>a</sup>	2008 Concentrations <sup>26</sup>
Eye makeup preparations				
Eye shadow	1 (576)	— <sup>b</sup> (229)	> 0.1% - 1%	— <sup>b</sup>
Eye lotions	— <sup>b</sup> (25)	— <sup>b</sup> (32)	— <sup>b</sup>	0.003%-0.04%
Mascara	— <sup>b</sup> (195)	— <sup>b</sup> (308)	— <sup>b</sup>	0.05%
Eye makeup remover	1 (100)	2 (114)	< 0.1%	0.0001%-0.001%
Fragrance preparations				
Other fragrance preparations	— <sup>b</sup> (173)	3 (187)	— <sup>b</sup>	— <sup>b</sup>
Noncoloring hair preparations				
Hair conditioners	— <sup>b</sup> (651)	26 (715)	— <sup>b</sup>	— <sup>b</sup>
Rinses	— <sup>b</sup> (42)	— <sup>b</sup> (46)	— <sup>b</sup>	0.02%
Tonics, dressings, and other hair-grooming aids	— <sup>b</sup> (598)	— <sup>b</sup> (623)	— <sup>b</sup>	0.02%
Hair-coloring preparations				
Bleaches	— <sup>b</sup> (120)	1 (103)	— <sup>b</sup>	— <sup>b</sup>
Hair lighteners	— <sup>b</sup> (5)	— <sup>b</sup> (14)	— <sup>b</sup>	0.04%
Makeup preparations				
Foundations	6 (324)	— <sup>b</sup> (530)	< 0.1%	0.0005%-0.03%
Makeup fixatives	— <sup>b</sup> (20)	— <sup>b</sup> (37)	— <sup>b</sup>	0.05%
Nail care products				
Cuticle softeners	1 (19)	— <sup>b</sup> (20)	< 0.1%	— <sup>b</sup>
Personal hygiene products				
Other personal hygiene products	— <sup>b</sup> (308)	3 (390)	— <sup>b</sup>	— <sup>b</sup>
Mouthwashes and breath fresheners	— <sup>b</sup> (46)	— <sup>b</sup> (57)	— <sup>b</sup>	0.2%
Underarm deodorant	— <sup>b</sup> (247)	— <sup>b</sup> (281)	— <sup>b</sup>	0.06%
Oral care products				
Dentifrices (aerosol, liquid, pastes, and powders)	— <sup>b</sup> (40)	— <sup>b</sup> (54)	— <sup>b</sup>	0.002%-0.01%
Shaving preparations				
Aftershave lotions	— <sup>b</sup> (231)	1 (260)	— <sup>b</sup>	— <sup>b</sup>
Skin care preparations				
Bath soaps and detergents	— <sup>b</sup> (143)	— <sup>b</sup> (207)	— <sup>b</sup>	0.02%
Skin cleansing creams, lotions, liquids, and pads	3 (775)	11 (1009)	< 0.1%	0.002%-0.05%
Face and neck skin care preparations		9 (546)		0.01%-0.03%
Body and hand skin care preparations	6 (1150)	7 (992)	< 0.1%	0.05%
Night skin care preparations	4 (200)	3 (229)	< 0.1%	— <sup>b</sup>
Skin fresheners	— <sup>b</sup> (184)	— <sup>b</sup> (212)	— <sup>b</sup>	0.05%
Moisturizers	— <sup>b</sup> (905)	— <sup>b</sup> (1200)	— <sup>b</sup>	0.001%-0.05%
Paste masks (mud packs)	6 (271)	4 (312)	< 0.1%	0.02%-0.05%
Other skin care preparations	— <sup>b</sup> (725)	6 (915)	— <sup>b</sup>	0.002%-0.05%
Suntan preparations				
Suntan gels, creams, and liquids	— <sup>b</sup> (131)	— <sup>b</sup> (138)	— <sup>b</sup>	0.05%
Total uses/ranges for chlorhexidine, chlorhexidine dihydrochloride, and chlorhexidine digluconate	30	61	< 0.1%-5%	0.0001%-0.13%

<sup>a</sup> 0.13% in oral rinse.

<sup>b</sup> Not reported. In some cases, the ingredient uses were not reported to Food and Drug Administration (FDA) in the voluntary industry product survey program, however, concentrations were provided. In other cases, the uses were reported, but no concentration was provided.

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## 2-Chloro-p-Phenylenediamine and 2-Chloro-p-Phenylenediamine Sulfate

### Conclusion

In a 1992 safety assessment of 2-chloro-p-phenylenediamine and 2-chloro-p-phenylenediamine sulfate, the Cosmetic Ingredient Review (CIR) Expert Panel stated that these ingredients are safe as "coal-tar" hair dye ingredients as used in cosmetic products.<sup>1</sup> The Expert Panel reviewed newly available studies since that assessment (see references),<sup>2-10</sup> along with updated information regarding types and concentrations of use and did not reopen this safety assessment. The Expert Panel confirmed that 2-chloro-p-phenylenediamine and 2-chloro-p-phenylenediamine sulfate are safe as cosmetic ingredients in the present practices of use and concentration.

### Discussion

Information supplied to the Food and Drug Administration (FDA) by industry as part of the Voluntary Cosmetic Ingredient Reporting Program (VCRP)<sup>1</sup> indicates that 2-chloro-p-phenylenediamine was being used in 1 hair dye at concentrations of  $\leq 0.1\%$  in 1984. Voluntary Cosmetic Ingredient Reporting Program data provided by FDA in 2006 and 2007 indicated no reported uses of 2-chloro-p-phenylenediamine,<sup>11,12</sup> and use concentrations of this dye were not reported in a 2007 industry survey.<sup>13</sup>

According to the information supplied to the FDA by industry as part of the VCRP,<sup>1</sup> 2-chloro-p-phenylenediamine sulfate was reported as being used in 61 hair dyes at concentrations of  $\leq 0.1\%$  to  $1\%$  in 1984. Voluntary Cosmetic Ingredient Reporting Program data provided by FDA in 2006 indicated that 2-chloro-p-phenylenediamine sulfate was being used in 24 hair dyes and in 11 hair tints.<sup>11</sup> Voluntary Cosmetic Ingredient Reporting Program data provided by FDA in 2007 indicated no reported uses of 2-chloro-p-phenylenediamine sulfate.<sup>12</sup> The results of a 2007 industry survey<sup>13</sup> indicated that 2-chloro-p-phenylenediamine sulfate was being used in hair dyes at a concentration of  $2\%$  (before dilution); use concentration data for this ingredient in hair tints were not included in this survey. Use frequency/use concentration data on 2-chloro-p-phenylenediamine and 2-chloro-p-phenylenediamine sulfate are included in Table 1.

The Expert Panel recognizes that there are data gaps regarding the use and concentration of these hair dyes. However, the overall information available on the types of products in which this ingredient is used and at what concentration indicate a pattern of use, which was considered by the Expert Panel in assessing safety. In order to gain more insight into ingredient use frequency patterns, the total number of products in a category could be considered along with the number of products in that category containing the ingredient.



**Table 1.** Historical and Current Cosmetic Product Uses and Concentrations for 2-Chloro-p-Phenylenediamine and 2-Chloro-p-Phenylenediamine Sulfate

Product Category <sup>11</sup>	1984 Uses (total number of products in category) <sup>1</sup>	2006 Uses (total number of products in category) <sup>11</sup>	1984 Concentrations (%) <sup>1</sup>	2007 Concentrations (%) <sup>13</sup>
2-Chloro-p-phenylenediamine				
Hair-coloring products				
Dyes and colors	1 (811)	- <sup>a</sup>	≤0.1	- <sup>b</sup>
Total uses/ranges for 2-chloro-p-phenylenediamine	1	-	≤0.1	-
2-Chloro-p-phenylenediamine sulfate				
Hair-coloring products				
Dyes and colors	61 (811)	24 (1600)	≤0.1-1	2% (before dilution)
Tints	- <sup>a</sup>	11 (56)	- <sup>a</sup>	-
Total uses/ranges for 2-chloro-p-phenylenediamine sulfate	61	35	≤ 0.1-1	2% (before dilution)

Abbreviation: FDA, Food and Drug Administration.

<sup>a</sup> In FDA's voluntary reporting system, no uses/use concentrations reported for this category in 1984; no uses reported for this category in 2006.

<sup>b</sup> In industry survey, no use concentrations reported for this category.

According to the Scientific Committee on Consumer Products (SCCP), 2-chloro-p-phenylenediamine and 2-chloro-p-phenylenediamine sulfate are reported to be used in oxidative hair dye formulations for eyebrows and eyelashes. The CIR Expert Panel strongly affirms that these practices of use are unsafe and should be discontinued.

The Expert Panel recognizes that 2-chloro-p-phenylenediamine and 2-chloro-p-phenylenediamine sulfate are used as hair dye ingredients and may be sensitizers. However, hair dyes containing these ingredients, as coal-tar hair dye products are exempt from the principal adulteration provision and from the color additive provisions in sections 601 and 706 of the Federal Food, Drug, and Cosmetic Act, when the label bears a caution statement and patch test instructions for determining whether the product causes skin irritation. The Expert Panel expects that continuing to follow this procedure will identify prospective individuals who would have an irritation/sensitization reaction and allow them to avoid significant exposures.

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 end points. The hair dye epidemiology data are available at <http://www.cir-safety.org/findings.shtml>.

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## 2,4-Diaminophenol and 2,4-Diaminophenol HCl

### Conclusion

In a 1994 safety assessment of 2,4-diaminophenol and 2,4-diaminophenol HCl (formerly 2,4-diaminophenol dihydrochloride), the Cosmetic Ingredient Review (CIR) Expert Panel stated that these ingredients are safe as (then) used in hair dyes at concentrations up to 0.2% (as the free base).<sup>1</sup> The Expert Panel reviewed newly available studies since that assessment (see references),<sup>2-11</sup> along with updated information regarding the type and concentration of use. The Panel determined to not reopen this safety assessment and confirmed that 2,4-diaminophenol and 2,4-diaminophenol HCl are safe as cosmetic ingredients in the current practices of use and concentration (Table 1).

### Discussion

2,4-Diaminophenol HCl had been used in 3 cosmetic products in 1981. Their use concentrations were not reported at that time. The Food and Drug Administration<sup>12</sup> reported that 2,4-diaminophenol HCl is used in 5 hair dyes and colors. A survey of current use concentrations conducted by the Personal Care Products Council<sup>13</sup> reported no use concentrations of 2,4-diaminophenol and 2,4-diaminophenol HCl.

Newly available data did not raise any issues regarding the safety of 2,4-diaminophenol and 2,4-diaminophenol HCl. The Expert Panel noted that the available hair dye epidemiology studies are insufficient to conclude there is a causal relationship between hair dye use and cancer and other end points based on lack of strength in the associations and inconsistency of findings. The hair dye epidemiology data is available at <http://www.cir-safety.org/findings.shtml>.

The Expert Panel recognized that 2,4-diaminophenol and 2,4-diaminophenol HCl are oxidizing hair dye ingredients and

may be sensitizers. However, hair dyes containing these ingredients, as coal-tar hair dye products, are exempt from the principal adulteration provision and color additive provisions in sections 601 and 706 of the Federal Food, Drug, and Cosmetic Act, when the label bears a caution statement and patch test instructions for determining whether the product causes skin irritation. The Expert Panel expects that continuing to follow the procedure will identify prospective individuals who would have an irritation/sensitization reaction and allow them to avoid significant exposures.

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**Table 1.** Historical and Current Cosmetic Product Uses and Concentrations for 2,4-diaminophenol HCl

Product Category	1981 Uses <sup>1</sup>	2008 Uses <sup>12</sup>	1981 Concentrations <sup>1</sup>	2009 Concentrations <sup>13</sup>
Hair-coloring preparations				
Hair dyes and colors	3 (1056)	5 (1600)	-	-
Total uses/ranges for 2,4-diaminophenol HCl	3	5	-	-

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## Diisopropylamine

### Conclusion

In a 1995 safety assessment of diisopropylamine, the Cosmetic Ingredient Review (CIR) Expert Panel stated that this ingredient is safe as a cosmetic ingredient as used, and that diisopropylamine should not be used in products containing *N*-nitrosating agents.<sup>1</sup> The Expert Panel reviewed newly available studies since that assessment along with updated frequency and concentration of use information.<sup>2-12</sup> The Expert Panel determined to not reopen this safety assessment and confirmed that diisopropylamine is safe as a cosmetic ingredient when used in products that do not contain *N*-nitrosating agents.

### Discussion

Diisopropylamine is reported to function as a pH adjuster, and reported use has increased very slightly from 1 "other skin care preparation" formulation<sup>1,10</sup> in 1993 to 3 bath soap and detergent formulations in 2009. Concentration of use was not reported to the Food and Drug Administration (FDA) in 1993, nor is it reported to FDA currently. A survey conducted by the Personal Care Products Council found that no uses of diisopropylamine were reported by industry<sup>11</sup> (Table 1).

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**Table 1.** Historical and Current Cosmetic Product Uses and Concentrations for Diisopropylamine

Product Category	Frequency of Use—1993 <sup>1</sup>	Frequency of Use—2009 <sup>10</sup>	Concentration of Use—1993 <sup>1</sup>	Concentration of Use—2009 <sup>11</sup>
Other skin care preparations	1		Not available	No uses reported
Bath soaps and detergents	—	3	Not available	No uses reported
Total	1	3	Not available	No uses reported

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## Disperse Blue 1

### Conclusion

In 1995, the Cosmetic Ingredient Review (CIR) Expert Panel<sup>1</sup> concluded that Disperse Blue 1 is "safe for use in hair dyes at concentrations up to 1%." In 2010, the Expert Panel reviewed new information available since the original assessment was published in 1995.<sup>2-18</sup> Current frequency of use data that indicate Disperse Blue 1 is no longer being used (personal communication, Don Havery, US FDA, Center for Food, Safety, and Applied Nutrition, Office of Colors and Cosmetics). The Expert Panel determined to not reopen this safety assessment and confirmed the existing conclusion.

### Discussion

In 2010, Disperse Blue 1 was not used in cosmetic formulations. However, if used in cosmetics, Disperse Blue 1 would function as a hair colorant.<sup>19</sup> In 1994, according to information supplied to the Food and Drug Administration (FDA) by industry as part of the Voluntary Cosmetic Registration Program, Disperse Blue 1 was used in 112 hair color formulations; industry reported that in 1994, Disperse Blue 1 was used at a concentration of 0.62% in semipermanent hair dyes and that it was not used in conjunction with hydrogen peroxide.<sup>1</sup>

Concern for the carcinogenic potential of Disperse Blue 1, as used in cosmetics, initially generated of opening a re-review of the safety assessment on Disperse Blue 1. In vitro dermal penetration data demonstrated that Disperse Blue 1 was poorly absorbed through rat skin. However, the most compelling data for not reopening the safety assessment of Disperse Blue 1 was the margin of safety (MOS) at a use concentration of 1%. Numerous risk assessments, presented below, were used to calculate the margin of safety; the results indicate that Disperse Blue 1 is safe for use in hair dyes at concentrations up to 1%.

### Food and Drug Administration Risk Assessment Information

Lifetime average daily exposure via hair dye use:

$$0.62 \text{ (g Disperse Blue 1 applied/application; assuming 100 mL formulation/application at a maximum concentration of 0.62\% in the formulation)} \times 0.002 \text{ (fraction Disperse Blue 1 absorbed)} \times 600 \text{ (applications/lifetime)} = 0.744 \text{ (g Disperse Blue 1 absorbed/lifetime)}$$

$$0.744 \text{ g/60 kg} = 0.0124 \text{ g/kg}$$

$$78 \text{ year (estimated life span)} \times 365 \text{ days} = 28\,470 \text{ days}$$

Estimated lifetime average daily absorbed-dose rate (hair dye use):  $0.0124 \text{ g/kg per } 28\,470 \text{ d} = 0.44 \text{ } \mu\text{g/kg per d}$ <sup>17,18</sup>

A simple linear regression analysis was used to estimate that 0.3  $\mu\text{g/kg per d}$  Disperse Blue 1 would be associated with an upper-bound 1 in 1 000 000 lifetime risk of developing a bladder cancer. The total lifetime daily exposure with hair dye use calculated above, 0.44  $\mu\text{g/kg per d}$ , is slightly greater than that value. This risk assessment indicates that the human cancer risks associated with the use of Disperse Blue 1 in hair-coloring formulations would be negligible, considering multiple conservative assumptions incorporated into the assessment.

Additionally, the acceptable daily intake (ADI) reported in the FDA document, using rat data from a National Toxicology Program (NTP) bioassay, was estimated to be 45  $\mu\text{g/kg per d}$ , which is 100 times greater than the estimated lifetime daily dose.<sup>18</sup>

Conclusions about the safe use of Disperse Blue 1 depend on whether its mechanism of action is viewed as genotoxic, thereby directly producing a carcinogenic event, or as a non-genotoxic. If it is viewed as nongenotoxic, the ADI and margin of safety indicated that potential exposure to Disperse Blue 1 would not increase the risk of developing cancer. If it is viewed as genotoxic, the estimated daily dose would be associated with an upper-bound cancer risk estimate slightly exceeding  $10^{-6}$  for humans (no uncertainty factor was applied for insufficient dermal penetration data).

### Industry-Prepared Quantitative Cancer Risk Assessment

A quantitative cancer risk assessment for Disperse Blue 1 was prepared based on the No Significant Risk Level (NSRL) of 200  $\mu\text{g/d}$  established under Proposition 65 by the State of California.<sup>8</sup> The NSRL was established using a linearized multistage model and the upper 95% confidence limit of the estimated cancer potency to extrapolate from the high oral doses used in the NTP rat bioassay to lower doses. Using the NSRL assumption of 70 kg as the adult human body weight, the equivalent average daily dose rate is 2.86  $\mu\text{g/kg per d}$ . This risk assessment incorporated the dermal penetration estimate of 0.2%, as determined by Yourick

et al.<sup>17</sup> For this risk assessment, the estimated lifetime average daily dose of Disperse Blue 1 from hair dye use was determined as follows<sup>18</sup>:

Amount of Disperse Blue 1 in contact with the skin =  $41 \mu\text{g}/\text{cm}^2$

Amount systemically absorbed per use:  $0.002 \times 41 \mu\text{g}/\text{cm}^2 \times 580 \text{ cm}^2$  (total scalp area) =  $47 \mu\text{g}/\text{application}$

Total lifetime exposure:  $47 \mu\text{g}/\text{application} \times 600$  applications/lifetime  $\times 1/60$  kg body weight (bw) =  $470 \mu\text{g}/\text{kg bw}$

Estimated lifetime average daily dose:  $470 \mu\text{g}/\text{kg bw}$  per 28 470 d (avg female life span) =  $0.0165 \mu\text{g}/\text{kg per d}$

Thus, the estimated human exposure is approximately 170-fold lower than the NSRL (expressed as a lifetime average daily dose rate) for Disperse Blue 1.

This risk assessment included a concentration of use value of 0.52% for Disperse Blue 1 in hair dyes. Since the existing CIR safety assessment of Disperse Blue 1 states that Disperse Blue 1 is safe at concentrations up to 1%, the risk assessment data were extrapolated to determine the margin of safety using 1% Disperse Blue 1. Assuming linear concentration dependence, the lifetime average daily dose rate from a 1% Disperse Blue 1 formulation would be  $0.032 \mu\text{g}/\text{kg per d}$ , which is approximately 90-fold lower than the NSRL.

The CIR considered these inputs and offered this perspective on the risk assessment for genotoxic versus nongenotoxic mechanisms of action:

**Assumptions.** FDA assessment, Disperse Blue 1 is carcinogenic via a genotoxic mechanism

- 0.62 g/100 mL Disperse Blue 1 in product
- 100 mL/application
- 12 applications/year
- 50-year exposure duration
- 60-kg bw and
- 78 years = 28 470 days averaging time for nonthreshold mechanisms

**Lifetime average daily-dose rate.** (no correction for the fraction that actually contacts the scalp in a hair product)

$[0.62 \text{ g}/100 \text{ mL} \times 100 \text{ mL}/\text{application} \times 12 \text{ applications}/\text{year} \times 50 \text{ years}]/[60 \text{ kg body weight} \times 28 \text{ 470 days}] = 2.18 \times 10^{-4} \text{ g}/\text{kg per d}$

$2.18 \times 10^{-4} \text{ g}/\text{kg per d} \times 10^6 \mu\text{g}/\text{g} = 2.18 \times 10^2 \mu\text{g}/\text{kg per d}$

- 0.002 (0.2%) of Disperse Blue 1 dermal penetration<sup>17</sup>  
 $2.18 \times 10^2 \mu\text{g}/\text{kg per d} \times 0.002 = 0.44 \mu\text{g}/\text{kg per d}$
- Uncertainty factor = 10 for lack of data on the amount remaining in the skin, which could be absorbed<sup>18</sup> (further investigation indicates that there is little potential for skin to serve as a reservoir,<sup>17</sup> so this uncertainty factor is not needed<sup>8</sup>)
- $0.44 \mu\text{g}/\text{kg per d} \times 10 = 4.4 \mu\text{g}/\text{kg per d}$

- 0.02 (2%) applied material contacts the scalp<sup>18</sup>
- $0.44 \mu\text{g}/\text{kg per d} \times 0.02 = 0.009 \text{ mg}/\text{kg per d} \sim 0.01 \mu\text{g}/\text{kg per d}$
- Industry risk assessment estimate<sup>8</sup>:  $0.0165 \mu\text{g}/\text{kg per d}$

### Cancer Potency of Disperse Blue 1

Extrapolated from an incidence of 41 (84%) of 49 rats exhibiting smooth muscle cell tumors at  $217 \text{ mg}/\text{kg per d}$  exposure to estimate that  $0.3 \mu\text{g}/\text{kg per d}$  is associated with a  $10^{-6}$  lifetime upper-bound cancer risk.<sup>18</sup>

A simple linear regression equation was used to extrapolate from dose rate of  $217 \text{ mg}/\text{kg per d}$  used in the NTP rat bioassay to low doses; the linearized multistage model or the upper 95% confidence limit was not used to estimate cancer potency.

The State of California NSRL of  $200 \mu\text{g}/\text{d}$  is based on<sup>8</sup>:

- 70 kg bw
- Linearized multistage model
- Linear multistage model to extrapolate from high to low doses in the NTP rat bioassay
- Upper 95% confidence limit of the linear term expressing upper bound potency

NSRL =  $200 \mu\text{g}/\text{d per } 70 \text{ kg} = 2.86 \mu\text{g}/\text{kg per d}$  (represents  $<10^{-5}$  lifetime cancer risk)

$2.86 \mu\text{g}/\text{kg per d}/10 = 0.286 \mu\text{g}/\text{kg per d}$  represents  $<10^{-6}$  lifetime cancer risk.

### Conclusion: Cancer Risk Assessment

Exposure estimates above<sup>8,18</sup> do not exceed lifetime average dose rates estimated to be associated with, at most, a  $10^{-6}$  lifetime cancer risk.

(MOS = 17.3-30)

**Assumption.** Disperse Blue 1 is Carcinogenic via a Nongenotoxic Mechanism.

Exposure averaging time for a nongenotoxic (ie, threshold) effect is generally taken to be equal to the exposure duration. Assuming an averaging time (and exposure duration) of 50 years (rather than 78 years), the average daily dose rate would be (adjusting the estimates calculated above assuming a genotoxic mechanism):

$0.01 \mu\text{g}/\text{kg per d} \times 78 \text{ years}/50 \text{ years} = 0.016 \mu\text{g}/\text{kg per d}$   
Reference Dose Assuming a Nongenotoxic Mechanism

NOAEL =  $45 \text{ mg}/\text{kg per d}$  (NTP rat bioassay)

Reference dose<sup>18</sup> =  $45 \text{ mg}/\text{kg per d}/1000$  uncertainty factor =  $45 \mu\text{g}/\text{kg per d}$

(MOS = 2812)

**Assumption.** Concentration<sup>8,18</sup> of Disperse Blue 1 is 1% (rather than 0.62% or 0.52%)

Exposure estimates<sup>8,18</sup>

$\sim 0.01 \mu\text{g}/\text{kg per d}$ , assuming 0.62%

$0.01 \mu\text{g/kg per d} \times 1\%/0.62\% = 0.016 \mu\text{g/kg per d at } 1\%;$   
 $-0.02 \mu\text{g/kg per d}$

$0.0165 \mu\text{g/kg per d, assuming } 0.52\%$

$0.0165 \mu\text{g/kg per d} \times 1\%/0.62\% = 0.0317; -0.032 \mu\text{g/kg per d}$

Thus, exposure estimates range from 0.02 to 0.032  $\mu\text{g/kg per d}$ .

*MOSs for product containing 1% Disperse Blue 1. Genotoxic effect:*

Range:  $[0.3 \mu\text{g/kg per d}/0.02 \mu\text{g/kg per d}]$  to  $[0.286 \mu\text{g/kg per d}/0.032 \mu\text{g/kg per d}] = 9$  to 15

Nongenotoxic effect:

Range:  $[45 \mu\text{g/kg per d}/0.032 \mu\text{g/kg per d}]$  to  $[45 \mu\text{g/kg per d}/0.02 \mu\text{g/kg per d}] = 1406$  to 2250

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## Disperse Violet 1

### Conclusion

In its 1991 safety assessment of Disperse Violet 1, the Cosmetic Ingredient Review (CIR) Expert Panel stated that this ingredient was safe as a cosmetic ingredient in the present

practices of use and concentration.<sup>1</sup> In 2007, the CIR Expert Panel reviewed newly available studies since that assessment, along with updated information regarding types and concentrations of use.<sup>2-50</sup> The CIR Expert Panel confirmed that Disperse

Violet 1 is safe in the practices of use and concentrations, as given in Table 1, and did not reopen this safety assessment.

## Discussion

This ingredient is a direct, non-oxidative hair dye used in 133 hair-coloring products in 1981, based on voluntary reports<sup>1</sup> submitted to Food and Drug Administration (FDA) by the industry, with concentrations of use  $\leq 1\%$ . In 2006, Disperse Violet 1 was reportedly used in 121 cosmetic products.<sup>51</sup> Data from an industry survey in 2007 indicated that Disperse Violet 1 was used at concentrations ranging from 0.1% to 0.7%.<sup>15</sup>

The available use and concentration data are given in Table 1, as a function of product category.

The Panel is aware that Disperse Red 15 is an impurity in Disperse Violet 1 but determined that the levels of this impurity have decreased since the original safety assessment. The Panel noted that Disperse Red 15 is a banned substance in Europe, except as it appears as an impurity in Disperse Violet 1.

While there is limited evidence of genotoxicity in certain assays (but not in others), the Panel noted a newly available negative oral reproductive study<sup>9</sup> and a negative 20-month dermal carcinogenicity in the original safety assessment that demonstrates an absence of carcinogenic or reproductive risk.

The CIR Expert Panel has concluded that the available epidemiology studies are insufficient to conclude there is a causal relationship between hair dye use and cancer and other end points, based on lack of strength of the associations and inconsistency of findings. A of hair dye epidemiology data are available at <http://www.cir-safety.org/findings.shtml>.

The Expert Panel recognizes that Disperse Violet 1 is used as a hair dye ingredient and may be a sensitizer. However, hair dyes containing this ingredient, as coal-tar hair products, are exempt from the principal adulteration provision and from the color additive provisions in sections 601 and 706 of the Federal Food, Drug, and Cosmetic Act, when the label bears a caution statement and patch test instructions for determining whether the product causes skin irritation. The Expert Panel expects that following this procedure will identify prospective individuals who have had an irritation/sensitization reaction and allow them to avoid significant exposure.

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**Table 1.** Historical and Current Cosmetic Product Uses and Concentrations of Disperse Violet 1

Product Category	1981 Uses <sup>1</sup>	2006 Uses <sup>52</sup>	1981 Concentrations <sup>1</sup>	2007 Concentrations <sup>15</sup>
Hair-coloring preparations				
Hair dyes and colors	133 (1056)	121 (1600)	$\leq 1$	0.1%-0.7%
Tints	(49) <sup>a</sup>	(56) <sup>a</sup>	<sup>a</sup>	0.5%
Rinses (coloring)	(42) <sup>a</sup>	(15) <sup>a</sup>	<sup>a</sup>	0.5%
Total uses/ranges of Disperse Violet 1	133	121	$\leq 1$	0.1%-0.7%

<sup>a</sup> Not reported. In some cases, uses of ingredient were not reported to Food and Drug Administration (FDA) in the voluntary industry product survey program; however, concentrations were provided. In other cases, the uses were reported but no concentration was provided.

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## Ethyl Hexanediol

### Conclusion

In 1994 earlier safety assessment of ethyl hexanediol, the Cosmetic Ingredient Review (CIR) Expert Panel stated that this ingredient is safe as (then) used as a cosmetic ingredient.<sup>1</sup> The Expert Panel reviewed newly available studies since that assessment along with updated frequency of use information.<sup>2-17</sup> The Panel determined to not reopen this safety assessment. Therefore, the Expert Panel confirmed that ethyl hexanediol is safe as a cosmetic ingredient.

### Discussion

Ethyl hexanediol was used in 3 cosmetic formulations in 1993. Use concentrations were not reported at that time.<sup>1</sup> The Food and Drug Administration (FDA)<sup>8</sup> reported that ethyl hexanediol is used in 1 cosmetic formulation in 2009. A survey conducted by the Personal Care Products Council reported no uses of ethyl hexanediol (Table 1).<sup>16</sup>

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**Table 1.** Historical and Current Cosmetic Product Uses and Concentrations for Ethyl Hexanediol

Product Category	1993 Frequency of Use <sup>1</sup>	2009 Frequency of Use <sup>8</sup>	1993 Use Concentration <sup>1</sup>	2009 Use Concentration <sup>16</sup>
Conditionics, dressings, and other hair grooming aids	1	—	a	No reported uses
Cleansing products	1	—	a	No reported uses
Other suntan preparations	1	—	a	No reported uses
Face and neck preparations (excluding shaving)	—	1	—	No reported uses
Total	3	1	a	No reported uses

Abbreviation: FDA, Food and Drug Administration.  
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## HC Blue No. 2

### Conclusion

In a 1994 safety assessment of HC Blue No. 2, the Cosmetic Ingredient Review (CIR) Expert Panel stated that HC Blue No. 2 is safe as (then) used as a coal-tar hair dye ingredient at the (then) current concentrations of use.<sup>1</sup> The Expert Panel reviewed newly available studies since that assessment,<sup>2-24</sup> along with updated information regarding types and concentrations of use. The Panel determined to not reopen this safety assessment. Therefore, the Panel confirms that HC Blue No. 2 is safe as a hair dye ingredient in the practices of use and concentration, as given in Table 1.

### Discussion

The Expert Panel recognizes that HC Blue No. 2 is used as a hair dye ingredient and may be a sensitizer. However, hair dyes, hair tints, hair rinses, hair color sprays, and coloring shampoos containing these ingredients as coal-tar hair dye products are exempt from the principal adulteration provision and from the color additive provisions in sections 601 and 706 of the Federal Food, Drug, and Cosmetic Act, when the label bears a caution statement and patch test instructions for determining whether the product causes skin irritation. The Expert Panel expects that continuing to follow this procedure will identify prospective

individuals who would have an irritation/sensitization reaction and allow them to avoid significant exposures.

While the Expert Panel noted that the Scientific Committee on Consumer Products (SCCP) limited the nitrosamine content of HC Blue No. 2 to < 50 ppb, the chemical structure of this ingredient is that of a nitro aryl compound and not of an *N*-nitroso compound.

The 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 end points based on lack of strength of the associations and inconsistency of findings. The hair dye epidemiology data are available at <http://www.cir-safety.org/findings.shtml>.

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**Table 1.** Historical and current cosmetic product uses and concentrations for HC Blue No. 2

Product Category	1993 Uses (total number of products in a category) <sup>1</sup>	2009 Uses (total number of products in category) <sup>25</sup>	1993 Concentrations <sup>1</sup> (%)	2009 Concentrations <sup>17</sup> (%)
Hair-coloring products			1.7 <sup>a</sup>	
Dyes and colors	136 (811)	163 (2481)	NA	2 <sup>b</sup>
Hair tints	7 (15)	1 (58)	NA	-
Hair rinses	NA	- (43)	NA	0.6
Hair shampoos (coloring)	NA	3 (48)	-	-
Other coloring preparations	2 (207)	- (166)	NA	-
Total uses/ranges for HC Blue No. 2	145	167	1.7	0.6-2

<sup>a</sup> Product category for concentration not reported.

<sup>b</sup> 1% after dilution.

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## HC Red No. 3

### Conclusion

In a 1992 safety assessment of HC Red No. 3, the Cosmetic Ingredient Review (CIR) Expert Panel stated that HC Red No. 3 is safe as (then) used as a coal-tar hair dye ingredient at the (then) current concentrations, with the condition that it should not be used in products containing *N*-nitrosating agents.<sup>1</sup> The Expert Panel reviewed newly available studies since that assessment (see references),<sup>1-22</sup> along with updated information regarding

types and concentrations of use and did not reopen the safety assessment. The Expert Panel confirmed that HC Red No. 3 is safe as a hair dye ingredient in the practices of use and concentration, as given in Table 1.

### Discussion

Although there is an increase in the number, type, and use concentration of HC Red No. 3, the CIR Expert Panel found

**Table 1.** Historical and Current Cosmetic Product Uses and Concentrations<sup>a</sup> of HC Red No. 3

Product Category	1984 Uses (Total Number of Products in a Category <sup>1</sup> )	2008 Uses (Total Number of Products in a Category <sup>23</sup> )	1992 Concentrations (%) <sup>1</sup>	2008 Concentrations (%) <sup>9</sup>
Hair-coloring products				
Dyes and colors	68 (811)	218 (1600)	≤0.1-1	0.1-2, 14 <sup>a</sup>
Hair tints	NA	2 (56)	NA	–
Hair rinses	NA	5 (15)	NA	2
Hair color sprays (aerosol)	NA	– (4)	NA	0.03
Shampoos (coloring)	NA	5 (27)	NA	–
Total uses/ranges for HC Red No. 3	68	230	≤0.1-1	NA

Abbreviation: NA, not available.

<sup>a</sup> Two percent after dilution.

that both the newly available studies and the studies in the original report support the safety of the new use and concentration of this ingredient in hair dye products. The Expert Panel determined the studies show that there is little to no dermal absorption of HC Red No. 3.

The Expert Panel recognizes that HC Red No. 3 is used as a hair dye ingredient and may be a sensitizer. However, hair dyes, hair tints, hair rinses, hair color sprays, and coloring shampoos containing these ingredients as coal-tar hair dye products are exempt from the principal adulteration provision and from the color additive provisions in sections 601 and 706 of the Federal Food, Drug, and Cosmetic Act, when the label bears a caution statement and patch test instructions for determining whether the product causes skin irritation. The Expert Panel expects that continuing to follow this procedure will identify prospective individuals who would have an irritation/sensitization reaction and allow them to avoid significant exposures.

The 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 end points based on lack of strength in the associations and inconsistency of findings. The hair dye epidemiology data are available at <http://www.cir-safety.org/findings.shtml>.

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## HC Yellow No. 2

### Conclusion

In a 1994 safety assessment of HC Yellow No. 2, the Cosmetic Ingredient Review (CIR) Expert Panel stated that this ingredient is safe as (then) used in cosmetic products.<sup>1</sup> The Expert Panel reviewed newly available studies since that assessment (see references),<sup>2-16</sup> along with updated information regarding types and concentrations of use. The Panel determined to not reopen this safety assessment. Therefore, the Panel confirmed that HC Yellow No. 2 is safe as a cosmetic ingredient in the practices of use and concentration, as given in Table 1.

### Discussion

HC Yellow No. 2 had been used in 91 cosmetic products in 1981. Use concentrations were not reported at that time. The Food and Drug Administration (FDA)<sup>17</sup> reported that HC Yellow No. 2 is used in 134 hair dyes and colors and 4 hair shampoos. A survey of current use concentrations conducted by the Personal Care Products Council<sup>18</sup> reported a range of 0.2% to 2.0% in hair dyes and colors.

Newly available data did not raise any new issues about the safety of HC Yellow No. 2. The Expert Panel noted that the available hair dye epidemiology studies are insufficient to conclude there is a causal relationship between hair dye use and cancer and other end points based on the lack of strength of the associations and inconsistency

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

The Expert Panel recognizes that HC Yellow No. 2 is used as a hair dye ingredient and may be a sensitizer. However, hair dyes containing these ingredients, as coal-tar hair dye products, are exempt from the principal adulteration provision and from the color additive provisions in sections 601 and 706 of the Federal Food, Drug, and Cosmetic Act, when the label bears a caution statement and patch test instructions for determining whether the product causes skin irritation. The Expert Panel expects that continuing to follow this procedure will identify prospective individuals who would have an irritation/sensitization reaction and allow them to avoid significant exposures.

The Expert Panel considered the addition of HC Yellow No. 5, 9, 11, and 12 to this safety assessment. It was decided that these dyes were chemically different from the original ingredient and that the available data on HC Yellow No. 2 could not be extended to these other hair dyes.

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**Table 1.** Historic and Current Cosmetic Product Uses and Concentrations for HC Yellow No. 2.

Product Category	1981 Uses <sup>1</sup>	2007 Uses <sup>17</sup>	1981 Concentrations <sup>1</sup> (%)	2008 Concentrations <sup>18</sup> (%)
Hair-coloring products				
Dyes and colors	91	134	-	0.2-2
Shampoos	-	4	-	-
Total uses/ranges for HC Yellow No. 2	91	138	-	0.2-2

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## Hydroxybenzomorpholine

### Conclusion

In its 1991 safety assessment of hydroxybenzomorpholine, the Cosmetic Ingredient Review (CIR) Expert Panel stated that this ingredient is safe as used in cosmetic products.<sup>1</sup> In 2007, the expert panel reviewed newly available studies since that assessment, along with updated information regarding types and concentrations of use.<sup>2-4</sup> The panel confirmed the safety of hydroxybenzomorpholine in hair dyes and colors in the practices of use and concentrations as given in Table 1 and did not reopen the safety assessment.

### Discussion

The Food and Drug Administration<sup>2</sup> voluntary reporting program included no uses for hydroxybenzomorpholine, compared to 43 uses in hair dyes and colors in 1989, mostly in the ≤0.1% range.<sup>1</sup> Cosmetic, Toiletry, and Fragrance Association (CTFA)<sup>3</sup> reported that this hair dye ingredient currently is used up to 0.03%, based on an industry survey.

The expert panel considered the opinion of the European Commission's Scientific Committee on Consumer Products (SCCP), which included unpublished data submitted by

**Table 1.** Historical and Current Cosmetic Product Uses and Concentrations for Hydroxybenzomorpholine

Product Category	1989 Ingredient Uses <sup>1</sup>	2006 Ingredient Uses <sup>2</sup>	1989 Use Concentrations <sup>1</sup>	2007 Use Concentrations <sup>3</sup>
Hair dyes and colors	43	–	≤0.1%-1%	0.03%
Total uses/ranges for hydroxybenzomorpholine	43	–	≤0.1%-1%	0.03%

industry.<sup>4</sup> It was noted that the SCCP limited nitrosamine content to 1% in any finished product. The CIR Expert Panel acknowledged that *N*-nitrosohydroxybenzomorpholine may be an impurity of hydroxybenzomorpholine. In addition, hydroxybenzomorpholine is subjected to nitrosation in the presence of *N*-nitrosating agents that may be included in a cosmetic formulation. Therefore, the expert panel reiterated that this ingredient should not contain *N*-nitroso impurities, nor should it be used in products where *N*-nitroso compounds may be formed.

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3. Cosmetic, Toiletry, and Fragrance Association (CTFA). 2007. Use concentration data for hydroxybenzomorpholine. Unpublished data submitted by CTFA. 1 page.
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# Isopropyl Isostearate

## Conclusion

In its 1992 safety assessment of isopropyl isostearate, the Cosmetic Ingredient Review (CIR) Expert Panel stated that this ingredient was safe as used in cosmetic products.<sup>1</sup> In 2007, the Expert Panel found no newly available studies since that assessment, but did review updated information regarding the types and concentrations of use. This re-review confirms that isopropyl isostearate is safe in the practices of use and concentration, as given in Table 1 and did not reopen this safety assessment.

## Discussion

Isopropyl isostearate was used in 78 cosmetic products in 1989, based on voluntary reports submitted to Food and Drug Administration (FDA by industry), with concentrations of use ranging from  $\leq 0.1\%$  to 50%.<sup>1</sup> In 2005, isopropyl isostearate was reportedly used in 69 cosmetic products.<sup>2</sup> Data from an industry survey in 2007 indicated that isopropyl isostearate was used at concentrations ranging from 0.5% to 65%.<sup>3</sup> The Panel noted that there was an increase in concentration to

**Table 1.** Historical and Current Cosmetic Product Uses and Concentrations of Isopropyl Isostearate in Cosmetics

Product Category	1989 Uses (total number of products in product category) <sup>4</sup>	2005 uses <sup>2</sup>	1989 Concentrations (total number of products in product category) <sup>4</sup>	2007 Concentrations <sup>3</sup>
Body products				
Lotions, oils, powders, and creams	- <sup>a</sup> (60)	2 (67)	- <sup>a</sup> (67)	-
Eye makeup preparations				
Eye eyebrow pencils	11 (1135) <sup>b</sup>	- <sup>a</sup> (124)	0.1%-10%	-
Eyeliner		- <sup>a</sup> (639)		-
Eye shadow		8 (1061)		2%-5%
Eye lotions		- <sup>a</sup> (32)		-
Eye makeup remover		1 (114)		3%
Mascara		- <sup>a</sup> (114)		0.6%
Other eye makeup preparations		- <sup>a</sup> (229)		2%
Fragrance preparations				
Powders	- <sup>a</sup> (273)	2 (324)	- <sup>a</sup> (324)	1%
Noncoloring Hair Preparations				
Shampoos	- <sup>a</sup> (884)	1 (1022)	- <sup>a</sup> (1022)	65%
Makeup preparations				
Blushers	40 (3194) <sup>b</sup>	- <sup>a</sup> (459)	$\leq 0.1\%$ -50%	0.5%-30%
Face powders		- <sup>a</sup> (447)		0.6%-30%
Foundations		- <sup>a</sup> (530)		12%-13%
Leg and body paints		- <sup>a</sup> (10)		-
Lipsticks		- <sup>a</sup> (1681)		12%-24%
Makeup bases		- <sup>a</sup> (273)		7%-30%
Rouges		- <sup>a</sup> (115)		6%
Makeup fixatives		- <sup>a</sup> (37)		- <sup>a</sup>
Other makeup preparations		19 (304)		1%-10%

(continued)

Table 1. (continued)

Product Category	1989 Uses (total number of products in product category) <sup>4</sup>	2005 uses <sup>2</sup>	1989 Concentrations (total number of products in product category) <sup>4</sup>	2007 Concentrations <sup>3</sup>
Personal hygiene products				
Underarm deodorants	- <sup>a</sup> (247)	- <sup>a</sup> (281)	- <sup>a</sup>	5%
Shaving Preparations				
Other shaving preparations	- <sup>a</sup> (63)	1 (64)	- <sup>a</sup> (64)	- <sup>a</sup>
Skin care preparations				
Skin cleansing creams, lotions, liquids, and pads	20 (3110) <sup>b</sup>	2 (1009)	≤0.1%-10%	2%-3%
Depilatories		- <sup>a</sup> (49)		- <sup>a</sup>
Face and neck skin care preparations		1 (546)		2%-4%
Body and hand skin care preparations		5 (992)		0.5%-4%
Foot powders and sprays		- <sup>a</sup> (43)		- <sup>a</sup>
Moisturizers		18 (1200)		0.7%-3%
Night skin care preparations		4 (229)		2%
Paste masks (mud packs)		1 (312)		- <sup>a</sup>
Skin fresheners		- <sup>a</sup> (212)		- <sup>a</sup>
Other skin care preparations	7	4 (915)	1%-25%	- <sup>a</sup>
Total uses/ranges for isopropyl isostearate	71	69	≤0.1%-50%	0.5%-65%

<sup>a</sup> Not reported. In some cases, ingredient uses were not reported to Food and Drug Administration (FDA) in the voluntary industry product survey program, however, concentrations were provided. In other cases, the uses were reported, but no concentration was provided.

<sup>b</sup> In 1989, these uses were combined.

65% in rinse-offs, but the original data supported the safety of this concentration.

The available usage and use concentration data are given in Table 1 as a function of product category.

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3. Cosmetic, Toiletry, and Fragrance Association. Use concentration survey results for isopropyl isostearate. Unpublished data submitted by CTFA; 2007.

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# Lauramine Oxide and Stearamine Oxide

## Conclusion

In 1994, the Cosmetic Ingredient Review (CIR) Expert Panel stated<sup>1</sup> that lauramine oxide and stearamine oxide are safe as cosmetic ingredients for rinse-off products, but that in leave-on products, the concentration of lauramine oxide should be limited to 3.7% and that of stearamine oxide should be limited to 5%. The Expert Panel reviewed newly available studies since that assessment (see references),<sup>2-4</sup> along with updated information regarding types and concentrations of use. The Panel decided to not reopen this safety assessment. Therefore, the panel confirmed that lauramine oxide and stearamine oxide are safe as cosmetic ingredients in rinse-off products, but that in leave-on products, the concentration of lauramine oxide and stearamine oxide should be limited to 3.7% and 5%, respectively.

## Discussion

The product formulation data submitted to the Food and Drug Administration (FDA) in 1992 reported that lauramine oxide and stearamine oxide were used in a total of 9 and 37 cosmetic product formulations, respectively (Table 1). According to information supplied to FDA by industry as part of the Voluntary Cosmetic Registration Program (VCRP), lauramine oxide and stearamine oxide were used in a total of 83 and 77 formulations, respectively, in 2009 (Table 1). A survey of current use concentrations conducted by the Personal Care Products Council<sup>5</sup> reported that lauramine oxide and stearamine oxide were used in ranges of 0.01% to 15% and 0.07% to 1%, respectively (Table 1).



**Table 1.** Historical and Current Cosmetic Product Uses and Concentrations of Lauramine Oxide and Stearamine Oxide

Product Category <sup>6</sup>	1992 Uses <sup>1</sup>	2007 Uses <sup>7</sup>	2009 Uses <sup>8</sup>	2008 Concentrations (%) <sup>5</sup>
Lauramine oxide				
Baby products				
Other		4 (138)	4 (138)	—
Bath products				
Soaps and detergents		24 (1329)	24 (1329)	0.2-15
Bubble baths		8 (262)	13 (262)	2
Noncoloring hair care products				
Conditioners		2 (1249)	2 (1249)	0.2 – 0.7
Permanent waves		2 (141)	—	—
Rinses	3 (83)	—	—	—
Shampoos	3 (953)	11 (1403)	10 (1403)	0.4
Tonics, dressings, etc	3 (548)	8 (1097)	8 (1097)	0.2-1
Other		2 (716)	1 (716)	—
Makeup				
Foundations		3 (635)	3 (635)	0.01
Personal hygiene products				
Other		1 (514)	6 (514)	0.5-2
Shaving products				
Shaving cream		1 (162)	1 (162)	0.08
Skin care products				
Cleansing creams, lotions, liquids, and pads		7 (1368)	7 (1368)	0.6-3
Body and hand creams, lotions, etc		1 (1513)	1 (1513)	0.2-0.9
Moisturizers		3 (2039)	3 (2039)	0.9
Total uses/ranges for lauramine oxide and total uses/ranges for ingredient	9	77	83	0.01-15
Stearamine oxide				
Noncoloring hair care products				
Conditioners	18 (666)	12 (1249)	8 (1249)	0.07-1
Rinses	5 (83)	—	—	—
Shampoos	9 (953)	3 (1403)	3 (1043)	—
Other		2 (716)	1 (716)	0.3
Hair-coloring products				
Dyes and colors		63 (2481)	63 (2481)	—
Tints		1 (58)	1 (58)	—
Skin care products				
Face and neck creams, lotions, etc		1 (1195)	1 (1195)	—
Paste masks/mud packs		1 (418)	—	—
Other	5 (848)	—	—	—
Total uses/ranges for stearamine oxide and total uses/ranges for Ingredient	37	83	77	0.07-1

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# Methenamine

## Conclusion

In a 1992 safety assessment of methenamine, the Cosmetic Ingredient Review (CIR) Expert Panel stated<sup>1</sup> that this ingredient is safe in cosmetic products at concentrations not to exceed 0.16%. The Expert Panel reviewed newly available studies since that assessment (see references),<sup>2-36</sup> along with updated information regarding product types and concentrations of use, and did not reopen this safety assessment. The Panel confirmed that methenamine is safe as cosmetic ingredients at concentrations not to exceed 0.16%.

## Discussion

Methenamine was used in 7 products in 1981, based on voluntary reports provided to Food and Drug Administration (FDA)<sup>1</sup> by industry with concentrations of use of <1%. In 2008, methenamine was reportedly used in 31 products.<sup>37</sup> For example, of the 288 "other" eye makeup products reported, only 1 contained methenamine. Most uses are in the shampoo product category, where 27 of 1403 products on the market were reported to contain methenamine. Data<sup>38</sup> from an industry survey in 2008 indicated that methenamine was used at 0.002%. Table 1 presents the available use and concentration information.

The Expert Panel noted that methenamine functions as a formaldehyde releaser. A fundamental equilibrium exists between these releasers and free formaldehyde itself, resulting in a steady state of availability of formaldehyde in aqueous

solutions. Data in the original safety assessment, along with all of the new data available since then, confirmed that, if the level of preservative is kept low, then the level of formaldehyde will not present any safety concerns.

The Expert Panel considered the addition of methenammium chloride to the safety assessment. It was decided that the methyl group added to the organic amine ring structure of methenammium chloride made the 2 ingredients too dissimilar to extrapolate the safety data of methenamine to methenammium chloride.

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**Table 1.** Historical and Current Cosmetic Product Uses and Concentrations for Methenamine

Product Category (total number of products in the category as given by FDA (2007)	1981 Uses <sup>1</sup>	2007 Uses <sup>37</sup>	1981 Concentrations <sup>1</sup> (%)	2007 Concentrations <sup>38</sup> (%)
Methenamine				
Eye makeup <sup>a</sup>	6	–	<1.0	–
Other (288)	–	1	–	–
Fragrance products				
Powders (278)	–	–	–	0.002
Noncoloring hair care products				
Conditioners (1249)	–	1	–	–
Shampoos (1403)	–	27	–	–
Makeup				
Other (406)	–	1	–	–
Skin care products <sup>b</sup>	1	–	<1.0	–
Skin cleansing creams, lotions, liquids, and pads (1368)	–	1	–	–
Total uses/ranges for methenamine	7	31	<1.0	0.002

Abbreviation: FDA, Food and Drug Administration.

<sup>a</sup> Listed as mascara and other eye makeup preparations in the original safety assessment.

<sup>b</sup> Listed as face, body, and hand skin care preparations (excluding shaving preparations) in the original safety assessment.

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# 1-Naphthol

## Conclusion

In its 1989 safety assessment of 1-naphthol, the Cosmetic Ingredient Review (CIR) Expert Panel<sup>1</sup> stated that this ingredient was safe for use as a cosmetic ingredient in the present practices of use and concentration. In 2007, the CIR Expert Panel reviewed newly available studies since that assessment,<sup>2-34</sup> along with updated information regarding types and concentrations of use. The CIR Expert Panel confirmed that 1-naphthol is safe in the practices of use and concentration, as given in Table 1 and did not reopen this safety assessment.

## Discussion

1-Naphthol, an oxidizing hair dye,<sup>1</sup> was reported to have use in a total of 236 hair dyes and colors at concentrations from less than 0.1% up to 5%. The Food and Drug Administration (FDA) in 2006 reported that there were 627 total cosmetic uses.<sup>20</sup> An industry survey<sup>15</sup> of current use concentrations found use concentrations between 0.01% and 3%. Table 1 presents the available use and use concentration data.

The CIR Expert Panel determined that the available epidemiology studies are insufficient to conclude there is a causal relationship between hair dye use and cancer and other end points, based on lack of strength of the associations and inconsistency of findings. A list of hair dye epidemiology data is available at <http://www.cir-safety.org/findings.shtml>.

The Expert Panel recognizes that 1-naphthol is used as a hair dye ingredient and may be a sensitizer. However, hair dyes containing these ingredients, such as coal-tar hair dye products, are exempt from the principal adulteration provision and from the color additive provisions in sections 601 and 706 of the Federal Food, Drug, and Cosmetic Act when the label bears a caution statement and patch test instructions for determining whether the product causes skin irritation. The Expert Panel expects that continuing to follow this procedure will identify prospective individuals who would have an irritation/sensitization reaction and allow them to avoid significant exposures.

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**Table 1.** Historical and Current Cosmetic Product Uses and Concentrations for 1-Naphthol

Product Category	1987 Uses (Total Number of Products in a Category) <sup>1</sup>	2006 Uses (Total Number of Products in a Category) <sup>20</sup>	1987 Concentrations (%) <sup>1</sup>	2006 Concentrations (%) <sup>15</sup>
Hair coloring products				
Dyes and colors	236	618 (1600)	≤0.1-5	0.01-3
Tints	–	8 (56)	–	–
Lighteners with color	–	1 (14)	–	–
Other hair coloring preparations <sup>a</sup>	–	(73)	–	0.1
Total uses/ranges for 1-naphthol	236	627	≤0.1-5	0.01-3

<sup>a</sup> Coloring shampoo.

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## Phenoxyethanol

### Conclusion

In its 1990 safety assessment of phenoxyethanol, the Cosmetic Ingredient Review (CIR) Expert Panel<sup>1</sup> stated that this ingredient is safe as a cosmetic ingredient in the present practices of use and concentration. In 2007, the Expert Panel reviewed newly available studies since that assessment,<sup>2-61</sup> along with updated information regarding types and concentration of use. The Panel

confirmed that phenoxyethanol is safe in the present practices of use and concentration given in Table 1 and did not reopen the safety assessment.

### Discussion

Phenoxyethanol was used in 253 products in 1987, based on voluntary reports provided to Food and Drug Administration

Table 1. Historical and Current Cosmetic Product Uses and Concentrations of Phenoxyethanol

Product Category <sup>62</sup>	1987 Uses <sup>1</sup>	Total Products in Category <sup>1</sup>	2006 Uses <sup>62</sup>	Total Products in Category <sup>62</sup>	1987 Concentrations (%) <sup>1</sup>	2006 Concentrations (%) <sup>63</sup>
<b>Baby products</b>						
Shampoos	— <sup>a</sup>		4	38	— <sup>a</sup>	0.3-0.7
Lotions, oils, powders, and creams	—		16	67	—	0.02-0.8
Other	—		5	64	—	0.6 (in baby wipes)
<b>Bath products</b>						
Oils, tablets, and salts	—		5	207	—	0.09-0.5
Bubble baths	—		24	256	—	0.5
Capsules	—		1	5	—	0.5
Soaps and detergents	—		21	594	—	0.4-1
Other	8 <sup>b</sup>	665 <sup>b</sup>	45	276	≤0.1 to 1 <sup>b</sup>	0.5
<b>Eye makeup</b>						
Eyebrow pencils	—		1	124	—	0.5-1
Eyeliners	23 <sup>b</sup>	1550 <sup>b</sup>	17	639	≤0.1 to 5 <sup>b</sup>	0.02-1
Eye shadow	—		51	1061	—	0.3-1
Eye lotions	—		10	32	—	0.3-0.5
Eye makeup remover	—		36	114	—	0.1-1
Mascara	—		121	308	—	0.1-1
Other	—		27	229	—	0.5-1 (in a brow powder and an eye gloss)
<b>Fragrance products</b>						
Colognes and toilet waters	—		5	948	—	— <sup>c</sup>
Perfumes	—		3	326	—	1
Powders	4 <sup>b</sup>	853 <sup>b</sup>	4	324	—	1
Sachets	—		— <sup>a</sup>	—	≤0.1 to 1 <sup>b</sup>	—
Other	—		23	187	—	0.7 (in an alcohol-free cologne)
<b>Noncoloring hair products</b>						
Conditioners	—		121	715	—	0.1-1
Sprays/aerosol fixatives	—		5	294	—	0.5
Straighteners	—		—	—	—	0.7 (0.4 after dilution)
Permanent waves	—		—	—	—	1 (0.5 after dilution)
Rinses	—		4	46	—	—
Shampoos	—		155	1022	—	0.2-1
Tonics, dressings, etc	—		71	623	—	0.2-1
Wave sets	54 <sup>b</sup>	3008 <sup>b</sup>	1	59	≤0.1 to 1 <sup>b</sup>	—
Other	—		93	464	—	0.8-1 (0.8 in a hair mask; 1 in a wax)
<b>Hair-coloring products</b>						
Dyes and colors	—		69	1600	—	0.05
Tints	—		—	—	—	—
Rinses	—		—	—	—	0.7
Shampoos	—		—	—	—	—
Color sprays	—		—	—	—	—
Lighteners with color	—		—	—	—	—
Bleaches	—		1	103	—	—
Other	—		1	73	—	—
<b>Makeup</b>						
Blushers	7	451	13	459	≤0.1 to 1	0.3-1
Face powders	—		35	447	—	0.1-1
Leg and body paints	—		1	10	—	—
Lipsticks	—		16	1681	—	0.4-0.9
<b>Makeup</b>						
Foundations	—		77	530	—	0.3-1
Makeup bases	20 <sup>b</sup>	645 <sup>b</sup>	17	273	≤0.1 to 1 <sup>b</sup>	0.001-1
Rouges	—		5	115	—	0.5
Makeup fixatives	—		8	37	—	0.5-0.7
Other	—		47	304	—	0.5-0.7 (0.5 in a concealer)

(continued)

Table 1. (continued)

Product Category <sup>62</sup>	1987 Uses <sup>1</sup>	Total Products in Category <sup>1</sup>	2006 Uses <sup>62</sup>	Total Products in Category <sup>62</sup>	1987 Concentrations (%) <sup>1</sup>	2006 Concentrations (%) <sup>63</sup>
<b>Nail care products</b>						
Basecoats and undercoats	- <sup>a</sup>		- <sup>a</sup>	43	- <sup>a</sup>	- <sup>c</sup>
Cuticle softeners	1	23	3	20	≤1	-
Nail creams and lotions	-			1	13	-
Nail polishes and enamels	-		3	398	-	-
Other	-		4	58	-	-
<b>Personal hygiene products</b>						
Underarm deodorants	-		14	281	-	0.3-1
Douches	-		2	8	-	0.2-1
Feminine deodorants	-		-	-	-	-
Other	-		31	390	-	0.3-1 (0.3, 0.5, 0.7, and 1 in body washes)
<b>Shaving products</b>						
Aftershave lotions	-		17	260	-	0.2-0.6
Preshave lotions	-		-	-	-	-
Shaving cream	-		7	135	-	0.3-0.7
Other	-		7	64	-	0.6-1 (1 in a skin balm)
<b>Skin care products</b>						
Skin cleansing creams, lotions, liquids, and pads			243	1009		0.2-1
Depilatories			-	49		0.5-1
Face and neck creams, lotions, powder and sprays			170	546		0.004-1 (1 in face and neck sprays)
Body and hand creams, lotions, powder and sprays			176	992		0.5-1
Foot powders and sprays	3684 <sup>b</sup>	109 <sup>c</sup>	15	43	≤0.1 to 5 <sup>b</sup>	0.5
Moisturizers			297	1200		0.2-1 (0.5 in moisturizing sprays)
Night creams, lotions, powder and sprays			69	229		0.3-1 (0.5 in night sprays)
Paste masks/mud packs			75	312		0.004-0.9
Skin fresheners			18	212		0.5-0.7
Other			178	915		0.0002 to 1 (0.8 in a bust firmer)
<b>Suntan products</b>						
Suntan gels, creams, and liquids	10 <sup>b</sup>	240 <sup>b</sup>	16	138	≤0.1 to 1 <sup>b</sup>	0.2-1
Indoor tanning preparations			32	74		0.5-1
Other			13	41		0.2-0.5
Total uses/ranges for phenoxyethanol	253		2550		≤0.1 to 5	≤0.0002-1

<sup>a</sup> FDA's voluntary reporting system, no uses/use concentrations reported for this category in 1987; no uses reported for this category in 2006.

<sup>b</sup> This category was combined when the original safety assessment was performed and is now 2 or more separate categories.

<sup>c</sup> In industry survey, no use concentrations reported for this category.

FDA)<sup>1</sup> by industry, at concentrations of ≤0.15% to 5%. Data provided to FDA in 2006 indicated that phenoxyethanol was being used in 2550 products.<sup>62</sup> Current use concentration data from a cosmetics industry survey<sup>63</sup> indicated that

phenoxyethanol was being used in cosmetics at concentrations ranging from ≤0.0002% to 1%.

The available usage and use concentration data are given in Table 1, as a function of product category.

The CIR Expert Panel recognized data gaps regarding in use and concentration data for this ingredient. However, the overall information available on types of products in which this ingredient is used and at what concentration indicates a pattern of use that was considered by the CIR Expert Panel in assessing safety. In order to gain more insight into ingredient use frequency patterns, the total number of products in a category could be considered along with the number of products in that category containing the ingredient.

The CIR Expert Panel acknowledged the significant increase in ingredient use frequency that has occurred and noted that this is probably driven primarily by the use of a preservative system that incorporates phenoxyethanol and methyl dibromo glutaronitrile (phenoxyethanol [4 parts]: methyl dibromo glutaronitrile [1 part]).<sup>13</sup> It has been suggested that methyl dibromo glutaronitrile is the allergen in this system.<sup>13</sup>

In considering that skin care products (sprays) are among the new product uses of phenoxyethanol, the CIR Expert Panel noted the absence of inhalation toxicity data from the safety assessment. However, in the absence of these data, the Panel determined that phenoxyethanol can be used safely in hair sprays because the ingredient particle size is not respirable. The Panel reasoned that the particle size of anhydrous hair sprays (60-80  $\mu\text{m}$ ) and pump hair sprays (>80  $\mu\text{m}$ ) is large compared to the median aerodynamic diameter of  $4.25 \pm 1.5 \mu\text{m}$  for a respirable particulate mass.

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# Phenyl Methyl Pyrazolone

## Conclusion

In a 1992 safety assessment of phenyl methyl pyrazolone (PMP), the Cosmetic Ingredient Review (CIR) Expert Panel concluded that "phenyl methyl pyrazolone is safe as a cosmetic ingredient in the present practices of use and concentration."<sup>1</sup> The Expert Panel reviewed the studies performed since that assessment<sup>2-16</sup> as well as updated use and concentration data. The Expert Panel confirmed that PMP is safe in the practices of use and concentration given in Table 1 and did not reopen the safety assessment.

## Discussion

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 end points based on lack of strength of the associations and inconsistency of findings. Information on the available hair dye epidemiology data is available at <http://www.cir-safety.org/findings.shtml>.

The Expert Panel recognizes that PMP is used as a hair dye ingredient and may be used as a sensitizer. However, hair dyes containing these ingredients, such as coal-tar hair dye products are exempt from the principal adulteration provision and from the color-additive provisions in sections 601 and 706 of the Federal Food, Drug, and Cosmetic Act, when the label bears a caution statement and patch test instructions for determining whether the product causes skin irritation. The Expert Panel expects that continuing to follow this procedure will identify prospective individuals who would have an irritation/sensitization reaction and allow them to avoid significant exposures.

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**Table 1.** Historical and Current Cosmetic Product Uses and Concentrations for Phenyl Methyl Pyrazolone

Product Category	1984 Uses <sup>1</sup>	2007 Uses <sup>17</sup>	1984 Concentrations <sup>1</sup> (%)	2007 Concentrations <sup>18</sup> (%)
<b>Hair coloring products</b>				
Dyes and colors	125	375	0.1-1	0.3-0.4
Tints	–	1	–	–
Lighteners with color	–	2	–	–
Total uses/ ranges for phenyl methyl pyrazolone	125	378	0.1-1	0.3-0.4

1%. CIT Study No. 9009 TAL. Unpublished data submitted by CTFA, November 8, 2007. 23 pages.

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## N-Phenyl-*p*-Phenylenediamine, N-Phenyl-*p*-Phenylenediamine HCl, and N-Phenyl-*p*-Phenylenediamine Sulfate

### Conclusion

In a 1994 safety assessment of *N*-phenyl-*p*-phenylenediamine, *p*-phenyl-*p*-phenylenediamine HCl, and *N*-phenyl-*p*-phenylenediamine sulfate, the Cosmetic Ingredient Review (CIR) Expert Panel stated that these ingredients are safe as (then) used in hair dyes at concentrations up to 1.7% (as the free base).<sup>1</sup> The expert panel reviewed newly available studies since that assessment along with updated information regarding type and frequency of use.<sup>1-39</sup> The expert panel determined not to reopen this safety assessment. Therefore, the panel confirmed that *N*-phenyl-*p*-phenylenediamine, *N*-phenyl-*p*-phenylenediamine HCl, and *N*-phenyl-*p*-phenylenediamine sulfate are safe for use in hair dyes at concentrations up to 1.7% (as the free base).

### Discussion

In 1993, *N*-phenyl-*p*-phenylenediamine and *N*-phenyl-*p*-phenylenediamine HCl were used in 9 and 11 hair dyes and

colors requiring caution statements, respectively; *N*-phenyl-*p*-phenylenediamine sulfate was not reported to be used in 1993. Use concentrations were not reported at that time.<sup>1</sup> In 2009, *N*-phenyl-*p*-phenylenediamine HCl was no longer reported to the Food and Drug Administration (FDA) as being used, while *N*-phenyl-*p*-phenylenediamine and *N*-phenyl-*p*-phenylenediamine sulfate increased in use to 25 and 105 hair dyes and colors requiring caution statements, respectively.<sup>40</sup> A survey by the Personal Care Products Council of current use concentrations found that *N*-phenyl-*p*-phenylenediamine is being used at 0.04%; no uses were reported for *N*-phenyl-*p*-phenylenediamine HCl or sulfate<sup>41</sup> (Table 1).

Newly available data did not raise any issues regarding the safety of *N*-phenyl-*p*-phenylenediamine, *N*-phenyl-*p*-phenylenediamine HCl, and *N*-phenyl-*p*-phenylenediamine sulfate. In considering hair dye epidemiology data, the CIR Expert Panel concluded that the available epidemiology studies are insufficient to conclude there is a causal relationship between hair dye use and cancer and other end

**Table 1.** Historical and Current Cosmetic Product Uses and Concentrations for *N*-Phenyl-*p*-Phenylenediamine, *N*-Phenyl-*p*-Phenylenediamine HCl, and *N*-Phenyl-*p*-Phenylenediamine Sulfate<sup>a</sup>

Product Category	1993 Frequency of Use <sup>1</sup>	2009 Frequency of Use <sup>45</sup>	1993 Concentration of Use <sup>1</sup>	2009 Concentration of Use <sup>46</sup>
<i>N</i> -Phenyl- <i>p</i> -Phenylenediamine				
hair dyes/colors (requiring caution stmt)	9	25	Not reported	0.04%
total	9	25	—	0.04%
<i>N</i> -Phenyl- <i>p</i> -phenylenediamine HCl				
hair dyes/colors (requiring a caution stmt)	11	None reported	Not reported	Not reported
total	11	—	—	—
<i>N</i> -Phenyl- <i>p</i> -phenylenediamine sulfate				
hair dyes/colors (requiring a caution stmt)	None reported	105	Not reported	Not reported
total		105	—	—

Refs. 1-6,8-13,15-27,30-32,34-38,42-44,47-52.

points, based on lack of strength of the associations and inconsistency of findings. The most recent comprehensive review of available epidemiology studies concluded that there is insufficient evidence to support a causal association between personal hair dye use and a variety of tumors and cancers. A summary of the available hair dye epidemiology data is available at <http://www.cir-safety.org/findings.shtml>.<sup>42-44</sup>

The expert panel recognizes that *N*-phenyl-*p*-phenylenediamine, *N*-phenyl-*p*-phenylenediamine HCl, and *N*-phenyl-*p*-phenylenediamine sulfate are oxidative hair dye ingredients and may be sensitizers. However, hair dyes containing these ingredients, as coal-tar hair dye products, are exempt from the principal adulteration provision and color-additive provisions in sections 601 and 706 of the Federal Food, Drug, and Cosmetic Act when the label bears a caution statement and patch test instructions for determining whether the product causes skin irritation. The expert panel expects that continuing to follow the procedure will identify prospective individuals who would have an irritation/sensitization reaction and allow them to avoid significant exposures.

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## Polyoxymethylene Urea

### Conclusion

In a 1995 safety assessment of polyoxymethylene urea, the Cosmetic Ingredient Review (CIR) Expert Panel stated that this ingredient is safe as a cosmetic ingredient. Cosmetics containing polyoxymethylene urea should be formulated to ensure that

concentrations of free formaldehyde do not exceed 0.2%. It cannot be concluded that polyoxymethylene urea is safe for use in cosmetic products intended to be aerosolized.<sup>1</sup> The Expert Panel reviewed newly available studies (see references)<sup>2-14</sup> since that assessment, along with updated frequency

**Table 1.** Historical and Current Cosmetic Product Uses and Concentrations for Polyoxymethylene Urea

Product Category	Frequency <sup>1</sup> of Use 1993	Frequency of Use 2009	Concentration <sup>1</sup> of use 1993	Concentration <sup>14</sup> of use 2009
Eye shadow	6	20	Not reported	0.02%
Perfumes	1	1	Not reported	—
Powders (dusting/talcum)	—	2	—	0.05%
Blushers (all types)	4	8	Not reported	0.1-5%
Face powders	8	1	Not reported	0.02%
Lipstick	2	—	Not reported	0.1%
Rouges	4	—	Not reported	—
Other makeup preps	—	2	—	—
Basecoats and undercoats	2	2	Not reported	—
Other manicuring preparations	1	1	Not reported	—
Other personal cleanliness products	—	1	—	—
Skin cleansing	—	—	—	0.005%
Total	28	38	Not reported	0.005-5%

and concentration of use information. The Expert Panel determined to not reopen this safety assessment and confirmed that polyoxymethylene urea is safe as a cosmetic ingredient, except those that are intended to be aerosolized, when formulated to ensure that concentrations of free formaldehyde do not exceed 0.2%.

## Discussion

Polyoxymethylene urea is reported to function as a bulking agent and reported use has increased from 28 cosmetic formulations<sup>1</sup> in 1993 to 38 formulations<sup>15</sup> in 2009, but product use did not change. Concentration of use was not reported to the Food and Drug Administration (FDA) in 1993, nor is it reported to the Food and Drug Administration (FDA) currently. In a survey conducted by the Personal Care Products Council, industry reported use concentrations in 2009 of 0.005% to 5% (Table 1).<sup>14</sup>

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# Polyquaternium-7

## Conclusion

In 1995, the Cosmetic Ingredient Review (CIR) Expert Panel concluded that polyquaternium-7 was safe as used in cosmetic formulations.<sup>1</sup> The expert panel reviewed the information available since that assessment,<sup>2,3</sup> along with updated frequency and concentration of use information. The Expert Panel confirmed the existing conclusion.

## Discussion

The use of polyquaternium-7 in cosmetic formulations has increased greatly, from 138 reported<sup>1,4</sup> uses in 1994 to 975 uses in 2010. Concentration of use was not reported to the

Food and Drug Administration (FDA) in 1994, nor is it reported to FDA currently. In response to a survey conducted by the Personal Care Products Council, industry reported current use concentrations of 0.009%-5% for polyquaternium-7 (Table 1).<sup>5</sup>

The Panel noted that polyquaternium-7 is now used in aerosolized products and noted the absence of inhalation toxicity data. However, in the absence of these data, the Panel determined that polyquaternium-7 can be used safely in hair sprays, because the product particle size is not respirable. The Panel reasoned that the particle size of aerosol hair sprays (around 38  $\mu\text{m}$ ) and pump hair sprays (>80  $\mu\text{m}$ ) is large compared to respirable particle sizes ( $\leq 10 \mu\text{m}$ ). Polyquaternium-7 is now also used in leave-on type

**Table 1.** Historical and Current Cosmetic Product Uses and Concentrations of Polyquaternium-7

Product	Frequency of Use 1994 (# in Category) <sup>1</sup>	Frequency of Use 2010 <sup>4</sup> (# in Category 2009) <sup>6</sup>	Concentration of Use 1994 <sup>1</sup>	Concentration of Use (%) 2010 <sup>5</sup>
Baby shampoos	2 (19)	7 (56)	NA	NR
Other baby products	1 (23)	8 (143)	NA	0.04
Bath oils, tablets, and salts	NR	NR (313)	NR	0.009
Bubble baths	2 (214)	15 (169)	NA	0.05-0.4
Other bath preparations	4 (132)	14 (234)	NA	NR
Eye shadow	NR	2 (1215)	NR	NR
Mascara	NR	6 (499)	NR	NR
Other fragrance preparation	2 (136)	1 (566)	NA	NR
Hair conditioner	16 (614)	31 (1226)	NA	0.01-0.3
Hair spray (aerosol fixatives)	NR	10 (312)	NR	NR
Permanent waves	4 (387)	1 (69)	NA	0.07-5
Rinses (non-coloring)	1 (58)	2 (33)	NA	0.2
Shampoos (non-coloring)	37 (852)	234 (1361)	NA	0.04-1
Tonics, dressings, and other hair grooming aids	19 (563)	34 (1205)	NA	0.2-3
Other hair preparations	3 (376)	21 (807)	NA	0.2-3
Hair dyes and colors (required caution statements)	NR	16 (2393)	NR	0.04
Hair shampoos (coloring)	3 (15)	1 (40)	NA	NR
Hair color sprays (aerosol)	NR	NR (7)	NR	0.02
Bath soaps and detergents	26 (343)	292 (1665)	NA	0.09-0.3
Other personal cleanliness products	3 (321)	198 (792)	NA	0.08-0.2
Aftershave lotion	1 (229)	3 (367)	NA	0.2
Shaving cream	4 (147)	2 (122)	NA	0.09
Shaving soap	NR	1 (10)	NR	NR
Cleansing	8 (746)	51 (1446)	NA	0.02-1
Face and neck (excluding shave)	NR	3 (1583)	NR	0.06-0.08
Body and hand (excluding shave)	NR	9 (1744)	NR	0.3
Moisturizing	NR	3 (2508)	NR	NR
Deodorant fresheners	NR	1 (259)	NR	NR
Other skin care preparations	1 (790)	8 (1308)	NA	0.4
Other suntan preparations	1 (61)	1 (62)	NA	NR
Total	138	975	NA	0.009-5

Abbreviations: NR, not reported as used in that category; NA, concentration of use data not reported at that time.

products and products that are applied to the eye. The panel was satisfied that data in the report supported the safety of these uses.

In the 1995 safety assessment, the Expert Panel<sup>1</sup> acknowledged the presence of acrylamide as an impurity in polyquaternium-7. An extrapolation using the current use concentration and the greatest amount of acrylamide impurity given in the 1995 report confirmed that the amount of residual acrylamide was not of concern. The Expert Panel confirmed that polyquaternium-7 is safe as used in cosmetic formulations.

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# Potassium Bromate and Sodium Bromate

## Conclusion

In a 1994 assessment of potassium bromate and sodium bromate, the Cosmetic Ingredient Review (CIR) Expert Panel stated that these ingredients may be used in cosmetic permanent wave formulations at concentrations not to exceed 10.17%, measured as sodium bromate.<sup>1</sup> The Expert Panel reviewed newly available studies since that assessment, along with updated information regarding types and concentrations of use<sup>2-96</sup> (Table 1). The Expert Panel determined not to reopen this safety assessment. Therefore, the Expert Panel confirms that potassium bromate and sodium bromate are safe as cosmetic permanent wave formulations at concentrations not to exceed 10.17%, measured as sodium bromate.

**Table 1.** Historical and Current Cosmetic Product Uses and Concentrations for Sodium Bromate

Product Category (no. of total products) <sup>97</sup>	1991 Uses <sup>1</sup>	2009 Uses <sup>98</sup>	1984 Concentrations <sup>1</sup> (%)	2009 Concentrations <sup>99</sup> (%)
Sodium bromate				
Noncoloring hair care products				
Straighteners (144)	61 <sup>a</sup>	—	—	8
Permanent waves (141)		—	10-25	8
Other (716)		1	—	—
Total uses/ranges for sodium bromate	61	1	10-25	8

<sup>a</sup>The uses were not broken down into categories but are assumed to have been within these categories.

## Discussion

The Expert Panel examined the large amount of new carcinogenicity data produced since the original safety assessment. The new biomarker and short- and long-term carcinogenicity studies did not reveal any new or different findings on potassium bromate and sodium bromate. As used in cosmetics, these chemicals do not present a carcinogenicity risk.

The Expert Panel did confirm that the conclusion restricts safe use in "cosmetic permanent wave formulations." Information was provided to the Expert Panel that the single use of sodium bromate in the "other" category is a nonaerosol hair spray product. This use is not covered by the conclusion in this safety assessment.

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## Quaternium-22

### Conclusion

In 1995, the Cosmetic Ingredient Review (CIR) Expert Panel concluded that quaternium-22 is safe in the present practices of use.<sup>1</sup> The Expert Panel reviewed information available since that assessment<sup>2,3</sup> along with updated frequency and concentration of use information. The Expert Panel confirmed the existing conclusion.

Quaternium-22 is reported to function as an antistatic agent, film former, and hair-conditioning agent.<sup>4</sup> Reported use<sup>1,5</sup> has decreased from 80 reported uses in 1994 to 58 uses in 2010, but the types of use have generally remained the same. Concentration of use was not reported to the Food and Drug Administration

(FDA) in 1994, nor is it reported to FDA currently. In response to a survey conducted by the Personal Care Products Council,<sup>6</sup> industry reported current use concentrations of 0.06% to 2% for quaternium-22 (Table 1).

### Discussion

The Panel noted that quaternium-22 is now used in aerosolized products and noted the absence of inhalation toxicity data. However, in the absence of these data, the Panel determined that quaternium-22 can be used safely in hair sprays, because the product particle size is not respirable. The Panel reasoned

**Table 1.** Historical and Current Cosmetic Product Uses and Concentrations of Quaternium-22

Product	Frequency of Use—1994 (# in Category) <sup>1</sup>	Frequency of Use—2010 <sup>5</sup> (# in Category) <sup>7</sup>	Concentration of Use (1994) <sup>1</sup>	Concentration of Use (%; 2010) <sup>6</sup>
Bubble baths	2 (208)	NR (169)	NA	0.5
Other bath preparations	3 (111)	NR (234)	NA	NR
Eye liner	NR	1 (754)	NR	NR
Mascara	34 (178)	17 (499)	NA	0.06-1
Hair conditioner	4 (597)	5 (1226)	NA	1
Hair spray (aerosol fixatives)	1 (294)	1 (312)	NA	NR
Hair straighteners	NR	NR (178)	NR	0.3
Permanent waves	NR	NR (69)	NR	0.2
Shampoos (non-coloring)	17 (845)	7 (1361)	NA	0.6
Tonics, dressings, and other hair grooming aids	2 (494)	3 (1205)	NA	0.06-0.7
Other hair preparations	2 (356)	3 (807)	NA	0.5
Hair dyes and colors (required caution statements)	NR	NR (1458)	NR	2 (1% after dilution)
Hair bleaches	NR	NR (149)	NR	2
Bath soaps and detergents	5 (335)	7 (1665)	NA	0.09-2
Other personal cleanliness products	1 (296)	NR (792)	NA	NR
Cleansing skin care preparations	1 (702)	5 (1446)	NA	0.2
Face and neck creams, lotions, and powders	NR	NR (1583)	NR	0.6
Moisturizing	1 (806)	7 (2508)	NA	NR
Paste masks (mud packs)	NR	1 (441)	NR	NR
Other skin care preparations	1 (745)	1 (1308)	NA	0.06
No. of uses listed under trade name	6	NR	NA	NR
<b>Total</b>	<b>80</b>	<b>58</b>	<b>NA</b>	<b>0.06-2</b>

Abbreviations: NR, not reported as used in that category; NA, concentration of use data not reported at that time.

that the particle size of aerosol hair sprays (around 38  $\mu\text{m}$ ) and pump hair sprays ( $>80 \mu\text{m}$ ) is large compared to respirable particle sizes ( $\leq 10 \mu\text{m}$ ).<sup>8-10</sup>

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# Shellac

## Conclusion

In a 1986 safety assessment of shellac, the Cosmetic Ingredient Review (CIR) Expert Panel stated that cosmetic-grade shellac is safe for use in cosmetic formulations at concentrations up to 6%. The Expert Panel reviewed studies performed since that assessment (see references)<sup>1-6</sup> as well as updated the use and concentration data. The Panel confirmed that shellac is safe in the present practices of use and concentration given in Table 1 and did not reopen the safety assessment.

## Discussion

In 1986, shellac was used in 69 reported product formulations at concentrations up to 1%. As of 2006, shellac is used in 11 reported product formulations at concentrations up to 6%. The reported use and concentration data are shown in Table 1. The Panel concluded that shellac continues to be safe in its present uses and concentrations.

The Panel considered adding Shellac Wax and Ammonium Shellacate to this safety assessment, but found the data inadequate to do so.

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**Table 1.** Historical and Current Cosmetic Product Uses and Concentrations for Shellac

Product Category	1986 Uses <sup>7</sup>	2006 Uses <sup>8</sup>	1986 Concentrations <sup>7</sup> (%)	2006 Concentrations <sup>9</sup> (%)
Eye makeup				
Eyeliners	21 (382)	4 (639)	1-10	
Mascara	42 (429)	6 (308)	0.01-0.25	2-6
Noncoloring hair care products				
Sprays/aerosol fixatives	6 (38)	1 (294)	0.01-1	
Total use/range	69 (859)	11 (1241)	0.01-10	2-6

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## Steapyrium Chloride and Lapyrium Chloride

### Conclusion

In its 1991 safety assessment of steapyrium and lapyrium chloride, the Cosmetic Ingredient Review (CIR) Expert Panel<sup>1</sup> concluded that these ingredients are safe as cosmetic ingredients in the present practice of use and concentration. In 2007, the Expert Panel found no newly available studies since that assessment but did review updated information regarding types and concentrations of use. The Panel confirmed the safety of steapyrium and lapyrium chloride in the practices of use given in Table 1 and did not reopen this safety assessment.

### Discussion

Steapyrium and lapyrium chloride were used in 36 and 38 products, respectively, in 1981, based on voluntary reports provided to Food and Drug Administration (FDA) by industry, at concentrations of >0.1% to 5% for steapyrium chloride and ≤0.1% to 5% for lapyrium chloride.<sup>1</sup> Data provided to FDA in 2007 indicated that steapyrium chloride and lapyrium chloride are being used in 18 and 12 products, respectively.<sup>2</sup> Current use concentration data from a cosmetics industry survey<sup>3</sup> indicated that steapyrium chloride is being used in cosmetics at

**Table 1.** Historical and Current Cosmetic Product Uses and Concentrations for Steapyrium and Lapyrium Chloride

Product Category	1986 Uses (Total Formulations) <sup>1</sup>	2007 Uses (Total Formulations) <sup>2</sup>	1986 Concentrations <sup>1</sup> (%)	2007 Concentrations <sup>3</sup> (%)
Steapyrium chloride				
Baby products				
Shampoos	1 (35)	—	>0.1-1	—
Noncoloring hair care products				
Conditioners	8 (478)	6 (715)	>0.1-5	1-3
Rinses	5 (158)	1 (46)	>0.1-5	—
Shampoos	1 (909)	—	>1-5	—
Other	—	1 (464)	—	—
Hair-coloring products				
Dyes and colors	1 (811)	—	>1-5	—
Tonics, dressings, and so on	—	1 (623)	—	0.1-3
Shaving products				
Aftershave lotions	2 (282)	—	>0.1-1	—
Skin care products				
Skin-cleansing creams, lotions, liquids, and pads	2 (680)	1 (1009)	>0.1-1	—
Depilatories				
Face and neck creams, lotions, powder, and sprays	7 (832)	—	>0.1-1	—
Body and hand creams, lotions, powder, and sprays	—	1 (992)	—	—
Foot powders and sprays				
Moisturizers	3 (747)	5 (1200)	>0.1-5	—
Night creams, lotions, powder, and sprays	2 (219)	—	>1-5	—
Suntan products				
Suntan gels, creams, liquids, and sprays	3 (164)	2 (138)	>0.1-1	—
Other	1 (28)	—	>0.1-1	—

(continued)

Table 1. (continued)

Product Category	1986 Uses (Total Formulations) <sup>1</sup>	2007 Uses (Total Formulations) <sup>2</sup>	1986 Concentrations <sup>1</sup> (%)	2007 Concentrations <sup>3</sup> (%)
Total uses/ranges for steapyrium chloride	36 (5343)	18 (5187)	>0.1-5	0.1-3
Lapyrium chloride				
Baby products	2 (56)		>0.1-1	
Lotions, oils, powders, and creams	–	2 (67)	–	–
Fragrance products				
Colognes and toilet waters	5 (1120)	1 (948)	>0.1-1	–
Noncoloring hair care products				
Conditioners	3 (478)	–	>0.1-1	–
Tonics, dressings, and so on	1 (290)	–	>0.1-1	–
Wave sets	1 (180)	1 (59)	≤0.1	–
Makeup				
Other	1 (530)	–	>0.1-1	–
Personal hygiene products				
Underarm deodorants	5 (239)	3 (281)	>0.1-1	–
Other	7 (227)	3 (390)	>0.1-5	0.03 (0.03 % in a body wash)
Shaving products				
Aftershave lotions	2 (282)	2 (260)	>0.1-1	–
Skin care products				
Skin cleansing creams, lotions, liquids, and pads	4 (680)	–	≤0.1-1	–
Depilatories				
Face and neck creams, lotions, powder, and sprays	4 (832)	–	≤0.1-5	–
Body and hand creams, lotions, powder, and sprays				
Foot powders and sprays				
Moisturizers	2 (747)	(1200)	>0.1-1	1
Night creams, lotions, powder, and sprays				
Paste masks/mud packs				
Skin fresheners	1 (260)		0.1-1	–
Skin lighteners				
Hormone preparations				
Other				
Total uses/ranges for lapyrium chloride	38 (5921)	12 (3205)	≤0.1- 5	0.03

concentrations ranging from 0.1% to 3% and that lapyrium chloride is being used at a concentration of 0.03%.

Historical and current product usage and use concentration data as a function of product category are given in Table 1. The CIR Expert Panel recognized that there are data gaps regarding the use and concentration of these ingredients. However, the overall information available on the types of products in which these ingredients are used and at what concentrations indicates a pattern of use, which was considered by the CIR Expert Panel in assessing safety. In order to gain more insight into the ingredient use frequency patterns, the total number of products in a category could be considered

along with the number of products in that category containing the ingredient.

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